FAO SPECIFICATIONS AND EVALUATIONS FOR AGRICULTURAL PESTICIDES

LAMBDA-CYHALOTHRIN

A reaction product comprising equal quantities of

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

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

FOOD AND AGRICULTURE ORGANIZATION *of* THE UNITED NATIONS

TABLE OF CONTENTS

DISCLAIMER[1]

FAO 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.

FAO disclaims any and all liability for any injury, death, loss, damage or other prejudice of any kind that may 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, FAO 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.

FAO 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, FAO does not in any way warrant or represent that any pesticide claimed to comply with a FAO specification actually does so.

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

INTRODUCTION

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

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

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

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

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

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

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

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

PART ONE

SPECIFICATIONS

LAMBDA-CYHALOTHRIN

LAMBDA-CYHALOTHRIN

INFORMATION

ISO common names:

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

Synonyms:

none

Chemical names:

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

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

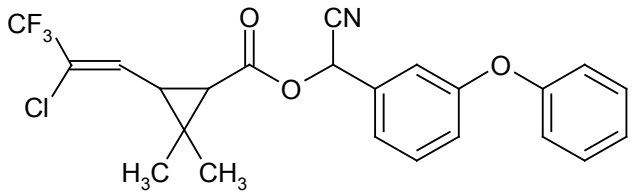
CAS No:

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.

LAMBDA-CYHALOTHRIN TECHNICAL MATERIAL

FAO Specification 463/TC (January 2013*)

*This specification, which is PART ONE of this publication, is based on an evaluation of data submitted by the manufacturers whose names are listed in the evaluation reports (*463/2003, 463/2006, 463/2012*). 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 specification. The specification may not be appropriate for TC produced by other manufacturers. The evaluation reports (*463/2003, 463/2006, 463/2012*), 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** (463/TC/M/2, CIPAC Handbook E, p.50, 1992)

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

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

The lambda-cyhalothrin content shall be declared (not less than 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_2SO_4.

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.fao.org/agriculture/crops/core-themes/theme/pests/jmps/ps-new/en/

LAMBDA-CYHALOTHRIN EMULSIFIABLE CONCENTRATE

FAO Specification 463/EC (January 2013*)

*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 sources. The specification is not an endorsement of those products, nor a guarantee that they comply with the specification. The specification may not be appropriate for the products of other manufacturers who use TC from other sources. The evaluation reports (*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 FAO specification 463/TC (January 2013), dissolved in suitable solvents (Note 1) together with any other necessary formulants. It shall be in the form of a clear to slightly hazy, stable homogeneous liquid, free from visible suspended matter and sediment, to be applied as an emulsion after dilution with water.

2 Active ingredient

2.1 **Identity tests** (463/EC/M/2, CIPAC Handbook E, p. 56, 1992)

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

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

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

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

3 Physical properties

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

pH range: 6.0 to 8.0.

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

3.2 **Emulsion stability and re-emulsification** (MT 36.3, CIPAC Handbook K, p.137, 2003) (Notes 3 and 4)

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

Time after dilution	Limits of stability
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, CIPAC Handbook F, p.152, 1995) (Note 5)

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

4 Storage stability

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

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

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

After storage at 54 ± 2°C for 14 days, the determined average active ingredient content shall not be lower than 95%, relative to the determined average content found under 2.2 before storage (Note 6), and the formulation shall continue to comply with the clauses for:

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

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

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

Note 3 This test will normally only be carried out after the heat stability test, 4.2.

Note 4 As outlined in CIPAC MT 36.3, the test concentrations should be based on those in the recommended directions for use supplied with the product. Where several concentrations are recommended, the highest and lowest concentrations within the scope of the method should be used.

Note 5 The mass of sample to be used in the test should correspond to the highest rate of use recommended by the supplier. The test is to be conducted in CIPAC standard water D.

Note 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.

