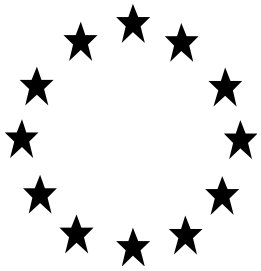
Regulation (EU) No 528/2012 concerning the making available on the market and use of biocidal products

Evaluation of active substances

Assessment Report



Cyphenothrin

Product-type 18
(insecticides, acaricides and products to control other arthropods)

February 2018

Greece

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1. STATEMENT OF SUBJECT MATTER AND PURPOSE

1.1. Procedure followed

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

Cyphenothrin (CAS No. 39515-40-70) was notified as an existing active substance by Sumitomo Chemical (U.K.) PLC in product-type 18, hereafter referred to as the applicant, in product-type 18.

Commission Regulation (EC) No 1451/2007 of 4 December 2007[1] lays down the detailed rules for the evaluation of dossiers and for the decision-making process.

In accordance with the provisions of Article 7(1) of that Regulation, Greece 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 Cyphenothrin as an active substance in Product Type 18 was 30/4/2006, in accordance with Annex V of Regulation (EC) No 1451/2007.

On 25/04/2006, the Greek competent authorities received a dossier from the applicant. The Rapporteur Member State accepted the dossier as complete for the purpose of the evaluation on 31/7/2006.

On 11/04/2013, the Rapporteur Member State submitted to the Commission and the applicant a copy of the evaluation report, hereafter referred to as the competent authority report.

In order to review the competent authority report and the comments received on it, consultations of technical experts from all Member States (peer review) were organised by the Agency. Revisions agreed upon were presented at the Biocidal Products Committee and its Working Groups meetings and the competent authority.

1.2. Purpose of the assessment report

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

For the implementation of the common principles of Annex VI, the content and conclusions of this assessment report, which is available from the Agency website 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

[1] 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

of another applicant, unless access to these data for that purpose has been granted to that applicant.

2. OVERALL SUMMARY AND CONCLUSIONS

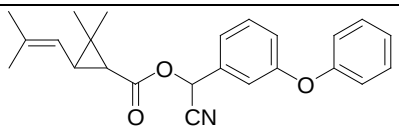
2.1. Presentation of the Active Substance

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

Identity of the active substance

Cyphenothrin is an insecticide, belonging to the pyrethroid family. Its identity is presented in the table below:

Table 2.1.1.2-1: Identity of the active substance cyphenothrin

Chemical name of cyphenothrin	IUPAC nomenclature: (RS)-α-cyano-3-phenoxybenzyl (1RS,3RS;1RS,3SR)-2,2-dimethyl-3-(2-methylprop-1-enyl)cyclopropanecarboxylate. or (RS)-α-cyano-3-phenoxybenzyl (1RS)-cis-trans-2,2-dimethyl-3-(2-methylprop-1-enyl)cyclopropanecarboxylate. or (±)-α-cyano-3-phenoxybenzyl (±)-cis-trans-chrysanthemate. CAS-name: cyano(3-phenoxyphenyl)methyl 2,2-dimethyl-3-(2-methyl-1-propenyl)cyclopropanecarboxylate.
CAS registry number	39515-40-7
EEC number	254-484-5
CIPAC number	804
Molecular formula	$C_{24}H_{25}NO_3$
Structural formula:	
Molecular weight	375.45 g/mol

Cyphenothrin is the ISO common name for a racemic mixture of 4 pairs of diastereoisomers. The minimum purity of cyphenothrin and the isomeric ratio are:

Purity of cyphenothrin based on Total Isomers: 92.0 %w/w minimum

Geometrical isomer ratio (Trans isomer ratio): 75.0%w/w (mimimum)

Optical isomer ratio (1R-isomer ratio): 95.0%w/w (minimum)

Detailed confidential information about the manufacturing process and batch analysis data on

cyphenothrin and all the impurities present, were provided.

Physico-chemical properties

Cyphenothrin is a yellow viscous liquid at room temperature. Its melting point is below -50°C (-25ºC pure active substance) and it decomposes before reaching its boiling point. The relative density of cyphenotrhin technical is about 1.08 and its vapour pressure is 2.9 x 10^{-7} Pa at 25°C. It is not expected to have oxidising or explosive properties and shows no reactivity towards its container material.

Two representative formulations have been evaluated in support of Cyphenothrin.

Gokilaht 5 EC is an emlusifiable concentrate containing 5% w/v cyphenothrin. It is not expected to have oxidising or explosive properties. Storage stability studies show that it remains stable for 2 weeks at 54ºC and for 7 days at 0ºC. The test material has been shown to undergo no significant physical or chemical change during storage at 25 ± 2°C for 24 months.

Pesguard LG OBA is an extremely flammable ready to use aerosol containing 0.31% cyphenothrin. Storage stability studies show that it remains stable for 8 weeks at 40ºC and for 7 days at 0ºC. The test material has been shown to undergo no significant physical or chemical change during storage at 25 ± 2°C for 24 months.

However, some points need to be clarified and new studies must be provided by the applicant. For more details see Document IIB.

Methods of Analysis

A fully validated GC-FID method has been submitted for the determination of the a.s. in cyphenothrin technical material which is acceptable. Additionally, for the determination of the R/S isomer ratio an acceptable GC–FID method has been submitted with sufficient validation data. Finally, acceptable and sufficiently validated methods have been submitted for the determination of impurities and additives in the technical material. However. some points need to be clarified by the applicant.

For residue analysis, fully validated analytical methods with acceptable data for linearity, specificity and recovery and with appropriate limits of detection (where applicable) were submitted for air. For drinking water some points need to be clarified. Methods for soil and surface water are also required. For more details see Document IIA.

2.1.2. Intended Uses and Efficacy

In order to support the inclusion of cyphenothrin in the Union List, the applicant has submitted efficacy studies with two representative products, Gokilaht 5EC (5% w/v cyphenothrin) and Pesguard LG OBA (oil-based-aerosol) (0.3% w/w cyphenothrin + 0.1% w/w imiprothrin).

Gokilaht 5EC is formulated as an emulsifiable concentrate (EC), containing 5% w/v cyphenothrin. This product will be used by a PCO (Pest Control Operator) indoors for remedial treatments in buildings (private housing, public buildings, etc.). Gokilaht 5EC is applied with hand held spray equipment with hydraulic nozzles (e.g. knapsack, 1-3 bars) by professional

users only. The product is diluted in water normally in 5 litre hand-held applicators and it is applied at a rate of 125 ml product /5 litre water for spraying 100 m^2 surfaces or 0.0625 gr a.i/ m^2. This product is intended to be used against German cockroaches (*Blattella germanica*) with directed spray onto the insects and against German and American (*Periplaneta americana*) cockroaches with surface residual treatment (including cracks and crevices) where insects may come into contact. The product is also intended to be used against black garden ants (*Lasius niger*) as directed spray onto the insects at 100 ml product/5 litre water/100 m^2 (0.05 gr a.i./m^2).

According to study B5.10/01, Gokilaht 5EC proved to be effective killing agent against German and American cockroaches by surface residual spray onto non-absorbent surfaces (e.g. overlaid plywood) for up to 12 weeks at a rate of 0.0625 gr a.i/ m^2. Moreover, Gokilaht 5EC proved to be effective as knockdown and killing agent against German cockroaches at 125 ml product diluted in water in 5 litre hand-held applicators for spraying 100 m^2 surfaces (equivalent to 0.0625 gr a.i./m^2).

According to study B5.10/02, Gokilaht 5EC proved to be effective against black garden ants by directed spray onto the insects at 1 ml product diluted in 50 ml water for spraying 1 m^2 (equivalent to 0.05 gr a.i./m^2).

Hence, based on the results of studies B5.10/01 and B.5.10/02 with Gokilaht 5EC, cyphenothrin proved to be effective as a direct spray against German cockroaches and as a surface residual spray (including crack and crevice treatment) against German and American cockroaches at 0.0625 gr a.i./m^2, and direct spray against black garden ants at 0.05 gr a.i./m^2.

The tests of the laboratory study on cockroaches (B.5.10/01) are acceptable for the purpose of inclusion of the active substance on the Union List but not sufficient for authorisation of the product Gokilaht 5EC. Only laboratory tests with the product against cockroaches were performed using low numbers of insects. No simulated use tests or field tests were provided. Similarly, the laboratory study on ants (B5.10/02) is acceptable for the purpose of active substance inclusion into Union List but not sufficient for authorisation of the product Gokilaht 5EC. Only laboratory tests against ants were performed with direct spray. Neither simulated use tests or field tests, nor tests assessing residual spray effectiveness against ants were provided. Hence, only basic activity of cyphenothrin against cockroaches and ants was demonstrated, while full efficacy should be demonstrated at product authorisation stage.

Pesguard LG OBA (oil-based-aerosol) is a hand held ready-to-use aerosol, which contains 0.3% w/w cyphenothrin and 0.1% w/w imiprothrin. This product will be used by a PCO (Pest Control Operator) indoors for remedial treatments where a large-scale treatment is not justified. It is intended to treat domestic or restaurant kitchens or small areas in large buildings where there is local or limited infestation. The product is intended to be used as surface spot, crack and crevice treatment at 6.6 gr product/m^2 against German cockroaches (*Blattella germanica*), bed bugs (*Cimex lectularius*) and cat fleas (*Ctenocephalides felis*).

In 2016, the applicant provided two new efficacy studies, a field study (B5.10.2/08) and a laboratory study (B5.10.02/09), with the representative product Pesguard LG OBA in order to support the new/revised intended use of the product, namely indoor application by professionals as surface spot, crack and crevice treatment at 6.6 gr product/m^2 against German cockroaches (*Blattella germanica*), bed bugs (*Cimex lectularius*) and cat fleas (*Ctenocephalides felis*). Since Pesguard LG OBA contains two active substances (0.3% cyphenothrin and 0.1% imiprothrin w/w), the laboratory study was also provided to prove the innate effect of cyphenothrin as indoor spot, crack and crevice treatment at 6.6 g Pesguard LG OBA/m^2.

These studies were discussed in Efficacy WG-I 2017 (early discussion) and as a follow up in Efficacy WG-III 2017. The EFF WG-III agreed with the evaluation made by the eCA for both efficacy studies.

In the laboratory study B5.10.02/09, tests were conducted using Pesguard LG OBA and Pesguard LG OBA containing only cyphenothrin as active substance at 0.3% or 0.1% (without imiprothrin) by increasing the content of one solvent in order to replace imiprothrin. A series of bioassays were performed to assess the direct and residual efficacy of Pesguard LG OBA (0.3% cyphenothrin and 0.1% imiprothrin w/w), New Formulation (High Level) (0.3% cyphenothrin w/w) and New Formulation (Low Level) (0.1% cyphenothrin w/w) against German cockroaches (*Blattella germanica*), bed bugs (*Cimex lectularius*) and cat fleas (*Ctenocephalides felis*) in terms of knockdown and mortality.

For the direct spray efficacy evaluation, the tested products were applied at a single rate of approximately 0.15g directly onto the insects in a container from a height of approximately 30cm. For the residual efficacy evaluation, treatments were applied directly onto ceramic (non-porous) and plywood (porous) surfaces at a rate of 6.6g per m^2.

In terms of direct spray, all tested products resulted in 100% knockdown within 30 minutes and 100% mortality 2-3 days post treatment for all test species.

Following exposure of cockroaches to Pesguard LG OBA and New formulation 0.3% on treated plywood aged up to 3 months, residual treatments showed low levels of mortality + knockdown (0-40%). However, contact of cockroaches with Pesguard LG OBA and New formulation 0.3% on treated ceramic substrates aged 1 and 2 days resulted in 80-95% mortality.

Following contact of bedbugs with Pesguard LG OBA and New formulation 0.3% on treated plywood aged 2 days, there were 97% affected (51% knocked down + 46% dead) and 100% affected (67.5% knocked down + 32.5% dead) insects, respectively. Contact of bedbugs on ceramic 1 and 2 day aged deposits resulted in 100% mortality of bed bugs.

Following contact of fleas with Pesguard LG OBA and New formulation 0.3% on treated plywood aged 1 day to 3 months, low levels of efficacy were observed, thus 0-10% knocked down and 5-38% dead insects. Contact of fleas on the ceramic 1 and 2 day aged deposits resulted in 100% mortality of fleas. Contact of fleas with Pesguard LG OBA and New formulation 0.3% on treated ceramic tiles aged 1 week resulted in 64% and 85.9% mortality, respectively.

Based on the results of study B5.10.02/09, the representative product Pesguard LG OBA and New formulation containing 0.3% cyphenothrin proved to be effective against German cockroaches, bedbugs and fleas as direct treatment onto the insects and surface treatment at 6.6 g product/m^2 when applied on non-porous surfaces with a residual activity of 1-2 days post treatment.

This study proves also the innate effect of cyphenothrin at 6.6 g Pesguard LG OBA/m^2 (0.0198 g cyphenothrin/m^2) as a spot, crack and crevice treatment against German cockroaches, bedbugs and fleas for Union-List inclusion purposes. At product authorization stage additional data should be required to support efficacy of the biocidal products in terms of duration of residual effect, residual effect on porous surfaces and field studies with spot, crack and crevice treatment against claimed target organisms.

Therefore, target pest organisms for cyphenothrin include the following insect species among others:

Blattella germanica - German Cockroach

Periplaneta americana - American Cockroach

Cimex lectularius - Bed bugs

Ctenocephalides felis - Cat fleas

Lasius niger – Black garden ant

Cyphenothrin is a synthetic pyrethroid insecticide with contact and stomach action. It affects the nervous system of insects causing pronounced repetitive activity and a prolongation of the transient increase in sodium permeability of nerve membranes in insects and other invertebrates. This results in continual nerve impulse transmission leading to tremors and death. This is demonstrated by the rapid knockdown action that pyrethroid compounds, e.g. cyphenothrin, have against target insects.

Pyrethroids should be expected to exert a rapid knockdown efficacy against target species. This effect is expected to be shown a few minutes after contact, although may take longer with larger less sensitive species.

Some resistance cases of cyphenothrin have been reported against houseflies (*Musca domestica*) and whiteflies (*Bemisia tabaci*). 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 cyphenothrin.

2.1.3. Classification and Labelling

Classification and labelling of the active substance

The following classification according to the (EC) Regulation 1272/2008 has been proposed for cyphenothrin:

Classification	Acute toxicity Category 4 Acute toxicity Category 4 Specific Target Organ Toxicity (Repeated Exposure) Category 1 Aquatic Acute 1; Acute M-factor: 1000 Aquatic Chronic 1; Chronic M-factor: 1000
GHS Pictograms	
Signal Word	Danger
Hazard Statements	H302: Harmful if swallowed H332: Harmful if inhaled. H372: Causes damage to respiratory system through prolonged or repeated exposure by inhalation H400: Very toxic to aquatic life H410: Very toxic to aquatic life with long lasting effects

Precautionary Statements	P260, P261, P264, P270, P271, P273, P301 + P312, P304- P340, P312, P314, P330, P273, P391, P501

Justification for the classification assigned to the active substance (Regulation 1272/2008):

Acute toxicity Category 4 – H302

According to Regulation (EC) 1272/2008 and taking into consideration that the LD_{50} values after oral administration of the a.i. cyphenothrin to male and female rats were in the range of 300-2000 mg/kg b.w., classification as Acute Tox. 4 with H302 (Harmful if swallowed), is triggered.

Acute toxicity Category 4 – H332

In the acute inhalation toxicity study the LC_{50} value was found to be greater than 1850 mg/m^3 in male and female rats for a 3-hr exposure period. Applying modified Haber's Law for exposure duration correction, the LC_{50} was calculated to be > 1387.5 mg/m^3 or > 1.39 mg/L (4-hours exposure). This value lies within the generic concentration limit of 1-5 mg/L for classification of the substance as Acute Tox. 4 with H332 (Harmful if inhaled) according to Regulation (EC) No 1272/2008.

Specific Target Organ Toxicity (Repeated Exposure) Category 1 – H372

STOT-RE 1 (inhalation, mist) is proposed based on adverse effects in a rat 29-day inhalation toxicity study, i.e. irregular respiration and/or sporadic nose discharge (males only) observed from the dose of 0.015 mg cyphenothrin/L air (equiv. 15.1 mg/m^3, whole body exposure, 4 h/day, 7 days/week).
It is noted that according to CLP, Category 1 classification of mists is applicable when significant toxic effects are observed in a rat 90-day repeated-dose study at ≤ 0.02 mg/L/6h/day. Although the repeated dose inhalation toxicity study in rats with cyphenothrin was a 29-day study, the eCA considers the guidance value still relevant, since it represents a worst-case (90-day inhalation exposure would lead to effects at same or lower doses).

Aquatic Acute 1

Cyphenothrin is classified as Aquatic Acute 1 as its acute toxicity to fish, Daphnia and algae is below the trigger of 1 mg/L. Further, since cyphenothrin $L(E)C_{50}$ for the most sensitive trophic level is in the range 0.0001 to 0.001 mg/L, the appropriate multiplying factor (M-factor) is 1000.

Aquatic Chronic 1

Cyphenothrin is classified as Aquatic Chronic 1 as its long-term toxicity to fish, Daphnia and algae is below the trigger of 0.1 mg/L and it is not readily biodegradable. Further, since cyphenothrin NOEC for the most sensitive trophic level is in the range 0.00001 to 0.0001 mg/L, the appropriate multiplying factor (M-factor) is 1000.

Classification and labelling of the biocidal products

Gokilath 5 EC

Classification	Aspiration Toxicity Category 1 Skin Irrit. Category 2

	STOT RE Category 2 Aquatic Acute 1 Aquatic Chronic 1
GHS Pictogram	
Signal Word	Danger
Hazard Statement	H315: Causes skin irritation H373: May cause damage to respiratory system through prolonged or repeated exposure by inhalation H304: May be fatal if swallowed and enters airways H400:Very toxic to aquatic life H410:Very toxic to aquatic life with long lasting effects
Precautionary Statement Prevention	P260: Do not breathe spray P264: Wash hands thoroughly after handling P280: Wear protective gloves/protective clothing/eye protection/face protection P273: Avoid release to the environment P391: Collect spillage
Precautionary Statement Response	P314: Get medical advice/attention if you feel unwell P301 + P310: IF SWALLOWED: Immediately call a POISON CENTER or doctor/physician P302+P352: IF ON SKIN: Wash with plenty of soap and water P332+P313: If skin irritation occurs: Get medical advice/attention P362: Take off contaminated clothing and wash before reuse P331: Do NOT induce vomiting
Precautionary Statement Storage	P405: Store locked up.
Precautionary Statement Disposal	P501: Dispose of contents/container to …in accordance with local/regional/national/ international regulation (to be specified).

Justification for the classification assigned to the product (Regulation 1272/2008):

Since the content of the Biocidal Product in aromatic hydrocarbon is above 10% and no data are available for the Surface Tension and the Kinematic Viscocity at 40 ^{O}C the product is classified in Category 1 for aspiration toxicity. In addition, based on the results of the available skin irritation study, Gokilaht 5EC was found to be a skin irritant and classification

as Skin Irrit. 2 with H315 should be applied. Also, following the proposed classification of cyphenothrin as STOT RE 1 ; H372 and considering the concentration levels of the active substance in the formulation, classification as STOT RE 2 with H373 is triggered for Gokilaht 5EC. Aquatic Acute 1 classification was assigned based on summation method. Aquatic Chronic 1 classification was assigned based on the summation method.

Pesguard LG OBA

Classification	Skin Sens. Category 1 Extremely Flammable Category 1 Aquatic Acute 1 Aquatic Chronic 1
GHS Pictogram	
Signal Word	Danger
Hazard Statement	H222: Extremely flammable aerosol H317: May cause an allergic skin reaction H400:Very toxic to aquatic life H410:Very toxic to aquatic life with long lasting effects
Precautionary Statement Response	P302 + P352: IF ON SKIN: Wash with plenty of soap and water P333 + P313: If skin irritation or rash occurs: Get medical advice/attention P363: Wash contaminated clothing before reuse
Precautionary Statement Prevention	P210: Keep away from heat/sparks/open f lames/hot surfaces. — No smoking P211: Do not spray on an open f lame or other ignition source P251: Pressurized container: Do not pierce or burn, even after use. P272: Contaminated work clothing should not be allowed out of the workplace P280: Wear protective gloves/protective clothing/eye protection/face protection P273: Avoid release to the environment P391: Collect spillage
Precautionary Statement Storage	P410+P412: Protect from sunlight. Do no expose to temperatures exceeding 50oC/122oF

Precautionary Statement Disposal	P501: Dispose of contents/container to …in accordance with local/regional/national/ international regulation (to be specified).
Other phrases	EUH066: Repeated exposure may cause skin dryness or cracking

Justification for the classification assigned to the product (Regulation 1272/2008):

From the available data the product is classified in Category 1 as Extremely Flammable Aerosol (H222).

Based on the results of the available M&K Maximization test, Pesguard LG OBA was found to be a skin sensitizer. In addition, and considering the toxicological properties of a solvent and its concentration levels in the formulation, the phrase EUH066 is triggered and should be assigned to the label of the product.

Aquatic Acute 1 classification was assigned based on summation method. Aquatic Chronic 1 classification was assigned based on the summation method.

2.2. Summary of the Risk Assessment

2.2.1. Human Health Risk Assessment

Hazard identification

The technical specification is well represented in the (eco)toxicity studies submitted in support of the cyphenothrin approval. No further testing is required. For the detailed evaluation please refer to Doc. III-A, Confidential Part, Section A2 – Identity of Active Substance.

- Toxicokinetics and metabolism

Both isomers of the active ingredient (a.i.) cyphenothrin are rapidly absorbed after single oral administration of a low (2.5 mg/kg bw) or a high (100 mg/kg bw) dose. They are extensively metabolised and efficiently excreted in urine (up to 47% of low dose within 24-hrs) and faeces (up to 60% of low dose within 24-hrs). The major metabolic reactions of both isomers involve either oxidation of the alcohol and acid moieties or cleavage of the ester linkage and conjugation of the resultant carboxylic acid and phenols with glucuronic acid, sulfuric acid or glycine. The ester-retained metabolites were found mainly in the faeces, whereas the ester-cleaved metabolited were found in the urine. The sulfate of 3-(4-hydroxyphenoxy) benzoic acid was a major metabolite of the (1R)-trans-isomer (17.6-50.2%) and the (1R)-cis-isomer (12.3-40.2%). Cyphenothrin tissue residues were very low and accounted for less than 1% of the orally dosed. Tissue residues in fat were slightly higher as compared with those in other tissues. However, repeated oral exposure to low dose isomers has indicated that there is no potential of accumulation in body fat. No marked sex and isomer differences were noted in the metabolism of cyphenothrin.

