WHO SPECIFICATIONS AND EVALUATIONS FOR PUBLIC HEALTH PESTICIDES

DELTAMETHRIN

(*S*)-α-cyano-3-phenoxybenzyl (1*R*,3*R*)-3-(2,2-dibromovinyl)-2,2-dimethylcyclopropane carboxylate

World Health Organization

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DISCLAIMER[1]

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

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

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

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

INTRODUCTION

WHO establishes and publishes specifications[2] for technical material and related formulations of public health pesticides with the objective that these specifications may be used to provide an international point of reference against which products can be judged either for regulatory purposes or in commercial dealings.

From 2002, the development of WHO specifications follows the **New Procedure**, described in the "Manual for development and use of FAO and WHO specifications for pesticides." This **New Procedure** follows a formal and transparent evaluation process. It describes the minimum data package, the procedure and evaluation applied by WHO and the experts of the FAO/WHO Joint Meeting on Pesticide Specifications (JMPS).

WHO specifications now only apply to products for which the technical materials have been evaluated. Consequently, from the year 2002 onwards, the publication of WHO specifications under the **New Procedure** has changed. Every specification consists now of two parts, namely the specifications and the evaluation report(s):

Part One: The Specification of the technical material and the related formulations of the pesticide in accordance with chapters 4 to 9 of the above-mentioned manual.

Part Two: The Evaluation Report(s) of the pesticide, reflecting the evaluation of the data package carried out by WHO and the JMPS. The data are provided by the manufacturer(s) according to the requirements of chapter 3 of the above-mentioned manual and supported by other information sources. evaluation reports include the name(s) of the manufacturer(s) whose technical material has been evaluated. Evaluation reports on specifications developed subsequently to the original set of specifications are added in chronological order to this report.

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

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

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

PART ONE: SPECIFICATIONS

DELTAMETHRIN

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Deltamethrin Information

ISO common names

Deltamethrin (BSI, E-ISO), deltaméthrine ((f) F-ISO)

Synonyms

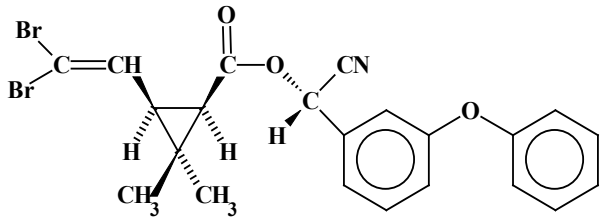
Decamethrin (rejected common name)

Chemical names

IUPAC (*S*)-α-cyano-3-phenoxybenzyl (1*R*,3*R*)-3-(2,2-dibromovinyl)-2,2-dimethylcyclopropane carboxylate

CA [1*R*-[1α(*S**),3α]]-cyano(3-phenoxyphenyl)methyl 3-(2,2-dibromoethenyl)-2,2-dimethylcyclopropanecarboxylate

Structural formula



Empirical formula

$C_{22}H_{19}Br_2NO_3$

Relative molecular mass

505.2

CAS Registry number

52918-63-5

CIPAC number

333

EEC number

258-256-6

Identity tests

Retention time in reversed phase and enantioselective HPLC; TLC; IR, NMR and mass spectra

Deltamethrin Technical Material (October 2023)

WHO specification 333/TC (October 2023*)

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 (333/2004, 333/2005, 333/2006.2, 333/2008.1, 333/2012.1, 333/2014.2, 333/2016.3, 333/2017.1, 333/2017.2, 333/2017.3, 333/2017.4, 333/2017.5, 333/2017.6, 333/2017.7, 333/2022). 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 (333/2004, 333/2005, 333/2006.2, 333/2008.1, 333/2012.1, 333/2014.2, 333/2016.3, 333/2017.1, 333/2017.2, 333/2017.3, 333/2017.4, 333/2017.5, 333/2017.6, 333/2017.7, 333/2022), as PART TWO, form an integral part of this publication.

1 Description

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

2 Active ingredient

2.1 **Identity tests** (333/TC/M2/2, CIPAC Handbook L, p.46, 2006 and 333/TC/M2/4, CIPAC Handbook O, p.39, 2017)

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 **Deltamethrin content** (333/TC/M2/3, CIPAC Handbook L, p.46, 2006 and 333/TC/M2/4, CIPAC Handbook O, p.39, 2017) (Note 1)

The deltamethrin content shall be declared (not less than 985 g/kg), and when determined, the average measured content shall not be lower than the declared minimum content.

3 Relevant impurities (Note 2)

Note 1 The determination of deltamethrin in deltamethrin TC in the possible presence of other stereoisomers relies on the combined use of the chemical purity method published in CIPAC Handbook L and of the peer validated stereospecific HPLC method for deltamethrin published in Handbook O.

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

Note 2 There are no relevant impurities to be controlled in products of the manufacturers identified in evaluation reports 333/2004, 333/2005, 333/2006.2, 333/2008.1, 333/2012.1, 333/2014.2, 333/2016.3, 333/2017.1, 333/2017.2, 333/2017.3, 333/2017.4, 333/2017.5, 333/2017.6, 333/2017.7 and 333/2022. However, becisthemic acid chloride [(1*R*,3*R*)-3-(2,2-dibromovinyl)-2,2-dimethylcyclopropane carboxoyl chloride], sometimes spelt bicisthemic acid chloride, can occur as a result of certain manufacturing processes. If this impurity could occur at ≥1 g/kg (of deltamethrin) in the products of other manufacturers, it would be designated as a relevant impurity and a clause would be required to limit its concentration.

Deltamethrin Dustable Powder (October 2023)

WHO specification 333/DP (October 2023*)

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 (333/2004, 333/2005, 333/2006.2). 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 (333/2004, 333/2005, 333/2006.2), as PART TWO, form an integral part of this publication.

1 Description

The material shall consist of a homogeneous mixture of technical deltamethrin, complying with the requirements of WHO specification 333/TC, together with carriers and any other necessary formulants. It shall be in the form of a fine, free-flowing powder, free from visible extraneous matter and hard lumps.

2 Active ingredient

2.1 **Identity tests** (333/DP/M2/2, CIPAC Handbook L, p.53, 2006)

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 **Deltamethrin content** (333/DP2/M/3, CIPAC Handbook L, p.53, 2006)

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

Declared content, g/kg	Tolerance
up to 25 Note: the upper limit is included in the range	± 25% of the declared content

3 Relevant impurities (Note 1)

4 Physical properties

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

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

The pH of an aqueous dispersion shall be 4.5 to 7.5.

4.2 **Dry sieve test** (MT 170, CIPAC Handbook F, p.420, 1995)

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

5 Storage stability

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

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

- pH range (4.1);
- dry sieve test (4.2).

Note 1 There are no relevant impurities to be controlled in products of the manufacturers identified in evaluation reports 333/2004, 333/2005 and 333/2006.2. However, becisthemic acid chloride [(1*R*,3*R*)-3-(2,2-dibromovinyl)-2,2-dimethylcyclopropane carboxoyl chloride], sometimes spelt bicisthemic acid chloride, can occur as a result of certain manufacturing processes. If this impurity could occur at ≥1 g/kg (of deltamethrin) in the products of other manufacturers, it would be designated as a relevant impurity, and a clause would be required to limit its concentration.

Note 2 Samples of the formulation taken before and after the accelerated storage stability test may be analyzed concurrently after the test in order to reduce the analytical error.

Deltamethrin Wettable Powder (October 2023)

WHO specification 333/WP (October 2023*)

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 (333/2004, 333/2005, 333/2006.2, 333/2008.1, 333/2017.7). 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 (333/2004, 333/2005, 333/2006.2, 333/2008.1, 333/2017.7), as PART TWO, form an integral part of this publication.

1 Description

The material shall consist of a homogeneous mixture of technical deltamethrin, complying with the requirements of WHO specification 333/TC, together with filler(s) and any other necessary formulants. It shall be in the form of a fine powder free from visible extraneous matter and hard lumps.

2 Active ingredient

2.1 **Identity tests** (333/WP/(M)/2, CIPAC Handbook L, p.50, 2006)

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 **Deltamethrin content** (333/WP/(M)/3, CIPAC Handbook L, p.50, 2006)

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

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

3 Relevant impurities (Note 1)

4 Physical properties

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

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

The pH of an aqueous dispersion shall be 4.5 to 7.5.

4.2 **Wet sieve test** (MT 185.1, CIPAC/5353) (Note 2)

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

4.3 **Suspensibility** (MT 184.1, CIPAC Handbook P, p.245, 2021) (Notes 3, 4 & 5)

Minimum: 60% after 30 min in CIPAC standard water D at 25 ± 5°C.

4.4 **Persistent foam** (MT 47.3, CIPAC Handbook O, p. 177, 2017) (Note 6)

Maximum: 60 ml after 1 min.

4.5 **Wettability** (MT 53.3.1, CIPAC Handbook F, p.164, 1995)

The formulation shall be completely wetted in 2 min without swirling.

5 Storage stability

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

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

- pH range (4.1);
- wet sieve test (4.2);
- suspensibility (4.3);
- wettability (4.5).

Note 1 There are no relevant impurities to be controlled in products of the manufacturers identified in evaluation reports 333/2004, 333/2005, 333/2006.2, 333/2008.1 and 333/2017.7. However, becisthemic acid chloride [(1*R*,3*R*)-3-(2,2-dibromovinyl)-2,2-dimethylcyclopropane carboxoyl chloride], sometimes spelt bicisthemic acid chloride, can occur as a result of certain manufacturing processes. If this impurity could occur at ≥1 g/kg (of deltamethrin) in the products of other manufacturers, it would be designated as a relevant impurity and a clause would be required to limit its concentration.

Note 2 The revised CIPAC method for wet sieve test (MT 185.1, CIPAC/5353) combining methods MT 182 and MT 185 into a single method was accepted as provisional CIPAC method in 2023. Prior to its publication in a next Handbook, the method can be obtained through the CIPAC prepublication scheme, https://www.cipac.org/index.php/m-p/pre-published-methods.

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 184.1.

Note 4 This test will normally only be carried out after the heat stability test, 5.1.

Note 5 Chemical assay is the only fully reliable method to measure the mass of active ingredient still in suspension. However, the simpler gravimetric method may be used on a routine basis provided that it has been shown to give equal results to those of chemical assay. In case of dispute, chemical assay shall be the referee method.

Note 6 The mass of sample to be used in the test should be at the highest rate of use recommended by the supplier. The test is to be conducted in CIPAC standard water D at 25 ± 5°C.

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

Deltamethrin Aqueous Suspension Concentrate (October 2023)

WHO specification 333/SC (October 2023*)

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 (333/2004, 333/2005, 333/2006.2, 333/2008.1). 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 (333/2004, 333/2005, 333/2006.2, 333/2008.1), as PART TWO, form an integral part of this publication.

1 Description

The material shall consist of a suspension of fine particles of technical deltamethrin, complying with the requirements of WHO specification 333/TC, in an aqueous phase together with suitable formulants. After gentle agitation, the material shall be homogeneous (Note 1) and suitable for further dilution in water.

2 Active ingredient

2.1 **Identity tests** (333/SC/M/2, CIPAC Handbook L, p.51, 2006)

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 **Deltamethrin content** (333/SC/M/3, CIPAC Handbook L, p.51, 2006)

The deltamethrin content shall be declared (10 g/kg or g/l at 20 ± 2ºC, Note 2), and, when determined, the average measured content shall not differ from that declared by more than ± 15%.

3 Relevant impurities (Note 3)

4 Physical properties

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

The pH of an aqueous dispersion shall be 4.5 to 7.5.

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

Maximum "residue": 5%.

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

4.3 **Spontaneity of dispersion** (MT 160.1, CIPAC/5323)(Notes 4 & 5)

Minimum: 90% after 5 min in CIPAC standard water D at 25 ± 5°C.

4.4 **Suspensibility** (MT 184.1, CIPAC Handbook P, p.245, 2021) (Notes 5 & 6)

Minimum: 90% after 30 min in CIPAC standard water D at 25 ± 5°C.

4.5 **Wet sieve test** (MT 185.1, CIPAC/5353) (Note 7)

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

4.6 **Persistent foam** (MT 47.3, CIPAC Handbook O, p.177, 2017) (Note 8)

Maximum: 50 ml after 1 min.

5 Storage stability

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

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

- suspensibility (4.4);
- wet sieve test (4.5).

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

After storage at 54 ± 2°C for 14 days, the determined average active ingredient content must not be lower than 95% relative to the determined mean content found before storage (Note 9), and the formulation shall continue to comply with the clauses for:

- pH range (4.1);
- pourability (4.2);
- spontaneity of dispersion (4.3);
- suspensibility (4.4);
- wet sieve test (4.5).

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

Note 2 Unless homogenization is carried out carefully, it is possible for the sample to become aerated. This can lead to errors in the determination of the mass per millilitre and in calculation of the active ingredient content (in g/l) if methods other

than OECD 109 or MT 3.3 are used. If the buyer requires both g/kg and g/l at 20°C, then in case of dispute, the analytical results shall be calculated as g/kg.

Note 3 There are no relevant impurities to be controlled in products of the manufacturers identified in evaluation reports 333/2004, 333/2005, 333/2006.2 and 333/2008.1. However, becisthemic acid chloride [(1*R*,3*R*)-3-(2,2-dibromovinyl)-2,2-dimethylcyclopropane carboxoyl chloride], sometimes spelt bicisthemic acid chloride, can occur as a result of certain manufacturing processes. If this impurity could occur at ≥1 g/kg (of deltamethrin) in the products of other manufacturers, it would be designated as a relevant impurity, and a clause would be required to limit its concentration.

Note 4 The revised CIPAC method for determination of the spontaneity of dispersion of liquid formulations forming suspensions on dilution with water (MT 160.1, CIPAC/5323) was adopted as full CIPAC method in 2023. Prior to its publication in the next Handbook, the method can be obtained through the CIPAC prepublication scheme, https://www.cipac.org/index.php/m-p/pre-published-methods.

Note 5 Chemical assay is the only fully reliable method to measure the mass of active ingredient still in suspension. However, the simpler gravimetric method may be used on a routine basis, provided that it has been shown to give equal results to those of chemical assay. In case of dispute, chemical assay shall be the referee method.

Note 6 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 the method MT 184.1.

Note 7 The revised CIPAC method for wet sieve test (MT 185.1, CIPAC/5353) combining methods MT 182 and MT 185 into a single method was accepted as provisional CIPAC method in 2023. Prior to its publication in a next Handbook, the method can be obtained through the CIPAC prepublication scheme, https://www.cipac.org/index.php/m-p/pre-published-methods.

Note 8 The mass of sample to be used in the test should be at the highest rate of use recommended by the supplier. The test is to be conducted in CIPAC standard water D at 25 ± 5°C.

Note 9 Samples of the formulation taken before and after the accelerated storage stability test may be analyzed concurrently after the test in order to reduce the analytical error.

Deltamethrin Polymer-Enhanced Suspension Concentrate (October 2023)

WHO interim specification 333/SC-PE (October 2023*)

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 (333/2013.1). 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 (333/2013.1), given in PART TWO, forms an integral part of this publication.

1 Description

The material shall consist of a suspension of fine particles of technical deltamethrin, complying with the requirements of WHO specification 333/TC, in an aqueous phase together with a polymer adjuvant and other suitable formulants (Note 1). After gentle agitation the material shall be homogeneous (Note 2) and suitable for further dilution in water.

2 Active ingredient

2.1 **Identity tests** (333/SC/M/2, CIPAC Handbook L, p.51, 2006)

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 **Deltamethrin content** (333/SC/M/3, CIPAC Handbook L, p.51, 2006)

The deltamethrin content shall be declared (62.5 g/kg or g/l at 20 ± 2ºC, Note 3), and, when determined, the average measured content shall not differ from that declared by more than ± 10%.

3 Relevant impurities (Note 4)

4 Physical properties

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* This specification is applicable to deltamethrin polymer-enhanced suspension concentrates produced by Bayer CropScience. In contrast to other formulations, an extension of this specification to nominally similar products of other manufacturers shall require biological testing. The SC-PE formulation code does not exist in the catalogue of pesticide formulation types and international coding system (CropLife International Technical Monograph No 2), but SC-PE was adopted for this formulation to distinguish it from the conventional SC (WHO specification 333/SC).

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

4.1 **Loss in weight** (MT 17.4, CIPAC Handbook F, p. 57, 1995)

Lower limit: 74%;
Upper limit: 81%.

4.2 **Glass transition temperature** (ISO 11357) (Note 5)

Minimum Tg: 43°C
Maximum Tg: 53°C

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

The pH of an aqueous dispersion shall be 4.5 to 7.5.

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

Maximum "residue": 5%.

4.5 **Spontaneity of dispersion** (MT 160.1, CIPAC/5323) (Notes 6 & 7)

Minimum: 70% after 5 min in CIPAC standard water D at 25 ± 5°C.

4.6 **Suspensibility** (MT 184.1, CIPAC Handbook P, p.245, 2021) (Notes 7 & 8)

Minimum: 90% after 30 min in CIPAC standard water D at 25 ± 5°C.

4.7 **Wet sieve test** (MT 185.1, CIPAC/5353) (Note 9)

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

4.8 **Persistent foam** (MT 47.3, CIPAC Handbook O, p. 177, 2017) (Note 10)

Maximum: 50 ml after 1 min.