LAMBDA-CYHALOTHRIN WATER DISPERSIBLE GRANULES

FAO Specification 463/WG (January 2013*)

*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 sources. The specification is not an endorsement of those products, nor a guarantee that they comply with the specification. The specification may not be appropriate for the products of other manufacturers who use TC from other sources. The evaluation reports (*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 FAO specification 463/TC (January 2013), together with carriers and any other necessary formulants. It shall be in the form of granules (Note 1) for application after disintegration and dispersion in water. The product shall be dry, free-flowing and free from visible extraneous matter and hard lumps.

2 Active ingredient

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

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

2.2 Lambda-cyhalothrin content (463/WP/M/3, CIPAC Handbook E, p.54, 1992) (Note 2)

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 amounts:

Declared content, g/kg	Permitted tolerance
up to 25 g/kg	± 25% of the declared content
above 25 g/kg up to 100 g/kg	± 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.fao.org/agriculture/crops/core-themes/theme/pests/jmps/ps-new/en/

3 Physical properties

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

pH range: 6.0 to 8.5.

3.2 **Wettability** (MT 53.3, CIPAC Handbook F, p.164, 1995)

The formulation shall be completely wetted in 5 seconds without swirling.

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

A maximum of 0.5 % w/w shall be retained on a 75 μm test sieve.

3.4 **Degree of dispersion** (MT 174, CIPAC Handbook F, p.435, 1995)

The minimum dispersibility shall be 70% after 1 minute of stirring.

3.5 **Suspensibility** (MT 184, CIPAC Handbook K, p.142, 2003) (Notes 3, 4 and 5)

A minimum of 50% of the lambda-cyhalothrin content found under 2.2 shall be in suspension after 30 minutes in CIPAC standard water D at 30 ± 2°C.

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

There shall be a maximum of 10 ml after 1 minute.

3.7 **Dustiness** (MT 171, CIPAC Handbook F, p.425, 1995) (Note 6)

The formulation shall be essentially non-dusty.

3.8 **Flowability** (MT 172.1, CIPAC Handbook F, p.430, 1995)

At least 98% of the formulation shall pass through a 5 mm test sieve after 20 drops of the sieve.

4 Storage stability

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

After storage at 54 ± 2°C for 14 days, the determined average active ingredient content shall not be lower than 95%, relative to the determined average content found under 2.2 before storage (Note 7), and the material shall continue to comply with the clauses for:

- pH range (3.1);
- wet sieve test (3.3);
- degree of dispersion (3.4);
- suspensibility (3.5);
- dustiness (3.7).

Note 1 Granules cylindrical, with a nominal diameter of 0.6 mm and varying in length from 2 to 6 mm.

Note 2 The collaboratively tested method for analysis of wettable powders (WP) is also applicable to water dispersible granules (WG). It is, however, recommended that samples be ground to a powder prior to analysis.

Note 3 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 4 Sample preparation should be carried out using MT 166. Quantitative determination of the sediment produced by MT 184 should be by chemical assay, using the capillary GC procedure described in CIPAC Handbook E, pp. 55–56 (1992).

Note 5 Chemical assay is the only fully reliable method to measure the mass of active ingredient still in suspension. In case of dispute, chemical assay shall be the "referee method".

Note 6 Measurement of dustiness must be carried out on the sample "as received" and, where practicable, the sample should be taken from a newly opened container, because changes in the water content of samples may influence dustiness significantly. The optical method, MT 171.2, usually shows good correlation with the gravimetric method, MT 171.1, and can, therefore, be used as an alternative where the equipment is available. Where the correlation is in doubt, it must be checked with the formulation to be tested. In case of dispute the gravimetric method shall be used.

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.

LAMBDA-CYHALOTHRIN RAPID-RELEASE CAPSULE SUSPENSIONS

(rapid-release CS) (Note 1)

FAO Specification 463/CS (January 2013*)

*This specification, which is PART ONE of this publication, is based on an evaluation of data submitted by the manufacturer whose name is listed in the evaluation report (*463/2003*). It should be applicable to relevant products of this manufacturer 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 report (*463/2003*), 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 FAO specification 463/TC (January 2013), in an aqueous phase, together with suitable formulants. After agitation, the material shall be homogeneous (Note 2) and suitable for further dilution in water.