The high radioactivity levels detected in feaces indicate the presence of an enterohepatic circulation. Since no study with bile-cannulated rats has been conducted, there is no information concerning the amount or the excretion rate of the test compound in the bile. An oral absorption value of 26% as a worst-case scenario has been considered as the most appropriate, based on the results for male rats and considering the cis isomer and the longest period examined.

Percentage of radiolabel (^{14}C) administered which was excreted by rats dosed once with 2.5 mg/kg

Sex/isomer	Percentage of radiolabel (^{14}C) administered/excreted	
	Day 0-1	Day 0-7
Male/Trans		
Urine	46.6	49.0
Faeces	47.4	49.5
Male/ Cis		
Urine	23.9	**26.2**
Faeces	60.4	69.4
Female / Trans		
Urine	40.0	43.9
Faeces	48.3	54.5
Female / Cis		
Urine	35.5	38.9
Faeces	51.0	59.5

The dermal absorption of cyphenothrin (1% w/v in ethanol) has been investigated in vitro through human epidermis. The formulation was applied to the epidermal membranes at a rate of 20µl/cm^2. Absorption of cyphenothrin from the 1% w/v formulation was relatively linear over the whole of the 24-hour exposure period (0.054µg/cm^2/h). The amounts absorbed during typical working day periods of 6, 8 and 10 hours were 0.205, 0.299 and 0.414µg/cm^2, respectively. The respective amounts expressed as percentages of the applied dose were 0.103, 0.149 and 0.207%. The amount absorbed over the entire 24-hour exposure period was 1.25µg/cm^2 (0.626% of the applied dose). According to the EFSA Guidance on Dermal Absorption (2012) when, less than 75% of total absorption occurs within half of the study duration, then the tape-stripped material cannot be excluded and the amount recovered from stratum corneum should be considered as potentially absorbed. As a result, for the derivation of the dermal absorption value, the amount directly absorbed and the one remaining in epidermis and in stratum corneum (all 5 tape-strips since results for each tape-strip were not available) have been considered. A dermal absorption value of 11% is concluded, corrected for low recovery and for SD being higher than 25% of the mean.

It was acknowledged that the applied volume was higher than the one recommended in the OECD protocol (20 µl/cm^2 instead of 10 µl/cm^2). However, this deviation was not considered to alter significantly the results by giving an underestimation of the dermal absorption. It is noted that for the calculated value the amount detected in all tape-strips was considered and correction has been performed twice for the SD and the low recovery. Therefore, overall any deviation that could change the absorption has been covered.
The “normalisation” approach rather than the addition of the missing material to absorption has been followed, in order to correct for low recovery. Normalization is one of two options the EFSA Guidance proposes for low recovery correction. In the study, the observed low recoveries were most likely to be as a result of poor extraction from the swabs. Therefore, the losses were considered to be from non-absorbed material and as such have no impact on the results according to the EFSA Guidance.

Overall, based on the available data, a value of 11% is concluded for a 1% cyphenothrin dilution in ethanol.

It is noted that the two supported formulations i.e. Gokilaht 5EC and Pesguard LG OBA, have no comparable compositions to the ethanolic solution tested. Therefore, read-across from the available *in vitro* dermal absorption study cannot be performed. A default value of 75% is applied for both formulations in accordance with the EFSA Guidance on Dermal Absorption

(2012).

The inhalation absortpion rate is considered by default to be 100%.

- Acute Toxicity

The acute oral toxicity of cyphenothrin was tested in Spraguw Dawley rats. Cyphenothrin appeared to be harmful by ingestion. The LD_{50} in males was 318 mg/kg bw and in females was 419 mg/kg bw. According to Regulation (EC) 1272/2008 and taking into consideration that the LD_{50} values after oral administration of the a.i. cyphenothrin to male and female rats are in the range of 300-2000 mg/kg bw, the a.i. cyphenothrin should be classified as **Acute Tox. 4 with H302** (Harmful if swallowed).

Cyphenothrin was of low acute dermal toxicity since there were no deaths and no overt signs of toxicity at any of the doses tested. The LD_{50} for males and females was greater than 5000 mg/kg bw. No remarkable macroscopic changes or skin irritation were observed in treated animals at necropsy. No classification is warranted.

The acute inhalation toxicity of cyphenothrin was tested in Spraguw Dawley rats. The LC_{50} in males and females was greater than 1850 mg/m^3 for a 3-hr exposure period. No remarkable macroscopic changes were observed in treated animals. Applying modified Haber's Law for exposure duration correction, the LC_{50} was calculated to be > 1387.5 mg/m^3 or > 1.39 mg/L (4-hours exposure).
This value lies within the generic concentration limit of 1-5 mg/L for classification of the substance as **Acute Tox. 4 with H332** (Harmful if inhaled) according to Regulation (EC) No 1272/2008.

- Irritation and Corrosivity

The skin and eye irritancy properties of the a.i. cyphenothrin were investigated in New Zealand White rabbits. No signs of irritation were observed in any of the animals with intact or abraded skin and no lesions were noted in the cornea and iris of any rabbit. However, slight conjunctival hyperaemia occurred in 2/6 animals with unwashed eyes at 1 hour reading only. Conjunctival effects were not observed in animals with washed eyes. Based on the above, cyphenothrin was considered to be non-irritating to rabbit skin and slightly irritating to rabbit eye. No classification is warranted.

- Sensitisation

A sensitisation study was conducted with cyphenothrin in male Hartley guinea pigs according to a modified Buehler method. Undiluted test material was used for both the induction and the challenge phase. Under the conditions of the study cyphenothrin was found to be not a skin sensitiser. It is noted that the method was a modified 10-induction application test. The study was conducted in accordance with generally accepted scientific principles while any methodological deficiencies are not considered to affect the quality of the results.
As in case of the 9-application modified Buehler test, the available study was considered acceptable for classification and labelling purposes.

- Repeated dose toxicity

Repeated dose toxicity was investigated by the oral route in several feeding studies in rats (13 and 104-week), mice (104-week) and dogs (4 and 13-week). In the 13-week study in rats, clinical chemistry changes indicative of liver toxicity were observed from the dose of 23.1 mg/kg bw/day, whereas clinical signs consistent with synthetic pyrethroid toxicity (i.e. tremors, irritability, facial staining and piloerection) were evident from the dose of 76.0 mg/kg bw/day. In the 104-week study, body weight and food consumption reduction was

observed in females, increase in relative-to-body liver weight in both sexes at 54 weeks, followed by increased liver/bile duct hyperplasia in females at 104 weeks from the dose of 48.16 mg/kg bw/day. The overall subchronic/chronic NOAEL in the rat was the value of 14.49 mg/kg b.w./day from the 104-week study, considering dose spacing. In mice 104-week study, the NOAEL was set at 14.6 mg/kg bw/day based on decreased kidney weight consistent with histopathology findings (males) and increased incidence of lymphoid hyperplasia of the mesenteric lymph node (males and females) from the dose of 42.91 mg/kg bw/day. In the 4-week feeding study in dogs, overt signs of pyrethroid toxicity were observed from Day 1 after dosing with 10 mg/kg bw/day. No NOAEL was set in this study. Thus, the NOAEL of 3 mg/kg bw/day from the 13-week feeding study in dogs was the overall NOAEL in dogs. This value was based on typical signs of pyrethroid toxicity (vomiting) from the dose of 10 mg/kg bw/day. Tremors, paleness and intense redness of the mucous membranes were evidenced at the top dose of 30 mg/Kg bw/day. Overall, the dog was identified as the most sensitive species by the oral route and Type I pyrethroid toxicity the most critical effect of cyphenothrin.

Repeated dose inhalation toxicity of cyphenothrin was tested in two 29-day studies in rats (whole body exposure for 4 h/day, 7 days/week) at dose levels of 7.76-152 mg/m^3. Treatment-related clinical signs, including irregular respiration (systemic effect) and sporadic nose discharge (local effect) were observed from the dose of 15.1 mg/m^3. Thus, the overall NOAEC for both systemic and local effects was set at 7.76 mg/m^3, equivalent to cyphenothrin intake of 5.73 mg/kg bw/day. It is noted that irregular respiration and/or sporadic nose discharge was observed on Day 1 after dosing from the dose of 0.015 mg cyphenothrin/L air, triggering classification of cyphenothrin as **STOT-RE 1** (inhalation, mist) **with H372** (Causes damage to respiratory system through prolonged or repeated exposure by inhalation). Although the repeated dose inhalation toxicity study in rats with cyphenothrin was a 29-day study, the guidance value is still relevant, since it represents a worst-case (90-day inhalation exposure would lead to effects at same or lower doses).

It was not considered essential to conduct repeated dose toxicity studies by the dermal route, since cyphenothrin is of low acute dermal toxicity.

- Genotoxicity

Cyphenothrin was tested in an *in vitro* genotoxicity battery, including mutagenicity in bacterial (*S.typ himurium*, *E.coli*) and mammalian (V79, HGPRT locus) cells, chromosome aberrations in Chinese Hamster Ovary (CHO) cells and sister chromatid exchange in CHO-K1 cells. Cyphenothrin was not genotoxic *in vitro.*

In vivo, cyphenothrin was assessed in a micronucleus study, wheremale ICR mice were dosed intraperitoneally. In both dose-response and time-response tests no significant increases in micronucleated cells were observed. Cyphenothrin was not genotoxic *in vivo*.

- Carcinogenicity

The potential carcinogenic properties of cyphenothrin were assessed in two 104-week feeding studies in the rat and mouse at doses of 0, 100, 300 and 1000 ppm. There was no evidence of carcinogenicity in both species up to the highest dose tested, equivalent to cyphenothrin intakes of 58.52 mg/kg bw/day in the rat and 154.5 mg/kg bw/day in the mouse.

- Reproductive toxicity

Developmental toxicity of cyphenothrin was tested in relevant subcutaneous studies in rats and rabbits. No treatment-related foetotoxic, teratogenic or behavioural effects of offspring were noted at doses up to 500 mg/kg bw/day in rats and 125 mg/kg bw/day in rabbits, where maternal toxicity was evidenced. In rats, the NOAEL for maternal toxicity was set at 150 mg/kg bw/day, based on decreased body weight gain, increased absolute weight of the

heart, spleen and kidneys, as well as mortality observed at the top dose of 500 mg/Kg bw/day. In rabbits, the NOAEL for maternal toxicity was set at 50 mg/kg bw/day, based on decreased body weight gain and food consumption at 125 mg/kg bw/day.

In a two-generation reproduction study in the rat, no apparent adverse effects on the reproductive parameters and/or the offspring development were observed. The overall NOAEL for parental systemic toxicity was set at 300 ppm (approx. equivalent to 23.7 mg/Kg bw/day), based on decreased bodyweight gains of F0 and FlA females at 1000 ppm.

- Neurotoxicity

Cyphenothrin neurotoxicity was tested in acute gavage studies and 90-day feeding studies in rats. In the acute gavage studies, adverse effects including markedly coarse tremors and severe neuromuscular findings (impaired mobility, dragging body clonic convulsions) were observed from the dose of 50 mg/kg b.w. The overall NOAEL was set at 25 mg/kg bw/day. In the 90-day feeding studies, the NOAEL was set at 73/90 mg/kg b.w./day, based on lower mean body weights, body weight gains, and food consumption as well as neurotoxic effects (slight to severe persistent tremors and clonic convulsions, resulting in moribundity and eventual euthanasia of all animals by study day 9) at 164/199 mg/kg bw/day, a dose considered as exceeding the MTD.

It is noted that the LOAEL = 50 mg/kg bw from the acute gavage neurotoxicity studies is below the NOAEL = 73/90 mg/kg b.w./day from the 90-day feeding neurotoxicity study. This indicates that perhaps gavage is not the most appropriate route for assessing cyphenothrin neurotoxicity or it could be attributed to the low oral absorption of the substance (approx. 26%). This observation is confirmed by findings in other studies. For instance, in the 2-generation reproductive toxicity (feeding) study there were no neurotoxic effects at doses up to approx. 76.8 mg/kg b.w./day in parents and offspring, which is in the same range with the NOAEL = 73/90 mg/kg b.w./day from the 90-day feeding neurotoxicity study. In the 13-week repeat dose feeding study in rats, clinical signs consistent with synthetic pyrethroid toxicity (i.e. tremors, irritability and piloerection) were evident at doses of ≥ 76.0/87.9 mg/kg b.w./day in males/females.

Regarding potential classification of cyphenothrin for neurotoxicity, it is noted that although STOT-SE 1 (nervous system) would be triggered based on findings from the acute neurotoxicity study where acute effects of type I pyrethroids are observed from the dose of 50 mg/kg b.w., this is not warranted. This is because the proposed classification for acute toxicity is stronger (Acute Tox. 4 – H302).

A DNT study has not been performed and it is not considered necessary. Overall, in the absence of treatment-related fetotoxic, teratogenic or behavioural effects of offspring and/or any evidence of greater sensitivity of younger animals, it is concluded that infants and children are not considered to be more sensitive than adults to cyphenothrin exposure. Therefore, infants and children are not considered to be more sensitive than adults to cyphenothrin exposure and the risk assessment for adults covers also for all other subgroups of the population.

- Human data

A review of the medical records of workers in the packaging department of the manufacturing plant showed no finding attributable to exposure to pyrethroids ([redacted], 2005). It is noted that the submitted report concerns worker exposure during the manufacturing process which is not relevant for the use as a biocide in EU.

Hazard characterisation

A summary of the hazard characterisation for cyphenothrin is presented in Table 2.2.1-1.

Table 2.2.1-1: Summary of the hazard characterisation for cyphenothrin

Reference	Study	NOAEL (LOAEL)	AF	Correction for oral absorption	Value
$AEL_{short-term}$	Dog 13-week oral (feeding) study ([redacted], 1987); supported by dog 4-week oral (feeding) study ([redacted], 1987).	3 mg/kg bw/d (10 mg/kg bw/d)	100	26% *	0.008** mg/kg bw
$AEL_{medium-term}$	Dog 13-week oral (feeding) study ([redacted] 1987)	3 mg/kg bw/d (10 mg/kg bw/d)	100	26% *	0.008** mg/kg bw/d
$AEL_{long-term}$	Dog 13-week oral (feeding) study ([redacted] 1987)	3 mg/kg bw/d (10 mg/kg bw/d)	100	26% *	0.008** mg/kg bw/d
$AEC_{short-term}$	Rat, 29-day inhalation; whole body, 4 h/day, 7 days/week ([redacted], 1983 & [redacted] 1984)	7.76 mg/m³ (15.1 mg/m³) Equivalent to: 5.73 / 11.1 mg/kg bw/d	25	100%	0.31 mg/m³
$AEC_{medium-term}$	Rat, 29-day inhalation; whole body, 4 h/day, 7 days/week ([redacted] 1983 & [redacted] 1984)	7.76 mg/m³ (15.1 mg/m³) Equivalent to: 5.73 / 11.1 mg/kg bw/d	25	100%	0.31 mg/m³
ARfD	Dog 13-week oral (feeding) study ([redacted] 1987); supported by dog 4-week oral (feeding) study ([redacted] 1987).	3 mg/kg bw/d (10 mg/kg bw/d)	100	-	0.03 mg/kg bw/d
ADI	Dog 13-week oral (feeding) study ([redacted], 1987)	3 mg/kg bw/d (10 mg/kg bw/d)	100	-	0.03 mg/kg bw/d

* Although the oral absorption of 26% is obtained from rat studies, consideration of this value in the estimation of AEL is expected to result in worst-case values and it is therefore considered relevant even when the NOAEL/starting point is from a dog study.
** The value is rounded to 0.008 mg/kg bw/day from 0.0078 mg/kg bw/day for risk characterisation (WG-II-2017).

Detailed justification on the doses selected for reference value setting and the associated uncertainties are presented in the following attached document (Chapter 14.1 & 14.2):

Cyphenothrin_draft Final CAR_Chapter 1

Exposure assessment

Pesguard LG OBA & Gokilaht 5 EC

It is noted that indented uses of both products include no non-professional use and hence this group has not been considered in the risk assessment.

Pesguard LG OBA

Primary exposure

Primary professional exposure during application has been calculated using data derived from laboratory-based studies of amateur and consumer exposure to aerosol sprays conducted since 1995 by the HSE Health and Safety Laboratory (UK). In addition, calculations have been performed using the surrogate values proposed in the TNsG part 2 version 2002. As a 1st Tier approach it has been assumed that no PPE is used and as a 2nd Tier PPE usage has been considered.

Table 2.2.1-2 Estimated exposure levels to cyphenothrin for professional operators during application of Pesguard LG OBA/ No PPE

Exposure parameter	**Central tendency** HSE Health & Safety	**Realistic worst** HSE Health & Safety	**TNsG, Part 2 (2002)**
Total dermal and inhalation systemic exposure (mg a.i./person)	2.18	4.74	3.73
Total systemic exposure to a.i. for a 60 kg adult (mg/kg a.i./day)	0.036	0.079	0.062
% of AEL (cyphenothrin: 0.008 mg/kg b.w./day)	**450**	**988**	**775**

Table 2.2.1-3 Estimated exposure levels to cyphenothrin for professional operators during application of Pesguard LG OBA/ PPE (gloves and impermeable coverall)

Exposure parameter	**Central tendency** HSE Health & Safety	**Realistic worst** HSE Health & Safety	**TNsG, Part 2 (2002)**
Total dermal and inhalation systemic exposure (mg a.i./person) Assuming gloves & impermeable coverall	0.196	0.43	0.325

Total systemic exposure to a.i. for a 60 kg adult (mg/kg a.i./day) Assuming gloves & impermeable coverall	0.0033	0.0072	0.0054
% of AEL (cyphenothrin: 0.008 mg/kg b.w./day)	**41**	**90**	**68**

Secondary exposure

The product is for professional application only and it may therefore be assumed that occupants and other bystanders will be excluded from treated areas during application and until surfaces are dry. However, a label instruction should be applied, to ensure that occupants and bystanders are excluded form treated areas shortly after application. Skin exposure may occur as a result of contact with treated surfaces and other surfaces onto which aerosolised material has deposited. For toddlers there is also the potential for oral exposure as a result of hand-to-mouth contact. The TNsG indicates that around 15 % of material released during a targeted spot or crack and crevice application may deposit on the floor away from the treated area (TNsG, part 2, page 256 and 260) while, for dried liquids the transfer coefficient from various types of surfaces is 18% (TNsG, version 2, page 102). For adults it has been assumed that all the surface residue of cyphenothrin is transferred to the palms (surface of both palms as indicated in HEEG Opinion 17: 410 cm^2). Children indirect dermal exposure has been assessed using the "rubbing-off" model from ConsExpo. For hand-to-mouth exposure and as indicated in HEEG Opinion 7, hands form about 20% of the total uncovered skin and is assumed that 50% of the product ending up on the hands is taken orally. Dermal exposure (hand contact) has not been assessed for the 'infant' (age group 6 to < 12 months old; reference: HEEG Opinion On 'Default Human Factor Values For Use In Exposure Assessments For Biological Products'- endorsed at TM II 2013) because such an age group is relatively immobile and infants tend to stay where they are placed. Therefore, it is anticipated that infants would be placed away from treated cracks/crevices and therefore be unable to touch treated surfaces negating dermal exposure. Inhalation exposure to volatilized active substance for the toddler was considered as negligible following HEEG Opinion 13, and this was also assumed for the child and adult.

Table 2.2.1-4 Exposure estimates for indirect exposure of adults and children following application of Pesguard LG OBA

Exposure Scenario		**Estimated Internal Exposures**				
	estimated oral uptake (mg a.s./kg bw/day)	**estimated inhalation uptake (mg a.s./kg bw/day)**	**estimated dermal uptake (mg a.s./kg bw/day)**	**estimated inhalation uptake of volatilized residues (mg a.s./kg bw/day)**	**estimated total uptake (mg a.s./kg bw/day)**	**Total exposure as % of medium term AEL of 0.008 mg/kg bw/d**
Adult	-	-	2.7×10^{-4}	negligible	2.7×10^{-4}	**3.4**
Child	-	-	3.4×10^{-3}	negligible	3.4×10^{-3}	**43**

Toddler	2.8×10^{4}	-	8×10^{3}	negligible	8.3×10^{3}	**104**

Risk characterisation - professional users (Pesguard LG OBA)

Workplace operation	PPE	Exposure path	Body dose (mg/kg bw/day)	% of the AEL *(cyphenothrin: 0.008 mg/kg b.w./day)*
Indoor surface spot, crack and crevice treatment	None	Dermal and Inhalation	0.036 (central tendecy) 0.079 (realistic worst case) 0.062 (TNsG, Part 2, 2002)	**450** **988** **775**
	Gloves & Impermeable coverall	Dermal and Inhalation	0.0033 (central tendecy) 0.0072 (realistic worst case) 0.0054 (TNsG, Part 2, 2002)	**41** **90** **68**

An acceptable risk has been identified for a professional user applying Pesguard LG OBA for indoor surface spot, crack and crevice treatment, considering gloves and coverall are used.

Local effects

Pesguard LG OBA is classified as skin sensitizer (Skin Sens. 1 – H317) and also been assigned with the phrase EUH066. The use of gloves and impermeable coverall by professionals is considered to adequately protect the users and as such, an acceptable risk can be concluded.

Risk characterisation - secondary exposure (Pesguard LG OBA)

Exposure Scenario		Estimated Internal Exposures				
	estimated oral uptake (mg a.s./kg bw/day)	estimated inhalation uptake (mg a.s./kg bw/day)	estimated dermal uptake (mg a.s./kg bw/day)	estimated inhalation uptake of volatilized residues (mg a.s./kg bw/day)	estimated total uptake (mg a.s./kg bw/day)	Total exposure as % of medium term AEL of 0.008 mg/kg bw/d
Adult	-	-	2.7×10^{4}	negligible	2.7×10^{4}	**3.4**
Child	-	-	3.4×10^{3}	negligible	3.4×10^{3}	**43**
Toddler	2.8×10^{4}	-	8×10^{3}	negligible	8.3×10^{3}	**104**

An acceptable risk has been identifiled for adults and children following secondary exposure to cyphenothrin after application of Pesguard LG OBA.
For toddlers, a borderline exposure estimate has been concluded. Given that the product is for spot, crack and crevice treatment and as such, toddlers will not have immediate access to treated residues, no particular concern is raised. In addition, it should be noted that exposure levels are overestimated since, the conservative default value of 75% for dermal absorption has been used in the calculations, in the absence of relevant to the product dermal absorption data. However, and as a precautionary measure, a label instruction for Pesguard LG OBA, to be applied to areas inaccessible to children, should be considered.

