WHO SPECIFICATIONS AND EVALUATIONS FOR PUBLIC HEALTH PESTICIDES

LAMBDA-CYHALOTHRIN

A reaction product comprising equal quantities of

(*S*)-*α*-cyano-3-phenoxybenzyl (*Z*)-(1*R*,3*R*)-3-(2-chloro-3,3,3-trifluoroprop-1-enyl)-2,2-dimethylcyclopropanecarboxylate and

(*R*)-*α*-cyano-3-phenoxybenzyl (*Z*)-(1*S*,3*S*)-3-(2-chloro-3,3,3-trifluoroprop-1-enyl)-2,2-dimethylcyclopropanecarboxylate

World Health Organization

TABLE OF CONTENTS

DISCLAIMER[1]

WHO specifications are developed with the basic objective of promoting, as far as practicable, the manufacture, distribution and use of pesticides that meet basic quality requirements.

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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[1] This disclaimer applies to all specifications published by WHO.

INTRODUCTION

WHO establishes and publishes specifications[2] for technical material and related formulations of public health 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 WHO specifications follows the **New Procedure**, described in the "Manual for development and use of FAO and WHO specifications for pesticides." This **New Procedure** follows a formal and transparent evaluation process. It describes the minimum data package, the procedure and evaluation applied by WHO and the experts of the FAO/WHO Joint Meeting on Pesticide Specifications (JMPS).

WHO specifications now only apply to products for which the technical materials have been evaluated. Consequently, from the year 2002 onwards, the publication of WHO 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 above-mentioned manual.

Part Two: The Evaluation Report(s) of the pesticide, reflecting the evaluation of the data package carried out by WHO and the JMPS. The data are provided by the manufacturer(s) according to the requirements of chapter 3 of the above-mentioned manual and supported by other information sources. Evaluation reports include 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 chronological order to this report.

WHO 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. WHO 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.

[2] The publications are available on the Internet under the WHO Prequalification Unit – Vector Control Product Assessment Team (PQT/VCP) website, https://extranet.who.int/pqweb/vector-control-products

PART ONE: SPECIFICATIONS FOR LAMBDA-CYHALOTHRIN

LAMBDA-CYHALOTHRIN

Lambda-Cyhalothrin Information

ISO common names

lambda-cyhalothrin (E-ISO)
lambda-cyhalothrine (F-ISO)

Synonyms

none

Chemical names

IUPAC A reaction product comprising equal quantities of (*S*)-*α*-cyano-3-phenoxybenzyl (*Z*)-(1*R*,3*R*)-3-(2-chloro-3,3,3-trifluoroprop-1-enyl)-2,2-dimethylcyclopropanecarboxylate and (*R*)-*α*-cyano-3-phenoxybenzyl (*Z*)-(1*S*,3*S*)-3-(2-chloro-3,3,3-trifluoroprop-1-enyl)-2,2-dimethylcyclopropanecarboxylate.

CA [1α(*S**),3α(*Z*)]-(±)-cyano(3-phenoxyphenyl)methyl 3-(2-chloro-3,3,3-trifluoro-1-propenyl)-2,2-dimethylcyclopropanecarboxylate.

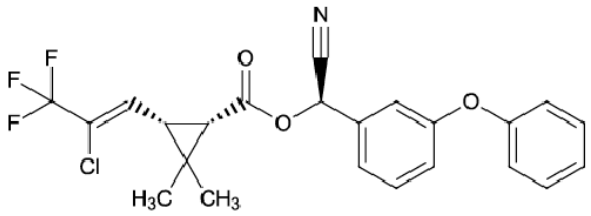
CAS Number

91465-08-6

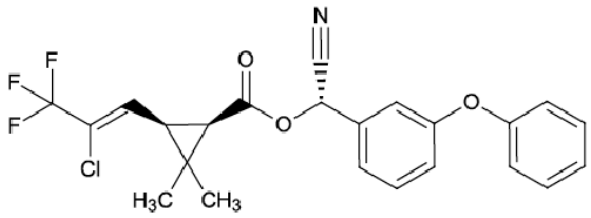
CIPAC Number

463

Structural formula



and



Molecular formula

$C_{23}H_{19}ClF_3NO_3$

Relative molecular mass

449.9

Identity tests

GC (relative retention time), NMR, IR.

Lambda-Cyhalothrin Technical Material - WHO Specification 463/TC (September 2021)

WHO specification 463/TC (September 2021*)

This specification, which is PART ONE of this publication, is based on an evaluation of data submitted by the manufacturers whose names are listed in the evaluation reports (463/2003, 463/2006, 463/2012, 463/2014, 463/2019, 463/2021.1, 463/2021.2, 463/2021.3). The specification 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 specification. The specification may not be appropriate for TC produced by other manufacturers. The evaluation reports (463/2003, 463/2006, 463/2012, 463/2014, 463/2019, 463/2021.1, 463/2021.2, 463/2021.3), as PART TWO, form an integral part of this publication.

1 Description

The material shall consist of lambda-cyhalothrin together with related manufacturing impurities and shall be a viscous brown/green semi-solid mass, which is liquid at 50°C and contains not more than a trace of insoluble material, and shall be free from extraneous matter and added modifying agents.

2 Active ingredient

2.1 **Identity tests** (463/TC/M/2, CIPAC Handbook E, p. 50, 1992)

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 **Lambda-cyhalothrin content** (463/TC/M/3, CIPAC Handbook E, p. 50, 1992)

The lambda-cyhalothrin content shall be declared (not less than 900 g/kg), and when determined, the average measured content shall not be lower than the declared minimum content.

3 Physical properties

3.1 **Acidity** (MT 31.2.1, CIPAC Handbook F, p. 98, 1995)

The maximum acidity shall be 0.5 g/kg, calculated as H_2SO_4.

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* Specifications may be revised and/or additional evaluations may be undertaken. Ensure the use of current versions by checking at the WHO Prequalification Unit – Vector Control Product Assessment Team (PQT/VCP) website, https://extranet.who.int/pqweb/vector-control-products

Lambda-Cyhalothrin Emulsifiable Concentrate - WHO Specification 463/EC (September 2021)

WHO specification 463/EC (September 2021*)

This specification, which is PART ONE of this publication, is based on an evaluation of data submitted by the manufacturers whose names are listed in the evaluation reports (463/2003, 463/2006, 463/2019). The specification should be applicable to relevant products of these manufacturers and those of any other formulators who use only TC from the evaluated source. 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 (463/2003, 463/2006, 463/2019), as PART TWO, form an integral part of this publication.

1 Description

The material shall consist of technical lambda-cyhalothrin, complying with the requirements of WHO specification 463/TC (September 2021), dissolved in suitable solvents (Note 1) together with any other necessary formulants. It shall be in the form of a clear to slightly hazy, 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** (463/EC/M/2, CIPAC Handbook E, p. 56, 1992)

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 **Lambda-cyhalothrin content** (463/EC/M/3, CIPAC Handbook E, p. 56, 1992)

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

Declared content (g/l at 20 ± 2°C)	Permitted tolerance
up to 25 g/l	± 15% of the declared content
above 25 g/l up to 100 g/l	± 10% of the declared content
Note: In each range the upper limit is included	

* Specifications may be revised and/or additional evaluations may be undertaken. Ensure the use of current versions by checking at the WHO Prequalification Unit – Vector Control Product Assessment Team (PQT/VCP) website, https://extranet.who.int/pqweb/vector-control-products.

3 Physical properties

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

pH range: 6.0 to 8.0.

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

The formulation, when diluted at 25 ± 5°C (Note 3) with CIPAC Standard Waters A and D, shall comply with the following:

Time after dilution	Limits of stability
0 h	Initial emulsion complete
0.5 h	'Cream', maximum: 1 ml
2.0 h	'Cream', maximum: 2 ml
	'Free oil', maximum: trace
24 h	Re-emulsification complete
24.5 h	'Cream', maximum: 2 ml
	'Free oil', maximum: trace
Note: tests after 24 h are required only where the results at 24 h are in doubt	

3.3 **Persistent foam** (MT 47.3, CIPAC Handbook O, p. 177, 2017) (Note 4)

Maximum: 15 ml after 1 minute

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 or liquid which separates shall not be more than 0.3 ml.

4.2 **Stability at elevated temperature** (MT 46.4, CIPAC Handbook P, p. 232, 2021)

After storage at 54 ± 2°C for 14 days, the determined average active ingredient content shall not be lower than 95%, relative to the determined average content found under 2.2 before storage (Note 5), and the formulation shall continue to comply with the clauses for:

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

Note 1 The flash point should not be lower than 38°C (MT 12). Attention is drawn to the appropriate national and international regulations on handling and transport of flammable materials.

Note 2 The mass per millilitre is expected to be in the range 0.895 to 0.915 g/ml at 20 ± 2°C but, in cases of doubt, the actual mass per millilitre should be determined (using CIPAC method MT 3) and used in the calculation. Where doubt remains, or in cases of dispute, the content should be expressed in g/kg.

Note 3 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 4 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 25 ± 5°C.

Note 5 Samples of the formulation taken before and after the storage stability test may be analysed concurrently after the test in order to reduce the analytical error.

Lambda-Cyhalothrin Wettable Powder - WHO Specification 463/WP (September 2021)

WHO specification 463/WP (September 2021*)

This specification, which is PART ONE of this publication, is based on an evaluation of data submitted by the manufacturers whose names are listed in the evaluation reports (463/2003, 463/2006, 463/2019). The specification should be applicable to relevant products of these manufacturers and those of any other formulators who use only TC from the evaluated source. 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 (463/2003, 463/2006, 463/2019), as PART TWO, form an integral part of this publication.

1 Description

The material shall consist of a homogeneous mixture of technical lambda-cyhalothrin, complying with the requirements of WHO specification 463/TC (September 2021), together with filler(s) and any other necessary formulants. It shall be in the form of a fine powder free from visible extraneous matter and hard lumps.

2 Active ingredient

2.1 **Identity tests** (463/WP/M/2, CIPAC Handbook E, p. 54, 1992)

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

2.2 **Lambda-cyhalothrin content** (463/WP/M/3, CIPAC Handbook E, p. 54, 1992)

The lambda-cyhalothrin content shall be declared (g/kg) and, when determined, the average content measured shall not differ from that declared by more than the following tolerances:

Declared content in g/kg	Permitted tolerance
up to 25	± 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

* Specifications may be revised and/or additional evaluations may be undertaken. Ensure the use of current versions by checking at the WHO Prequalification Unit – Vector Control Product Assessment Team (PQT/VCP) website, https://extranet.who.int/pqweb/vector-control-products.

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

pH range: 5.5 to 9.0.

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

Maximum: 2% retained on a 75 µm test sieve.

3.3 **Suspensibility** (MT 184.1 CIPAC Handbook P, p. 245, 2021) (Notes 1 & 2)

Suspensibility: minimum 50% after 30 minute in CIPAC Standard Water D at 25 ± 5°C.

3.4 **Persistent foam** (MT 47.3, CIPAC Handbook O, p. 177, 2017) (Note 3)

Maximum: 60 ml after 1 minute

3.5 **Wettability** (MT 53.3.1, CIPAC Handbook F, p. 165, 1995)

The formulation shall be completely wetted in 1 minute without swirling.

4 Storage stability

4.1 **Stability at elevated temperature** (MT 46.4, CIPAC Handbook P, p. 232, 2021)

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 (3.5).

Note 1 The formulation should be tested at the highest and lowest rates of use recommended by the supplier, provided this does not exceed the conditions given in method MT 184.1.

Note 2 Chemical assay is the only fully reliable method to measure the mass of active ingredient still in suspension. However, the simpler gravimetric method may be used on a routine basis provided that it has 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 25 ± 5°C.

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

Lambda-Cyhalothrin Wettable Powder in Sealed Water Soluble Bag (WP-SB) - Who Specification 463/WP-SB (September 2021)

WHO Specification 463/WP-SB (September 2021*)

This specification, which is PART ONE of this publication, is based on an evaluation of data submitted by the manufacturers whose names are listed in the evaluation reports (463/2003, 463/2006, 463/2019). The specification should be applicable to relevant products of these manufacturers and those of any other formulators who use only TC from the evaluated source. 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 (463/2003, 463/2006, 463/2019), as PART TWO, form an integral part of this publication.

1 Description

The material shall consist of a defined quantity of a homogeneous mixture of technical lambda-cyhalothrin, complying with the requirements of WHO specification 463/TC (September 2021), together with filler(s) and any other necessary formulants. It shall be in the form of a fine powder, free from visible extraneous matter and hard lumps, contained in a sealed water-soluble bag.

2 Active ingredient (Note 1)

2.1 Identity tests (463/WP/M/2, CIPAC Handbook E, p. 54, 1992)

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

2.2 Lambda-cyhalothrin content (463/WP/M/3, CIPAC Handbook E, p. 54, 1992)

The lambda-cyhalothrin content shall be declared (g/kg) and, when determined, the average content measured shall not differ from that declared by more than the following tolerances:

Declared content in g/kg	Permitted tolerance
up to 25	± 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 (Note 1)

* Specifications may be revised and/or additional evaluations may be undertaken. Ensure the use of current versions by checking at the WHO Prequalification Unit – Vector Control Product Assessment Team (PQT/VCP) website, https://extranet.who.int/pqweb/vector-control-products.

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

pH range: 5.5 to 9.0.

3.2 **Wettability** (MT 53.3.1, CIPAC Handbook F, p. 165, 1995)

The formulation shall be completely wetted in 1 minute without swirling.

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

Maximum: 2% retained on a 75 µm test sieve.

3.4 **Suspensibility** (MT 184.1, CIPAC Handbook P, p. 245, 2021) (Notes 2 & 3)

The suspensibility shall be tested on a suspension containing the WP and the bag material in the actual ratio of application, prepared according to the procedure described in Note 4.

Suspensibility: minimum 50% after 30 minute in CIPAC Standard Water D at 25 ± 5°C.

3.5 **Persistent foam** (MT 47.3, CIPAC Handbook O, p. 177, 2017) (Note 5)

The persistent foam shall be tested on a suspension containing the WP and the bag material in the actual ratio of application in CIPAC Standard Water D, prepared according to the procedure described in Note 4.

Maximum: 60 ml after 1 minute

3.6 **Dissolution of the bag** (MT 176, CIPAC Handbook F, p. 444, 1995) (Notes 1 & 6)

The dissolution of the bag shall be tested on a sample of the emptied and cleaned bag together with an appropriate proportion of the WP in CIPAC Standard Water D taken according to the procedure described in Note 6.

Flow time of the suspension: maximum 30 sec.

4 Storage stability

4.1 **Stability at elevated temperature** (MT 46.4, CIPAC Handbook P, p. 232, 2021)

The package should be enclosed in a watertight sachet, box or any other container at 30 ± 2°C for 18 weeks. 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 formulation shall continue to comply with the clauses for:

- pH range (3.1);
- wet sieve test (3.3);
- suspensibility (3.4);
- persistent foam(3.5);
- dissolution of the bag (3.6).

None of the bags tested should show signs of leakage or rupture during normal handling, before and after storage. _____

Note 1 Sub-sampling.

Lay the bag on a bench and carefully open one side of the bag with a cutter, taking care not to damage the seals. Transfer the contents of the bag into a suitable flask. This material shall be used to carry out the tests for:

- active ingredient identity (2.1),
- active ingredient content (2.2),
- pH range (3.1),
- wettability (3.2),
- wet sieve test (3.3),
- suspensibility (3.4),
- persistent foam (3.5),
- dissolution of the bag (3.6).

The bag is then opened on three sides, completely cleaned from adhering powder by brushing or suction and weighed to the nearest 0.01 g. Aliquots of an aqueous solution of the bag material shall be used in the suspensibility (3.4) and persistent foam (3.5) tests.

In the case of delay of the above tests, the bag shall be stored in a watertight container (glass bottle or equivalent) to avoid any change in its properties.

Note 2 The formulation should be tested at the highest and lowest rates of use recommended by the supplier, provided this does not exceed the conditions given in method MT 184.1.

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

Note 4 The procedure for adding the bag material to the solution for the suspensibility and persistent foam tests should be as follows:

Prepare a stock solution of the bag material (1 mg/ml) by weighing a sample (n mg) of the bag (excluding sealed parts). Dissolve this sample by stirring in the standard water used for the tests to give a final volume of n ml. Store the stock solution in a stoppered bottle before use.

Calculate the volume (V ml) of the stock solution of the bag to be added to the test suspension of the water dispersible granule according to the following equation:

$$V(\text{ml}) = X \times \frac{1000B}{W}$$

Where: B (g) = weight of the emptied and cleaned bag
W (g) = nominal weight of the WP contained in the bag
X (g) = weight of the WP sample used in the test

Note 5 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 25 ± 5°C.

Note 6 The sampling of the bag for the dissolution test should be as follows:

Lay the empty cleaned bag in its original configuration (double layer). Delineate and then cut up a test sample including part of the upper seal (5 cm) and symmetrically including the vertical seal (10 cm). If the size of the bag is less than this dimension, use the whole bag.

Carry out the dissolution test immediately to avoid any modification of the sample.

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

Lambda-Cyhalothrin Slow-Release Capsule Suspension - (Slow-Release Cs) (Note 1) - WHO Specification 463/CS (August 2015)

WHO Specification 463/CS (August 2015*)

This specification, which is PART ONE of this publication, is based on an evaluation of data submitted by the manufacturers whose names are listed in the evaluation reports (463/2003, 463/2011). The specification should be applicable to relevant products of these manufacturers, but it 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, irrespective of the source of TC. The evaluation reports (463/2003, 463/2011), as PART TWO, forms an integral part of this publication.

1 Description

The material shall consist of a suspension of micro-capsules containing technical lambda-cyhalothrin, complying with the requirements of WHO specification 463/TC (August 2015), in an aqueous phase, together with suitable formulants. After agitation, the material shall be homogeneous (Note 2) and suitable for further dilution in water.

2 Active ingredient

2.1 **Identity tests** (463/CS/M/2, CIPAC Handbook K, p.86, 2003)

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 **Total lambda-cyhalothrin content** (463/CS/M/3, CIPAC Handbook K, p.86, 2003)

The lambda-cyhalothrin content shall be declared (g/l at 20 ± 2°C) (Note 3), and, when determined, the average content measured shall not differ from that declared by more than the following tolerances:

Declared content (g/l at 20 ± 2°C)	Permitted tolerance
up to 25 g/l	± 15% of the declared content
above 25 up to 100**	± 10% of the declared content
Note: the upper limit is included in each range	

* Specifications may be revised and/or additional evaluations may be undertaken. Ensure the use of current versions by checking at the WHO Prequalification Unit, Vector Control Products (PQT/VCP) website.

** The >25-100 g/l range was added in 2007, following a WHOPES Working Group (2006) recommendation for use of the 100 g/l formulation in indoor residual spraying.

2.3 **"Free" ("non-encapsulated") lambda-cyhalothrin content** (MT 189, CIPAC Handbook L, p.137, 2005)

The “free” (“non-encapsulated”) lambda-cyhalothrin content shall not exceed 4% of the total lambda-cyhalothrin content, determined according to clause 2.2.

2.4 **Release of lambda-cyhalothrin** (MT 190, CIPAC Handbook L, p.140, 2005)

The release of lambda-cyhalothrin from the capsules shall be:

at 15 min, 30 to 75% of that released at 180 min; and
at 30 min, 50 to 90% of that released at 180 min; and
at 180 min, a minimum of 80% of the total lambda-cyhalothrin content, determined according to clause 2.2.

3 Physical properties

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

pH range: 4.5 to 9.0.

3.2 **Pourability** (MT 148.1, CIPAC Handbook J, p.133, 2000)

Maximum “residue”: 5%.