2 Active ingredient

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

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

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

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

Declared content (g/l at 20 ± 2°C)	Permitted tolerance
up to 25 g/l	± 15% of the declared content
above 25 g/l up to 100 g/l	± 10% of the declared content
above 100 g/l up to 250 g/l	± 6% of the declared content
Note: In each range the upper limit is included.	

3 Physical properties

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

pH range: 4.0 to 6.0.

---

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

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

Maximum "residue": 1.5%.

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

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

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

A minimum of 80% of the lambda-cyhalothrin content found under 2.2 shall be in suspension after 30 minutes in CIPAC standard water D at 30°C ± 2° C.

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

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

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

There shall be a maximum of 2 ml after 1 minute.

4 Storage stability

4.1 **Freeze/thaw stability** (Note 5)

After undergoing 4 freeze/thaw cycles, and following homogenization, the formulation shall continue to comply with the clauses for:

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

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

After storage at 54 ± 2°C for 14 days the determined average active ingredient content must not be lower than 95%, relative to the determined average content found before storage (Note 6), and the material shall continue to comply with the clauses for:

- total active ingredient content (2.2);
- 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 rapid-release capsule suspension formulations, intended for foliar application in agriculture. Measurement of particle size distribution permits this type of product to be differentiated rapidly from the lambda-cyhalothrin slow-release CS products used in public health. Using CIPAC MT 187 (CIPAC Handbook K, 2003), the following criteria should be met by the rapid-release CS, intended for agricultural applications:

$D_{(10)}$, >0.25 µm;
$D_{(50)}$, 1.0 to 3 µm;
$D_{(90)}$, <8 µm.

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

Before sampling to verify formulation quality, the commercial container must be inspected carefully. On standing, suspensions usually develop a concentration gradient from the top to the bottom of the container. This may even result in the appearance of a clear liquid on the top and/or 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 ± 2°C, the actual mass per millilitre shall be determined and used in the calculation, using MT 3.3. Where doubt remains or in cases of dispute, the content should be expressed as g/kg. Unless homogenization is carried out carefully, it is possible for the sample to become aerated. This can lead to errors in the determination of the mass per millilitre and thereby in the determination of the active ingredient content (g/l), if methods other than MT 3.3 are used.

Note 4 Chemical assay is the only fully reliable method to measure the mass of active ingredient still in suspension. However, simpler methods such as gravimetric and solvent-extraction determination may be used on a routine basis provided that these methods have been shown to give equal results to those of the chemical assay method. In cases of dispute, the chemical method shall be the “Referee method”.

Note 5 This test applies only to freeze-protected formulations. Non-protected products will carry a label warning to protect from freezing temperatures. The test shall cycle the formulation between room temperature (e.g. 20 ± 2°C) and –10 ± 2°C. The cycles shall be 18-hour freeze, 6-hour melt.

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.

PART TWO

EVALUATION REPORTS

LAMBDA-CYHALOTHRIN

LAMBDA-CYHALOTHRIN

FAO/WHO EVALUATION REPORT 463/2012

Recommendations

The Meeting recommended that:

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

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

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

Appraisal

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

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

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

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

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

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

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

Bharat Rasayan Limited produces lambda-cyhalothrin TC at two manufacturing sites, but has provided the 5-batch analysis data for only one manufacturing site. The manufacturer did not submit data for the other manufacturing site and confirmed

that purity/impurities profile is similar for the both production sites, and this was considered acceptable by the Meeting.

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

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

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

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

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

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

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

SUPPORTING INFORMATION

FOR

EVALUATION REPORT 463/2012

Physico-chemical properties of lambda-cyhalothrin

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

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

Table 2. Chemical composition and properties of lambda-cyhalothrin technical material (TC)

Manufacturing process, maximum limits for impurities ≥ 1 g/kg, 5 batch analysis data	Confidential information supplied and held on file by FAO and WHO. Mass balances were 99.81–99.85%. Percentage of unknowns were 0.15-0.20%.
Declared minimum lambda-cyhalothrin content	965 g/kg
Relevant impurities ≥ 1 g/kg and maximum limits for them	None
Relevant impurities **<** 1 g/kg and maximum limits for them	None
Stabilizers or other additives and maximum limits for them	None

Background information on toxicology / ecotoxicology

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

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

It is used in agriculture and for public health use.