Local effects

Pesguard LG OBA is classified as skin sensitizer (Skin Sens. 1 – H317) and also been assigned with the phrase EUH066. Taking into account that according to the intended uses the product is applied once at each application site and considering also that immediate and routine access to treated residues will not occur as the application method refers to spot, crack and crevice treatment, potential exposure can be considered minimal and thus, no concern is identified.

COMBINED EXPOSURE (Pesguard LG OBA)

Combined exposure can occur for a person (professional user) applying the product (primary exposure) and being resident in the treated premises subsequently (secondary exposure to volatilized residues *via* inhalation).

Inhalation exposure to volatilized active substance was found to be negligible for the toddler and consequently for the infant, child and adult, in accordance with HEEG Opinion No. 13. The combined scenario is summarised in Table below.

Table 2.2.1-5 Summary of systemic exposures for combined scenario

User	Total systemic exposure during primary exposure (mg/kg bw/d)	Total systemic exposure during secondary exposure to volatilized a.s. (mg/kg bw/d)	Combined exposure (mg/kg bw/d)	Combined exposure as % of acute AEL of 0.008 mg/kg bw/d
Professional application and resident in premises	0.0033 (central tendecy) 0.0072 (realistic worst case) 0.0054 (TNsG, Part 2, 2002)	negligible	0.0033 (central tendecy) 0.0072 (realistic worst case) 0.0054 (TNsG, Part 2, 2002)	**41** **90** **68**

Combined systemic exposures from the application of Pesguard LG OBA by professional users, residents in the treated building, present an acceptable risk.

A dietary risk assessment was not undertaken due to the use pattern. Possible food contamination can be avoided by label restrictions. If use of the product can lead to contamination of food, a proper risk assessment via food exposure should be performed at product authorization.

Gokilaht 5 EC

Primary exposure

Spraying model 1 (TNsG part 2, p 143) was considered in order to assess primary exposure of professionals. A task duration of 120 min was selected according to the parameters described in the TNsG part 2 version 1 (2002). Furthermore, with regard to the personal protective equipment used and the penetration rate, a value of 5% has been used for impermeable coveralls as indicated in the ECHA Biocides Human Health Exposure Methodology (October, 2015). Respiratory protection equipment (FF P2 half mask) was considered to provide 90% protection.
With regard to the inhalation exposure a breathing rate of 1.25 m^3/hour has been used based on the TNsG.
A dermal absorption value of 75% has been concluded for Gokilaht 5EC (please refer to Doc IIA). As a 1st Tier approach it has been assumed that no PPE is used and as a 2nd Tier PPE/RPE usage has been considered.

Table 2.2.1-6 Primary Exposure estimates for professional operators during mixing/loading/application of Gokilaht 5EC – No PPE

Exposure	Value
Total dermal and inhalation systemic exposure (mg a.i./person)	49.66
Total systemic exposure to a.i. for a 60 kg adult (mg/kg a.i./day)	0.828
% of AEL (cyphenothrin: 0.008 mg/kg b.w./day)	**10350**

Table 2.2.1-7 Primary Exposure estimates for professional operators during mixing/loading/application of Gokilaht 5EC – PPE

Exposure	Value
Total dermal and inhalation systemic exposure (mg a.i./person)	3.27
Total systemic exposure to a.i. for a 60 kg adult (mg/kg a.i./day) PPE: gloves & impermeable coverall	0.0545
% of AEL (cyphenothrin: 0.008 mg/kg b.w./day)	**681**

Table 2.2.1-8 Primary Exposure estimates for professional operators during mixing/loading/application of Gokilaht 5EC – PPE/RPE

Exposure	Value
Total dermal and inhalation systemic exposure (mg a.i./person)	2.8
Total systemic exposure to a.i. for a 60 kg adult (mg/kg a.i./day) PPE: gloves & impermeable coverall & RPE (FF P2 half mask)	0.0467
% of AEL (cyphenothrin: 0.008 mg/kg b.w./day)	**584**

For assessing primary exposure during cleaning of the application equipment, the surrogate values from BEAT model database have been used.

Detailed exposure calculations are presented in the following tables:

Table 2.2.1-9 Primary exposure estimates for professional operators during cleaning of application equipment of Gokilaht 5EC – no PPE

Exposure Description	
Total systemic exposure to a.s. for a 60 kg adult (mg a.s./kg bw/day)	0.00003
% of AEL (cyphenothrin: 0.008 mg/kg b.w./day)	**0.375**

Table 2.2.1-10 Primary exposure estimates for professional operators during cleaning of application equipment of Gokilaht 5EC – PPE

Exposure Description	
Total systemic exposure to a.s. for a 60 kg adult (mg a.s./kg bw/day)	1×10^{-5}
% of AEL (cyphenothrin: 0.008 mg/kg b.w./day)	**0.125**

The following table summarises the exposure estimates for primary exposure during mixing/loading, application and cleaning of application equipment for Gokilaht 5EC.

Table 2.2.1-11 Estimated primary systemic operator exposure levels to cyphenothrin [mg/kg bw/day] during mixing/loading, application and cleaning of Gokilaht 5EC without and with PPE/RPE

Systemic exposure in mg/kg bw/day resulting from	**no PPE**	**with PPE**	**With PPE/RPE**
- Mixing/loading & application	0.828	0.0545	0.0467
- Cleaning application equipment	3×10^{-5}	1×10^{-5}	1×10^{-5}
Total systemic exposure [mg/kg bw/day]	0.828	0.0545	0.0467
% of AEL (cyphenothrin: 0.008 mg/kg b.w./day)	**10350**	**681**	**584**

Secondary exposure

The product is for professional application only and it may therefore be assumed that occupants and other bystanders will be excluded from treated areas during application and until surfaces are dry. However, a label instruction should be applied, to ensure that occupants and bystanders are excluded form treated areas shortly after application. Skin exposure may occur as a result of contact with treated surfaces and other surfaces onto which aerosolised material has deposited. For toddlers and infants there is also the potential for oral exposure as a result of hand-to-mouth contact.
The TNsG indicates that for dried liquids the transfer coefficient from various types of surfaces is 18% (TNsG, version 2, page 102). For adults it has been assumed that all the surface residue of cyphenothrin is transferred to the palms (surface of both palms as indicated in HEEG Opinion 17: 410 cm^2). Children indirect dermal exposure has been assessed using the “rubbing-off” model from ConsExpo. For hand-to-mouth exposure and as indicated in HEEG Opinion 7, hands form about 20% of the total uncovered skin and is assumed that 50% of the product ending up on the hands is taken orally. Inhalation exposure to volatilized active substance for the toddler was considered as negligible following HEEG Opinion 13, and this was also assumed for the infant, child and adult.

Table 2.2.1-12 Exposure estimates for indirect exposure of adults and children following application of Gokilaht 5EC

Exposure Scenario	**Estimated Internal Exposures**					
	estimated oral uptake (mg	**estimated inhalation uptake (mg**	**estimated dermal uptake (mg**	**estimated inhalation uptake of volatilized**	**estimated total uptake (mg**	**Total exposure as % of medium term**

	a.s./kg bw/day)	**a.s./kg bw/day)**	**a.s./kg bw/day)**	**residues (mg a.s./kg bw/day)**	**a.s./kg bw/day)**	**AEL of 0.008 mg/kg bw/d**
Adult	-	-	9.2×10^{3}	negligible	9.2×10^{3}	**115**
Child	-	-	$1.1 \times 10^{-}$	negligible	$1.1 \times 10^{-}$	**1375**
Toddler	9.4×10^{3}	-	$2.7 \times 10^{-}$	negligible	$2.8\times 10^{-}$	**3493**
Infant	1.2×10^{2}	-	$3.4 \times 10^{-}$	negligible	$3.5\times 10^{-}$	**4400**

Risk characterisation - professional users (Gokilaht 5EC)

Workplace operation	**PPE**	**Exposure path**	**Body dose (mg/kg bw/day)**	**% of the AEL *(cyphenothrin: 0.008 mg/kg b.w./day)***
Indoor low pressure handheld spray application	None	Dermal and Inhalation	0.828	**10350**
	Gloves & Impermeable coverall	Dermal and Inhalation	0.0545	**681**
	Gloves & Impermeable coverall & FFp2 half mask	Dermal and Inhalation	0.0467	**584**

An unacceptable risk has been identified for a professional user applying Gokilaht 5EC indoor *via* low pressure hand-held equipment, even when PPE and RPE is used.

Local effects

Gokilaht 5EC is classified as skin irritant (Skin Irrit. 2 – H315) and also as STOT RE Category 2 with H373 for local effects to the respiratory system.

- Dermal effects: The use of gloves and impermeable coverall by professionals is considered to adequately protect the users and as such, an acceptable risk can be concluded.

- Respiratory effects:

Table 2.2.1-13 Risk for local respiratory effects

Local (external) respiratory exposure estimate [mg/m³]	**Local respiratory AEC [mg/m³]**	**% (Local respiratory exposure / AEC)**
0.208	0.31	67

An acceptable risk can be concluded.

Risk characterisation - secondary exposure (Gokilaht 5EC)

Exposure Scenario		Estimated Internal Exposures				
	estimated oral uptake (mg a.s./kg bw/day)	estimated inhalation uptake (mg a.s./kg bw/day)	estimated dermal uptake (mg a.s./kg bw/day)	estimated inhalation uptake of volatilized residues (mg a.s./kg bw/day)	estimated total uptake (mg a.s./kg bw/day)	Total exposure as % of medium term AEL of 0.008 mg/kg bw/d
Adult	-	-	9.2×10^{-3}	negligible	9.2×10^{-3}	**115**
Child	-	-	1.1×10^{-2}	negligible	1.1×10^{-2}	**1375**
Toddler	9.4×10^{-3}	-	2.7×10^{-2}	negligible	2.8×10^{-2}	**3493**
Infant	1.2×10^{-2}	-	3.4×10^{-2}	negligible	3.5×10^{-2}	**4400**

An unacceptable risk has been identifiled for both adults and children following secondary exposure to cyphenothrin after application of Gokilaht 5EC.

Local effects

Gokilaht 5EC is classified as skin irritant (Skin Irrit. 2 – H315) and also as STOT RE Category 2 with H373 for local effects to the respiratory system.
Dermal effects: Taking into account that possible exposure will occur to the diluted product and according to the intended uses the product is applied once at each application site potential exposure can be considered minimal and thus, no concern is identified.
Respiratory effects: Taking into account the frequency of use of the product and that inhalation exposure to volatilized active substance has been concluded to be negligible, an acceptable risk is identified.

COMBINED EXPOSURE (Gokilaht 5EC)

Combined exposure can occur for a person (professional user) applying the product (primary exposure) and being resident in the treated premises subsequently (secondary exposure to volatilized residues *via* inhalation).

Inhalation exposure to volatilized active substance was found to be negligible for the toddler and consequently for the infant, child and adult, in accordance with HEEG Opinion No. 13. The combined scenario is summarised in Table below.

Table 2.2.1-14 Summary of systemic exposures for combined scenario

User	Total systemic exposure during primary exposure (mg/kg bw/d)	Total systemic exposure during secondary exposure to volatilized a.s. (mg/kg bw/d)	Combined exposure (mg/kg bw/d)	Combined exposure as % of acute AEL of 0.008 mg/kg bw/d
Professional application and resident in premises	0.0467	negligible	0.0467	**584**

Combined systemic exposures from the application of Gokilaht 5EC by professional users, residents in the treated building, present an unacceptable risk.

A dietary risk assessment was not undertaken due to the use pattern. Possible food contamination can be avoided by label restrictions. If use of the product can lead to contamination of food, a proper risk assessment via food exposure should be performed at product authorization.

2.2.2. Environmental Risk Assessment

Fate and distribution in the environment

The composition of cyphenothrin technical material consists in a ratio of *trans:cis* of 75:25 approximately. The detailed composition is presented in the confidential part of this CAR. The submitted studies have been performed using mixtures of cyphenothrin as a test substance in a range of trans:cis ratios. For risk and PBT assessment purposes cis and trans isomers have been considered individually.

Hydrolysis: Cyphenothrin was shown to be hydrolytically stable at pH 4. The half-life of cyphenothrin in pH 7 buffer at 25°C was calculated to be 112 days (316.9 days at 12^0C), by extrapolation from the plot of the half-lives obtained at higher temperatures (48, 60, 70) using the Arrhenius equation. The Arrhenius activation energy was calculated as 621.7 KJ/mol.The half-life of cyphenothrin in pH 9 at 25^0C was calculated to be 4.6 days (13 days at 12^0C). Furthermore, 3-phenoxybenzaldehyde and d-trans-cyphenothrin-$CONH_2$ have been identified as major hydrolysis products at pH 7 and pH 9.

Photolysis: Photolysis of *trans*-cyphenothrin was investigated in non-GLP study performed according to OECD Guideline 316. The half-life of cyphenothrin was calculated to be 9.2 hrs at 25^oC, in a solution buffered to pH 4 and exposed continuously under xenon arc lamp for 26 total hours. (RS)-α-cyano-3-phenoxybenzyl (1R)-trans-2,2-dimethyl-3-formylcyclopropanecarboxylate (CHO-GKL, 49.4% of AR at 20 hr) and 3-phenoxybenzaldehyde (PBald, 14.4% at 12 hr) were identified as major degradation products.

Phototransformation in air: The photchemical degradation in air has been calculated using AOPWIN (version 1.92) model. The half-life was estimated to be 3.675 hrs for overall OH rate constant.

Ready biodegradability: Cypenothrin was investigated for its ready biodegradability in a manometric respirometry test over 28 days based on EU Commission Directive 92/69 EEC, C.4-D (1992) and OECD Guideline for Testing of Chemicals No. 301 F (1992).

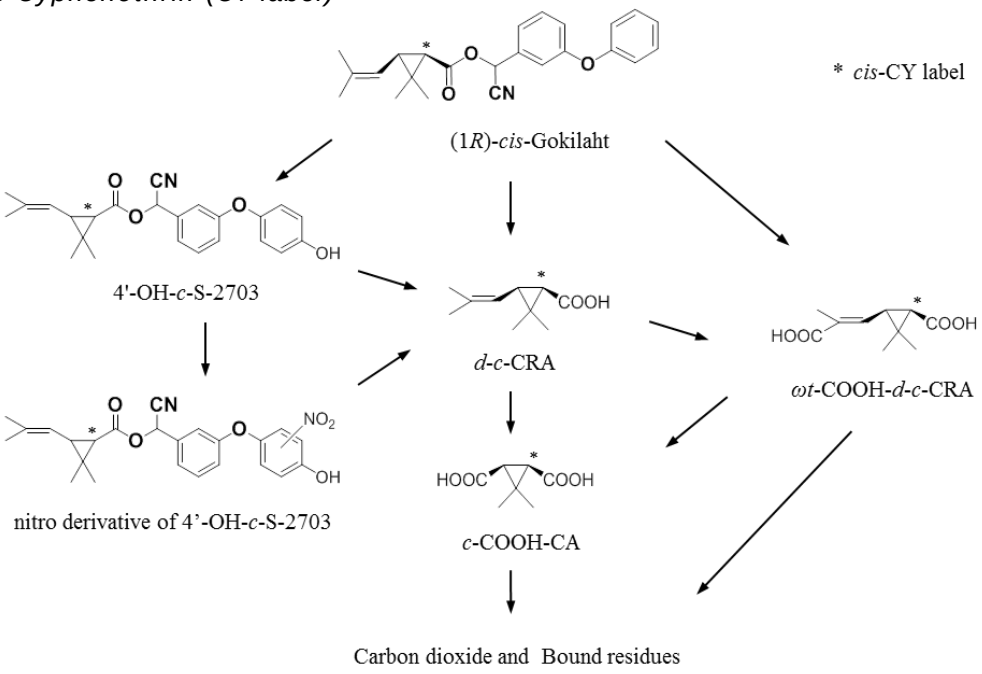
Consequently, cypenothrin was found to be not biodegradable under the test conditions within 28 days.

Aerobic soil degradation: A laboratory study was performed according to OECD-Guideline 307. The aerobic degradation behaviour of Cyphenothrin has been tested in four soil types at 20 ± 2^0C under dark conditions. Three radiolabelled species of Cyphenothrin were investigated (trans-cyclopropyl-1-^{14}C-Cyphenothrin, trans-phenoxyphenyl-U-14C-Cyphenothrin, cis-cyclopropyl-1-14C-Cyphenothrin), however trans-CY has been tested only in sandy loam soil (Barrow, UK). For the cis-CY and trans-CY labels, samples were collected immediately after treatment (time 0) and after 1, 3, 7, 14, 30, 62, and 120 days of incubation. For the trans-PH label, samples were collected immediately after treatment (time 0) and after 1, 3, 7, 14, 29, 60 and 123 days of incubation. Four major degradation products have been observed and

identified to be 4'-OH-c-S-2703 with max. AR of 10.9% in Empingham soil at day 3, PBacid with max. 15.8% in Barrow soil at day 3 and ωt-COOH-d-c-CRA with max. AR of 8.4% in Brierlow soil at the end of the study and a nitro-derivative of 4'-OH-c-S-2703, initially identified as "Met-59", was observed at maximum concentration of 8.3% of AR in Ingleby soil at 62nd day. Several minor metabolites have been identified with AR% less than 5%. The calculated DT_{50} values for cyphenothrin and its major metabolites are summarised in the following tables.

Figure 1: Proposed degradation pathway for [^{14}C]cyphenothrin in soil under aerobic conditions.

(1R)-cis-Cyphenothrin (CY label)



(1R)-trans-Cyphenothrin (PH label and CY label)

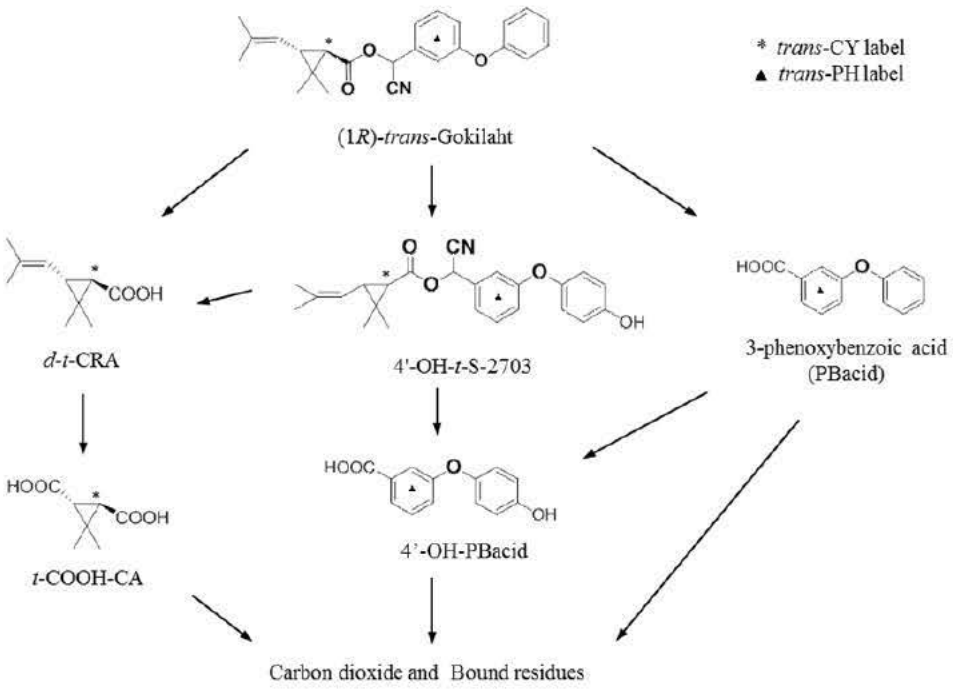


Table 2.2.2-1: Major metabolites in the aerobic soil degradation

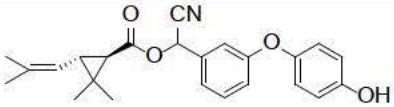
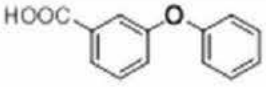
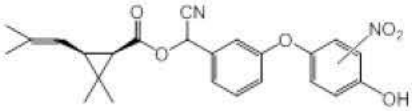
Code	Max.% AR	Precursor	Structure
4'-OH-*c*-S-2703	10.9	*cis*-CY	
PBacid	15.8	*trans*-PH	
ωt-COOH-*d*-*c*-CRA	8.4	*cis*-CY	
nitro derivative of 4'-OH-*c*-S-2703	8.3	*cis*-CY	

Table 2.2.2-2: DT50 values calculated at 20 and 12°C.

Modelling endpoints*						
Soil	**Label**	**Kinetic fit**	**Visual assessment**	**Chi² % error**	**DT_{50} at 20°C (days)**	**DT_{50} at 12°C (days)**
Empingham, UK	*cis*-CY	FOMC	Excellent	5.1	6.2	13.2
	trans-PH	FOMC	Excellent	4	6.04	12.8
Ingleby, UK	*cis*-CY	DFOP	Excellent	4.3	1000	1000
	trans-	FOMC	Excellent	5.8	14.2	30.3

	PH					
Barrow, UK	*cis*-CY	DFOP	Excellent	2.9	154	328.7
	trans-PH	FOMC	Very good	10.7	11.3	24.1
	trans-CY	FOMC	Excellent	4.06	9.64	20.6
Brierlow, UK	*cis*-CY	DFOP	Very good	3.9	65.1	138.9
	trans-PH	FOMC	Acceptable	12.4	20.5	43.8
Geometric mean**		cis				**156.68**
		trans				**24.3**

* DT50 for FOMC was calculated from DT90/3.32 and for DFOP the slow phase DT50 was considered.
**The geometric mean value for its isomer should be considered for risk assessment purposes.