5 Storage stability

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

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

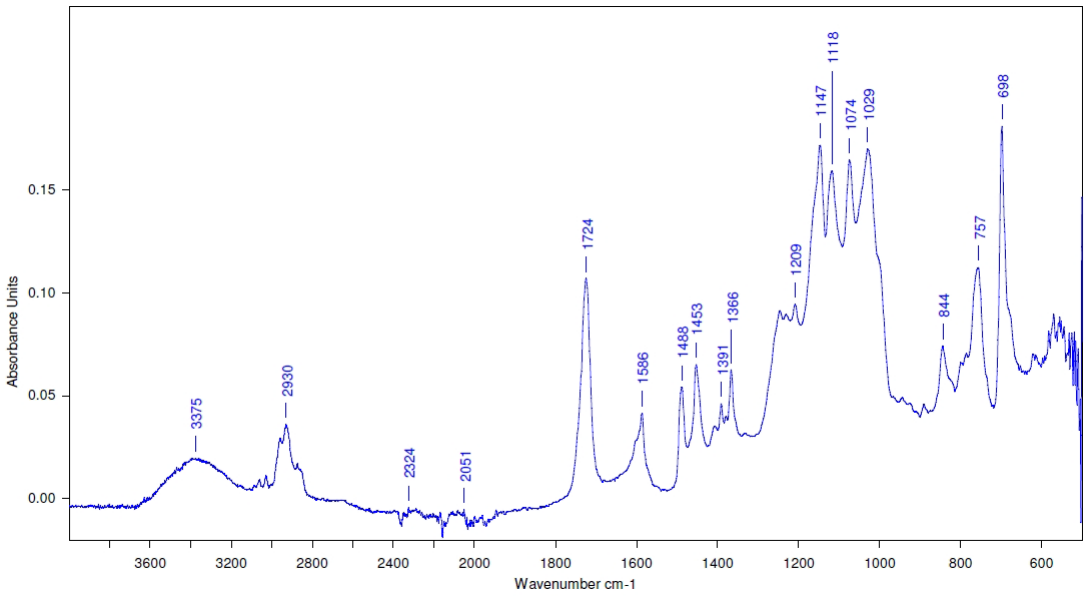
- suspensibility (4.6);
- wet sieve test (4.7).

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

After storage at 54 ± 2°C for 14 days, the determined average active ingredient content must not be lower than 95% relative to the determined mean content found before storage (Note 11), and the formulation shall continue to comply with the clauses for:

- pH range (4.3);
- pourability (4.4);
- spontaneity of dispersion (4.5);
- suspensibility (4.6);
- wet sieve test (4.7).

Note 1 IR spectrum of Deltamethrin 62.5 SC-PE



Sample preparation for the IR spectrum recording:
1rst option:
- The formulation is dried at 105°C at constant weight.

Alternate and preferred option:
- Dilute 10 time the formulation with water.
- After shaking, the formulation is centrifuged, and the supernatant is separated.
- The supernatant is dried at 105°C at constant weight.

Note 2 Before sampling to verify the formulation quality, inspect the commercial container carefully. On standing, suspension concentrates usually develop a concentration gradient from the top to the bottom of the container. This may even result in the appearance of a clear liquid on the top and/or of sediment on the bottom. Therefore, before sampling, homogenize the formulation according to the instructions given by the manufacturer or, in the absence of such instructions, by gentle shaking of the commercial container (for example, by inverting the closed container several times). Large containers must be opened and stirred adequately. After this procedure, the container should not contain a sticky layer of non-dispersed matter at the bottom. A suitable and simple method of checking for a non-dispersed sticky layer "cake" is by probing with a glass rod or similar device adapted to the size and shape of the container. All the physical and chemical tests must be carried out on a laboratory sample taken after the recommended homogenization procedure.

Note 3 Unless homogenization is carried out carefully, it is possible for the sample to become aerated. This can lead to errors in the determination of the mass per millilitre and in calculation of the active ingredient content (in g/l) if methods other than OECD 109 or MT 3.3 are used. If the buyer requires both g/kg and g/l at 20°C, then in case of dispute, the analytical results shall be calculated as g/kg.

Note 4 There are no relevant impurities to be controlled in products of the manufacturers identified in evaluation report 333/2013.1. However, becisthemic acid chloride [(1*R*,3*R*)-3-(2,2-dibromovinyl)-2,2-dimethylcyclopropane carboxoyl chloride], sometimes spelt bicisthemic acid chloride, can occur as a result of certain manufacturing processes. If this impurity could occur at ≥1 g/kg (of deltamethrin) in the products of other manufacturers, it would be designated as a relevant impurity, and a clause would be required to limit its concentration.

Note 5 Sample preparation for the Glass Transition Temperature determination:
- Coat the formulation on a glass plate with approximately 100 µm wet film thickness.
- Dry the coated film at room temperature for at least 4 days at a relative humidity of less than 2% (e.g., in a nitrogen flushed glove box).
- Load 10 mg of dried film into a suitable DSC sample pan.
- Compress the sample to ensure a good thermal contact with the sample pan.
- Store open the sample pan with specimen for at least another 24h at a relative humidity of less than 2%.
- Under these humidity conditions (e.g., in a glove box), crimp the DSC sample pan with a suitable lid.
- Put closed sample pan with specimen into differential scanning calorimeter (eg. Perkin-Elmer DSC-7 with cooling accessory).

Note 6 The revised CIPAC method for determination of the spontaneity of dispersion of liquid formulations forming suspensions on dilution with water (MT 160.1, CIPAC/5323) was adopted as full CIPAC method in 2023. Prior to its publication in the next Handbook, the method can be obtained through the CIPAC prepublication scheme, https://www.cipac.org/index.php/m-p/pre-published-methods.

Note 7 Chemical assay is the only fully reliable method to measure the mass of active ingredient still in suspension. However, the simpler gravimetric method may be used on a routine basis, provided that it has been shown to give equal results to those of chemical assay. In case of dispute, chemical assay shall be the referee method.

Note 8 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 the method MT 184.1.

Note 9 The revised CIPAC method for wet sieve test (MT 185.1, CIPAC/5353) combining methods MT 182 and MT 185 into a single method was accepted as provisional CIPAC method in 2023. Prior to its publication in the next Handbook, the method can be obtained through the CIPAC prepublication scheme, https://www.cipac.org/index.php/m-p/pre-published-methods.

Note 10 The mass of sample to be used in the test should be at the highest rate of use recommended by the supplier. The test is to be conducted in CIPAC standard water D at 25 ± 5°C.

Note 11 Samples of the formulation taken before and after the accelerated storage stability test may be analyzed concurrently after the test in order to reduce the analytical error.

Deltamethrin Emulsifiable Concentrate (October 2023)

WHO specification 333/EC (October 2023*)

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 (333/2004, 333/2005, 333/2006.2, 333/2008.1, 333/2012.1, 333/2012.2). 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 (333/2004, 333/2005, 333/2006.2, 333/2008.1, 333/2012.1, 333/2012.2), as PART TWO, form an integral part of this publication.

1 Description

The material shall consist of technical deltamethrin, complying with the requirements of WHO specification 333/TC, dissolved in suitable solvents, together with any other necessary formulants. It shall be in the form of a stable homogeneous liquid, free from visible suspended matter and sediment, to be applied as an emulsion after dilution in water.

2 Active ingredient

2.1 **Identity tests** (333/EC/M2/2, CIPAC Handbook L, p.50, 2006)

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 **Deltamethrin content** (333/EC/M2/3, CIPAC Handbook L, p.51, 2006)

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

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

3 Relevant impurities (Note 2)

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

4 **Physical** properties

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

The pH of an aqueous dispersion shall be 4.5 to 7.5.

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

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

Time after dilution	Limits of stability
0 h	Initial emulsification complete
0.5 h	"Cream": none
2.0 h	"Cream", maximum: 1 ml "Free oil": none
24 h	Re-emulsification complete
24.5 h	"Cream": none "Free oil": none
Note: tests at 24 h are required only where the results at 2 h are in doubt.	

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

Maximum: 50 ml after 1 min.

5 **Storage stability**

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

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

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

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

- pH range (4.1);
- emulsion stability and re-emulsification (4.2).

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

Note 2 There are no relevant impurities to be controlled in products of the manufacturers identified in evaluation reports 333/2004, 333/2005, 333/2006.2, 333/2008.1, 333/2012.1 and 333/2012.2. However, becisthemic acid chloride [(1*R*,3*R*)-3-(2,2-dibromovinyl)-2,2-dimethylcyclopropane carboxoyl chloride], sometimes spelt bicisthemic acid chloride, can occur as a result of certain manufacturing processes. If this impurity could occur at ≥1 g/kg (of deltamethrin) in the products of other manufacturers, it would be designated as a relevant impurity, and a clause would be required to limit its concentration.

Note 3 As outlined in CIPAC MT 36.3, the test concentrations should be based on those in the recommended directions for use supplied with the product. Where several concentrations are recommended, the highest and lowest concentrations within the scope of the method should be used.

Note 4 The mass of sample to be used in the test should correspond to the highest rate of use recommended by the supplier. The test is to be conducted in CIPAC standard water D at 25 ± 5°C.

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

Deltamethrin Ultra Low Volume Liquid (October 2023)

WHO specification 333/UL (October 2023*)

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 (333/2004, 333/2005, 333/2006.2, 333/2008.1). 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 (333/2004, 333/2005, 333/2006.2, 333/2008.1), as PART TWO, form an integral part of this publication.

1 Description

The material shall consist of technical deltamethrin, complying with the requirements of WHO specification 333/TC, together with any necessary formulants (Note 1). It shall be in the form of a stable homogeneous liquid, free from visible suspended matter and sediment.

2 Active ingredient

2.1 **Identity tests** (333/UL/(M2)/2, CIPAC Handbook L, p.56, 2006)

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 **Deltamethrin content** (333/UL/(M2)/3, CIPAC Handbook L, p.56, 2006)

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

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

3 Relevant impurities (Note 3)

4 Physical properties (Notes 4 & 5)

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

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

The pH of an aqueous dispersion shall be 4.5 to 7.5.

5 Storage stability

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

After storage at 0 ± 2°C for 7 days, no separation of solid and/or oily material shall occur.

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

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

- pH range (4.1).

Note 1 Although it is not included in this specification, the flash point of the product shall comply with national and/or international transport regulations for flammable materials.

Note 2 If the buyer requires both g/kg and g/l at 20°C, then in case of dispute, the analytical results shall be calculated as g/kg.

Note 3 There are no relevant impurities to be controlled in products of the manufacturers identified in evaluation reports 333/2004, 333/2005, 333/2006.2 and 333/2008.1. However, becisthemic acid chloride [(1*R*,3*R*)-3-(2,2-dibromovinyl)-2,2-dimethylcyclopropane carboxoyl chloride], sometimes spelt bicisthemic acid chloride, can occur as a result of certain manufacturing processes. If this impurity could occur at ≥1 g/kg (of deltamethrin) in the products of other manufacturers, it would be designated as a relevant impurity, and a clause would be required to limit its concentration.

Note 4 Viscosity can be critically important for successful application of a UL formulation, but the requirements are dependent upon both the formulation and the application technique or equipment. For this reason, no clause is provided for kinematic viscosity.

Note 5 Loss of droplet mass by volatilisation can be critical for UL formulations because, if the losses are significant, the proportion of the spray which drifts from the target, and the distance over which the drift occurs, is likely to increase. The volatilization and additional drift that occur in practice are dependent on the initial droplet size spectrum and the height through which droplets fall, the air temperature and wind speed. In addition, a degree of volatilization which may be unacceptable for one type of application may be of little or no consequence in another case. At present, no method is available to allow measurement of loss by volatilization to be related to the potential increase in drift and therefore no clause is provided for volatility.

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

Deltamethrin Water Dispersible Granules (October 2023)

WHO specification 333/WG (October 2023*)

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 (333/2004, 333/2005, 333/2006.2, 333/2007, 333/2014.2, 333/2014.3). 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 (333/2004, 333/2005, 333/2006.2, 333/2007, 333/2014.2, 333/2014.3), as PART TWO, form an integral part of this publication.

1 Description

The material shall consist of a homogeneous mixture of technical deltamethrin, complying with the requirements of WHO specification 333/TC, together with carriers and any other necessary formulants. It shall be in the form of granules for application after disintegration and dispersion in water. The formulation shall be dry, free-flowing, nearly dust-free or essentially non-dusty, and free from visible extraneous matter and hard lumps.

2 Active ingredient

2.1 **Identity tests** (333/WG/M/2, CIPAC Handbook L, p.48, 2006)

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 **Deltamethrin content** (333/WG/M/3, CIPAC Handbook L, p.48, 2006)

The deltamethrin content shall be declared (250 g/kg), and when determined, the average measured content shall not differ from that declared by more than ± 6%.

3 Relevant impurities (Note 1)

4 Physical properties

4.1 **Acidity** (MT 191, CIPAC Handbook L, p.143, 2006)

Maximum acidity: 20 g/kg calculated as H_2SO_4.

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

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

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

4.3 **Wet sieve test** (MT 185.1, CIPAC/5353) (Note 2)

Maximum: 1% retained on a 75 µm test sieve.

4.4 **Dispersibility** (MT 174, CIPAC Handbook F, p.435, 1995)

Minimum: 90% after 2 min stirring.

4.5 **Suspensibility** (MT 184.1, CIPAC Handbook P, p.245, 2021) (Notes 3 & 4)

Minimum: 70% after 30 min in CIPAC standard water D at 25 ± 5°C.

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

Maximum: 40 ml after 1 min.

4.7 **Dustiness** (MT 171.1, CIPAC Handbook P, p.235, 2021) (Note 6)

The formulation shall have a maximum collected dust of 30 mg by the gravimetric method or a maximum dust factor of 25 by the optical method.

4.8 **Flowability** (MT 172.2, CIPAC Handbook P, p.241, 2021)

At least 99% of the formulation shall pass through a 5 mm test sieve after 20 drops of the sieve (Note 7).

5 Storage stability

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

After storage at 54 ± 2°C for 14 days, the determined average active ingredient content must not be lower than 95% relative to the determined average content found before storage (Note 8) and the formulation shall continue to comply with the clauses for:

- acidity (4.1);
- wet sieve test (4.3);
- dispersibility (4.4);
- suspensibility (4.5);
- dustiness (4.7).

Note 1 There are no relevant impurities to be controlled in products of the manufacturers identified in evaluation reports 333/2004, 333/2005, 333/2006.2, 333/2007, 333/2014.2 and 333/2014.3. However, becisthemic acid chloride [(1*R*,3*R*)-3-(2,2-dibromovinyl)-2,2-dimethylcyclopropane carboxoyl chloride], sometimes spelt bicisthemic acid chloride, can occur as a result of certain manufacturing processes. If this impurity could occur at ≥1 g/kg (of deltamethrin) in the products of other manufacturers, it would be designated as a relevant impurity and a clause would be required to limit its concentration.

Note 2 The revised CIPAC method for wet sieve test (MT 185.1, CIPAC/5353) combining methods MT 182 and MT 185 into a single method was accepted as provisional CIPAC method in 2023. Prior to its publication in the next Handbook, the method

can be obtained through the CIPAC prepublication scheme, https://www.cipac.org/index.php/m-p/pre-published-methods.

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 the method MT 184.1.

Note 4 Chemical assay is the only fully reliable method to measure the mass of active ingredient still in suspension. However, the simpler gravimetric method may be used on a routine basis provided that it has been shown to give equal results to those of chemical assay. In case of dispute, chemical assay shall be the referee method.

Note 5 The mass of sample to be used in the test should be at the highest rate of use recommended by the supplier. The test is to be conducted in CIPAC standard water D at 25 ± 5°C.

Note 6 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 of MT 171.1 usually shows good correlation with the gravimetric method, 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 The flowability test (MT 172.2) includes the accelerated storage conditions to be used.

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

Deltamethrin Water Dispersible Granules in Sealed Water-Soluble Bag (October 2023)

WHO specification 333/WG-SB (October 2023*)

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 (333/2013.2, 333/2014.4, 333/2016.2). 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 (333/2013.2, 333/2014.4, 333/2016.2), as PART TWO, form an integral part of this publication.

1 Description

The material shall consist of a defined quantity of a homogeneous mixture of technical deltamethrin, complying with the requirements of WHO specification 333/TC, together with carriers and any other necessary formulants. It shall be in the form of granules, contained in a sealed water-soluble bag, for application after disintegration and dispersion in water. The formulation shall be dry, free-flowing, nearly dust-free or essentially non-dusty, and free from visible extraneous matter and hard lumps.

2 Active ingredient

2.1 **Identity tests** (333/WG/M/2, CIPAC Handbook L, p.48, 2006)

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 **Deltamethrin content** (333/WG/M/3, CIPAC Handbook L, p.48, 2006)

The deltamethrin content shall be declared (250 g/kg), and when determined, the average measured content shall not differ from that declared by more than ± 6%.

3 Relevant impurities (Note 1)

4 Physical properties (Note 2)

4.1 **Acidity** (MT 191, CIPAC Handbook L, p.143, 2006)

Maximum acidity: 20 g/kg calculated as H_2SO_4.

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

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

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

4.3 **Wet sieve test** (MT 185.1, CIPAC/5353) (Note 3)

Maximum: 1% retained on a 75 µm test sieve.

4.4 **Dispersibility** (MT 174, CIPAC Handbook F, p.435, 1995)

Minimum: 90% after 2 min stirring.

4.5 **Suspensibility** (MT 184.1, CIPAC Handbook P, p.245, 2021) (Notes 4 & 5)

The suspensibility shall be tested on a suspension containing the WG and the bag material in the actual ratio of application, prepared according to the procedure described in Note 6.

Minimum: 70% after 30 min in CIPAC standard water D at 25 ± 5°C.

4.6 **Persistent foam** (MT 47.3, CIPAC Handbook O, p. 177, 2017) (Note 7)

The persistent foam shall be tested on a suspension containing the WG and the bag material in the actual ratio of application, prepared according to the procedure described in Note 6.

Maximum: 40 ml after 1 min.

4.7 **Flowability** (MT 172.2, CIPAC Handbook P, p.241, 2021)

At least 99% of the formulation shall pass through a 5 mm test sieve after 20 drops of the sieve (Note 8).

4.8 **Dissolution of the bag** (MT 176, CIPAC Handbook F, p. 440, 1995) (Notes 2 & 9)

The dissolution of the bag shall be tested on a sample of the emptied and cleaned bag taken according to the procedure described in Note 9.

Flow time of the suspension: maximum 30 sec.

5 Storage stability

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

The package should be enclosed in a watertight sachet, box or any other container at 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 10), and the formulation shall continue to comply with the clauses for:

- acidity (4.1);
- wet sieve test (4.3);
- dispersibility (4.4);
- suspensibility (4.5);
- persistent foam (4.6);

– dissolution of the bag (4.8).