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

Methods of analysis and testing

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

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

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

Containers and packaging

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

Expression of the active ingredient

The active ingredient content is expressed as lambda-cyhalothrin, in g/kg.

ANNEX 1

HAZARD SUMMARY PROVIDED BY THE PROPOSER

Note:

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

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

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

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

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

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

ANNEX 2. REFERENCES

Author and year or study number	Study title. Study identification number. Report identification number. Company conducting the study.
Bharat Rasayan Limited, 10/2010	FAO/WHO Specifications for Pesticides – Proposers (Bharat Rasayan Limited) template with (i) Manufacturing Process and 5 batch analysis (Confidential) & (ii) specifications including physico-chemical properties, toxicological summaries & references (Non-confidential).
Bharat Rasayan Limited, 8/2011	FAO/WHO Specifications for Pesticides – Proposers (Bharat Rasayan Limited) template with (i) updated Manufacturing Process and (ii) Impurity profile of Key Starting Materials.
Bharat Rasayan Limited, 8/2011	FAO/WHO Specifications for Pesticides – Proposers (Bharat Rasayan Limited) 5 batch analysis using CIPAC methods of analysis.
Government of India, 19/04/2005	Certificate of Registration for Lambda-cyhalothrin Technical for indigenous manufacture Government of India, Ministry of Agriculture, provided for comparison of manufacturing process & DoC.
Bharat Rasayan Limited, 8/2011	Bharat Rasayan Letter of Access for DoC.
Bharat Rasayan Limited, 10/2010	Method of Analysis of the composition (Lambda-cyhalothrin content) of Bharat Rasayan TC by GCMS.
CIPAC 1992	CIPAC Handbook E - Analysis of Technical and Formulated Pesticides Lambda-cyhalothrin 463/TC pages 49-57.
JRF Study number 227-2-12-0971	Preliminary Analyses of five representative production batches of Lambda-cyhalothrin Technical Grade Active Ingredient (TGAI) to determine % Lambda-cyhalothrin and to quantify its associated impurities. Jai Research Foundation (JRF). Guideline U.S.EPA OPPTS 830.1700, 830.1800.
JRF Study number 10200	Validation of Analytical Method for active ingredient analysis of Lambda-cyhalothrin Technical. Test Facility Jai Research Foundation (JRF) Guideline U.S.EPA OPPTS 830.1800.
JRF Study number 10194	Appearance, colour report. Test Facility Jai Research Foundation (JRF) Guideline U.S.EPA OPPTS 830.1800, 830.6302, 6303, 6304.
JRF Study number 10197	Vapour pressure of Lambda-cyhalothrin Technical. Jai Research Foundation (JRF) Guideline: EC A.4, OECD 104, U.S. EPAOPPTS 830.7950.
JRF Study number 10199	Melting point/Melting range of Lambda-cyhalothrin Technical. Test Facility Jai Research Foundation (JRF). Guideline: U.S. EPA OPPTS 830.7200.
JRF Study number 10195	Water solubility of Lambda-cyhalothrin Technical. Jai Research Foundation (JRF). Guideline: EEC A.6, OECD No. 105 and U.S.EPA OPPTS 830.7840.
JRF Study number 10198	Partition co-efficient of Lambda-cyhalothrin Technical by HPLC Method. Jai Research Foundation (JRF). Guideline: U.S. EPA OPPTS 830.7570, OECD 117.
JRF Study number 10196	Solubility of Lambda-cyhalothrin Technical in organic solvents. Jai Research Foundation (JRF) Guideline: CIPAC MT 181.
Report number 000122145	Acute Oral toxicity study in rats with Lambda-cyhalothrin technical. Project no. TOX/438. Guideline: OECD 423 (section 4).
Report number 000122145	Acute Dermal toxicity study in rats with Lambda-cyhalothrin technical. Project no. TOX/438. Guideline: OECD 402 (section 4).
Report number 000122145	Acute Inhalation toxicity study in rats with Lambda-cyhalothrin technical Project no. TOX/438. Guideline: OECD 403 (section 4).
Report number 000122145	Acute Dermal Irritation in rabbits with Lambda-cyhalothrin technical. Project no. TOX/438. Guideline: OECD 404 (section 4).