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

A minimum of 90% of the lambda-cyhalothrin content found under 2.2 shall be in suspension after 5 minutes in CIPAC standard water D at 30 ± 2°C.

3.4 **Suspensibility** (MT 184, CIPAC Handbook K, p.142, 2003) (Note 4)

A minimum of 75% of the lambda-cyhalothrin content found under 2.2 shall be in suspension after 30 minutes in CIPAC standard water D at 30 ± 2°C.

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

A maximum of 0.1% w/w shall be retained on a 75 μm test sieve.

3.6 **Persistent Foam** (MT 47.3) (Notes 5 & 6)

Maximum: 5 ml after 1 minute

4 Storage stability

4.1 **Freeze/thaw stability** (Note 7)

After undergoing 4 freeze/thaw cycles (between 20 ± 2°C and -3 ± 2°C in 18-hour freeze/6-hour thaw cycles) and following homogenization, the formulation 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).

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 shall not be lower than 96% relative to the determined average content found before storage (Note 8), and the material shall continue to comply with the clauses for:

- "free" ("non-encapsulated") lambda-cyhalothrin content (2.3);
- release of lambda-cyhalothrin (2.4);
- pH range (3.1);
- pourability (3.2);
- spontaneity of dispersion (3.3);
- suspensibility (3.4);
- wet sieve test (3.5).

Note 1 This specification is applicable only to slow-release capsule suspension formulations intended for public health applications. Measurement of particle size distribution permits this type of product to be differentiated rapidly from the lambda-cyhalothrin rapid-release CS products used in agriculture. Using CIPAC MT 187 (CIPAC Handbook K, p.153, 2003), the following criteria should be met by the slow-release CS, intended for public health applications:

$D_{(10)}$, >1 µm;
$D_{(50)}$, 7 to 12 µm;
$D_{(90)}$, <50 µm.

Note 2 All physical and chemical tests listed in this specification are to be performed with a laboratory sample taken after the recommended homogenization procedure.

Before sampling to verify formulation quality, the commercial container must be inspected carefully. On standing, suspensions 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 sediment on the bottom. Therefore before sampling, the formulation must be homogenized 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.

Note 3 In determining active ingredient in g/l at 20 ± 2°C, the actual mass per millilitre shall be determined and used in the calculation, using MT 3.3. Where doubt remains, or in cases of dispute, the content should be expressed as g/kg. 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 thereby in the determination of the active ingredient content (g/l), if methods other than MT 3.3 are used.

Note 4 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 the chemical assay method. In cases of dispute, the chemical method shall be the "referee method".

Note 5 The CIPAC method MT 47.2 published in Handbook F for determination of persistent foam created when formulations are added to water before use was updated to MT 47.3. This new method was accepted as a full CIPAC method in 2013. Prior to its publication in the next Handbook, copies of the method can be obtained through the CIPAC website, http://www.cipac.org/cipacpub.htm.

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.

Note 7 After manufacture and during shipping, it may be impossible for the buyer or seller to be sure that the formulation has not been exposed to freezing temperatures. As freezing of an aqueous capsule suspension may result in undesirable and irreversible changes, including (but not limited to) capsule failure, caused by crystallization of the active ingredient, the ability of the formulation to successfully withstand repeated freezing and thawing is an important property. To avoid such undesirable changes, lambda-cyhalothrin CS formulations for use in public health must not be allowed to freeze, which occurs at about –5ºC.

Note 8 Samples of the formulation taken before and after the storage stability test should be analysed concurrently after the test in order to reduce the analytical error.

PART TWO: EVALUATION REPORTS FOR LAMBDA-CYHALOTHRIN

LAMBDA-CYHALOTHRIN

LAMBDA-CYHALOTHRIN

WHO Summary Report 463/2021

Based on the appraisals and recommendations provided by the JMPS expert panel in the 2019, 2020 and 2021 evaluation reports, the following actions were taken by WHO:

1. The amended lambda-cyhalothrin TC specification denoting the change in clause 2.2 to increase the minimum content from 810 /kg to 900 g/kg was adopted.
2. Manufacturers of lambda-cyhalothrin TC for whom the specification had been extended were requested to submit the relevant information to confirm the continued compliance of the respective TC products in relation to the increased minimum purity. These applicants responded to the request, and their submissions were evaluated. The respective 2021 evaluation reports confirmed continued compliance by all three manufacturers.
3. The editorial changes to the EC, WP and WP-SB specifications were confirmed and adopted.
4. The proposed changes to the slow-release CS specification were withheld from the publication of the updated specification. An analysis of the submitted information indicated that the proposed changes could impact other characteristics of WHO prequalified products which are supported by this specification. WHO therefore requested that post-prequalification change applications be submitted by the applicant to ensure that a complete assessment of the change and its effects on the product is undertaken.

Recommendations

The Meeting recommended that:

(i) The lambda-cyhalothrin TC produced by Jiangsu Yangnong Chemical Co. Ltd. should be accepted as equivalent to the lambda-cyhalothrin TC (revised) from Syngenta.

(ii) The revised FAO specification for lambda-cyhalothrin TC should be extended to encompass the product of Jiangsu Yangnong Chemical Co. Ltd.

(iii) The revised WHO specification for lambda-cyhalothrin TC should be extended to encompass the product of Jiangsu Yangnong Chemical Co. Ltd.

Appraisal

The Meeting considered a data package submitted by Jiangsu Yangnong Chemical Co. Ltd. in 2020 in support of continued compliance of their product with the FAO and WHO reference specifications for lambda-cyhalothrin TC, revised and adopted in 2019 and 2020 with the minimum purity raised from 810 g/kg to 900 g/kg.

The data submitted were in accordance with the requirements of the “Manual for development and use of FAO and WHO specifications for pesticides” (2016, third revision of the First Edition).

The Meeting was provided with commercially confidential information on the manufacturing process, the manufacturing specification and 5-batch analysis data together with supporting documentation and toxicity summaries. The declared minimum purity of the lambda-cyhalothrin TC is 950 g/kg, which is the same as at the time of previous extension in 2014 to the product of the proposer and higher than the revised FAO and WHO reference specification (minimum 900 g/kg). The mass balances range between 989.5 g/kg and 996.5 g/kg.

The manufacturing process, impurity profile and 5-batch analyses were compared with that of Syngenta in the revised reference profile . The proposer’s manufacturing process is unchanged since the original assessment by the JMPS and consists of three steps, whereas Syngenta’s manufacturing process comprises six steps. However, the starting material of the first step of the proposer’s process is the same as that of the third step in case of the reference and, thereafter, it follows the same pathway to obtain the lambda-cyhalothrin TC. The steps for preparation of cyhalothrin and epimerization have been merged in the process of the proposer. A total of five compounds have been identified in the TC – lambda-cyhalothrin and four impurities at or above 1 g/kg. The impurity profile of the proposer is different when compared to the reference. Of the four impurities so identified, two impurities, including the one as a residual aromatic solvent, are far below 1 g/kg in all the batches, although their manufacturing limits have been proposed at or above 1 g/kg. None of the impurities present in the TC of the proposer is considered relevant.

The proposer maintained the same toxicity profile of the product as at the time of previous extension (2014). Syngenta has also maintained the same acute toxicity studies as at the time of first evaluation (1999). Therefore, the comparison and

evaluation of toxicity studies of the proposer with those of the reference at the time of previous evaluation (2014) are still valid. The conclusion of the Meeting that lambda-cyhalothrin produced by the proposer was not more hazardous and, thus, equivalent to the toxicology profile of the reference TC based on Tier-2 evaluation still remains valid for the present evaluation.

The quantification of the active ingredient in the 5-batch study was performed using the CIPAC method 463/TC/M/3. The lambda-cyhalothrin was determined by GC-FID using a CP-Sil 5 CB capillary column, dichloromethane as solvent and hexacosane as internal standard. The proposer has provided three different methods (GC-MS, NMR and FTIR) for identity of active ingredient. The organic impurities were also determined by GC-FID after validation with respect to specificity, linearity, precision and accuracy at an acceptable LOQ. The water content was determined by Karl Fischer titration method. Test methods for determination of physico-chemical properties of the technical active ingredient were OECD and CIPAC.

The proposer also maintained the same data as were provided at the time of previous evaluation on physical-chemical properties like vapour pressure, melting point, solubility in water and some organic solvents, pH value, partition coefficient and photolysis for technical material ($\geq$ 95.0%). The data still remain valid.

In view of the purity and impurity profile as well as toxicology profile of the material of the proposer and its equivalence to that of the revised reference TC on Tier-2 evaluation, the Meeting concluded that the lambda-cyhalothrin TC of Jiangsu Yangnong Chemical Co. Ltd. continue to comply with the revised reference FAO and WHO specification.

Supporting Information
for
Evaluation Report 463/2021.3

Physico-chemical properties of lambda-cyhalothrin

Table 1. Chemical composition and properties of the Jiangsu Yangnong lambda-cyhalothrin 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 or WHO. Mass balances were 98.95 – 99.65%, and percentages of unknowns were 0.35 – 1.05%.
Declared minimum Lambda-cyhalothrin 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
Stabilisers or other additives and maximum limits for them	None

Parameter	Value and conditions	Purity %	Method reference	Study number
Melting temperature range of the TC	49.6 °C	97.1	OECD 102 EC 440/2008	3510010019
Solubility in organic solvents	40-50 g/l n-heptane at 25 °C ＞ 250 g/l p-xylene at 25°C ＞ 250 g/l 1,2-dichloroethane at 25°C 80-100 g/l propane-2-ol at 25°C ＞ 250 g/l acetone at 25°C ＞ 250 g/l ethyl acetate at 25°C	97.1	CIPAC MT 181	1010010099

Annex 1: References

Study number	Author(s)	Year	Study title. Study identification number. Report identification number. GLP [if GLP]. Company conducting the study
YN-2020-002	Yuan Zhou	2020	Validation of Analytical Methodology for the Assay of Active Ingredient and Related Significant Impurities and Subsequent five batches Qualitative and Quantitative Analysis of Lambda-cyhalothrin TC. Yangnong GLP Laboratory, China. Study number: YN-2020-002. GLP, Unpublished.
3510010019	Zhang minghong	2010	Determination of the Melting Point/Melting Range of 95% Lambda-Cyhalothrin Technical. Shanghai Research Institute of Chemical Industry Testing Centre, China. Study number: 3510010019. GLP, Unpublished.
1010010099	Zhang xiaoqin	2010	Determination of the solubility in organic solvents of 95% lambda-cyhalothrin Technical. Shanghai Research Institute of Chemical Industry Testing Centre, China. Study number: 1010010099. GLP, Unpublished.

Recommendations

The Meeting recommended that:

(i) The lambda-cyhalothrin TC produced by Bharat Rasayan Limited should be accepted as equivalent to the lambda-cyhalothrin TC (revised) from Syngenta.

(ii) The revised FAO specification for lambda-cyhalothrin TC should be extended to encompass the product of Bharat Rasayan Limited.

(iii) The revised WHO specification for lambda-cyhalothrin TC should be extended to encompass the product of Bharat Rasayan Limited.

Appraisal

The Meeting considered a data package submitted by Bharat Rasayan Limited (Bharat) in 2020 in support of continued compliance of their product with the FAO and WHO reference specifications for lambda-cyhalothrin TC, revised and adopted in 2019 and 2020 with the minimum purity raised from 810 g/kg to 900 g/kg.

The data submitted were in accordance with the requirements of the “Manual for development and use of FAO and WHO specifications for pesticides” (2016, third revision of the First Edition).

The Meeting was provided with commercially confidential information on the manufacturing process and five batch analysis data on all impurities present at or above 1 g/kg, and their manufacturing limits in the TC. Mass balances ranged between 991.4 g/kg and 995.9 g/kg in the 5-batch data. The maximum limits for the impurities were supported by the 5-batch data, and they are statistically justified. The proposer declared the minimum purity of the lambda-cyhalothrin TC as 970 g/kg, which is statistically justified (mean value - 3 standard deviation = 970 g/kg) and is higher than the minimum purity declared at the time of the first submission to FAO and WHO (965 g/kg) and higher than the minimum purity in the revised FAO/WHO reference specification (900 g/kg).

The confidential data provided on the manufacturing process of lambda-cyhalothrin TC from Bharat were stated to be identical to those submitted for registration in Europe, Brazil and Australia.

The manufacturing process, impurity profile and five batch analyses were compared with the data submitted by Syngenta in the revised reference profile.

The Bharat manufacturing process involves a synthesis route, which is the same as that of Syngenta. Bharat have made some improvements to the manufacturing plant process and are using starting materials of higher purity since the original assessment by the JMPS, although the synthesis pathway is unchanged. The impurity profile of the Bharat TC is similar to the profile of the reference TC but with fewer impurities.

No new impurities were identified in the Bharat TC. Batches were analysed for the presence of process solvents used during manufacture; these were not found at levels above 0.5 g/kg in the batches.

A new mutagenicity study (Ames test) for lambda-cyhalothrin TC has been conducted as Tier-1 data. Lambda-cyhalothrin TC from Bharat does not show mutagenicity in *in vitro* bacterial assays (OECD 471). New acute toxicity studies and studies on eye irritation and skin sensitization were also submitted to update the data package originally submitted by Bharat.

The analytical method for the active ingredient (including identity tests) is the CIPAC method 463/TC/M/3. The lambda-cyhalothrin is determined by GC-FID, using internal standardisation.

The CIPAC method was used for the determination of lambda-cyhalothrin in the batch analysis study. Although not required, validation data were also provided for this method and are acceptable.

Other impurities were determined by in-house methods using GC-FID. The methods are considered fully validated.

Data on acidity of 5-batches of TC were provided and determined using CIPAC method MT31.2.1. These demonstrated that the TC from Bharat complies with the specification clause of 0.5 g/kg, calculated as H_2SO_4.

Test methods for determination of physico-chemical properties of the technical active ingredient were OECD test methods.

The Meeting was provided with data on the melting point, vapour pressure, octanol/water partition coefficient, solubility in water and organic solvents and hydrolysis and photolysis behaviour on pure lambda-cyhalothrin. Although not required, these physical-chemical properties were in agreement with the reference material and with the physical-chemical data submitted in support of the previous extension (2012).

The Meeting concluded that Bharat lambda-cyhalothrin TC is equivalent to the revised lambda-cyhalothrin reference TC based on a Tier-1 evaluation and continues to comply with the revised reference FAO and WHO specification.

Supporting Information
for
Evaluation Report 463/2021.2

Physico-chemical properties of lambda-cyhalothrin

Table 1. Physico-chemical properties of pure lambda-cyhalothrin

New data were provided by Bharat Rasayan Limited. Properties for vapour pressure, melting point, solubility in water, octanol/water partition coefficient and solubility in organic solvents were already considered in the evaluation report 463/2012; the new data agree with that submitted previously.

Parameter	Values and conditions	Purity %	Method reference	Study number
Vapour pressure	7.75×10^{-5} Pa at 40°C and 2.17×10^{-7} Pa (2.17×10^{-4} mPa) at 20°C	98.15	OECD 104 / OPPTS 830.7950 / EEC A.4	20191
Melting point	47°C - 50°C	98.15	OECD 102, OPPTS 830.7200, EEC A.1, CIPAC MT 2, U.S. EPA	20189
Solubility in water	0.0000054 g/L (5.4 µg/L) at 20 ± 0.5°C (pH – approx. 7.0)	98.15	EEC A.6, OECD 105, and OPPTS 830.7840	10192
Octanol/water partition coefficient	log P_{OW} = 6.61 at 25 ± 1°C	98.15	EEC A.8, OECD 117, OPPTS 830.7530	20194
Hydrolysis characteristics	Half-life = 7.43 days at 20°C at pH 9 Half-life = 5.54 days at 35°C at pH 9 Half-life = 4.33 days at 45°C at pH 9	98.15	EEC C.7, OECD 111, OPPTS 835.2120	10196
Photolysis characteristics	DT50 = 13 days at pH 4 DT50 = 18 days at pH 7	98.15	OECD 316, OPPTS 835.2210	20197
Solubility in organic solvents	Acetone > 250 g/L; 1,2-Dichloroethane > 250g/L; Ethyl Acetate > 250 g/L; n-Heptane 72.2 g/L; Methanol > 250 g/L; p-Xylene > 250 g/L (all at 20 ± 0.50˚C)	98.15	EEC A.6, OECD 105, OPPTS 830.7840	20193
Acidity	0.012%	98.15	CIPAC MT 31.1	20188
Density	1.3224 g/mL at 20.2°C	98.15	OPPTS 830.7300, OECD 109 EEC A.3	20190
Accelerated Storage Stability at 54 ± 2°C for 14 days	Product is stable at elevated temperature 54 ± 2 °C for 14 days	98.15	OPPTS 830.6317, OPPTS 830.6303, OPPTS 830.6302, OPPTS 830.6304, OPPTS 830.7200, OECD 102 and 830.6320	20195

Table 2. Chemical composition and properties of Bharat lambda-cyhalothrin 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 99.14 – 99.59 % and percentages of unknowns were 0.41 – 0.86%.
Declared minimum lambda-cyhalothrin 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
Stabilisers or other additives and maximum limits for them	None

Parameter	Value and conditions	Purity %	Method reference	Study number
Melting temperature range of the TC	47°C - 50°C	98.15	OECD 102, OPPTS 830.7200, EEC A.1, CIPAC MT 2, U.S. EPA	20189

Annex 1: Hazard Summary Provided by the Proposer

Notes.

(i) The proposer confirmed that the toxicological data included in the summary below were derived from lambda-cyhalothrin having impurity profiles similar to those referred to in the table above.

(ii) The conclusions expressed in the summary below are those of the proposer unless otherwise specified.