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

Note 1 There are no relevant impurities to be controlled in products of the manufacturers identified in evaluation reports 333/2013.2, 333/2014.4 and 333/2016.2. However, becisthemic acid chloride [(1*R*,3*R*)-3-(2,2-dibromovinyl)-2,2-dimethylcyclopropane carboxoyl chloride], sometimes spelt bicisthemic acid chloride, can occur as a result of certain manufacturing processes. If this impurity could occur at ≥1 g/kg (of deltamethrin) in the products of other manufacturers, it would be designated as a relevant impurity, and a clause would be required to limit its concentration.

Note 2 Sub-sampling.

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

- active ingredient identity (2.1)
- active ingredient content (2.2)
- acidity (4.1)
- wettability (4.2)
- wet sieve test (4.3)
- dispersibility (4.4)
- suspensibility (4.5)
- persistent foam (4.6)
- flowability (4.7)
- dissolution of the bag (4.8)

The bag is then opened on three sides, completely cleaned from adhering powder by brushing or suction and weighed to the nearest 0.01 g. Aliquots of an aqueous solution of the bag material shall be used in the suspensibility (4.5) and persistent foam (4.6) tests.

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

Note 3 The revised CIPAC method for wet sieve test (MT 185.1, CIPAC/5353) combining methods MT 182 and MT 185 into a single method was accepted as provisional CIPAC method in 2023. Prior to its publication in the next Handbook, the method can be obtained through the CIPAC prepublication scheme, https://www.cipac.org/index.php/m-p/pre-published-methods.

Note 4 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 the method MT 184.1.

Note 5 Chemical assay is the only fully reliable method to measure the mass of active ingredient still in suspension. However, the simpler gravimetric method may be used on a routine basis, provided that it has been shown to give equal results to those of chemical assay. In case of dispute, chemical assay shall be the referee method.

Note 6 The procedure for adding the bag material to the solution for the suspensibility and persistent foam tests should be as follows:

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

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

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

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

Note 7 The mass of sample to be used in the test should be at the highest rate of use recommended by the supplier. The test is to be conducted in CIPAC standard water D at 25 ± 5°C.

Note 8 The flowability test (MT 172.2) includes the accelerated storage conditions to be used.

Note 9 The sampling of the bag for the dissolution test should be as follows:

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

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

Note 10 Samples of the formulation taken before and after the accelerated storage stability test may be analyzed concurrently after the test in order to reduce the analytical error.

Deltamethrin Emulsion, Oil in Water (October 2023)

WHO specification 333/EW (October 2023*)

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 (333/2004, 333/2005, 333/2006.2, 333/2008.2, 333/2012.2). 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 (333/2004, 333/2005, 333/2006.2, 333/2008.2, 333/2012.2), as PART TWO, form an integral part of this publication.

1 Description

The formulation shall consist of an emulsion of technical deltamethrin, complying with the requirements of WHO specification 333/TC, in an aqueous phase together with suitable formulants. After gentle agitation, the formulation shall be homogeneous (Note 1) and suitable for dilution in water.

2 Active ingredient

2.1 **Identity tests** (333/EW/(M)/2, CIPAC Handbook L, p.55, 2006)

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 **Deltamethrin content** (333/EW/(M)/3, CIPAC Handbook L, p.55, 2006)

The deltamethrin content shall be declared (20 g/kg or g/l at 20 ± 2ºC, Note 2) and, when determined, the mean measured content shall not differ from that declared by more than ± 15%.

3 Relevant impurities (Note 3)

4 Physical properties

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

The pH of an aqueous dispersion shall be 3.0 to 7.5.

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

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

Maximum "residue": 5%

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

The formulation, when diluted at 25 ± 5°C (Note 4) with CIPAC standard waters A and D, shall comply with the following:

Time after dilution	Limits of stability
0 h	Initial emulsification complete
0.5 h	“Cream”: none
2.0 h	"Cream": none "Free oil": none
24 h	Re-emulsification complete
24.5 h	"Cream": none "Free oil": none.
Note: tests at 24 h are required only where the results at 2 h are in doubt.	

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

Maximum: 40 ml after 1 min.

5 Storage stability

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

After storage at 0 ± 2°C for 7 days, no separation of particulate or oily matter shall be visible after gentle agitation.

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

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

- pH range (4.1),
- emulsion stability and re-emulsification (4.3).

Note 1 All physical and chemical tests listed in this specification are to be performed with a laboratory sample taken after the recommended homogenisation procedure.

Before sampling to verify the formulation quality, the commercial container must be inspected carefully. On standing, emulsions may develop a concentration gradient, which could even result in the appearance of a clear liquid on the top (sedimentation

of the emulsion) or on the bottom (creaming up of the emulsion). Therefore, before sampling, the formulation must be homogenised 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.

Note 2 If the buyer requires both g/kg and g/l at 20°C, then in case of dispute, the analytical results shall be calculated as g/kg.

Note 3 There are no relevant impurities to be controlled in products of the manufacturers identified in evaluation reports 333/2004, 333/2005, 333/2006.2, 333/2008.2 and 333/2012.2. However, becisthemic acid chloride [(1*R*,3*R*)-3-(2,2-dibromovinyl)-2,2-dimethylcyclopropane carboxoyl chloride], sometimes spelt bicisthemic acid chloride, can occur as a result of certain manufacturing processes. If this impurity could occur at ≥1 g/kg (of deltamethrin) in the products of other manufacturers, it would be designated as a relevant impurity, and a clause would be required to limit its concentration.

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 be at the highest rate of use recommended by the supplier. The test is to be conducted in CIPAC standard water D at 25 ± 5°C.

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

PART TWO: EVALUATION REPORTS

DELTAMETHRIN

DELTAMETHRIN

FAO/WHO Evaluation Report 333/2023

Summary of Action

The last revision of the deltamethrin WT formulation specification included clauses as disintegration of tablets (MT 197), wet sieve test (MT 185.1), suspensibility (MT 184.1), persistent foam (MT 47.3), tablet integrity and attrition resistance of tablets (MT 178.2).

The deltamethrin WT formulation submitter was contacted to inquiry for its willingness to continue supporting the established specification. The submitter did not wish to continue supporting the WT specification. Hence, the WT specification is withdrawn.

The deltamethrin WT formulation specification can be re-established based on a new submission.

DELTAMETHRIN

FAO/WHO Evaluation Report 333/2022

Recommendations

The Meeting recommended the following:

(i) The deltamethrin TC as proposed by Hemani Industries Ltd should be accepted as equivalent to the deltamethrin reference profile.

(ii) The existing FAO specification for deltamethrin TC should be extended to encompass the technical material produced by Hemani Industries Ltd.

(iii) The existing WHO specification for deltamethrin TC should be extended to encompass the technical material produced by Hemani Industries Ltd.

Appraisal

The Meeting considered a data package submitted by M/s Hemani Industries Ltd (Hemani) in 2021 in support of extension of the existing FAO and WHO specifications for deltamethrin TC. The reference specifications for deltamethrin TC and formulated products were initially submitted by Bayer CropScience and published in 2004. After several extensions and a revision in 2016 to better reflect the ISO common name definition of deltamethrin, the current TC specification was published in 2017 with a minimum purity of 985 g/kg.

The data submitted were in accordance with the requirements of the Manual on the development and use of FAO and WHO specifications for chemical pesticides (2022, Second Edition).

The Meeting was provided with commercially confidential information on the manufacturing process and five-batch analysis data on deltamethrin and all impurities present at or above 1 g/kg, and their manufacturing limits in the TC.

The confidential data provided on the manufacturing process and five-batch analysis data of deltamethrin TC from Hemani were stated to be identical to those submitted for registration in the EU, Brazil, Mexico and Australia. Certificates of registration were provided from the Australian and French authorities, reflecting the minimum purity of 985 g/kg.

The manufacturing process, impurity profile and five-batch analyses were comparable with the data submitted by Bayer in the reference profile.

The mass balance in the five-batch data ranged from 993.25 g/kg to 995.39 g/kg. The maximum limits for the impurities were supported by the five-batch data and they are statistically justified. The proposer declared the minimum purity of the deltamethrin TC as 985 g/kg which is statistically justified (mean value – 3 standard deviations = 985 g/kg) and is identical to the minimum purity in the FAO/WHO reference specification.

No new organic impurities were identified in the Hemani deltamethrin technical material. Batches were analysed for the presence of process solvents used during manufacture; these were not detected in the batches at the respective LODs which were much lower than 0.5 g/kg.

The determination of deltamethrin in deltamethrin TC in the possible presence of other stereoisomers relies on the combined use of the chemical purity normal phase HPLC method 333/TC/M2/3 published in CIPAC Handbook L and of the peer-validated stereospecific HPLC method 333/TC/M2/4 published in CIPAC Handbook O. These CIPAC methods were used for the determination of deltamethrin in the five-batch analysis study. Although not required, validation data were also provided for the chemical purity method and are acceptable.

Water was determined by CIPAC method MT 30.6. Other impurities were determined by in-house methods using HPLC-UV, GC-MS, UV spectroscopy and GC-FID. The methods are considered fully validated.

The Meeting was provided with data on the melting point, vapour pressure, octanol/water partition coefficient, and solubility in water and organic solvents for technical deltamethrin. Although not all required, these physical-chemical properties were agreement with those of the reference technical material. Test methods employed for determination of physico-chemical properties were OECD test methods.

A mutagenicity study (Ames test) was conducted as part of the Tier 1 data package and reviewed by the Meeting. Deltamethrin TC from Hemani did not show mutagenicity in *in vitro* bacterial assays under the conditions of this study (OECD 471).

On basis of Tier-1 data provided by Hemani (manufacturing process, purity/impurity profile, 5-batch analysis data, mutagenicity profile), the meeting concluded that the deltamethrin TC from Hemani Industries Ltd. should be considered as equivalent to the reference profile supporting the existing FAO and WHO specifications 333/TC (FAO/WHO evaluation report 333/2004).

Additional action proposed by the Meeting

The Meeting recommended updating the FAO and WHO formulation specifications aligning them with the most recent versions of the specification templates in the Manual, in particular with the current and latest versions of CIPAC MT methods. They include:

- replacement of method for dry sieve test MT 59.1 by MT 170 as published in CIPAC Handbook F, for the DP;
- replacement of method for wet sieve test MT 185 by MT 185.1 as accepted as provisional CIPAC method in 2023, for the WP, SC, SC-PE, WG, WG-SB and EG;
- replacement of method for suspensibility MT 184 by MT 184.1 as published in CIPAC Handbook P, for the WP, SC, SC-PE, WG and WG-SB;
- replacement of method for spontaneity of dispersion MT 160 by MT 160.1 as accepted as full CIPAC method in 2023, for the SC and SC-PE;
- referencing of the CIPAC method MT 171.1 for dustiness as published in CIPAC Handbook P, for the WG and EG;
- replacement of method for flowability MT 172.1 by MT 172.2 as published in CIPAC Handbook P, for the WG and WG-SB;
- replacement of method for stability at elevated temperature MT 46.3 by MT 46.4 as published in CIPAC Handbook P, for the DP, WP, SC, SC-PE, EC, UL, WG, WG-SB, EW, WT, EG and LB;

- referencing of the CIPAC method MT 195 for wash resistance index as published in CIPAC Handbook O, for the LB;
- update of some footnotes.

These revised MT methods are considered to provide equivalent results as the previous versions, so all limits in the concerned clauses remain the same as for the previous versions.

Supporting Information
for
Evaluation Report 333/2022

Physico-chemical properties of deltamethrin

Table 1. Chemical composition and properties of deltamethrin 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 99.3–99.5% and percentages of unknowns were 0.46–0.68%.
Declared minimum deltamethrin content	985 g/kg
Relevant impurities ≥ 1 g/kg and maximum limits for them	None
Relevant impurities < 1 g/kg and maximum limits for them	None
Stabilisers or other additives and maximum limits for them	None

Parameter	Value and conditions	Purity %	Method reference	Study number
Melting point of the TC	100.3°C (range 98.8 – 100.4°C)	98.9	OECD 102, OPPTS 830.7200	G16652
Solubility in organic solvents at 20°C	acetone > 250 g/L methanol 8.085 g/L 1,2-dichloroethane > 250 g/L ethyl acetate > 250 g/L p-xylene 160-200 g/L n-heptane 2.694 g/L	98.9	OECD 105, OPPTS 830.7840	G20284

Annex 1: Hazard Summary Provided by the Proposer

Notes.

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

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

Table 2. Mutagenicity profile of deltamethrin technical material based on *in vitro* tests

Species	Test	Purity %	Guideline, duration, doses and conditions	Result	Study number
Salmonella typhimurium (TA1537, TA1535, TA98, TA100) *Escherichia coli* WP2uvrA (pKM101)	Bacterial reverse mutation (*in vitro*)	98.9	OECD 471, 68 h, doses: 16 - 5000 µg/plate in DMSO, with and without metabolic activation	Negative	G16668

Annex 2: References

Study number	Author(s)	Year	Study title. Study identification number. Report identification number. GLP [if GLP]. Company conducting the study
FAO/WHO Manual	FAO/WHO	2022	Manual on the Development and Use of FAO and WHO Specifications for Chemical Pesticides, Second Edition. Food and Agriculture Organization of the United Nations / World Health Organization, Rome and Geneva.
CIPAC L	Dobrat W. and Martijn A.	2005	CIPAC Handbook Volume L. Analysis of Technical and Formulated Pesticides. CIPAC methods 333/TC/M2/2 & 3, p. 46.
CIPAC O	de Oliveira M. C. C. Garvey J. and Patrian B.	2017	CIPAC Handbook Volume O. Analysis of Technical and Formulated Pesticides. CIPAC method 333/TC/M2/4, p. 39.
G16652	Bhavya V.	2020	Determination of Melting Point and Melting Range of Deltamethrin Technical. GLP. Eurofins Advinus Ltd. Unpublished.
G16668	Rani S.D.	2020	Deltamethrin Technical: Bacterial Reverse Mutation Test. GLP. Eurofins Advinus Ltd. Unpublished.
G20284	Bhavya V.	2021	Determination of Solubility of Deltamethrin Technical in Organic Solvents. GLP. Eurofins Advinus Ltd. Unpublished.
G16647	Gogineni R.	2020	Five Batch Analysis of Deltamethrin Technical. GLP. Eurofins Advinus Ltd. Unpublished.

DELTAMETHRIN

FAO/WHO Evaluation Report 333/2017.7

Recommendations

The Meeting recommended the following:

(i) The deltamethrin TC as proposed by Sharda CropChem Limited should be accepted as equivalent to the deltamethrin reference profile.

(ii) The FAO and WHO specifications for deltamethrin TC (November 2017) should be extended to encompass the TC from Sharda CropChem Limited.

(iii) The existing WHO specification for deltamethrin WP should be extended to encompass the corresponding product of Sharda Cropchem Limited.

(iv) The existing WHO specification for deltamethrin SC should not be extended to encompass the corresponding product of Sharda Cropchem Limited.

Appraisal

The Meeting considered data and information submitted by Sharda Cropchem Limited (India) in support of extension of the existing FAO and WHO specifications for deltamethrin TC, and the existing WHO specifications for deltamethrin SC and WP. The data submitted by Sharda Cropchem Limited were largely in accordance with the requirements of the Manual on development and use of FAO and WHO specifications for pesticides (November 2010 - second revision of the First Edition) (Section 3.2).

The Meeting was provided by Sharda Cropchem Limited with commercially confidential data on the manufacturing process, the manufacturing specification and 5-batch analysis data for deltamethrin and all detectable impurities. The manufacturing process provided by Sharda Cropchem Limited is not exactly the same as the one from the reference process but based on an overall assessment of the synthetic routes, it is not expected that there will be any significant difference with regards to relevant impurities.

Sharda Cropchem Limited stated that their deltamethrin TC have been submitted for registration in the UK. The confidential information (manufacturing process, purity and impurity profile) submitted to FAO/WHO was confirmed by the Chemicals Regulation Directorate as being identical to that submitted for registration in UK, and was evaluated and considered acceptable by the UK.

The 5-batch analysis study was performed according to GLP guidelines. The CIPAC method 333/TC/M2/3 (normal phase HPLC-DAD) was used for determination of deltamethrin in combination with the CIPAC chiral identity test (333/TC/M2/4). Sharda used a reference standard mixture of all 8 isomers for this purpose and this mixture was provided by Bayer CropScience. Sharda used the CIPAC method 333/TC/M2/4 on 5-batches of TC and confirmed the complete separation of all 8 isomers. The deltamethrin manufacturing impurities were determined by either

reverse phase or normal phase HPLC-DAD (with confirmation by MS) or GC-FID. Sharda used GC-FID for the analysis of a chlorinated solvent used in the manufacturing process. All the analytical methods used in the 5-batch analysis study were fully validated with respect to their specificity, linearity of response, accuracy, repeatability and limits of quantification.

The minimum purity of deltamethrin in the TC is 985 g/kg and complies with the revised FAO/WHO specification. Mass balances are high (99.7 – 100.1%), with no unknowns detected. The proposed manufacturing maximum limits for the only two impurities included in the manufacturing QC limits were fully supported by the 5-batch analysis data. All the other manufacturing impurities were below the LOQ and well below 1 g/kg.

The becisthemic acid chloride [(1*R*,3*R*)-3-(2,2-dibromovinyl)-2,2-dimethylcyclo propane carboxoyl chloride], which would be designed as a relevant impurity if it would occur at ≥ 1g/kg (of deltamethrin) according to the existing FAO/WHO specification, is well below this threshold (below the LOQ of 0.05 g/kg in 5-batch). The Meeting agreed therefore that becisthemic acid chloride should remain a non-relevant impurity. The Meeting agreed also that water is not a relevant impurity in the TC at a concentration < 1 g/kg.

The manufacturer was questioned about the possible presence of chlorinated solvents, catalysts and other raw materials in the final TC. The manufacturer answered that substances other than those identified and quantified in the 5-batch were not present at levels ≥ 1.0 g/kg and this statement was supported by HPLC-DAD analysis. The applicant also used a fully validated GC-FID method that confirmed that a potential chlorinated solvent was not present at levels > 0.1 g/kg. The analysis was supported by a very high mass balance in the 5-batch analysis data (99.7 - 100.1%). The Meeting agreed that the chlorinated solvents, catalysts and other raw materials should not be considered relevant impurities in the final TC.

