FAO SPECIFICATIONS AND EVALUATIONS

FOR AGRICULTURAL PESTICIDES

ALPHA-CYPERMETHRIN

A racemic mixture of:
(*S*)-α-cyano-3-phenoxybenzyl-(1*R*,3*R*)-3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropane-carboxylate and
(*R*)-α-cyano-3-phenoxybenzyl-(1*S*,3*S*)-3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropane-carboxylate

FOOD AND AGRICULTURE ORGANIZATION of THE UNITED NATIONS

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Compliance with the specifications does not constitute an endorsement or warranty of the fitness of a particular pesticide for a particular purpose, including its suitability for the control of any given pest, or its suitability for use in a particular area. Owing to the complexity of the problems involved, the suitability of pesticides for a particular purpose and the content of the labelling instructions must be decided at the national or provincial level.

Furthermore, pesticides which are manufactured to comply with these specifications are not exempted from any safety regulation or other legal or administrative provision applicable to their manufacture, sale, transportation, storage, handling, preparation and/or use.

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INTRODUCTION

FAO establishes and publishes specifications* for technical material and related formulations of agricultural pesticides, with the objective that these specifications may be used to provide an international point of reference against which products can be judged either for regulatory purposes or in commercial dealings.

From 2002, the development of FAO specifications follows the **New Procedure**, described in the Manual on Development and Use of FAO and WHO Specifications for Pesticides, which is available only on the internet through the FAO and WHO web sites. This **New Procedure** follows a formal and transparent evaluation process. It describes the minimum data package, the procedure and evaluation applied by FAO and the Experts of the FAO/WHO Joint Meeting on Pesticide Specifications (JMPS). [Note: prior to 2002, the Experts were of the FAO Panel of Experts on Pesticide Specifications, Registration Requirements, Application Standards and Prior Informed Consent, which now forms part of the JMPS, rather than the JMPS.]

FAO Specifications now only apply to products for which the technical materials have been evaluated. Consequently from the year 2000 onwards the publication of FAO specifications under the **New Procedure** has changed. Every specification consists now of two parts namely the specifications and the evaluation report(s):

Part One: **The Specification** of the technical material and the related formulations of the pesticide in accordance with chapters 4 to 9 of the "Manual on development and use of FAO and WHO specifications for pesticides".

Part Two: **The Evaluation Report(s)** of the plant protection product reflecting the evaluation of the data package carried out by FAO and the JMPS. The data are to be provided by the manufacturer(s) according to the requirements of Appendix A, annex 1 or 2 of the "Manual on the development and use of FAO specifications for plant protection products" and supported by other information sources. The Evaluation Report includes the name(s) of the manufacturer(s) whose technical material has been evaluated. Evaluation reports on specifications developed subsequently to the original set of specifications are added in a chronological order to this report.

FAO specifications under the **New Procedure** do not necessarily apply to nominally similar products of other manufacturer(s), nor to those where the active ingredient is produced by other routes of manufacture. FAO has the possibility to extend the scope of the specifications to similar products but only when the JMPS has been satisfied that the additional products are equivalent to that which formed the basis of the reference specification.

Specifications bear the date (month and year) of publication of the current version. Evaluations bear the date (year) of the meeting at which the recommendations were made by the JMPS.

* NOTE: PUBLICATIONS ARE AVAILABLE ON THE INTERNET AT (http://www.fao.org/agriculture/crops/core-themes/theme/pests/jmps/ps-new/en/)

PART ONE

SPECIFICATIONS

Page

ALPHA-CYPERMETHRIN

ALPHA-CYPERMETHRIN

INFORMATION

Common name

alpha-cypermethrin (E-ISO, BSI), alpha-cyperméthrine (F-ISO)

Synonyms

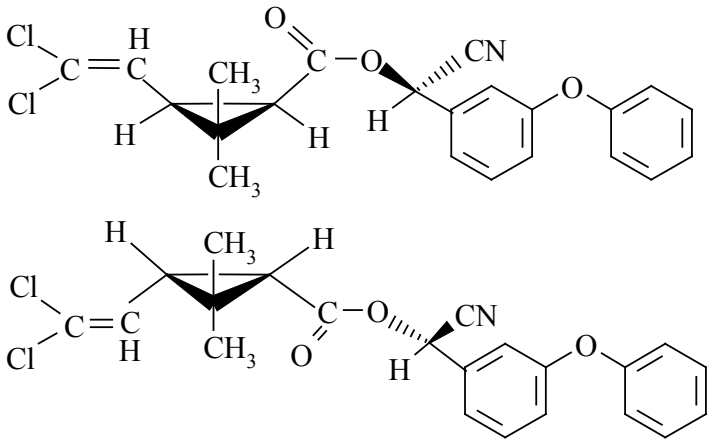
alphamethrin (rejected common name), alfoxylate

Chemical names

IUPAC: a racemic mixture of: (*S*)-α-cyano-3-phenoxybenzyl-(1*R*,3*R*)-3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropanecarboxylate and (*R*)-α-cyano-3-phenoxybenzyl-(1*S*,3*S*)-3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropanecarboxylate

CA: [1α(*S**), 3α]-(±)-cyano(3-phenoxyphenyl)methyl 3-(2,2-dichloroethenyl)-2,2-dimethylcyclopropanecarboxylate

Structural formula



Empirical formula

$C_{22}H_{19}Cl_2NO_3$

Relative molecular mass

416.3

CAS Registry number

67375-30-8

CIPAC number

454

Identity tests

GC retention time, IR spectrum.

ALPHA-CYPERMETHRIN TECHNICAL MATERIAL

FAO specification 454/TC (January 2013*)

This specification, which is PART ONE of this publication, is based on evaluations of data submitted by the manufacturers whose names are listed in the evaluation reports (454/2005, 454/2007, 454/2009, 454/2011, 454/2012). It should be applicable to TC produced by these manufacturers but it is not an endorsement of those products, nor a guarantee that they comply with the specifications. The specification may not be appropriate for TC produced by other manufacturers. The evaluation reports (454/2005, 454/2007, 454/2009, 454/2011, 454/2012), as PART TWO, form an integral part of this publication.

1 Description

The material shall consist of alpha-cypermethrin together with related manufacturing impurities and shall be a white- to cream-coloured crystalline powder with characteristic odour, free from visible extraneous matter and added modifying agents.

2 Active ingredient

2.1 **Identity tests** (454/TC/(M)/2, CIPAC Handbook H, p.15, 1998)

The active ingredient shall comply with an identity test and, where the identity remains in doubt, shall comply with at least one additional test.

2.2 **Alpha-cypermethrin content** (454/TC/(M)/3, CIPAC Handbook H, p.15, 1998)

The alpha-cypermethrin content shall be declared (not less than 930 g/kg) and, when determined, the average measured content shall not be lower than the declared minimum content.

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* Specifications may be revised and/or additional evaluations may be undertaken. Ensure the use of current versions by checking at:
http://www.fao.org/agriculture/crops/core-themes/theme/pests/jmps/ps-new/en/

ALPHA-CYPERMETHRIN WETTABLE POWDER

FAO specification 454/WP (January 2013*)

This specification, which is PART ONE of this publication, is based on evaluations of data submitted by the manufacturers whose names are listed in the evaluation reports (454/2005, 454/2007, 454/2009, 454/2011). It should be applicable to relevant products of these manufacturers, and those of any other formulators who use only TC from the evaluated sources. The specification is not an endorsement of those products, nor a guarantee that they comply with the specification. The specification may not be appropriate for the products of other manufacturers who use TC from other sources. The evaluation reports (454/2005, 454/2007, 454/2009, 454/2011), as PART TWO, form an integral part of this publication.

1 Description

The material shall consist of a homogeneous mixture of technical alpha-cypermethrin, complying with the requirements of FAO specification 454/TC (January 2013), together with filler(s) and any other necessary formulants. It shall be in the form of a freely flowing fine powder, free from visible extraneous matter and hard lumps.

2 Active ingredient

2.1 **Identity tests** (454/WP/(M)/2, CIPAC Handbook H, p.18, 1998)

The active ingredient shall comply with an identity test and, where the identity remains in doubt, shall comply with at least one additional test.

2.2 **Alpha-cypermethrin content** (454/WP/(M)/3, CIPAC Handbook H, p.18, 1998)

The alpha-cypermethrin content shall be declared (g/kg) and, when determined, the average measured content shall not differ from that declared by more than the following tolerance.

Declared content in g/kg	Tolerance
above 25 up to 100 above 100 up to 250 Note: the upper limit is included in the range.	± 10% of the declared content ± 6% of the declared content

3 Physical properties

3.1 **pH range** (MT 75.3, CIPAC Handbook J, p.131, 2000)

pH range: 4 to 8.

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* Specifications may be revised and/or additional evaluations may be undertaken. Ensure the use of current versions by checking at:
http://www.fao.org/agriculture/crops/core-themes/theme/pests/jmps/ps-new/en/

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3.2 **Wet sieve test** (MT 185, CIPAC Handbook K, p.149, 2003)

Maximum: 2% of the formulation shall be retained on a 75 µm test sieve.

3.3 **Suspensibility** (MT 184, CIPAC Handbook K, p.142, 2003) (Notes 1)

A minimum of 70% of the alpha-cypermethrin content found under 2.2 shall be in suspension after 30 min in CIPAC standard water D at 30 ± 2°C (Note 2).

3.4 **Wettability** (MT 53.3.2, CIPAC Handbook F, p.164, 1995)

The formulation shall be completely wetted in 1 min with swirling.

3.5 **Persistent foam** (MT 47.2, CIPAC Handbook F, p.152, 1995) (Note 3)

Maximum: 60 ml after 1 min.

4 Storage stability

4.1 **Stability at elevated temperature** (MT 46.3, CIPAC Handbook J, p.128, 2000)

After storage at 54 ± 2°C for 14 days, the determined average active ingredient content must not be lower than 95%, relative to the determined average content found before storage (Note 4), and the formulation shall continue to comply with the clauses for:

- pH range (3.1),
- wet sieve test (3.2),
- suspensibility (3.3),
- wettability (3.4).

Note 1 The formulation should be tested at the highest and lowest rates of use recommended by the supplier, provided it does not exceed the conditions given in method MT 184.

Note 2 Chemical assay is the only fully reliable method to measure the mass of active ingredient still in suspension. However, simpler methods such as gravimetric and solvent extraction determination may be used on a routine basis provided that these methods have been shown to give equal results to those of chemical assay. In case of dispute, chemical assay shall be the "referee method".

Note 3 The mass of sample to be used in the test should be at the highest rate of use recommended by the supplier. The test is to be conducted in CIPAC standard water D at 30°C ± 2°C.

Note 4 Samples of the formulation taken before and after the storage stability test should be analyzed concurrently after the test in order to reduce the analytical error.

ALPHA-CYPERMETHRIN SUSPENSION CONCENTRATE

FAO specification 454/SC (January 2013*)

This specification, which is PART ONE of this publication, is based on evaluations of data submitted by the manufacturers whose names are listed in the evaluation reports (454/2005, 454/2007, 454/2009, 454/2011). It should be applicable to relevant products of these manufacturers, and those of any other formulators who use only TC from the evaluated sources. The specification is not an endorsement of those products, nor a guarantee that they comply with the specification. The specification may not be appropriate for the products of other manufacturers who use TC from other sources. The evaluation reports (454/2005, 454/2007, 454/2009, 454/2011), as PART TWO, form an integral part of this publication.

1 Description

The material shall consist of a suspension of fine particles of technical alpha-cypermethrin, complying with the requirements of FAO specification 454/TC (January 2013), in an aqueous phase together with suitable formulants. After gentle agitation the material shall be homogeneous (Note 1) and suitable for further dilution in water.

2 Active ingredient

2.1 **Identity tests** (454/SC/(M)2, CIPAC Handbook H, p.20, 1998)

The active ingredient shall comply with an identity test and, where the identity remains in doubt, shall comply with at least one additional test.

2.2 **Alpha-cypermethrin content** (454/SC/(M)/3, CIPAC Handbook H, p.20, 1998)

The alpha-cypermethrin content shall be declared (g/kg or g/l at 20 ± 2°C, Note 2) and, when determined, the average measured content shall not differ from that declared by more than the following tolerances:

Declared content in g/kg or g/l at 20 ± 2°C	Tolerance
up to 25 above 25 up to 100 above 100 up to 250 Note: in each range the upper limit is included.	± 15% of the declared content ± 10% of the declared content ± 6% of the declared content

3 Physical properties

3.1 **pH range** (1% aqueous dispersion) (MT 75.3, CIPAC Handbook J, p.131, 2000)

pH range: 5 to 8.

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* Specifications may be revised and/or additional evaluations may be undertaken. Ensure the use of current versions by checking at:
http://www.fao.org/agriculture/crops/core-themes/theme/pests/jmps/ps-new/en/

3.2 **Pourability** (MT 148.1, CIPAC Handbook J, p.133, 1995)

Maximum "residue": 3%.

3.3 **Spontaneity of dispersion** (MT 160, CIPAC Handbook F, p.391, 1995) (Notes 3 & 4)

A minimum of 60% of the alpha-cypermethrin content found under 2.2 shall be in suspension after 5 min in CIPAC standard water D at 30 ± 2°C.

3.4 **Suspensibility** (MT 184, CIPAC Handbook K, p.142, 2003) (Note 3)

A minimum of 60% of the alpha-cypermethrin content found under 2.2 shall be in suspension after 30 min in CIPAC standard water D at 30 ± 2°C.

3.5 **Wet sieve test** (MT 185, CIPAC Handbook K, p.149, 2003) (Note 5)

Maximum: 2% of the formulation shall be retained on a 75 µm test sieve.

3.6 **Persistent foam** (MT 47.2, CIPAC Handbook F, p.152, 1995) (Note 6)

Maximum: 60 ml after 1 min.