Table 3. Toxicology profile of the Bharat lambda-cyhalothrin technical material, based on acute toxicity, irritation and sensitization

(Additional data generated since, or not included in the FAO/WHO evaluation report 463/2012)

Species	Test	Purity %	Guideline, duration, doses and conditions	Result	Study number
Wistar Rats, Female	Oral	98.15	OECD 423	LD50 > 50 ≤ 300 mg/kg bw. Category 3 as per GHS classification	20_26_145
Wistar Rats, Male and Female	Dermal	98.15	OECD 402 and OCSPP 870.1200	LD50 >1400 < 2000 mg/kg bw. Category 4 as per GHS classification	20_26_146
Wistar Rats, Male and Female	Inhalation	98.15	OECD 403 and OCSPP 870.1300	LC50 = 0.32 mg/mL of air Category 2 as per GHS classification	20_26_147
New Zealand white rabbits, Male	Skin irritation	98.15	OECD 404 and OCSPP 870.2500	Non-irritant to rabbit skin	20_26_149
New Zealand white rabbits, Female	Eye irritation	98.15	OECD 405 and OCSPP 870.2400	Non-irritant to rabbit eye	20_26_150
Cavia porcellus (Guinea pig), Female	Skin sensitisation	98.15	OECD 406 and OCSPP 870.2600	Not a sensitizer	20_26_148

Table 4. Mutagenicity profile of the Bharat technical material based on *in vitro* tests
(Additional data generated since, or not included in the FAO/WHO evaluation report 463/2012)

Species	Test	Purity %	Guideline, duration, doses and conditions	Result	Study number[4]
Salmonella Typhimurium TA1537, TA98, TA100, TA102 and TA1535	Bacterial reverse mutation assay Ames Test	98.15	OECD 471 and OCSPP 870.5100 Trial 1: (+S9 and -S9): 312.5, 625, 1250, 2500 and 5000 µg/plate Trial 2: (+S9): 128, 320, 800, 2000 and 5000 µg/plate	Non-mutagenic	20_26_151

Annex 2: References

Study number	Author(s)	Year	Study title. Study identification number. Report identification number. GLP [if GLP]. Company conducting the study
20131	Ch. Rajasekharam	2020	Chemical Composition of Five Batches of Lambda-cyhalothrin Technical Preliminary Analysis and Enforcement Analytical Methods for Lambda-cyhalothrin TGAI, fulfilling the Requirements of OPPTS Guideline 830.1700 and 830.1800 and EU Commission Regulation No. 283/2013 IIBAT Study No: 20131 (Final Report) – Volumes I and II International Institute of Biotechnology and Toxicology (IIBAT) GLP, Unpublished.
20187	S. Pandiselvi	2020	Lambda-cyhalothrin Technical: Laboratory Study of Appearance (Physical State, Colour and Odour) International Institute of Biotechnology and Toxicology (IIBAT)GLP, Unpublished.
20188	S. Pandiselvi	2020	Lambda-cyhalothrin Technical: Laboratory study of Acidity International Institute of Biotechnology and Toxicology (IIBAT)GLP, Unpublished.
20189	S. Pandiselvi	2020	Lambda-cyhalothrin Technical: Laboratory study of Melting point International Institute of Biotechnology and Toxicology (IIBAT)GLP, Unpublished.
20190	S. Pandiselvi	2020	Lambda-cyhalothrin Technical: Laboratory study of Density International Institute of Biotechnology and Toxicology (IIBAT)GLP, Unpublished.
20191	S. Nagachandrudu	2020	Lambda-cyhalothrin Technical: Laboratory study of Vapour Pressure/Volatility International Institute of Biotechnology and Toxicology (IIBAT)GLP, Unpublished.
20192	J. Rupa Piriyadarsini	2020	Lambda-cyhalothrin Technical: Laboratory study of Water Solubility International Institute of Biotechnology and Toxicology (IIBAT)GLP, Unpublished.
20193	J. Rupa Piriyadarsini	2020	Lambda-cyhalothrin Technical: Laboratory study of Solubility in Organic Solvent International Institute of Biotechnology and Toxicology (IIBAT)GLP, Unpublished.
20194	Uma Venkata Satish Pakki	2020	Lambda-cyhalothrin Technical: Laboratory study of Partition Coefficient International Institute of Biotechnology and Toxicology (IIBAT)GLP, Unpublished.
20195	P.E. Ravi	2020	Lambda-cyhalothrin Technical: Laboratory study of Accelerated Storage Stability at 54 ± 2°C for 14 days International Institute of Biotechnology and Toxicology (IIBAT)GLP, Unpublished.
20196	S. Kousalya	2020	Lambda-cyhalothrin Technical: Laboratory study of Hydrolysis in Buffer solutions of pH 4, 7 and 9

Study number	Author(s)	Year	Study title. Study identification number. Report identification number. GLP [if GLP]. Company conducting the study
			International Institute of Biotechnology and Toxicology (IIBAT)GLP, Unpublished.
20197	B. Saranya	2020	Lambda-cyhalothrin Technical: Laboratory study of Photolysis International Institute of Biotechnology and Toxicology (IIBAT)GLP, Unpublished.
20_26_151	Sam Koshy	2021	Bacterial Reverse Mutation Test of Lambda-cyhalothrin Technical in Salmonella Typhimurium Tester Strain Test Facility: sa-FORD GLP, Unpublished.
20_26_145	-	2021	Acute oral Toxicity study (Acute Toxic Class Method) of Lambda-cyhalothrin Technical in Wistar Rats. GLP, Unpublished.
20_26_146	-	2021	Acute Dermal Toxicity Study of Lambda-cyhalothrin Technical in Wistar Rats GLP, Unpublished.
20_26_147	-	2021	Acute Inhalation Toxicity Study of Lambda-cyhalothrin Technical in Wistar Rats. GLP, Unpublished.
20_26_149	-	2021	Acute Dermal Irritation /Corrosion Study of Lambda-Cyhalothrin Technical in Rabbits GLP, Unpublished.
20_26_150	-	2021	Acute Eye Irritation/corrosion study of Lambda-cyhalothrin technical in Rabbits GLP, Unpublished.
20_26_148	-	2021	Skin Sensitization Maximization Study (GPMT) of Lambda-cyhalothrin Technical in Guinea Pigs GLP, Unpublished.

Recommendations

The Meeting recommended that:

(i) The lambda-cyhalothrin TC produced by Tagros Chemicals India Private Limited should be accepted as equivalent to the lambda-cyhalothrin TC (revised) from Syngenta.

(ii) The revised FAO specification for lambda-cyhalothrin TC should be extended to encompass the product of Tagros Chemicals India Private Limited.

(iii) The revised WHO specification for lambda-cyhalothrin TC should be extended to encompass the product of Tagros Chemicals India Private Limited.

Appraisal

The Meeting considered a data package submitted by Tagros Chemical India Private Limited in 2020 in support of continued compliance of their product with the FAO and WHO reference specifications for lambda-cyhalothrin TC, revised and adopted in 2019 and 2020, with the minimum purity raised from 810 g/kg to 900 g/kg.

The data submitted were not fully in accordance with the requirements of the “Manual for development and use of FAO and WHO specifications for pesticides” (2016, third revision of the First Edition) but were considered sufficient by the Meeting.

The Meeting was provided with commercially confidential information on the manufacturing process and 5-batch analysis data (GLP study) for the lambda-cyhalothrin content and acidity only. In addition, manufacturing QC data of 15 batches that were analysed for lambda-cyhalothrin content, acidity and impurities present at or above 1 g/kg were provided to support the stated manufacturing limits in the TC.

The proposer declared the minimum purity of the lambda-cyhalothrin TC as 950 g/kg, which is statistically justified (mean value - 3 standard deviation = 950 g/kg) and is higher than the minimum purity declared at the time of the first submission to FAO and WHO (840 g/kg) and higher than the minimum purity in the revised FAO/WHO reference specification (900 g/kg). The levels of the other manufacturing impurities were the same or lower than declared previously and were supported by analytical quality control data. The Meeting considered that sufficient analytical data had been provided to support the declared manufacturing specification.

The manufacturing process, impurity profile and five batch analyses were compared with the data submitted by Syngenta in the revised reference profile.

The Tagros manufacturing process involves a synthesis route which is the same as that of Syngenta and is unchanged since the original submission to FAO and WHO.

One of the impurities in Tagros TC did not appear in the reference Syngenta profile; this same impurity was already considered in Tagros TC by the JMPS in 2006:

> “equivalence was assessed by comparing the Tagros acute toxicity data with those of the reference profile. The oral, dermal, inhalation, skin irritation and skin

sensitization hazard data indicated equivalence. However, the data for mucous membrane irritation were more difficult to compare, because the Tagros data related to vaginal mucous membrane irritation, whereas the data from the reference profile related to eye irritation. WHO/PCS noted that vaginal mucous membrane irritation data are a requirement under the Gaitonde protocol, whereas eye irritation data are a requirement under the OECD protocol. From a detailed consideration of the data and protocols, WHO/PCS concluded that, although no comparative studies of the two protocols are available, the absence of vaginal mucous membrane irritation produced by Tagros lambda-cyhalothrin meant that the product could be considered equivalent to the reference, which is characterized as mildly irritating to the eye (PCS 2006). The Meeting therefore agreed that the products should be considered equivalent."

The level of this impurity in the current Tagros manufacturing specification is lower than considered previously; therefore, the Meeting agreed that the conclusion of the previous evaluation is still valid.

Another impurity, which is present in both Tagros TC and the reference profile, is present in the current Tagros TC at levels that are higher than in the revised reference Syngenta TC. The level of this impurity remains unchanged in Tagros TC when compared to the previous Tagros specification. The Meeting noted that Syngenta, the reference profile, maintained the same acute toxicity studies in their revised data package as at the time of the first evaluation (1999), and at that time, the Syngenta manufacturing specification for this impurity was the same as for Tagros. Therefore, the presence of this impurity at both the original and current level in the Tagros TC specification has been sufficiently covered by the data package for the reference profile, the conclusion of the previous evaluation is still valid, and no further consideration is needed.

A mutagenicity study (Ames test) for lambda-cyhalothrin was not initially provided. This is required as Tier-1 data for equivalence assessment. Upon request, Tagros provided a study conducted on a batch of TC manufactured in 2020. The lambda-cyhalothrin TC of Tagros is considered non-mutagenic under the conditions of the test.

The proposer maintained the same acute toxicity, irritation and sensitization data as submitted at the time of previous extension (2006). Syngenta has also maintained the same acute toxicity studies as at the time of first evaluation (1999). Therefore, the comparison and evaluation of these toxicity studies of the proposer with those of the reference at the time of previous evaluation (2006) are still valid.

The analytical method for the active ingredient (including identity tests) is the CIPAC method 463/TC/M/3. The lambda-cyhalothrin is determined by GC-FID using internal standardisation.

The CIPAC method was used for the determination of lambda-cyhalothrin in the batch analysis study. Although not required, validation data were also provided for this method and are acceptable.

Data on acidity of 5-batches of TC were provided and were determined using CIPAC method MT 31.2.1. These demonstrated that the TC from Tagros complies with the specification clause of 0.5 g/kg, calculated as H_2SO_4.

The proposer maintained the same data, as were provided at the time of the previous evaluation on physical-chemical properties like vapour pressure, melting point,

solubility in water and some organic solvents, pH value, partition coefficient and photolysis.

The Meeting concluded that Tagros lambda-cyhalothrin TC complies with the clauses for active ingredient content and acidity of the revised reference specification. The Meeting also concluded that although the data submitted were not fully in line with the requirements of the Manual, there is sufficient data to conclude that the Tagros lambda-cyhalothrin TC is equivalent to the revised lambda-cyhalothrin reference TC and continues to comply with the revised reference FAO and WHO specification.

Supporting Information
for
Evaluation Report 463/2021.1

Physico-chemical properties of lambda-cyhalothrin

Table 1. Physico-chemical properties of pure lambda-cyhalothrin

No new data were provided.

Table 2. Chemical composition and properties of Tagros lambda-cyhalothrin 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 99.32 – 99.98 % w/w and percentages of unknowns were 0.02 – 0.68%.
Declared minimum lambda-cyhalothrin 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
Stabilisers or other additives and maximum limits for them	None

Annex 1: Hazard Summary Provided by the Proposer

Notes.

(i) The proposer confirmed that the toxicological data included in the summary below were derived from lambda-cyhalothrin having impurity profiles similar to those referred to in the table above.

(ii) The conclusions expressed in the summary below are those of the proposer unless otherwise specified.

Table 3. Mutagenicity profile of the Tagros technical material based on *in vitro* tests

Species	Test	Purity %	Guideline, duration, doses and conditions	Result	Study number[4]
Salmonella Typhimurium TA98, TA100, TA1535 and TA1537 *Escherichia Coli* WP2uvrA (pKM101)	Bacterial reverse mutation assay Ames Test	98 % w/w	OECD 471 (2020) Preliminary (TA100): 50, 100, 200, 400, 800, 1600, 3200 and 5000 µg/plate. Main test (+S9 and -S9): 10, 32, 102, 321, 1013 and 3200 µg/plate	Non-mutagenic	G23158

Annex 2: References

Study number	Author(s)	Year	Study title. Study identification number. Report identification number. GLP [if GLP]. Company conducting the study
G20285	Ravikanth gogineni	2020	Five Batch Analysis of Lambda-Cyhalothrin Technical. Study identification Number: G20285. Report identification Number: Not available. Eurofins Advinius Limited, GLP, Unpublished.
QC data	P. Pandiyarajan	2021	Quality Control Data of Lambda-Cyhalothrin. Study identification Number: N/A. Report identification Number: N/A. Tagros Chemical India Private Limited, Non-GLP, Unpublished.
G23158	Ashwini, C.	2021	Lambda-cyhalothrin Technical : Bacterial Reverse Mutation Test.Study identification Number: G23158 Eurofins Advinius Limited, GLP, Unpublished.

Recommendations

The Meeting recommended that:

(i) The existing FAO specifications for lambda-cyhalothrin TC, EC, WG and rapid-release CS (see below) should be converted into time-limited interim specifications valid until June 2021.

(ii) The existing WHO specifications for lambda-cyhalothrin TC, EC, WP, WP-SB and slow release CS (see below) should be converted into time-limited interim specifications valid until June 2021.

Appraisal

The Meeting considered the recently revised FAO and WHO specifications for lambda-cyhalothrin TC, EC, WG, WP, WP-SB and rapid- and slow-release CS that had been proposed by Syngenta in 2018 and adopted in 2019 and 2020. The revision mainly included a new confidential data package for the TC, an editorial update of the EC, WP and WG specifications, and a major revision of the rapid- and slow-release CS specifications. As for the TC, the data supported an increase in minimum purity from 810 to a minimum of 900 g/kg, and none of the impurities identified were deemed to be relevant.

In order to offer the companies that have been granted extensions of the previous versions of TC and formulations specifications to their products, to provide adequate supporting documentations to demonstrate within a reasonable time that their products still comply with the revised reference specifications, the Meeting recommended that these specifications should be converted into time-limited interim specifications (until end of June 2021). Concurrently, the manufacturers should be invited to submit appropriate data packages to JMPS to demonstrate continued equivalence of their product. This will also safeguard unfettered supply of these products, especially for public health use.

These provisions refer to the following manufacturers, their products and FAO and WHO specifications:

- Tagros Chemicals India Ltd, for TC (FAO and WHO), EC (FAO and WHO), WP and WP-SB (WHO) (2006) and slow-release CS (WHO, 2011)
- Bharat Rasayan Limited, India for TC (FAO and WHO, 2012)
- Jiangsu Yangnong Chemical Co., Ltd, China for TC (FAO and WHO, 2014).

Recommendations

The Meeting recommended the following:

(i) The revised FAO specifications for lambda-cyhalothrin TC and rapid-release CS, and the editorially updated WG and EC specifications, proposed by Syngenta, and as amended, should be adopted by FAO as new reference specifications.

(ii) The revised WHO specification for lambda-cyhalothrin TC and the editorially updated specifications for EC, WP and WP-SB, proposed by Syngenta, and as amended, should be adopted by WHO as new reference specifications.

(iii) The previous FAO and WHO specifications for lambda-cyhalothrin TC and formulated products should be converted into time-limited interim specifications valid for the products of those manufacturers (Tagros, Bharat Rasayan, Jiangsu Yangnong) whose the previous lambda-cyhalothrin reference specifications had been extended to.

Appraisal

The Meeting considered a data package in support of the revision of the existing FAO and WHO specifications for lambda-cyhalothrin TC, WP and EC and the FAO specification for CS (rapid-release). The data package also included updated hazard summaries beside two studies on *in-vitro* reverse mutation of the technical material produced in the two production sites (see below) as part of the Tier-1 equivalence assessment.

Lambda-cyhalothrin is a pyrethroid insecticide with rapid knock down effect and good photostability. It is used in agriculture and public health, to control a wide range of pests and vectors such as mosquitoes and flies. Lambda-cyhalothrin is not under patent. The first FAO and WHO specifications for lambda-cyhalothrin under "New procedure" were evaluated and published by FAO in 1999 and by WHO in 2003. The minimum purity of the active ingredient was 810 g/kg.

The compound was last evaluated by JMPR in 2007 where a group ADI for cyhalothrin and lambda-cyhalothrin of 0 - 0.02 mg/kg bw and an ARfD of 0.02 mg/kg were established on the basis of systemic neurotoxicity, using a safety factor of 25.

Lambda-cyhalothrin was also re-evaluated by the European Commission in 2015. The compound is included in the positive list of EU Regulation 540/2011 with a minimum purity of 900 g/kg, hence significantly higher than in the published FAO and WHO specifications for the TC (810 g/kg).

The ISO 1750 common name definition for lambda-cyhalothrin is a "reaction product comprising equal quantities of (*R*)-*α*-cyano-3-phenoxybenzyl (1*S*,3*S*)-3-[(*Z*)-2-chloro-3,3,3-trifluoropropenyl]-2,2-dimethylcyclopropanecarboxylate and (*S*)-*α*-cyano-3-phenoxybenzyl (1*R*,3*R*)-3-[(*Z*)-2-chloro-3,3,3-trifluoropropenyl]-2,2-dimethyl-cyclopropane - carboxylate". Whereas cyhalothrin consists of 4 possible stereoisomers all having *cis*-configuration at the cyclopropyl-moiety and *Z*- configuration at the double bond, lambda-cyhalothrin is a single diastereomer and a racemate comprised of the (*Z*) α-*S*-1-*R*-*cis*- and (*Z*) α-*R*-1-*S*-*cis* enantiomers using the Rothamsted nomenclature.

The CIPAC method to determine the content of lambda-cyhalothrin in TC, WP, EC and UL formulations is published in Handbook E. The capillary GC method is capable of quantifying lambda-cyhalothrin in the possible presence of the other cyhalothrin diastereomer. The method utilizes internal standardization with hexacosane.

The Meeting was provided with commercially confidential information in relation to the proposed new technical specification, the manufacturing process and the supporting 5-batch analysis, together with updated supporting documentation and toxicity summaries.

The manufacturing process of lambda-cyhalothrin as described in the data package supporting the 1999 specifications and in the recently submitted confidential data are quite similar. Main differences lie in the more detailed description of the manufacturing of the cyhalothric acid moiety and the final step in preparation of the finished lambda-cyhalothrin TC.

Mass balances ranged from 99.7 to 100.8% in the 5-batch data and no unidentified impurities exceeding 1 g/kg were reported. There are no relevant impurities in the technical material as manufactured. The main differences in the purity/impurity profile lie in the higher minimum purity with a minimum of 900 g/kg lambda-cyhalothrin. The analytical methods for active ingredient and impurities were CIPAC for lambda-cyhalothrin, whereas the majority of impurities were determined by GC-FID and GC-MS. Some polar impurities needed derivatization prior to determination, and water was determined by coulometric Karl Fischer water determination.

The 2018 confidential data package refers to two production sites - one at a Syngenta site within Europe and one outside, where lambda-cyhalothrin is toll manufactured. The two sites produce lambda-cyhalothrin with the same starting materials using the same process and differ slightly in the final step, the non-European source achieving a somewhat higher minimum purity. The Meeting considered the purity-impurity profile of the two sources and concluded, that the TC produced in the two sites are deemed equivalent by Tier-1 and that the TC produced at the Syngenta site is considered as the reference profile. None of the impurities identified should be considered as relevant.

Issues identified with particular specifications:

TC: The previous FAO and WHO TC specifications had a clause for flash point. As the content of residual solvent in the 2018 5-batch data was very low, the Meeting concluded that the flash point clause was no longer required and could be removed. The clause for acidity however was justified, as the last manufacturing step includes controlled addition of a mineral acid. In order to avoid excessive amounts of acids present that could be detrimental for the stability of formulations and cause phytotoxicity, the acid clause was kept.

Rapid-release CS formulation: The formation of the capsules involves a reaction step of plastic monomers together with the active ingredient and other materials to form the capsule shells with the majority of active ingredient encapsulated. During that reaction, a shift of pH is expected to occur. Minor modifications in the encapsulation process may therefore lead to changes of pH range in the finished CS formulation. Quality control data have shown, that a pH range shift from 4 to 6 to 4.5 to 7.5 has been observed in batches. In addition, a somewhat higher residue in pourability has been observed (from 1.5 to 5 %), together with a slight increase in wet sieve residue (from 0.1 to 0.2 %). The other clauses and limits remain the same. The Meeting considered the proposed changes and concluded, that neither of these changes are expected to have an adverse effect on the quality of the fast-release CS formulation.