Sharda Cropchem Limited provided the Meeting with mutagenicity data (supported by GLP studies) on *Salmonella typhimurium* (reverse mutation Ames test) showing that no mutagenic effect was observed.

It was noted that there are two new impurities in the new source of TC when compared with the reference source. Both impurities are isomers of each other with one impurity being present at < 1 g/kg and the other impurity being present at ≥ 5.0 g/kg. Therefore, on the basis of all Tier-1 data provided by Sharda Cropchem Limited (manufacturing process, impurity profile, 5-batch analysis data, mutagenicity profile), the Meeting could not conclude that the Sharda Cropchem Limited deltamethrin TC should be considered as equivalent to the reference profile supporting the existing FAO and WHO specifications (FAO/WHO evaluation report 333/2004). Therefore the Meeting considered Tier-2 data.

Sharda Cropchem Limited also provided the Meeting with acute toxicity, irritation and sensitization data, as well as data on the physico-chemical properties of pure deltamethrin (vapour pressure, melting point, solubility in water and in organic solvents, octanol / water partition coefficient). These studies were performed using OECD, EU or CIPAC methods and according to GLP principles. A detailed comparison of acute tox endpoints such as acute oral, skin and eye irritation and skin sensitization did not indicate that the material produced by Sharda should be considered as more hazardous than the reference material.

These additional Tier-2 data indicated equivalence of the Sharda Cropchem Limited deltamethrin TC with the reference profile supporting the existing FAO and WHO specifications (FAO/WHO evaluation report 333/2016).

The Meeting also considered the possibility of requesting 28 or 90 days toxicity studies based on new criteria, however the Meeting considered that the information would not be necessary in this case.

The Meeting was provided by Sharda Cropchem Limited with data on the physical and chemical properties of their deltamethrin 2.5% SC and 2.5% WP formulations. The Meeting noted that the deltamethrin 2.5% SC did not comply with the existing WHO specification for deltamethrin SC, and therefore had not a reference product to be compared with, so the evaluation of this product could not progress further.

Sharda provided a GLP 5-batch analysis report for the WP formulation. The most recent CIPAC methods were used for the 5-batch WP study and the specification clause limits were met in all cases for the WP. The proposer used the published method for content in the WP (CIPAC 333/WP/(M)/3).

The Meeting agreed also, in the specifications for deltamethrin WP, SC, SC-PE, EC, WG, WG-SB, EW and EG, to refer to the CIPAC method MT 47.3 for persistent foam as published in Handbook O, and in the specification for deltamethrin WG, to update the CIPAC method for dustiness (MT 171.1 instead of MT 171) to be in line with the current CIPAC methods.

Supporting Information

for

Evaluation Report 333/2017.7

Physico-chemical properties of deltamethrin

Table 1. Chemical composition and properties of deltamethrin technical material (TC)

Manufacturing process, maximum limits for impurities ≥ 1 g/kg, 5 batch analysis data	Confidential information supplied and held on file by FAO and WHO. Mass balances were 99.7 – 100.1% with no unknowns.
Declared minimum deltamethrin content	985 g/kg
Relevant impurities ≥ 1 g/kg and maximum limits for them	None
Relevant impurities < 1 g/kg and maximum limits for them	None
Stabilisers or other additives and maximum limits for them	None

Parameter	Value and conditions	Purity %	Method reference	Study number
Melting temperature range of the TC	92.5 - 95.0°C (No decomposition occurs)	98.5	OECD 102EEC A.	CH-200/2008
Solubility in organic solvents	2 g/l n-hexane at 22°C 8 g/l methanol at 22°C 675 g/l acetone at 22°C 550 g/l ethyl acetate at 22°C 725 g/l dichloromethane at 22°C 275 g/l xylene at 22°C	98.5	CIPAC MT 181	CH-210/2008

Formulations and co-formulated active ingredients

The main formulation types available are SC, AL, DP and WP as public health formulations.

Deltamethrin may be co-formulated with piperonyl butoxide, abamectin, alpha-cypermethrin, azaconazole, buprofezin, chlorpyrifos, dichlorvos, difethialone, diflubenzuron, dimethoate, endosulfan, esbiothrin, fenitrothion, imidacloprid, pirimicarb, S-bioallethrin, tetramethrin, thiacloprid and triazophos.

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

Methods of analysis and testing

The analytical methods for the active ingredient (including identity tests) are CIPAC method 333/SC/M/2 and CIPAC method 333/SC/M/3 for SC formulation, CIPAC method 333/WP/M/2 and CIPAC method 333/WP/M/3 for WP formulation

The method(s) for determination of impurities are based on CIPAC method 333/TC/M2/3.

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

Containers and packaging

No special requirements for containers and packaging have been identified.

Expression of the active ingredient

The active ingredient is expressed as deltamethrin.

Annex 1: Hazard Summary Provided by the Proposer

Notes.

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

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

Table 2. Toxicology profile of deltamethrin technical material, based on acute toxicity, irritation and sensitization

Species	Test	Purity %	Guideline, duration, doses and conditions	Result	Study number
Rat (Rattus norvegicus) Strain: Wistar Females	Oral acute	Batch SWL-0291 98.5	Guidelines of OECD N° 423 (December 2001). Female Wistar rats fasted overnight were dosed with deltamethrin technical in vegetable oil as single oral gavage, using intubation cannula. The feed was withheld until 3 h post dosing. The first set (set I) of three female rats was given a single dose of 300 mg deltamethrin technical/kg body weight. All three rats were found dead at this dose level hence the second set (set II) of three female rats was given at the lower dose. level of 50 mg deltamethrin technical/kg body weight. One mortality was observed at this dose level so the third set (set III) of three female rats was given at the same dose level of 50 mg deltamethrin technical/kg body weight. One mortality was observed at this dose, so the endpoint was achieved and further testing was not required.	LD_{50} >50 mg/kg bw	SCL-A-01-001 JRF: 401-1-01-6589
Rat (Rattus norvegicus) Strain: Wistar Females	Dermal acute	Batch SWL-0291 98.5	The method followed was as per the guideline of OECD N° 402 (February 1987). This study was performed as a limit study. Two groups of Wistar rats, each comprising 5 males and 5 females were randomly selected for the study. An area greater than, 10 percent of the body surface was clipped 24 h prior to the dermal application of the test item. One group (group I) served as the control and was treated with 0.2 mL distilled water. The other group (group II) was given a limit dose of 2000 mg deltamethrin technical/kg body weight. A calculated dose quantity (472 to 598 mg) of deltamethrin technical (moistened with 0.2 mL distilled water) was applied over the clipped area (approximately 7 x 5 cm of body surface) by single dermal application and observed for a period of 14 days.	LD_{50} = 2000 mg/kg bw	SCL-A-01-002 JRF: 403-1-01-6590
Rat (Rattus norvegicus) Strain: Wistar Females	Inhalation acute	Batch SWL-0291 98.53 ± 0.0924 % w/w	The method followed was as per the guidelines of OECD N° 403 (September 2009). The study was conducted using inhalation equipment (head/nose only exposure). A group of rats	LC_{50} > 689 mg/m^3	SCL-A-01-003 JRF: 405-1-01-6591

			comprising three males and three females were used for the study. The rats from group I were exposed to the maximum achievable breathing zone concentration (0.689 mg/L air) of deltamethrin technical. Rats from group I were exposed for 4 h followed by observation for a period of 14 days.		
Rabbit (Oryctolagus cuniculus) Strain : New Zealand White. Male	Skin irritation acute	Batch SWL-0291 98.53 ± 0.0924 % w/w	The method followed was as per the guidelines of the OECD N° 404 (April 2002). Three healthy, adult male albino rabbits of the New Zealand White strain were selected for the study. Initially one rabbit was tested with a single patch for a period of 4 h. Based on the observation at 24 h post patch removal, the irritation response was confirmed by testing two additional rabbits simultaneously. An amount of 500 mg of deltamethrin technical (moistened with 0.5 mL distilled water) was applied evenly to the intact skin of rabbits. The control skin site of the rabbits was applied with 0.5 mL distilled water and was found normal throughout the experimental period. The treated and the control sites were covered with gauze patch and secured at the margins by non-irritating tape for a period of 4 h. At the end of 4 h exposure period, the residual test item was removed with cotton soaked in distilled water. The skin reactions were observed at 1, 24, 48 and 72 h post patch removal.	Non irritant	SCL-A-01-004 JRF: 406-1-01-6592
Rabbit (Oryctolagus cuniculus) Strain : New Zealand White Females	Eye irritation acute	Batch SWL-0291 98.53 ± 0.0924 % w/w	The method followed was as per guidelines of the OECD N° 405 (October 2012) Three healthy, adult, female albino rabbits of New Zealand White strain were selected for the study. Initiallyone rabbit was tested. Based on the results obtained at 24 h post test item application (TIA) observation, the irritation response was confirmed by testing two additional rabbits simultaneously. A volume of 0.1 mL deltamethrin technical was applied into one eye of each rabbit and the contralateral eye served as the control. Observations were made following the method described in the guidelines at 1 h (on day 0), 24, 48 and 72 h post application.	Non irritant	SCL-A-01-005 JRF: 407-1-01-6593

Guinea pig Species (strain) : Cavia porcellus (Hartley) Males	Skin sensitisation acute	Batch SWL-0291 98.53 ± 0.0924 % w/w	The method followed was as per the guidelines of OECD N° 406 (July 1992) using the Guinea-pig Maximization Test Method. Fifteen Hartley strain male guinea pigs were randomly divided into two groups. The control group comprised 5 guinea pigs and the treatment group comprised 10 guinea pigs. Based on the results of the pilot study, 1.0% (w/v) deltamethrin technical in propylene glycol was selected for intradermal injection during induction exposure on day 0. Since deltamethrin technical was found to be non-irritant when applied topically (Refer: pilot study), clipped site was applied on day 6 with 0.5 mL 10% (w/v) sodium lauryl sulphate in vaseline to augment the local skin irritation. A quantity of 100 mg deltamethrin technical moistened with 0.2 mL 80% ethanol was selected for topical application during induction on day 7 and 100 mg deltamethrin technical moistened with 0.2 mL acetone was selected for challenge exposure on day 21.	Non sensitizing agent	SCL-A-01-006 JRF: 408-1-01-6594

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

Species	Test	Purity %	Guideline, duration, doses and conditions	Result	Study number
Salmonella typhimurium viz. Strains: TA1537, TA1535, TA98, TA100 and TA102	Test in Vitro. Code 481-1-06-8041	Batch SWL-0291 98.53 ± 0.0924 % w/w	OECD 471 “Bacterial Reverse Mutation Test” Based on the results of the cytotoxicity test, the test concentrations of 156.25, 312.5, 625, 1250, 2500 and 5000 µg/plate of deltamethrin technical in the absence and presence (5% v/v S9 mix) of metabolic activation were tested.	From the results of this study, under the specified experimental conditions, deltamethrin technical is concluded to be non-mutagenic in the bacterial reverse mutation assay using *Salmonella typhimurium*	SCL-A-01-007 JRF: 481-1-06-8041

Annex 2: References

Study number	Author(s)	Year	Study title. Study identification number. Report identification number. GLP [if GLP]. Company conducting the study
	FAO/WHO	2016	Manual on development and use of FAO and WHO specifications for pesticides. First edition - third revision, http://www.fao.org/3/a-i5713e.pdf and http://www.who.int/whopes/resources/9789251092651/en/
41204558	A.J. Woolley	2013	Deltamethrin 2.5% SC. Determination of physico-chemical properties. Study No. 41204558. GLP. Harlan laboratories LTD. Unpublished.
	Escudero J.A.	2017	Physico-Chemical Characterization of Deltamethrin 2.5% WP. GLP. Laboratorios Munuera.
JRF 401-1-01-6589		2013	Acute Oral Toxicity Study of Deltamethrin Technical in Rats. GLP.
JRF 403-1-01-6590		2013	Acute Dermal Toxicity of Deltamethrin Technical in Rats. GLP.
JRF 405-1-01-6591		2013	Acute Inhalation Toxicity Study of Deltamethrin Technical in Rats. GLP.
JRF – 406-1-01-6592		2013	Acute Dermal Irritation Study of Deltamethrin Technical in Rabbits. GLP.
JRF – 407-1-01-6593		2013	Acute Eye Irritation of Deltamethrin Technical in Rabbits. GLP.
JRF – 408-1-01-6594		2013	Skin Sensitization Study of Deltamethrin Technical in Guinea Pigs. GLP.
JRF-481-1-06-8041	Gaikwad, S.S.	2014	Bacterial Reverse Mutation Test of Deltamethrin Technical Using Salmonella typhimurium.

DELTAMETHRIN

FAO/WHO Evaluation Report 333/2017.6

Recommendations

The Meeting recommended the following:

(i) The deltamethrin TC produced by Youth Chemical Co., Ltd. (a subsidiary company of Jiangsu Yangnong Chemical Co. Ltd.) should be accepted as equivalent to the deltamethrin reference profile.

(ii) The FAO and WHO specifications for deltamethrin TC (November 2017) should be extended to encompass the TC manufactured by Youth Chemical Co., Ltd. (a subsidiary company of Jiangsu Yangnong Chemical Co. Ltd.).

Appraisal

The Meeting considered data for deltamethrin TC submitted by Jiangsu Yangnong Chemical Co. Ltd. (Jiangsu Yangnong) in October 2016.

The data were evaluated in support of an extension of the revised FAO/WHO specification 333/TC (November 2017). The reference specification and supporting data were provided by Bayer CropScience, published in 2005 and revised in 2016.

The data were broadly in accordance with the requirements of the March 2016 (3rd revision of the 1st edition) of the FAO/WHO Manual.

The manufacturer submitted confidential data on the manufacturing process together with the manufacturing specification and batch analysis data on purity and impurities ≥ 1 g/kg.

The confidential data presented are claimed to be identical to those submitted to ICAMA for registration in China. A Letter of Access and a certificate of registration were submitted by the company.

The manufacturing process is similar to the one used by Bayer CropScience with regard of starting materials and reaction conditions, so in principle no major new impurities in comparison to the reference product may be expected.

In the revised FAO and WHO deltamethrin TC specifications published in November 2017, an enantioselective analytical method in combination with a chemical purity method is used to determine the deltamethrin content in the possible presence of other stereoisomers but not belonging to deltamethrin. The data submitted by Jiangsu Yangnong using these methods demonstrate that the content of deltamethrin in all batches is above the minimum purity of 985 g/kg. The analysed batches were produced over a period of three years.

In addition, analytical data on the content of the potentially relevant impurity becisthemic acid chloride in deltamethrin TC were submitted on request. The content of becisthemic acid chloride in all batches is clearly below the threshold of relevance.

The company utilizes a catalyst system in the manufacturing process where two intermediates react to form deltamethrin. The Meeting questioned the efficiency how the catalyst is removed from the crude reaction product. On request, the manufacturer submitted further confidential information on that catalyst and how it is removed from the TC. The Meeting considered the additional information and concluded that the catalyst can be efficiently removed from the crude reaction product and that residues of the catalyst should not be part of the manufacturing specification.

The content of an aromatic solvent which is used in the manufacturing process was determined and found to be below the LOQ (0.002 %) in 8 batches.

According to the Bacterial reverse mutation test submitted the TC of the manufacturer is not mutagenic.

The Meeting therefore concluded that based on the data submitted the deltamethrin TC from Jiangsu Yangnong can be considered as equivalent to the reference profile on Tier-1.

The manufacturer did not propose specifications for deltamethrin formulated products.

Supporting Information
for
Evaluation Report 333/2017.6

Physico-chemical properties of deltamethrin

Table 1. Chemical composition and properties of deltamethrin 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 98.98 - 99.27% and percentages of unknowns were 0.73 - 1.02%			
Declared minimum deltamethrin content	985 g/kg			
Relevant impurities ≥ 1 g/kg and maximum limits for them	None			
Relevant impurities < 1 g/kg and maximum limits for them	None			
Stabilisers or other additives and maximum limits for them	None			
Parameter	Value and conditions	Purity %	Method reference	Study number
Melting temperature range of the TC	103.1°C	98.6%	OECD 102	2016G76

Formulations and co-formulated active ingredients

No formulation specifications were proposed by the company.

Methods of analysis and testing

The analytical method for the active ingredient (including identity tests) is 333/TC/M2/2 and 333/TC/M2/3, CIPAC Handbook L, p. 46, 2006 and Handbook O, p. 39, 2017.

Deltamethrin is determined by normal phase HPLC, using UV detection at 230 nm and external standardisation.

The enantiomeric purity is determined by HPLC on a chiral column.

Test method for determination of physico-chemical properties (only melting point) of the technical active ingredient was OECD 102 (DSC).

Containers and packaging

No special requirements for containers and packaging have been identified.

Expression of the active ingredient

The active ingredient is expressed as deltamethrin.

Annex 1: Hazard Summary Provided by the Proposer

Notes.

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

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

Table 2. Mutagenicity profile of deltamethrin technical material based on *in vitro* tests

Species	Test	Purity %	Guideline, duration, doses and conditions	Result	Study number
Salmonella enteric serovar typhimurium Test strains: TA97a,TA98, TA100, TA102 and TA1535	Ames Test	98.6	OECD 471 0.128, 0.32, 0.8, 2.0 and 5.0 mg/plate mixed in DMSO (with and without S9 mix) 37℃ for 70 hours	Not mutagenic	2016-419-01-7

Annex 2: References

Study number	Author(s)	Year	Study title. Study identification number. Report identification number. GLP [if GLP]. Company conducting the study
	FAO/WHO	2016	Manual on development and use of FAO and WHO specifications for pesticides. March 2016 1st Edition 3rd revision. FAO Plant Production and Protection Paper. www.fao.org/ag/AGP/AGPP/Pesticid/Default.htm and http://apps.who.int/iris/bitstream/10665/246192/1/WHO-HTM-NTD-WHOPES-2016.4-eng.pdf?ua=1
2016G76	Hou Songmei	2016	Melting Point Test of Deltamethrin TC. RF 2016G76. GLP. Pesticides Test Laboratory of Shenyang Research Institute of Chemical Industry.
2016-419-01-07	Li LiLy	2016	Bacterial Reverse Mutation Test of Deltamethrin TC. 2016-419-01-07. RF2016-419-01-07. GLP. Suzhou Xishan Zhongke Drug R & D Co., Ltd.
YNGF-2016-002	Sun Chunyan	2016	Determination of active ingredient in Deltamethrin TC. YNGF-2016-002. RF YNGF-2016-002. GLP. Jiangsu Yangnong Chemical Co., Ltd.
YA-008	Vlado Damnjanovic	2014	Determination of the Active Content and Impurity Profile of Deltamethrin. YA-008. RF.YA-008. GLP. Agrifor Scientific Pty Ltd.
-	-	2017	Additional information on catalyst (Template).
YNGF-2017-0003	Weilian Shi	2017	Determination of (aromatic solvent XYZ) in deltamethrin TC, Report No YNGF-2017-003, 17/08/2017, GLP, Jiangsu Yangnong Chemical Co., Ltd.