4 Storage stability

4.1 **Stability at 0°C** (MT 39.3, CIPAC Handbook J, p.126, 2000)

After storage at 0 ± 2°C for 7 days, the formulation shall continue to comply with the clauses for:

- suspensibility (3.4),
- wet sieve test (3.5).

4.2 **Stability at elevated temperature** (MT 46.3, CIPAC Handbook J, p.128, 2000)

After storage at 54 ± 2°C for 14 days the determined average active ingredient content must not be lower than 95%, relative to the determined average content found before storage (Note 7), and the product shall continue to comply with the clauses for:

- pH range (3.1),
- pourability (3.2),
- spontaneity of dispersion (3.3),
- suspensibility (3.4),
- wet sieve test (3.5).

Note 1 Before sampling to verify the formulation quality, inspect the commercial container carefully. On standing, suspension concentrates usually develop a concentration gradient from the top to the bottom of the container. This may even result in the appearance of a clear liquid on the top and/or of sediment on the bottom. Therefore, before sampling, homogenize the formulation according to the instructions given by the manufacturer or, in the absence of such instructions, by gentle shaking of the commercial container (for example by inverting the closed container several times). Large containers must be opened and stirred adequately. After this procedure, the container should not contain a sticky layer of non-dispersed matter at the bottom. A suitable and simple method of checking for a non-dispersed sticky layer "cake" is by probing with a glass rod or similar device adapted to the size and shape of the container. All the physical and chemical tests must be carried out on a laboratory sample taken after the recommended homogenization procedure.

Note 2 Unless homogenization is carried out carefully, it is possible for the sample to become aerated. This can lead to errors in the determination of the mass per millilitre and in the calculation of the active ingredient content (in g/l) if methods other than MT 3.3 are used. If the buyer requires both g/kg and g/l at 20°C, then in case of dispute the analytical results shall be calculated as g/kg.

Note 3 Chemical assay is the only fully reliable method to measure the mass of active ingredient still in suspension. However, simpler methods such as gravimetric and solvent extraction determination may be used on a routine basis provided that these methods have been shown to give results equal to those of the chemical assay method. In case of dispute, the chemical method shall be the referee method.

Note 4 The test should be conducted at 0.5% concentration (248.75 ml water, 1.25 ml formulation, corresponding to the maximum recommended concentration for application), instead of the 5% specified in MT 160.

Note 5 This test detects coarse particles (e.g. caused by crystal growth) or agglomerates (crust formation) or extraneous materials, which could cause blockage of spray nozzles or filters in the spray tank.

Note 6 The mass of sample to be used in the test should correspond to the highest rate of use recommended by the supplier. The test is to be conducted in CIPAC standard water D at 30°C ± 2°C.

Note 7 Samples of the formulation taken before and after the storage stability test should be analyzed concurrently after the test in order to reduce the analytical error.

ALPHA-CYPERMETHRIN EMULSIFIABLE CONCENTRATE

FAO specification 454/EC (January 2013*)

This specification, which is PART ONE of this publication, is based on evaluations of data submitted by the manufacturers whose names are listed in the evaluation reports (454/2005, 454/2007). It should be applicable to relevant products of these manufacturers, and those of any other formulators who use only TC from the evaluated sources. The specification is not an endorsement of those products, nor a guarantee that they comply with the specification. The specification may not be appropriate for the products of other manufacturers who use TC from other sources. The evaluation reports (454/2005, 454/2007), as PART TWO, form an integral part of this publication.

1 Description

The material shall consist of technical alpha-cypermethrin, complying with the requirements of FAO specification 454/TC (January 2013), dissolved in suitable solvents together with any other necessary formulants. It shall be in the form of a stable homogeneous liquid, free from visible suspended matter and sediment, to be applied as an emulsion after dilution with water.

2 Active ingredient

2.1 **Identity tests** (454/EC/(M)/2, CIPAC Handbook H, p.19, 1998)

The active ingredient shall comply with an identity test and, where the identity remains in doubt, shall comply with at least one additional test.

2.2 **Alpha-cypermethrin content** (454/EC/(M)/3, CIPAC Handbook H, p.20, 1998)

The alpha-cypermethrin content shall be declared (g/kg or g/l at 20 ± 2°C, Note 1) and, when determined, the average measured content shall not differ from that declared by more than the following tolerances:

Declared content in g/kg or g/l at 20 ± 2°C	Tolerance
up to 25 above 25 up to 100 above 100 up to 250 Note: in each range the upper limit is included.	± 15% of the declared content ± 10% of the declared content ± 6% of the declared content

3 Physical properties

3.1 **pH range** (1% aqueous emulsion) (MT 75.3, CIPAC Handbook J, p.131, 2000)

pH range: 4 to 8.

* Specifications may be revised and/or additional evaluations may be undertaken. Ensure the use of current versions by checking at: http://www.fao.org/agriculture/crops/core-themes/theme/pests/jmps/ps-new/en/.

3.2 **Emulsion stability and re-emulsification** (MT 36.3, CIPAC Handbook K, p.137, 2003) (Note 2)

The formulation, when diluted at 30 ± 2°C with CIPAC standard waters A and D, shall comply with the following:

Time after dilution	Limits of stability, MT 36.3
0 h	Initial emulsification complete
0.5 h	"Cream", maximum: 2 ml
2 h	"Cream", maximum: 5 ml "Free oil", maximum: 1
24 h	Re-emulsification complete
24.5 h	"Cream", maximum: 5 ml "Free oil", maximum: 1 ml
Note: tests after 24 h are required only where results at 2 h are in doubt.	

3.3 **Persistent foam** (MT 47.2, CIPAC Handbook F, p.152, 1995) (Note 3)

Maximum: 60 ml after 1 min.

4 Storage stability

4.1 **Stability at 0°C** (MT 39.3, CIPAC Handbook J, p.126, 2000)

After storage at 0 ± 2°C for 7 days, the volume of solid and/or liquid which separates shall not be more than 0.3 ml.

4.2 **Stability at elevated temperature** (MT 46.3, CIPAC Handbook J, p.128, 2000)

After storage at 54 ± 2°C for 14 days, the determined average active ingredient content must not be lower than 95% relative to the determined average content found before storage (Note 4) and the product shall continue to comply with the clauses for:

- pH range (3.1),
- emulsion stability and re-emulsification (3.2).

Note 1 If the buyer requires both g/kg and g/l at 20°C, then in case of dispute the analytical results shall be calculated as g/kg.

Note 2 The test will normally be carried out after the heat stability test 4.2. As outlined in CIPAC MT 36.3, the test concentrations should be based on those in the recommended directions for use supplied with the product. Where several concentrations are recommended, the highest and lowest concentrations within the scope of the method should be used.

Note 3 The mass of sample to be used in the test should correspond to the highest rate of use recommended by the supplier. The test is to be conducted in CIPAC standard water D.

Note 4 Samples of the formulation taken before and after the storage stability test should be analyzed concurrently after the test in order to reduce the analytical error.

ALPHA-CYPERMETHRIN ULTRA LOW VOLUME LIQUID

FAO specification 454/UL (January 2013*)

This specification, which is PART ONE of this publication, is based on evaluations of data submitted by the manufacturers whose names are listed in the evaluation reports (454/2005, 454/2007). It should be applicable to relevant products of these manufacturers, and those of any other formulators who use only TC from the evaluated sources. The specification is not an endorsement of those products, nor a guarantee that they comply with the specification. The specification may not be appropriate for the products of other manufacturers who use TC from other sources. The evaluation reports (454/2005, 454/2007), as PART TWO, form an integral part of this publication.

1 Description

The material shall consist of a technical alpha-cypermethrin, complying with the requirements of FAO specification 454/TC (January 2013), together with any necessary formulants. It shall be in the form of a stable homogeneous liquid, free from visible suspended matter and sediment.

2 Active ingredient

2.1 **Identity tests** (454/UL/(M)/2, CIPAC Handbook H, p.21, 1998)

The active ingredient shall comply with an identity test and, where the identity remains in doubt, shall comply with at least one additional test.

2.2 **Alpha-cypermethrin content** (454/UL/(M)/3, CIPAC Handbook H, p.21, 1998)

The alpha-cypermethrin content shall be declared (g/kg or g/l at 20 ± 2°C, Note 1) and, when determined, the average measured content shall not differ from that declared by more than the following tolerances:

Declared content in g/kg or g/l at 20 ± 2°C	Tolerance
up to 25 g/l	± 15% of the declared content
above 25 up to 100	± 10% of the declared content
Note in each range the upper limit is included	

3 Physical properties (Notes 2 and 3)

3.1 **pH range** (MT 75.3, CIPAC Handbook J, p.131, 2000)

pH range: 4 to 8.

* Specifications may be revised and/or additional evaluations may be undertaken. Ensure the use of current versions by checking at: http://www.fao.org/agriculture/crops/core-themes/theme/pests/jmps/ps-new/en/.

4 Storage stability

4.1 **Stability at 0°C** (MT 39.3, CIPAC Handbook J, p.131, 2000)

After storage at 0 ± 2°C for 7 days, the volume of solid and/or liquid which separates shall not be more than 0.3 ml.

4.2 **Stability at elevated temperature** (MT 46.3, CIPAC J, p.128, 2000)

After storage at 54 ± 2°C for 14 days the determined average active ingredient content must not be lower than 95%, relative to the determined average content found before storage (Note 4), and the product shall continue to comply with the clause for:

- pH range (3.1).

Note 1 If the buyer requires both g/kg and g/l at 20°C, then in case of dispute the analytical results shall be calculated as g/kg.

Note 2 Viscosity can be critically important for successful application of a UL formulation but the requirements are dependent upon both the formulation and the application technique or equipment. For this reason, no clause is provided for kinematic viscosity.

Note 3 Loss of droplet mass by volatilization can be critical for UL formulations because, if the losses are significant, the proportion on the spray which drifts from the target, and the distance over which drift occurs, is likely to increase. The volatilization and additional drift that occur in practice are dependent on the initial droplet size spectrum and the height through which droplets fall, the air temperature and wind speed. In addition, a degree of volatilization, which may be unacceptable for one type of application, may be of little or no consequence in another case. At present, no method is available to allow measurement of loss by volatilization to be related to the potential increase in drift and therefore no clause is provided for volatility.

Note 4 Samples of the formulation taken before and after the storage stability test should be analyzed concurrently after the test in order to reduce the analytical error.

PART TWO

EVALUATION REPORTS

ALPHA-CYPERMETHRIN

ALPHA-CYPERMETHRIN

FAO/WHO EVALUATION REPORT 454/2012

Recommendations

The Meeting recommended that:

(i) The alpha-cypermethrin TC as proposed by Bharat Rasayan Limited should be accepted as equivalent to the alpha-cypermethrin reference profile.

(ii) The existing FAO specification for alpha-cypermethrin TC should be extended to encompass the corresponding product of Bharat Rasayan Limited.

(iii) The existing WHO specification for alpha-cypermethrin TC should be extended to encompass the corresponding product of Bharat Rasayan Limited.

Appraisal

The Meeting considered data and information on alpha-cypermethrin submitted by Bharat Rasayan Limited (India) in support of the extension of the existing FAO and WHO TC specifications.

The Meeting was provided with a detailed description of the manufacturing process for the technical grade active ingredient, the 5-batch analysis data for alpha-cypermethrin and all impurities ≥ 1 g/kg and their manufacturing limits in the TC. The manufacturing process utilized by Bharat Rasayan Limited is similar to that from BASF and supported the 5-batch data.

Mass balances in the 5-batch data were high with a narrow range of 99.87-99.93% (batches manufactured from January to March 2010). The minimum purity of alpha-cypermethrin in the TC is 970 g/kg and complies with the existing specification. The percentage of unknowns was from 0.07 to 0.13% and considered acceptable by the Meeting. The manufacturer stated that all impurities > 1 g/kg were quantified. The Meeting concluded that there are no relevant impurities in the TC.

Bharat Rasayan Limited produces alpha-cypermethrin TC at two manufacturing sites, but has provided the 5-batch analysis data for only one manufacturing site. The manufacturer did not submit data for the other manufacturing site and confirmed that purity/impurities profile is similar for the both production sites, and this was considered acceptable by the Meeting.

The CIPAC analytical method published in Handbook H is based on capillary gas chromatography with flame ionization detection (GC-FID) and separates alpha-cypermethrin from diastereomers not belonging to the active ingredient. The company however used an in-house method based on HPLC-UV with external standard calibration. At the request of the Meeting, the manufacturer provided a bridging study where same batches were analysed using the internal HPLC-UV and the CIPAC GC-FID methods. Results of analysis showed that the two methods gave comparable results.

The content of residual solvents used in the manufacturing process of alpha-cypermethrin was determined by GC-FID using the external standard calibration. The Meeting found the methods acceptable. The identity of alpha-cypermethrin and

its impurities in the 5 batches of alpha-cypermethrin TC were confirmed by HPLC or GC based on the retention time and by LC-MS.

The data package (manufacturing process, purity and impurity profile) submitted to FAO/WHO was confirmed by the Central Insecticides Board and Registration Committee of India as being comparable to that submitted for registration in India.

No data on acute toxicity, irritation and sensitization, genotoxicity and ecotoxicology using alpha-cypermethrin TC from Bharat Rasayan Limited have been submitted to the Meeting. Nevertheless the company submitted a study on *in-vitro* mutagenicity indicating negative results for its alpha-cypermethrin TC.

On basis of all Tier-1 data provided by Bharat Rasayan Limited (manufacturing process, impurity profile, 5-batch analysis data, mutagenicity profile), the Meeting concluded that the alpha-cypermethrin TC from Bharat Rasayan Limited should be considered as equivalent to the reference profile supporting the existing FAO and WHO specifications (FAO/WHO evaluation report 454/2005). Bharat Rasayan Limited did not propose specifications for formulated products.