Table 2.2.2-3: DT_{50} values for soil metabolites

Metabolite	DT50 (days)	DT90 (days)	DT50 at 12°C (days)
4'-OH-c-*S-2703*	2.59	8.6	4.9
	11.9	39.7	22.6
	5.8	19.3	11.0
	35.1	117	66.6
Geometric mean			16.9
PBacid	0.287	0.954	0.5
	77.8	259	148
	43.9	146	83.3
	77.5	257	147
Geometric mean			30.85

Adsorption desorption study: The adsorption of cyphenothrin was determined by the HPLC method OECD guideline 121:

log Koc = 5.58 which is equal to Koc = 380189 (peak 1)

log Koc = 5.79 which is equal to Koc = 616595 (peak 2)

(Cyphenothrin is a racemic mixture and is detected as a double peak).

Koc values have been estimated for cyphenothrin's major soil metabolites using EPIWEB 4.1 (KOCWIN 2.1) model, based on their SMILES structures.

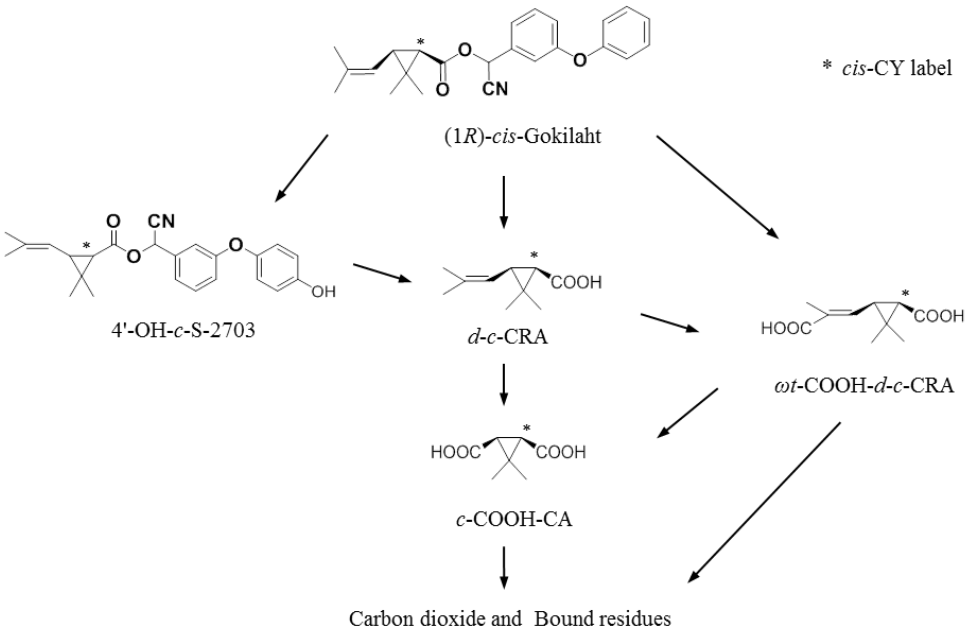
Table **2.2.2-4**: Estimated Koc (KOCWIN 2.1) for soil metabolites

Metabolite	Koc (MCI method) (L/kg)
4'-OH-c-S-2703	1.024E+5
Nitro derivative of 4'-OH-c-S-2703	1.62E+5
Ωt-COOH-d-c-CRA	217.8
PBacid	59.47

Aerobic aquatic degradation: Two water/sediment systems have been considered for the aerobic degradation in water/sediment systems. Cyphenothrin was radiolabelled in two positions in cyclopropyl ring (both *trans* and *cis*) and in phenyl ring (*trans*). The temperature was maintained at a range of 18-22^{0}C, under dark conditions. Six major metabolites have been identified in both tested systems considering both of the radiolabelled positions of *cis* and *trans* cyphenothrin isomers. Further details regarding maximum occurrence of the metabolites in the two systems and DT_{50} values for cyphenothrin and its metabolites are presented in the following tables.

Figure 2: Proposed degradation pathway for [^{14}C]cyphenothrin in water / sediment systems under aerobic conditions.

(1*R*)-*cis*-*Gokilaht (CY label)*



(1*R*)-*trans*-Gokilaht *(PH label and CY label)*

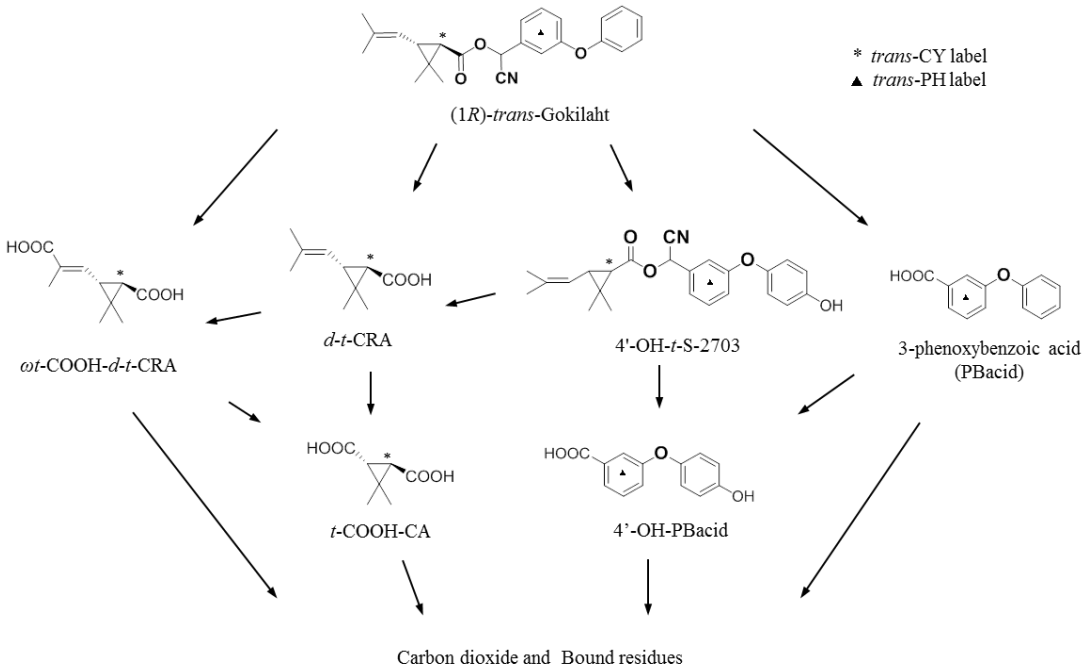


Table 2.2.2-5: Major metabolites chemical structures

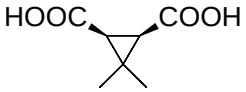
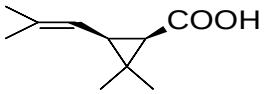
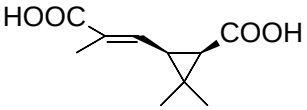
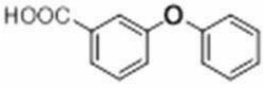
Code / Name	Chemical structure
c-COOH-CA	
d-c-CRA	
t-COOH-CA	
d-t-CRA	
ωt-COOH-d-c-CRA	
PBacid	

Table 2.2.2-6: Major metabolites observed in two water-sediment systems

Code / Name	Max occurrence %			Precursor
	Whole system	Water	Sediment	
c-COOH-CA	13.7	5.1 (end of study)	8.6 (end of study)	*cis*-CY
d-*c*-CRA	34.4	17.3	28.6	*cis*-CY
t-COOH-CA	46.5	39.9	19.9	*trans*-CY
d-*t*-CRA	56.3	26.4	36.2	*trans*-CY
ωt-COOH-*d*-*c*-CRA	16.3	11.5	7.8	*cis*-CY
PBacid	60.9	29.8	31.9	*trans*-PH

Table 2.2.2-7: DT_{50} and DT_{90} results for the water/sediment total system at 12^0C

System	Label	DT_{50} (days)	DT_{50} (days) 12^0C*
Calwich Abbey	*c*-CY	0.7	1.3
	t-CY	0.4	0.8
	t-PH	0.7	1.3
SwissLake	*c*-CY	7.2	13.7
	t-CY	0.9	1.7
	t-PH	1.4	2.7

*Worst case DT50 should be considered for risk assessment purposes for each isomer.

Table 2.2.2-8: DT_{50} and DT_{90} results for the water/sediment total system at 12^0C

System	Label	DT_{50} (days)	DT_{50} (days) 12^0C
Calwich Abbey	*c*-CY	36.7	69.6
	t-CY	5.7	10.8
	t-PH	6.8	12.9
SwissLake	*c*-CY	35.4	67.1
	t-CY	14.1	26.7
	t-PH	6.5	12.3

*Worst case DT50 should be considered for risk assessment purposes for each isomer.

Table 2.2.2-9: Summary of $DT_{50/90}$ values for major metabolites

Metabolite	DT_{50} (days)	DT_{90} (days)	DT_{50} at 12^0C (days)
d-*c*-CRA	18.1	60.2	34.3
	27.9	92.8	52.9
d-*t*-CRA	18.9	62.8	35.8

Metabolite	DT_{50} (days)	DT_{90} (days)	DT_{50} at 12^0C (days)
	11.7	38.7	22.2
c-COOH-CA	Not calculated	Not calculated	Not calculated
t-COOH-CA	27.6	91.6	52.3
	53.5	178	101
ωt-COOH-*d*-*c*-CRA	14.7	48.7	27.9
	12.5	41.5	23.7
PBacid	28.6	94.9	54.2
	60.1	200	114

Bioaccumulation: The log octanol:water partition coefficients of cyphenothrin (5.79-6.09; measured) and its metabolites 4'OH-c-S-2703 (6.01; predicted *via* QSAR analysis), nitro derivative of 4'-OH-*c*-S-2703 (5.56 – 6.40 predicted *via* QSAR analysis), *d*-*t*-CRA / *d*-*c*-CRA (3.49; predicted *via* QSAR analysis) and PBacid (3.93; predicted *via* QSAR analysis) are above the trigger of 3 suggesting that these substances may have significant potential for bioconcentration in both aquatic and terrestrial biota, with the possibility of bioaccumulation leading to secondary poisoning.

The aquatic bioaccumulation potential of cyphenothrin was experimentally investigated using the bluegill sunfish (*Lepomis macrochirus*). The kinetic and steady-state BCF values in whole fish were calculated to be 894.9 and 618 L/kg, respectively. The bioaccumulation potential of cyphenothrin in terrestrial organisms was predicted by using the relationship of [redacted](1998) since no experimentally derived earthworm bioconcentration data were available. The earthworm bioconcentration factor ($BCF_{earthworm}$) was estimated to be 14764 mg/kg.

As regards metabolites 4'OH-c-S-2703, nitro derivative of 4'-OH-*c*-S-2703, *d*-*t*-CRA / *d*-*c*-CRA and PBacid, their bioaccumulation potential in both aquatic (fish) and terrestrial (earthworms) organisms was predicted by using the equations developed by [redacted] et al. (1979) and [redacted](1998), respectively. The fish BCF values for the aquatic metabolites *d*-*t*-CRA / *d*-*c*-CRA and PBacid were estimated to be 185 and 437 L/kg, respectively, while the earthworm BCF for the soil metabolites 4'OH-*c*-S-2703, nitro derivative of 4'-OH-*c*-S-2703, and PBacid were estimated to be 12280, 12280 and 103 mg/kg, respectively.

Effects assessment

The ecotoxicological properties of the active substance cyphenothrin were investigated in acute and long-term toxicity studies performed with representative species of non-target organisms inhabiting the aquatic environment. In case of sediment and soil compartments, due to the lack of measured toxicity data, the effects assessment was based on predicted toxicity data derived from standardized EU agreed equations (i.e. Equilibrium Partitioning Method).

The ecotoxicological properties of the major metabolites of cyphenothrin were assessed on the basis of appropriate QSAR analyses. For the major metabolites t-COOH-CA and PBacid (3-Phenoxybenzoic acid), in addition to the estimated toxicity values, measured aquatic toxicity data were available. Where necessary, worst-case assumptions based on the available ecotoxicity data for the parent compound were employed.

It is noted that the effects assessment (in line with the exposure assessment) of major metabolites has been conducted without consideration of precursor isomers of the parent compound. Thus, *d*-*t*-CRA and *d*-*c*-CRA as well as *t*-COOH-CA and *c*-COOH-CA have been considered as one and the same substance, respectively.

Effects assessment for the aquatic compartment

Effects on aquatic organisms

The toxicity of cyphenothrin to aquatic organisms was investigated in acute and chronic toxicity tests with fish and aquatic invertebrates as well as a toxicity test on inhibitory effects on algae growth. The toxicity of major metabolites to aquatic organisms was investigated mainly via QSAR analysis. For the major metabolites t-COOH-CA and PBacid (3-Phenoxybenzoic acid), in addition to the estimated toxicity values, measured data on their acute toxicity to fish, Daphnia and algae were submitted.

The available data demonstrated that cyphenothrin is highly toxic to aquatic organisms under both acute and long-term exposure conditions. The acute effect endpoints calculated for rainbow trout *Salmo gairdneri* (96-hour LC_{50} 0.34 µg a.s./L) and the cladoceran freshwater flea *Daphnia magna* (48-hour EC_{50} 0.43 µg a.s./L) were below 1 µg/L while the growth rate-related acute effect endpoint (72-hour E_rC_{50}) for the green algae *Pseudokirchneriella subcapitata* was calculated to be greater than 14 µg a.s./L. The long-term effect endpoints calculated for fathead minnow *Pimephales promelas* (NOEC 0.54 µg a.s./L) and the cladoceran freshwater flea *Daphnia magna* (NOEC 0.081 µg a.s./L) were below 1 µg/L and 0.1 µg/L, respectively, while the growth rate-related chronic effect endpoint (72-hour NOE_rC) for the green algae *Pseudokirchneriella subcapitata* was calculated to be 5 µg a.s./L. Based on the available acute and chronic toxicity data, cyphenothrin is characterized as very toxic to aquatic life with long-lasting effects.

The $PNEC_{aquatic}$ for cyphenothrin, i.e. 0.0081 µg /L **=** 8.1 x 10^{-6} mg/L, was derived by applying an assessment factor of 10 to the lowest available NOEC of 0.081 µg a.s./L for *Daphnia magna*. It is acknowledged that the most sensitive species tested under acute exposure conditions was the rainbow trout S*almo gairdneri* while the available fish long-term toxicity study was conducted with fathead minnow *Pimephales promelas*. However, taking into account that the lowest long-term NOEC was calculated for *Daphnia magna* and the acute toxicity endpoints for fish (96-hour LC_{50} 0.34 µg/L) and *Daphnia magna* (48-hour EC_{50} 0.43 µg/L) are not significantly different from each other (i.e. the sensitivity difference is less than 10), the eCA's considers that application of an assessment factor of 10 to the lowest NOEC of 0.081 µg/L for *Daphnia magna* would be sufficiently protective for the aquatic ecosystem.

Regarding the four major aquatic metabolites of cyphenothrin, i.e. *t*-COOH-CA / *c*-COOH-CA, *d-t*-CRA / *d-c*-CRA, *ωt*-COOH-*d-c*-CRA, PBacid, limited testing toxicity data were available to assess their toxicity to aquatic organisms. Acute toxicity data on fish, Daphnia and algae from laboratory tests were available only for metabolites *t*-COOH-CA / *c*-COOH-CA and PBacid. The acute toxicity of *t*-COOH-CA / *c*-COOH-CA to fathead minnow (*Pimephales promelas*), *Daphnia magna* and *Pseudokirchneriella subcapitata* was calculated to be >94, >92 and 75 (based on growth rate) mg/L, respectively. The acute toxicity of PBacid to rainbow trout (*Oncorhynchus mykiss*), *Daphnia magna* and *Selenastrum capricornutum* was calculated to be 14.3, 35.4 and 51.92 (based on growth rate) mg/L, respectively. These results indicate that both metabolites are of relatively low acute toxicity to aquatic organisms particularly in relation to the parent compound. The lowest acute toxicity endpoints of 75 mg/L and 14.3 mg/ were used to derive the $PNEC_{water}$ values of 0.075 and 0.0143 mg/L for *t*-COOH-CA / *c*-COOH-CA and PBacid, respectively, by applying an assessment factor of 1000. For metabolites *d-t*-CRA / *d-c*-CRA and *ωt*-COOH-*d-c*-CRA no testing toxicity data were available but QSAR predictions (EpiSuite ECOSAR, version 1.11) of their aquatic toxicity were provided by the applicant. Given the uncertainty of the estimated via QSAR analysis $L(E)C_{50}$ values and taking into account the structure of these metabolites and the likely impact of structural changes relative to the parent compound on their toxicity, it was considered appropriate to assume that their aquatic toxicity is equal to that of the parent cyphenothrin (please refer to Doc IIA, section 4.2.1.3 for further details). Thus, the $PNEC_{water}$ of 0.0081 µg a.s./L calculated for cyphenothrin was also used to characterize the risk to aquatic organisms

from these metabolites. It is acknowledged that this approach is potentially conservative but it is considered reasonable based on the reliability of the available information.

Effects on sediment-dwelling organisms

No tests investigated the toxicity of cyphenothrin or its major metabolites to sediment-dwelling organisms were provided.

In accordance with ECHA Guidance on the BPR (Volume IV, Part B – Risk Assessment (active substance), Version 1.0, April 2015), the $PNEC_{sed}$ for cyphenothrin and the metabolites *t*-COOH-CA / *c*-COOH-CA and PBacid for which testing aquatic toxicity data were available was derived by taking into account the $PNEC_{water}$ for aquatic organisms and the sediment/water partitioning coefficient. In order to account for the high log K_{OW} value (>5) of cyphenothrin, an additional factor of 10 was applied to the $PNEC_{sed}$. The $PNEC_{sed}$ values for cyphenothrin, *t*-COOH-CA / *c*-COOH-CA and PBacid were calculated to be 0.0067, 0.0623 and 0.0789 mg/kg wwt, respectively.

For *d*-*t*-CRA / *d*-*c*-CRA and *ωt*-COOH-*d*-*c*-CRA, for which no testing aquatic toxicity data were available, the $PNEC_{sed}$ for the parent compound was used to characterise the sensitivity of sediment-dwelling organisms to these metabolites.

Effects on STP microorganisms

Cyphenothrin had no significant inhibitory effects on the respiration rate of activated sludge (representing combined carbonaceous and nitrogenous oxidation processes) up to and including the highest test concentration of 100 mg a.s./L. Taking into that this concentration exceeds the water solubility of cyphenothrin (0.0132 mg/L at 20^0C; Doc IIA, Table 1.3-1), the PNEC for STP microorganisms was set equal to the water solubility value of 0.0132 mg/L.

Effects on terrestrial organisms

Effects on soil organisms

No tests investigated the toxicity of cyphenothrin or its major metabolites to soil-dwelling organisms were provided.

In accordance with ECHA Guidance on the BPR (Volume IV, Part B – Risk Assessment (active substance), Version 1.0, April 2015), the $PNEC_{soil}$ for cyphenothrin and the soil metabolite PBacid for which testing aquatic toxicity data were available was derived by taking into account the $PNEC_{water}$ for aquatic organisms and the soil/water partitioning coefficient. In order to account for the high log K_{OW} value (>5) of cyphenothrin, an additional factor of 10 was applied to the $PNEC_{soil}$. The $PNEC_{soil}$ values for cyphenothrin and PBacid were calculated to be 0.0054 and 0.0550 mg/kg wwt, respectively.

For 4'OH-*c*-S-2703 and *ωt*-COOH-*d*-*c*-CRA, for which no testing aquatic toxicity data were available, the $PNEC_{soil}$ for the parent compound was used to characterise the sensitivity of soil-dwelling organisms to these metabolites.

Effects on other terrestrial non-target organisms

No studies investigating the effects of cyphenothrin on bees and other beneficial arthropods were submitted by the applicant. However, taking into account the intended uses of formulated cyphenothrin in PT18 indoor applications, no exposure of non-target arthropods is expected and the associated risk was considered to be acceptable.

Further, no avian toxicity data on cyphenothrin were provided. Thus, the risk assessment of secondary poisoning via the terrestrial and aquatic food chain was based on the available

mammalian long-term toxicity endpoints. The $PNEC_{mammal, oral}$, i.e. 1.33 mg a.s./kg food, was derived by applying an assessment factor of 90 to the lowest oral NOAEL of 3 mg/kg bw/day from the repeated-dose toxicity study in dogs ([redacted] et al., 1987; III-A.6.4.1/02).

A summary of the estimated PNEC values for the parent compound cyphenothrin and major metabolites is provided in table 2.2.2-10.

Table 2.2.2-10: Summmary of PNEC values for cyphenothrin and major metabolites

Substance	PNEC values for environmental compartments under concern				
	Surface water [$PNEC_{aquatic}$ (mg/L)]	Sediment [$PNEC_{sediment}$ (mg/kg wwt)]	STP microorganisms [$PNEC_{STP(micro-organisms)}$ (mg/L)]	Soil [$PNEC_{soil}$ (mg/kg soil wwt)]	Mammals [$PNEC_{oral, mammals}$ (mg/kg diet)]
Cyphenothrin (parent)	8.1×10^{-6}	0.0067	0.0132	5.4×10^{-3}	1.33
4'OH-*c*-S-2703	Not relevant	Not relevant	Not relevant	5.4×10^{-3} [1]	1.33 [1]
***d-t*-CRA / *d-c*-CRA**	8.1×10^{-6} [1]	0.0067 [1]	Not relevant	Not relevant	1.33 [1]
***ωt*-COOH-*d-c*-CRA**	8.1×10^{-6} [1]	0.0067 [1]	Not relevant	5.4×10^{-3} [1]	Not relevant
***t*-COOH-CA / *c*-COOH-CA**	0.075	0.0623	Not relevant	Not relevant	Not relevant
PBacid	0.0143	0.0789	Not relevant	0.0550	1.33 [1]
Nitro derivative 4'OH-c-S-2703	Not relevant	Not relevant	Not relevant	5.4×10^{-3} [1]	1.33 [1]

[1] No relevant toxicity data were available; as a worst-case approach, cyphenothrin metabolites have been considered to be as toxic to the respective non-target organisms as the parent compound

Exposure assessment

The environmental exposure was assessed using all the relevant information. All the assumptions and equations used were taken from the submitted studies and the OECD Task Force Documents, the Emission Scenario Document (ESD) for Insecticides, Acaricides and Products to control arthropods (PT 18) for household and professional use, the Technical Guidance Document on Risk Assessment (TGD, Part II; EC, 2003) and the more recent versions of TAB (June, 2016 and August, 2017).

Separate environmental exposure assessments were conducted for the two representative cyphenothrin-containing products, i.e. Gokilaht 5EC and Pesguard LG OBA.