DELTAMETHRIN

FAO/WHO Evaluation Report 333/2017.5

Recommendations

The Meeting recommended the following:

(i) The deltamethrin TC produced by Tagros Chemicals India Ltd. should be accepted as equivalent to the deltamethrin TC (revised) from Bayer CropScience.

(ii) The revised FAO specification for deltamethrin TC (November 2017) should again be extended to encompass the TC from Tagros Chemicals India Ltd.

(iii) The revised WHO specification for deltamethrin TC (November 2017) should again be extended to encompass the TC from Tagros Chemicals India Ltd.

Appraisal

The Meeting considered data for deltamethrin TC submitted in February 2017 by Tagros Chemicals India Ltd. (Tagros). The data were requested by the Meeting as a consequence of the revision of the deltamethrin reference specification (published in November 2017) and was evaluated to allow a conclusion, whether or not the deltamethrin TC produced by Tagros was still equivalent.

The reference specification and supporting data were provided by Bayer CropScience, published in 2005 and revised in 2016.

In the revised specification for deltamethrin TC, an additional enantioselective analytical method was introduced, allowing to resolve and quantify deltamethrin in the possible presence of other stereoisomers.

The data submitted by the manufacturer Tagros using this method allow the conclusion that the content of deltamethrin in all batches is above the minimum purity of 985 g/kg. The Meeting accepted this as other parameters like manufacturing process or impurity profile had already been evaluated in the original evaluations and had not changed since then.

Based on the data submitted the existing equivalence for TC should be regarded as valid also for the revised specification.

As the original batches were no longer available (the batches had been analyzed under GLP and had expired) different, recently produced batches were used for the analysis. This was considered acceptable by the Meeting.

The new enantioselective method is only applicable to the TC, not for formulated products. The Meeting regarded the method used for the formulated products in the published specifications as still acceptable. The equivalence for formulated product mentioned in evaluation reports 333/2005 and 333/2014.4 is valid without further review.

Annex 1: References

Study number	Author(s)	Year	Study title. Study identification number. Report identification number. GLP [if GLP]. Company conducting the study
		2017	Determination of deltamethrin content and enantiomeric purity in five batches of deltamethrin technical, Tagros Chemicals India Private Limited, 87 pages.

DELTAMETHRIN

FAO/WHO Evaluation Report 333/2017.4

Recommendations

The Meeting recommended the following:

(i) The deltamethrin TC produced by Rotam Agrochemical Co., Ltd. should be accepted as equivalent to the deltamethrin TC (revised) from Bayer CropScience.

(ii) The revised FAO specification for deltamethrin TC (November 2017) should again be extended to encompass the TC from Rotam Agrochemical Co., Ltd.

(iii) The revised WHO specification for deltamethrin TC (November 2017) should again be extended to encompass the TC from Rotam Agrochemical Co., Ltd.

Appraisal

The Meeting considered data for deltamethrin TC submitted in June 2017 by Rotam Agrochemical Co., Ltd. (Rotam). The data were requested by the Meeting as a consequence of the revision of the deltamethrin reference specification (published in November 2017) and was evaluated to allow a conclusion, whether or not the deltamethrin TC produced by Rotam was still equivalent.

The reference specification and supporting data were provided by Bayer CropScience, published in 2005 and revised in 2016.

In the revised specification for deltamethrin TC, an additional enantioselective analytical method was introduced, allowing to resolve and quantify deltamethrin in the possible presence of other stereoisomers.

The data submitted by the manufacturer Rotam using this method allow the conclusion that the content of deltamethrin in all batches is above the minimum purity of 985 g/kg. The Meeting accepted this as other parameters like manufacturing process or impurity profile had already been evaluated in the original evaluations and had not changed since then.

Based on the data submitted the existing equivalence for TC should be regarded as valid also for the revised specification.

As the original batches were no longer available, different, recently produced batches were used for the analysis. This was considered acceptable by the Meeting.

The new enantioselective method is only applicable to the TC, not for formulated products. The Meeting regarded the method used for the formulated products in the published specifications as still acceptable. The equivalence for formulated product mentioned in evaluation report 333/2014.2 is valid without further review.

Annex 1: References

Study number	Author(s)	Year	Study title. Study identification number. Report identification number. GLP [if GLP]. Company conducting the study
2044	Scott Luo	2017	Determination of enantiomer content in five representative production batches of deltamethrin technical, Study No 2044, Rotam Research Laboratory, 1 June 2017.

DELTAMETHRIN

FAO/WHO Evaluation Report 333/2017.3

Recommendations

The Meeting recommended the following:

(i) The deltamethrin TC produced by ISAGRO S.p.A. should be accepted as equivalent to the deltamethrin TC (revised) from Bayer CropScience.

(ii) The revised FAO specification for deltamethrin TC (November 2017) should again be extended to encompass the TC from ISAGRO S.p.A.

(iii) The revised WHO specification for deltamethrin TC (November 2017) should again be extended to encompass the TC from ISAGRO S.p.A.

Appraisal

The Meeting considered data for deltamethrin TC submitted in November 2017 by ISAGRO S.p.A. (Isagro). The data were requested by the Meeting as a consequence of the revision of the deltamethrin reference specification (published in November 2017) and was evaluated to allow a conclusion, whether or not the deltamethrin TC produced by Isagro was still equivalent.

The reference specification and supporting data were provided by Bayer CropScience, published in 2005 and revised in 2016.

In the revised specification for deltamethrin TC, an additional enantioselective analytical method was introduced, allowing to resolve and quantify deltamethrin in the possible presence of other stereoisomers.

The data submitted by the manufacturer Isagro using this method allow the conclusion that the content of deltamethrin in all batches is above the minimum purity of 985 g/kg. The Meeting accepted this as other parameters like manufacturing process or impurity profile had already been evaluated in the original evaluations and had not changed since then.

Based on the data submitted the existing equivalence for TC should be regarded as valid also for the revised specification.

As the original batches were no longer available, different, recently produced batches were used for the analysis. This was considered acceptable by the Meeting. No reference material for the deltamethrin enantiomer *αR, 1S-cis* was available, so the company used standards for the stereoisomers *αR, 1R-cis* and *αS, 1R-trans*. Additionally the content of the potential relevant impurity bicisthemic acid chloride was determined in the five batches and found to be below the LOQ of 0.1%.

The new enantioselective method is only applicable to the TC, not for formulated products. The Meeting regarded the method used for the formulated products in the published specifications as still acceptable. The equivalence for formulated product mentioned in evaluation report 333/2012.1 is valid without further review.

Annex 1: References

Study number	Author(s)	Year	Study title. Study identification number. Report identification number. GLP [if GLP]. Company conducting the study
17039-01C	L. Gazzotti	2017	Analytical characterization (chemical content and stereoisomer content) of 5 representative batches of Deltamethrin Technical Material, Stud No 17039-01C, GLP, RenoLab S.r.l., 12 July 2017.

DELTAMETHRIN

FAO/WHO Evaluation Report 333/2017.2

Recommendations

The Meeting recommended the following:

(i) The deltamethrin TC produced by Heranba Industries Ltd. should be accepted as equivalent to the deltamethrin TC (revised) from Bayer CropScience.

(ii) The revised FAO specification for deltamethrin TC (November 2017) should again be extended to encompass the TC from Heranba Industries Ltd.

(iii) The revised WHO specification for deltamethrin TC (November 2017) should again be extended to encompass the TC from Heranba Industries Ltd.

Appraisal

The Meeting considered data for deltamethrin TC submitted in April 2017 by Heranba Industries Ltd. (Heranba). The data were requested by the Meeting as a consequence of the revision of the deltamethrin reference specification (published in November 2017) and was evaluated to allow a conclusion, whether or not the deltamethrin TC produced by Heranba was still equivalent.

The reference specification and supporting data were provided by Bayer CropScience, published in 2005 and revised in 2016.

In the revised specification for deltamethrin TC, an additional enantioselective analytical method was introduced, allowing to resolve and quantify deltamethrin in the possible presence of other stereoisomers.

The data submitted by the manufacturer Heranba using this method allow the conclusion that the content of deltamethrin in all batches is above the minimum purity of 985 g/kg. The Meeting accepted this as other parameters like manufacturing process or impurity profile had already been evaluated in the original evaluations and had not changed since then.

Based on the data submitted the existing equivalence for TC should be regarded as valid also for the revised specification.

As the original batches were no longer available, different, recently produced batches were used for the analysis. This was considered acceptable by the Meeting.

The new enantioselective method is only applicable to the TC, not for formulated products. The Meeting regarded the method used for the formulated products in the published specifications as still acceptable. The equivalence for formulated product mentioned in evaluation report 333/2006.2 is valid without further review.

Annex 1: References

Study number	Author(s)	Year	Study title. Study identification number. Report identification number. GLP [if GLP]. Company conducting the study
17009	A. Vijayakumar	2017	Active and Enantiomer Analysis of Five Batches of Deltamethrin Technical Enforcement Analytical Methods for Deltamethrin TGAI, fulfilling the Requirements of WHO specification 333/TC, OPPTS Guidelines 830.1800 and EU Commission regulation No. 283/2013 . Study No 17009, GLP, International Institute of Biotechnology and Toxicology (IIBAT), 26 April 2017.

DELTAMETHRIN

FAO/WHO Evaluation Report 333/2017.1

Recommendations

The Meeting recommended the following:

(i) The deltamethrin TC produced by Gharda Chemicals Ltd. should be accepted as equivalent to the deltamethrin TC (revised) from Bayer CropScience.

(ii) The revised FAO specification for deltamethrin TC (November 2017) should again be extended to encompass the TC from Gharda Chemicals Ltd.

(iii) The revised WHO specification for deltamethrin TC (November 2017) should again be extended to encompass the TC from Gharda Chemicals Ltd.

Appraisal

The Meeting considered data for deltamethrin TC submitted in May 2017 by Gharda Chemicals Ltd. (Gharda). The data were requested by the Meeting as a consequence of the revision of the deltamethrin reference specification (published in November 2017) and was evaluated to allow a conclusion, whether or not the deltamethrin TC produced by Gharda was still equivalent.

The reference specification and supporting data were provided by Bayer CropScience, published in 2005 and revised in 2016.

In the revised specification for deltamethrin TC, an additional enantioselective analytical method was introduced, allowing to resolve and quantify deltamethrin in the possible presence of other stereoisomers.

The data submitted by the manufacturer Gharda using this method allow the conclusion that the content of deltamethrin in all batches is above the minimum purity of 985 g/kg. The Meeting accepted this as other parameters like manufacturing process or impurity profile had already been evaluated in the original evaluations and had not changed since then.

Based on the data submitted the existing equivalence for TC should be regarded as valid also for the revised specification.

As the original batches were no longer available, different, recently produced batches were used for the analysis. This was considered acceptable by the Meeting.

The new enantioselective method is only applicable to the TC, not for formulated products. The Meeting regarded the method used for the formulated products in the published specifications as still acceptable. The equivalence for formulated product mentioned in evaluation reports 333/2008.1 and 2014.3 is valid without further review.

Annex 1: References

Study number	Author(s)	Year	Study title. Study identification number. Report identification number. GLP [if GLP]. Company conducting the studyN1701
SN1701	S. R. Nayak	2017	Analysis and certification of limits for deltamethrin technical. Study No SN1701, Report No FR 1701 FB, GLP, Gharda Chemicals Ltd., 29 April 2017.

DELTAMETHRIN

FAO/WHO Evaluation Report 333/2016.3

Recommendations

The Meeting recommended that the published FAO/WHO specification for deltamethrin TC should be revised to better reflect the ISO common name definition of deltamethrin as single pyrethroid stereoisomer.

Appraisal

The reference specification for deltamethrin was published in 2004 and supported by a data package provided by Bayer CropScience (BCS). The company submitted a new data package in 2015 (BCS, 2015) and requested the JMPS to revise the deltamethrin TC specification for the following reasons:

Despite deltamethrin being a pyrethroid insecticide consisting of a single stereoisomer (out of theoretically 8) - the *(S)*-α-cyano-3-phenoxybenzyl (*1R,3R*)-3-(2,2-dibromovinyl)-2,2-dimethylcyclopropane carboxylate according to IUPAC nomenclature - a robust quantitative identity test capable to determine deltamethrin in the presence of other stereoisomers was not available at the time of first submission in 2003. Since 2005, the content of deltamethrin in the TC was determined by a CIPAC method based on normal phase liquid chromatography using a cyano-substituted silica column capable of quantifying deltamethrin in the presence its *(R)*-α-epimer. The method - published in Handbook L - is therefore considered as suitable to determine the chemical purity of technical deltamethrin.

A previous method published in CIPAC Handbook D used normal phase HPLC on a silica column and contains a sub-method (333/TC/M/2.2) where technical deltamethrin is analyzed on a commercially available phenylglycine substituted HPLC column (Pirkle phase). However, this method is no longer recommended due to limited availability and stability of the phenylglycine column.

In order to alleviate this discrepancy between claim made in the specification and possibility to enforce that claim by a suitable and validated analytical method, BCS developed an enantioselective HPLC method capable of separating deltamethrin from all 7 stereoisomers that are related to deltamethrin but with different configurations at the stereogenic centers. That method was peer-validated, presented at the 2013 CIPAC meeting in Kiev and adopted as stereospecific quantitative identity test by CIPAC.

As the specification is actually a clarification of a composition that now can also be enforced by the new stereoselective method, a letter of access for the comparison of the confidential data and registration with the data package submitted to a regulatory authority was considered as not being necessary by the Meeting. Nevertheless, a letter of access was submitted by the BCS and CRD/UK confirmed that all data submitted to FAO/WHO were also submitted to CRD with some additional information (CRD, 2016).

For the potentially relevant impurity becisthemic acid chloride no data were provided in the 5-batch data submitted to FAO/WHO, but obviously was part of the 5-batch data submitted to CRD. The content was not detectable (LOQ = 0.5 g/kg) in all batches and so well ≤ 1 g/kg, the GHS threshold of relevance.

The content of deltamethrin in the TC remains unchanged (985 g/kg). However, the reference to the new peer validated stereospecific HPLC method is added under clause 2.1 and 2.2 and a footnote to explain that only the combined use of the chemical purity method in Handbook L and the stereospecific HPLC method provides the full information to confirm the minimum purity of deltamethrin in TC with 985 g/kg.

Annex 1: References

Study number	Author(s)	Year	Study title. Study identification number. Report identification number. GLP [if GLP]. Company conducting the study
	Bayer CropScience	2015	Data package on revision of deltamethrin submitted in October 2015 (confidential data) and January 2016 (TC specification).
	CRD UK	2016	CRD UK: e-mail confirming the similarity of data package submitted to UK and to JMPS. Date: 27/05/2016.

DELTAMETHRIN

FAO/WHO Evaluation Report 333/2016.2

Recommendations

The Meeting recommended that the existing WHO specification for deltamethrin WG-SB should be extended to encompass the corresponding product of Gharda Chemicals Ltd.

Appraisal

The Meeting considered data and information submitted by Gharda Chemicals Ltd. (India) to support the extension of the existing WHO specification 333/WG-SB (January 2015). The data submitted by Gharda were in accordance with the requirements of the Manual on development and use of FAO and WHO specifications for pesticides (November 2010 - second revision of the First Edition).

The Meeting noted that the current description for WG-SB contains ”nearly dust free or essentially non-dusty”. The Meeting discussed whether it was appropriate to retain a reference to dust in the specification description, considering that “dustiness” is not a clause in the current reference specification. The Meeting agreed to keep the reference to dust in the specification description on the basis that dust will be included as a clause in the updated Manual.

The Gharda specification was supported by results from 5 batches of deltamethrin WG-SB. Gharda provided acceptable accelerated storage stability results on the basis of WG-SB material tested at 54°C for 2 weeks. Although the actual study report did not provide information in relation to the bag integrity after accelerated storage, it was confirmed by Gharda that the bag integrity was maintained in terms of softening, deformation, shrinkage and weight change. Gharda also provided a test report from the supplier of the bag material that reported stability up to temperatures of at least 70°C over a 10 day period.

The meeting noted that WHOPES trials of deltamethrin WG had been successfully completed (WHO 2002). WHOPES evaluation on the neat formulation is also applicable to WG-SB. WHOPES recommended deltamethrin WP and WG use for indoor residual spraying (IRS) against malaria vectors at 20-25 mg active ingredient / m^2 with an expected residual effect of 3-6 months.

Annex 1: References

Study number	Author(s)	Year	Study title. Study identification number. Report identification number. GLP [if GLP]. Company conducting the study
C.DM2.0 752	Limae D. K.	2015	Physical and chemical properties of deltamethrin 25% WG-SB in accordance with WHO specification 333/WG-SB. January 2015, GLP Unpublished.
	WHO	2002	Report of the Sixth WHOPES Working Group Meeting, WHO/HQ, Geneva, 6-7 November 2002. WHO, Geneva, document WHO/CDS/WHOPES/2002.6.

DELTAMETHRIN

FAO/WHO Evaluation Report 333/2014.4

Recommendations

The Meeting recommended that the existing WHO specification for deltamethrin water dispersible granules in sealed water soluble bag (WG-SB) should be extended to encompass the corresponding product of Tagros.

