

# WHO SPECIFICATIONS AND EVALUATIONS FOR PUBLIC HEALTH PESTICIDES

## LAMBDA-CYHALOTHRIN

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

---

	Page
DISCLAIMER	3
INTRODUCTION	4
<b>PART ONE</b>	
SPECIFICATIONS FOR LAMBDA-CYHALOTHRIN	
LAMBDA-CYHALOTHRIN INFORMATION	6
LAMBDA-CYHALOTHRIN TECHNICAL MATERIAL (2003)	7
LAMBDA-CYHALOTHRIN EMULSIFIABLE CONCENTRATE (2003)	8
LAMBDA-CYHALOTHRIN WETTABLE POWDER (2003)	11
LAMBDA-CYHALOTHRIN SLOW-RELEASE CAPSULE SUSPENSION (SEPTEMBER 2011)	15
<b>PART TWO</b>	
EVALUATIONS OF LAMBDA-CYHALOTHRIN	
2011 FAO/WHO EVALUATION REPORT ON LAMBDA-CYHALOTHRIN	20
SUPPORTING INFORMATION	21
ANNEX 2: REFERENCES	24
2006 FAO/WHO EVALUATION REPORT ON LAMBDA-CYHALOTHRIN	25
SUPPORTING INFORMATION	27
ANNEX 1: HAZARD SUMMARY PROVIDED BY THE PROPOSER	29
ANNEX 2: REFERENCES	31
2003 FAO/WHO EVALUATION REPORT ON LAMBDA-CYHALOTHRIN	32
2000 FAO EVALUATION REPORT ON LAMBDA-CYHALOTHRIN	36
1999 FAO EVALUATION REPORT ON LAMBDA-CYHALOTHRIN	39

## Disclaimer<sup>1</sup>

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.

WHO disclaims any and all liability for any injury, death, loss, damage or other prejudice of any kind that may be arise as a result of, or in connection with, the manufacture, sale, transportation, storage, handling, preparation and/or use of pesticides which are found, or are claimed, to have been manufactured to comply with these specifications.

Additionally, WHO wishes to alert users to the fact that improper storage, handling, preparation and/or use of pesticides can result in either a lowering or complete loss of safety and/or efficacy.

WHO is not responsible, and does not accept any liability, for the testing of pesticides for compliance with the specifications, nor for any methods recommended and/or used for testing compliance. As a result, WHO does not in any way warrant or represent that any pesticide claimed to comply with a WHO specification actually does so.

---

<sup>1</sup> This disclaimer applies to all specifications published by WHO.

## INTRODUCTION

WHO establishes and publishes specifications\* 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 Specifications of the technical material and the related formulations of the pesticide in accordance with chapters 4 to 9 of the “FAO/WHO Manual on Pesticide Specifications.”

**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 “FAO/WHO Manual on Pesticide Specifications” and supported by other information sources. The Evaluation Report includes the name(s) of the manufacturer(s) whose technical material has been evaluated. Evaluation reports on specifications developed subsequently to the original set of specifications are added in a chronological order to this report.

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. Dates of publication of the earlier versions, if any, are identified in a footnote. Evaluations bear the date (year) of the meeting at which the recommendations were made by the JMPS.**

\* Footnote: The publications are available on the Internet under [\(http://www.who.int/whopes/quality/en/\)](http://www.who.int/whopes/quality/en/).

**PART ONE**  
**SPECIFICATIONS**

---

LAMBDA-CYHALOTHRIN

	Page
LAMBDA-CYHALOTHRIN INFORMATION	<b>6</b>
LAMBDA-CYHALOTHRIN TECHNICAL MATERIAL (2003)	<b>7</b>
LAMBDA-CYHALOTHRIN EMULSIFIABLE CONCENTRATE (2003)	<b>8</b>
LAMBDA-CYHALOTHRIN WETTABLE POWDER (2003)	<b>11</b>
LAMBDA-CYHALOTHRIN SLOW-RELEASE CAPSULE SUSPENSION (SEPTEMBER 2011)	<b>15</b>

# WHO SPECIFICATIONS FOR PUBLIC HEALTH PESTICIDES

## LAMBDA-CYHALOTHRIN

### INFORMATION

#### ISO common names

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

#### Synonyms

none

#### Chemical names

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

**CA** [1 $\alpha$ (*S*<sup>\*</sup>),3 $\alpha$ (*Z*)]-( $\pm$ )-cyano(3-phenoxyphenyl)methyl 3-(2-chloro-3,3,3-trifluoro-1-propenyl)-2,2-dimethylcyclopropanecarboxylate.