SUPPORTING INFORMATION
FOR
EVALUATION REPORT 454/2012

Physico-chemical properties of alpha-cypermethrin

Table 1. Physico-chemical properties of pure alpha-cypermethrin

Parameter	Value(s) and conditions	Purity %	Method	Reference
Vapour pressure	7.83 x 10^{-5} Pa at 20°C	97.86%	OECD 104, U.S.EPA OPPTS 830.7950	Study Number 10205 06-08-2010
Melting point	81.6 ± 0.0°C	97.86%	U.S. EPA OPPTS 830.7200	Study Number 10202 01-09-2010
Solubility in water	At pH 5.02 : 0.000014 ± 0.000001 g/L at 20 ± 1.0°C At pH 7.05 : 0.000013 ± 0.000001 g/L at 20 ± 1.0°C At pH 9.02 : 0.000016 ± 0.000001 g/L at 20 ± 1.0°C	97.9%	EC A.6, OECD 105, U.S. EPA OPPTS 830.7840	Study Number 10203 15-09-2010
Octanol/water partition coefficient	log P_{OW} = 6.83	97.86%	OECD 117, U.S.EPA OPPTS 830.7570	Study Number 10206 07-09-2010
Solubility in organic solvents	Acetone : >250 g/L 1,2-Dichloroethane : >250 g/L Ethyl acetate : >250 g/L n-Heptane : 10-14 g/L Methanol : 25-29 g/L p-Xylene : >250 g/L at 20 ± 1.0°C	97.86%	CIPAC MT 181	Study Number 10204 20-07-2010

Table 2. Chemical composition and properties of alpha-cypermethrin technical material (TC)

Manufacturing process, maximum limits for impurities ≥ 1 g/kg, 5 batch analysis data	Confidential information supplied and held on file by FAO and WHO. Mass balances were 99.87-99.93%. Percentage of unknowns was 0.07-0.13%.
Declared minimum alpha-cypermethrin content	970 g/kg
Relevant impurities ≥ 1 g/kg and maximum limits for them	None
Relevant impurities < 1 g/kg and maximum limits for them	None
Stabilizers or other additives and maximum limits for them	None
Melting temperature of the TC (97.86% purity)	81.6°C

Formulations

The analytical method for the active ingredient (including identity tests) was HPLC-UV. The manufacturer conducted a bridging study using the CIPAC GC-FID method and a comparison of the batch analyses demonstrated there are no significant differences between the two methods. This confirms that the CIPAC method is applicable to the manufacturer's TC.

Expression of the active ingredient

The active ingredient is expressed as alpha-cypermethrin, in g/kg.

ANNEX 1

HAZARD SUMMARY PROVIDED BY THE PROPOSER

Note:

Bharat Rasayan Limited provided written confirmation that the toxicological data included in the following summary were derived from alpha-cypermethrin having impurity profiles similar to those referred to in Table 2, above.

The conclusions expressed in the summary below are those of the proposer, unless otherwise specified.

Table A. Mutagenicity profile of alpha-cypermethrin technical material based on bacterial *in vitro* tests

Species	Test	Purity %	Conditions and guideline	Result	Reference
S*almonella typhimurium* TA 98, TA 100, TA 1535, TA 1537, TA 102	Ames Mutagenicity test - Bacterial Reverse Mutation assay - In Vitro	98%	Dosage up to 5000 ug/plate on 5 strains of salmonella typhimurium Trial 1 in the absence and presence of 5% v/v S-9 mix at dose levels 156.25, 312.5, 625, 1250, 2500 and 5000 µg/plate Trial 2 in the absence and presence of 10% v/v S-9 mix at dose levels 51.2, 128, 320, 800, 200 and 5000 µg/plate Guideline :OECD 471	Negative	Study Number 481-1-06-2018

ANNEX 2. REFERENCES

Reference of the studies	Year	Title of report or publication details
Study number 10202	2010	Melting point/Melting range of Alphacypermethrin Technical.
Study number 10203	2010	Water solubility of Alphacypermethrin Technical.
Study number 10204	2010	Solubility of Alphacypermethrin Technical in organic solvents.
Study number 10205	2010	Vapour pressure of Alphacypermethrin Technical.
Study number 10206	2010	Partition co-efficient of Alphacypermethrin.
Study number 227-2-12-0977 (part I)	2010	Analysis of five representative production batches of alphacypermethrin technical grade active ingredient (TGAI) to determine % alphacypermethrin and to quantify its associated impurities
Study number 227-2-12-0977 (part II)	2010	Validation of the analytical method for the determination of alphacypermethrin active ingredient and its associated impurities
Study number 481-1-06-2018	2011	Bacterial reverse mutation test of alphacypermethrin technical using *Salmonella typhimurium*.
FAO/WHO Eval. Report 454/2005	2005	FAO/WHO specifications and Evaluation for Public Health Pesticides- Alphacypermethrin. Project/Report no.: FAO/WHO Evaluation Report 454/2005.
FAO/WHO Eval. Report 454/2007	2007	FAO/WHO specifications and Evaluation for Public Health Pesticides- Alphacypermethrin. Project/Report no.: FAO/WHO Evaluation Report 454/2007.
FAO/WHO Eval. Report 454/2009	2009	FAO/WHO specifications and Evaluation for Public Health Pesticides- Alphacypermethrin. Project/Report no.: FAO/WHO Evaluation Report 454/2009.
Pesticide Manual, 2003	2003	Pesticide Manual, 13th Edition, British Crop Protection Council, UK (2003).
CIPAC handbook H	1998	CIPAC 1998, Collaborative International Pesticides Analytical council 1998.

ALPHA-CYPERMETHRIN

FAO/WHO EVALUATION REPORT 454/2011

Recommendations

The Meeting recommended the following.

(i) The existing WHO specifications for alpha-cypermethrin TC, WP and SC should be extended to encompass the corresponding products of Meghmani Organics Limited.

(ii) The existing FAO specifications for alpha-cypermethrin TC, WP and SC should be extended to encompass the corresponding products of Meghmani Organics Limited..

Appraisal

The Meeting considered data and information submitted by Meghmani Organics Limited (India) in support of extension of the existing FAO and WHO specifications for alpha-cypermethrin TC, WP and SC.

The Meeting was provided with a detailed description of the manufacturing process for the technical grade active ingredient and 5-batch analysis data for alpha-cypermethrin and all impurities ≥1 g/kg and their manufacturing limits in the TC. The 5-batch analysis study was performed according to GLP guidelines. The manufacturer stated that all impurities ≥1 g/kg were quantified.

The manufacturing process provided by Meghmani Organics Limited is similar to those supporting the existing FAO and WHO specifications. Mass balances in the 5-batch data were high with a narrow range of 99.55-99.81% (2 batches manufactured on June 2004 and 3 batches manufactured on July 2004). The minimum purity of alpha-cypermethrin in the TC is 950 g/kg and complies with the existing specification. The percentage of unknowns was not declared but as the mass balance is high it was considered acceptable by the Meeting. The Meeting and the manufacturer agreed that there are no relevant impurities in the TC.

Meghmani Organics Limited stated that the manufacturing specifications have been submitted for registration in Australia, Indonesia, Malaysia, China, Saudi Arabia, Syria, Thailand and USA. The manufacturing process and minimum purity of the TC was confirmed by the Australian Pesticides and Veterinary Medicines Authority (APVMA) as being identical to that submitted for registration in Australia. Nevertheless impurities and their maximum limits in the manufacturing specification were not confirmed to be identical to those provided to the APVMA. The Pesticide Board of Malaysia for registration of pesticides confirmed also that the manufacturing process provided to FAO/WHO was more complete than this one provided to them. The 5-batch analysis data were not the same than those provided to FAO/WHO but the Meeting agreed that they were similar.

Alpha-cypermethrin was determined using the CIPAC method 454/TC/M/3 (GC-FID). The diastereoisomers content (*cis* and *trans* impurities) were determined by HPLC-UV using the CIPAC method 332/TC/M/3.2 for cypermethrin. External standard calibration was used to quantify the levels of alpha-cypermethrin and associated

impurities (*cis* and *trans* impurities). The content of solvents used in the manufacturing process of alpha-cypermethrin was determined by GC-FID using the external standard calibration. The Meeting found the methods acceptable. The identity of alpha-cypermethrin and its impurities in the five batches of alpha-cypermethrin TC were confirmed by IR spectroscopy and mass spectrometry.

Meghmani Organics Limited provided data on physical and chemical properties of pure alpha-cypermethrin using a test item with a purity of 97.9% except for photolysis characteristics for which data are from WHO evaluation. The Meeting agreed therefore to not include the photolysis characteristics in the table 1. Results on vapour pressure, solubility in water, hydrolysis, n-octanol/water coefficient partition and melting point are in the range of the data submitted by the reference manufacturer (and other manufacturers). Studies were performed according to GLP guidelines and using OECD methods. A certificate of analysis of the test item used in these studies was provided showing that results are within the proposed specifications.

The same test item was used for studies on skin irritation, eye irritation, skin sensitisation and acute toxicity on fish and toxicity on earthworm. Ames mutagenicity test and some ecotoxicological studies have been performed with a test item with a purity of 98 % for which a certificate of analysis was also provided and showed that results are within the proposed specifications. Other data were generated using a test item with a purity of 98.2 % for which the exact composition is unknown. Nevertheless, as all the impurities were considered as non-relevant, the Meeting considered the studies/results provided as acceptable.

The Meeting concluded that the purity/impurity, acute dermal, skin irritation, eye irritation, mutagenicity, genotoxicity and ecotoxicology profiles of the TC produced by Meghmani Organics Limited indicated equivalence with the reference profile supporting the existing FAO and WHO specifications (FAO/WHO evaluation report 454/2005).

A full CIPAC method is available for the determination of alpha-cypermethrin in the TC and all formulations for which specifications were proposed. The Meeting concluded that the specification for alpha-cypermethrin TC complies with the existing FAO/WHO specification. Regarding the specifications for formulations produced by Meghmani Organics Limited, modification and clarification were required to the manufacturer in order to comply with the published specifications, and the Meeting finally agreed that the WP and SC formulations comply with the existing FAO/WHO specifications.

The Meeting proposed to amend the specification for the WP to take into account the 50 g/kg formulation produced by Meghmani Organics Limited. The table of tolerances for the active ingredient content was therefore modified to include the WP containing 50 g/kg of alpha-cypermethrin.

The Meeting agreed also to update in the SC specification the CIPAC methods for some physical properties (pourability - MT 148.1 instead of MT 148, suspensibility - MT 184 instead of MT 161) to be in line with the guideline for SC specification of the November 2010 – second revision of the first edition of the FAO/WHO Manual and the CIPAC methods actually recommended.

SUPPORTING INFORMATION
FOR
EVALUATION REPORT 454/2011

Physico-chemical properties of alpha-cypermethrin

Table 1. Physico-chemical properties of pure and technical alpha-cypermethrin

Parameter	Value(s) and conditions	Purity %	Method	Reference
Vapour pressure	2.11 x 10^{-5} Pa at 20°C measurement made with powder active substance 3 97 x 10^{-4} Pa at 40°C	97.9%	OECD guideline 104	Report 07162
Melting point	Melting point: 80-82°C	97.9%	OECD guideline 102	Report 07163
Boiling point, temperature of decomposition	Decomposition temperature: 270°C	97.9%	OECD guideline 103	Report 07164
Solubility in water	0.01 mg/L at 20 ± 0.5°C	97.9 %	OECD guideline 105	Report 07165
Octanol/water partition coefficient	log P_{OW} = 6.25 - 6.27 at 23°C and pH 4-7 log P_{OW} = 5.57 at 23°C and pH 9	97.9%	OECD guideline 107	Report 07166
Hydrolysis characteristics	DT_{50} : 8.94 - 17.34 d at pH 9 and 50°C and 20°C respectively	97.9%	OECD Guideline 111	Report 07167
Dissociation characteristics	Does not dissociate	97.9%	OECD Guideline 112	Report 07168

Table 2. Chemical composition and properties of alpha-cypermethrin technical material (TC)

Manufacturing process, maximum limits for impurities ≥1 g/kg, 5 batch analysis data	Confidential information supplied and held on file by FAO and WHO. Mass balances were 99.55-99.81%. Percentage of unknows not given but calculated to be < 0.5%.
Declared minimum alpha-cypermethrin content	950 g/kg
Relevant impurities ≥ 1 g/kg and maximum limits for them	None
Relevant impurities < 1 g/kg and maximum limits for them	None
Stabilizers or other additives and maximum limits for them	None
Melting temperature of the TC	80-82°C

Formulations

Meghmani Organics Limited stated that the main formulations available are EC, SC, WP and UL formulations. These formulations are registered and sold in many countries in Europe, South Africa, Australia and Asia.

Nevertheless Meghmani Organics Limited has deposited specifications only for TC, WP and SC formulations. SC formulations are used in agriculture and for public health programme and WP formulations are used in public health programme only.

Methods of analysis and testing

Specifications for alpha-cypermethrin TC and formulations produced by Meghmani Organics Limited comply with the existing FAO/WHO specifications. CIPAC methods are available for determination of alpha-cypermethrin in TC and formulations and for the determination of the physico-chemical properties of the WP and SC formulations.

ANNEX 1

HAZARD SUMMARY PROVIDED BY THE PROPOSER

Note: Meghmani Organics Limited provided written confirmation that the toxicological data included in the following summary were derived from alpha-cypermethrin having impurity profiles similar to those referred to in Table 2, above.