WP formulation: The previous WP formulation was still the combined template for a neat wettable powder and a WP packed in water soluble bags. The latest edition of the Manual now has two new model specifications - one for the neat and one for the formulation packed in water soluble bags. The company explained that both WP formulations - the neat and the soluble-bag packed - are intended for public health use.

The Meeting also recommended that the revised lambda-cyhalothrin specifications, before publication, should be provided to the manufacturers of hitherto equivalent TC and formulated products and they should be requested to submit data packages within a reasonable time demonstrating that their TC and formulated products continue to be equivalent with the revised reference specifications.

Supporting Information
for
Evaluation Report 463/2019

Physico-chemical properties of lambda-cyhalothrin

Table 1. Physico-chemical properties of pure lambda-cyhalothrin

Parameter	Value(s) and conditions	Purity %	Method reference (and technique if the reference gives more than one)	Study number
Vapour pressure	2 x 10^{-10} kPa at 20°C	99.0	OECD 104	RJ0366B ***PP321/1616 (1984)***
Melting point	49.2°C (322.4 K)	99.0	OECD 102	RJ0366B ***PP321/1616 (1984)*** 1291/016 ***PP321/1807 (2001)***
Temperature of decomposition	No boiling point at atmospheric or reduced pressure, decomposition occurs at 239°C (purity 99.0%) and at 234°C at 1 mm Hg pressure (purity 85.9% and 96.5%) Methods: EEC A2, EEC A4 and OECD 103 for boiling point, OECD 103 and EEC A4 for temperature of decomposition.	99.1 85.9 96.5	OECD 103 EEC A2 and A4	RJ0366B ***PP321/1616 (1984)***
Solubility in water	4 x 10^{-3} mg/l at pH 5.0 5 x 10^{-3} mg/l at pH 6.5 4 x 10^{-3} mg/l at pH 9.2	96.5	EEC A6	RJ0366B ***PP321/1616 (1984)***
Octanol/water partition coefficient	log P_{OW} 7.0	99.0	EEC A8	RJ0366B ***PP321/1616 (1984)***

Parameter	Value(s) and conditions	Purity %	Method reference (and technique if the reference gives more than one)	Study number
Hydrolysis characteristics	Study of the acid moiety, over a period of 30 days at 25°C, indicated that lambda-cyhalothrin is stable to hydrolysis at pH 5, hydrolyses very slowly at pH 7 and rapidly at pH 9. However, the material failed to remain completely in solution and these data are questionable. At both pH 7 and 9, the cyclopropane acid was the major product of hydrolysis (2% produced at pH 7 and 73% at pH 9). Polar compounds, which remained at the origin of thin layer chromatograms, were formed but did not exceed 10% of the radioactivity recovered into dichloromethane. Studies on the alcohol moiety, over a period of up to 29 days at 25°C, indicated that hydrolysis occurred very slowly at pH 4, slowly at pH 7 and fairly rapidly at pH 9. At all pH values, 3-phenoxybenzaldehyde and 3-phenoxybenzoic acid were formed, with 3-phenoxybenzaldehyde being the major compound formed at pH 9 (up to 78% of the applied radioactivity). Two unidentified compounds were also formed, representing 10.7% and 3.4% of the applied radioactivity after 29 days at pH 9. These unknowns occurred at much lower levels at pH 4 and 7 (radio-labelled material purity >95%).	>95	EPA CG5000	RJ0338B ***PP321/1023 (1984)*** RJ0117B ***CGA55186/ 0653 (1980)***
Photolysis characteristics	Studies at pH 5 for 31 days at 25°C produced four values for the lambda-cyhalothrin remaining at each sampling interval. The values were used to estimate a half-life of 24 d for lambda-cyhalothrin at 30°N in autumn. This value is only approximate because lambda-cyhalothrin was too hydrophobic to remain totally in solution during the irradiation (radiolabeled material purity > 95%).	>95	EPA CG6000	RJ0605B ***PP321/1022 (1988)***
Dissociation characteristics	Not measurable due to hydrolysis.	-	-	RJ0366B ***PP321/1616 (1984)***
Solubility in organic solvents	See Table 2.			

Table 2. Chemical composition and properties of lambda-cyhalothrin 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 99.7 – 100.8% and percentages of unknowns were n.d. – 0.04%.			
Declared minimum lambda-cyhalothrin content	900 g/kg			
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			
Parameter	Value and conditions	Purity %	Method reference	Study number
Melting temperature range of the TC and/or TK	47.5-48.5°C (320.6-321.6 K)	96.5	OECD 102	RJ0366B ***PP321/1616 (1984)***
Solubility in organic solvents	The solubility of technical lambda-cyhalothrin in organic solvents was determined at 20°C: Xylene: 847-875 g/kg n-Heptane: 742-758 g/kg Acetone: 924 - 948 g/kg Ethyl acetate: 875 - 900 g/kg Methanol: 761 - 769 g/kg n-Octanol: 202 - 223 g/kg Dichloroethane: 898 - 924 g/kg	83.3	OECD 105	1291/016 ***PP321/1807 (2001)***

Formulations and co-formulated active ingredients

The main formulation types available are EC, WG, WP and CS.

Lambda-cyhalothrin may be co-formulated with other insecticides or fungicides.

These formulations are registered and sold in many countries throughout the world.

Methods of analysis and testing

The analytical method for the active ingredient (including identity tests) is CIPAC method 1990 (463/TC/M/2, CIPAC Handbook E, p.50, 1992).

Lambda-cyhalothrin is determined according to the analytical method CIPAC 1990, by gas chromatography (GC) with internal standard calibration, and flame ionization detection (FID). Analytical method AMP10020-02B (active substance) is equivalent to CIPAC method 1990 (463/TC/M/2, CIPAC Handbook E, p.50, 1992) and was used for studies described in this document.

The method(s) for determination of impurities are according to the analytical methods AMP10020-02B (GC-FID) and AMP10106-01B (HPLC-UV).

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

Physical properties

The physical properties, the methods for testing them and the limits proposed for the noted formulations, comply with the requirements of the FAO/WHO Manual (2006 edition).

Containers and packaging

No special requirements for containers and packaging have been identified.

Expression of the active ingredient

The active ingredient is expressed as lambda-cyhalothrin.

Annex 1: Hazard Summary Provided by the Proposer

Note:

(i) The proposer confirmed that the toxicological and ecotoxicological data included in the summary below were derived from lambda-cyhalothrin having impurity profiles similar to those referred to in the table above.

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

(iii) References noted in tables 3, 4 and 5 are those generated since, or not included in, the JMPS evaluation in 1999 (FAO/WHO EVALUATION REPORT 463/1999).

No additional acute toxicity data has been generated since the JMPS evaluation in 1999 (FAO/WHO EVALUATION REPORT 463/1999)

Table 3. Toxicology profile of lambda-cyhalothrin technical material, based on acute toxicity, irritation and sensitization.

Species	Test	Purity %[3]	Guideline, duration, doses and conditions	Result [(isomer/form)]	Study number
not applicable	not applicable	not applicable	not applicable	not applicable	not applicable

[3] Purity is the content of pure lambda-cyhalothrin in the technical material unless otherwise stated, expressed as a percentage.

Additional repeated administration data generated since, or not included in, the JMPS evaluation in 1999 (FAO/WHO EVALUATION REPORT 463/1999)

Table 4. Toxicology profile of lambda-cyhalothrin technical material based on repeated administration (subacute to chronic)

Species	Test	Purity %[4]	Guideline, duration, doses and conditions	Result [(isomer/form)]	Study number
Rat (m)	Reversibility Study	96.8 Cyhalothrin	Repeat-dose (28-Day Reversibility Study) Toxicity (Rat) 28 d diet oral Alderley Park Wistar derived rats Dose level: 0, 250 ppm	Administration of 250 ppm cyhalothrin in diet produced reversible and adaptive changes in the liver, characterised by SER proliferation and increased APDM activity. This level of cyhalothrin also produced a decrease in bodyweight gain which was still apparent 28 days after the cessation of treatment	Lindsay. S *et al*., (1982) ***PP563/0180, IAD ASF356_11154***
Dog	6 Week Oral	87.7	No guideline 6 Week gelatine capsule oral Beagle dogs Dose levels: 0.75, 1.5, 3.0 or 4.0 mg/kg/day	NOAEL = 0.75 mg/kg/day. There were no signs of neuroactivity at 1.5 mg/kg/day except for one dog which exhibited slight tremors on day one of treatment. The NOAEL is therefore conservatively established at 0.75 mg/kg/day in the dog for acute exposure	Horner. S., (1996) ***PP321/1741, IAD PP321/1734***
Rat	21 Days sub-acute inhalation	81.5	No guideline 21 Days sub-acute inhalation Alpk: APfSD (Wistar-derived) rats	NOEL = 0.3 µg/L	Hext P.M., (1990) ***PP321/1739***

[4] Purity is the content of pure lambda-cyhalothrin in the technical material unless otherwise stated, expressed as a percentage.

Species	Test	Purity %[4]	Guideline, duration, doses and conditions	Result [(isomer/form)]	Study number
			Dose levels (mean particulate concentrations measured gravimetrically): 0.3, 3.3 and 16.7 µg/L		
Rat	21-Day Dermal	96.6	OECD 410 (1981): OPPTS 870.3200 (1998): 92/69/EEC B.9 (1992) 21-Day Dermal Alpk: APfSD (SPF) rats Dose levels: 1, 10, 100 mg/kg (reduced to 50 mg/kg after two or three applications)	NOAEL = 10 mg/kg	Leah A., (1989) ***PP321/1582, IAD PP321/1732***
Rat	Sub-chronic Neurotoxicity	87.7	OECD 424 (1997): OPPTS 870.6200 (1998): 2004/73/EC B.43 (2004) 90 d dietary oral Alpk: APfSD (Wistar-derived) rats Dose levels: 0, 25, 60 or 150 ppm	NOEL = 150ppm	Brammer A., (2001) ***PP321/1469; IAD PP321/1485***
Rat	Preliminary Developmental Neurotoxicity	87.7	No guideline Dams dosed from gestation day 7 to lactation day 22 (approx. 5 weeks). Alpk: APfSD (Wistar-derived) rats Dose levels: 0, 25, 60 or 150 ppm	Dose levels acceptable for main study	Williams J., (2001) ***PP321/1537***
Rat	Developmental Neurotoxicity	87.7	OPPTS 870.6300 (83-6); OECD 426 (2007) Dams dosed from gestation day 7 to lactation day 22 (approx. 5 weeks). Alpk: APfSD (Wistar-derived) rats Dose levels: 0, 25, 60 or 150 ppm	NOEL for toxicity = 25 ppm NOEL for developmental neurotoxicity = 150 ppm	Milburn G., (2004) ***PP321/2475***

Additional mutagenicity data generated since, or not included in, the JMPS evaluation in 1999 (FAO/WHO EVALUATION REPORT 463/1999)

Table 5. Mutagenicity profile of the lambda-cyhalothrin technical materials based on in vitro and in vivo tests

Species	Test	Purity %[5]	Source	Guideline, duration, doses and conditions	Result [(isomer/form)]	Study number
Salmonella typhimurium strains TA1535, TA1537, TA1538, TA98 and TA100	Bacterial Reverse Gene Mutation (in vitro)	81.5	Syngenta	OECD 471 (1997): OPPTS 870.5100 (1998): 2000/32/EEC B.13/B.14 (2000) Dose levels: 1.6, 8, 40, 200, 1000 or 5000 µg/plate +/- S9 DMSO	Negative +/-S9	Callander R., and Priestley K, 1989 ***PP321/2164***
Salmonella typhimurium strains TA1535, TA1537, TA98, and TA100, and the Escherichia coli strains WP2 uvrA pKM101 and WP2 pKM101	Bacterial Reverse Gene Mutation (in vitro)	90.5	Syngenta	OECD 471 (1997): OPPTS 870.5100 (1998): EC 440/2008 B.13/14 (2008) Dose levels: Pre-Experiment/ Experiment I: 3; 10; 33; 100; 333; 1000; 2500; and 5000 µg/plate and Experiment II: 10; 33; 100; 333; 1000; 2500; and 5000 µg/plate +/- S9	Negative +/-S9	Sokolowski A., (2012) ***PP321_11497***
Salmonella typhimurium strains TA1535, TA1537, TA98, and TA100, and the Escherichia coli strains WP2 uvrA pKM101 and WP2 pKM101	Bacterial Reverse Gene Mutation (in vitro)	99.5	Toll-manufacturing	OECD 471 (1997): OPPTS 870.5100 (1998): EC 440/2008 B.13/14 (2008) Dose levels: Pre-Experiment/ Experiment I: 3; 10; 33; 100; 333; 1000; 2500; and 5000 µg/plate and Experiment II: 10; 33; 100; 333; 1000; 2500; and 5000 µg/plate +/- S9	Negative +/- S9	Sokolowski A., (2012) Study number 1447901

[5] Purity is the content of pure lambda-cyhalothrin in the technical material unless otherwise stated, expressed as a percentage.

Additional ecotoxicological data generated since the JMPS evaluation in 1999 (FAO/WHO EVALUATION REPORT 463/1999)

Table 6. Ecotoxicology profile of the technical material

Species	Test	Purity % [6]	Guideline, duration, doses and conditions	Result [(isomer/form)]	Study number
Chironomus riparius	Acute toxicity	92.1	OECD Guidelines for Testing of Chemicals, Section 2 - Effects on Biotic Systems, Method 202 OECD Guidelines for Testing of Chemicals, Section 2 - Effects on Biotic Systems, Method 219 0.16, 0.50, 1.6, 5.0, 15.7 and 50 µg/L	48-hour EC_{50} is 1.5 µg/L.	Memmert U and Bader U., ***PP321/3507***
Pimephales promelas	Chronic toxicity	96.7	EPA 72-5, 540/9-86-137 (1986) 0.03, 0.06, 0.12, 0.25 and 0.50 µg/L	LOEC and NOEC values are 0.062 and 0.031 µg *lambda*-cyhalothrin/L, respectively.	Tapp *et al*., ***PP321/1443***
Eisenia fetida	Acute toxicity	96.8	OECD 207, (1984) 0, 32, 56 and 100 mg/kg soil (dry weight)	14 day LC_{50} value is >1000 mg a.i./kg soil (dry weight).	Yearsdon *et al*., ***PP321/1141***
Leuciscus idus	Acute toxicity	87.7	EPA 72-1 (1985); OECD 203 (1992) 0.03, 0.06, 0.12, 0.24, 0.48 and 0.96 µg a.i./L	96h LC_{50} was 0.078 µg a.i./L, NOEC is 0.056 µg a.i./L	Kent SJ and Shillabeer N ***PP321/1161***

[6] Note: Purity is the content of pure active ingredient in the technical material, expressed as a percentage.

Lambda-cyhalothrin was evaluated by the WHO IPCS in 2007. Lambda-cyhalothrin was evaluated by the FAO/WHO JMPR in 2008 and 2015.

The IPCS hazard classification of lambda-cyhalothrin is:

Hazard Class and Category Code(s)
Acute Tox. 3 - H301 (oral)
Acute Tox. 2 - H330 (inhalation)
Acute Tox. 4 - H312 (dermal)
Aquatic Acute 1 – H400
Aquatic Chronic 1 – H410

Annex 2: References

Study number	Author(s)	Year	Study title. Study identification number. Report identification number. GLP [if GLP]. Company conducting the study

LAMBDA-CYHALOTHRIN

FAO/WHO Evaluation Report 463/2014

Recommendations

The Meeting recommended that:

(i) The existing FAO specification for lambda-cyhalothrin TC should be extended to encompass the product of Jiangsu Yangnong Chemical Co., Ltd., China.

(ii) The existing WHO specification for lambda-cyhalothrin TC should be extended to encompass the product of Jiangsu Yangnong Chemical Co., Ltd., China.

Appraisal

The Meeting considered data and information on lambda-cyhalothrin submitted by Jiangsu Yangnong Chemical Co., Ltd., China (Yangnong) in 2013 in support of the extension of the existing FAO/WHO TC specifications. The data submitted were broadly in accordance with the requirements of the Manual on Development and Use of FAO and WHO Specifications for Pesticides (November 2010 - second revision of the First Edition) and supported the existing specifications.

Lambda-cyhalothrin is the ISO common name for a racemate of the ester of cis-cyhalothric acid with the *R*- and *S*- α-cyanophenylbenzyl alcohol moitey, respectively. These two enantiomers show higher insecticidal activity as compared to cyhalothrin.

Lambda-cyhalothrin is an agricultural and public health broad spectrum insecticide that is used to control a range of insects and mites. Lambda-cyhalothrin is not under patent. It has been evaluated by the European Commission as part of the EU review of the existing active substances for inclusion in Annex I of the Council Directive 91/414/EEC on January 2002. Initially, it was included with a minimum purity of 810 g/kg, which was equal to what is given in the available FAO and WHO specifications for lambda-cyhalothrin, however the specification was revised and finally it was included in Annex I with a minimum purity of 900 g/kg.

The data for lambda-cyhalothrin were first evaluated in 1999 in support of new FAO/WHO specifications based on the draft specifications and the supporting data provided by Zeneca Agrochemicals (a predecessor of Syngenta).

The Meeting was provided with the proposer’s confidential information on the manufacturing process, the manufacturing specification and respective 5-batch analysis data on impurities present at or above 1g/kg. The declared minimum purity of the lambda-cyhalothrin TC is 950 g/kg, which was found to be statistically justified. The declared minimum content is higher than that of the existing FAO and WHO specifications (minimum 810 g/kg). The mass balance range is 997.2 - 1002.9 g/kg, which is considered acceptable.

The manufacturing process, impurity profile and five batch analyses were compared with the data submitted by Zeneca in 1999. Yangnong's synthesis pathway is comprised of three steps, while the Zeneca process has two steps. The Meeting noted that the last two steps in Yangnong pathway are the same as Zeneca's. However, in the case of Yangnong, the first step is actually the formation of a main building block whereas in the case of Zeneca this intermediate was also manufactured but no further

information was provided. The impurity profile of Yangnong's TC is different as compared to that of the Zeneca TC as it has a lower amount of impurities at or above 1 g/kg (5 compounds identified). One new impurity was identified and a compound also present in Zeneca's profile was increased above the acceptable range (according to the equivalence criteria as laid down in the FAO/WHO Manual). Furthermore, the mutagenicity studies required had not been performed according to the OECD Guideline 471 (Bacterial Reverse Mutation Test, OECD 1997). At that stage of the evaluation, the Meeting concluded that:

- The data package in support of the equivalence of Yangnong's TC with the reference profile was incomplete on Tier-1 as the studies on bacterial reverse mutation did not cover all required strains of *S. typhimurium* and *E. coli.*
- The evidence presented on 5-batch composition was not conclusive enough to allow a decision on equivalence even after submission of a complemented bacterial reverse mutation study and a data package on acute toxicity would be needed to allow a decision to be taken on Tier-2.

Toxicity studies were conducted by using one batch of the 5-batch study and submitted to the Meeting. The evaluation of the studies allowed the following conclusions:

- Rat, acute oral LD_{50}: 126 mg/kg bw (female) and 171 mg/kg bw (male)
- Rat, acute dermal LD_{50}: > 2000 mg/kg bw
- Rat, acute inhalation LC_{50}: 512 mg/m^3
- Rabbit, eye irritation: Slightly irritating
- Rabbit, skin irritation: non-irritant
- Guinea-pig skin sensitization: non-sensitizer
- Mutagenicity tests *in vitro* and *in vivo*: non-mutagenic, negative

Considering the outcome of the toxicity studies, the Meeting concluded that lambda-cyhalothrin produced by Yangnong was not more hazardous and hence it is equivalent to the toxicology profile of the reference TC based on Tier-2 evaluation.