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

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 ≥1 g/kg. Mass balances in the 5-batch data were very high (99.5-99.8%). The confidential data were confirmed as sufficiently similar to those supporting registration of Tagros lambda-cyhalothrin in India to conclude that the national evaluations should be applicable to the profile submitted to WHO.

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

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

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

SUPPORTING INFORMATION

FOR

EVALUATION REPORT 463/2006

Physico-chemical properties of Tagros lambda-cyhalothrin

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

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

Table 2. Chemical composition and properties of Tagros technical lambda-cyhalothrin (TC)

Manufacturing process, maximum limits for impurities ≥ 1 g/kg, 5 batch analysis data	Confidential information supplied and held on file by FAO and WHO. Mass balances were 99.44–99.82%, with 11.86-12.29% impurities (including other cyhalothrin isomers) and no unknowns >1 g/kg.
Declared minimum lambda-cyhalothrin content	840 g/kg
Relevant impurities ≥ 1 g/kg and maximum limits for them	None
Relevant impurities < 1 g/kg and maximum limits for them	None
Stabilizers or other additives and maximum limits for them	None

Formulations

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

Methods of analysis and testing

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

ANNEX 1

HAZARD SUMMARY PROVIDED BY THE PROPOSER

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

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

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

ANNEX 2. REFERENCES

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

LAMBDA-CYHALOTHRIN

FAO/WHO EVALUATION REPORT 463/2003

Explanation

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

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

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, 1997 and 2001).

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

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

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

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

Other than minor editorial amendments and changes to the notes (as mentioned for the TC), the meeting agreed that no other changes were necessary.

The 1999 WHO specification for the EC included a clause for water content, with a limit of 0.5 g/kg. Originally, the proposer had requested a clause to limit water in the 1999 FAO specification for EC of 5 g/kg, although this was subsequently withdrawn because, at that concentration, the formulation would no longer comply with the description clause which specifies"….a clear to slightly hazy, stable homogeneous liquid, free from visible suspended matter and sediment….". The proposer confirmed that an appropriate limit would be 5 g/kg but agreed that, because the formulation would not comply with the description clause at this concentration, a separate clause (and test) is not necessary. The 1999 WHO specification for the EC included a clause for acidity or alkalinity, whereas the corresponding clause in the 1999 FAO specification is for pH range. The proposer agreed that a clause for pH range should be adopted for the WHO specification. The 1999 WHO specification for the EC included a clause for flash point, whereas in the 1999 FAO specification this appears as a note. The meeting agreed that the WHO specification should be amended accordingly. The clause for heat stability test in the 1999 WHO specification for the EC made no allowance for any loss of active ingredient. This contrasted with the 1999 FAO specification for EC, which permits a loss of up to 5%. The proposer agreed that the WHO specification should be amended accordingly. With these amendments, the existing WHO specification for EC is harmonized with that of the FAO specification.

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

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

Users must be able to distinguish immediately between the FAO and WHO specifications for CS and understand the different purposes for which the two products are intended. The meeting was informed by CropLife International that standard codes are not available to distinguish CS formulations with differing release characteristics because, although the present case of lambda-cyhalothrin provides

clear-cut extremes, there are other (unrelated) products with either intermediate or mixed characteristics. The meeting therefore concluded that the titles of CS formulation specifications should be decided on a case-by-case basis. In the present case, meeting agreed that the FAO specification should be entitled "Lambda-cyhalothrin rapid-release capsule suspension (rapid-release CS)" and the WHO specification should be entitled "Lambda-cyhalothrin slow-release capsule suspension (slow-release CS)".

Recommendations

The Meeting recommended that:

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

References

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

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

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

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

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

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

WHO 2001 World Health Organization, 2001. Report of the 4th WHOPES Working Group meeting - IR3535, KBR3023, (RS)-methoprene 20% EC, pyriproxyfen 0.5% GR and lambda-cyhalothrin 2.5% CS, 4-5 December 2000, Geneva, doc. WHO/CDS/WHOPES/2001.2.