Table A. Toxicology profile of the alpha-cypermethrin technical material, based on acute toxicity, irritation and sensitization

Species	Test	Purity %	Guideline, duration, doses and conditions	Result	Reference
Wistar Rats (5 m and 5 f)	Acute oral	98.2%	OECD 401 Duration : 14 days Dosage : 0, 90, 108, 130 mg/kg bw	LD_{50} = 98 (85-112) mg/kg bw	Report JRF/1157
Wistar Rats (5 m and 5 f)	Acute dermal	98.2%	OECD 402 Duration : 14 days Dosage : 0, 2000 mg/kg bw	LD_{50} > 2000 mg/kg bw	Report 1158
Wistar Rats (5 m and 5 f)	Acute Inhalation	98.2%	OECD 403 Duration : 14 days Dosage : 0, 0.376, 0.745, 1.485 mg/l	LC_{50} = 0.510 (0.305-0.854) mg/l	Report 1159
Rabbit, New Zealand white male and female	Skin irritation	97.9%	OECD 404 Duration : after 1, 24, 48, 72 hour Dosage : 0.5 gm	Non irritant	Report 07169
Rabbit, New Zealand white (3 f)	Eye irritation	97.9%	OECD 405 Duration : after 1, 24, 48, 72 hour Dosage : 100 mg	Non irritant	Report 07170
Guinea pigs *Cavia porcellus* (20 m)	Skin sensitisation	97.9%	OECD 406 Duration : 28 days Dosage : 2000 mg	Non sensitizer	Report 07171

Table B. Mutagenicity profile of the technical material based on in vitro and in vivo tests

Species	Test	Purity %	Guideline, duration, doses and conditions	Result	Reference
S*alomonella typhimurium* TA 98, TA 100, TA 1535, TA 1537	Ames Mutagenicity test - Bacterial Reverse Mutation assay - In Vitro	98%	Guideline : OECD 471 Dosage : 0.5, 5.0, 50, 500 or 5000 µg/plate	negative	Report 10708
Albino Mice	Chromosomal aberration test in bone marrow	98.2%	Guideline : OECD 475 Dosage : oral dose of 20 mg/kg bw (1 day)	negative	Report 1166
Albino Mice (Bone marrow)	Micronuclei test	98.2%	Guideline : OECD 474 Dosage : 5, 10, 20 mg/kg bw	negative	Report 1167

Table C. Ecotoxicology profile of the technical material

Species	Test	Purity %	Guideline, duration, doses and conditions	Result	Reference
Daphnia magna (water flea)	Acute toxicity	98%	Guideline : OECD 202 Duration : 24 hour Dosage : 0, 0.04, 0.06, 0.09, 0.135, 0.2 µg/l	EC_{50} = 0.09 µg/l (Range : 0.07-0.11)	Report 1164
Chlorella vulgaris (Green Alga)	Growth Inhibition	98%	Guideline : OECD 201 Duration : 24, 48, 72 hour	EC_{50}(72 hrs) = 6.89 µg/ml	Report 10755
Danio rerio (Fresh water fish)	Acute toxicity	97.90%	Guideline : OECD 203 Duration : 24, 48, 72, 96 hour mortality Dosage : 0, 1.0, 1.60, 2.56, 4.10, 6.55 ug/l	LC_{50} = 2.20 µg/l at 24 h (Range : 1.65 - 2.75) LC_{50} = 2.14 µg/l at 48 h (Range : 1.65 - 2.63) LC_{50} = 2.04 µg/l at 72 h (Range : 1.55 - 2.53) LC_{50} = 1.84 µg/l at 96 h (Range : 1.41 - 2.2)	Report 07172
Eisenia fetida	(Earthworm)	97.90%	Guideline: OECD 207 Acute toxicity Dosage : 62.50 - 1000 mg/kg (dry wt. of soil)	LC_{50} >1000 mg/kg of soil	Report 07173
Honeybees *(Apis indica)*	Acute toxicity	98%	Guideline : EPPO 170 Duration : 24 hour	LD_50 = 0.027 µg/bee	Report 10382
Coturnix coturnix japonica (Japanese Quails)	Dietary toxicity	98%	Guideline : OECD 205 Duration : 8 days Dosage : 200, 400, 800, 1600, 3200 ppm	LC_{50} = 1230.60 ppm (Range : 951.63 - 1509.56 ppm)	Report 10416

ANNEX 2. REFERENCES

Reference of the studies	Date	Title of report or publication details
Study No. 14920	01/10/2004	Alphacypermethrin Technical: Five Batch Analysis
Study No. 07162	12/12/2007	Alphacypermethrin Technical: Laboratory Study on Vapour Pressure
Study No. 07163	17/12/2007	Alphacypermethrin Technical: Laboratory Study on Melting Point
Study No. 07164	17/12/2007	Alphacypermethrin Technical: Laboratory Study on Boiling Point
Study No. 07165	12/12/2007	Alphacypermethrin Technical: Laboratory Study of Water Solubility
Study No. 07166	19/12/2007	Alphacypermethrin Technical: Laboratory Study of partition coefficient
Study No. 07167	11/12/2007	Hydrolysis of Alphacypermethrin in Buffer Solutions of pH 4, 7 and 9
Study No. 07168	19/12/2007	Alphacypermethrin Technical: Laboratory Study of Dissociation Constant
Study No. 1157	29/12/1997	Acute oral toxicity study of Alphacypermethrin Technical in rat
Study No. 1158	11/03/1998	Acute dermal toxicity study of Alphacypermethrin Technical in rats
Study No. 1159	18/09/1997	Acute Inhalation toxicity study of Alphacypermethrin Technical to rats
Study No. 07169	01/02/2008	A Study on Acute Dermal irritation of Alphacypermethrin Technical in New Zealand white rabbits
Study No.: 07170	01/02/2008	A study on Acute Eye Irritation of Alphacypermethrin Technical in New Zealand White Rabbits
Study No. 07171	01/02/2008	Skin Sensitization Potential of Alphacypermethrin Technical in Guinea Pigs
Study No. 10708	15/05/2002	Mutagenecity evaluation of Alphacypermethrin Technical by Ames Salmonella Typhimurium- Reverse mutation Assay
Study No. 1166	18/12/1997	Chromosomal aberration Study of Alphacypermethrin technical to mice
Study No. 1167	18/12/1997	Micronucleus test of Alphacypermethrin technical to mice
Study No. 1164	01/09/1997	Alphacypermethrin Technical: Acute immobilization test to Daphnia Magna
Study No. 10755	15/05/2002	Effect of Alphacypermethrin Technical on the Growth of Green Alga (Chlorella vulgaris)
Study No. 07172	27/02/2008	Acute toxicity study of Alphacypermethrin Technical to Freshwater fish (Danio rerio)
Study No. 07173	27/02/2008	Toxicity of Alphacypermethrin Technical to Earthworm, Eisenia fetida
Study No. 10382	21/05/2008	Toxicity of Alphacypermethrin Technical to Honey Bee, Apis indica
Study No. 10416	30/04/2002	Dietary toxicity study with Alphacypermethrin Technical in Japanese Quails
Pesticide Manual	2003	13th Edition, British Crop Protection Council, UK
WHO	2006	WHO Specification and Evaluations for Public Health Pesticides - Alphacypermethrin

ALPHA-CYPERMETHRIN

FAO/WHO EVALUATION REPORT 454/2009

Recommendations

The Meeting recommended the following.

(i) The existing WHO specifications for alpha-cypermethrin TC, WP and SC should be extended to encompass the corresponding products of Gharda Chemicals Limited.

(ii) The existing FAO specifications for alpha-cypermethrin TC, WP and SC should be extended to encompass the corresponding products of Gharda Chemicals Limited.

Appraisal

The Meeting considered data and information submitted by Gharda Chemicals Limited (India) in support of extension of the existing FAO and WHO specifications for alpha-cypermethrin TC, WP and SC.

The Meeting was provided a detailed description of the manufacturing process for the technical grade active ingredient, 5-batch analysis data (GLP study) for alpha-cypermethrin and all impurities ≥1 g/kg and their manufacturing limits in the TC. The manufacturing process provided by Gharda is similar to those supporting the existing FAO and WHO specifications. Mass balances for the 5-batch data (batches manufactured on September 1998) were 99.39-100.1%. A narrow range of mass balances was observed in the batches. The percentage of unknowns was not declared but it was considered acceptable by the Meeting. The declared impurities content ranged from 5 to 35 g/kg. No relevant impurities were declared and it was accepted by the Meeting. The Meeting agreed that the purity/impurity profile of Gharda TC indicated equivalence with the reference profile supporting the existing FAO and WHO specifications.

In the primary dossier, alpha-cypermethrin and impurities (*cis* and *trans* impurities) content were determined using HPLC with UV detection and external standard calibration. This method was validated. Reagents or solvents were determined using a titrimetric method or GC-FID, respectively, depending on the nature of the compound. As the HPLC-UV method used for determination of alpha-cypermethrin in the TC is not the CIPAC method, the Meeting required new batch analysis using the CIPAC method 454/TC/M/3 (GC-FID method). The new batch analysis data (performed according to GLP guidelines) were received on March 2009. These batches were manufactured from December 2007 to May 2008. Alpha-cypermethrin content ranged from 98.0 % to 98.5 %. For comparison, the same batches were analysed using HPLC-UV and the CIPAC method (GC-FID), and the Meeting concluded that results are similar. The alpha-cypermethrin content in the TC is in compliance with the existing FAO and WHO specifications. Following the request of the Meeting, Gharda Chemicals Limited provided also data on the content of two non-relevant impurities. No detectable residue was found.

Gharda stated that the manufacturing specifications have been submitted for registration in Argentina, Australia, India, China and Taiwan. The impurities and their maximum limits in the manufacturing specifications were confirmed to be

identical to the alpha-cypermethrin impurity profile provided to the Australian authorities for support of registration.

The Meeting agreed to consider the studies for the physical and chemical properties (GLP studies) acceptable and similar to those provided by previous proposers Nevertheless, an explanation was required regarding the solubility in water for which results were given in mg/L and not in µg/L as given in studies submitted by other applicants. A new study was provided in March 2009 indicating that the unit of the first results for the solubility in water was wrong. In the new study, a value of 6 µg/L was given and it was accepted by the Meeting.

The studies on acute dermal, skin irritation, eye irritation, mutagenicity, genotoxicity submitted by Gharda were performed according to GLP guidelines. Results are in accordance with the data provided by previous applicants and supporting the existing FAO and WHO specifications.

Ecotoxicological studies are old, not performed according to GLP and not performed on the same species than those of the reference profile. The studies on toxicity to honeybees provided by Gharda showed that the effect of alpha-cypermethrin Gharda was comparable to those previously provided by other proposers. Data on daphnia and earthworm were not considered because not performed using the alpha-cypermethrin TC from Gharda.

On basis of all the data provided by Gharda (manufacturing process, impurity profile, 5-batch analysis data, physical and chemical properties of active ingredient, chemical composition of TC and toxicological data), the Meeting concluded that the Gharda alpha-cypermethrin TC is equivalent to the reference profile supporting the existing FAO and WHO specifications (FAO/WHO evaluation report 454/2005).

Full CIPAC methods are available for determination of alpha-cypermethrin in the TC and formulations (WP, SC) for which specifications were proposed. The Meeting agreed that specifications for alpha-cypermethrin TC and formulations (WP, SC) produced by Gharda (WP, SC) comply with the existing FAO/WHO specifications.

SUPPORTING INFORMATION
FOR
EVALUATION REPORT 454/2009

Physico-chemical properties of alpha-cypermethrin

Table 1. Physico-chemical properties of pure and technical alpha-cypermethrin

Parameter	Value(s) and conditions	Purity %	Method	Reference
Vapour pressure	9.0×10^{-6} Pa at 25°C	95%	EEC A.4	1 C.AMO.029
Melting point, boiling point and/or temperature of decomposition	Melting point: 81-83°C	95%	OECD guideline 102	2 C.AMO.027
Solubility in water	6 µg/L (at 20 ± 0.5°C and pH ≈ 7)	97.8 %	OECD guideline 105	3 C.AMO.059
Octanol/water partition coefficient	log P_{OW} = 6.64 at 25 °C	95%	OECD guideline 107	4 C.AMO.033
Hydrolysis characteristics	No information	95%	OECD Guideline 105	5 C.AMO.034
Photolysis characteristics	No information	95%	EPA guideline, "Photolysis of aqueous solution in sunlight CG-6000"	6 C.AMO.039
Dissociation characteristics	The structure indicates that it is unlikely to undergo dissociation	-	-	-

Table 2. Chemical composition and properties of alpha-cypermethrin technical material (TC)

Manufacturing process, maximum limits for impurities ≥1 g/kg, 5 batch analysis data	Confidential information supplied and held on file by FAO and WHO. Mass balances were 99.39-100.1%. Percentage of unknows not given but calculated to be < 0.6%.
Declared minimum alpha-cypermethrin content	950 g/kg
Relevant impurities ≥ 1 g/kg and maximum limits for them	None
Relevant impurities **<** 1 g/kg and maximum limits for them	None
Stabilizers or other additives and maximum limits for them	None
Melting temperature of the TC	81-83°C

Formulations

Gharda Chemicals Limited stated that:

- Alpha-cypermethrin 10 EC is sold in Argentina, Bulgaria, Estonia, France, Hungary, Kazakastan, Moldova, Kenya, Poland, Ukraine and Taiwan.
- Alpha-cypermethrin 5 WP is sold in India and Nepal.
- Alpha-cypermethrin 10 SC is sold in India.

Gharda has deposited specifications only for TC, WP and SC formulations used in public health programme. However the EC formulation complies with FAO specifications.

Methods of analysis and testing

Specifications for alpha-cypermethrin TC and formulations produced by Gharda comply with the existing FAO/WHO specifications. Existing CIPAC methods are given in the specifications for the determination of alpha-cypermethrin in TC and formulations.

ANNEX 1

HAZARD SUMMARY PROVIDED BY THE PROPOSER

Note: Gharda Chemicals Limited provided written confirmation that the toxicological data included in the following summary were derived from alpha-cypermethrin having impurity profiles similar to those referred to in Table 2, above.