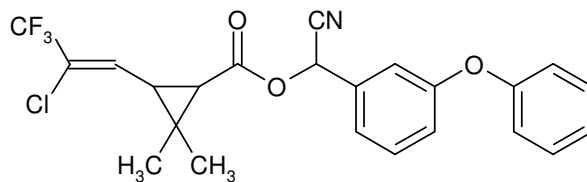
#### CAS Number

91465-08-6

#### CIPAC Number

463

#### Structural formula



#### Molecular formula

C<sub>23</sub>H<sub>19</sub>ClF<sub>3</sub>NO<sub>3</sub>

#### Relative molecular mass

449.9

#### Identity tests

GC (relative retention time), NMR, IR.

# WHO SPECIFICATIONS FOR PUBLIC HEALTH PESTICIDES

## LAMBDA-CYHALOTHRIN TECHNICAL MATERIAL

WHO Specification 463/TC (2003\*)

*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). It should be applicable to TC produced by these manufacturers but it is not an endorsement of those products, nor a guarantee that they comply with the specifications. The specification may not be appropriate for TC produced by other manufacturers. The evaluation reports (463/2003, 463/2006), 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 (Note 1) 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 (CIPAC 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 (CIPAC 463/TC/M/3, CIPAC Handbook E, p.50, 1992)

The lambda-cyhalothrin content shall be declared (not less than 810 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)

The maximum acidity shall be 0.5 g/kg, calculated as H<sub>2</sub>SO<sub>4</sub>.

---

**Note 1** The flash point of the product should not be lower than 44 °C when determined using the Abel Closed Cup (MT 12). Attention is drawn to the appropriate national and international regulations on handling and transport of flammable materials.

---

\* Specifications may be revised and/or additional evaluations may be undertaken. Ensure the use of current versions by checking at: <http://www.who.int/whopes/quality/en/>.

# WHO SPECIFICATIONS FOR PUBLIC HEALTH PESTICIDES

## LAMBDA-CYHALOTHRIN EMULSIFIABLE CONCENTRATE

WHO Specification 463/EC (2003\*)

*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). It 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), 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 (2003), 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 (CIPAC 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 (CIPAC 463/EC/M/3, CIPAC Handbook E, p.56, 1992)

The lambda-cyhalothrin content shall be declared (g/l at  $20 \pm 2^\circ\text{C}$ , 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 $20 \pm 2^\circ\text{C}$ )	Permitted tolerance
up to 25 g/l	$\pm 15\%$ of the declared content
above 25 g/l up to 100 g/l	$\pm 10\%$ 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: <http://www.who.int/whopes/quality/en/>.

### 3 Physical properties

#### 3.1 pH range (1% aqueous dispersion) (MT 75)

pH range: 6.0 to 8.0.

#### 3.2 Emulsion stability and re-emulsification (MT 36.1) (Notes 3 and 4)

The formulation, when diluted at  $30 \pm 2^\circ\text{C}$  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 47.2)

There shall be a maximum of 15 ml after 1 minute.

### 4 Storage stability

#### 4.1 Stability at $0^\circ\text{C}$ (MT 39.1)

After storage at  $0 \pm 2^\circ\text{C}$  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 46.3)

After storage at  $54 \pm 2^\circ\text{C}$  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  $38^\circ\text{C}$  (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  $20 \pm 2^\circ\text{C}$  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 This test will normally only be carried out after the heat stability test, 4.2.

Note 4 Field dilution rates include concentrations below 5% but the MT 36.1 test has been shown to be indicative of performance over the recommended range of dilutions.

Note 5 Samples taken before and after this test should be analyzed concurrently to reduce analytical error.

# WHO SPECIFICATIONS FOR PUBLIC HEALTH PESTICIDES

## LAMBDA-CYHALOTHRIN WETTABLE POWDER

WHO Specification 463/WP (2003<sup>\*</sup>)

*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). It 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), as PART TWO, form an integral part of this publication.*

### 1 Description

The material shall consist of an homogeneous mixture of technical lambda-cyhalothrin, complying with the requirements of WHO specification 463/TC (2003), 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.

Where the material is packaged in sealed water soluble bags (Note 1), the material shall consist of a defined quantity of a lambda-cyhalothrin wettable powder, complying with the requirements of WHO specification 463/WP, contained in a sealed water soluble bag.