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

LAMBDA-CYHALOTHRIN

FAO EVALUATION REPORT 463/2000

Explanation

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

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

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

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

Formulations

CS formulations are registered in USA and Argentina.

Methods of analysis and testing

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

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

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

---

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

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

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

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

Appraisal

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

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

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

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

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

Recommendations

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

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

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

LAMBDA-CYHALOTHRIN

FAO EVALUATION REPORT 463/1999

Explanation

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

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

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

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

Uses

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

Identity

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

Synonyms: none

Chemical names

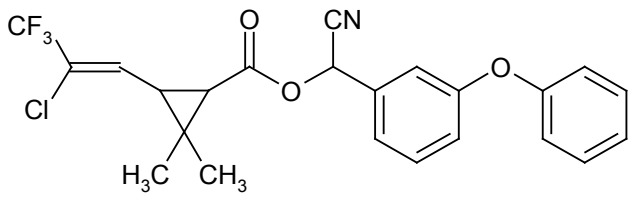
IUPAC: alpha-cyano-3-phenoxybenzyl 3-(2-chloro-3,3,3-trifluoroprop-1-enyl)-2,2-dimethylcyclopropane carboxylate, a 1:1 mixture of the (Z)-(1R,3R),S-ester and the (Z)-(1S,3S),R-ester

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

CAS No: 91465-08-6

CIPAC No: 463

Structural formula:



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

Relative molecular mass: 449.9

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

Physical and chemical properties of lambda-cyhalothrin

Physical and chemical properties of pure lambda-cyhalothrin

Parameter	Value(s), method(s), conditions and purity
Vapour pressure:	2×10^{-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:	4×10^{-3} mg/l at pH 5.0 5×10^{-3} mg/l at pH 6.5 4×10^{-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.
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 $\geq$ 95%). Method: EPA CG6000.

Chemical composition of the technical material (TC)

Manufacturing process, maximum limits for impurities ≥ 1 g/kg, 5 batch analysis data.	Confidential information supplied and held on file by FAO. Mass balances were 97.5 to 98.1%, with 10.5 to 11.7% impurities (including other cyhalothrin isomers) and with <0.1 to 0.5% present as unknowns.
Declared minimum lambda-cyhalothrin content:	810 g/kg.
Total alpha-cyano-3-phenoxybenzyl-3-(2-chloro-3,3,3-trifluoropropenyl)-2,2-dimethylcyclopropanecarboxylate minimum content, as lambda-cyhalothrin and other diastereoisomers:	900 g/kg.
Relevant impurities ≥ 1 g/kg and maximum limits for them:	none.
Relevant impurities **<** 1 g/kg and maximum limits for them:	none.
Stabilisers or other additives, and maximum limits for them:	none.

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

Hazard summary

Notes.

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

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

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

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

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

In the rat, lambda-cyhalothrin is less toxic by the dermal route but is highly toxic by inhalation. WHO (WHO 1990B) considered only the potential for irritation of the upper respiratory tract by inhalation of fine dust or mist, and the potential for chemical pneumonitis resulting from aspiration into the lungs of the solvent used for liquid formulations, not the inhalation toxicity of lambda-cyhalothrin itself. WHO (WHO 1990B) concluded that lambda-cyhalothrin is a mild irritant to the rabbit eye and skin. It is not a skin sensitizer in the guinea pig.