The following scenarios have been assessed for the two representative products (Gokilaht 5EC and Pesguard LG OBA).

Formulation	Scenarios	Application rate (g cyphenothrin/m^2)
Gokilaht 5EC	Indoor general surface treatment by professionals once per day (F_{sim}=0.0552) using low	0.1**

	pressure spray equipment with hydraulic nozzles.	
	Indoor general surface treatment by professionals using low pressure handheld spray equipment with hydraulic nozzles considering 1 or 2 applications per year (F_{sim}=0.00204).	
	Indoor spraying applications in cracks and crevices by professionals using hand held aerosol sprayer, considering 1 or 2 applications per year. (F_{sim}=0.00204).	
Pesguard LG OBA	Indoor spraying applications in cracks and crevices by professionals using hand held ready-touse aerosol sprayer, considering it's applied once per month. (F_{sim}=0.0139)*.	0.654
	Indoor spraying applications in cracks and crevices by professionals using hand held ready-touse aerosol sprayer, considering it's applied once per month. (F_{sim}=0.0139)	0.02***

*This scenario is presented only for consistency purposes, since the newest lower application rate (0.02 g a.s./m^2) should only be considered.
**Rounded value of the initially proposed application rate of 0.0625 g a.i./m^2.
*** Rounded value of the initially proposed application rate of 0.0198 g a.i./m^2.

Gokilaht 5EC is formulated as an emulsifiable concentrate (EC), containing 5% w/v cyphenothrin and is intended for indoor use by a PCO (Pest Control Operator) for remedial treatments in buildings (private housing, public buildings, etc.). Gokilaht 5EC is intended to be applied with hand held spray equipment with hydraulic nozzles (e.g. knapsack, 1-3 bars) by professional users only. According to the proposed use pattern, local scale environmental emissions were considered to be the worst case scenario of predicted environmental concentrations. Releases at any life cycle stage of substance were considered in the exposure assessment. The direct and indirect routes of potential environmental exposure following the intended use of Gokilaht 5EC are summarised in the following table.

Table 2.2.2-11: Environmental compartments predicted to be exposed during the use of Gokilaht 5 EC.

Use scenario	**Environmental compartments of concern**						
	Air	STP	Surface water	Sediment	Soil	Groundwater	Biota
Indoor treatment	(+)	++	+	+	+	+	(+)

++ Compartment directly exposed
+ Compartment indirectly exposed
(+) Compartment potentially exposed

Pesguard LG OBA is a hand held Oil Based ready-to-use aerosol. The canister contains 0.3 % w/w cyphenothrin and 0.1 % w/w imiprothrin as active substances. Pesguard LG OBA is intented for indoor use for spot, crack and crevice treatment by professional operators. According to the proposed use pattern, two applications with an interval of 4 weeks are foreseen. The direct and indirect routes of potential environmental exposure following the intended use of Pesguard LG OBA are summarised in the following table.

Table 2.2.2-12: Environmental compartments predicted to be exposed during the use of Pesguard LG OBA

Use scenario	Environmental compartments of concern						
	Air	STP	Surface water	Sediment	Soil	Groundwater	Biota
Indoor treatment	(+)	++	+	+	+	+	(+)

++ Compartment directly exposed
+ Compartment indirectly exposed
(+) Compartment potentially exposed

For a detailed presentation of the results and the used scenarios please refer to the corresponding sections (Section 3.3) of Document IIB.

Risk characterization

The environmental risk characterisation for the active substance cyphenothrin and its major metabolites was based on the proposed use pattern of the biocidal products Gokilaht 5EC, an emulsifiable concentrate containing 5% w/w (50 g/L) cyphenothrin, and Pesguard LG OBA, an oil based aerosol containing 0.3% w/w (3 g/kg) cyphenothrin and 0.1% w/w (0.1 g/kg) imiprothrin. Current environmental risk assessment is performed in support of the evaluation of the active substance cyphenothrin for inclusion in Annex I of the BPR, other active substances contained in the representative biocidal products, i.e. imiprothrin in Pesguard LG OBA, have not been further considered.

Using the Predicted No Effect Concentrations (PNEC) estimated in Document IIA (Section 4.3) and the Predicted Environmental Concentrations estimated in Document IIB (Section 3.3), PEC/PNEC ratios were calculated in order to assess the environmental risk associated with the intended use of formulated cyphenothrin. Separate PEC/PNEC ratios were calculated for each representative product. PEC/PNEC ratios less than 1 indicated no unacceptable risk, while PEC/PNEC ratios greater than 1 indicated an unacceptable risk to the environmental compartment under concern.

The risk characterization for the aquatic compartment (including surface water organisms, sediment-dwelling organisms and STP microorganisms) and the terrestrial compartment (including soil organisms and top predators exposed via the food chain) was conducted on the basis of the respective PEC/PNEC calculations. The risk to the groundwater has been assessed via comparison of the calculated $PEC_{goundwater}$ values with the threshold concentration of 0.1 µg/L stipulated under Drinking Water Directive.

As the current environmental risk assessment is performed in support of the evaluation of the active substance cyphenothrin for inclusion in Annex I of the BPR, other active substances contained in the representative biocidal products, i.e. imiprothrin in Pesguard LG OBA, were not evaluated. Information on the ecotoxicological properties and environmental fate and behaviour of the active substance imiprothrin can be found in the respective assessment report.

The risk characterization (PEC/PNEC) ratios calculated for the environmental compartments under concern considering the intended indoor uses of formulated cyphenothrin as Gokilaht 5EC and Pesguard LG OBA are presented in the following tables (2.2.2.5-1 and 2.2.2.5-2).

Table 2.2.2.5-1: Summary of PEC/PNEC ratios for the biocidal product Gokilaht 5EC

Scenario/Compartment		PEC/PNEC								
		Cyphenothrin (parent)			4'OH-*c*-S-2703	Nitro derivative 4'OH-c-S-2703	*d-t*-CRA / *d-c*-CRA	*ωt*-COOH-*d-c*-CRA	*t*-COOH-CA / *c*-COOH-CA	PBacid
		trans	cis	total						
STP microorganisms	F_{sim1}*	**1.6667**	0.5455	**2.21**	not relevant	not relevant	not relevant	not relevant	not relevant	not relevant
	F_{sim2}**	0.0606	0.0205	0.0811						
	C&C***	0.0025	0.0008	0.0033						
Surface water – aquatic organisms	F_{sim1}*	**148.15**	**50.62**	**199**	not relevant	not relevant	**51.85**	**17.28**	4.3E-03	3.99E-02
	F_{sim2}**	**5.80**	**1.98**	**7.78**			**1.98**	0.67	1.6E-04	1.54E-03
	C&C***	0.23	0.08	0.31			0.08	0.03	6.7E-06	6.15E-05
Sediment-dwelling organisms	F_{sim1}*	**2000**	**672**	**2672**	not relevant	not relevant	**672**	**224**	**56**	**79**
	F_{sim2}**	**74.6**	**25.4**	**100**			**25**	**8.96**	**2.09**	**2.92**
	C&C***	**3.0**	**1.12**	**4.1**			**1.06**	0.36	0.09	0.12
Soil organisms	F_{sim1}*	**110**	**64**	**175**	**25**	**21**	not relevant	**9.8**	not relevant	**1.964**
	F_{sim2}**	**3.68**	**2.39**	**6.08**	0.94	0.74		0.368		0.074
	C&C***	0.17	0.10	0.27	0.04	0.03		0.015		0.003
Fish-eating mammals	F_{sim1}*	0.804	0.28	**1.08**	not relevant	not relevant	5.9E-02	not relevant	not relevant	1.9E-01
	F_{sim2}**	0.03	0.01	4.2E-2			2.3E-03			7.2E-03
	C&C***	0.9E-03	3.1E-04	1.28E-3			6.4E-05			2.0E-04
Earthworm-eating mammals	F_{sim1}*	2.0E-01	3.2E-01	5.20E-1	0.241	0.602	not relevant	not relevant	not relevant	**1.8**
	F_{sim2}**	6.9E-03	1.2E-02	1.89E-2	0.009	0.023				5.94E-02
	C&C***	0.98	0.24	4.4E-4	2.7E-4	8.8E-4				2.11E-03

*General surface treatment, Fsim=0.0552
**General surface treatment, Fsim=0.00204
***Cracks and crevices, Fsim=0.00204

Based on the PEC/PNEC calculations summarized in table 2.2.2.5-1 the following conclusions were drawn regarding the risks posed to non-target environmental organisms following the intended use of Gokilaht 5EC:

Aquatic compartment (including STP, surface water and sediment)

The risk to STP microorganisms was calculated to be acceptable when a usage restriction of 1-2 applications per year (F_{sim2}) by surface treatment is considered. The risk to aquatic and sediment-dwelling organisms was calculated to be unacceptable for both surface treatment scenarios ($F_{sim1,}$ F_{sim2}).

The risk to STP microorganisms and aquatic organisms was calculated to be acceptable when the product is applied to cracks and crevices. The risk to sediment-dwelling organisms was calculated to be unacceptable (for parent compound and *d-t*-CRA / *d-c*-CRA metabolite), even when the product is applied to cracks and crevices.

Terrestrial compartment (including soil, groundwater, fish- and earthworm-eating predators)

The risk to soil organisms was calculated to be unacceptable for both surface treatment scenarios ($F_{sim1,}$ F_{sim2}). The risk to fish-eating and earthworm-eating mammals was calculated to be acceptable when a usage restriction of 1-2 applications per year (F_{sim2}) by surface treatment is considered. Regarding groundwater, the risk has been calculated to be unacceptable when the F_{sim1} is considered. When 1-2 applications per year are proposed, the risk for groundwater contamination has been identified to be acceptable.

The risk to soil organisms, fish-eating and earthworm-eating mammals and groundwater was calculated to be acceptable when the product is applied to cracks and crevices.

Table 2.2.2.5-2: Summary of PEC/PNEC ratios for the biocidal product Pesguard LG OBA

Scenario/Compartment		PEC/PNEC								
		Cyphenothrin (parent)			4'OH-*c*-S-2703	Nitro derivative 4'OH-c-S-2703	*d*-*t*-CRA / *d*-*c*-CRA	*ωt*-COOH-*d*-*c*-CRA	*t*-COOH-CA / *c*-COOH-CA	PBacid
		trans	cis	Total						
STP microorganisms	Ap. dose 1*	0.0082	0.0027	1.09E-2	not relevant	not relevant	not relevant	not relevant	not relevant	not relevant
	Ap. dose 2**	0.0003	0.0001	4E-3						
Surface water – aquatic organisms	Ap. dose 1*	0.77	0.26	**1.02**	not relevant	not relevant	0.26	0.09	2.1E-05	2.03E-04
	Ap. dose 2**	0.02	0.01	0.03			7.90E-03	2.72E-03	6.5E-07	6.15E-06
Sediment-dwelling organisms	Ap. dose 1*	**10**	**3.28**	**13.28**	not relevant	not relevant	**3.3**	**1.15**	0.32	0.38
	Ap. dose 2**	0.28	0.09	0.38			0.1	0.04	0.008	0.01
Soil organisms	Ap. dose 1*	0.55	0.31	0.87	0.07	0.10	not relevant	0.049	not relevant	0.007
	Ap. dose 2**	0.02	0.01	0.03	2.2E-03	3.31E-03		1.5E-03		2.2E-04
Fish-eating mammals	Ap. dose 1*	7.5E-03	1.4E-03	8.9E-3	not relevant	not relevant	2.9E-04	not relevant	not relevant	9.8E-04
	Ap. dose 2**	1.3E-04	4.2E-05	1.72E-4			9.0E-06			2.9E-05
Earthworm-eating mammals	Ap. dose 1*	1.1E-03	1.6E-03	2.6E-03	1.33E-02	3.01E-03	not relevant	not relevant	not relevant	7.52E-03
	Ap. dose 2**	4.1E-05	4.8E-05	9.0E-05	3.76E-05	9.02E-05				2.41E-04

*0.654 g a.s./m² (cracks and crevices). This scenario is presented only for consistency purposes.

**0.02 g a.s./ m²(cracks and crevices)

Based on the PEC/PNEC calculations summarized in table 2.2.2.5-2, the following conclusions were drawn regarding the risks posed to non-target environmental organisms following the intended use of Pesguard LG OBA:

Aquatic compartment (including STP, surface water and sediment)

The risk to STP microorganisms was calculated to be acceptable. The risk to aquatic organisms (surface water) from the parent compound has been calculated to be acceptable only when a reduced application rate ($2x10^{-5}$ kg/m^2) is considered. The risk to aquatic organisms (surface water) from the relevant metabolites has been calculated to be acceptable at both application rates examined. The risk to sediment-dwelling organisms from the parent compound and its metabolites *d*-*t*-CRA / *d*-*c*-CRA and *ωt*-COOH-*d*-*c*-CRA has been calculated to be acceptable only when a reduced application rate ($2x10^{-5}$ kg/m^2) is considered. For metabolites *t*-COOH-CA / *c*-COOH-CA and PBacid, the risk to sediment-swelling organisms has been calculated to be acceptable for both application rates examined. Overall, the risk to aquatic and sediment-dwelling non-target organisms following the intended use of the biocidal product Pesguard LG OBA has been calculated to be acceptable only when a reduced application rate ($2x10^{-5}$ kg/m^2) is considered

Terrestrial compartment (including soil, groundwater, fish- and earthworm-eating predators)

The risk to soil organisms has been calculated to be acceptable at both application rates examined. Regarding groundwater, the risk has been calculated to be acceptable for the parent compound cyphenothrin (at both application rates examined) and its soil metabolites ωt-COOH-d-c-CRA and PBacid (following reduced dose application). The risk to fish- and earthworm- eating predators has been calculated to be acceptable for the parent compound and relevant metabolites (4'OH-c-S-2703, d-t-CRA / d-c-CRA, PBacid) at both application rates examined. Overall, the risk to terrestrial compartment is acceptable only following application of formulated cyphenothrin as Pesguard LG OBA at the reduced application rate of $2x10^{-5}$ kg a.s./m^2.

Based on the PEC/PNEC calculations presented in tables 2.2.2.5-1 and 2.2.2.5-2, and the risk assessment conducted for the groundwater, it is concluded that the overall risk to the environement (non-target organisms and ground water) is acceptable only following application of formulated cyphenothrin as Pesguard LG OBA at the reduced application rate of $2x10^{-5}$ kg a.s./m^2.

2.2.3. PBT and POP assessment

PBT assessment

The PBT assessment presented below covers the active substance cyphenothrin and the major soil and aquatic/sediment metabolites.

Persistence criteria (P)

Cyphenothrin (parent)

Cyphenothrin was found to be not biodegradable under the test conditions within 28 days. Furthermore, was shown to be hydrolytically stable at pH 4. The half-life of cyphenothrin in pH 7 buffer at 25^0C was calculated by extrapolation. The half-life at 25^0C was calculated to be 112 days.
An aerobic soil degradation study of Cyphenothrin has been performed on four soils considering. Both cis- and trans- isomers have been considered in the study (3 radio-labelled positions). As agreed in the ENV WG-II 2017, the P assessment is separately performed for

cis- and trans- isomers.

Table 2.2.3-1: Normalised soil DT_{50} values for *cis* and *trans* cyphenothrin.

***cis*-CY**		***trans*-PH**		***trans*-CY**	
Soil	**DT50 days**	**Soil**	**DT50 days**	**Soil**	**DT50 days**
Empingham, UK Loam	13.2	**Empinhgham, UK** Loam	12.8		
Ingleby, UK Sand	1000	**Ingleby, UK** Sand	30.3		
Barrow, UK Sandy loam	328.7	**Barrow, UK** Sandy loam	24.1	**Barrow, UK** Sandy loam	20.6
Brierlow, UK Loam soil	138.9	**Brierlow, UK** Loam soil	43.8		
Geomean	**156.7**	**Geomean**	25.3		**24.3**[1]

[1]Geometric mean calculated for *trans*-cyphenothrin (both PH and CY labeled).

Furthermore, data presented in Hiler, 2015 (Doc IIIA 7.1.2.2.2) regarding the behaviour of cyphenothrin in water/sediment systems show the following DT_{50} values in the whole systems.

Table 2.2.3-2: Normalised water/sediment DT_{50} values for *cis* and *trans* cyphenothrin.

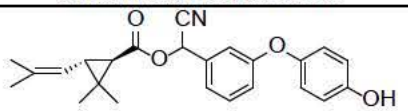
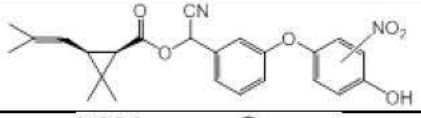
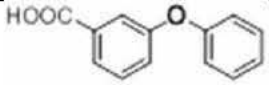
cis-CY		*trans*-PH		*trans*-CY	
System	**DT50 days**	**System**	**DT50 days**	**System**	**DT50 days**
Calwich Abbey	69.6	Calwich Abbey	12.9	Calwich Abbey	10.8
Swiss Lake	67.1	Swiss Lake	12.3	Swiss Lake	26.7

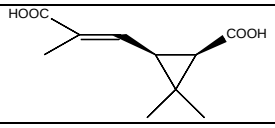
Based on the geometric mean DT_{50} value of 156.7 days in soil (12°C), the *cis* isomer of cyphenothrin fulfills **P** criterion. On the other hand, *trans*-cyphenothrin does not fulfil either P or vP criteria.

Metabolites identified in soil and water/sediment systems:

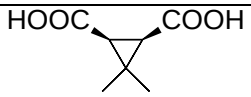
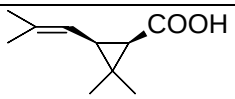
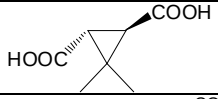
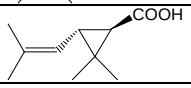
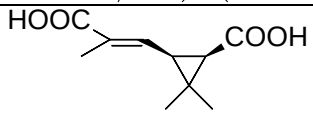
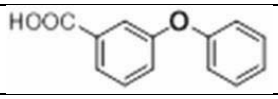
The following major metabolites have been identified in soil and water/sediment studies and are assessed for the P and vP criteria:

Table 2.2.3-3: Soil metabolites

Code	Chemical structure
4'-OH-*c*-S-2703	
nitro derivative of 4'-OH-*c*-S-2703	
PBacid	

Code	Chemical structure
ωt-COOH-*d*-*c*-CRA	

Metabolites in water/sediment

Code / Name	Chemical structure
c-COOH-CA	
d-c-CRA	
t-COOH-CA	
d-t-CRA	
ωt-COOH-d-c-CRA	
PBacid	

4'-OH-*c*-S-2703

The following DT_{50} values normalized to 12^0C have been derived from the aerobic soil study.

Metabolite	DT_{50} (days)	DT_{90} (days)	DT_{50} at 12^0C (days)
4'-OH-*c*-S-2703	2.59	8.6	4.9
	11.9	39.7	22.6
	5.8	19.3	11.0
	35.1	117	66.6
Geomean	-	-	**16.9**

Based on the normalized to 12^0C, geometric mean (n=4), DT_{50} value of 16.9 days in soil, 4'-OH-*c*-S-2703 is **not** considered to be persistent (P) or very persistent (vP).

nitro derivative of 4'-OH-*c*-S-2703:

A major metabolite, initially identified as "Met-59" was observed at a maximum of 8.3% of AR in one soil (Ingleby). No experimental DT50 could be calculated. The EPISuite output was compared to the PBT criteria as described in "Guidance on Information Requirements and Chemical Safety Assessment Chapter R.11: PBT/vPvB assessment, Version 2.0, November 2014".

R.11 criteria		Nitro 4'-OH-c-S-2703	Outcome
Biowin 2 (non-linear model prediction) and Biowin 3 (ultimate biodegradation time)	Does not biodegrade fast (probability < 0.5) and ultimate biodegradation timeframe prediction: ≥ months (value < 2.25 (to 2.75)	Biowin2: Probability = 0.9886 (biodegrades fast Biowin3: Probability = 1.9090 (months)	**No conclusion**

or			
Biowin 6 (MITI non-linear model prediction) and Biowin 3 (ultimate biodegradation time)	Does not biodegrade fast (probability < 0.5) and ultimate biodegradation timeframe prediction: ≥ months (value < 2.25 (to 2.75))	Biowin6: Probability = 0.0013 (does not biodegrade fast) Biowin3: Probability = 1.9090 (months)	**Potentially P**

Based on the results of Biowin 6 and 3, nitro derivative of 4'-OH-*c*-S-2703 should be considered as P substance.

PBacid

The following DT_{50} values normalized to 12^0C have been derived from the aerobic soil study.

Metabolite	DT_{50} (days)	DT_{90} (days)	DT_{50} at 12^0C (days)
PBacid	0.287	0.954	0.5
	77.8	259	148
	43.9	146	83.3
	77.5	257	147
Geomean	-	-	**30.9**

Furthermore, PBacid was also present in the two water/sediment systems. The normalized to 12^0C, DT_{50} values are presented below.

Metabolite	DT_{50} (days)	DT_{90} (days)	DT_{50} at 12^0C (days)
PBacid	28.6	94.9	54.2
	60.1	200	114

Based on the geometric mean DT_{50} value in soil and the highest DT_{50} value in the whole aquatic system, PBacid is not considered as P or vP substance in soil and sediment.

ωt-COOH-d-c-CRA

No DT_{50} soil is available for this metabolite since it was present only in one soil (Brierlow soil, *cis*-CY) reaching up 8.4% of applied radioactivity. However, the following DT_{50} values have been calculated for water/sediment systems.

Metabolite	DT_{50} (days)	DT_{90} (days)	DT_{50} at 12^0C (days)
ωt-COOH-d-c-CRA	14.7	48.7	27.9
	12.5	41.5	23.7

Furthermore, metabolite ωt-COOH-d-c-CRA seems to be highly water soluble (7317.7 mg/L, WATERNT v.1.01) and highly mobile (Koc 11.86 l/kg). Therefore, the half-lives for the whole system should be compared to the water criterion.

Based on the available information, *ωt*-COOH-d-c-CRA is not considered as P or vP substance.

d-c-CRA:

The following DT_{50} values have been calculated for water/sediment systems.