The data package (manufacturing process, purity and impurity profile) submitted to FAO/WHO was confirmed by ICAMA (Chen T., 2014) through e-mail that it is consistent to that submitted for registration in China.

The proposer used an in-house method for the determination of the content of lambda-cyhalothrin in lambda-cyhalothrin TC instead of the CIPAC method (463/TC/M/3) published in CIPAC Handbook E. The in-house method for the determination of the active ingredient content is validated with respect to specificity, linearity, precision and accuracy in one laboratory. This method is also a gas chromatographic method with a flame ionization detector, as the CIPAC method, while using different internal standard and chromatographic analysis parameters. Following the Meeting request, the proposer provided a bridging study between the in-house and the CIPAC method, with no significant difference between results. This confirms that the CIPAC method is applicable to the manufacturer’s TC.

The proposer determined one of the impurities by an internal standardization GC-FID method, whereas all the other impurities (four impurities) were determined by an external standardization HPLC-DAD method. The methods are validated with respect to specificity, linearity, precision, accuracy and LOQ.

Test methods for determination of physico-chemical properties of the technical active ingredient were mainly OECD and CIPAC.

Three different identity tests for lambda-cyhalothrin had been provided: HPLC-DAD-MS, GC-MS and NMR.

The Meeting agreed also to update, in the FAO specifications for lambda-cyhalothrin EC, WG and rapid-release CS and in the WHO specifications for lambda-cyhalothrin EC, WP and slow-release CS, the CIPAC method for persistent foam (MT 47.3 instead of MT 47.2) to be in line with the current CIPAC method.

Supporting Information
for
Evaluation Report 463/2014

Uses

Lambda-cyhalothrin is an agricultural and public health insecticide, controlling a wide spectrum of insects and mites, at all developmental stages, on a wide range of crops. It is non-systemic, with very little translaminar activity. It is of low volatility and short persistence in soil and therefore has only limited uses as a soil insecticide (JMPR 1986). However, lambda-cyhalothrin WP, EC and slow-release CS are also used, respectively, for indoor residual spraying, space spraying and treatment of mosquito nets, for the control of vectors and pests of public health importance.

Physico-chemical properties of lambda-cyhalothrin

Table 1. Chemical composition and properties of lambda-cyhalothrin 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 99.72 – 100.29 % and percentages of unknowns were 0.00 - 0.28 %.			
Declared minimum lambda-cyhalothrin 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			
Stabilisers or other additives and maximum limits for them	None			
Parameter	Value and conditions	Purity %	Method reference	Study number
Melting temperature range of the TC	49.6 °C	97.1	OECD 102 EC 440/2008	3510010019
Solubility in organic solvents (all at 25 °C)	40-50 g/l in n-heptane at 25 °C > 250 g/l in p-xylene > 250 g/l in 1,2-dichloroethane 80-100 g/l in propane-2-ol at 25 °C > 250 g/l in acetone > 250 g/l in ethyl acetate	97.1	CIPAC MT 181	1010010099

Formulations and co-formulated active ingredients

Yangnong did not propose a specification for a formulated product. The main formulation types available are EC and WP, used in agricultural and public health, respectively. Lambda-cyhalothrin is not co-formulated with other pesticides. The EC is registered and sold in India, Kyrgyzstan and Azerbaijan. The WP is registered and sold in India.

Methods of analysis and testing

The analytical method for the determination of the active ingredient is an internal standardization GC-FID method which is different than the official CIPAC method (463/TC/M) regarding internal standard used and chromatographic analysis parameters. According to this in-house method lambda-cyhalothrin is dissolved in an internal standard solution (DOP). Following the Meeting request, the proposer provided a bridging study between the in-house and the CIPAC method, with no significant difference between results.

Two different method(s) were submitted for determination of the five detected impurities. One method is a GC-FID method (impurity IV) and the other one used for the determination of the other four impurities is a reversed phase HPLC method.

Physical properties

Test methods for determination of physico-chemical properties of the technical active ingredient were mainly OECD and CIPAC.

Containers and packaging

No special requirements were identified for containers and packaging.

Expression of the active ingredient

The lambda-cyhalothrin is expressed as lambda-cyhalothrin in g/kg.

Annex 1: Hazard Summary Provided by the Proposer

Note:

(i) The proposer confirmed that the toxicological and ecotoxicological data included in the summary below were derived from lambda-cyhalothrin having impurity profiles similar to those referred to in the table above.

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

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

Species	Test	Purity %	Guideline, duration, doses and conditions	Result	Study number
Rat (M/F)	Oral	≥ 95.0	OECD 401 Edible oil Single dose/14 day observations 46.4, 100, 215, and 464 mg/kg bw	LD_{50} : 126 mg/kg·bw (female) 171 mg/kg·bw (male)	bg-09NYQT-WT002-1a
Rat (M/F)	Dermal	≥ 95.0	OECD 402 Edible oil Single dose/14 day observations 2000 mg/kg bw	LD_{50} > 2000 mg/kg·bw	bg-09NYQT-WT002-1b
Rat (M/F)	Inhalation	≥ 95.0	OECD 403 Whole-body exposure 14 day observations 4 hour exposure 890.20, 333.75, 294.29 and 230.37 mg/m^3	LC_{50} = 512.29 mg/m^3	09NYQT-WT002-1
Rabbit	Skin irritation	≥ 95.0	OECD 404 4 hour exposure 0.5 g/2×3 cm^2	Non-irritant (PII = 0)	10NYQT-WT004-1
Rabbit	Eye irritation	≥ 95.0	OECD 405 72 hour exposure 0.1 g	Slightly irritating	10NYQT-WT004-1
Guinea pig	Skin sensitisation	≥ 95.0	OECD 406 The skin sensitization test for 95% lambda-cyholathrin TC was conducted with guinea pigs. Induction contact on day 0, 7 and 14 for 6 h. 14 days after final induction application, challenge contact for 6 h. Sites were evaluated for skin reactions at approximately 24 and 48 h after challenge phase using the scoring scale. The negative control group was treated as test group except for test item exposure.	Non-sensitizer	2013-114-01-01

Table B. Mutagenicity profile of lambda-cyhalothrin technical material based on *in vitro* and *in vivo* tests

Species	Test	Purity %	Guideline, duration, doses and conditions	Result	Reference
Salmonella typhimurium TA97a, TA98, TA100, TA102 and 1535	Bacterial Reverse Mutation Test	≥ 95.0	OECD 471 0.5, 5, 50, 500, and 5000 µg/plate In both initial and confirmatory mutagenicity assays, in the absence and presence of S9 metabolic activation at 0.5, 5, 50, 500, and 5000 µg/plate. The initial mutagenicity assay was conducted using the plate incorporation method. The confirmatory mutagenicity assay was conducted using the preincubation method.	Negative	09NYQT-WT002-2a and 2014-175-01-01
Chinese Hamster Lung Fibroblasts (CHL) Cells	In Vitro Mammalian Chromosome Aberration Test	≥ 95.0	OECD 473 DMSO was used as solvent for the test article and was the solvent control. In the non-activated 3 hour exposure group, in the non-activated 24 hour exposure group, and in the S9 activated 3 hour exposure group, CHL cultures were exposed to 95% Lambda-cyhalothrin technical at 160, 80, and 40 µg/mL.	Negative	09NYQT-WT002-2b
Mouse (M/F)	Mammalian Erythrocyte Micronucleus Test	≥ 95.0	OECD 474 24 hour exposure Oral by gavage 0, 2.5, 5.0, and 10 mg/kg bw	Negative	09NYQT-WT002-2c

Annex 2: References

Study number	Author(s)	Year	Study title. Study identification number. Report identification number. GLP [if GLP]. Company conducting the study
	FAO	2013	FAO specification: 463/TC and evaluation reports 463/1999, 463/2003, 463/2006, 463/2012, accessible at http://www.fao.org/agriculture/crops/core-themes/theme/pests/jmps/ps-new/en/
NC-2008-031		2010	Preliminary Analysis and Enforcement Analytical Method of Lambda-cyhalothrin TGAI. NC-2008-031. GLP. Nutrichem Laboratory Co., Ltd., China.
	Chen T.	2014	E-mail from Chen Tiechun, Director ICAMA to E. Karasali sent 28 May 2014 confirming the similarity of the data packages submitted to ICAMA for registration and to JMPS.
NC-2011-019		2011	Identification of 5 batch Lambda-cyhalothrin TGAI for Active Ingredient and impurities (I-V) and the spiked recovery assay of methods for impurities (I-V). NC-2011-019. GLP. Nutrichem Laboratory Co., Ltd., China.
3513080009		2013	Determination of the vapour pressure of 95% Lambda-cyhalothrin Technical. 3513080009. GLP.
3510010019		2010	Determination of the Melting Point/Melting Range of 95% Lambda-Cyhalothrin Technical. 3510010019. GLP. Shanghai Research Institute of Chemical Industry Testing Centre, China.
1010010099		2010	Determination of the solubility in organic solvents of 95% lambda-cyhalothrin Technical. 1010010099. GLP. Shanghai Research Institute of Chemical Industry Testing Centre, China.
bg-09NYQT-WT002-1a		2009	Acute Oral Toxicity Study for 95% Lambda-Cyhalothrin Technical in Rats. bg-09NYQT-WT002-1a. GLP. Institute of Applied Toxicology, Nanjing Medical University, China.
bg-09NYQT-WT002-1b		2009	Acute Dermal Toxicity Study for 95% Lambda-Cyhalothrin Technical in Rats. bg-09NYQT-WT002-1b. GLP. Institute of Applied Toxicology, Nanjing Medical University, China.
09NYQT-WT002-1		2011	Acute Inhalation Toxicity Study for 95% Lambda-Cyhalothrin Technical in Rats. bg-09NYQT-WT002-1. bg-09NYQT-WT002-1cG2. GLP.
10NYQT-WT004-1		2010	Acute Skin Irritation Study for Lambda-Cyhalothrin 95% TC in Rabbits. 10NYQT-WT004-1. bg-10NYQT-WT004-1b. GLP.
10NYQT-WT004-1		2010	Acute Eye Irritation Study for Lambda-Cyhalothrin 95% TC in Rabbits. 10NYQT-WT004-1. bg-10NYQT-WT004-1a. GLP.
2013-114-01-01		2013	Skin Sensitization Study of 95% Lambda-cyholathrin TC in Guinea Pigs-Buehler Test. 2013-114-01-01. GLP.
09NYQT-WT002-2a		2009	Bacterial Reverse Mutation Test with Salmonella Typhimurium for 95% Lambda-Cyhalothrin Technical. 09NYQT-WT002-2a. bg-09NYQT-WT002-2a. GLP.
2014-175-01-01		2014	Bacterial Reverse Mutation Test of Lambda-Cyhalothrin 95% TC. 2014-175-01-01. GLP.
09NYQT-WT002-2b		2009	In Vitro Mammalian Chromosome Aberration Test in Chinese Hamster Lung Fibroblasts(CHL)Cells for 95% Lambda-Cyhalothrin Technical. 09NYQT-WT002-2b. bg-09NYQT-WT002-2b. GLP.

Recommendations

The Meeting recommended that:

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

(ii) The existing FAO specifications for lambda-cyhalothrin TC should be extended to encompass the corresponding products of Bharat Rasayan Limited.

(iii) The existing WHO specifications for lambda-cyhalothrin TC should be extended to encompass the corresponding products of Bharat Rasayan Limited.

Appraisal

The Meeting considered data and information on lambda-cyhalothrin submitted by Bharat Rasayan Limited (India) in support of the extension of the existing (2003) FAO/WHO specifications of the TC.

The Meeting was provided with confidential information on the manufacturing process, the manufacturing specification and 5 batch analyses. The proposer declared the minimum purity of the lambda-cyhalothrin TC is 965 g/kg, but the five batch analysis gave a mean result which was slightly higher. The mass balance range is 99.81 – 99.85 g/kg total lambda-cyhalothrin.

The manufacturing process, impurity profile and 5 batch analyses was compared with the data submitted by Syngenta in 2003. The manufacturing process was the same but the impurity profile is very different. The proposers 5 batch analysis has less impurities than in the reference profile of Syngenta. The proposer stated this is because the manufacturing process has been optimised to minimise impurity formation.

The company also provided an impurity profile of the key starting materials which demonstrated that these materials were of high purity with very few impurities.

The Meeting was provided with data on the physico-chemical properties which are similar to those of the reference material (Syngenta). No hydrolysis and photolysis studies were provided.

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.

The Meeting concluded that there are no relevant impurities in the lambda-cyhalothrin produced by Bharat.

Bharat Rasayan Limited produces lambda-cyhalothrin 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.

Acute toxicity data and a mutagenicity study for lambda-cyhalothrin were provided by the manufacturer. The acute toxicity of lambda-cyhalothrin was moderate to high and it is a mild eye irritant. Lambda-cyhalothrin does not show mutagenicity in *in vitro* bacterial assays.

Bharat Rasayan Limited used a GC-MS method for analysis of the active ingredient and also for the identity tests. The method used external standard calibration and validation data were provided by the proposer. The method is essentially the same as the CIPAC method 463/TC/M/3 except that the GC detector is a mass spectrometer. The proposer provided a bridging study using the CIPAC method with no significant difference between the results. This confirms the CIPAC method is applicable to the manufacturer's TC.

Bharat Rasayan Limited determined the impurities by GC-MS, GC-FID and CIPAC methods. The methods used for physico-chemical properties and chemical composition are all referenced USEPA OPPTS, OECD and CIPAC methods.

The proposed specification for TC was in accordance with the requirements of the FAO/WHO Manual.

The Meeting concluded that lambda-cyhalothrin TC of Bharat Rasayan Limited is equivalent to the specification of the reference profile (Syngenta).

The Meeting agreed also to update the CIPAC methods and to revise some footnotes in the following specifications to be in line with the specification guidelines of the November 2010 – second revision of the first edition of the FAO/WHO Manual and the current CIPAC methods:

- FAO and WHO specifications for EC: MT 36.3 instead of MT 36.1 for emulsion stability, MT 39.3 instead of MT 39.1 for stability at 0°C.
- WHO specification for WP: MT 185 instead of MT 59.3 for wet sieve test.
- FAO specification for WG: MT 185 instead of MT 167 for wet sieve test, MT 184 instead of MT 168 for suspensibility, MT 172.1 instead of MT 172 for flowability, deletion of the flowability test after the stability at elevated temperature.
- FAO specification for rapid-release CS: MT 148.1 instead of MT 148 for pourability, MT 184 instead of MT 161 for suspensibility, MT 185 instead of MT 59.3 for wet sieve test.

Supporting Information
for
Evaluation Report 463/2012

Physico-chemical properties of lambda-cyhalothrin

Table 1. Physico-chemical properties of pure lambda-cyhalothrin

Parameter	Value(s) and conditions	Purity %	Method	Reference
Vapour pressure	7.48 x 10^{-7} Pa at 20°C	97.25%	OECD 104, U.S.EPA OPPTS 830.7950	Study Number 10197 06-08-2010
Melting point, boiling point and/or temperature of decomposition	47.3 ± 0.1°C	97.25%	U.S. EPA OPPTS 830.7200	Study Number 10199 01-09-2010
Solubility in water	At pH 5.04 : 0.0000063 ± 0.0000003 g/L at 20±1.0°C At pH 7.03 : 0.0000058 ± 0.0000004 g/L at 20±1.0°C At pH 9.04 : 0.0000063 ± 0.0000002 g/L at 20±1.0°C	97.25%	EC A.6 / OECD 105 / U.S. EPA OPPTS 830.7840	Study Number 10195 16-09-2010
Octanol/water partition coefficient	log POW = 6.61	97.25%	OECD 117, U.S.EPA OPPTS 830.7570	Study Number 10198 22-07-2010
Dissociation characteristics	Not applicable	-	-	-
Solubility in organic solvents	Acetone : >250 g/L 1,2-Dichloroethane : >250 g/L Ethyl acetate : >250 g/L n-Heptane : 67-80 g/L Methanol : >250 g/L p-Xylene : >250 g/L at 20 ± 1.0°C	97.25%	CIPAC MT 181	Study Number 10196 20-07-2010

Table 2. Chemical composition and properties of lambda-cyhalothrin 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 99.81–99.85%. Percentage of unknowns were 0.15-0.20%.
Declared minimum lambda-cyhalothrin content	965 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

Background information on toxicology / ecotoxicology

Bharat Rasayan Limited provided data on the acute toxicity, skin irritation and sensitization, and mutagenicity of the lambda-cyhalothrin technical material.

Acute toxicity was moderate to high in male and female rats in general toxicity and neurotoxicity terms, as shown by the LD_{50} and LC_{50}. It caused mild irritation but not skin sensitivity. The mutagenicity study concluded that the lambda-cyhalothrin is non-mutagenic.

It is used in agriculture and for public health use.

JMPR have defined an acceptable daily intake (ADI) of 0-0.02 mg/kg bw (2007). The IPCS hazard classification of Lambda-cyhalothrin is: moderately hazardous, class II. (1999).

Methods of analysis and testing

The analytical method for the active ingredient (including identity tests) was GC-MS by an in-house validated external standard method under the EU and U.S. EPA guidelines (EU 91/414/EEC and U.S. EPA OPPTS 830.1700, 830.1800). The proposer conducted bridging study using the CIPAC method and a comparison of the 5 batch analyses demonstrated there are no significant differences between the two methods. This confirms that the CIPAC method is applicable to the proposer's TC.

The methods used for the determination of impurities are GC-MS.

Test methods for determination of physico-chemical properties of the technical active ingredient were OECD, EC, USEPA or CIPAC.

Containers and packaging

The product will be packed in polyethylene lined mild steel drums (composite), lacquered inside, of 25 kg capacity.