Table A. Toxicology profile of the alpha-cypermethrin technical material, based on acute toxicity, irritation and sensitization

Species	Test	Purity %	Guideline, duration, doses and conditions	Result	Reference
Rat (Albino)	Acute oral	97.5	OECD 401	LD_{50} = 360 mg/kg bw	7 T.AMO.070
Rat (Albino)	Acute dermal	97.5	OECD 402	LD_{50} > 2000 mg/kg bw	8 T.AMO.036
Rat (Albino)	Acute Inhalation	97.5	OECD 403	LC_{50} > 0.593 mg/l	9 T.AMO.073
Rabbit, New Zealand white	Skin irritation	97.5	OECD 404	Non irritant	10 T.AMO.072
Rabbit, New Zealand white	Eye irritation	97.5	OECD 405	Not irritant to eyes	11 T.AMO.074
Guinea pig	Skin sensitisation	97.5	OECD 406	Non sensitizer	12 T.AMO.122

Table B. Toxicology profile of the technical material based on repeated administration (sub-acute to chronic)

Species	Test	Purity %	Guideline, duration, doses and conditions	Result	Reference
Rat (Wistar)	Sub acute oral	97.5	90 days	Did not show any toxicity up to the dose of 4000 ppm	13 T.AMO.007
Dog (Mongrel)	Sub acute oral	97.5	90 days	NOEL: 3 mg/kg/day	14 T.AMO.008
Rabbit (Albino)	Sub acute dermal	97.5	21 days	NOEL: 2000 mg/kg/day	15 T.AMO.009
Rat (Wistar)	Sub acute inhalation	97.5	14 days	NOEL: 0.029 mg/l	16 T.AMO.010
Mice (Albino)	Carcinogenecity	99.0	Dose: M: 6.5, 13.0 and 65 ppm/kg/day F: 7.8, 15.6 & 78 ppm/kg/day Period: 24 months	NOEL: M: 65 mg/kg/day F: 78 mg/kg/day	17 T.AMO.013
Rat (Albino)	Teratogenecity & developmental toxicity	99.0	Dose: 5,10 and 20 mg/kg/day Duration: 24 months	No teratological potential for rats	18 T.AMO.020
Rat (Albino)	2 generation reproduction study	99.0	Dose: 2.5,10, 25 mg/kg/day Duration: 2 years	No adverse reproductive effects	19 T.AMO.011
Chicken	Delayed neurotoxicity	99.0	Dose: 0, 70, 140 and 700 mg/kg bw Duration:21 days	Does not have neurotoxic potential NOEL: 70 mg/kg bw	20 T.AMO.016

Table C. Mutagenicity profile of the technical material based on in vitro and in vivo tests

Species	Test	Purity %	Guideline, duration, doses and conditions	Result	Reference
S*alomonella Typhimurium* TA 98, TA 100, TA 1535, TA 1537 and one tryptophan dependent auxotroph of *Escherichia coli*, strain CM891	Bacterial reverse mutation assay	97.8	OECD (5) Concentrations up to 5000 μg/plate	Non-mutagenic	21 T.AMO.015
Albino Mice (Bone marrow)	Chromosomal aberration test	97.8	Gaitonde Committee Guideline Dosages: 6.5, 12.5 and 25 mg/kg	Non mutagenic	22 T.AMO.014
Albino Mice (Bone marrow)	Dominant lethal test	97.8	Gaitonde Committee Guideline Dosages: 5, 10 and 15 mg/kg 5 consecutives days	Non mutagenic	22 T.AMO.014
Albino Mice (Bone marrow)	Micronuclei test	97.8	Gaitonde Committee Guideline Dosages: 5, 25 and 30 mg/kg	Non mutagenic	22 T.AMO.014

Table D. Ecotoxicology profile of the technical material

Species	Test	Purity %	Guideline, duration, doses and conditions	Result	Reference
Fresh water fish (*Tilapia mussambica)*	Acute toxicity	99.0	Litchfield & Wilcoxon method Duration: 10 days at room temperature Dosage: 1, 10, 100 and 1000 ppm	LC_{50}: > 1000 ppm	24 T.AMO.023
Honeybees *(Apis indica)*	Acute toxicity	99.0	Duration : 12 h Temp: 28 ± 2°C Topical application	LC_{50} (24 h): 0.044 μg/bee	25 T.AMO.024
Chicken	Acute oral toxicity (MLD)	99.0	Litchfield & Wilcoxon method (1949) Duration: 14 days Test levels: 4000, 6000, 7000,8000 and 12000 mg/kg	LD_{50}: 7000 ± 800 mg/kg	26 T.AMO.022
Pigeon	Acute oral Toxicity (MLD)	99.0	Duration: 21 days Test levels:1000, 2000, 4000 and 8000 mg/kg	MLD: 2500 mg/kg	27 T.AMO.021

ANNEX 2. REFERENCES

Gharda document number or other references		Year	Title of report or publication details
1	C.AMO.029	2000	Physical & chemical characteristics of Alpha-cypermethrin - vapour pressure
2	C.AMO.027	2000	Physical & chemical characteristics of Alpha-cypermethrin - Melting point
3	C.AMO.031	2000	Physical & chemical characteristics of Alpha-cypermethrin – solubility in water
	C.AMO.059	2009	Physical & chemical characteristics of Alpha-cypermethrin – solubility in water
4	C.AMO.033	2000	Physical & chemical characteristics of Alpha-cypermethrin – n-Octanol/Water partition coefficient
5	C.AMO.034	2000	Physical & chemical characteristics of Alpha-cypermethrin – Hydrolysis
6	C.AMO.039	2000	Physical & chemical characteristics of Alpha-cypermethrin – Direct photo-transformation in water
7	T.AMO.070	1994	Acute oral toxicity to Albino rat
8	T.AMO.036	1992	Acute dermal toxicity study in rat
9	T.AMO.073	1994	Acute inhalation toxicity to Albino rat
10	T.AMO.072	1994	Acute dermal irritation / corrosion study in rabbit
11	T.AMO.074	1994	Acute eye irritation / corrosion study in rabbit
12	T.AMO.122	2007	Skin sensitisation test in Guinea pig
13	T.AMO.007	1988	Sub acute oral toxicity for 90 days in Rats
14	T.AMO.008	1988	Sub acute oral toxicity in Dogs (for 90 days)
15	T.AMO.009	1988	Sub acute dermal toxicity (for 21 days in Rabbits)
16	T.AMO.010	1988	Sub acute inhalation toxicity in Rats (for 14 days)]
17	T.AMO.013	1989	Long-term carcinogenicity in Albino mice
18	T.AMO.020	1989	Teratogenicity studies in Rats
19	T.AMO.011	1989	Reproduction study in Rats
20	T.AMO.016	1989	Delayed neurotoxicity study in chicken
21	T.AMO.015	1998	Bacterial Mutation Assay
22	T.AMO.014	1989	Mutagenicity studies – chromosomal aberration test, Dominant Lethal test, Micronuclei test
23	Pesticide Manual		The Pesticide Manual 13th Edn. – Alpha-cypermethrin, Crop Protection Publication
24	T.AMO.023	1988	Acute toxicity to fresh water fish
25	T.AMO.024	1988	Acute toxicity to honey bees (*Apis indica)*
26	T.AMO.022	1988	Acute toxicity (MLD) in chicken
27	T.AMO.021	1988	Acute oral toxicity (MLD) to Pigeon

ALPHA-CYPERMETHRIN

FAO/WHO EVALUATION REPORT 454/2007

Recommendations

The Meeting recommended the following.

(i) The existing WHO specifications for alpha-cypermethrin TC, WP and SC, should be extended to encompass the products of Heranba Industries Ltd.

(ii) The existing FAO specifications for alpha-cypermethrin TC, WP, SC, EC, UL, should be extended to encompass the products of Heranba Industries Ltd.

(iii) The emulsion stability clause of the existing FAO specification for alpha-cypermethrin EC should be corrected, to refer to CIPAC method MT 36.3 instead of MT 173.

Appraisal

The Meeting considered data and information submitted by Heranba Industries Ltd (Mumbai, India) in support of extension of the existing FAO and WHO specifications.

The Meeting was provided a detailed description of the manufacturing process for the technical grade active ingredient, 5-batch analysis data for all impurities ≥1 g/kg and their manufacturing limits in the TC. Mass balances for the 5-batch data (batches manufactured in 2005) were 99.85-99.94%, with no unknowns. The narrow range of mass balances reflected the uniformly high purity of TC batches and use of a very accurate and precise analytical method (6293). The data were confirmed to be identical to those submitted in support of registration in Thailand and were stated also to be identical to those submitted in support of registration India.

Certain impurities, initially proposed as relevant by the manufacturer, were agreed to be non-relevant, in accordance with the manual (FAO/WHO 2006).

The Meeting agreed that the purity/impurity, acute toxicology, mutagenicity and ecotoxicology profiles of Heranba TC indicated equivalence with the reference profile supporting the existing FAO and WHO specifications (FAO/WHO evaluation report 454/2005).

Heranba alpha-cypermethrin TC was classified by the manufacturer as a “minimal irritant” of eyes, which is an unusual designation. Following discussion, the manufacturer agreed that “mild irritant” would be an appropriate classification.

Heranba confirmed that the alpha-cypermethrin TC and formulations produced by the company comply with existing FAO and WHO specifications. The company also confirmed that existing CIPAC methods for identification and determination of alpha-cypermethrin were acceptable for analysis of the company’s TC and formulations.

The Meeting noted that the emulsion stability clause of the existing FAO specification for alpha-cypermethrin EC referred, incorrectly, to CIPAC method MT 173. The specified limits related, correctly, to CIPAC method MT 36.3 and the method reference should therefore be corrected.

SUPPORTING INFORMATION
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Physico-chemical properties of alpha-cypermethrin

Table 1. Physico-chemical properties of pure alpha-cypermethrin

Parameter	Value(s) and conditions	Purity %	Method	Reference
Vapour pressure	3.85×10^{-5} Pa at 20°C 2.45×10^{-4} Pa at 40°C	97.83	EEC A.4, OECD 104	06181
Melting point	78-80°C	97.83	EEC A.1, OECD 102	06182
Temperature of decomposition	218-221ºC	97.83	OECD 103	06182
Solubility in water	0.01 mg/l at 20 ± 0.5°C	97.83	EEC A.6, OECD 105	06183
Octanol/water partition coefficient	K_{ow} log P = 6.29 ± 0.02, at 23 ± 1ºC	97.83	EEC A.8, OECD 107	06184
Hydrolysis characteristics	Aqueous abiotic hydrolysis should not contribute significantly to degradation at pH 4 but would contribute significantly at pH 7 and 9.	97.83	EEC C.7, OECD 111	06180

Table 2. Chemical composition and properties of technical alpha-cypermethrin (TC)

Manufacturing process, maximum limits for impurities ≥1 g/kg, 5 batch analysis data	Confidential information supplied and held on file by FAO and WHO. Mass balances were 99.85-99.94%, with no unknowns.
Declared minimum alpha-cypermethrin content	950 g/kg
Relevant impurities ≥ 1 g/kg and maximum limits for them	None
Relevant impurities < 1 g/kg and maximum limits for them	None
Stabilizers or other additives and maximum limits for them	None
Melting temperature of the TC	78-80°C

Formulations

Heranba alpha-cypermethrin formulations are registered and sold in India and Thailand.

Methods of analysis and testing

Heranba confirmed that the existing CIPAC methods for the determination of active ingredient content and for testing physical properties are satisfactory for use with their products.

ANNEX 1

HAZARD SUMMARY PROVIDED BY THE PROPOSER

Note: Heranba provided written confirmation that the toxicological data included in the following summary were derived from alpha-cypermethrin having impurity profiles similar to those referred to in Table 2, above.

Table A. Toxicology profile of alpha-cypermethrin technical material, based on acute toxicity, irritation and sensitization

Species	Test	Purity %	Duration and conditions or guideline adopted	Result	Reference
Rat, Wistar (m,f)	Oral	97.83	OECD 401 Observation: 14 days Dosage: 0, 100, 150 & 200 mg/kg bw Vehicle: corn oil	LD_{50} = 118.51 mg/kg bw (f) LD_{50} = 138.98 mg/kg bw (m) (118.79 to 159.19)	06165
Rat, Wistar (m,f)	Dermal	97.83	OECD 402 Observation: 14 days Dosage: 0 & 2000 mg/kg bw	LD_{50} >2000 mg/kg bw	06166
Rat, (m,f)	Inhalation	97.83	OECD 403 Observation: 14 days Dosage: 0, 0.35, 0.75 & 1.02 mg/l	LC_{50} = 0.70 mg/l (0.61 to 0.79)	06169
Rabbit	Skin irritation	97.83	OECD 404 Observation: 1, 24, 48 & 72 h after treatment Dosage: 500 mg (4 h)	Non-irritant	06167
Rabbit	Eye irritation	97.83	OECD 405 Observation: 1, 24, 48 & 72 h after treatment Dosage: 100 mg	Mild irritant	06168
Guinea pig (m)	Skin sensitization	97.83	OECD 406 Observation: 28 d Dosage: 250 mg	Non-sensitizer	06170

Table B. Mutagenicity profile of technical alpha-cypermethrin based on *in vitro* and *in vivo* tests

Species	Test	Purity %	Guideline & conditions	Result	Reference
Salmonella typhimurium	Ames test, reverse mutation assay *in vitro*	97.83	OECD 471 Doses: 1000, 320, 100, 32 & 10 µg/plate ± S9 activation	Negative	06171
Mouse	Micronucleus assay, *in vivo*	97.83	OECD 474 Doses: 20, 10 & 5 mg/kg bw Vehicle: vegetable oil	Negative	06172
Human lymphocytes	Chromosomal aberration, *in vitro*	97.83	OECD 473 Culture 32 h (incubated 4 h) Doses, pre-test: 5000, 2000 & 1000 µg/ml ± S9. Doses, main study: 200, 100, 50, 25 & 12.5 µg/ml ± S9	Negative	06173