Appraisal

The Meeting considered data and information submitted by Tagros to support the extension of the existing WHO specification 333/WG-SB (May 2014). The Tagros specification was supported by results from 31 batches of deltamethrin WG-SB.

Tagros proposed the introduction of a new pH clause. The current specification (Bayer CropScience) does not contain a pH clause, however Bayer provided a clause for acidity. The Meeting considered whether pH or acidity was the appropriate clause to include in the WG-SB specification. The Meeting decided that, as Tagros has an extension to the reference WG specification which specifies maximum 20 g/kg calculated as H_2SO_4, the existing clause of maximum 20 g/kg calculated as H_2SO_4 should be maintained in the specification for the WG-SB. Tagros agreed to provide acidity results for WG-SB.

Tagros proposed to extend the clause for dissolution of the bag from maximum 30 seconds to 1 minute. The meeting disagreed to extend the clause for dissolution of the bag to maximum 1 minute for the flow time suspension because the recommended CIPAC method recommends a maximum time of 30 seconds for flow time suspension. Tagros agreed to retest their WG-SB for dissolution of the bag and confirmed their deltamethrin WG-SB complies with the current specification.

Tagros had proposed additional clauses for dustiness, attrition resistance and flowability, however the Meeting considered that there was no need to include the clauses for dustiness and attrition resistance as additional clauses on the basis that exposure of the user to dust from WG-SB formulations is considered to be negligible. The Meeting agreed to include the clause for flowability, as also stated in the WG specification.

Tagros provided accelerated storage stability results on the basis of WG-SB material tested at 45°C for 6 weeks. The reference specification for WG-SB specifies test conditions of 54°C for 2 weeks under the accelerated storage stability clause. The Meeting requested Tagros to retest their WG-SB using 54°C for 2 weeks in order to obtain an extension to the WG-SB specification. Tagros agreed to carry out a new accelerated storage stability study using test conditions of 54°C for 2 weeks and confirmed that their deltamethrin WG-SB complies with the current specification.

Annex 1: References

Study number	Author(s)	Year	Study title. Study identification number. Report identification number. GLP [if GLP]. Company conducting the study
	S.K. Marne	2013	Determination of Preliminary Analysis of Deltamethrin 25% WG (PALI 250 WG) Water Soluble Bag. Report No. R/AUT1336/PANL/13. GLP.
	P.Y. Naik	2013	Determination of the Time of Complete Wetting of Deltamethrin 25% WG (PALI 250 WG) Water Soluble Bag. Report No. R/PCP1339/WET/13. GLP.
	K. Senthil	2014	QC Control data Deltamethrin 250 WG-SB.
	D.B. Waghade	2013	Determination of Dispersibility of Deltamethrin 25% WG (PALI 250 WG) Water Soluble Bag. Report No. R/PCP1341/SPDISP/13. GLP.
	D.B. Waghade	2013	Determination of Wet Sieve Test of Deltamethrin 25% WG (PALI 250 WG) Water Soluble Bag. Report No. R/PCP1340/WSVE/13. GLP.
	D.B. Waghade	2013	Determination of the Time of Complete Wetting of Deltamethrin 25% WG (PALI 250 WG) Water Soluble Bag. Report No. R/PCP1339/WET/13. GLP.
	D.B. Waghade	2013	Determination of persistent foamability of Deltamethrin 25% WG (PALI 250 WG) Water Soluble Bag. Report No. R/PCP1380/PERFM/13. GLP.
	D.B. Waghade	2013	Determination of Suspensibility of Deltamethrin 25% WG (PALI 250 WG) Water Soluble Bag Before Accelerated Storage with Proportionate Quantity of Water Soluble Bag. Report No. R/PCP1342/STBSP/13. GLP
	D.B. Waghade	2014	Determination of flowability of Granules of Deltamethrin 25% WG (PALI 250 WG) Water Soluble Bag After Heat test under pressure. Report No. R/PCP1345/FLOW/14. GLP

DELTAMETHRIN

FAO/WHO Evaluation Report 333/2014.3

Recommendations

The Meeting recommended that the existing WHO specification for deltamethrin water dispersible granules (WG) should be extended to encompass the corresponding product of Gharda Chemicals Ltd.

Appraisal

The Meeting considered data and information submitted by Gharda Chemicals Ltd. (India) in support of extension of the existing WHO specification for deltamethrin WG. The formulation is an insecticide for vector control, developed for use in indoor residual spraying programs (IRS), and therefore, is limited to WHO. The neat product was successfully evaluated by WHOPES in 2002 and has a recommendation for IRS (WHO 2002).

Gharda provided quality control data in order to support their specification. The data submitted by Gharda Chemicals Ltd. were broadly in accordance with the requirements of the Manual on development and use of FAO and WHO specifications for pesticides (November 2010 - second revision of the First Edition) and complied with the existing specification for deltamethrin WG.

Gharda tested their WG for acidity and persistent foam using the most recent CIPAC methods (CIPAC MT 191 and MT 47.3).

The stability of the WG in the accelerated storage test MT 46.3 without pressure was demonstrated to be acceptable, and no significant deterioration of the formulation was observed in terms of active ingredient content, acidity, residue after wet sieving, dispersibility, suspensibility and formation of dust.

DELTAMETHRIN

FAO/WHO Evaluation Report 333/2014.2

Recommendations

The Meeting recommended the following.

(i) The deltamethrin TC as proposed by Rotam Agrochemical Co., Ltd. should be accepted as equivalent to the deltamethrin reference profile.

(ii) The existing FAO and WHO specifications for deltamethrin TC should be extended to encompass the corresponding product of Rotam Agrochemical Co., Ltd.

(iii) The existing WHO specification for deltamethrin WG should be extended to encompass the corresponding product of Jiangsu Rotam Chemistry Co., Ltd.

Appraisal

The Meeting considered data and information submitted by Rotam Agrochemical Co., Ltd. (Hong Kong) in support of extension of the existing FAO and WHO specifications for deltamethrin TC and submitted by Jiangsu Rotam Chemistry Co., Ltd. (China) in support of extension of the existing WHO specification for deltamethrin WG. The data submitted by Rotam were in accordance with the requirements of the Manual on development and use of FAO and WHO specifications for pesticides (November 2010 - second revision of the First Edition).

Deltamethrin TC

The Meeting was provided by Rotam with commercially confidential information on the manufacturing process, the manufacturing quality control limits (technical specifications) and 5-batch analysis data for active ingredient and impurities equal or above 1 g/kg. The manufacturer stated that all impurities present in the TC with a content ≥ 1.0 g/kg were quantified.

Deltamethrin from Rotam (same manufacturing site) was evaluated by Spain and was declared similar to the reference profile agreed at the EU level (certificate of registration signed on February 11, 2011).

The manufacturing process was considered by the Meeting and was concluded to be similar to those previously provided for FAO/WHO specifications for deltamethrin TC. In the 5-batch data (commercial scale batches manufactured from June to October 2008), mass balances were very high (99.32 - 99.94%). Percentage of unknown compounds was from 0.06 to 0.68 % which is considered acceptable. The minimum purity of deltamethrin in the TC of Rotam is 985 g/kg.

No relevant impurities were declared in the Rotam deltamethrin TC. Nevertheless as mentioned in the FAO/WHO specifications on deltamethrin and as decided by the 2005 JMPS, becisthemic acid chloride [(1*R*,3*R*)-3-(2,2-dibromovinyl)-2,2-dimethylcyclopropane carboxoyl chloride], can occur as a result of certain manufacturing processes. Rotam was questioned about results for becisthemic acid

chloride which was declared at a level < 1 g/kg in the submitted specifications. The manufacturer confirmed that this impurity cannot occur at a level ≥ 1 g/kg. The analysis of two recent batches confirmed that the level of this impurity is below 1 g/kg. Also, as required by the Meeting, the manufacturer determined the level of one chlorinated solvent in two batches. Results were well below 1 g/kg and confirmed that the solvent is efficiently removed during the manufacturing process. The Meeting considered these data as similar to those previously published for deltamethrin TC and concluded that the Rotam deltamethrin TC comply with the existing FAO/WHO specification.

In the 5-batch analysis data submitted by the manufacturer, the method from the old specification WHO/24.R1 was used for determination of deltamethrin and impurities. The study was performed according to GLP guidelines. Nevertheless, this method is different from the CIPAC method published in Handbook L, and a revised 5-batch analysis study or a bridging study between the two methods was required by the Meeting. A bridging study was submitted showing that results are very similar. No other data were required and the results provided in the 5-batch analysis were considered acceptable.

The manufacturer provided full validation data (specificity, linearity of response, accuracy, repeatability, LOQ) for analytical methods for active ingredient and impurities content. The Meeting concluded that the analytical methods for the determination of active ingredient and significant impurities are acceptable. Water was determined using the CIPAC method. The identity of deltamethrin and impurities was confirmed using GC-MS, FT-IR and NMR.

The Meeting agreed that the purity/impurity profile of deltamethrin TC from Rotam indicated equivalence with the reference profile supporting the existing FAO and WHO specifications (FAO/WHO evaluation report 333/2004).

Studies on acute toxicology (acute oral, dermal and inhalation, skin and eye irritation and skin sensitization) and on mutagenicity were performed using deltamethrin from Rotam with a purity of 98.3 - 98.5 % depending on the studies. Rotam provided also data on the physico-chemical properties of pure deltamethrin (purity > 98.5%).

No study on ecotoxicology profile was provided. Nevertheless, this was agreed as acceptable as the purity/impurity profile and the mutagenicity profile were considered to be equivalent to the reference profile.

The Meeting therefore concluded that the Rotam deltamethrin TC should be considered as equivalent to the reference profile and those previously included and supporting the existing FAO and WHO specifications.

Deltamethrin WG

The Meeting considered data and information submitted by Jiangsu Rotam Chemistry Co., Ltd. (China) in support of extension of the existing WHO specification for deltamethrin WG. The formulation is an insecticide for vector control, developed for use in indoor residual spraying programs (IRS), and therefore, is limited to WHO. The neat product was successfully evaluated by WHOPES in 2002 and has a recommendation for IRS (WHO 2002).

Rotam provided quality control data in order to support their specification. The data submitted by Rotam were broadly in accordance with the requirements of the Manual on development and use of FAO and WHO specifications for pesticides (November 2010 - second revision of the First Edition) and complied with the existing specification for deltamethrin WG.

Rotam tested their WG for acidity and persistent foam using the most recent CIPAC methods (CIPAC MT 191 and MT 47.3).

The stability of the WG in the accelerated storage test MT 46.3 without pressure was demonstrated to be acceptable, and no significant deterioration of the formulation was observed in terms of active ingredient content, acidity, residue after wet sieving, dispersibility, suspensibility and formation of dust.

The Meeting noted that only the WG with a declared deltamethrin content of 250 g/kg is used for public health, and decided therefore to delete the other deltamethrin content ranges in the WHO specification.

The Meeting proposed to revise in the WG specification the limit for dustiness from “Essentially non-dusty” to “The formulation shall have a maximum collected dust of 30 mg by the gravimetric method or a maximum dust factor of 25 by the optical method”, as recommended in the amendments to the FAO/WHO specification Manual published on the FAO and WHO websites.

The Meeting agreed also to update in the specifications for deltamethrin WP, EC and EW the CIPAC method for persistent foam (MT 47.3 instead of MT 47.2) to be in line with the current CIPAC method.

Supporting Information
for
Evaluation Report 333/2014.2

Physico-chemical properties of deltamethrin

Table 1. Physico-chemical properties of pure deltamethrin

Parameter	Value(s) and conditions	Purity %	Method reference (and technique if the reference gives more than one)	Study number
Vapour pressure	3.936×10^{-6} Pa at 25°C	98.59%	EEC A.4, OECD 104, CIPAC 333/TC/M/-	0722
Melting point	101.2°C - 101.9°C	98.59%	EEC A.1	0721
Temperature of decomposition	The decomposition of the test item begins at 506 K (233°C) and the test item is totally decomposed at 513 K (240°C)	98.51%	EEC A2	R B2205
Solubility in water	0.035 mg/L at 20.0°C	98.59%	EEC A.6	0721
Octanol/water partition coefficient	log Pow = 6.0	98.59%	EEC A.8	0721
Hydrolysis characteristics	pH 4.0: $t_{0.5}$ > 1 year at 25°C pH 7.0: $t_{0.5}$ > 1 year at 25°C pH 9.0: $t_{0.5}$ = 2.41 days at 25°C (No major hydrolysis products those representing ≥ 10% of the applied dose were observed)	98.51%	EEC C.7, OECD 111	0963
Photolysis characteristics	No pH dependence is observed in the UV spectra recorded under acidic, neutral nor basic medium. Under the experimental conditions used (pH = 5.9 and T^o = 30°C ± 2°C), the half life time of the test item, $t_{1/2}$ (mean) = 2.0 hours	98.51%	OECD 316	R B2205
Dissociation characteristics	No dissociation constant	98.51%	OECD 112	0963
Solubility in organic solvents	n-heptane: 2.53 g/L at 20.0°C methanol: 8.43 g/L at 20.0°C acetone: > 250g/L at 25.0°C ethyl acetate: > 250 g/L at 25.0°C 1,2-dichloroethane: >250 g/L at 25.0°C o-xylene: > 250 g/L at 25.0°C	98.59%	EEC A.6	0721

Table 2. Chemical composition and properties of deltamethrin technical material (TC)

Manufacturing process, maximum limits for impurities ≥ 1 g/kg, 5 batch analysis data	Confidential information supplied and held on file by FAO and WHO. Mass balances were 99.32-99.94% with unknowns from 0.06 to 0.68%.
Declared minimum deltamethrin content	985 g/kg
Relevant impurities ≥ 1 g/kg and maximum limits for them	None
Relevant impurities < 1 g/kg and maximum limits for them	None
Stabilisers or other additives and maximum limits for them	None

Parameter	Value and conditions	Purity %	Method reference	Study number
Melting temperature range of the TC	101.2°C - 101.9°C	98.5%	EEC A.1	0721

Formulations and co-formulated active ingredients

The main formulation type available is WG.

Methods of analysis and testing

Rotam confirmed that the existing CIPAC methods for the determination of active ingredient content is appropriate for the analysis of their products.

Impurities are determined using HPLC on an Agilent ZORBAX RX-SIL (5 µm particle size) column with iso-octane and 1,4-dioxane as eluent, UV detector at 230 nm and external standardization. The methods used for the determination of impurities in deltamethrin technical material are specific and were validated.

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

Containers and packaging

No special requirements for containers and packaging have been identified.

Annex 1: Hazard Summary Provided by the Proposer

Note:

Rotam Agrochemical Co. Ltd. provided written confirmation that the toxicological data included in the following summary were derived from deltamethrin 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.

All data has been generated only with the Rotam technical grade active ingredient.

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

Species	Test	Purity %	Guideline, duration, doses and conditions	Result	Study number
Wistar Rats, Females	oral	98.3%	OECD 423, OPPTS 870.1100; 50, 300, 2000 mg/kg bw	GHS category 3 LD_{50} > 50 - 300 mg/kg bw	09045
Wistar Rats, Females & Males	dermal	98.3%	OECD 402, OPPTS 870.1200, EEC B.3; 2000 mg/kg bw	LD_{50} > 2000 mg/kg bw	09046
Wistar Rats, Females & Males	inhalation	98.3%	OECD 403, OPPTS 870.1300, EC Directive 93/21 No. L110, B2, 1993; 4 hour; 0.64, 1.50, 3.00 mg/L of Deltamethrin Technical	LC_{50} = 1.4519 mg/L	09049
New Zealand White Rabbit, Females	skin irritation	98.3%	OECD 404, OPPTS 870.2500, EC directive 2004/73 No L152, B4, 2004; 4 hour	Non-irritating	09047
New Zealand White Rabbit, Females	eye irritation	98.3%	OECD 405, OPPTS 870.2400, EC directive 2004/73 No L152, B5, 2004	Non-irritant	09048
Guinea Pigs; Females & Males	skin sensitisation	98.3%	OECD 406, OPPTS 870.2600, EC directive 96/54 No L248, B6, 1996	Non-sensitizer	09050

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

Species	Test	Purity %	Guideline, duration, doses and conditions	Result	Study number
Salmonella typhimurium	Reverse Mutation Assay, *in vitro*	98.51%	OECD 471, OPPTS 870.1500 (1998), EC directive No. 440/2008 B13/14 (2008). With and without liver microsomal activation. Concentrations: 0.078, 0.156, 0.313, 0.625 and 1.25 mg/plate.	The test item Deltamethrin Technical did not induce gene mutations by base pair changes or frameshifts in the genome of the strains used.	3483

Annex 2: References

Study number	Author(s)	Year	Study title. Study identification number. Report identification number. GLP [if GLP]. Company conducting the study
0534		2009	Preliminary Analysis of Five Representative Production Batches of Deltamethrin Technical Grade Active Ingredient (TGAI) to Determine % Deltamethrin and to Quantify Its Associated Impurities. Study No. 0534. Rep. GLP. Rotam Research Laboratory (RRL), China. Unpublished.
0721		2010	Study on the Physico-Chemical Properties of Deltamethrin Technical. Study No. 0721. GLP. Rotam Research Laboratory (RRL), China. Unpublished.
0722		2010	Study on Vapour Pressure of Deltamethrin Technical. Study No. 0722. GLP. Rotam Research Laboratory (RRL), China. Unpublished.
R B2205		2012	Determination of Direct Phototransformation & Temperature Decomposition of Deltamethrin Technical. Report No. R B2205. GLP. ANADIAG, France. Unpublished.
0963		2012	Study on The Physico-Chemical Properties of Deltamethrin Technical. Study No. 0963. GLP. Rotam Research Laboratory (RRL), China. Unpublished.
09045		2010	Acute Oral Toxicity Study with Deltamethrin Technical in Wistar Rats. Study No. 09045. GLP. International Institute of Biotechnology and Toxicology (IIBAT), India. Unpublished.
09046		2010	Acute Dermal Toxicity Study with Deltamethrin Technical in Wistar Rats. Study No. 09046. GLP. International Institute of Biotechnology and Toxicology (IIBAT), India. Unpublished.
09049		2010	Acute Inhalation Toxicity Study with Deltamethrin Technical in Wistar Rats. Study No. 09049. GLP. International Institute of Biotechnology and Toxicology (IIBAT), India. Unpublished.
09047		2010	Acute Dermal Irritation / Corrosion of Deltamethrin Technical in New Zealand White Rabbits. Study No. 09047. GLP. International Institute of Biotechnology and Toxicology (IIBAT), India. Unpublished.
09048		2010	Acute Eye Irritation / Corrosion of Deltamethrin Technical in New Zealand White Rabbits. Study No. 09048. GLP. International Institute of Biotechnology and Toxicology (IIBAT), India. Unpublished.
09050		2010	Skin Sensitization Potential of Deltamethrin Technical in Guinea Pigs (Guinea Pig maximization Test of Magnusson and Kligman Method). Study No. 09050. GLP. International Institute of Biotechnology and Toxicology (IIBAT), India. Unpublished.
3483		2012	*Salmonella typhimurium* Reverse Mutation Assay with Deltamethrin Technical. Study No. 3483. GLP. RCC Laboratories India Private Limited, India. Unpublished.
1132		2013	Study on the active ingredient content of deltamethrin technical. Study N° 1132. GLP. RRL. Unpublished.
1138		2013	Study on the physic-chemical properties of deltamethrin 250 g/kg water dispersible granule. Study N° 1138. GLP. RRL. Unpublished.
		2013	Data sheet on analysis of Ethylene Dichloride In Deltamethrin TC.
	FAO/WHO	2010	Manual on development and use of FAO and WHO specifications for pesticides. November 2010 – second revision of the First Edition. FAO Plant Production and Protection Paper. Revised.