Expression of the active ingredient

The active ingredient content is expressed as lambda-cyhalothrin, 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 lambda-cyhalothrin 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. Toxicology profile of lambda-cyhalothrin technical material, based on acute toxicity, irritation and sensitization

Species	Test	Purity %	Guideline, duration, doses and conditions	Result	Study number
Rats, (Wistar)	Oral	97.17%	OECD 423	LD_{50} = 5-50 mg/kg bw	Report No. 000122145 28-03-2009
Rats, (Wistar) (f, m)	Dermal	97.17%	OECD 402	LD_{50} >2000 mg/kg bw for (f, m)	Report No. 000122145 28-03-2009
Rats, (Wistar)	Inhalation	97.17%	OECD 403	Male : LC_{50} 1.0 mg a.i./l Female : LC_{50} 0.55 mg a.i./l	Report No. 000122145 28-03-2009
Rabbit, New Zealand White	Skin irritation	97.17%	OECD 404	Non irritant	Report No. 000122145 28-03-2009
Rabbit, New Zealand White	Eye irritation	97.17%	OECD 405	Moderate irritant	Report No. 000122145 28-03-2009
Guinea Pigs	Skin sensitivity	97.17%	OECD 406	Non sensitizer	Report No. 000122145 28-03-2009

Table B. Mutagenicity profile of lambda-cyhalothrin technical material based on bacterial *in vitro* tests

Species	Test	Purity %	Conditions and guideline	Result	Reference
Salmonella typhimurium TA1537, TA1535, TA98 TA100 and TA102	Bacterial reverse mutation assay (In vitro)	96.75%	Dosage 156.25, 312.5, 625, 1250, 2500 and 5000 ug/plate Trial 1 in the absence and presence of 5% v/v S-9 mix 51.2, 128, 320, 800, 2000 and 5000 ug/plate Trial 2 in the absence and presence of 10% v/v S-9 mix Guideline : OECD 471	Negative	JFR Study No. 481-1-06-3231 December 2011

Annex 2. References

Author and year or study number	Study title. Study identification number. Report identification number. Company conducting the study.
Bharat Rasayan Limited, 10/2010	FAO/WHO Specifications for Pesticides – Proposers (Bharat Rasayan Limited) template with (i) Manufacturing Process and 5 batch analysis (Confidential) & (ii) specifications including physico-chemical properties, toxicological summaries & references (Non-confidential).
Bharat Rasayan Limited, 8/2011	FAO/WHO Specifications for Pesticides – Proposers (Bharat Rasayan Limited) template with (i) updated Manufacturing Process and (ii) Impurity profile of Key Starting Materials.
Bharat Rasayan Limited, 8/2011	FAO/WHO Specifications for Pesticides – Proposers (Bharat Rasayan Limited) 5 batch analysis using CIPAC methods of analysis.
Government of India, 19/04/2005	Certificate of Registration for Lambda-cyhalothrin Technical for indigenous manufacture Government of India, Ministry of Agriculture, provided for comparison of manufacturing process & DoC.
Bharat Rasayan Limited, 8/2011	Bharat Rasayan Letter of Access for DoC.
Bharat Rasayan Limited, 10/2010	Method of Analysis of the composition (Lambda-cyhalothrin content) of Bharat Rasayan TC by GCMS.
CIPAC 1992	CIPAC Handbook E - Analysis of Technical and Formulated Pesticides Lambda-cyhalothrin 463/TC pages 49-57.
JRF Study number 227-2-12-0971	Preliminary Analyses of five representative production batches of Lambda-cyhalothrin Technical Grade Active Ingredient (TGAI) to determine % Lambda-cyhalothrin and to quantify its associated impurities. Jai Research Foundation (JRF). Guideline U.S.EPA OPPTS 830.1700, 830.1800.
JRF Study number 10200	Validation of Analytical Method for active ingredient analysis of Lambda-cyhalothrin Technical. Test Facility Jai Research Foundation (JRF) Guideline U.S.EPA OPPTS 830.1800.
JRF Study number 10194	Appearance, colour report. Test Facility Jai Research Foundation (JRF) Guideline U.S.EPA OPPTS 830.1800, 830.6302, 6303, 6304.
JRF Study number 10197	Vapour pressure of Lambda-cyhalothrin Technical. Jai Research Foundation (JRF) Guideline: EC A.4, OECD 104, U.S. EPAOPPTS 830.7950.
JRF Study number 10199	Melting point/Melting range of Lambda-cyhalothrin Technical. Test Facility Jai Research Foundation (JRF). Guideline: U.S. EPA OPPTS 830.7200.
JRF Study number 10195	Water solubility of Lambda-cyhalothrin Technical. Jai Research Foundation (JRF). Guideline: EEC A.6, OECD No. 105 and U.S.EPA OPPTS 830.7840.
JRF Study number 10198	Partition co-efficient of Lambda-cyhalothrin Technical by HPLC Method. Jai Research Foundation (JRF). Guideline: U.S. EPA OPPTS 830.7570, OECD 117.
JRF Study number 10196	Solubility of Lambda-cyhalothrin Technical in organic solvents. Jai Research Foundation (JRF) Guideline: CIPAC MT 181.
Report number 000122145	Acute Oral toxicity study in rats with Lambda-cyhalothrin technical. Project no. TOX/438. Guideline: OECD 423 (section 4).
Report number 000122145	Acute Dermal toxicity study in rats with Lambda-cyhalothrin technical. Project no. TOX/438. Guideline: OECD 402 (section 4).
Report number 000122145	Acute Inhalation toxicity study in rats with Lambda-cyhalothrin technical Project no. TOX/438. Guideline: OECD 403 (section 4).

Author and year or study number	Study title. Study identification number. Report identification number. Company conducting the study.
Report number 000122145	Acute Dermal Irritation in rabbits with Lambda-cyhalothrin technical. Project no. TOX/438. Guideline: OECD 404 (section 4).
Report number 000122145	Acute Eye Irritation in rabbits with Lambda-cyhalothrin technical. Project no. : TOX/438. Guideline: OECD 405 (section 4).
Report number 000122145	Skin Sensitization study in guinea pigs with Lambda-cyhalothrin technical Project no. TOX/438. Guideline: OECD 406 (section 4).
JMPR, 2007	Acceptable Daily Intake of Lambda-cyhalothrin. Pesticide Residues in Food – 2007. FAO Plant Production and Protection Paper, 191. Lambda cyhalothrin (146), pp 91-98.
Jai Research Foundation, 12/2011	Bacterial Reverse Mutation Test of Lambdacyhalothrin Technical using Salmonella typhimurium. JRF No. 481-1-06-3231 (Final Report) JRF for Bharat Rasayan Ltd.
Research and Development Centre, Bharat Rasayan Limited, December 31, 2011	Analysis Report - Analysis of Lambda-cyhalothrin Active Ingredient content in five representative batches of Lambda-cyhalothrin Technical. Bridging study using the CIPAC Method for the analysis of Lambda-cyhalothrin Active Ingredient content in TC.

Recommendations

The Meeting recommended that the existing WHO specification for lambda-cyhalothrin "slow release CS" should be extended to encompass the corresponding product of Tagros Chemicals India Limited.

Appraisal

The Meeting considered data provided by Tagros Chemicals India Limited, in support of the extension of the existing WHO specifications for lambda-cyhalothrin "slow-release" CS (2007). This was evaluated for equivalence with the reference specification of Syngenta (2007).

The total lambda-cyhalothrin content and "free" ("non-encapsulated") lambda-cyhalothrin content of the Tagros product comply with the WHO specification for lambda-cyhalothrin "slow release" CS (2007). There are no relevant impurities.

The Meeting was provided with data on the physico-chemical properties of lambda-cyhalothrin CS and these are equivalent to those of Syngenta. The storage stability data (freeze/thaw and elevated temperature) are the same as for normal temperature and equivalent to those of the WHO specifications for lambda-cyhalothrin "slow release" CS (2007).

Tagros used CIPAC methods to determine the total and "free" lambda-cyhalothrin content of the CS as referenced in the specification. The methods used to determine the physico-chemical properties and chemical composition are all referenced CIPAC methods.

The Tagros lambda-cyhalothrin "slow release" CS complies with the requirements of the FAO/WHO Manual and can be considered equivalent to the product of Syngenta.

The Meeting agreed also to update in the CS specification the CIPAC methods for some physical properties (pH range - MT 75.3 instead of MT 75, pourability - MT 148.1 instead of MT 148, suspensibility - MT 184 instead of MT 161, wet sieve test -MT 185 instead of MT 59.3) to be in line with the guideline for CS 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 463/2011

Physico-chemical properties of Tagros lambda-cyhalothrin 10% CS

Table 1. Chemical properties

Parameter	Value(s) and conditions	Method	Reference/date
Identity test	Confirmation of the identity by comparing the retention time of active ingredient in test item and active ingredient in standard. The retention time of lambda-cyhalothrin in the test item and reference analytical standard are identical	CIPAC E 463/TC/M/2	Report No. 09135 (27/10/2009)
Total active ingredient content	104.30 g/kg	CIPAC K 463/CS/M/3	Report No. 09135 (27/10/2009)
Free lambda-cyhalothrin content (Relative active)	0.32%	CIPAC L MT 189	Report No. 09135 (27/10/2009)
Release of lambda-cyhalothrin (Relative active)	15 min – 59.80% 30 min – 81.21% 180 min – 97.12%	CIPAC L MT 190	Report No. 09135 (27/10/2009)

Table 2. Physical properties

Parameter	Value(s) and conditions	Method	Reference/date
pH (1% aqueous dispersion)	6.80 at 25.7°C	CIPAC MT 75	Report No. 09136 (18/09/2009)
Pourability	Residue: 2.5% at 20°C Rinsed residue: 0.35% at 20°C	CIPAC MT 148	Report No. 09136 (18/09/2009)
Spontaneity of dispersion	98.52% at 20°C	CIPAC MT 160	Report No. 09136 (18/09/2009)
Suspensibility	96.97% at 20°C	CIPAC MT 161	Report No. 09136 (18/09/2009)
Wet sieve test	No particles were retained on 75 µm sieve	CIPAC MT 59.3	Report No. 09136 (18/09/2009)
Persistent Foam	Time interval - Volume of foam 10 seconds - 4 ml 1 minute - 2 ml 3 minute - 2 ml 12 minute - 2 ml	CIPAC MT 47.2	Report No. 09136 (18/09/2009)

Table 3. Storage stability - freeze/thaw stability

Parameter	Value(s) and conditions	Method	Reference/date
Total active ingredient content	104.4 g/kg	CIPAC K 463/CS/M/3	Report No.09137 (28/10/2009)
Free lambda-cyhalothrin content (Relative active)	0.33%	CIPAC L MT 189	Report No.09137 (28/10/2009)

Release of lambda-cyhalothrin (Relative active)	15 min – 59.48% 30 min – 81.49% 180 min – 97.31%	CIPAC L MT 190	Report No.09137 (28/10/2009)
pH of 1% solution at 25 ± 0.5°C	6.81 at 25.4°C	CIPAC MT 75	Report No.09137 (28/10/2009)
Pourability	Residue: 2.09% Rinsed residue: 0.24%	CIPAC MT 148	Report No.09137 (28/10/2009)
Spontaneity of dispersion	99.80%	CIPAC MT 160	Report No.09137 (28/10/2009)
Suspensibility	98.49%	CIPAC MT 161	Report No.09137 (28/10/2009)
Wet sieve test passing through 75 µm sieve	0.1%	CIPAC MT 59.3	Report No.09137 (28/10/2009)
Persistent foaming at 1 minute	2 ml	CIPAC MT 59.3	Report No.09137 (28/10/2009)

Table 4. Storage stability - stability at elevated temperature

Parameter	Value(s) and conditions	Method	Reference/date
Total active ingredient content	104.65 g/kg	CIPAC K 463/CS/M/3	Report No.09137 (28/10/2009)
Free lambda-cyhalothrin content (Relative active)	0.33%	CIPAC L MT 189	Report No.09137 (28/10/2009)
Release of lambda-cyhalothrin (Relative active)	15 min – 60.80% 30 min – 82.76% 180 min – 98.93%	CIPAC L MT 190	Report No.09137 (28/10/2009)
pH of 1% solution at 25 ± 0.5°C	6.79 at 25.2°C	CIPAC MT 75	Report No.09137 (28/10/2009)
Pourability	Residue: 2.07% Rinsed residue: 0.24%	CIPAC MT 148	Report No.09137 (28/10/2009)
Spontaneity of dispersion	99.62 %	CIPAC MT 160	Report No.09137 (28/10/2009)
Suspensibility	98.89%	CIPAC MT 161	Report No.09137 (28/10/2009)
Wet sieve test passing through 75 µm sieve	0.1%	CIPAC MT 59.3	Report No.09137 (28/10/2009)
Persistent foaming at 1 minute	2 ml	CIPAC MT 59.3	Report No.09137 (28/10/2009)

Methods of analysis and testing

Tagros confirmed that the existing CIPAC methods were used for total and “free” lambda-cyhalothrin in slow release CS.

Test methods for the determination of physico-chemical properties were CIPAC as indicated in the specifications.

Annex 1: References

Author and year	Study title. Study identification number. Report identification number. Company conducting the study.
Tagros, 2010	Proposers (Tagros). Specifications for Lambda-Cyhalothrin Slow-Release Capsule Suspension (CS).
Report No. 09135	M. Uma Ganesh, 2009. Study report of Laboratory Study of Identity test, Total a.i. content, Free Lambda-cyhalothrin content, Release of Lambdacyhalothrin of Lambdacyhalothrin 10% CS. Unpublished report International Institute of Biotechnology and Toxicology, Padappai, Tamil Nadu, India, sponsored by M/s Tagros Chemicals India Ltd., Chennai, India.
Report No. 09136 Revision No. 1	D. Radhakrishanan, 2011. Study report of Laboratory Study of pH range, Pourability, Spontaneity of dispersion, Suspensibility, Wet Sieve test, Persistent foam of Lambdacyhalothrin 10% CS. Unpublished report International Institute of Biotechnology and Toxicology, Padappai, Tamil Nadu, India, sponsored by M/s Tagros Chemicals India Ltd., Chennai, India.
Report No. 09137 Revision No. 1	R. Nageshwara Rao, 2011. Study report of Laboratory Study of Storage Stability (Freeze/Thaw stability, Stability at elevated temperature) of Lambdacyhalothrin 10% CS. Unpublished report International Institute of Biotechnology and Toxicology, Padappai, Tamil Nadu, India, sponsored by M/s Tagros Chemicals India Ltd., Chennai, India.

Recommendations

The Meeting recommended that:

(i) the existing FAO specifications for lambda-cyhalothrin TC, EC and WG should be extended to encompass Tagros products;

(ii) the existing WHO specifications for lambda-cyhalothrin TC, EC and WP should be extended to encompass Tagros products;

(iii) the existing FAO specification for lambda-cyhalothrin rapid-release CS, and the existing WHO specification for lambda-cyhalothrin slow-release CS, should remain restricted to Syngenta products.

Appraisal

The Meeting considered data provided by Tagros Chemicals, India Ltd, to support extensions of the existing (2003) FAO specifications for lambda-cyhalothrin (TC, EC, WG) and the existing (2003) WHO specifications for lambda-cyhalothrin (TC, EC, WP).

The manufacturer did not seek extension of the existing (2003) FAO specification for lambda-cyhalothrin rapid-release CS and of the existing (2003) WHO specification for lambda-cyhalothrin slow-release CS.

The Meeting was provided with confidential information on the manufacturing process, together with 5-batch analytical data and manufacturing specifications for purity and all impurities ≥1 g/kg. Mass balances in the 5-batch data were very high (99.5-99.8%). The confidential data were confirmed as sufficiently similar to those supporting registration of Tagros lambda-cyhalothrin in India to conclude that the national evaluations should be applicable to the profile submitted to WHO.

The Tagros product complied with the existing specifications for lambda-cyhalothrin TC but one of the impurities did not appear in the reference profile of impurities and therefore equivalence was assessed by comparing the Tagros acute toxicity data with those of the reference profile. The oral, dermal, inhalation, skin irritation and skin sensitization hazard data indicated equivalence. However, the data for mucous membrane irritation were more difficult to compare, because the Tagros data related to vaginal mucous membrane irritation, whereas the data from the reference profile related to eye irritation. WHO/PCS noted that vaginal mucous membrane irritation data are a requirement under the Gaitonde protocol, whereas eye irritation data are a requirement under the OECD protocol. From a detailed consideration of the data and protocols, WHO/PCS concluded that, although no comparative studies of the two protocols are available, the absence of vaginal mucous membrane irritation produced by Tagros lambda-cyhalothrin meant that the product could be considered equivalent to the reference, which is characterized as mildly irritating to the eye (PCS 2006). The Meeting therefore agreed that the products should be considered equivalent.

The Tagros lambda-cyhalothrin EC complied with the existing FAO specification and the WP complied with the existing WHO specification.

Tagros confirmed that the existing CIPAC analytical methods for determination of lambda-cyhalothrin content of TC, EC and WP are satisfactory for the analysis of the company's products.

Supporting Information
for
Evaluation Report 463/2006

Physico-chemical properties of Tagros lambda-cyhalothrin

Table 1. Physico-chemical properties of Tagros technical lambda-cyhalothrin (TC)

Parameter	Value(s) and conditions	Purity %	Method	Reference
Vapour pressure	2.80×10^{-7} Pa at 20°C 3.65×10^{-5} Pa at 40°C	87.63%	EEC A.4, OECD 104	0704156
Melting point	47-49°C	87.63%	EEC A.1, OECD 102	0704157
Boiling point, temperature of decomposition	228-230°C	87.63%	EEC A.2, OECD 103	0704157
Solubility in water at 20°C	0.0009 mg/l at pH 4.0 0.001 mg/l at pH 7.0 0.004 mg/l at pH 9.0	87.63%	OECD 105, EEC A6	0704158
Partition coefficient	6.28 ± 0.02 at 24±1°C	87.63%	OECD 107, EEC A8, shake flask method	0704159
Hydrolysis characteristics	Half life values: pH 4 = 4.27 days at 20°C 2.41 days at 35°C pH 7 = 5.03 days at 20°C 3.28 days at 35°C pH 9 = 3.36 days at 20°C 2.34 days at 35°C	87.63%	OECD 111, EEC C7	0704160

Table 2. Chemical composition and properties of Tagros technical lambda-cyhalothrin (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 99.44–99.82%, with 11.86-12.29% impurities (including other cyhalothrin isomers) and no unknowns >1 g/kg.
Declared minimum lambda-cyhalothrin content	840 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

Formulations

The main formulation types available are EC and WP, used in agricultural and public health, respectively. Lambda-cyhalothrin is not co-formulated with other pesticides. The EC is registered and sold in India, Kyrgyzstan, Azerbaijan. The WP is registered and sold in India.

Methods of analysis and testing

The manufacturer confirmed that the existing CIPAC methods, designated in the specifications, are suitable for analysis and testing of the Tagros products.

Annex 1: Hazard Summary Provided by the Proposer

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

Table A. Toxicology profile of Tagros lambda-cyhalothrin technical material, based on acute toxicity, irritation and sensitization

Species	Test	Duration and conditions	Result	Reference
Rat, Sprague-Dawley, m & f	Acute oral MLD	14 d. Dosage: 63, 80 ,100, 130 mg/kg bw. Vehicle: corn oil. Guideline: Gaitonde Committee Recommendation, CIB, Ministry of Agriculture, India. Purity 87.72%	LD_{50} = 91 mg/kg bw (74.50-111.16)	222802
Mouse, Swiss albino, m & f	Acute oral MLD	14 d. Dosage: 30,40mg, 50, 63 mg/kg bw. Vehicle: corn oil. Guideline: Gaitonde Committee Recommendation, CIB, Ministry of Agriculture, India. Purity 87.72%	LD_{50} = 44 mg/kg bw (36.03-56.73)	222801
Rabbit, NZ white, m & f	Acute dermal	14 d. Dosage: 2000 mg/kg bw. Guideline: Gaitonde Committee Recommendation, CIB, Ministry of Agriculture, India. Purity 87.72%	LD_{50} >2000 mg/kg bw	222803
Rat, Sprague-Dawley, m & f	Acute inhalation (MLC)	14 d. Dosage: 0.16, 0.25, 0.44 mg/l. Guideline: Gaitonde Committee Recommendation, CIB, Ministry of Agriculture, India. Purity 87.72%	LC_{50} = 0.23 mg/l (0.14-0.37)	222804
Rabbit, NZ white, m & f	Primary skin irritation	72 h. Dosage:0.5 g. Guideline: Gaitonde Committee Recommendation, CIB, Ministry of Agriculture, India. Purity 87.72%	Non-irritant	222805
Rabbit, NZ white, m & f	Vaginal mucous membrane irritation	72 h. Dosage: 0.1 g. Guideline: Gaitonde Committee Recommendation, CIB, Ministry of Agriculture, India. Purity 87.72%	Non-irritant	222806
Guinea pig	Skin sensitization	OECD 4/406 (1992). Purity 87.63%	Non-sensitizer	0705162

Annex 2: References

Tagros document number or other reference	Year and title of report
0704156	2007. Lambda-Cyhalothrin Technical: Laboratory Study of Vapour Pressure.
0704157	2007. Lambda-cyhalothrin Technical : Laboratory Study on Melting point and Boiling Point.
0704158	2007. Lambda-cyhalothrin Technical: Laboratory Study of Water Solubility.
0704159	2007. Lambda-cyhalothrin Technical : Laboratory Study of partition coefficient.
0704160	2007. Hydrolysis of Lambda-cyhalothrin in Buffer Solutions of pH 4,7 and 9.
0705162	2007. Skin Sensitization potential of Lambda-Cyhalothrin technical in Guinea Pigs.
222801	2004, Acute oral toxicity of Lambda-cyhalothrin to Mouse.
222802	2004, Acute oral toxicity of Lambda-cyhalothrin to Rat.
222803	2004, Acute Dermal toxicity of Lambda-cyhalothrin to Rabbits.
222804	2004, Acute Inhalation toxicity of Lambda-cyhalothrin to Rat.
222805	2004, Primary Skin Irritation study of Lambda-cyhalothrin in Rabbit.
222806	2004, Mucous Membrane Irritation Study of Lambda-cyhalothrin to Rat.
PCS 2006	2006. JMPS enquiry on Lambda-cyhalothrin, revision 1.