Table C. Ecotoxicology profile of technical alpha-cypermethrin

Species	Test	Guideline & conditions	Result	Reference
Daphnia magna (water flea)	Acute immobilization test	OECD 202 Dosage: 0.08, 0.18, 0.39, 0.85 & 1.87 µg/l, purity: 97.83%	EC_{50} (48 h) = 0.57 µg/l (0.50-0.64 µg/l)	06175
Poecilia reticulata (freshwater fish)	Acute toxicity	OECD 203 Dosage: 4, 5.6, 7.8, 11 & 15.4 µg/l (semi-static bioassay), purity: 97.83%	LC_{50} (24 h) >15.4 µg/l LC_{50} (48 h) = 12.28 µg/l LC_{50} (72 h) = 9.26 µg/l LC_{50} (96 h) = 8.36 µg/l	06174
Lampito mauritii (earthworm)	Acute toxicity	OECD 207 Dosage : 62.5-1000 mg/kg dry soil, purity 97.83%	LC_{50} >1000 mg/kg dry wt. (14 d)	06179
Apis mellifera (honey bee)	Acute oral toxicity	OECD 213 Purity 97.83%	LD_{50} = 0.015 µg/bee (48 h)	06177
	Acute contact toxicity	OECD 214 Dosage: 0.0025, 0.0044, 0.0077, 0.013, 0.023 & 0.041 µg/bee, purity 97.83%	LD_{50} = 0.010 µg/bee (48 h)	06178
Coturnix coturnix japonica (Japanese quail)	Dietary toxicity	OECD 205 Dosage: 5000 ppm; 5 days, purity 97.83%	LC_{50} >5000 ppm	06176

ANNEX 2. REFERENCES

Heranba document number or other reference	Year and title of report or publication details
06180	2007. Hydrolysis of alpha cypermethrin in buffer solutions of pH 4, 7, 9.
06181	2007. Alpha cypermethrin technical – Laboratory study of vapour pressure.
06182	2006. Alpha cypermethrin technical – Laboratory study on melting point and boiling point.
06183	2006. Alpha cypermethrin technical – Laboratory study of water solubility.
06184	2006. Alpha cypermethrin technical – Laboratory study of partition coefficient.
06165	2006. Acute oral toxicity study with Alpha cypermethrin technical in Wistar rats.
06166	2006. Acute dermal toxicity study with Alpha cypermethrin technical in Wistar rats.
06167	2006. A study on primary skin irritation of Alpha cypermethrin technical in New Zealand white rabbits.
06168	2006. A study on eye irritation of Alpha cypermethrin technical in New Zealand white rabbits.
06169	2006. Acute inhalation toxicity study with Alpha cypermethrin technical in Wistar rats.
06170	2006. Skin sensitisation potential of Alpha cypermethrin technical in guinea pigs.
06171	2006. Mutagenicity evaluation of Alpha cypermethrin technical by Ames *Salmonella typhimurium* - Reverse Mutation Assay.
06172	2006. Mutagenicity evaluation of Alpha cypermethrin technical by *In vivo* mouse micronucleus assay.
06173	2006. *In vitro* Cytogenetic Assay measuring chromosomal aberration frequencies induced by Alpha cypermethrin technical in human lymphocytes.
06174	2006. Acute toxicity study of Alpha cypermethrin technical to Freshwater Fish, *Poecilia reticulata*.
06175	2006. Acute immobilisation test with Alpha cypermethrin technical in *Daphnia magna*.
06176	2006. Dietary toxicity study with Alpha cypermethrin technical in Japanese quail.
06177	2006. Acute toxicity of alpha cypermethrin technical to honeybees *Apis mellifera.*
06178	2006. Acute toxicity of alpha cypermethrin technical to honeybees.
06179	2006. Acute toxicity of alpha cypermethrin technical to Earthworm *Lampito mauritti.*
6293	2006. Preliminary analyses of five representative production batches of alpha cypermethrin technical grade active ingredient (TGAI) to determine % alpha cypermethrin and to quantify its associated impurities.
FAO/WHO 2006	Manual on development and use of FAO and WHO specifications for Pesticides. March 2006 revision, published on the internet at http://www.fao.org/ag/agp/agpp/pesticid/ and http://www.who.int/quality/en/.

ALPHA-CYPERMETHRIN

FAO/WHO EVALUATION REPORT 454/2005

Recommendations

The Meeting recommended the following.

(i) That the existing WHO specifications for alpha-cypermethrin TC, SC and WP should be withdrawn.

(ii) That the specifications for alpha-cypermethrin TC, WP (100 g/kg only) and SC proposed by BASF and Tagros, as amended, should be adopted by WHO.

(iii) That the specifications for alpha-cypermethrin TC, WP(>100-250 g/kg range), SC, EC and UL proposed by BASF and Tagros, as amended, should be adopted by FAO.

Appraisal

The Meeting considered data on alpha-cypermethrin, submitted by BASF and Tagros, in support of new FAO specifications for TC, SC, EC and UL, and for the review of existing WHO full specifications for TC (WHO/SIT/32, 1999) and SC (WHO/SIF/61, 1999) and the WHO interim specification for WP (WHO/IS/98.1.2.R1, 2000).

Alpha-cypermethrin is not under patent.

Draft specifications and supporting data were provided by BASF Aktiengesellschaft, Germany, and Tagros Chemicals India Ltd, in 2004.

The cypermethrin molecule has 3 chiral centres and cypermethrin exists as 8 different enantiomers, or 4 pairs of diastereoisomers. Alpha-cypermethrin is a racemate of one diastereoisomeric pair: [*S*, 1*R*,3*R*] and [*R*, 1*S*,3*S*]. When analyzed by non-chiral chromatography, cypermethrin may be resolved into 4 peaks, one of which represents alpha-cypermethrin.

The Meeting was presented with information from both manufacturers on the manufacturing process, data from 5-batch analyses, and summary data on toxic hazards. Mass balances were high: 99.0-100.3% (BASF) and 99.70–99.94% (Tagros). The minimum content of alpha-cypermethrin declared by BASF was 930 g/kg, whereas that declared by Tagros was 950 g/kg. Both BASF and Tagros reported unknown impurities, the maximum for the sum of them exceeded 1 g/kg in both cases but the maximum for any individual unknown compound was <1 g/kg. The BASF data were confirmed as similar to those presented to Belgium, in support of the EU review of alpha-cypermethrin. The Tagros data were confirmed as identical (except for the limit for a solvent impurity) to those presented for registration in Australia.

The Meeting agreed that the impurity profile of BASF should be considered the reference profile, as it was supported by a full data package on hazards. The Tagros TC appeared to be equivalent to that of BASF on the basis of the impurity profiles. However, on the basis of the data provided for skin and eye irritation, the alpha-cypermethrin produced by Tagros (mild irritant) did not appear to be equivalent to that of BASF (non-irritant). A review of the Tagros original study reports by WHO/PCS secretariat (PCS 2005) concluded that the Tagros TC is not an irritant to

either skin or eyes, according to the GHS classification (GHS 2003), and that the two manufacturers' TCs should also be considered equivalent on the basis of the toxicological data. The Meeting agreed with this conclusion.

The Meeting agreed that none of impurities is relevant.

A full CIPAC method is available for the determination of alpha-cypermethrin in the TC and all formulations for which specifications were proposed.

The proposed specifications were broadly in accordance with the requirements of the manual (FAO/WHO 2002) but the Meeting considered certain exceptions.

TC and formulations. Both manufacturers included clauses to specify the minimum amount of total cypermethrin isomers present, in addition to the minimum for alpha-cypermethrin isomers. Similar clauses appeared in the existing WHO specifications for alpha-cypermethrin. While recognising that the low levels of minor cypermethrin isomers present might contribute (minimally) to the overall activity, the Meeting concluded that they are not components of alpha-cypermethrin (as defined by the common name) and that they should be designated as non-relevant impurities and therefore not included in the specification.

TC. The existing WHO specification for alpha-cypermethrin included clauses for hydrocarbon solvent and triethylamine content. Neither manufacturer included these clauses in the proposed specifications and the Meeting accepted that they were not required.

The Meeting agreed that the limit for minimum alpha-cypermethrin content should be that of BASF (930 g/kg).

Formulations. The Meeting questioned the apparently high upper limits given for pH range in the specifications (pH 8 or higher), given the potential for slow hydrolysis of alpha-cypermethrin at pH 9 (half-life of several days at room temperatures). The existing WHO specification for SC (the formulation in which hydrolysis might occur most readily) included an upper limit for pH range of 8.7. The manufacturers confirmed that the active ingredient is stable during storage of products at pH 8 and this limit was therefore agreed by the Meeting.

WP. The clause for wettability proposed by Tagros specified a wetting time limit of 5 min, without swirling. The Meeting acknowledged that pyrethroids have virtually no affinity for water but considered this to be an unacceptably long time. The manufacturer explained that a limit of 1 min, with swirling, was readily achievable and the Meeting accepted this.

The existing WHO specification incorporated a limit of 90 ml for persistent foam but the manufacturers acknowledged that their products comply with the standard maximum of 60 ml (FAO/WHO 2002) and this limit was agreed by the Meeting.

The Meeting noted that the WHO specification for WP is restricted to a 10% formulation, whereas a >100-250 g/kg range is appropriate for FAO specifications.

Tagros stated that their WP is sold in metallized-film sachets but the Meeting did not consider this to require a clause or Note in the specification.

SC. The proposed limits for wet sieve test differed slightly between the manufacturers but they agreed with the Meeting to adopt a limit of 2%.

The Meeting agreed that the limit for pourability of 2.5%, proposed by BASF, should be rounded to 3 ml. The proposed limit for the Tagros product was within this limit.

BASF stated that spontaneity of dispersion should be tested at 0.5% concentration (instead of the usual 5% indicated in method MT 160) because the lower concentration represented both the maximum application rate and a more reasonable test of formulation quality. This requirement for the test did not appear in the existing WHO specification but the existing limit (60% dispersion) was the same as that proposed. The Meeting accepted that testing at the higher concentration was unrealistic in this case and agreed to the proposed deviation from the normal requirement.

The limit proposed by BASF for active ingredient content after storage was lower than that proposed by Tagros but, being within the acceptable range, it was accepted by the Meeting.

EC. Both manufacturers provided limits for method MT 36.1 and MT 173. Following discussions of the methods to be employed, the Meeting and manufacturers agreed that limits should be provided for method MT 36.3 only.

SUPPORTING INFORMATION
FOR
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Uses

Alpha-cypermethrin is a non-systemic, broad spectrum, insecticidal pyrethroid, with rapid knockdown activity. It is effective by contact and ingestion against target pests at relatively low application rates. It acts by preventing transmission of nerve impulses, by blocking the passage of sodium ions through channels in nerve membranes, thus preventing signals passing down axons. Typically this intoxication results in a rapid "knockdown" and mortality.

It is used in to control a wide range of chewing and sucking insects (particularly Lepidoptera, Coleoptera and Hemiptera) in fruit (including citrus), vegetables, vines, cereals, maize, beet, oilseed rape, potatoes, cotton, rice, soya beans, forestry and other crops. In public health it is used to control cockroaches, mosquitoes, flies and other insect pests. It is also used in animal health as an ectoparasiticide.

Identity

Common name

alpha-cypermethrin (E-ISO, BSI), alpha-cyperméthrine (F-ISO)

Synonyms

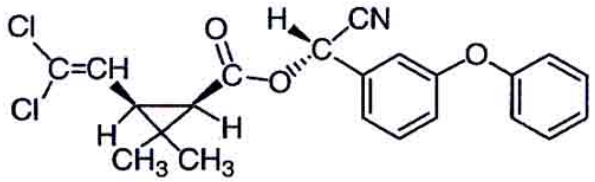
alphamethrin (rejected common name), alfoxylate

Chemical names

IUPAC: a racemic mixture of: (*S*)-α-cyano-3-phenoxybenzyl-(1*R*,3*R*)-3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropanecarboxylate and (*R*)-α-cyano-3-phenoxybenzyl-(1*S*,3*S*)-3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropanecarboxylate

CA: [1α(*S**), 3□α]-(±)-cyano(3-phenoxyphenyl)methyl 3-(2,2-dichloroethenyl)-2,2-dimethylcyclopropanecarboxylate

(*S*) (1*R*)-*cis*-



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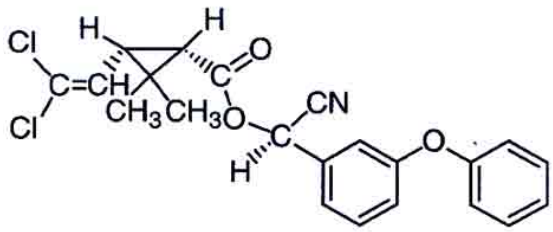

(*R*) (1*S*)-*cis*-

Structural formula

Empirical formula

$C_{22}H_{19}Cl_2NO_3$

Relative molecular mass

416.3

CAS Registry number

67375-30-8

CIPAC number

454

Identity tests

GC retention time, IR spectrum.