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

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

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

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

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

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

Test system	Target cells	Concentration	Purity	Results
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
In vivo studies				
Mouse bone marrow micronucleus assay	Mouse bone marrow	22 and 35 mg/kg (single dose)	96.5% w/w	Negative

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

Table 4. Ecotoxicological profile of the technical material

Species	Test type, duration, concentrations, etc.	Result
Daphnia magna (water flea)	48 h immobilization,	EC_{50} 0.36 µg/l
Oncorhynchus mykiss (rainbow trout)	96 h mortality	LC_{50} 0.24 µg/l
Lepomis macrochirus (bluegill sunfish)	96 h mortality	LC_{50} 0.21 µg/l
Selenastrum capricornutum (green alga) (*Note 1)*	96 h growth	EC_{50} >1000 µg/l
Daphnia magna (water flea)	21 d reproduction	NOEC 0.002 µg/l
Cyprinodon variegatus (sheepshead minnow)	28 d early life-stage.	NOEC 0.25 µg/l
Mallard duck	Acute oral, 0, 739, 1040, 1620, 2580, 3950 mg a.i./kg bw	Acute Oral LD_{50}, lowest lethal dose (LLD) and NOEL all >3950 mg/kg bw
Bobwhite quail	Sub-acute oral toxicity, 0, 500, 1000, 2000, 4000 and 5000 mg a.i./kg diet	Dietary LC50 >5300 mg/kg diet. LLC = 577 mg/kg diet
Mallard duck	Sub-acute oral toxicity, 0, 500, 1000, 2000, 3000, 4000 and 5000 mg a.i./kg diet	Dietary LC50 = 3948 mg/kg diet
Mallard duck	Reproduction, 0, 0.5, 5.0, 15 and 30 mg a.i./kg diet	Reproductive NOEL = 30 mg/kg diet for 20 weeks
Bee (note 2)	24 h contact toxicity	mean LD_{50} 0.051 µg a.i./bee
Bee (note 2)	48 h contact toxicity	mean LD_{50} 0.038 µg a.i./bee
Bee (note 2)	24 h oral toxicity	mean LD_{50} 0.965 µg a.i./bee
Bee (note 2)	48 h oral toxicity	mean LD_{50} 0.909 µg a.i./bee

Note 1. The 96-hour E_rC_{50} and E_bC_{50} of lambda-cyhalothrin to the green alga (*Selenastrum capricornutum*) are both greater than 1.0 mg/litre, the 96-hour NOEC was 1.0 mg/litre. In a different study, assessing the effect of a 5% w/v EC formulation of lambda-cyhalothrin on the green alga

(*Selenastrum capricornutum*), the 96-hour E_rC_{50} was calculated to be 31 mg formulation (1.6 mg lambda-cyhalothrin)/litre). The results obtained for technical and formulated products were therefore in agreement.

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

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

Formulations

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

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

Methods of analysis and testing

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

A modification of the CIPAC method is required for analysis of CS formulations, to extract the lambda-cyhalothrin, although the remainder of the method is unchanged. The linearity, repeatability and reproducibility of the modification has been validated by the company but these data have not yet been assessed by CIPAC. At the time of submission, there were no validated methods available to differentiate between the free and encapsulated active ingredient in the CS formulations. In principle, the very low water solubility of lambda-cyhalothrin should ensure that the free active ingredient content is very low.

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

All methods for testing the physical properties of the TC, WP, EC and SE, for compliance with the proposed FAO specifications, have been published by CIPAC

(CIPAC 1995). They are referenced in the specifications and were used to develop the data on which the specifications are based.

Containers and packaging

No special requirements were identified for containers and packaging.

Expression of active ingredient

The active ingredient is expressed as lambda-cyhalothrin.

Appraisal

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

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

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

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

Confidential information on the manufacturing process, and on impurities at or above 1 g/kg, was provided by the proposer, together with limits for the impurities (1 to 100 g/kg, including other cyhalothrin isomers) in the TC. Limits for the impurities were

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

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

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

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

The JMPR allocated an ADI of 0-0.02 mg/kg bodyweight for cyhalothrin, based on short term and chronic testing on rats, mice, rabbits, guinea pigs and dogs. The data were considered by the JMPR and WHO to be applicable to lambda-

cyhalothrin. The purity of the technical material used in these studies was similar to that of commercial products and within the TC specification.

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

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

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

Recommendations

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

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

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

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

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, 10th ed. p. 57. FAO Rome.

Codex 1999 Codex Alimentarius, volume 2, 3rd edition, Cyhalothrin 146, Pesticide Residues in Food, FAO Rome.

FAO 1994 Manual on the development and use of FAO specifications for plant protection products, 4th 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, 5th 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.