LAMBDA-CYHALOTHRIN

FAO/WHO Evaluation Report 463/2003

Explanation

FAO full specifications for lambda-cyhalothrin TC, EC and WG were developed in 1999 (FAO 1999a), according to the new procedure. In 2000, the FAO specifications were extended to “rapid-release” CS formulations intended for use in agriculture (FAO 2000).

WHO full specifications for lambda-cyhalothrin TC, EC and WP were developed in 1999 (WHO 1999), according to the old procedure. In 2002, a WHO interim specification (WHO 2002a) was developed for a “slow-release” CS formulation (micro-capsule suspension) intended for public health uses (net treatments).

The objective of the 2003 evaluation was to harmonize, under the new procedures of both WHO and FAO, the existing specifications and, in particular, to improve and clarify specifications for the two different types of CS formulation.

The supporting data for the existing specifications and the data in support of the review were provided by Syngenta (formerly Zeneca Agrochemicals) UK. At the time of review, the FAO specifications applied only to the lambda-cyhalothrin products of Syngenta, whereas the WHO specifications developed under the old procedure could, in principle, have been applied to the products of any manufacturer of lambda-cyhalothrin products. In practice, because lambda-cyhalothrin had patent protection in many countries, the WHO specifications had been largely restricted to the Syngenta products, although there were some exceptions.

Most of the supporting information and data are unchanged from those presented in the FAO evaluation reports 463/1999 (FAO 1999a) and 463/2000 (FAO 2000) and these should be consulted for detailed background information. Apart from certain new information, the only data repeated from the earlier FAO evaluations are those required for a comparison between the FAO (new procedure) and WHO (old procedure) data.

Syngenta stated that the manufacturing process and manufacturing specifications for lambda-cyhalothrin TC are the same for all products, irrespective of whether they are ultimately intended for use in agriculture or public health.

Uses

In addition to the information provided in evaluation reports 463/1999 (FAO 1999a) and 463/2000 (FAO 2000), lambda-cyhalothrin WP, EC and slow-release CS are also used, respectively, for indoor residual spraying, space spraying and treatment of mosquito nets, for the control of vectors and pests of public health importance.

Formulations

Evaluation reports 463/1999 (FAO 1999a) and 463/2000 (FAO 2000) provided no information on the slow-release lambda-cyhalothrin CS formulation intended for public health use. This formulation type is registered for use in Albania, Cyprus, Greece, Indonesia, S. Korea, Taiwan, Thailand, Vietnam, Cameroon, Ethiopia, Ghana, Ivory Coast, Kenya, Liberia, Malawi, Nigeria, South Africa, Tanzania, Zimbabwe, Columbia, Ecuador, Guatemala, Honduras and Nicaragua.

The capsules of the rapid-release CS formulation for use in agriculture are generally smaller than those of the slow-release CS formulation for use in public health, so that measurement of the particle size distribution provides a rapid means for identifying the product type. Due to the very different release characteristics of the active ingredient, the two product types cannot be used interchangeably.

Methods of analysis and testing

Chemical analysis and physical test methods are all CIPAC methods. Test methods for determination of “free” active ingredient (MT 189) and release rate (MT 190) in slow-release CS were adopted by CIPAC in 2003.

Containers and packaging

No special requirements were identified for containers and packaging.

Appraisal

The WHO Pesticide Evaluation Scheme (WHOPES) has evaluated the WP, EC and slow-release CS formulations of lambda-cyhalothrin for indoor residual spraying against malaria vectors, space spraying against mosquitoes, and treatment of mosquito nets for malaria vector control, respectively (WHO, 2002b).

Existing FAO specifications for lambda-cyhalothrin TC, EC, WG and “rapid-release” CS were adopted in 1999 and 2000, following comprehensive evaluation under the new procedure and therefore they were used as benchmarks for evaluating the existing WHO full and interim specifications (note: WG and rapid-release CS formulations are not used in public health applications).

It was not necessary for the meeting to consider the equivalence of the TC used in agriculture and public health because the same material is used – batches are not manufactured specifically for one area of application or the other – and there had been no change in the manufacturing process.

The meeting agreed that the following clauses or notes in the 1999 WHO specification for TC should be removed: (i) low-activity isomers of cyhalothrin (the cis A and cis B’ pairs of diastereoisomers, which are non-relevant impurities); (ii) melting point; (iii) water content (lambda-cyhalothrin has exceptionally low affinity for water and it is normally impossible to exceed the limit); and (iv) analytical methods for the active ingredient and the non-relevant impurities. With these amendments, the existing WHO specification for TC is harmonized with that of the 1999 FAO specification.

There is no FAO counterpart of the 1999 WHO specification for the WP, which complied with the requirements of the FAO manual (FAO 1999b), with one exception: after the heat stability test there was no requirement for continued compliance with the clause for wettability. The proposer agreed that this clause should be included. The 1999 WHO specification also made no allowance for any loss of active ingredient, which contrasted with the FAO specifications for EC and WG, which permit a loss of up to 5%. The proposer agreed that the WHO specification should be amended to include this limit, though it was stated that, in practice, the loss is expected to be significantly less than the maximum allowed. Other than minor editorial amendments and changes to the notes (as mentioned for the TC), the meeting agreed that no other changes were necessary.

The 1999 WHO specification for the EC included a clause for water content, with a limit of 0.5 g/kg. Originally, the proposer had requested a clause to limit water in the

1999 FAO specification for EC of 5 g/kg, although this was subsequently withdrawn because, at that concentration, the formulation would no longer comply with the description clause which specifies“….a clear to slightly hazy, stable homogeneous liquid, free from visible suspended matter and sediment….”. The proposer confirmed that an appropriate limit would be 5 g/kg but agreed that, because the formulation would not comply with the description clause at this concentration, a separate clause (and test) is not necessary. The 1999 WHO specification for the EC included a clause for acidity or alkalinity, whereas the corresponding clause in the 1999 FAO specification is for pH range. The proposer agreed that a clause for pH range should be adopted for the WHO specification. The 1999 WHO specification for the EC included a clause for flash point, whereas in the 1999 FAO specification this appears as a note. The meeting agreed that the WHO specification should be amended accordingly. The clause for heat stability test in the 1999 WHO specification for the EC made no allowance for any loss of active ingredient. This contrasted with the 1999 FAO specification for EC, which permits a loss of up to 5%. The proposer agreed that the WHO specification should be amended accordingly. With these amendments, the existing WHO specification for EC is harmonized with that of the FAO specification.

Although the specifications for EC formulations used in public health and agriculture thus become identical and are applicable to both kinds of product, this does not imply that the products are necessarily the same, nor that they can be used interchangeably. The meeting noted that users must adhere to the label recommendations, to ensure acceptable safety and efficacy.

The 2002 WHO specification for (slow-release) CS and the 2000 FAO specification for (rapid-release) CS included clauses for mass per millilitre. The clause was included in the FAO manual (FAO 1999b) but is not included in the guideline for CS given in the new FAO/WHO manual (FAO/WHO 2002). The proposer agreed that it is not an appropriate quality criterion for FAO and WHO specifications purposes. The 2002 WHO interim specification for (slow-release) CS includes a clause for particle size, which is not included in the manual (FAO 1999b, FAO/WHO 2002). The purpose of the clause in the 2002 WHO specification was to permit rapid-release and slow-release CS formulations of lambda-cyhalothrin to be differentiated quickly, thus avoiding confusion and the unnecessary testing of a rapid-release CS for “free” active ingredient and release rate. The meeting agreed that particle size, as determined by CIPAC MT 187, would provide a useful screening test but that it is not appropriate as a criterion for product quality. The meeting therefore agreed that the test and suitable limits for d_{10}, d_{50} and d_{90} should be appended to the specifications in the form of a note to the “description”, not in the form of a specification clause.

Users must be able to distinguish immediately between the FAO and WHO specifications for CS and understand the different purposes for which the two products are intended. The meeting was informed by CropLife International that standard codes are not available to distinguish CS formulations with differing release characteristics because, although the present case of lambda-cyhalothrin provides clear-cut extremes, there are other (unrelated) products with either intermediate or mixed characteristics. The meeting therefore concluded that the titles of CS formulation specifications should be decided on a case-by-case basis. In the present case, meeting agreed that the FAO specification should be entitled “Lambda-cyhalothrin rapid-release capsule suspension (rapid-release CS)” and the WHO specification should be entitled “Lambda-cyhalothrin slow-release capsule suspension (slow-release CS)”.

Recommendations

The Meeting recommended that:

1) the existing WHO specifications for lambda-cyhalothrin TC, EC, WP and slow-release CS, developed under the old procedure, should be withdrawn;
2) the existing FAO specifications for TC and EC do not require amendment and should be retained by FAO and adopted by WHO;
3) the existing WHO specification for WP, amended as described in the appraisal, above, should be adopted by WHO;
4) the existing FAO specification for WG does not require amendment and should be retained by FAO (it should not be adopted by WHO);
5) the existing FAO specification for rapid-release CS, amended as described in the appraisal, above, should be adopted by FAO;
6) the existing WHO specification for slow-release CS, amended as described in the appraisal, above, should be adopted by WHO.

References

FAO 1999a — FAO specifications: 463/TC, 463/WG, 463EC and evaluation report 463/1999, accessible at http://www.fao.org/ag/ap/agpp/pesticid/.

FAO 1999b — Manual on the development and use of FAO specifications for plant protection products, 5th edition, 1999. FAO Plant production and protection paper 149, FAO, Rome.

FAO 2000 — FAO specification: 463/CS and evaluation report 463/2000, accessible at http://www.fao.org/ag/ap/agpp/pesticid/.

FAO/WHO 2002 — Manual on the development and use of FAO and WHO specifications for pesticides, 1st edition, 2002. FAO Plant production and protection paper 173, FAO, Rome.

WHO 1997 — Chavasse, D.C. and H.H. Yap, 1997. Chemical methods for the control of vectors and pests of public health importance. World Health Organization, Geneva, doc. WHO/CTD/WHOPES/97.2.

WHO 1999 — Full specifications: TC, WHO/SIT/31; WP, WHO/SIF/59; EC, WHO/SIF/60.

WHO 2002a — Interim specification: CS, WHO/IS/CS/463/2002.

WHO 2002b — Najera, J.A. and M. Zaim. Malaria vector control – Decision making criteria and procedures for judicious use of insecticides. World Health Organization, Geneva, Doc. WHO/CDS/WHOPES/2002.5 Rev.1.

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LAMBDA-CYHALOTHRIN

FAO Evaluation Report 463/2000

Explanation

Information on lambda-cyhalothrin capsule suspension (CS) formulations was evaluated in support of a new FAO specification. A full data package for lambda-cyhalothrin was evaluated in 1999 and, at that Meeting, specifications were adopted for TC, EC and WG (evaluation report 463/1999).

A draft specification for lambda-cyhalothrin CS formulations was also considered in 1999. Most of the clauses had been considered satisfactory but additional information was required in respect of two critical clauses forming part of the guideline specification provided in the FAO Manual[1]. The Meeting requested validated methods for total and free (non-encapsulated) lambda-cyhalothrin and wished to evaluate a specification for the free active ingredient.

The draft CS specification under consideration was for lambda-cyhalothrin products encapsulated for foliar application only. The capsules of these products are thin-walled: they are intended to burst and release the active ingredient immediately when the spray deposits dry. This type of formulation may be considered somewhat analogous to an EW but it contains no organic solvent. This type of CS is very different from the thick-walled products intended for slow- or controlled-release of active ingredients, which may be used for soil applications, etc.

The draft specification and supporting information were provided by Zeneca Agrochemicals, UK, in 2000.

Formulations

CS formulations are registered in USA and Argentina.

Methods of analysis and testing

The analytical method (463/CS/M/-) for total active ingredient was adopted as a provisional CIPAC method in 2000 but has not yet been published by CIPAC. It is provided as a Note to the specification. The method involves two modifications to the original CIPAC method for lambda-cyhalothrin[2]: one being the addition of acetone to extract the active ingredient from the capsules; the other, reported in the 463/1999 evaluation, being the addition of trifluoroacetic acid to ensure stability of the active ingredient. The method is based on capillary GC with internal standardisation and detection by FID.

The Proposer had been unable to develop a method for the determination of free active ingredient in the lambda-cyhalothrin CS formulations, intended for foliar application.

The proposer stated that, even employing the most sophisticated techniques available, it was impossible to develop a method that would provide a meaningful result for the free active ingredient content.

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1 Manual on the development and use of FAO specifications for plant protection products, 5th edition, FAO Plant production and protection paper 149, page 109. FAO, Rome.

2 Martijn A. and Dobrat W., Eds, CIPAC Handbook E, Lambda-cyhalothrin 463, pp 49-57. CIPAC, Harpenden.

The meeting accepted that, for this type of rapid-release product, it may not be possible to define free active ingredient and that, even if a satisfactory definition could be developed, the analytical result may not be meaning for practical purposes.

Methods for testing the physical properties of the CS, for compliance with the proposed FAO specifications, have been published by CIPAC (CIPAC 1995). They are referenced in the specifications and were used to develop the data on which the specifications are based.

Appraisal

The lambda-cyhalothrin CS formulations described by the draft specification are “rapid-release” products, containing thin-walled capsules, intended for foliar application after dilution.

The Proposer provided a method for the determination of total lambda-cyhalothrin content but was unable to provide a method for the determination of the free (non-encapsulated) active ingredient. The Meeting accepted that, in this case, free active ingredient may be impossible to define or to measure in a meaningful way.

Lambda-cyhalothrin has extremely low water solubility and, if capsules rupture, the active ingredient can only form a separate liquid layer, adhere to the capsule material and/or adhere to the walls of the container. The Proposer stated that the physical properties (e.g. description, wet sieve test) of the formulation would be adversely affected if a significant proportion of capsules became ruptured or were imperfectly formed during formulation.

The Meeting agreed that, in this case, a specification clause limiting free active ingredient content was not appropriate. The Meeting agreed that, because of the rapid-release nature intended for the products, there were no implications for operator or environmental risk from free active ingredient in the formulation.

The Meeting was informed of the existence of slow-release formulations of lambda-cyhalothrin for use in public health applications, by the representative of WHOPES. The Meeting was therefore concerned that the specification should be restricted to products intended for foliar application. The Meeting also considered that the inclusion/exclusion of a clause specifying free active ingredient in CS formulations of other pesticides should be decided on a case-by-case basis.

Recommendations

The Meeting recommended that the proposed specification for CS, lacking the guideline clause for free active ingredient content, should be adopted as an FAO specification. The Meeting recommended that the specification should be restricted to rapid-release CS formulation intended for foliar application.

The Meeting recommended that the Proposer should submit data to FAO to demonstrate the adverse effects (or otherwise) of capsule rupture, or poor capsule formation, on the physical properties of the formulation.

The Meeting recommended that clarification should be sought by FAO from Industry, regarding the descriptions, codes and most appropriate specification guidelines for the different types of CS products.

LAMBDA-CYHALOTHRIN

FAO Evaluation Report 463/1999

Explanation

The data for lambda-cyhalothrin were evaluated in support of new FAO specifications.

Lambda-cyhalothrin is sold under various trade names (e.g. “Karate”, “Kung-Fu” and “Icon”) and is protected in most major markets by patents (and in some European countries by supplementary protection certificates) until mid- to late-2003.

Cyhalothrin (as the mixture of equal parts of the four *Z-cis*-isomers) was evaluated by the FAO/WHO Joint Meeting on Pesticide Residues (JMPR 1984), for toxicology and residues, and an acceptable daily intake (ADI) of 0.00 to 0.02 mg/kg bodyweight was established. Lambda-cyhalothrin (as one of the two diastereoisomeric pairs of enantiomers) was subsequently evaluated for residues and environmental data (JMPR 1986, JMPR 1988). Codex maximum residue limits have been established, for the sum of cyhalothrin isomers, of 0.2 mg/kg on pome fruit and cabbages and 0.02 mg/kg on cottonseed, cottonseed oil and potatoes (Codex 1999).

The draft specifications and supporting data were provided by Zeneca Agrochemicals, UK, in 1999.

Uses

An agricultural and public health insecticide, controlling a wide spectrum of insects and mites, at all developmental stages, on a wide range of crops. It is non-systemic, with very little translaminar activity. It is of low volatility and short persistence in soil and therefore has only limited uses as a soil insecticide. (JMPR 1986).

Identity

ISO common names: Lambda-cyhalothrin (draft E-ISO),
Lambda-cyhalothrine (draft F-ISO).

Synonyms: none

Chemical names

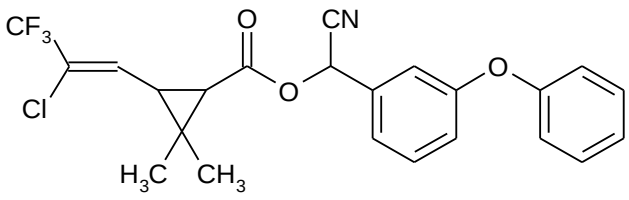
IUPAC: alpha-cyano-3-phenoxybenzyl 3-(2-chloro-3,3,3-trifluoroprop-1-enyl)-2,2-dimethylcyclopropane carboxylate, a 1:1 mixture of the (Z)-(1R,3R),S-ester and the (Z)-(1S,3S),R-ester

CA: [1-alpha(S*),3-alpha(Z)]-cyano(3-phenoxyphenyl)methyl-3-(2-chloro-3,3,3-trifluoro-1-propenyl)-2,2-dimethylcyclopropanecarboxylate (9CI)

CAS No: 91465-08-6

CIPAC No: 463

Structural formula:



Molecular formula: $C_{23}H_{19}ClF_3NO_3$

Relative molecular mass: 449.9

Identity tests: GC (relative retention time), NMR, IR.