### 2 Active ingredient

#### 2.1 Identity tests (CIPAC 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 (CIPAC 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
<u>Note:</u> 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: <http://www.who.int/whopes/quality/en/>.

### 3 Physical properties

#### 3.1 pH range (MT 75.2)

pH range: 5.5 to 9.0.

#### 3.2 Wet sieve test (MT 59.3)

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

#### 3.3 Suspensibility (MT 184) (Notes 2 and 3)

A minimum of 50 % of the lambda-cyhalothrin content found under 2.2 shall be in suspension after 30 min in CIPAC Standard Water D at  $30 \pm 2^\circ\text{C}$  (Note 4).

In the case of water soluble bag packaging, the provisions of clause 5.2 should be applied.

#### 3.4 Persistent foam (MT 47.2) (Note 5)

Maximum: 60ml after 1 min.

In the case of water soluble bag packaging, the provisions of clause 5.3 should be applied.

#### 3.5 Wettability (MT 53.3)

The formulation shall be completely wetted in 1 min, without swirling.

### 4 Storage stability

#### 4.1 Stability at elevated temperature (MT 46.3)

After storage at  $54 \pm 2^\circ\text{C}$  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 6) 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).

In the case of water soluble bag packaging, the package should be enclosed in a watertight sachet, box or any other container, at  $30^\circ\text{C}$  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 6) and the formulation shall continue to comply with the clauses for:

- pH range (3.1);
- wet sieve test (3.2);
- dissolution of the bag (5.1);
- suspensibility (5.2);
- persistent foam (5.3).

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

## 5 **Material packaged in a sealed water soluble bag** (Note 7)

### 5.1 **Dissolution of the bag** (MT 176) (Note 8)

The dissolution of the bag shall be tested on a sample of the emptied and cleaned bag taken according to the procedure described in Note 8, together with an appropriate proportion of the WP.

Flow time of the suspension: maximum 30 sec.

### 5.2 **Suspensibility** (MT 184) (Notes 2 and 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 9.

A minimum of 50% shall be in suspension after 30 min in CIPAC Standard Water D at  $30 \pm 2^\circ\text{C}$  (Note 4).

### 5.3 **Persistent foam** (MT 47.2) (Note 5)

The persistent foam shall be tested on a suspension containing the WP and the bag in the actual ratio of application, prepared according to the procedure described in Note 9.

Maximum: 60ml after 1 min.

---

Note 1 For record keeping purposes, the suffix "SB" should be added to the formulation code (WP-SB).

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.

Note 3 This test will normally only be carried out after the heat stability test 4.1.

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 chemical assay. In case of dispute, chemical assay shall be the "referee method".

Note 5 The mass of sample to be used in the test should be at the highest rate of use recommended by the supplier.

Note 6 Samples of the formulation taken before and after the storage stability test should be analyzed concurrently after the test in order to reduce the analytical error.

Note 7 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);
- wet sieve test (3.2);
- wettability (3.5);
- dissolution of the bag (5.1);
- suspensibility (5.2);
- persistent foam (5.3).

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. It shall be used to carry out the dissolution test (5.1). Aliquots of an aqueous solution of the bag material shall be used in the suspensibility (5.2) and persistent foam (5.3) 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 8** 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 9** The procedure for adding the bag material to the solution for the suspensibility and the persistent foam tests should be as follows:

Prepare a stock solution of the bag material (1 mg/ml) by weighing approximately a 100 mg sample ( $\underline{n}$  mg) of the bag (excluding sealed parts) to the nearest mg. Dissolve this sample by stirring in the standard water used for the tests to give a final volume of  $\underline{n}$  ml. Store the stock solution in a stoppered bottle before use.

Calculate the volume ( $\underline{V}$  ml) of the stock solution of the bag to be added to the test suspension of the wettable powder 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.

# WHO SPECIFICATIONS FOR PUBLIC HEALTH PESTICIDES

## LAMBDA-CYHALOTHRIN SLOW-RELEASE CAPSULE SUSPENSION

(slow-release CS) (Note 1)

WHO Specification 463/CS (2011\*)

*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). It 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 (2003), 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  $20 \pm 2^\circ\text{C}$ ) (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 $20 \pm 2^\circ\text{C}$ )	Permitted tolerance
up to 25 g/l	$\pm 15\%$ of the declared content
above 25 up to 100**	$\pm 10\%$ 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: <http://www.who.int/whopes/quality/en/>.

\*\* 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  $30 \pm 2^\circ\text{C}$ .

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  $30 \pm 2^\circ\text{C}$ .