Metabolite	DT_{50} (days)	DT_{90} (days)	DT_{50} at 12°C (days)
d-c-CRA	18.1	60.2	34.3
	27.9	92.8	52.9

Whole system DT50 values are compared with freshwater trigger values, since d-c-CRA metabolite shows moderate to high water solubility and low soil adsorption, based on QSAR predictions (EPIsuite).
Based on the abovementioned DT_{50} values, *d*-*c*-CRA is considered as P substance.

t-COOH-CA

The following DT_{50} values have been calculated for water/sediment systems.

Metabolite	DT_{50} (days)	DT_{90} (days)	DT_{50} at 12°C (days)
t-COOH-CA	27.6	91.6	52.3
	53.5	178	101

Whole system DT50 values are compared with freshwater trigger values, since t-COOH-CA metabolite shows very high water solubility and low soil adsorption, based on QSAR predictions (EPIsuite). Based on the abovementioned DT_{50} values, *t*-COOH-CA is considered as vP substance.

c-COOH-CA

No DT_{50} values have been calculated for *c*-COOH-CA either for soil, or for water/sediment, instead, the results of the Biowin models 2 and 3, 3 and 6 have been compared in order to conclude on the persistency. Based on the following information *c*-COOH-CA is not considered as P or vP substance.

R.11 criteria		*c*-COOH-CA	Outcome
Biowin 2 (non-linear model prediction) and Biowin 3 (ultimate biodegradation time)	Does not biodegrade fast (probability < 0.5) and ultimate biodegradation timeframe prediction: ≥ months (value < 2.25 (to 2.75)	Biowin2: Probability = 0.5808 (biodegrades fast Biowin3: Probability = 3.3668 (days-weeks)	**Non P or vP**
or			
Biowin 6 (MITI non-linear model prediction) and Biowin 3 (ultimate biodegradation time)	Does not biodegrade fast (probability < 0.5) and ultimate biodegradation timeframe prediction: ≥ months (value < 2.25 (to 2.75))	Biowin6: Probability = 0.6006 (biodegrades fast) Biowin3: Probability = 3.3668 (days-weeks)	**Non P or vP**

d-t-CRA

The following DT_{50} values have been calculated for water/sediment systems.

Metabolite	DT_{50} (days)	DT_{90} (days)	DT_{50} at 12°C (days)
d-t-CRA	18.9	62.8	35.8
	11.7	38.7	22.2

Based on the abovementioned DT_{50} values, *d*-*t*-CRA is not considered as P or vP substance.

Conclusion on persistence (P) criterion:

Substance	Persistence (P)
Cyphenothrin (cis)	P
Cyphenothrin (trans)	Not P, not vP
4'OH-*c*-S-2703	not P, not vP
nitro derivative of 4'-OH-*c*-S-2703	P
d-*t*-CRA	not P, not vP
d-*c*-CRA	P
ωt-COOH-*d*-*c*-CRA	not P, not vP
t-COOH-CA	vP
c-COOH-CA	not P, not vP
PBacid	not P, not vP

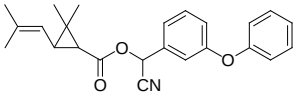
Bioaccumulation criteria (B)

The fish bioconcentration factor for the parent compound cyphenothrin was experimentally determined to be 894.9 L/kg (whole fish, kinetic) and 618 L/kg (whole fish, steady-state) (III-A7.4.2; [redacted]), e.g. lower than the both trigger values of 2000 and 5000 L/kg. Thus, nor B neither vB criterion was found to be fulfilled for cyphenothrin.

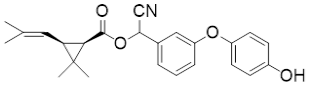
Regarding cyphenothrin metabolites, no testing data on their bioaccumulation potential were available. Therefore, based on the recommendations given in the ECHA Guidance on IR & CSA (Part V: PBT/vPvB assessment, Version 2.0, November 2014) their QSAR estimated log P_{OW} values (Doc IIA, Section 4.1.3) were further considered to elucidate the B criterion. For all metabolites except 4'OH-*c*-S-2703 and nitro derivative of 4'-OH-*c*-S-2703, the QSAR estimated log P_{OW} values were below the trigger of 4.5 indicating that these metabolites (*d*-*t*-CRA / *d*-*c*-CRA, *ωt*-COOH-*d*-*c*-CRA, *t*-COOH-CA / *c*-COOH-CA, PBacid) do not fulfil the B or vB criterion. Regarding metabolites 4'OH-*c*-S-2703 (QSAR estimated log P_{OW} = 6.01) and nitro derivative of 4'-OH-*c*-S-2703 (QSAR estimated log P_{OW} = 5.56 – 6.40), the BCF_{fish} values measured for the parent compound were considered to decide on its aquatic bioaccumulation potential based on the following assumptions:

(i) similarity between the log P_{OW} values for the parent compound cyphenothrin (5.79 - 6.09) and the metabolites 4'OH-*c*-S-2703 (6.01) and nitro derivative of 4'-OH-*c*-S-2703 (5.56 – 6.40),

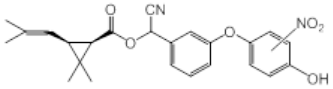
(ii) structural similarity between the parent compound cyphenothrin and the metabolites 4'OH-*c*-S-2703 and nitro derivative of 4'-OH-*c*-S-2703; the addition of one hydroxyl group directly connected to the benzene ring is not expected to have a significant impact on the overall bioaccumulation potential of metabolites 4'OH-c-S-2703 and nitro derivative 4'OH-c-S-2703 compared to the parent compound cyphenothrin. Furthermore, the addition of one nitro group to the benzene ring is not expected to have a significant impact on the bioaccumulation potential of the metabolite nitro derivative 4'OH-c-S-2703 compared to the metabolite 4'OH-c-S-2703.



cyphenothrin



4'OH-c-S-2703



nitro derivative 4'OH-c-S-2703

(iii) all possible efforts should be made to avoid further vertebrate testing (3R principle)

Based on the worst-case BCF (kinetic) of 894.9 L/kg for the parent compound, metabolites 4'OH-*c*-S-2703 and nitro derivative of 4'-OH-*c*-S-2703 are not considered to fulfil the B or vB criterion.

Toxicity criteria (T)

Cyphenothrin does not meet the criteria for classification as CMR. Nevertheless, there is other evidence of chronic toxicity, meeting the criteria for classification as STOT RE 1 according to the CLP regulation, indicating that the T criterion is fulfilled for cyphenothrin.

As regards long-term aquatic toxicity, the lowest endpoint (NOEC), i.e. 0.081 µg/L for the water flea *Daphnia magna* (Shaw, 2015; III-A 7.4.3.4), is below the trigger value of 0.01 mg/L indicating that T criterion is fulfilled for the parent compound.

Regarding cyphenothrin metabolites, no mammalian or long-term aquatic toxicity data were available. Thus, their T assessment was based on the available acute aquatic toxicity data, either derived from laboratory testing or QSAR analysis. The lowest experimentally derived L(E)C_{50}s for *t*-COOH-CA / *c*-COOH-CA (75 mg/L for green algae) and PBacid (14.3 mg/L for fish) were above the trigger value of 0.01 mg/L indicating that T criterion is not fulfilled for these metabolites. The same conclusion applies for metabolites *d*-*t*-CRA / *d*-*c*-CRA and *ωt*-COOH-*d*-*c*-CRA for which the lowest QSAR estimated L(E)C_{50}s were 42 mg/L (Daphnia) and 1200 mg/L (for algae), respectively. Regarding 4'OH-*c*-S-2703, the lowest QSAR estimated L(E)C_{50} is 0.0012 mg/L (Daphnia) indicating that this metabolite fulflls the T criterion. The same conclusion applies also for the metabolite nitro-derivative 4'OH-*c*-S-2703, for which the lowest QSAR estimated L(E)C_{50} is 0.00085 mg/L.

The PBT assessment for cyphenothrin and its major metabolites is summarized in the table below.

Table 2.2.3-4: Summary of PBT assessment

Substance	PBT properties		
	Persistence (P)	Bioaccumulation (B)	Toxicity (T)
Cyphenothrin (cis)	P	not B, not vB[1]	T[1]
Cyphenothrin (trans)	not P, not vP	not B, not vB[1]	T[1]
4'OH-*c*-S-2703	not P, not vP	not B, not vB	T
nitro derivative of 4'-OH-*c*-S-2703	P	not B, not vB	T
d-*t*-CRA	not P, not vP	not B, not vB	not T
d-*c*-CRA	P		
ωt-COOH-*d*-*c*-CRA	not P, not vP	not B, not vB	not T
t-COOH-CA	vP	not B, not vB	not T
c-COOH-CA	not P, not vP		
PBacid	not P, not vP	not B, not vB	not T

[1] The assessment was performed for Cyphenothrin as mixture of *cis* and *trans* isomers and not individually for each isomer.

POP assessment

The criteria for a substance being a persistent organic pollutant (POP) are 'P', 'B' and having the potential for long range transport. In addition, high toxicity can breach the 'B' criterion, in which case a substance will be a persistent organic pollutant if it is 'P', demonstrates the potential for long range transport, and is either 'B' or 'T'.

Cyphenothrin is not expected to be prone for long-range transport. With an an estimated atmospheric half-life of < 4 h (assuming a 12 h day and an OH radical concentration of 7 x 10^{11} mol OH^-/ cm^3 when estimated using the AOPWIN v 1.92 QSAR modelling tool) will not pose a possible risk for a long-range transport. This conclusion is further supported by the compound's very low vapour pressure (2.9 x 10^{-7} Pa at 25°C), low predicted Henry's Law constant plus limited environmental exposure from use patterns.

In conclusion, cyphenothrin does not meet the criteria for being a persistent organic pollutant.

3. EXCLUSION CRITERIA

3.1 EXCLUSION CRITERIA

3.1.1. Assessment of CMR properties

Criteria (BPR Article 5[1])	Assessment
Active substances which have been classified in accordance with Regulation (EC) No 1272/2008 as, or which meet the criteria to be classified as, carcinogen category 1A or 1B.	Cyphenothrin does not meet the criteria to be classified as, carcinogen category 1A or 1B.
Active substances which have been classified in accordance with Regulation (EC) No 272/2008 as, or which meet the criteria to be classified as, mutagen category 1A or 1B.	Cyphenothrin does not meet the criteria to be classified as, mutagen category 1A or 1B.
Active substances which have been classified in accordance with Regulation (EC) No 1272/2008 as, or which meet the criteria to be classified as, toxic for reproduction category 1A or 1B.	Cyphenothrin does not meet the criteria to be classified as, toxic for reproduction category 1A or 1B.

Conclusion on CMR properties	Cyphenothrin does not meet the criteria for classification as CMR.

3.1.2. Assessment on endocrine disrupting properties

Criteria (BPR Article 5)	Assessment
Active substances which, on the basis of the criteria specified pursuant to the first subparagraph of paragraph 3 are considered as having endocrine-disrupting properties that may cause adverse effects in humans.	The criteria are not yet published.
Pending the adoption of those Criteria[1], active substances that are classified in accordance with Regulation (EC) No 1272/2008 as, or meet the criteria to be classified as, carcinogen category 2 and toxic for reproduction category 2 and toxic for reproduction category 2[2].	Cyphenothrin does not meet the criteria to be classified as, carcinogen category 2 and toxic for reproduction category 2 and toxic for reproduction category 2.
Substances such as those that are classified in accordance with Regulation (EC) No 1272/2008 as, or that meet the criteria to be classified as, toxic for reproduction category 2 and that have toxic effects on the endocrine organs[3]	Cyphenothrin does not meet the criteria to be classified as, toxic for reproduction category 2 and that have toxic effects on the endocrine organs.
Active substances which are identified in accordance with Articles 57(f) and 59(1) of Regulation (EC) No 1907/2006 as having endocrine disrupting properties	Not relevant for BPR.

[1] This refers to the criteria mentioned in the 1st row
[2] These active substances shall be considered as having endocrine-disrupting properties
[3] These active substances may considered as having endocrine-disrupting properties

Conclusion on ED properties	Cyphenothrin does not fulfil the interim criteria specific in BPR and thus it is not considered as having endocrine-disrupting properties.

3.1.3. PBT assessment

Substance	PBT properties		
	Persistence (P)	Bioaccumulation (B)	Toxicity (T)
Cyphenothrin (cis)	P	not B, not vB[1]	T[1]
Cyphenothrin (trans)	non P or vP	not B, not vB[1]	T[1]
4'OH-*c*-S-2703	non P or vP	not B, not vB	T
nitro derivative of 4'-OH-*c*-S-2703	P	not B, not vB	T
d-*t*-CRA	non P or vP	not B, not vB	not T

Substance	PBT properties		
	Persistence (P)	**Bioaccumulation (B)**	**Toxicity (T)**
d-*c*-CRA	P		
ωt-COOH-*d*-*c*-CRA	non P or vP	not B, not vB	not T
t-COOH-CA	vP	not B, not vB	not T
c-COOH-CA	non P or vP		
PBacid	non P or vP	not B, not vB	not T

[1] The assessment was performed for Cyphenothrin as mixture of *cis*- and *trans*- isomers and not individually for each isomer.

For more details please refer to point 2.2.2.3.

Conclusion on PBT/vPvB properties	Based on the available data, cyphenothrin is considered as persistent (P) and toxic (T) substance.

3.2. SUBSTITUTION CRITERIA

Substitution criteria (BPR, Article 10)	**Assessment**
One of the exclusion criteria listed in Article 5(1) is met but AS may be approved in accordance with Article 5(2)	Cyphenothrin does not meet the criteria for classification as CMR, is not considered as having endocrine-disrupting properties and does not meet the criteria for being PBT or vPvB.
The criteria to be classified, in accordance with Regulation (EC) No 1272/2008, as a respiratory sensitiser is met	Cyphenothrin is not a respiratory sensitiser.
The acceptable daily intake, acute reference dose or acceptable operator exposure level, as appropriate, is significantly lower than those of the majority of approved active substances for the same product-type and use scenario	The reference values are in the same range as those of other pyrethroid insecticides.
Two of the criteria for being PBT in accordance with Annex XIII to Regulation (EC) No 1907/2006 are met	Cyphenothrin is considered as persistent (P) and toxic (T) substance.
There are reasons for concern linked to the nature of the critical effects which, in combination with the use patterns, amount to use that could still cause concern, such as high potential of risk to groundwater, even with very restrictive risk management measures	Not relevant
The AS contains a significant proportion of nonactive isomers or impurities.	Cyphenothrin is ≥ 92.0 % pure. All isomers are considered as part of the active substance.

Conclusion on substitution criteria	The substitution criteria in BPR Article 10(1)a-f are met.

4. ASSESSMENT OF LONG-RANGE ENVIRONMENTAL TRANSPORT AND IMPACT ON ENVIRONMENTAL COMPARTMENTS

The active substance or a degradation product is a persistent organic pollutant (POP) listed in Annex I of EC 850/2004	No
Assessment of long-range transport potential (LRTAP) • Vapour pressure <1000 Pa and • Half-life in air >2 days or • Monitoring data in remote area showing that the substance is found in remote regions or result of multimedia modelling	• Vapour pressure: 2.9 x 10^{-7} Pa at 25^{0}C • T1/2 in reaction with OH-radicals: 3.675 hrs • T1/2 in reaction with ozone: 38.378 min
The active substance or a degradation product is **vP/vB or T?**	Based on screening data, cyphenothrin is considered as persistent (P) and toxic (T).

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

4.1. Assessment of endocrine disruptor properties

No endocrine specific studies, e.g. *in vitro* or *in vivo* screening assays or *in vivo* confirmatory tests, were submitted to investigate the potential endocrine mode of action of cyphenothrin. Therefore, the assessment of potential endocrine disrupting activity of cyphenothrin is based on available mammalian toxicity data and available information and evidence from the scientific literature.

Standard mammalian toxicology studies with cyphenothrin such as repeated dose toxicity, long-term toxicity and carcinogenicity, reproductive and developmental toxicity, did not provide any indication of endocrine activity that could be attributed to cyphenothrin administration, including effects on the sexual hormone system and on thyroid activity. Non-standard studies on specific endocrine mechanisms in mammals were not conducted and were not considered necessary.

However, further information to assess the potential for endocrine disruption of cyphenothrin may be required when EU harmonised guidelines are established for test methods and risk assessment.

4.2. Overall conclusions

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

4.3. List of endpoints

The most important endpoints, as identified during the evaluation process, are listed in Appendix I.

5. DECISION

5.1. BACKGROUND TO THE PROPOSED DECISION

The proposed use for cyphenothrin is as an active ingredient for insecticide formulations (product Type 18: insecticides, acaricides and product to control other arthropods).
In order to support inclusion of cyphenothrin in Union List, the applicant has submitted efficacy studies with two representative products, Gokilaht 5EC (5% w/v cyphenothrin) and Pesguard LG OBA (oil-based-aerosol) (0.3% w/w cyphenothrin + 0.1% w/w imiprothrin).
Gokilaht 5EC is formulated as an emulsifiable concentrate (EC), containing 5% w/v cyphenothrin. This product will be used by a PCO (Pest Control Operator) indoors for remedial treatments in buildings (private housing, public buildings, etc.). Gokilaht 5EC is applied with hand held spray equipment with hydraulic nozzles (e.g. knapsack, 1-3 bars) by professional users only. The product is diluted in water normally in 5l hand-held applicators and it is applied at a rate of 125 ml product /5 lt water for spraying 100 m^2 surfaces or 0.0625 gr a.i/ m^2. This product is intended to be used against German cockroaches (*Blattella germanica*) with directed spray onto the insects and against German and American (*Periplaneta americana*) cockroaches with surface residual treatment (including cracks and crevices) where insects may come into contact. The product is also intended to be used against black garden ants (*Lasius niger*) as directed spray onto the insects at 100 ml product/5 lt water/100 m^2 (0.05 gr a.i./m^2).
Based on the results of efficacy studies with Gokilaht 5EC, cyphenothrin proved to be effective as direct spray against German cockroaches and surface residual spray (including crack and crevice treatment) against German and American cockroaches at 0.0625 gr a.i./m^2, and direct spray against black garden ants at 0.05 gr a.i./m^2.
Pesguard LG OBA (oil-based-aerosol) is a hand held ready-to-use aerosol, which contains 0.3% w/w cyphenothrin and 0.1% w/w imiprothrin. This product will be used by a PCO (Pest Control Operator) indoors for remedial treatments where a large-scale treatment is not justified. It is intended to treat domestic or restaurant kitchens or small areas in large buildings where there is local or limited infestation. The product is intended to be used as surface spot, crack and crevice treatment at 6.6 gr product/m^2 against German cockroaches (*Blattella germanica*), bed bugs (*Cimex lectularius*) and cat fleas (*Ctenocephalides felis*).
In 2016, the applicant provided two new efficacy studies, a field study and a laboratory study, with the representative product Pesguard LG OBA in order to support the new/revised intended use of the product, namely indoor application by professionals as surface spot, crack and crevice treatment at 6.6 gr product/m^2 against German cockroaches (*Blattella germanica*), bed bugs (*Cimex lectularius*) and cat fleas (*Ctenocephalides felis*). Since Pesguard LG OBA contains two active substances (0.3% cyphenothrin and 0.1% imiprothrin w/w), the laboratory study was also provided to prove the innate effect of cyphenothrin as indoor spot, crack and crevice treatment at 6.6 g Pesguard LG OBA/ m^2.
These studies were discussed in Efficacy WG-I 2017 (early discussion) and as a follow up in Efficacy WG-III 2017. The EFF WG-III agreed with the evaluation made by the eCA for both efficacy studies.
In the laboratory study, tests were conducted using Pesguard LG OBA and Pesguard LG OBA containing only cyphenothrin as active substance at 0.3% or 0.1% (without imiprothrin) by increasing the content of one solvent in order to replace imiprothrin. A series of bioassays were performed to assess the direct and residual efficacy of Pesguard LG OBA (0.3% cyphenothrin and 0.1% imiprothrin w/w), New Formulation (High Level) (0.3% cyphenothrin w/w) and New Formulation (Low Level) (0.1% cyphenothrin w/w) against German cockroaches (*Blattella germanica*), bed bugs (*Cimex lectularius*) and cat fleas (*Ctenocephalides felis*) in terms of knockdown and mortality. This study proved innate effect of cyphenothrin at 6.6 g Pesguard LG OBA/m^2 (0.0198 g cyphenothrin/m^2) as a spot, crack and crevice treatment against German cockroaches, bedbugs and fleas for Union-List inclusion purposes.

Regarding human health, cyphenothrin is classified as Acute Tox. 4 with H302 (Harmful if

swallowed) and H332 (Harmful if inhaled) and as STOT RE 1 with H372 (Causes damage to respiratory system through prolonged or repeated exposure by inhalation). Based on the risk assessment performed, a safe use has been demonstrated for Pesguard LG OBA. An acceptable risk for the professional user has been identified when PPE (gloves & impermeable coverall) is used and in accordance with the label instructions. Likewise, no unacceptable risk through indirect exposure was determided for adults and children. For toddlers, a borderline exposure estimate has been concluded. Given that the product is for spot, crack and crevice treatment and as such, toddlers will not have immediate access to treated residues, no particular concern is raised. In addition, it should be noted that in the absence of relevant to the product dermal absorption data, the conservative default value of 75% has been used in the calculations leading to an overestimation of exposure. As a precautionary measure, a label instruction for Pesguard LG OBA, to be applied to areas inaccessible to children, should be considered.
For Gokilaht 5 EC, no safe use has been demonstrated for both primary and secondary exposure.

Regarding the environment, cyphenothrin is classified as Aquatic Acute 1 and Aquatic Chronic 1 with H400 (Very toxic to aquatic) and H410 (Very toxic to aquatic life with long lasting effects) respectively. Unacceptable environmental risk was identified for Gokilaht for both total surface and crack and crevice treatments. More specifically, for the total area surface treatment no safe use could be demonstrated because of the risk identified for the aquatic (i.e. aquatic organisms, sediment-dweling organisms and STP microorganism) and the terrestrial compartment (i.e. soil organisms, fish- and earthworm-eating predators and grownd water). Regarding the application of Gokilaht on cracks and crevices, unacceptable risk has been identified only for sediment-dwelling organisms.
Safe use has been demonstrated for Pesguard LG OBA considering the new/revised application dose of 6.6 g Pesguard LG OBA/m^2 (0.0198 g cyphenothrin/m^2).

5.2. PROPOSED DECISION

In view of the conclusions of the evaluation, it is proposed that cyphenothrin shall be approved and be included in the Union list of approved active substances.