DELTAMETHRIN

FAO/WHO Evaluation Report 333/2013.2

Recommendations

The Meeting recommended that the specification for deltamethrin water dispersible granules in sealed water soluble bag (WG-SB), proposed by Bayer CropScience, as amended, should be adopted by WHO.

Appraisal

Supporting data and draft specification for deltamethrin water dispersible granules in sealed water soluble bag (WG-SB), provided by Bayer CropScience, were considered by the Meeting for development of a new WHO specification.

The formulation is an insecticide for vector control, developed for use in indoor residual spraying programs (IRS), and therefore, is limited to WHO. The neat product was successfully evaluated by WHOPES in 2002 and has a recommendation for IRS (WHO 2002). As the fundamental properties of the formulated product are considered not to change with the packaging in water soluble bags, the WHOPES recommendation is also valid for the deltamethrin WG-SB.

The proposed specification for deltamethrin WG-SB was broadly in agreement with the guidelines given in the Manual (FAO/WHO 2010).

Formulation type, description, content of active ingredient and analytical method

Deltamethrin is formulated as a water dispersible granule packed in a water soluble bag. Up to now, FAO and WHO specifications were available for neat deltamethrin WG. The clauses dealing with the formulation itself remain the same. Additional clauses for the WG-SB which require testing of the soluble bag as part of the formulation and testing of suspensibility and persistent foam with a part of the soluble bag have been included in the WG-SB specification. The Meeting concluded that deltamethrin WG and deltamethrin WG-SB should be standalone specifications.

Description clause

The formulation is intended for IRS with a target dose of 0.02 to 0.025 g deltametrin per m^2. A certain defined amount of deltamethrin WG with a declared content of 250 g/kg is packed in a water soluble sachet so that dosing in a certain amount of water is facilitated without direct contact of the operator with the granule.

Physical-chemical properties

In certain tests to be carried out to assess the physical-chemical parameters of the WG-SB, the neat formulation is used (e.g. in wet sieve test and wettability). Suspensibility and persistent foam tests have to be carried out on the neat formulation with the bag material in the actual ratio of application.

Storage stability

The clauses and limits in the physical-chemical subsection were mainly in agreement with the requirement of the Manual. The WG-SB remains stable upon storage and the soluble bag retains its integrity. In addition to standard clauses for a WG-SB formulation, the persistent foam after storage was included, in agreement with the latest amendments of the Manual.

The Meeting agreed also to update in the specifications for deltamethrin WG and WG-SB the CIPAC method for persistent foam (MT 47.3 instead of MT 47.2) to be in line with the current CIPAC method.

Annex 1: References

Study number	Author(s)	Year	Study title. Study identification number. Report identification number. GLP [if GLP]. Company conducting the study
Mo4522	BioGenius GmbH Analytics	2013	Interim Report 2 Weeks. Determination of physico-chemical properties and storage stability for Deltamethrin WG-SB 25: 2 weeks at 54˚C, 8 weeks at 40˚C and up to 36 months at 20˚C. Unpublished report. BioGenius GmbH Analytics, 51429 Bergisch Gladbach, Germany.
Mo4522	BioGenius GmbH Analytics	2013	Amendment No. 1 to Interim Report 2 Weeks. Determination of physico-chemical properties and storage stability for Deltamethrin WG-SB 25: 2 weeks at 54˚C, 8 weeks at 40˚C and up to 36 months at 20˚C. Unpublished report. BioGenius GmbH Analytics, 51429 Bergisch Gladbach, Germany.
Mo4522	BioGenius GmbH Analytics	2013	Amendment No. 2 to Interim Report 2 Weeks. Determination of physico-chemical properties and storage stability for Deltamethrin WG-SB 25: 2 weeks at 54˚C, 8 weeks at 40˚C and up to 36 months at 20˚C. Unpublished report. BioGenius GmbH Analytics, 51429 Bergisch Gladbach, Germany.
	FAO/WHO	2010	Manual on development and use of FAO and WHO specifications for pesticides. Second revision of the 1st edition. FAO, Rome and WHO, Geneva, November 2010 (internet publications).
	WHO	2002	Report of the Sixthn WHOPES Working Group Meeting, WHO/HQ, Geneva, 6-7 November 2002. WHO, Geneva, document WHO/CDS/WHOPES/2002.6

DELTAMETHRIN

FAO/WHO Evaluation Report 333/2013.1

Recommendations

The Meeting recommended that a time-limited interim specification (until January 2017) for deltamethrin polymer-enhanced suspension concentrate (SC-PE) proposed by Bayer CropScience, as amended, should be adopted by WHO.

Appraisal

Supporting data and draft specification for a new deltamethrin suspension concentrate (deltamethrin 62.5 g/L SC) for indoor residual spraying applications, provided by Bayer CropScience were considered by the Meeting for development of a new WHO specification. This new formulation was successfully evaluated by WHOPES and a recommendation for its use in malaria prevention and control was recently published (WHO 2013).

The extended residual activity of this new SC formulation is closely related to the use of a polymer adjuvant which stabilizes deltamethrin against degradation on chemically aggressive, alkaline and porous surfaces. At the same time, upon drying of the sprayed formulation after application, this polymer adjuvant does not encapsulate the active ingredient which would lead to a reduction of the biological availability.

The manufacturer had initially proposed to the Meeting to extend the existing WHO specification 333/SC (April 2005) in order to encompass the new formulation, and had requested to change the clause for spontaneity of dispersion from minimum 90% to minimum 70%. Nevertheless, as the formulation has an extended residual effect, the Meeting proposed to develop a separate specification for this new formulation. The Meeting noted that there is no specific guideline for “long-lasting” SC formulations and required the company to develop physico-chemical parameters which would permit to characterize the extended residual effect.

The manufacturer initially proposed SC-LL as the formulation code for this “long-lasting” aqueous suspension concentrate to differentiate this new formulation from the classical SC formulations, but the Meeting did not agree with the term long-lasting because the extended residual effect cannot be measured directly by physico-chemical testing. The Meeting finally proposed to name this new formulation as deltamethrin polymer-enhanced suspension concentrate with the code SC-PE, and the manufacturer agreed. The SC-PE formulation code does not exist in the catalogue of pesticide formulation types and international coding system (CropLife International Technical Monograph No 2). Nevertheless SC-PE was adopted for this formulation to distinguish it from the conventional SC (WHO specification 333/SC), and this was explained in a footnote added in the specification. Because the polymer co-formulant is part of the business confidential information, the Meeting and the manufacturer agreed that it should not be disclosed in the specification.

The manufacturer developed and proposed to include in the new specification three additional physical tests and criteria in order to indirectly characterize the long-lasting effect and therefore the presence of the polymer adjuvant in quality and in quantity.

Infrared spectrum

The IR spectrum of a dried suspension (at 105°C until constant weight) provides a chemical identification of the formulation. This spectrum reflects strongly the chemistry of the selected polymer adjuvant. Alternatively, the IR spectrum of dried supernatant of a 10 times diluted formulation after centrifugation can be analysed. This spectrum reflects even more in detail the chemistry of the selected polymer adjuvant. The manufacturer provided the IR spectrum of the product with the sample preparation for the IR spectrum recording. The Meeting noted that the IR spectrum can only provide an indication of the presence of the polymer and that no limit can be specified, and therefore it cannot be included in the physical properties of the specification. The Meeting finally concluded that the IR spectrum and the procedure used to do the measurement should be included in a footnote attached to the description clause.

Solid content or loss in weight

The choice and amount of polymer in the formulation was optimized by the manufacturer to provide a good residuality on all type of treated surfaces. To guarantee the extended residual effect, the polymer concentration of the formulation has to be within a certain specified concentration range. Together with the active ingredient, the amount of polymer dominates the solid content and therefore also the drying loss of the formulation. The manufacturer proposed to measure the loss in weight using the CIPAC method MT 17.4 (weight loss at 100°C for 4 hours) and specified a lower limit of 74% and an upper limit of 81%.

Glass transition temperature

One essential property of the polymer adjuvant is its glass transition temperature (Tg), which presents a solid state property. The liquid-glass transition (or glass transition, Tg) is the reversible transition in amorphous materials (or in amorphous regions within semi-crystalline materials) from a hard and relatively brittle state into a molten or rubber-like state. The manufacturer proposed to include in the specification the determination of the glass transition temperature using Differential Scanning Calorimetry (DSC) according to the ISO 11357 standard, in order to characterise the polymer and distinguish it from other potential polymer additives.

The experimental Tg value of complex polymeric system may be influenced not only by the interaction between polymer and other formulation components, but also by the preparation method of the specimen and by the experimental conditions. The manufacturer specified a minimum Tg of 43°C and a maximum Tg of 53°C and proposed to include in a footnote to the specification the sample preparation for the determination of the glass temperature transition. The manufacturer confirmed that the glass transition temperature is not significantly affected by the accelerated storage of the product and that there was no reason to specify this test after storage at 54°C for 14 days, and this was agreed by the Meeting.

The Meeting noted that these 3 additional tests are not standard tests but permit to indirectly characterise this new polymer-enhanced SC formulation. All the other tests proposed by the manufacturer for this product (active ingredient identity and content, pH range, pourability, spontaneity of dispersion, suspensibility, wet sieve test,

persistent foam, stability at 0°C and at elevated temperature are those recommended in the SC guideline of the FAO/WHO specification Manual.

The proposed physico-chemical parameters (Infrared spectrum, loss in weight and glass transition temperature) are indirect measurements of the extended residual effect. The Meeting proposed therefore to publish the specification as a time-limited (for a 3 years period) interim specification and to invite the manufacturer to develop a more appropriate standard test to measure directly the extended residual effect (in a similar way as tests developed for slow release formulations), and the manufacturer agreed. The Meeting agreed also to specify in a footnote that extensions of this specification to nominally similar products of other manufacturers shall require biological testing.

The Meeting agreed also:

- to update in the specification for deltamethrin SC the CIPAC method for pourability (MT 148.1 instead of MT 148) to be in line with the specification guidelines of the November 2010 – second revision of the first edition of the FAO/WHO Manual and the current CIPAC method;
- and to update in the specifications for deltamethrin SC and SC-PE the CIPAC method for persistent foam (MT 47.3 instead of MT 47.2) to be in line with the current CIPAC method.

Annex 1: References

Study number	Author(s)	Year	Study title. Study identification number. Report identification number. GLP [if GLP]. Company conducting the study
	Bascou J.-P.	2012	Revised draft specification and supporting data for deltamethrin long-lasting aqueous suspension concentrate. Bayer CropScience, March 23, 2012.
	Bascou J.-P.	2012	Revised draft specification for deltamethrin long-lasting aqueous suspension concentrate. Bayer CropScience, November 09, 2012.
	Bascou J.-P.	2013	Revised draft specification for deltamethrin polymer-enhanced suspension concentrate. Bayer CropScience, June 03, 2013.
	ISO	2010	DIN EN ISO 11357-1. Plastics – Differential scanning calorimetry (DSC) – Part 1 : General principles (ISO 11357-1:2009). March 2010.
	Kijlstra J.	2012	WHO specification limits for Deltamethrin SC 62.5. Bayer CropScience, May 11, 2012.
Mo4002	Manka Sven	2010	Determination of physico-chemical properties and storage stability test for Deltamethrin SC 62,5 in HDPE bottles. Report Mo4002 of BioGenius GmbH for Bayer CropScience, December 16, 2010.
	Patty L.	2011	Draft JMPS specification for deltamethrin SC formulations encompassing deltamethrin SC62.5, Bayer CropScience, February 10, 2011.
	Patty L.	2011	Information provided by Bayer CropScience on Deltamethrin SC 62.5 to JMPS, December 21, 2011.
	WHO	2013	Report of the Sixteenth WHOPES Working Group Meeting, WHO/HQ, Geneva, 22-30 July 2013. WHO, Geneva, document ISBN 978 92 4 150630 4 and WHO/HTM/NTD/WHOPES/2013.6

DELTAMETHRIN

FAO/WHO Evaluation Report 333/2012.2

Recommendations

The Meeting recommended the following.

(i) The existing FAO and WHO specifications for deltamethrin EC and EW should be revised as proposed by Bayer CropScience and as amended by the Meeting.

(ii) The existing WHO specification for deltamethrin WT should be revised as proposed by the Meeting.

Appraisal

Deltamethrin EC

The Meeting considered data and information submitted by Bayer CropScience to support the revision of the existing WHO specification 333/EC (April 2005) and the existing FAO specification 333/EC (May 2005). During the EU deltamethrin post Annex I re-registration, some regulatory authorities have reported that emulsion stability values were not compliant with the existing FAO and WHO specifications for deltamethrin EC formulations.

In order to align the specifications with the quality of the products placed on the market, the manufacturer requested to change the clause for ECs emulsion stability limits from “no cream” to “maximum 1 ml cream” after 0.5 h, from “no cream” to “maximum 5 ml cream” after 2 h” and from “no cream” to “maximum 2 ml cream” after 24.5 h. The manufacturer had provided the Meeting with study reports as well as quality control data on several batches to support these change.

The Meeting did not accept the 5 mL limit proposed by the company because an important amount of the active ingredient could be present in the cream. The Meeting proposed to replace the CIPAC method MT 36.1.1 (at 5% concentration) which is no longer supported by CIPAC by the MT 36.3, and this was accepted by the company who confirmed that their EC formulations are recommended to be used at concentrations less than 5% and that the MT 36.3 is applicable for their EC formulations. The company informed later the Meeting that new studies performed on deltamethrin 100 g/L EC using the MT 36.3 had shown that their formulations fully comply with the existing tolerance for emulsion stability and re-emulsification. The Meeting concluded that the change requested by Bayer CropScience was no longer necessary because the method was changed from MT 36.1.1 to MT 36.3.

The Meeting proposed also to adapt the footnotes of the current specification for emulsion stability and persistent foam according to the recommendations of the EC guideline of the FAO/WHO Manual (November 2010 – second revision of the first edition).

Deltamethrin EW

The Meeting considered data and information submitted by Bayer CropScience to support the revision of the existing WHO specification 333/EW (March 2009) and the existing FAO specification 333/EW (March 2009). During the EU deltamethrin post Annex I re-registration, some regulatory authorities have reported that the pH values were not compliant with the existing FAO and WHO specifications for deltamethrin EW formulations.

In order to align the specifications with the quality of the products placed on the market, the manufacturer requested to change the EWs pH limits from 4.5 - 7.5 to 3.0 - 7.5. The manufacturer provided the Meeting with study reports as well as quality control data on several batches to support these changes. The Meeting judged the proposal regarding the stability of deltamethrin to hydrolysis and epimerization under acidic conditions acceptable. As the new tolerances are somewhat less stringent than the older ones, this has no negative impact on the deltamethrin EW formulation specifications proposed by other proposers who had been granted equivalence.

The Meeting proposed to replace the CIPAC method MT 36.1.1 (at 5% concentration) which is no longer supported by CIPAC by the MT 36.3, and this was accepted by the company who confirmed that their EW formulations are recommended to be used at concentrations less than 5% and that the MT 36.3 is valid for their EW formulations.

For the pourability of the EW formulation, the Meeting proposed to change the CIPAC method MT 148 to the MT 148.1 as recommended by CIPAC for testing pourability. The Meeting proposed also to adapt the footnote of the current specification for emulsion stability according to the recommendations of the EW guideline of the FAO/WHO Manual (November 2010 – second revision of the first edition).

Deltamethrin WP, SC, WG, EG and WT

As the analytical methods for deltamethrin identity and content in tablets are now published in the CIPAC handbook M, the Meeting proposed to update the WHO specification 333/WT for deltamethrin water dispersible tablet by referencing the active ingredient identity and content clauses with the relevant CIPAC methods 333/TB/M/2 and 333/TB/M/3.

The Meeting proposed also to update some footnotes in the WP, SC, WG and EG 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.

DELTAMETHRIN

FAO/WHO Evaluation Report 333/2012.1

Recommendations

The Meeting recommended the following.

(i) The deltamethrin TC as proposed by ISAGRO S.p.A. should be accepted as equivalent to the deltamethrin reference profile.

(ii) The existing FAO specifications for deltamethrin TC and EC should be extended to encompass the corresponding products of ISAGRO S.p.A.

(iii) The existing WHO specifications for deltamethrin TC and EC should be extended to encompass the corresponding products of ISAGRO S.p.A.

Appraisal

The Meeting considered data and information submitted by ISAGRO S.p.A. (Italy) in support of extension of the existing FAO and WHO specifications for deltamethrin TC and EC. The data submitted by ISAGRO S.p.A. were in accordance with the requirements of the Manual on development and use of FAO and WHO specifications for pesticides (November 2010 - second revision of the First Edition).