Physico-chemical properties of alpha-cypermethrin

Table 1. Physico-chemical properties of pure alpha-cypermethrin

Parameter	Value	Purity %	Method	Reference
Vapour pressure	3.4 x 10^{-7} Pa at 25°C 1.9 x 10^{-5} Pa at 51°C (BASF)	97.3	EEC A4	PML 1992-C39
	2.3 X 10^{-5} Pa at 20°C (Tagros)	97.4	EEC A4	10802
Melting point	81.5°C (range 81.4-83.7°C) (BASF)	97.3	OECD 102	AL-303-001
	Melting point: 77.8-80.8°C (Tagros)	97.4	EEC A1, A2	10781

Table 1. Physico-chemical properties of pure alpha-cypermethrin

Parameter	Value	Purity %	Method	Reference
Boiling point	200°C at 0.07 mm Hg (BASF) Cannot be determined at atmospheric pressure as decomposition occurs before boiling	99.0	OECD 102	AL-303-001
	195.8-197.8°C at 9.3 Pa (Tagros)	97.4	EEC A1, A2	10781
Decomposition temperature	Decomposition temperature starts at ca 270°C (below boiling point at atmospheric pressure) (BASF)	97.3	-	AL-303-001
Solubility in water (all in µg/l at 25°C)	pH *cis*-1 *cis*-2 total 4.08 3.92 0.67 4.59 7.12 1.83 3.97 5.80 9.06 3.33 4.54 7.87 distilled water, unbuffered 0.81 1.25 2.06 (BASF)	98.0	EEC A.6	AL-311-002
	10 at 30°C (Tagros)	97.4	OECD 105	10778
Octanol/water partition coefficient	log P K_{OW} = 5.5 at ambient temperature (BASF)	95.4	OECD 117, HPLC method	AL-315-001
	log P_{OW} = 6.93 at 25°C, pH 7.0 (Tagros)	97.4	EEC A8 GC-ECD method	10805
Hydrolysis characteristics (half-life)	measured: pH 4, stable at 40ºC pH 7, 27 days at 50ºC pH 7, 5.3 days at 60ºC pH7, 2.0 days at 75ºC pH 9, 3.5 days at 25ºC pH 9, 3.0 hours at 50ºC Calculated: pH 7, 101 days at 20ºC pH 7, 67 days at 25ºC pH 9, 7.3 days at 20ºC pH 9, 3.5 days at 25ºC (BASF)	radio-labelled purity 99.0, unlabelled purity 97.3	OECD 111	AL-322-002
	pH 4, stable at 50ºC pH 7, stable at 50ºC pH 9.0, 15.41 days at 40ºC pH 9.0, 21.02 days at 30ºC (Tagros)	97.4	OECD 111	12327
Photolysis characteristics	Conditions: pH 5 (sterile buffer, no hydrolytic decomposition), 22°C, artificial sunlight over 15 and 28 days, two radiolabelled test substances, dark control samples. benzene-label: DT_{50} = 2.2 days continuous irradiation DT_{50} = 6.3 days calculated for solar exposure cyclopropane-label: DT_{50} = 1.2 days continuous irradiation DT_{50} = 3.4 days calculated for solar exposure Environmental half-life, 2.9 days, calculated from quantum yield for latitude 40°N during spring (BASF)	each radio-labelled compound >99	SETAC Part 1: 10	AL-324-003

Table 1. Physico-chemical properties of pure alpha-cypermethrin

Parameter	Value	Purity %	Method	Reference
Dissociation characteristics	Does not dissociate	-	-	EU 2004

Alpha-cypermethrin is not flammable or auto-flammable and does not have explosive or oxidizing properties.

Table 2. Chemical composition and properties of alpha-cypermethrin technical material (TC)

Manufacturing process, maximum limits for impurities ≥ 1 g/kg, 5 batch analysis data	Confidential information supplied and held on file by FAO. Mass balances were 99.0-100.3% and percentages of unknowns were in the range of <0.05-0.14% for the sum of six impurities, each <0.1% (BASF). Mass balances were 99.70–99.94%, percentages of unknowns were in the range of <0.06-0.3% for their sum, each <0.1% (Tagros).
Declared minimum alpha-cypermethrin content	930 g/kg (BASF) 950 g/kg (Tagros)
Relevant impurities ≥ 1 g/kg and maximum limits for them	None.
Relevant impurities < 1 g/kg and maximum limits for them:	None.
Stabilisers or other additives and maximum limits for them:	None.
Melting temperature range of the TC	81.4-83.7°C (BASF) 77.8-80.8°C (Tagros)

Pure alpha-cypermethrin consists of colourless crystals, the TC is a white to cream powder with a mild chemical odour.

Hazard summary

IPCS initially made a full evaluation of cypermethrin (IPCS 1989) and later a full evaluation of alpha-cypermethrin (IPCS 1992). IPCS concluded that, when applied according to good agricultural practice, exposure of the general population to alpha-cypermethrin is low and is unlikely to present a hazard. With good work practices, hygiene measures, and safety precautions, the use of alpha-cypermethrin is unlikely to present a hazard to those occupationally exposed to it. The occurrence of "facial sensations" is an indication of exposure and, if they occur, work practices should be reviewed. With recommended application rates, it is unlikely that alpha-cypermethrin will attain levels of environmental significance. It is highly toxic to aquatic arthropods, fish and honeybees under laboratory conditions. Significant toxic effects on non-target invertebrates and fish are only likely to occur in cases of spillage, over-spraying and misuse.

Evaluations of alpha-cypermethrin by the FAO/WHO JMPR and JECFA (JMPR 1980, 1982; JECFA 1996, 1998, 2000, 2002 and 2003) have produced conclusions which are in agreement with those of IPCS The JECFA allocated an ADI of 0-0.02 mg/kg bw/d and no acute RfD for alpha-cypermethrin (JECFA 1996).

An EU review concluded that alpha-cypermethrin fulfils the safety requirements of Articles 5(1)(a) and (b) of Directive 91/414/EEC, and that residues arising from the proposed uses, with good plant protection practice, should have no harmful effects

on human or animal health (EU 2004). The following toxicological reference doses were allocated: ADI = 0-0.015 mg/kg bw/d (1-year toxicity in dog, 100 safety factor); ARfD = 0.04 mg/kg bw (acute oral rat neurotoxicity, 100 safety factor); AOEL (systemic) = 0.01 mg/kg bw/d (90-d dog study, 100 safety factor); AOEL (dermal) = 0.2 mg/kg bw/d (15-d rabbit dermal study, 100 safety factor).

The WHO hazard classification of alpha-cypermethrin is: moderately hazardous, class II (WHO 2002).

Formulations and co-formulated active ingredients

The main formulation types available for use in public health applications (primarily indoor residual spraying) are WP and SC (SC is also used for bed net treatment). The main formulation types available for use in agriculture are EC, SC and UL. The EC formulation is also used to control ectoparasites on animals. These formulations are registered and sold in many countries in Europe, South America, Africa, Australasia and Asia.

Alpha-cypermethrin may be formulated alone or co-formulated with other insecticides, such as flufenoxuron or teflubenzuron.

Methods of analysis and testing

The analytical method for the active ingredient (including identity tests) is a full CIPAC method (CIPAC H, CIPAC K) for the analysis of TC, WP, EC, UL, SC and oil-enhanced SC. Alpha-cypermethrin is determined by capillary GC, with FID and internal standardization with dioctyl phthalate. Alpha-cypermethrin (a pair of enantiomers) produces a single GC peak.

Impurities in alpha-cypermethrin are determined by GC-FID and HPLC-UV methods.

Test methods for determination of physico-chemical properties of the technical active ingredient were OECD or EC, while those for the formulations are CIPAC, as indicated in the specifications.

Physical properties

The physical properties, the methods for testing them and the limits proposed for the formulations comply with the requirements of the FAO/WHO manual (FAO/WHO 2002), with the exception of determination of spontaneity of dispersion (SC specification) which is tested at the maximum application rate (0.5% instead of the usual 5%).

Containers and packaging

No special requirements for containers and packaging have been identified. The WP may be packaged in metallized film (“alupoly”) sachets but not water-soluble bags.

Expression of the active ingredient

The active ingredient is expressed as alpha-cypermethrin in g/kg or g/l at 20 ± 2ºC.

ANNEX 1

HAZARD SUMMARY PROVIDED BY THE PROPOSER

Note: BASF and Tagros provided written confirmation that the toxicological and ecotoxicological data included in the following summary were derived from alpha-cypermethrin having impurity profiles similar to those referred to in Table 2, above.

Table A. Toxicology profile of technical alpha-cypermethrin, based on acute toxicity, irritation and sensitization

Species	Test	Purity %	Duration and conditions or guideline adopted	Result	Reference
Rat (m, f)	oral	95.6	Single exposure. Study conducted according to B.1 92/69/EEC	LD_{50} = 57 mg/kg bw (m) LD_{50} = 71 mg/kg bw (f) (BASF)	SBTR.92.033
Rat, Wistar (m,f)	oral MLD	98	OECD 401, 14 d. 0, 80, 120, 180 mg/kg bw (in peanut oil)	LD_{50} = 132 (104-168) mg/kg bw (Tagros)	1361
Rat (m, f)	dermal	96	Single exposure. Study conducted according to B.3 92/69/EEC	LD_{50} >2000 mg/kg bw (BASF)	SBTR.92.033
Rat, Wistar (m,f)	dermal MLD	98	OECD 402, 14 d, 0 & 2000 mg/kg bw	LD_{50} >2000 mg/kg bw (Tagros)	1363
Rat (m, f)	inhalation	95.6	Single 4-hour exposure. Study conducted according to B.2 92/69/EEC	LC_{50} >1.59 mg/l (BASF)	SLL 266/930770
Rat, Wistar (m,f)	inhalation MLC	98	OECD 403, 14 d, 0, 0.614, 0.451, 0.273 mg/l	LC_{50} = 0.313 (0.109-0.893) mg/l (Tagros)	1364
Rabbit (m, f)	skin irritation	95.6	Single exposure, Study conducted according to B.4 92/69/EEC	Non-irritant (BASF)	SBTR.92.033
Rabbit	skin irritation	98	OECD 404, 500 mg (4 h), observed 1, 24, 48 & 72 h after treatment	Mild irritant (Tagros)	1365
Rabbit (m, f)	eye irritation	95.6	Single exposure. Study conducted according to B.5 92/69/EEC	Non-irritant (BASF)	SBTR.92.033
Rabbit	eye irritation	98	OECD 405, 100 mg, observed 1, 24, 48 & 72 h after treatment	Mild irritant (Tagros)	1369
Guinea pig (m, f)	skin sensitization	95.6	Maximization test. Study conducted according to B.6 84/449/EEC	Non-sensitizing (BASF)	SBTR.92.033
Guinea pig, Hartley	skin sensitization	98	OECD 406, 250 mg, observed for 28 d.	Not a sensitizer	1366

ECB, Ispra, has classified alpha-cypermethrin as R37 (irritant for respiratory system).

Table B. Toxicology profile of technical alpha-cypermethrin, based on repeated administration (sub-acute to chronic)

Species	Test	Purity %	Duration and conditions or guideline adopted	Result	Reference
Rat (m, f)	5-week feeding	96.5	B.7 92/69/EEC, 35 d (normal duration is 28 d).	NOAEL = 20 mg/kg bw/d (m) (BASF)	SBGR.81.212
Rat (m, f)	Oral, 6-week	95.6	B.7 92/69/EEC, 35 d (normal duration is 28 d).	NOEL = 20 mg/kg bw/d (m) (BASF)	SBTR.93.002
Mouse (m, f)	Oral, 29-d	95.4	B.7 92/69/EEC, 29 d	NOAEL = 56 mg/kg bw/d (m, f) (BASF)	LSR 92/SHL008/0346

Table B. Toxicology profile of technical alpha-cypermethrin, based on repeated administration (sub-acute to chronic)

Species	Test	Purity %	Duration and conditions or guideline adopted	Result	Reference
Dog (m, f)	Oral, increasing dose feeding study (range-finding)	Batch F8300 47B	B.7 92/69/EEC (not fully compliant), 14 d	NOAEL = 5 mg/kg bw/d, based on clinical signs of toxicity in 1f (BASF)	3107
Rat (m, f)	Oral, 90 d	96.5	OECD 408 (1981)	NOAEL = 9 mg/kg bw/d (BASF)	SBGR.81.293
Rat	90 d	97.1	OECD 408	NOAEL = 25 mg/kg bw/d (Tagros)	10378
Dog (m, f)	Oral, 90 d	95.8	OECD 408 (1981)	NOAEL = 2.3 mg/kg bw/d (BASF)	3197
Mouse, CD-1 (m, f)	Oral feeding, 13-week	95.4	Study approximated OECD 408 (1981). Groups 12 m, 12 f, fed 13 weeks at 0, 50, 250, or 1000 ppm in diet.	NOAEL = 6.3 mg/kg bw/d (BASF)	92/SHL009/0849
Dog (m, f)	1 year feeding	95.4	US EPA Guideline No. 83-1	NOAEL = 1.5 mg/kg bw/d (based on clinical signs of skin irritation in 1 f) (BASF)	11110
Rat, Wistar (m, f)	Carcinogenicity, 2 year feeding	98	Directive 87/302/EEC, method B but 24 rats (not 50) included in 2 y sacrifice. Cypermethrin (WL 43467) (approx. 25% alpha-cypermethrin) fed to 48/sex/group at 1, 10, 100, 1000 ppm in diet (0.05, 0.5, 5, and 50 mg/kg/day). Observations after sacrifice at 6, 12, 18 & 24 months.	NOAEL = 5 mg/kg bw/d (chronic effects) No evidence of carcinogenicity at 50 mg/kg bw/d (highest concentration tested). (BASF)	TLGR 78.189
Mouse (m, f)	Carcinogenicity, 78-week feeding	95.4	Directive 87/302/EEC method B. Alpha-cypermethrin at 0, 30, 100, 300 ppm in diet (3, 10.6, 35.2 mg/kg/day males, 3.5, 11.5, and 37.7 mg/kg/day females)	NOAEL = 3 mg/kg bw/d = 30 ppm(based on reduced body weight gain in males at 100 ppm). No evidence of carcinogenicity at 300 ppm (highest dose tested).(BASF)	95/SHL010/0596

Table B. Toxicology profile of technical alpha-cypermethrin, based on repeated administration (sub-acute to chronic)