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  $\mu\text{m}$  test sieve.

3.6 **Persistent Foam** (MT 47.2, CIPAC Handbook F, p.152, 1995) (Note 5)

Maximum: 5 ml after 1 min.

### 4 Storage stability

4.1 **Freeze/thaw stability** (Note 6)

After undergoing 4 freeze/thaw cycles (between  $20 \pm 2^\circ\text{C}$  and  $-3 \pm 2^\circ\text{C}$  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  $54 \pm 2^\circ\text{C}$  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 7) 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:

- $D_{(10)}$ ,  $>1 \mu\text{m}$ ;
- $D_{(50)}$ , 7 to  $12 \mu\text{m}$ ;
- $D_{(90)}$ ,  $<50 \mu\text{m}$ .

**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 of 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  $20 \pm 2^\circ\text{C}$ , 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 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.

Note 6 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  $-5^{\circ}\text{C}$ .

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

## PART TWO

### EVALUATION REPORTS

---

#### LAMBDA-CYHALOTHRIN

	Page
<b>2011</b> <b>FAO/WHO evaluation report</b> based on submission of data from Tagros (slow-release CS)	<b>20</b>
<b>Supporting information</b>	<b>21</b>
<b>Annex 1: References</b>	<b>24</b>
<b>2006</b> <b>FAO/WHO evaluation report</b> based on submission of data from Tagros (TC, EC, WP)	<b>25</b>
<b>Supporting information</b>	<b>27</b>
<b>Annex 1: Hazard summary provided by the proposer</b>	<b>29</b>
<b>Annex 2: References</b>	<b>31</b>
<b>2003</b> <b>FAO/WHO evaluation report</b> based on submission of data from Syngenta, UK (TC, EC, WP, WG, slow-release CS, rapid-release CS).	<b>32</b>
<b>2000</b> <b>FAO evaluation report</b> based on submission of data from Zeneca Agrochemicals, UK (rapid-release CS).	<b>36</b>
<b>1999</b> <b>FAO evaluation report</b> based on submission of data from Zeneca Agrochemicals, UK (TC, EC, WG).	<b>39</b>

# WHO SPECIFICATIONS FOR PUBLIC HEALTH PESTICIDES

## LAMBDA-CYHALOTHRIN

### FAO/WHO EVALUATION REPORT 463/2011

#### **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.

# WHO SPECIFICATIONS FOR PUBLIC HEALTH PESTICIDES

## LAMBDA-CYHALOTHRIN

### FAO/WHO EVALUATION REPORT 463/2006

#### 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  $\geq 1$  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 x 10 <sup>-7</sup> Pa at 20°C 3.65 x 10 <sup>-5</sup> 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 <sub>50</sub> = 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 <sub>50</sub> = 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 <sub>50</sub> >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 <sub>50</sub> = 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.

# WHO SPECIFICATIONS FOR PUBLIC HEALTH PESTICIDES

## 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, 5<sup>th</sup> 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, 1<sup>st</sup> 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.
-

# WHO SPECIFICATIONS FOR PUBLIC HEALTH PESTICIDES

## 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<sup>1</sup>. 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<sup>2</sup>: 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.

---

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

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

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.

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 meaningful 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.

---

# WHO SPECIFICATIONS FOR PUBLIC HEALTH PESTICIDES

## FAO EVALUATION REPORT 463/1999

### LAMBDA-CYHALOTHRIN

#### 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

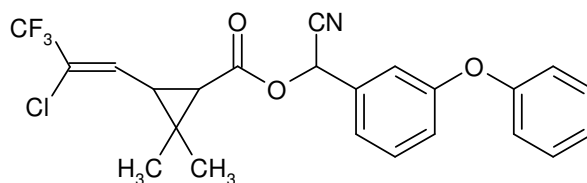
IUPAC: alpha-cyano-3-phenoxybenzyl 3-(2-chloro-3,3,3-trifluoroprop-1-enyl)-2,2-dimethylcyclopropane carboxylate, a 1:1 mixture of the (Z)-(1R,3R),S-ester and the (Z)-(1S,3S),R-ester

CA: [1- $\alpha$ (S<sup>\*</sup>),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:	$2 \times 10^{-10}$ 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:	$4 \times 10^{-3}$ mg/l at pH 5.0 $5 \times 10^{-3}$ mg/l at pH 6.5 $4 \times 10^{-3}$ mg/l at pH 9.2 (purity 96.5%). Method: EECA6.
Octanol/water partition coefficient:	Log $P_{ow}$ = 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 $\geq 95\%$ ). Method: EPA CG5000.