5.3. ELEMENTS TO BE TAKEN INTO ACCOUNT WHEN AUTHORISING PRODUCTS

Efficacy

- At product authorization stage additional simulated-use and field tests should be required to support efficacy of Gokilaht 5EC against cockroaches and ants. The lab tests against cockroaches should be performed with adequate number of insects as described in the TNsG for PT18&19. Also, studies assessing residual spray effectiveness against ants should be provided, depending on the label claim.

- At product authorization stage, additional data should be required to support efficacy of Pesguard LG OBA in terms of duration of residual effect, residual effect on porous surfaces and field studies with spot, crack and crevice treatment against claimed target organisms.

- A strategy for management of the development of resistance is required on the label of the representative products Gokilaht 5EC and Pesguard LG OBA, at product authorization level. There is reason to expect resistance development in insects (e.g. cockroaches and ants) in particular when the products are used as surface treatment because of the persistent activity on surfaces over time. The selection pressure can be

high and continuous use of the a.s. may lead to resistance in due time.

- Resistance to cyphenothrin has been reported for some insect 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 cyphenothrin.

Human health

Considering the hazardous properties and the proposed classification of the product as well as the outcome of the specific risk assessment for the intended uses, the following protective measures should be considered at product authorisation:

- **Pesguard LG OBA**
  - Unprotected persons and animals should be kept away from treated areas until surfaces are dry.
  - The product should be applied to areas inaccessible to children.
  - Do not contaminate foodstuffs, eating utensils or food contact surfaces.

- **Gokilaht 5 EC**
  Not relevant; no safe use has been demonstrated.

Environment

- **Gokilaht 5 EC**

Not relevant; no safe use has been demonstrated.

- **Pesguard LG OBA**

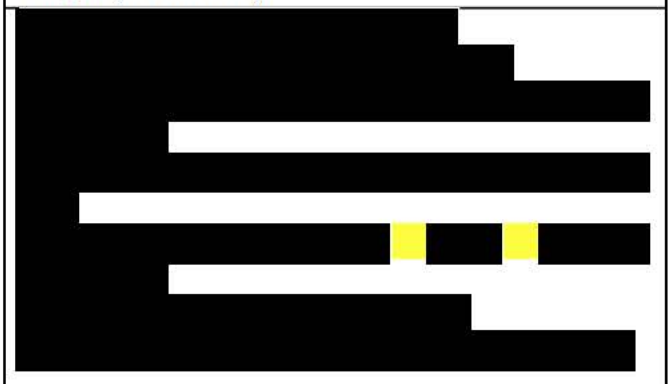
No protective measures are proposed.

Appendix I: List of endpoints

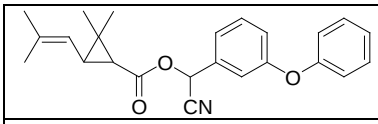
Chapter 1: Identity, Physical and Chemical Properties, Classification and Labelling

Active substance (ISO Common Name)	Cyphenothrin
Product-type	PT 18 (insecticides, acaricides and products to control other arthropods)

Identity

Chemical name (IUPAC)	(RS)-α-cyano-3-phenoxybenzyl (1RS,3RS;1RS,3SR)-2,2-dimethyl-3-(2-methylprop-1-enyl)cyclopropanecarboxylate. or (RS)-α-cyano-3-phenoxybenzyl (1RS)-cis-trans-2,2-dimethyl-3-(2-methylprop-1-enyl)cyclopropanecarboxylate. or (±)-α-cyano-3-phenoxybenzyl (±)-cis-trans-chrysanthemate
Chemical name (CA)	cyano(3-phenoxyphenyl)methyl 2,2-dimethyl-3-(2-methyl-1-propenyl)cyclopropanecarboxylate
CAS No	39515-40-7
EC No	254-484-5
Other substance No.	CIPAC: 804
Minimum purity of the active substance as manufactured (g/kg or g/l)	Purity of cyphenothrin based on Total Isomers: 92.0 %w/w minimum Geometrical isomer ratio (Trans isomer ratio): 75.0 %w/w (mimimum) Optical isomer ratio (1R-isomer ratio): 95.0 %w/w (minimum)
Identity of relevant impurities and additives (substances of concern) in the active substance as manufactured (g/kg)[2]	
Molecular formula	$C_{24}H_{25}NO_3$

[2] Disclaimer ECHA 6 July 2018: the information provided here is 'blackened out' pending the assessment of a confidentiality claim.

Molecular mass	
Structural formula	375.45 g/mol

Physical and chemical properties

Melting point (state purity)	-25ºC (100%)
Boiling point (state purity)	At atmospheric pressure technical cyphenothrin decomposes before it boils (technical material, purity not stated)
Temperature of decomposition	>180ºC (100%)
Appearance (state purity)	Viscous yellow / amber liquid (95%) Viscous slightly yellow/clear (99/3%)
Relative density (state purity)	1.08 (100%)
Surface tension	Not applicable (low solubility).
Vapour pressure (in Pa, state temperature)	Temperature: 20°C Result: 1.8 x 10^{-7} Pa Temperature: 25°C Result: 2.9 x 10^{-7} Pa
Henry's law constant (Pa m^3 mol^{-1})	0.005 Pa m^3 mol^{-1} at 20ºC 0.008 Pa m^3 mol^{-1} (based on results of vapour pressure at 25 ºC and water solubility at 20ºC)
Solubility in water (g/l or mg/l, state temperature)	1.321 × 10^{-5} g/l, 20°C, distilled water
Solubility in organic solvents (in g/l or mg/l, state temperature)	Non-analytical, solvent addition procedure at nominally 20°C n-Heptane: >250 g/L Methanol: >250 g/L
Stability in organic solvents used in biocidal products including relevant breakdown products	There is no requirement to perform this test as the active substance as manufactured does not include an organic solvent. Also the active substance remains stable after storage in the products.
Partition coefficient (log P_{OW}) (state temperature)	The test substance eluted with three distinct peaks with retention times corresponding to log Pow values of +5.79, +6.03 and +6.09, which were within 95% confidence ranges of +5.56 to +6.06, +5.78 to +6.32 and +5.83 to +6.38, respectively (95% technical material).
Hydrolytic stability (DT_{50}) (state pH and temperature)	pH = 4 , stable pH =7, DT_{50} = 112 days at 25 ºC
Dissociation constant	No dissociation

UV/VIS absorption (max.) (if absorption > 290 nm state ε at wavelength)	

Conditions	Maximum absorbance wavelength (nm)	Extinction coefficient (ε)
Acidic	204	45300
	278	2930
Unadjusted	204	44100
	278	2940
Basic	220	17600
	306	1160

Quantum yield of direct phototransformation in water at Σ > 290 nm	Pending. For more details see Environmental Section.
Flammability	Auto-flammability: 366 ± 2°C (95%) Flash Point: >110°C (95%)
Explosive properties	Not explosive.
Oxidising properties	Not oxidising.

Classification and proposed labelling

with regard to physical/chemical data	None
with regard to toxicological data	Acute Tox. 4; H302 Acute Tox. 4; H332 STOT RE 1; H372
with regard to fate and behaviour data	
with regard to ecotoxicological data	Aquatic Acute 1; Acute M-factor: 1000 Aquatic Chronic 1; Chronic M-factor: 1000

Chapter 2: Methods of Analysis

Analytical methods for the active substance

Technical active substance (principle of method)	Cyphenothrin: GC with Flame Ionisation Detector Optical isomer ratio: GC with Flame Ionisation Detector Geometrical isomer ratio: GC with Flame Ionisation Detector
Impurities in technical active substance (principle of method)	GC-FID and Titration

Analytical methods for residues

Soil (principle of method and LOQ)	Method should be provided.
Air (principle of method and LOQ)	GC-MS No confirmatory method is required. LOQ= 0.0008 mg/m^{3}LOQ= 0.0008 mg/m^3
Water (principle of method and LOQ)	Drinking water: GC-ECD: LOQ=0.1 µg/L Information on clean-up is required. Validated method required for surface water is required.
Body fluids and tissues (principle of method and LOQ)	Not required.
Food/feed of plant origin (principle of method and LOQ for methods for monitoring purposes)	Not required.
Food/feed of animal origin (principle of method and LOQ for methods for monitoring purposes)	Not required.

Chapter 3: Impact on Human Health

Absorption, distribution, metabolism and excretion in mammals

Rate and extent of oral absorption:	Rapid, 26.2-49% (based on urinary excretion) For risk assessment a 26% oral absorption value was assumed as a worst case scenario
Rate and extent of dermal absorption:	• Slow, dermal absorption accounted for 11% for a 1% w/v cyphenothrin in ethanol (*in vitro* human skin) • 75% default value used in the risk assessment of Pesguard LG OBA & Gokilaht 5EC
Distribution:	Tissues residues accounted fro less than 1% of the dose (day 7 post administration). Fat residues were slightly higher compared with other tissues
Potential for accumulation:	Limited
Rate and extent of excretion:	Rapid, 84.3-94% *via* urine and faeces within 24 hrs: Urine – males: 23.9-46.6% Faeces – males: 47.4-60.4% Urine – females: 35.5-40% Faeces – females: 48.3-51%
Toxicologically significant metabolite(s)	Parent compound and metabolites (metabolites formed either by oxidation of the alcohol and acid moieties or by cleavage of the ester linkage and conjugation of the resultant carboxylic acid and phenols with glucuronic acid, sulfuric acid or glycine)

Acute toxicity

Rat LD_{50} oral	318 mg/kg b.w. (male rat), 419 mg/kg b.w. (female rat), **Acute Tox. 4; H302**
Rat LD_{50} dermal	> 5000 mg/kg b.w., (rat)
Rat LC_{50} inhalation	> 1850 mg/m^3 (rat), 3-hr exposure. Applying modified Haber's Law: > 1387.5 mg/m^3, 4-hr exposure. **Acute Tox. 4; H332**
Skin irritation	Not irritating
Eye irritation	Slightly irritating
Skin sensitization (test method used and	Not sensitising (modified Buehler method)

result)	

Repeated dose toxicity

Species/ target / critical effect	Target organs: nervous system & liver (rat, dog) Critical effects: - typical signs of pyrethroid toxicity, i.e. vomiting, paleness and intense redness of the mucous membranes (dog), irritability, facial staining and piloerection (rat) and tremors (dog, rat) - clinical chemistry changes, i.e. decreased total cholesterol levels, increased A/G ratio, albumin and total protein (rat) and raised total bilirubin (dog)
Lowest relevant oral NOAEL	3 mg/kg bw/day, 13-week feeding dog
Lowest relevant dermal NOAEL	Not available. Not required.
Lowest relevant inhalation NOAEL	NOAEC = 7.76 mg/m^3, 29-day inhalation rat (equiv. to NOAEL = 5.73 mg/kg bw/d) **STOT RE 1; H372**

Genotoxicity	No genotoxic potential

Carcinogenicity

Species / target / critical effect	No carcinogenic potential (rat, mouse)
Lowest dose with tumours	Not relevant

Reproductive toxicity

Species/ Reproduction target / critical effect	No adverse effects on reproductive performance or fertility. Decreased maternal body weight gain. (Rat)
Lowest relevant reproductive NOAEL	- systemic parental: 23.7 mg/kg bw/day - reproductive: 76.8 mg/kg bw/day - offspring: 76.8 mg/kg bw/day
Species/Developmental target / critical effect	No developmental effects (rat, rabbit) in the presence of maternal toxicity, i.e. decreased body weight gain (rat, rabbit), mortality, increased absolute heart, spleen and kidneys weight (rat)
Lowest relevant developmental NOAEL	maternal: 50 mg/kg bw/day (rabbit) foetal: 125 mg/kg bw/day (rabbit)

Neurotoxicity / Delayed neurotoxicity

Species/ target/critical effect	Rat / nervous system / clinical signs typical of pyrethroids toxicity (acute, repeated exp.)
Lowest relevant NOAEL	73 mg/kg b.w./day, 90-day feeding neurotoxicity rat

Other toxicological studies

....	Data not available. Not considered necessary.

Medical data

....	No findings attributable to pyrethroid exposure in workers involved in the manufacturing process.

Summary	Value	Study	Safety factor
AELshort-term *	0.008 mg/kg bw	13-week dog	100
AELmedium-term *	0.008 mg/kg bw/day	13-week dog	100
AELlong-term *	0.008 mg/kg bw/day	13-week dog	100
AECshort-term	0.31 mg/m^3	29-day inhalation, rat	25
AECmedium-term	0.31 mg/m^3	29-day inhalation, rat	25
ADI (acceptable daily intake)	0.03 mg/kg bw/day	13-week dog	100
ARfD (acute reference dose)	0.03 mg/kg bw	13-week dog	100
Dermal absorption	11% 75%	*In vitro* human data (1% w/v cyphenothrin in ethanol) Default value used in risk assessment	

** considering 26% oral absorption; values are rounded from 0.0078 mg/kg bw/day*

Chapter 4: Fate and Behaviour in the Environment

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

Hydrolysis of active substance and relevant metabolites (DT_{50}) (state pH and temperature)	pH 4 stable	
	pH 7 at 25°C half life = 112 days (calculation)	
	pH 9 at 25°C half life = 4.6 days (calculation)	
	3-phenoxybenzaldehyde (47.4% at pH7, 78.2% at pH9), d-trans-cyphenothrin-$CONH_2$ (9.8% at pH7)	
Photolytic / photo-oxidative degradation of active substance and resulting relevant metabolites	DT50: 9.2 hrs (RS)-α-cyano-3-phenoxybenzyl(1R)-trans-2,2-dimethyl-3-formylcyclopropanecarboxylate (CHO-GKL): 49.9% of AR at 20 hr 3-phenoxybenzaldehyde (PBald): 14.4% of AR at 12 hr	
Readily biodegradable (yes/no)	No	
Inherent biodegradable (yes/no)	Not performed	
Biodegradation in freshwater	-	
Biodegradation in seawater	Not applicable	
Non-extractable residues	-	
Distribution in water / sediment systems (active substance)	**Calwich Abbey**: *cis*-CY: water: 73.7% (0 d) sediment: 79.9% (3 d) *trans*-CY: water: 76.5% (0 d) sediment: 75.2% (1 d) *trans*-PH: water: 68.2% (0 d) sediment: 63.9% (3 d)	**Swiss Lake**: *cis*-CY: water: 84.8% (0 d) sediment: 35.0% (3 d) *trans*-CY: water: 93.8% (0 d) sediment: 41.6% (1 d) *trans*-PH: water: 81.5% (0 d) sediment: 44.7% (3 d)
Distribution in water / sediment	The following major meatbolites have been	

systems (metabolites)

identified:

Code/Name	Max occurrence %			Precursor
	Whole system	Water	Sediment	
c-COOH-CA	13.7	5.1 (end of study)	8.6 (end of study)	*cis*-CY
d-c-CRA	34.4	17.3	28.6	*cis*-CY
t-COOH-CA	46.5	39.9	19.9	*trans*-CY
d-t-CRA	56.3	26.4	36.2	*trans*-CY
ωt-COOH-d-c-CRA	16.3	11.5	7.8	*cis*-CY
PBacid	60.9	29.8	31.9	*trans*-PH

The following DT_{50} values are normalized to 12^0C

Metabolite	DT50 (days)
d-c-CRA	34.3
	52.9
d-t-CRA	35.8
	22.2
c-COOH-CA	Not calculated
t-COOH-CA	52.3
	101
ωt-COOH-d-c-CRA	27.9
	23.7
PBacid	54.2
	114

DT50 water (12^0C)

2.1 days (geometric mean, n=6)

DT50 sediment (12^0C)

Not calculated

DT50 whole system (12^0C)

System	Label	DT_{50} (days)	DT_{50} (days) 12^0C
Calwich Abbey	*c*-CY	36.7	69.6
	t-CY	5.7	10.8
	t-PH	6.8	12.9
SwissLake	*c*-CY	35.4	67.1

	t-CY	14.1	26.7
	t-PH	6.5	12.3
Mineralization	CO_2 maximum levels 21.5-24.3% AR (*cis*) and 26.4-42.2% AR (*trans*)		
Non-extractable residues	Bound residues 13.4-31.4% AR (*cis*) and 10.5-35.6% AR (*trans*)		

Route and rate of degradation in soil

Mineralization (aerobic)	CO_2 at last day of the study		
	Empingham *cis*-CY: 56.9% *trans*-PH: 51.1%	Ingleby *cis*-CY: 43.4% *trans*-PH: 56.9%	Barrow *cis*-CY: 49.5% *trans*-PH: 56.7%
Laboratory studies (range or median, with number of measurements, with regression coefficient)			

DT_{50lab} (20°C, aerobic):

Soil	Label	Kinetic fit	DT_{50} at 20^0C (days)	DT_{50} at 12^0C (days)
Empingham, UK	*cis*-CY	FOMC	6.2	13.2
	trans-PH	FOMC	6.04	12.8
Ingleby, UK	*cis*-CY	DFOP	1000	1000
	trans-PH	FOMC	14.2	30.3
Barrow, UK	*cis*-CY	DFOP	154	328.7
	trans-PH	FOMC	11.3	24.1
	trans-CY	FOMC	9.64	20.6
Brierlow, UK	*cis*-CY	DFOP	65.1	138.9
	trans-PH	FOMC	20.5	43.8
Geometric mean[*]		Cis		156.68
		trans		24.3

[*] The geometric mean value for its isomer should be considered for risk assessment purposes

DT_{90lab} (20°C, aerobic):

Soil	Label	Kinetic fit	DT_{90} at 20^0C (days)
Empingham, UK	*cis*-CY	FOMC	20.6
	trans-PH	FOMC	20.1
Ingleby, UK	*cis*-CY	DFOP	>1000
	trans-PH	FOMC	47
Barrow, UK	*cis*-CY	DFOP	158
	trans-PH	FOMC	37.6
	trans-CY	FOMC	32
Brierlow, UK	*cis*-CY	DFOP	122
	trans-PH	FOMC	68.2

Mineralization (aerobic)

43.4-56.9% CO_2 after 120 days (n=9)

Non-extreactable residues

17.2-47.1% after 120 days (n=9)

Relevant metabolites - name and/or code, % of applied a.i. (range and maximum)

Code	Max.% AR	Precursor
4'-OH-*c*-S-2703	10.9	*cis*-CY
PBacid	15.8	*trans*-PH
ωt-COOH-*d*-*c*-CRA	8.4	*cis*-CY
nitro derivative of 4'-OH-*c*-S-2703	8.3	*cis*-CY

Metabolite	DT50 (days)	DT50 at 12^0C (days)
4'-OH-c-S-2703	2.59	4.9
	11.9	22.6
	5.8	11.0

	35.1	66.6
Geometric mean		16.9
PBacid	0.287	0.5
	77.8	148
	43.9	83.3
	77.5	147
Geometric mean		30.85

DT_{50lab} (20°C, anaerobic):	-
Degradation in the saturated zone:	-
Field studies (state location, range or median with number of measurements)	
Soil photolysis	-
Non-extractable residues	-
Relevant metabolites - name and/or code, % of applied a.i. (range and maximum)	Not applicable
Soil accumulation and plateau concentration	-

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

Ka , Kd	-
Ka_{oc}	log Koc = 5.58 which is equal to Koc = 380189 (peak 1) log Koc = 5.79 which is equal to Koc = 616595 (peak 2) (Cyphenothrin is a racemic mixture and is detected as a double peak).
pH dependence (yes / no) (if yes type of dependence)	Not reported

Fate and behaviour in air

Direct photolysis in air	No test
Quantum yield of direct photolysis	No test
Photo-oxidative degradation in air	Atkinson model (via AOPWIN version 1.92 DT_{50}: 3.675 hrs (12-hr, 0.5E6 OH/cm^3)
Volatilization	Not applicable

Reference value for groundwater

According to BPR Annex VI, point 68	0.0001 mg/L (Directive 98/83EC)

Monitoring data, if available

Soil (indicate location and type of study)	Not applicable
Surface water (indicate location and type of study)	Not applicable
Ground water (indicate location and type of study)	Not applicable
Air (indicate location and type of study)	Not applicable

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 (mg a.s./L)
Cyphenothrin (parent)			
Fish			
Salmo gairdneri	96 hours	LC_{50}	0.00034 (m.m.)
Pimephales promelas	28-day post hatch	NOEC	0.00054 (m.m.)
Invertebrates			
Daphnia magna	48 hours	EC_{50}	0.00043 (m.m.)
	21 days	NOEC	0.000081 (m.m.)
Algae			
Pseudokirhneriella subcapitata	72 hours	E_rC_{50} E_bC_{50} NOE_rC NOE_bC	> 0.014 (m.m.) > 0.014 (m.m.) 0.005 (m.m.) 0.014 (m.m.)
Microorganisms			
Activated sludge	30 minutes	NOEC	0.0132 *
***t*-COOH-CA (metabolite)**			
Fish			
Pimephales promelas	96 hours	LC_{50}	> 94 (m.m.)
Invertebrates			
Daphnia magna	48 hours	EC_{50}	> 92 (m.m.)

Species	Time-scale	Endpoint	Toxicity (mg a.s./L)
Algae			
Pseudokirchneriella subcapitata	96 hours	E_rC_{50}	75 (m.m.)
PBacid or 3-Phenoxybenzoic acid (metabolite)			
Fish			
Oncorhynchus mykiss	96 hours	LC_{50}	14.3 (m.m.)
Invertebrates			
Daphnia magna	48 hours	EC_{50}	35.4 (nom.)
Algae			
Selenastrum capricornutum	72 hours	E_rC_{50} E_bC_{50} NOE_rC NOE_bC	> 51.92 (m.m.) > 33.79 (m.m.) 18.4 (m.m.) 18.4 (m.m.)

m.m.: results were based on mean measured concentrations
nom.: results were based on nominal concentrations
* cyphenothrin had no significant inhibitory effects on the respiration rate of activated sludge up to and including the highest test concentration of 100 mg/L. Taking into that this concentration exceeds the limit of water solubility of cyphenothrin, the NOEC was set equal to the water solubility value of 0.0132 mg/L.