Physical and chemical properties of lambda-cyhalothrin

Physical and chemical properties of pure lambda-cyhalothrin

Parameter	Value(s), method(s), conditions and purity
Vapour pressure:	2 x 10-10 kPa at 20°C (purity 99.0%). Method: OECD104, estimated by extrapolation using Henry's law.
Melting point/range:	49.2°C (99.0% purity). 47.5 to 48.5°C (purity 96.5%) Method: OECD102.
Temperature of decomposition:	No boiling point at atmospheric or reduced pressure, decomposition occurs at 239°C (purity 99.0%) and at 234°C at 1 mm Hg pressure (purity 85.9% and 96.5%) Methods: EECA2, EECA4 and OECD103 for boiling point, OECD103 and EECA4 for temperature of decomposition.
Solubility in water:	4 x 10-3 mg/l at pH 5.0 5 x 10-3 mg/l at pH 6.5 4 x 10-3 mg/l at pH 9.2 (purity 96.5%). Method: EECA6.
Octanol/water partition coefficient:	Log Pow = 7.0. (purity 99.0%). Method: EECA8.
Hydrolysis characteristics:	Study of the acid moiety, over a period of 30 days at 25°C, indicated that lambda-cyhalothrin is stable to hydrolysis at pH 5, hydrolyses very slowly at pH 7 and rapidly at pH 9. However, the material failed to remain completely in solution and these data are questionable. At both pH 7 and 9, the cyclopropane acid was the major product of hydrolysis (2% produced at pH 7 and 73% at pH 9). Polar compounds, which remained at the origin of thin layer chromatograms, were formed but did not exceed 10% of the radioactivity recovered into dichloromethane. Studies on the alcohol moiety, over a period of up to 29 days at 25°C, indicated that hydrolysis occurred very slowly at pH 4, slowly at pH 7 and fairly rapidly at pH 9. At all pH values, 3-phenoxybenzaldehyde and 3-phenoxybenzoic acid were formed, with 3-phenoxybenzaldehyde being the major compound formed at pH 9 (up to 78% of the applied radioactivity). Two unidentified compounds were also formed, representing 10.7% and 3.4% of the applied radioactivity after 29 days at pH 9. These unknowns occurred at much lower levels at pH 4 and 7 (radio-labelled material purity ≥ 95%). Method: EPA CG5000.
Photolysis characteristics:	Studies at pH 5 for 31 days at 25°C produced four values for the lambda-cyhalothrin remaining at each sampling interval. The values were used to estimate a half-life of 24 d for lambda-cyhalothrin at 30°N in autumn. This value is only approximate because lambda-cyhalothrin was too hydrophobic to remain totally in solution during the irradiation (radio-labelled material purity ≥ 95%). Method: EPA CG6000.

Chemical composition of the 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 97.5 to 98.1%, with 10.5 to 11.7% impurities (including other cyhalothrin isomers) and with <0.1 to 0.5% present as unknowns.

Declared minimum lambda-cyhalothrin content:	810 g/kg.
Total alpha-cyano-3-phenoxybenzyl-3-(2-chloro-3,3,3-trifluoropropenyl)-2,2-dimethylcyclopropanecarboxylate minimum content, as lambda-cyhalothrin and other diastereoisomers:	900 g/kg.
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.

WHO/IPCS and the FAO/WHO JMPR did not identify any impurities as toxicologically relevant.

Hazard summary

Notes.

(i) In some cases, the proposer did not identify the purity of materials used for the toxicological and ecotoxicological tests but it was stated that all data summarized below were generated using technical materials of similar composition to commercial products.

(ii) Except where otherwise stated, the summaries presented below are those of the proposer and are in agreement with the conclusions of the WHO and JMPR.

Table 1. Toxicological profile of the lambda-cyhalothrin technical material, based on acute toxicity, irritation and sensitization

Species	Test	Result
Rat (male)	Oral MLD	79 mg/kg bw
Rat (female)	Oral MLD	56 mg/kg bw
Mouse (male)	Oral MLD	20 mg/kg bw
Mouse (female)	Oral MLD	20 mg/kg bw
Rat (male)	Inhalation MLC	0.06 mg/l
Rat (female)	Inhalation MLC	0.06 mg/l
Rat (male)	Dermal MLD	632 mg/kg bw
Rat (female)	Dermal MLD	696 mg/kg bw
Rabbit	Skin irritation	Mild Irritant (WHO 1990B)
Rabbit	Eye irritation	Mild Irritant (WHO 1990B)
Guinea pig	Skin sensitization	Not a sensitizer

Lambda-cyhalothrin has moderate to high acute toxicity when administered orally to the rat or mouse, the mouse being the more susceptible than the rat. Clinical signs are consistent with pyrethroid toxicity (e.g. abnormal motor function).

In the rat, lambda-cyhalothrin is less toxic by the dermal route but is highly toxic by inhalation. WHO (WHO 1990B) considered only the potential for irritation of the upper respiratory tract by inhalation of fine dust or mist, and the potential for chemical

pneumonitis resulting from aspiration into the lungs of the solvent used for liquid formulations, not the inhalation toxicity of lambda-cyhalothrin itself. WHO (WHO 1990B) concluded that lambda-cyhalothrin is a mild irritant to the rabbit eye and skin. It is not a skin sensitizer in the guinea pig.

Table 2. Toxicological profile of the technical material based on repeated administration (sub-acute to chronic)

Species	Study Type	Cyhalothrin results	Lambda-cyhalothrin results
Rat	90 day toxicity	NOAEL: 50 ppm (2.8-3.6 mg/kg/day)	50 ppm (~5 mg/kg/day)
Dog	26 week toxicity 12 month toxicity	NOAEL: 2.5 mg/kg/day	NOAEL: 0.5 mg/kg/day
Rat	2 year toxicity and carcinogenicity	Not carcinogenic NOAEL: 50 ppm (~2.5 mg/kg/day)	
Mouse	2 year carcinogenicity	Not carcinogenic NOAEL: 20 ppm (~1.9 mg/kg/day)	
Rat	Three-generation reproduction	Not a reprotoxin NOAEL: 30 ppm (~2 mg/kg/day)	
Rat	Teratogenicity Maternal toxicity Developmental toxicity	Not teratogenic NOAEL: 10 mg/kg/day NOAEL: >15 mg/kg/day	
Rabbit	Teratogenicity Maternal toxicity Developmental toxicity	Not teratogenic NOAEL: 10 mg/kg/day NOAEL: >30 mg/kg/day	

Based on the stereochemistry of the molecules, the equivalence of metabolism, and the sub-chronic toxicology of cyhalothrin and lambda-cyhalothrin, data on cyhalothrin were used to assess the toxicity of lambda-cyhalothrin.

Table 3. Mutagenicity profile of the technical material based on *in vitro* and *in vivo* tests

Test system	Target cells	Concentration	Purity	Results
In vitro studies				
Bacterial mutation assay	*Salmonella typhimurium* TA98, TA100, TA1535, TA1537, TA1538	1.6-5000 mg/plate (+ and - S9-mix)	96.5% w/w	Negative
Mammalian cell gene mutation assay	L5178Y cells	125-2000 mg/ml (test 1) 250-2000 mg/ml (test 2) 250-4000 mg/ml (test 3) (+ and - S9-mix)	96.6% w/w	Negative
Mammalian cell cytogenetic assay	Human lymphocytes (chromosomal aberrations)	100, 500 and 1000 mg/ml (+ and - S9-mix)	96.5% w/w	Negative

Table 3. Mutagenicity profile of the technical material based on *in vitro* and *in vivo* tests

Test system	Target cells	Concentration	Purity	Results
Rat hepatocyte culture, unscheduled DNA synthesis assay	Rat hepatocytes (UDS)	10^{-8}, 10^{-7}, 10^{-6} and 10^{-5}M	96.6% w/w	Negative
In vivo studies				
Mouse bone marrow micronucleus assay	Mouse bone marrow	22 and 35 mg/kg (single dose)	96.5% w/w	Negative

All of the assays conducted were negative and it was concluded that lambda-cyhalothrin is not genotoxic.

Table 4. Ecotoxicological profile of the technical material

Species	Test type, duration, concentrations, etc.	Result
Daphnia magna (water flea)	48 h immobilization,	EC_{50} 0.36 µg/l
Oncorhynchus mykiss (rainbow trout)	96 h mortality	LC_{50} 0.24 µg/l
Lepomis macrochirus (bluegill sunfish)	96 h mortality	LC_{50} 0.21 µg/l
Selenastrum capricornutum (green alga) (*Note 1)*	96 h growth	EC_{50} >1000 µg/l
Daphnia magna (water flea)	21 d reproduction	NOEC 0.002 µg/l
Cyprinodon variegatus (sheepshead minnow)	28 d early life-stage.	NOEC 0.25 µg/l
Mallard duck	Acute oral, 0, 739, 1040, 1620, 2580, 3950 mg a.i./kg bw	Acute Oral LD_{50}, Lowest lethal Dose (LLD) and NOEL all >3950 mg/kg bw
Bobwhite quail	Sub-acute oral toxicity, 0, 500, 1000, 2000, 4000 and 5000 mg a.i./kg diet	Dietary LC50 >5300 mg/kg diet. LLC = 577 mg/kg diet
Mallard duck	Sub-acute oral toxicity, 0, 500, 1000, 2000, 3000, 4000 and 5000 mg a.i./kg diet	Dietary LC50 = 3948 mg/kg diet
Mallard duck	Reproduction, 0, 0.5, 5.0, 15 and 30 mg a.i./kg diet	Reproductive NOEL = 30 mg/kg diet for 20 weeks

Table 4. Ecotoxicological profile of the technical material

Species	Test type, duration, concentrations, etc.	Result
Bee (note 2)	24 h contact toxicity	mean LD_{50} 0.051 μg a.i./bee
Bee (note 2)	48 h contact toxicity	mean LD_{50} 0.038 μg a.i./bee
Bee (note 2)	24 h oral toxicity	mean LD_{50} 0.965 μg a.i./bee
Bee (note 2)	48 h oral toxicity	mean LD_{50} 0.909 μg a.i./bee

Note 1. The 96-hour E_rC_{50} and E_bC_{50} of lambda-cyhalothrin to the green alga (*Selenastrum capricornutum*) are both greater than 1.0 mg/litre, the 96-hour NOEC was 1.0 mg/litre. In a different study, assessing the effect of a 5% w/v EC formulation of lambda-cyhalothrin on the green alga (*Selenastrum capricornutum*), the 96-hour E_rC_{50} was calculated to be 31 mg formulation (1.6 mg lambda-cyhalothrin)/litre). The results obtained for technical and formulated products were therefore in agreement.

Note 2. Individual mean and 95% confidence interval data were provided from duplicate trials. Positive controls with dimethoate demonstrated normal responses to toxic compounds.

WHO/IPCS has evaluated lambda-cyhalothrin and classified it as 'Moderately Hazardous' (Class II), on the basis of acute oral toxicity data (WHO 1999). The hazards and risks were summarised as follows. Harmful; irritating to eyes, skin and upper respiratory system; ingestion could lead to neurological symptoms such as tremors and convulsions; a hazard of ingested liquid formulations is aspiration of the solvent into the lungs (chemical pneumonitis); very toxic to fish and honey bees. Exposure of the general population to lambda-cyhalothrin is expected to be very low and not likely to represent a hazard under normal conditions of use. With good work practices, hygiene measures and safety precautions, lambda-cyhalothrin is unlikely to present an occupational exposure hazard. Although very toxic to fish bees and aquatic arthropods in the laboratory, in the field last effects are not likely to occur under recommended conditions of use (WHO 1990A).

Formulations

The main formulation type available for agricultural uses is EC, although WG, 'fast-release' CS and EW formulations are available in some countries. WP formulations are sold in some countries, exclusively for public health purposes.

EC formulations are registered in 84 countries world-wide, including those countries where CS or WG are also registered. CS formulations are registered in USA and Argentina. WG is registered in 6 countries of the European Union.

Methods of analysis and testing

Chemical analysis for the active ingredient utilises CIPAC methods (CIPAC 1992) to identify and quantify the active ingredient content of technical materials (463/TC/M/-) and formulated products 463/WP/M/- and 463/EC/M/-). The method involves capillary GC with internal standardisation and detection by FID. The proposer recommended a minor modification to the published method, i.e. trifluoroacetic acid should be added to the standard and sample solutions, to ensure stability of the lambda-cyhalothrin.

A modification of the CIPAC method is required for analysis of CS formulations, to extract the lambda-cyhalothrin, although the remainder of the method is unchanged. The linearity, repeatability and reproducibility of the modification has been validated by the company but these data have not yet been assessed by CIPAC. At the time of

submission, there were no validated methods available to differentiate between the free and encapsulated active ingredient in the CS formulations. In principle, the very low water solubility of lambda-cyhalothrin should ensure that the free active ingredient content is very low.

There are no relevant impurities in lambda-cyhalothrin and thus approved methods are not required to support the specifications. Non-relevant organic impurities in the TC were determined by capillary GC with FID, with the exception of two impurities which were determined by HPLC.

All methods for testing the physical properties of the TC, WP, EC and SE, for compliance with the proposed FAO specifications, have been published by CIPAC (CIPAC 1995). They are referenced in the specifications and were used to develop the data on which the specifications are based.

Containers and packaging

No special requirements were identified for containers and packaging.

Expression of active ingredient

The active ingredient is expressed as lambda-cyhalothrin.

Appraisal

Lambda-cyhalothrin is a patented active ingredient that had not previously been the subject of FAO specifications.

Lambda-cyhalothrin is fat soluble and of very low water solubility. It is hydrolysed very slowly at pH 4 but is degraded fairly rapidly at pH 9, mainly by hydrolysis. Dilute aqueous solutions are subject to photolysis, which occurs at a moderate rate.

The purity of the TC quoted by the JMPR (JMPR 1986) and WHO (WHO 1990A) was a minimum of 90% as lambda-cyhalothrin, with (noted by the JMPR only) small amounts of other isomers present. The lambda-cyhalothrin purity quoted in the WHO interim specification is 83% (WHO 1997). The minimum purity given in the specification is 810 g/kg as lambda-cyhalothrin, with total cyhalothrin isomers at a minimum of 900 g/kg. The proposer stated that the minimum contents of the isomers had always been reported as given in the specification and that the lower limit for lambda-cyhalothrin had been notified to, and accepted by, regulatory authorities world-wide. The 90% minimum content of lambda-cyhalothrin, reported by the JMPR, was a mistake that had not been recognised previously by the proposer. The 83% minimum interim specification of WHO for lambda-cyhalothrin was based on the convention previously utilised by FAO for technical materials (FAO 1994). The proposer stated that lambda-cyhalothrin batches produced over a period of several years had a mean active ingredient content of about 87%, with fewer than 1% of batches containing less than 83%. The previous FAO convention for TC specifications permitted a tolerance (±2.5%) which, in this case, effectively corresponded to an absolute minimum of approximately 81%. FAO limits now reflect the absolute minimum measured content and the proposer redefined the limit accordingly. The purity of the cyhalothrin (mixed isomers) on which the ADI was based was not quoted by the JMPR (JMPR 1984). The proposer confirmed that data on toxicity and ecotoxicity of lambda-cyhalothrin were generated using TC materials with impurity contents within the maximum limits of the impurity profile notified for the FAO specifications. WHO and the JMPR considered

cyhalothrin and lambda-cyhalothrin to be toxicologically and ecotoxicologically equivalent.

The purity of the TC used to establish the physicochemical data was 96.5% lambda-cyhalothrin. Later studies, which included some repeated determinations, employed typical commercial technical material of 85.9% lambda-cyhalothrin and >90% total cyhalothrin. The meeting accepted that physico-chemical data generated from material of higher isomeric purity are valid for the normal technical materials.

Confidential information on the manufacturing process, and on impurities at or above 1 g/kg, was provided by the proposer, together with limits for the impurities (1 to 100 g/kg, including other cyhalothrin isomers) in the TC. Limits for the impurities were supported by 5 batch analyses, in which unidentified components accounted for <1 - 5.2 g/kg and the mass balances were high. Limits for four impurities exceeded the mean plus 10 s.d. for the 5 batch data. The proposer explained that the 5 batch data formed only a very small proportion of the data available and that the limits were based on all data. The proposer provided additional information to show that a potential relevant impurity, postulated by the evaluator, does not occur in practice. With the possible exception of water (see following paragraph), there are no impurities, present above or below 1 g/kg, in technical lambda-cyhalothrin which are known or suspected to affect adversely the overall safety of the product. No stabilisers or other compounds are added to the TC.

The proposer identified water as a relevant impurity. It was proposed that water in the TC and EC should be limited to 3 g/kg and 5 g/kg, respectively, to avoid undesirable epimerisation. In the case of the WG, the proposer indicated that the water content should be limited to 10 g/kg, to avoid aggregation of the granules during storage. These requirements were logical but no data were available to support the values as appropriate limits or to demonstrate that the water content must be limited in practice. In principle, the very low water solubility of lambda-cyhalothrin should limit the water content of the TC. However, water in the EC could be present in the form of emulsion droplets, providing a larger reservoir of water for epimerisation. In the case of the WG, the proposer believed that a water content >10 g/kg could lead to granule aggregation. The specified tests for storage at elevated temperature and flowability should, in principle, identify significant changes of this kind. The proposer reported that a water content >10 g/kg exacerbates aggregation over an extended period at normal temperatures but was unable to show that this would not be detected by the tests of storage at elevated temperature and flowability. The meeting invited the proposer to provide evidence to support their assertions but agreed that, in the absence of supporting data, water should not be defined as a relevant impurity in the specifications.

Analytical and physical test methods are full CIPAC methods, with the exception of the analytical method for the CS formulation. The proposer reported that the CIPAC analytical methods should be modified by the addition of trifluoroacetic acid to standard and sample solutions to prevent epimerisation. The method proposed for determination of total a.i. in the CS was an extension of the CIPAC method, with the introduction of an initial acetone extraction step. The company submitted validation data to support the extension of the method. The meeting agreed that this aspect of the proposed specification for CS would become acceptable when the extension is adopted by CIPAC.

Valid methods are not available for the separate determination of free and encapsulated active ingredient in any CS formulation. In the case of lambda-cyhalothrin, the levels of free active ingredient in true aqueous solution should be very low and the proposer stated that the active ingredient is not further solubilised by the low concentration of emulsifiers present. The meeting agreed that it may be appropriate to accept defining methods (method type I, Codex 1997) for this purpose.

The JMPR allocated an ADI of 0-0.02 mg/kg bodyweight for cyhalothrin, based on short term and chronic testing on rats, mice, rabbits, guinea pigs and dogs. The data were considered by the JMPR and WHO to be applicable to lambda-cyhalothrin. The purity of the technical material used in these studies was similar to that of commercial products and within the TC specification.

WHO concluded that in normal use, and with good work practices and safety precautions, lambda-cyhalothrin is unlikely to present hazards to the general population, or to those who are occupationally exposed. The WHO assessment of inhalation hazard appears to have been based on the hazards of aspiration of the solvent from liquid formulation, or irritation of the upper respiratory system by dust or mist, and not on the inhalation toxicity data presented in support of the proposed specification. The meeting recommended that FAO should refer the matter to WHO. Lambda-cyhalothrin is highly toxic to fish, aquatic arthropods and honey-bees but WHO concluded that recommended use rates would not lead to levels presenting environmental hazards.

The WG specification requires a minimum suspensibility of 50%, which is lower the 60% minimum recommended in the Manual (FAO 1999, section 3.5.43). The proposer stated that the suspensibility is normally higher than 50% but the CIPAC test may give results approaching this value. The proposer stated the product is sold in many markets, including those in which knapsack sprayers are commonly used, and has had a consistent record of customer satisfaction, with no negative feedback concerning the distribution of product within a spray tank or its spray performance.

The proposed specification for CS provided, in a note, the full details of the modifications proposed for the CIPAC method. The meeting agreed that the extension of the analytical method for total active ingredient content should be considered by CIPAC. The meeting also agreed that a defining method could be utilised for the determination of free active ingredient content of the CS. The meeting agreed that the draft CS specification should be reconsidered in 2000.

Recommendations

The specifications for TC, EC and WG were recommended for adoption.

The draft specification for CS should be reconsidered in 2000, subject to the proposer submitting the methods for free and total active ingredient content for adoption by CIPAC, AOAC or equivalent. The proposer should be invited to provide a draft specification for free active ingredient content.

The proposer should be invited to provide data to support inclusion of water as a relevant impurity in the TC, EC and WG and the specifications should be reviewed when these data become available.

FAO should notify WHO that the inhalation hazard associated with lambda-cyhalothrin may require review.

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