## Physical and chemical properties of pure lambda-cyhalothrin

Parameter	Value(s), method(s), conditions and purity
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

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

Species	Test	Result
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
<i>In vitro</i> studies				
Bacterial mutation assay	<i>Salmonella typhimurium</i> 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
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
<i>In vivo</i> 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
<i>Daphnia magna</i> (water flea)	48 h immobilization,	EC <sub>50</sub> 0.36 µg/l
<i>Oncorhynchus mykiss</i> (rainbow trout)	96 h mortality	LC <sub>50</sub> 0.24 µg/l
<i>Lepomis macrochirus</i> (bluegill sunfish)	96 h mortality	LC <sub>50</sub> 0.21 µg/l
<i>Selenastrum capricornutum</i> (green alga) (Note 1)	96 h growth	EC <sub>50</sub> >1000 µg/l
<i>Daphnia magna</i> (water flea)	21 d reproduction	NOEC 0.002 µg/l
<i>Cyprinodon variegatus</i> (sheepshead minnow)	28 d early life-stage.	NOEC 0.25 µg/l

**Table 4. Ecotoxicological profile of the technical material**

Species	Test type, duration, concentrations, etc.	Result
Mallard duck	Acute oral, 0, 739, 1040, 1620, 2580, 3950 mg a.i./kg bw	Acute Oral LD <sub>50</sub> , 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
Bee (note 2)	24 h contact toxicity	mean LD <sub>50</sub> 0.051 µg a.i./bee
Bee (note 2)	48 h contact toxicity	mean LD <sub>50</sub> 0.038 µg a.i./bee
Bee (note 2)	24 h oral toxicity	mean LD <sub>50</sub> 0.965 µg a.i./bee
Bee (note 2)	48 h oral toxicity	mean LD <sub>50</sub> 0.909 µg a.i./bee

*Note 1.* The 96-hour E<sub>r</sub>C<sub>50</sub> and E<sub>b</sub>C<sub>50</sub> 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<sub>r</sub>C<sub>50</sub> 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 ( $\pm 2.5\%$ ) 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 than 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.

## References

- CIPAC 1992 Martijn A. and Dobrat W., Eds, CIPAC Handbook E, Lambda-cyhalothrin 463, pp 49-57.
- CIPAC 1995 Dobrat W and Martijn A, Eds, CIPAC Handbook F.
- Codex 1997 Procedural manual of the Codex Alimentarius Commission, 10<sup>th</sup> ed. p. 57. FAO Rome.
- Codex 1999 Codex Alimentarius, volume 2, 3<sup>rd</sup> edition, Cyhalothrin 146, Pesticide Residues in Food, FAO Rome.
- FAO 1994 Manual on the development and use of FAO specifications for plant protection products, 4<sup>th</sup> edition, FAO Plant production and protection paper 128, FAO, Rome.
- FAO 1999 Manual on the development and use of FAO specifications for plant protection products, 5<sup>th</sup> edition, FAO Plant production and protection paper 149, FAO, Rome.
- JMPR 1984 Report of the FAO/WHO Joint Meeting on Pesticide Residues on Cyhalothrin, 1984. FAO Plant Production and Protection Paper Nos: 62 (pp. 30-32) and 67 (pp. 173-185).
- JMPR 1986 Report of the FAO/WHO Joint Meeting on Pesticide Residues on Cyhalothrin, 1986. FAO Plant Production and Protection Paper No: 78 (pp. 95-138).
- JMPR 1988 Report of the FAO/WHO Joint Meeting on Pesticide Residues on Cyhalothrin, 1988. FAO Plant Production and Protection Paper No: 93/1 (p. 57).
- WHO 1990A 'Cyhalothrin' Environmental Health Criteria 99, International Programme on Chemical Safety. World Health Organization, Geneva 1990 (ISBN 92 4 154299 3).
- WHO 1990B 'Cyhalothrin and Lambda-cyhalothrin Health and Safety Guide' Health and Safety Guide No. 38, International Programme on Chemical Safety. World Health Organization, Geneva 1990 (ISBN 92 4 151038 2).

- WHO 1997 'Interim specifications for pesticides used in public health' WHO/CTD/WHOPES/97.7, WHO, Geneva.
- WHO 1998 IPCS, the WHO recommended classification of pesticides by hazard and guidelines to classification 1998-1999. WHO/PCS/98.21/Rev.1. p. 20, entry no. II160. WHO, Geneva.
-