Effects on earthworms or other soil non-target organisms

Acute toxicity	Data not available
Reproductive toxicity	Data not available

Effects on soil micro-organisms

Nitrogen mineralization	Data not available
Carbon mineralization	Data not available

Effects on terrestrial vertebrates

Acute toxicity to mammals	Please refer to Chapter 3 (Impact on Human Health)
Acute toxicity to birds	Data not available
Dietary toxicity to birds	Data not available
Reproductive toxicity to birds	Data not available

Effects on honeybees

Acute oral toxicity	Data not available

Acute contact toxicity	Data not available

Effects on other beneficial arthropods

Acute oral toxicity	Data not available
Acute contact toxicity	Data not available

Bioconcentration

Bioconcentration factor (BCF)	$BCF_{SS, L}$ = 618 L/kg (whole body, at 0.1 µg/L) $BCF_{SS, L}$ = 617 L/kg (whole body, at 0.3 µg/L) BCF_K = 894.9 L/kg (whole body, at 0.1 µg/L) BCF_K = 864.6 L/kg (whole body, at 0.3 µg/L)
Depration time (DT_{50})	8.8 days (whole body, at 0.1 µg/L) 5.1 days (whole body, at 0.3 µg/L)
Depration time (DT_{90})	Not determined (by the end of the depuration period (28 days), the concentration of cyphenothrin in whole fish was more than 10%, i.e. 14% and 11% of the steady-state concentration in the low (0.1 µg/L) and high (0.3 µg/L) exposure levels, respectively)
Level of metabolites (%) in organisms accounting for > 10 % of residues	polar (comprising of multiple components, each of which amounted to less than 10%TRR): 38.4% TRR (whole body) ωt-COOH-d-c-CRA: 19.3% TRR (whole body) ωc-COOH-d-c-CRA: 10.8% TRR (whole body) d-t-CRA: 16.0% TRR (whole body)

Chapter 6: Other End Points

No other data required

Appendix II: List of Intended Uses

Object and/or situation (a)	Member State or Country	Product name	Organisms controlled (c)	Formulation		Application			Applied amount per treatment			Remarks: (m)
				Type (d-f)	Conc. of as (i)	Method Kind (f-h)	Number min max (k)	Interval between applications (min)	g as/L min max	water L/m^2 min max	g as/m^2 min max	
Public health insecticide for professional use by a PCO (Pest Control Operator) as an insecticidal direct and residual surface spray indoors against cockroaches and ants.	All EU member states	Gokilaht 5 EC	Cockroaches (*Blattella germanica, Periplanata americana*) Ants (*Lasius niger)*	EC – emulsifiable concenrtrate low pressure spraying	5% w/v cyphenothrin 50g/l	Direct spray against German cockroaches, surface residual spray (including crack and crevice treatment) against German and American cockroaches, and direct spray against ants with low pressure sprayer (1-3 bars).	It will be used indoors for remedial treatments in buildings (private housing, public buildings, etc.) Treatments would be made as necessary.	For surface residual treatments the treated surfaces (non absorbent) may retain residual activity against German and American cockroaches for up to 12 weeks.	1.25 gr as/lt water for direct and surface residual treatment against cockroaches 1 gr as/lt water for direct spray onto ants	0.05	0.05 – 0.0625 0.0625 for direct and surface residual treatment against cockroaches 0.05 for direct spray onto ants	
Public health insecticide for professional use by a PCO (Pest Control Operator) as an insecticidal surface spot, crack and crevice treatment indoors	All EU member states	Pesguard LG OBA	German cockroaches (*Blattella germanica*), Bed bugs (*Cimex lectularius*) Cat fleas (*Ctenocephalides felis*)	Hand held ready to use oil –based aerosol	0.3% w/w Cyphenothrin and 0.1% w/w Imiprothrin	Surface spot, crack and crevice treatment	It will be used for remedial treatments where large-scale treatment is not justified. It is intended to treat indoor domestic or public places where there is local or limited	Not specified	-	-	0.0198 g cyphenothrin/ m^2 (6.6 g product/m^2)	

							infestation. Treatments would be made as necessary.					

(a) *e.g.* biting and suckling insects, fungi, molds

(b) *e.g.* wettable powder (WP), emulsifiable concentrate (EC), granule (GR)

(c) GCPF Codes - GIFAP Technical Monograph No 2, 1989 ISBN 3-8263-3152-4)

(d) All abbreviations used must be explained

(e) g/kg or g/l;(f) Method, *e.g.* high volume spraying, low volume spraying, spreading, dusting, drench

(g) Kind, *e.g.* overall, broadcast, aerial spraying, row, bait, crack and crevice equipment used must be indicated

(h) Indicate the minimum and maximum number of application possible under practical conditions of use

(i) Remarks may include: Extent of use/economic importance/restrictions

(j)

Appendix III: List of studies

Reference list by Annex Point

List of studies for Cyphenothrin

Section No / Reference No	Author	Year	Title. Source (where different from company) Company, Report No. GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes/No)	Owner
A2.7 A2.8	[redacted]	2002	Preliminary Analysis of Gokilaht Technical Grade [redacted] GLP Unpublished	Yes	Sumitomo
A3.1.1	[redacted]	2000	Gokilaht: Determination of melting and freezing temperature [redacted] GLP Unpublished	Yes	Sumitomo
A3.1.2	[redacted]	2002	Determination of boiling temperature [redacted] GLP Unpublished	Yes	Sumitomo
A3.1.3 A3.2 A3.2.1 A3.3.1 A3.2.2 A3.2.3 A3.3 A3.4 A3.7 A3.8 A3.9 A3.10 A3.11 A3.12 A3.14	[redacted]	2006	Cyphenothrin: Evaluation of Physico-Chemical Properties [redacted] GLP Unpublished	Yes	Sumitomo
A3.5 A3.13	[redacted]	2007	Cyphenothrin: Evaluation of the Water Solubility and Surface Tension [redacted] GLP Unpublished	NA	Sumitomo
A3.17	[redacted]	2005	Reactivity of pyrethroid technical materials towards container materials	Yes	Sumitomo

Section No / Reference No	Author	Year	Title. Source (where different from company) Company, Report No. GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes/No)	Owner
			[redacted] Non GLP Unpublished		
A4.1	[redacted]	2003	Enforcement Analytical Methods of Gokilaht Technical Grade [redacted] GLP Unpublished	Yes	Sumitomo
A4.2	[redacted]	2006	Gokilaht (cyphenothrin): Validation of an Analytical Method for the Determination of residues in Air [redacted] GLP Unpublished	Yes	Sumitomo
A4.2	[redacted]	2001	Validation of a Multi-Residue Method for the Determination of Gokilaht in Drinking Water [redacted] GLP Unpublished	Yes	Sumitomo
A6.1.1/01	[redacted]	1983(a)	Acute oral toxicity of S-2703 Forte in rats [redacted] GLP Unpublished	Yes	Sumitomo
A6.1.2/01	[redacted]	1983(b)	Acute dermal toxicity of S-2703 Forte in rats [redacted] GLP Unpublished	Yes	Sumitomo
A6.1.2/01	[redacted]	2005	Review on medical evaluation of factory workers exposed to pyrethroids [redacted] GLP Unpublished	Yes	Sumitomo
A6.1.3/01	[redacted]	1981	Acute inhalation toxicity of S-2703 Forte in rats [redacted] GLP Unpublished	Yes	Sumitomo
A6.1.4.1/01	[redacted]	1981	Primary eye and skin irritation tests of S2703 Forte technical in rabbits [redacted]	Yes	Sumitomo

Section No / Reference No	Author	Year	Title. Source (where different from company) Company, Report No. GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes/No)	Owner
			[redacted] GLP Unpublished		
A6.1.4.2/01	[redacted]	1981	Primary eye and skin irritation tests of S2703 Forte technical in rabbits [redacted] GLP Unpublished	Yes	Sumitomo
A6.1.5/01	[redacted]	1983(c)	Dermal sensitization test of S-2703 Forte in guinea pigs [redacted] GLP Unpublished	Yes	Sumitomo
A6.2.2/01	[redacted]	2006	Protocol GOKILAHT: In vitro absorption from a 1% Gokilaht formulation through human epidermis. [redacted]	n.a	Sumitomo
A6.3.1.01	[redacted]	1984	A five week sub acute feeding Toxicity Study of S-2703 in Rats [redacted] GLP Unpublished	Yes	Sumitomo
A6.3.1/02	[redacted]	1987	S-2703F. Preliminary toxicity study by oral (capsule) administration to beagle dogs for four weeks [redacted] GLP Unpublished	Yes	Sumitomo
A6.3.3/01	[redacted]	1983	Subacute Inhalation Toxicity of S-2703 Forte in Rats. [redacted] GLP Unpublished	Yes	Sumitomo
A6.3.3/02	[redacted]	1984	Subacute Inhalation Toxicity of S-2703 Forte in Rats. [redacted] GLP	Yes	Sumitomo

Section No / Reference No	Author	Year	Title. Source (where different from company) Company, Report No. GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes/No)	Owner
			Unpublished		
A6.4.1/01	[redacted]	1985	S-2703F: Thirteen week range finding toxicity study in rats [redacted] GLP Unpublished	Yes	Sumitomo
A6.4.1/02	[redacted]	1987	Subacute (13week) oral toxicity study of S-2703F in beagles [redacted] GLP Unpublished	Yes	Sumitomo
A6.5/01	[redacted]	1988	S2703F: Combined oncogenicity and toxicity study in rats [redacted] GLP Unpublished	Yes	Sumitomo
A6.6.1/01	[redacted]	1982	Gene Mutation Test of S-2703 Forte in Bacterial System [redacted] GLP Unpublished	Yes	Sumitomo
A6.6.1/02	[redacted]	1983	In vitro sister chromatid exchanges test of S-2703 forte in CHO-K1 cells [redacted] GLP Unpublished	Yes	Sumitomo
A6.6.2/01	[redacted]	1989	Mutagenicity test on Gokilaht in an in vitro cytogenetic assay measuring chromosomal aberration frequencies in Chinese hamster ovary (CHO) cells [redacted] GLP Unpublished	Yes	Sumitomo
A6.6.3/01	[redacted]	1989	In vitro gene mutation test of S-2703 Forte in V79 Chinese hamster cells in culture [redacted] GLP Unpublished	Yes	Sumitomo
A6.6.4/01	[redacted]	1983	Micronucleus Test of S-2703 Forte [redacted]	Yes	Sumitomo

Section No / Reference No	Author	Year	Title. Source (where different from company) Company, Report No. GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes/No)	Owner
			[redacted] GLP Unpublished		
A6.7/01	[redacted]	1989	S 2703F Oncogenicity study by dietary administration to B6CF1 mice for 104 days [redacted] GLP Unpublished	Yes	Sumitomo
A6.8.1/01	[redacted]	1984	Teratology study in rats treated subcutaneously with S-2703 Forte [redacted] GLP Unpublished	Yes	Sumitomo
A6.8.1/02	[redacted]	1984b	Teratology study of S-2703 forte in the rabbit (second study) [redacted] GLP Unpublished	Yes	Sumitomo
A6.8.2/01	[redacted]	1986	S-2703F: Effects upon reproductive performance of rats treated continuously throughout two successive generations [redacted] GLP Unpublished	Yes	Sumitomo
A6.9	[redacted]	2006	General Statement of Neurotoxicity for Pyrethroids [redacted] GLP Unpublished	Yes	Sumitomo
A6.9/01	[redacted]	2012	An Oral (Gavage) Dose Range-Finding Acute Neurotoxicity Study of Cyphenothrin in Rats. [redacted] GLP Unpublished	Yes	Sumitomo
A6.9/02	[redacted]	2012	An Oral (Gavage) Acute Neurotoxicity Study of Cyphenothrin in Rats. [redacted] GLP Unpublished	Yes	Sumitomo
A6.9/03	[redacted]	2012	A 28-day Dietary Dose Range-	Yes	Sumitomo

Section No / Reference No	Author	Year	Title. Source (where different from company) Company, Report No. GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes/No)	Owner
			Finding Subchronic Study of Cyphenothrin in Rats. [redacted] GLP Unpublished		
A6.9/04	[redacted]	2012	A 90-day Oral Dietary Neurotoxicity Study of Cyphenothrin in Rats. [redacted] GLP Unpublished	Yes	Sumitomo
A7.1.1.1.1/01	[redacted]	2002	Hydrolysis of [phenoxy phenyl-^{14}C] Gokilaht (GKL) at pH 7, 7 and 9 [redacted] GLP Unpublished	Yes	Sumitomo
A7.1.1.2.1/01	[redacted]	2002	Ready biodegradability of Gokilaht in a manometric respirometry test [redacted] GLP Unpublished	Yes	Sumitomo
A7.1.3/01	[redacted]	2001	Estimation of the adsorption coefficient of Gokilaht/Gokilaht-s on soil using high performance Liquid chromatography (HPLC) [redacted] GLP Unpublished	Yes	Sumitomo
A7.4.1.1/01	[redacted]	1989	Acute flow-through toxicity of Gokilaht to rainbow trout (S*almo gairdneri*) [redacted] GLP Unpublished	Yes	Sumitomo
A7.4.1.1/02	[redacted]	2005	3-Phenoxybenzoic acid: Acute toxicity test with rainbow trout (Oncorhynchus mykiss) under static conditions. [redacted] GLP Unpublished	Yes	Sumitomo

A7.4.1.1/03	[redacted]	2013b	Acute Toxicity of t-COOH-CA to Freshwater Green Alga, Daphnid and Fish. [redacted] Non-GLP Unpublished	Yes	Sumitomo
A7.4.1.2/01	[redacted]	1989	Acute Flow-Through Toxicity of Gokilaht to Daphnia magna [redacted] GLP Unpublished	Yes	Sumitomo
A7.4.1.2/02	[redacted]	2005	3-Phenoxybenzoic acid: Acute immobilisation test with daphnids (Daphnia magna) under static conditions. [redacted] GLP Unpublished	Yes	Sumitomo
A7.4.1.3/01	[redacted]	2002	Gokilaht – Toxicity to the fresh water green algae *Pseudokirhneriella subcapitata* [redacted] GLP Unpublished	Yes	Sumitomo
A7.4.1.3/02	[redacted]	2005	3-Phenoxybenzoic acid: Alga growth inhibition test with Pseudokirchneriella subcapitata (syn Selenastrum capricornutum). [redacted] GLP Unpublished	Yes	Sumitomo
A7.4.1.4/01	[redacted]	2002	Toxicity of Gokilaht to Activated Sludge [redacted] GLP Unpublished	Yes	Sumitomo
A7.4.2	[redacted]	2015	[^{14}C]Cyphenothrin: Flow-through Bioconcentration and Metabolism Study with Blugill Sunfish (Lepomis macrochirus) [redacted] GLP Unpublished	Yes	Sumitomo
A7.4.3.2	[redacted]	2015	Fish Early Life Stage Test (Pimephales promelas) [redacted] GLP Unpublished	Yes	Sumitomo

A7.4.3.4	[redacted]	2015	Cyphenothrin – Full Life-Cycle Toxicity Test with Water Fleas, Daphnia magna, Under Flow-Through Conditions Following OECD Guideline #211 [redacted] GLP Unpublished	Yes	Sumitomo

List of studies for Gokilaht 5 EC

Section No / Reference No	Author	Year	Title. Source (where different from company) Company, Report No. GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes/No)	Owner
B3.1.1 B3.1.2 B3.5 B3.7 B3.8	[redacted]	2006 (b)	Determination of accelerated storage stability, low temperature stability and physico-chemical characteristics. [redacted] GLP	Yes	Sumitomo
B3.7	[redacted]	2008	Determination long term storage stability and physico-chemical characteristics. [redacted] GLP	Yes	Sumitomo
B4.1	[redacted]	2005	Gokilaht 5 EC – Determination of analytical method validation [redacted] GLP; Unpublished	Yes	Sumitomo
B5.10.2/01	[redacted]	1989	Efficacy of Gokilaht MC against Cockroaches. Sumitomo Chemical (UK) plc Study Number EEE-0108 Unpublished	Yes	Sumitomo
B5.10.2/02	[redacted]	2008	Laboratory bioassay to determine the efficacy of products applied as a direct spray against black ants, Lasius niger i2LResearch Ltd Report No: 0875 12 November 2008 Unpublished.	Yes	Sumitomo
B6.2.1/01	[redacted]	1997(a)	Primary skin irritation test of Gokilaht-S 5% EC in rabbits. [redacted] GLP Unpublished	Yes	Sumitomo
B6.2.2/01	[redacted]	1997(b)	Primary eye irritation test of Gokilaht-S 5% EC in rabbits. [redacted] GLP Unpublished	Yes	Sumitomo
B6.3/01	[redacted]	2006	Skin sensitisation of Gokilaht-S 5EC in guinea pigs. [redacted] Unpublished GLP	Yes	Sumitomo

List of studies for Pesguard LG OBA

Section No / Reference No	Author	Year	Title. Source (where different from company) Company, Report No. GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes/No)	Owner
B3.1.1 B3.1.2 B3.7	[redacted]	2006	Determination of Accelerated Storage Stability, Low Temperature Stability and Physico-Chemical Characteristics [redacted] GLP Unpublished	Yes	Sumitomo
B3.7	[redacted]	2008	Determination of Long term Storage Stability and Physico-Chemical Characteristics [redacted] GLP Unpublished	Yes	Sumitomo
B4.1	[redacted]	1991	Analytical Method for the determination of 5-41311 and Gokilaht in S-41311/Gokilaht OBA. [redacted] GLP Unpublished	Yes	Sumitomo
B4.1	[redacted]	2006	Determination of method validation [redacted] GLP Unpublished	Yes	Sumitomo
B5.10.2/01	[redacted]	1996(a)	Biological efficacy of Pesguard LG13 oil-based aerosol formulation against cockroaches Sumitomo Chemical Co Ltd SGE-0018 GLP Unpublished	yes	Sumitomo
B5.10.2/02	[redacted]	1996(b)	Biological efficacy of Pesguard LG13 oil-based aerosol formulation against cockroaches Sumitomo Chemical Co Ltd SGE-0019 GLP Unpublished	yes	Sumitomo
B5.10.2/03	[redacted]	1997(a)	A Laboratory Test of The Efficacy of Residues of Pesguard Aerosol (Active Ingredients Imiprothrin And Cyphenothrin) against the Oriental Cockroach (*Blatta orientalis*) and the German Cockroach The University of Southampton, UK SGE 0021 GLP Unpublished	yes	Sumitomo

Section No / Reference No	Author	Year	Title. Source (where different from company) Company, Report No. GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes/No)	Owner
B5.10.2/04	[redacted]	1997(b)	A Laboratory Test for the rate of effect of Pesguard Aerosol (Active Ingredients Imiprothrin And Cyphenothrin) against the Oriental Cockroach (*Blatta Orientalis*) and the German Cockroach The University of Southampton, UK SGE 0022 GLP Unpublished	yes	Sumitomo
B5.10.2/05	[redacted]	1997(c)	A Laboratory Test of the Flushing ability of Pesguard Aerosol (Active Ingredients Imiprothrin And Cyphenothrin) against the Oriental Cockroach (*Blatta Orientalis*) and the German Cockroach (B*lattella germanica*) The University of Southampton, UK SGE 0023 GLP Unpublished	yes	Sumitomo
B5.10.2/06	[redacted]	1997	Biological efficacy of Pesguard LG13 oil-based aerosol formulation against cockroaches. Confined contact method Sumitomo Chemical Co Ltd SGE-0020 GLP Unpublished	yes	Sumitomo
B5.10.2/07	[redacted]	1977	A Laboratory Test Efficacy of residues of Pesguard Aerosol (Active Ingredients Imiprothrin and Cyphenothrin) against the Black Garden Ant (*Lazius niger)* The University of Southampton, UK SUM 96-5 GLP Unpublished	yes	Sumitomo
B5.10.2/08	[redacted]	2012	Field trial to determine the efficacy of Pesguard LG OBA against bed bugs, *Cimex lectularius.* i2LResearch Ltd Study Code 10/135B UK	yes	Sumitomo
B5.10.2/09	[redacted]	2017	Laboratory bioassay to determine the direct contact and residual efficacy of an active ingredient (cyphenothrin) against multiple insect species. i2LResearch Ltd Study Code 16/409 UK	yes	Sumitomo

Section No / Reference No	Author	Year	Title. Source (where different from company) Company, Report No. GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes/No)	Owner
B6.1.1/01	[redacted]	1991(a)	Acute oral toxicity study of S-4l3ll/GKL AEROSOL BASE LIQUID in rats [redacted] GLP Unpublished	yes	Sumitomo
B6.1.2/01	[redacted]	1991(b)	Acute dermal toxicity study of S-4l3ll/GKL AEROSOL BASE LIQUID in rats [redacted] GLP Unpublished	yes	Sumitomo
B6.1.3/01	[redacted]	1992	Acute inhalation toxicity study of S-4l3ll/GKL aerosol in rats [redacted] GLP Unpublished	yes	Sumitomo
B6.1.4/01	[redacted]	1991	Primary eye and skin irritation tests with S-41311/GKL AEROSOL BASE LIQUID in rabbits [redacted] GLP Unpublished	yes	Sumitomo
B6.1.5/01	[redacted]	1991	Primary eye and skin irritation tests with S-41311/GKL AEROSOL BASE LIQUID in rabbits [redacted] GLP Unpublished	yes	Sumitomo
B6.1.6/01	[redacted]	1992	S-41311/Gokilaht aerosol base liquid: Skin sensitisation in the guinea-pig [redacted] GLP Unpublished	yes	Sumitomo
-	[redacted]	1997a	The change of the discharge rate and aerosol particle size of Pesguard LG 13 oil based aerosol as consumed. [redacted] Non-GLP Unpublished	Yes	Sumitomo
-	[redacted]	1997b	The discharge rate and aerosol particle size of Pesguard LG 13 oil based aerosol [redacted] Non-GLP Unpublished	Yes	Sumitomo

Section No / Reference No	Author	Year	Title. Source (where different from company) Company, Report No. GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes/No)	Owner
-	[redacted]	1997c	The deposit on the floor by spraying Pesguard LG13 oil based aerosol [redacted] Non-GLP Unpublished	Yes	Sumitomo
-	[redacted]	1999	Transfer of contaminants from surface to hands: experimental assessment of linearity of exposure process , adherence to the skin and area exposed during fixed pressure and recontact with surfaces contaminated with a powder. Appl. Occup. Environ. Hyg. 14(4) 231 -239 GLP – not applicable Published	No	-
-	[redacted]	1992	Dermal exposure of occasional user of pesticide products: Flea-spray in aerosol cans. HSL Report No. IR/A/96/10.(interpreted in paper presented to the Medical and Toxicolgical Panel of the Advisory Committee on Pesticides meeting, May 2001)., Pesticide Application Methods, 2nd Edition. Longman Scientific & Technical. ISBN 0-5824-0905-5 Published	No	-