Species	Test	Purity %	Duration and conditions or guideline adopted	Result	Reference
Rats (m, f)	Reproductive toxicity 3-generation	99	Directive 87/302/EEC method B. Males up to 25 mg/kg/day, females up to 20 mg/kg/day.	No adverse reproductive effect up to 5 mg/kg bw/d. NOAEL = 5 mg/kg bw/d = 100 ppm (maternal) based on reduced premating body weight and food consumption at 500 ppm. NOAEL = 5 mg/kg bw/d = 100 ppm (reproduction), based on reduced litter size at birth primarily in F1a generation, and reduced mean pup weights on day 21 for F1b females and F3b males at 500 ppm. (BASF)	TLGR.78.188
Rat (m, f)	Teratogenicity & developmental toxicity	95.6	OECD 414 (1981). Pregnant females received 0, 3, 9, or 15 mg/kg/day on gestation days 6-18.	No maternal or developmental toxicity at 3 or 9 mg/kg/day. NOAEL = 9 mg/kg bw/d (maternal) NOAEL = 9 mg/kg bw/d (fetal) (BASF)	SLN/3/92 & SLN/4/92
Rabbit (m, f)	Teratogenicity & developmental toxicity	95.6	OECD 414 (1981); US EPA 83-3 (1982); JMAFF (1985) Pregnant females received 0, 3, 15 or 30 mg/kg/day on gestation days 7-19.	No maternal or developmental toxicity at 3 or 15 mg/kg/day. NOAEL = 15 mg/kg bw/d (maternal) NOAEL = 30 mg/kg bw/d (fetal). (BASF)	SLN/3/92 & SLN/4/92
Rat (m, f)	Acute neurotoxicity	95.4	US EPA (40 CFR 160); UK DoH (London, 1989); OECD (Paris, 1982); JMAFF (59 Nohsan 3850) Single oral dose of 0, 4, 20, or 40 mg/kg	NOAEL = 4 mg/kg bw (BASF)	SBTR.93.002

In chronic toxicity studies (≥1 y), dietary administration of alpha-cypermethrin to mice, rats and dogs resulted in clinical signs of treatment that were limited to adverse effects on the skin and hair. Decreases in body weight gains were observed in mice treated with doses ≥100ppm (approximately

14.3 mg/kg bw/day). The dog appeared more sensitive than the mouse to the effects of alpha-cypermethrin, as indicated by NOAELs of 1.5 mg/kg bw/day and 3 mg/kg bw/day for dogs and mice, respectively.

Alpha-cypermethrin was not carcinogenic in long-term studies in mice after administration via the diet. Results from the carcinogenicity study with cypermethrin (the two alpha-cypermethrin isomers comprised approximately 25% of the total cypermethrin) have been used to fulfil data requirements for alpha-cypermethrin. Developmental toxicity tests conducted in rabbits and rats with alpha-cypermethrin revealed no teratogenic effects for either species.

Alpha-cypermethrin is neurotoxic to all species.

Table C. Mutagenicity profile of technical alpha-cypermethrin, based on *in vitro* and *in vivo* tests

Species	Test	Purity %	Conditions	Result	Reference
Salmonella typhimurium TA98, TA100, TA1535, TA1537, TA1538 *E. coli* WP2 uvrA	Point mutation, Ames test, *in vitro*	95.6	92/69/EEC Dose range: 31.25, 62.5, 125, 250, 500, 1000 and 5000 µg/plate with and without S9.	Not mutagenic (BASF)	SBTR.93.007
Salmonella typhimurium TA98, TA100, TA1535, TA1537, TA1538	Point mutation, Ames test, *in vitro*	99	92/69/EEC method B14 50, 150, 500, 1500, and 5000 µg/plate with and without S9.	Not mutagenic (BASF)	SBTR.93.007
Salmonella typhimurium TA98, TA100, TA1535, TA1537	Bacterial reverse mutation assay	98	OECD 471 12.5-1000 µg/plate	Negative (Tagros)	1367
L5178Y mouse lymphoma cells	Gene Mutation Test *In vitro*	95.4	0, 0.03, 0.1, 0.3, 3.3, 10, 33, 50 µg/ml with and without S9. Study conducted following method B of 87/303/EEC	Not mutagenic (BASF)	087378
Chinese hamster ovary cell lines	Chromosomal aberration	98	OECD 473 5.5,6.5 & 7.5 µM with S-9 4, 5 & 6 µM without S-9	Negative (Tagros)	10402
Human lymphocytes	Chromosome aberrations, cytogenic investigation*, in vitro*	95.6	92/69/EEC method B In culture for 24 or 48 h (S9 incubated 3 h) Dose range: trial #1: 125, 500, 1000 µg/ml trial #2: 93.75, 375, 500, 750 µg/ml, with and without S9 125, 500 and 1000 µg/ml in 2 trials with S9	Not genotoxic (BASF)	SBTR.93.007

Table C. Mutagenicity profile of technical alpha-cypermethrin, based on *in vitro* and *in vivo* tests

Species	Test	Purity %	Conditions	Result	Reference
TK6 human lymphoblastoid cells	Mammalian cell gene mutation test	97.1	OECD 476 0.005, 0.01, 0.04, 0.06 mM with S-9 0.005, 0.01, 0.02, 0.04 mM without S-9	Negative (Tagros)	10404
Bone marrow cells (Wistar rats, Charles River)	Chromosome aberration, cytogenic investigation, *in vivo*	95.8	Rat femoral bone marrow, 6 per sex per group 0, 2, 4, 8 mg/kg orally, single dose	Not genotoxic (BASF)	SBGR.84.120
Rat, hepatocytes (Albino Wistar)	UDS after partial hepatectomy, *in vivo*	96.5	0, 40 mg/kg, single oral dose, 6 h exposure	Not genotoxic (BASF)	SBGR.81.225
Mouse, Swiss, femoral bone marrow	Micronucleus assay *in vivo*	95.4	0, 1, 5, 10 mg/kg orally, single dose 24, 48, 72 h harvest	Not genotoxic (BASF)	087367
Mouse, Swiss albino (m, f)	Micronucleus assay *in vivo*	98	OECD 474 25, 50 & 75 mg/kg, vegetable oil vehicle	Negative (Tagros)	10403
Mouse (m, f)	Dominant lethal test, *in vivo*.	99	87/302/EEC, method B 0, 5, 10, or 15 mg/kg bw for 5 consecutive days	Not mutagenic (BASF)	TLGR.0042.77
Mouse	Mouse bone marrow chromosome study	98	OECD 475 0, 10, 20 & 40 mg/kg bw	Negative (Tagros)	1368
Saccharomyces cerevisiae XV 185-14C	Gene mutation	95.8	0, 31.25, 62.5, 125, 250, 500, 1000, 2000, or 4000 µg/plate, with or without S9	Not mutagenic (BASF)	SBGR.84.117

Table D. Ecotoxicology profile of technical alpha-cypermethrin

Species	Test	Purity %	Duration and conditions	Result	Reference
Daphnia magna (water flea)	Acute toxicity	93.4-95.7	48 h, semi-static test system with renewal after 24 h OECD 202 I	EC_{50} = 0.3 µg/l (BASF)	SBGR.81.277
Daphnia magna (water flea)	24 h acute immobilization	98	24 h. 0, 0.03, 0.06, 0.12, 0.24, 0.48 µg/l	EC_{50} = 0.14 (0.1-0.18) µg/l water (Tagros)	1360
Daphnia magna (water flea)	Chronic toxicity	98-98.5	21 d, semi-static test system with renewal after 24 h OECD 202 II	NOEC = 0.03 µg/l (BASF)	SBGR.81.277
Salmo gairdneri (rainbow trout)	Acute toxicity	98-98.5	96 h, semi-static with renewal every 12 h. OECD 203	LC_{50} = 2.8 µg/l NOEC = 1.5 µg/l (BASF)	SBGR.81.026

Table D. Ecotoxicology profile of technical alpha-cypermethrin

Species	Test	Purity %	Duration and conditions	Result	Reference
Cyprinus carpio (common carp)	Acute toxicity	98	OECD 203 96 h mortality 0, 0.0003, 0.0005, 0.0008, 0.001 & 0.002 mg/l	LC_{50} = 0.00084 (0.0007-0.0009) mg/l (Tagros)	1358
Pimephales promelas (fathead minnow)	Fish early life stage toxicity	91.5	60 embryos per concentration. The embryos were obtained within 48 hours after fertilization and were followed up to day 30	NOEC = 0.25 µg/l (BASF)	BW-80-9-723
Pimephales promelas (fathead minnow)	Fish early life stage toxicity	98.2-99.4	Embryos within 24 h after fertilization, observed 34 d 30 embryos/ concentration	NOEC = 0.03 µg/l (BASF)	SBGR.82.298
Rainbow trout	Bioconcentration	96.1	73 d study. 0.2 µg/l 18 d exposure in flow-through system at 15ºC. Study with cypermethrin	Bioaccumulation factor calculated as 1204, uptake rate constant of 0.11/L water/g fish, depuration rate constant 0.09 L water/g fish/day. Cypermethrin rapidly taken up and eliminated, alpha-cypermethrin expected to be similar. (BASF)	SBGR.81.026
Selenastrum capricornutum (green alga)	Acute toxicity	93.4-95.7	96 h, static water, OECD (201)	EC_{50} >100 µg/l (growth rate) EC_{50} >100 µg/l (biomass) no morphological effects observed under test conditions. (BASF)	SBGR.81.277
Pseudo-kirchneriella subcapitata (green alga)	Growth inhibition test	96	Static, 72 h; 5 concentrations, 3 replicates, plus control with 5 replicates; daily assessments of growth. EEC 92/69, OECD 201	Effect on biomass: EbC_{50} (0-72 h) >1 mg/l EbC_{10} (0-72 h) <0.05 mg/l Effect on growth rate: ErC_{50} (0-72 h) >1 mg/l ErC_{10} (0-72 h) >1 mg/l (BASF)	AL-520-002

Table D. Ecotoxicology profile of technical alpha-cypermethrin

Species	Test	Purity %	Duration and conditions	Result	Reference
Chlorella vulgaris (green alga)	Growth inhibition	97.1	OECD 201, 72h	EC_{50} = 15.26 μg/ml (Tagros)	11441
Chironomus riparius Meigen	Chronic toxicity sediment dwelling organisms	97	Static system containing standard sediment (according to OECD 207) and water (Elendt, M4-medium); two definitive tests conducted, each with test duration 28 days; 7 test concentrations, each with 4 replicates plus a control with 4 and a solvent control with 4 replicates; assessment of larval development and emergence.	NOEC = 0.024 μg a.s./l LOEC = 0.048 μg a.s./l EC_{50} = 0.227 μg a.s./l (95% confidence limits: 0.120 – 1.066 μg a.s./l) (BASF)	AL-523-002
Macro-invertebrates, zooplankton and algae	Effect on freshwater ecosystem	Min. 93%	Natural assemblages of freshwater macro-invertebrates, zooplankton and algae in ponds	overall Ecologically Acceptable Concentration (EAC) = 0.015 μg/, single and repeated applications (BASF)	AL-560-023
Eisenia foetida (earthworm)	Acute toxicity	98.2-99.4	14 d, OECD (207)	14-day LC_{50} >100 mg a.s./kg soil NOEC = 100 mg/kg soil (BASF)	SBGR.83.071
Lampito mauritii (earthworm)	Acute toxicity	98	OECD 207 0-80 mg/kg dry soil	EC_{50} = 57.4 (39.2-84) mg/kg artificial soil (Tagros)	1359
Apis mellifera (honey bee)	Acute oral toxicity	99.5	48 h, OECD (213), according to recommendations of ICPBR (1999)	LD_{50} >0.059 μg/bee (BASF)	SBGR.82.023
Apis mellifera (honey bee)	Contact toxicity	99.5	48 h, OECD (214), according to recommendations of ICPBR (1999)	LD_{50} >0.033 μg/bee (BASF)	SBGR.82.023
Northern bobwhite quail (*Colinus virginianus*)	Acute toxicity	96.1	EPA 71-1, SETAC	Highest dose (2025 mg a.s. /kg body weight) caused no compound-related mortality (BASF)	ETX-00-107

Table D. Ecotoxicology profile of technical alpha-cypermethrin

Species	Test	Purity %	Duration and conditions	Result	Reference
Northern bobwhite quail (*Colinus virginianus*)	Dietary toxicity	96.1	U.S. EPA. Guideline 71-2, OPPTS 850.2200; OECD 205	LC_{50} >5000 mg a.s./kg diet NOEC = 5000 mg a.s./kg diet (BASF)	ETX-00-182 / AL-534-003
Northern bobwhite quail (*Colinus virginianus*)	Sub-chronic toxicity and reproduction	96.1	U.S. EPA Guideline 71-4; USEPA OPPTS 850.2300; OECD 206.	NOEC = 150 mg a.s./kg diet (BASF)	AL-534-002

Based on lower tier data, alpha-cypermethrin appeared to be potentially hazardous to aquatic organisms. Therefore, a higher-tier evaluation of the potential risk to aquatic environments was conducted using results from pond ("mesocosm") studies. Based on these mesocosm results and data from a series of single-species laboratory toxicity tests with sensitive organisms, a conservative Ecologically Acceptable Concentration (EAC) of 0.015 µg alpha-cypermethrin/l (water solubility approximately 5 µg/l) was recommended for single and repeated applications.

Although alpha-cypermethrin was toxic in acute tests in which honey bees were directly exposed to fresh residue, the results from numerous field tests indicate that application of alpha-cypermethrin is of low risk to honey bees This is because direct exposure to alpha-cypermethrin, through contact and ingestion, is very limited due to its repellent effect on foraging bees.

Alpha-cypermethrin poses negligible risks to birds through acute, short-term, and chronic (reproductive) exposure.

ANNEX 2. REFERENCES

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BASF or Tagros document number or other reference	Year and title of report or publication details
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