ISAGRO S.p.A. provided the Meeting with commercially confidential data on the manufacturing process, the manufacturing specification and 5-batch analysis data for deltamethrin and all detectable impurities. The manufacturing process provided by ISAGRO S.p.A. is not exactly the same than this one from the reference process but can be considered as very similar as regards the synthesis route and the potential impurities.

ISAGRO S.p.A. stated that their deltamethrin TC and EC have been submitted for registration in different EC countries and in Latin America. The confidential information (manufacturing process, purity and impurity profile) submitted to FAO/WHO was confirmed by the Chemicals Regulation Directorate as being identical to that submitted for registration in UK, and was evaluated and considered acceptable by the UK.

In the 5-batch analysis study a method very similar to the CIPAC method 333/TC/M2/3 (normal phase HPLC-DAD) was used for determination of deltamethrin. A bridging study confirmed that the use of a silicagel column and detection at 250 nm gave comparable results to the CIPAC method using a cyanophenyl column and detection at 230 nm. The deltamethrin manufacturing impurities were determined by reverse phase HPLC-DAD (with confirmation by GC-MS), except water, loss on drying and sulphated ashes which were determined using the appropriate titration or gravimetric CIPAC methods. All the analytical methods used in the 5-batch analysis study were fully validated on their specificity, linearity of response, accuracy, repeatability and limits of detection and quantification (for impurities).

The minimum purity of deltamethrin in the TC is 985 g/kg and complies with the existing FAO/WHO specification. Mass balances are very high (99.6 – 100.4%), with no unknown detected, and similar to those of the reference profile of Bayer CropScience (98.6 – 99.5%). The proposed manufacturing maximum limit for deltamethrin R-alpha isomer [(*R*)-α-cyano-3-phenoxybenzyl (1*R*,3*R*)-3-(2,2-dibromovinyl)-2,2-dimethylcyclopropane carboxylate)], a non relevant impurity, was 5 g/kg and was consistent with the 5-batch analysis data. All the other manufacturing impurities were below the LOQ or the LOD level and well below 1 g/kg. All these impurities were already evaluated by WHO/PCS who confirmed the non-relevance of these impurities (FAO/WHO evaluation reports 333/2004, 333/2005, 333/2006.2 and 333/2008.1).

The becisthemic acid chloride [(1*R*,3*R*)-3-(2,2-dibromovinyl)-2,2-dimethylcyclo propane carboxoyl chloride], which would be designed as a relevant impurity if it occurs at ≥ 1g/kg (of deltamethrin) according to the existing FAO/WHO specification, is well below this threshold with a manufacturing QC limit of 0.28 g/kg (LOQ). The Meeting agreed therefore that becisthemic acid chloride should remain a non-relevant impurity with a note that the compound could become relevant in products of other manufacturers. The Meeting agreed also that water (with a manufacturing QC limit of 1 g/kg), loss on drying and sulphated ashes are not relevant impurities.

The manufacturer provided the Meeting with detailed information on the solvents and catalysts used in the manufacturing process and confirmed that they are completely removed during the manufacturing steps.

Tolune is used as solvent in the manufacturing process. Using data from experimental animals and humans, JMPS has earlier derived a tolerable inhalation concentration for toluene, which may be a relevant impurity in the present deltamethrin TC. This tolerable concentration in the air will be reached if the concentration of the solvent in the deltamethrin TC is 1.5 g/kg and the air-borne deltamethrin concentration is 4030 mg/m^3, *i.e.*, the LC_{50} for deltamethrin. Therefore, the toxicity of the active ingredient, deltamethrin, greatly outweighs that of the solvent, and the contribution of the solvent to the total hazard of the product is negligible. The Meeting thus concluded that, at concentrations less than 1.5 g/kg, the solvent is not a relevant impurity in the deltamethrin TC.

ISAGRO S.p.A. provided the Meeting with mutagenicity data on *Salmonella typhimurium* (reverse mutation Ames test) and on mouse - *Mus musculus* (erythrocyte micronucleous test) showing that no mutagenic effect nor induction of chromosomal damages could be observed.

On basis of all Tier-1 data provided by ISAGRO S.p.A. (manufacturing process, impurity profile, 5-batch analysis data, mutagenicity profile), the Meeting concluded that the ISAGRO S.p.A. deltamethrin TC should be considered as equivalent to the reference profile supporting the existing FAO and WHO specifications (FAO/WHO evaluation report 333/2004).

ISAGRO S.p.A. provided also the Meeting with acute toxicity, irritation and sensitization data, as well as data on the physico-chemical properties of pure deltamethrin (vapour pressure, melting point, solubility in water and in organic solvents, octanol / water partition coefficient). These studies were performed using OECD, EU or CIPAC methods. These additional Tier-2 data indicated equivalence of the ISAGRO S.p.A. deltamethrin TC with the reference profile supporting the existing FAO and WHO

specifications (FAO/WHO evaluation report 333/2004).

The Meeting was provided by ISAGRO S.p.A. with data on the physical and chemical properties of their deltamethrin 25 g/L EC formulation and including appearance, deltamethrin identity and content, pH, emulsion stability, persistent foam, stability at 0°C and after storage at 54 ± 2°C for 14 days. The deltamethrin content in the EC was determined by a reverse phase HPLC-DAD method which was fully validated on its specificity, linearity of response, accuracy and repeatability. The company stated also that the existing CIPAC methods for determination of deltamethrin and for determination of physical properties are appropriate for their formulation. Results of the physical and chemical properties of the EC showed that the formulation fully complies with the existing FAO/WHO specifications for deltamethrin EC.

Supporting Information
for
Evaluation Report 333/2012.1

Physico-chemical properties of deltamethrin

Table 1. Physico-chemical properties of pure deltamethrin

Parameter	Value(s) and conditions	Purity %	Method	Reference
Vapour pressure	1.9×10^{-8} Pa at 20°C 4.9×10^{-8} Pa at 25°C 4.2×10^{-6} Pa at 50°C	99.3%	EEC A.4 OECD 104 and 113	4160
Melting point	Melting point = 97.8-99.3°C	99.3%	EEC A.1	4153
Solubility in water	1.3×10^{-6} g/L at 20°C pH value of medium has no effect on the solubility of deltamethrin	99.3%	OECD 105	4148
Octanol/water partition coefficient	log P_{OW} = 4.59 at 20°C	99.3%	OECD 107	4164
Solubility in organic solvents	n-hexane: 0.53 g/L at 20°C toluene: > 250 g/L at 20°C dichloromethane: > 250 g/L at 20°C ethanol: 10-14 g/L at 20°C acetone: > 250 g/L at 20°C ethyl acetate: > 250 g/L at 20°C	99.3%	CIPAC MT 181 OECD 105	4156

Table 2. Chemical composition and properties of deltamethrin 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 99.6-100.4 % % with no unknowns.		
Declared minimum deltamethrin content		985 g/kg		
Relevant impurities ≥ 1 g/kg and maximum limits for them		None		
Relevant impurities < 1 g/kg and maximum limits for them		None		
Stabilisers or other additives and maximum limits for them		None		
Parameter	Value and conditions	Purity %	Method reference	Study number
Melting temperature range of the TC and/or TK	97.8-99.3°C [at 99.3ºC the substance becomes completely liquid]	99.3%	EEC A.1	4153
Solubility in organic solvents (at 20°C)	n-hexane: 0.53 g/L toluene: > 250 g/L dichloromethane: > 250 g/L ethanol: 10-14 g/L acetone: > 250 g/L ethyl acetate: > 250 g/L	99.3%	CIPAC MT 181 OECD 105 Methods adapted for solubility below 10 g/L	4156

Formulations and co-formulated active ingredients

The main formulation types available are, for Isagro products, only an EC (emulsifiable concentrate) containing 25 g/L of deltamethrin dissolved in suitable solvents and formulants for agricultural uses and also public health uses.

Deltamethrin produced by Isagro is not co-formulated with other pesticides.

This formulation (Deltamethrin 25 g/L EC) is on going in registration process in different countries of EC (Greece, Italy, Spain, France, Portugal, Bulgary, Cyprus, Malta) and Latin America (Argentina, Colombia) and will be sold when is authorized.

Methods of analysis and testing

The analytical method for the active ingredient content in the TC (including identity tests) is similar to the CIPAC method 333/TC/M2. Deltamethrin is determined by HPLC with PDA detector. The validation study was conducted by Mapelli E. (2007). The working solution was the analyte dissolved with isooctane:dioxane (80:20, v/v); column: Lichrospher 60 A Si, 250 x 4 mm, 5 µm; temperature 25ºC; flow: 1 ml/min; mobile phase: Isooctane:dioxane 95:5 (v/v), isocratic system. The method was successfully validated.

Phuong Lien (2008) used and validated a HPLC-UV method in order to analyse deltamethrin in the formulation at a nominal concentration of 25 g/L. The sample was analyzed after dilution in acetonitrile; detection wavelength: 205 nm; column: Luna 100 C18 (2), 5 µm particle size, 150 x 2 mm; pre-column: Phenomenex C18, 4 x 2 mm; column temperature : 40°C; injection volume: 2-10 µL; mobile phase A: 70% acetonitrile; mobile phase B: 30% water containing 0.05% glacial acetic acid; flow rate: 0.5 mL/min. The method has been successfully validated for the determination of deltamethrin in EC formulations.

The methods for determination of impurities are based on HPLC. Technical deltamethrin does not contain relevant impurities. The validated method for deltamethrin proved to be suitable also for the determination of its R-isomer which is liable to be present in the final product at levels higher than 0.1 %. Methods for all impurities were successfully validated for specificity, linearity, repeatability and accuracy.

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

Physical properties

The physical properties, the methods for testing them and the limits proposed for the EC formulation, comply with the requirements of the FAO/WHO manual.

Containers and packaging

No special requirements for containers and packaging have been identified.

Annex 1: Hazard Summary Provided by the Proposer

Note:

ISAGRO S.p.A. provided written confirmation that the toxicological data included in the following summary were derived from deltamethrin 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.

All data has been generated only with the ISAGRO technical grade active ingredient.

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

Species	Test	Duration and conditions or guideline adopted	Result	Reference
HsdRccHan: WIST rats (Full-Barrier) Sex: female	oral	The study followed the first addendum to OECD guidelines for testing of chemicals, section 4, No 423. Deltamethrin purity: 99.3%	LD50: 50 mg/kg bw	4132
HsdRccHan: WIST rats (Full-Barrier) Sex: male and female	dermal	The study followed the first addendum to OECD guidelines for testing of chemicals, section 4, No 402. Deltamethrin purity: 99.3%	LD50: > 2000 mg/kg bw	4133
Sprague-Dawley Crl:CD (SD) IGS BR strain rats. Male and female	inhalation	The study followed the OECD guidelines for testing of chemicals, No 403 method B2. Deltamethrin purity: 99.3%	LC50: 3.43-4.03 mg/L	4121
New Zealand White Rabbits Hsdlf:NZW. Male and female	skin irritation	The study followed the first addendum to OECD guidelines for testing of chemicals, section 4, No 404. Deltamethrin purity: 99.3%	Non irritant	4129
New Zealand White Rabbits Hsdlf:NZW. Male and female	eye irritation	The study followed the first addendum to OECD guidelines for testing of chemicals, section 4, No 405. Deltamethrin purity: 99.3%	Non irritant	4130
Hsd Poc: DH – guinea pigs (Full-Barrier)	skin sensitization	The study followed the first addendum to OECD guidelines for testing of chemicals, section 4, No 406. Deltamethrin purity: 99.3%	Not sensitizing agent	4134

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

Species	Test	Conditions and guideline	Result	Reference
Salmonella typhimurium (TA 98, TA100, TA1535, TA1537), 10^9-10^9 cells/ml	Ames test, reverse mutation assay (*in vitro)*	OECD 471; ±S9 metabolic activation; 0.2, 2, 20, 200 and 2000 µg/plate mixed in DMSO. Deltamethrin purity: 98.85%	No mutagenic effect was observed within the testes doses Negative effect	4131
Mouse (Mus musculus, strain CF1	Mammalian erythrocyt micronucleus	OECD 474; Dose level of 2000 mg/kg/bw of deltamethrin technical dissolved in corn oil administred orally as a single dose to 5 males + 5 females Deltamethrin purity: 98.85%	No induction of chromosomal damages Negative effect	4128

Annex 2. References

References Section 1. Confidential data (sorted by study number)

Study number	Author(s)	year	Study title. Study identification number. Report identification number. GLP [if GLP]. Company conducting the study.
3563	Mapelli, E.	2007	Determination of the assay of deltamethrin technical. Report No. AM1682, GLP. Biolab. Unpublished.
3564	Mapelli, E.	2007	Methods validation for the determination of assay and related substances of deltamethrin. BIOLAB Report No AM1394i-1.rev1, GLP unpublished.
3565	Porcelli, C.	2009	Methods validation for the determination of assay and related substances of deltamethrin. BIOLAB Report No AM1394i-1.rev2, GLP unpublished.
3566	Mapelli, E.	2007	Analytical characterization of 5 batches of deltamethrin technical. BIOLAB Report No AM1394i-2.rev1, GLP unpublished.
4135	Mapelli, E.	2007	Chemical characterization as analytical standards. BIOLAB Report No AM1527i-rev1, GLP unpublished.
4136	Porcelli, C.	2009	Analytical characterization of 5 batches of deltamethrin technical. BIOLAB Report No AM1394i-2.rev2, GLP unpublished.

References Section 2. Tier I (sorted by study number)

Study number	Author(s)	year	Study title. Study identification number. Report identification number. GLP [if GLP]. Company conducting the study.
4128	Parodi F.	2008	Mouse (mus musculus) Erythrocyte Micronucleus Test of DELTAMETRINA TECNICA. LOTE N113/07. MICROQUIM, Report BIBR 6 – 12735, GLP unpublished.
4131	Lope N.	2008	Reverse Mutation Assay of DELTAMETRINA TECNICA. LOTE N113/07 in Salmonella typhirium. MICROQUIM, Report No. BIBR 6 – 12730, GLP unpublished.
4137	Phuong Lien T.	2008	Physico-chemical properties of the formulation Deltamethrin 25 g/l EC (unstored test item). Eurofins/GAB, Report No. S08-02718, GLP unpublished.
4138	Phuong Lien T.	2008	Flash Point of the Formulation Deltamethrin 25 g/l EC. Eurofins/GAB, Report No. S08-02660, GLP unpublished.
4139	Phuong Lien T.	2008	Certificate of Analysis including Development and Validation of an Analytical Method for Determination of the content of Deltamethrin in the formulation Deltamethrin 25 g/l EC. Eurofins/GAB, Report No. S08-02667, GLP unpublished.
4140	Krack M.	2008	Auto-Flammability (Determination of them temperature of self-ignition of volatile liquids and of gases) A.15. SIEMENS, Report No. 20080707.02, GLP unpublished.
4141	Krack M.	2008	Explosive properties A.14. SIEMENS, Report No. 20080707.01, GLP unpublished.
4142	Krack M.	2008	Oxidising properties of liquids A.21. SIEMENS, Report No. 20080707.01, GLP unpublished.
4143	Phuong Lien T.	2008	Physico-chemical properties of the formulation Deltamethrin 25 g/l EC after Cold Storage at 0°C for 7 days. Eurofins/GAB, Report No. S08-02668, GLP unpublished.
4147	Phuong Lien T.	2008	Physico-chemical properties of the formulation Deltamethrin 25 g/l EC after accelerated storage at 54°C for 2 weeks. Eurofins/GAB, Report No. S08-02669, GLP unpublished.
4148	Rizzo F., Ferrario F.	2008	Deltamethrin: solubility in water. ISAGRO RICERCA Report No. MEF.07.23, GLP unpublished.

4153	Gazzotti L.	2007	Melting Point of Deltamethrin Technical. GAB Study code: 20075513/01-PCMP, GLP unpublished.
4155	Phuong Lien T.	2008	Relative Density of Formulation Deltamethrin 25 g/l EC. Eurofins/GAB, Report No. S08-02663, GLP Unpublished.
4156	Rizzo F., Ferrario F.	2007	Deltamethrin: solubility in organic solvents. ISAGRO RICERCA Report No. MEF.07.24, GLP unpublished.
4157	Phuong Lien T.	2008	Viscosity of the formulation Deltamethrina 25 g/l EC. Eurofins/GAB, Report No. S08-02661, GLP unpublished.
4159	Burkhard A.	2011	Physico-chemical properties of the formulation Deltamethrin 25 g/l EC over 2 years at 20°C. Eurofins/GAB, Report No. S08-02670, GLP unpublished.
4160	Smeykal H.	2007	Vapour Pressure A.4. SIEMENS Report-No: 20071068.01 GLP unpublished.
4161	Phuong Lien T.	2008	Surface tension of Deltamethrin 25 g/l EC (Pure Formulation). Eurofins/GAB, Report No. S08-02662, GLP unpublished.
4162	Phuong Lien T.	2008	Persistent foaming of Deltamethrin 25 g/l EC. Eurofins/GAB, Report No. S08-02664, GLP unpublished.
4163	Phuong Lien T.	2008	Pourability of the formulation Deltamethrin 25 g/l EC. Eurofins/GAB, Report No. S08-02665, GLP unpublished.
4164	Rizzo F., Ferrario F.	2008	Deltamethrin: n-octanol/water partition coefficient. ISAGRO RICERCA Report No. MEF.07.25, GLP unpublished.
4910	Burkhard A.	2011	Final report. Emulsion stability (CIPAC MT 36.3) of the formulation Deltamethrin 25 g/l EC over 2 Years at 20°C, GLP unpublished.

References Section 2. Tier II (sorted by study number)

Study number	Author(s)	year	Study title. Study identification number. Report identification number. GLP [if GLP]. Company conducting the study.
	FAO/WHO	2010	Manual on development and use of FAO and WHO specifications for pesticides. November 2010 Revision of First Edition. FAO Plant Production and Protection Paper. Revised. www.fao.org/ag/AGP/AGPP/Pesticid/Default.htm and http://whqlibdoc.who.int/publications/2006/9251048576_eng_update2.pdf
	INCHEM	2001	IPCS International Programme on Chemical Safet. ICSC: 0247 http://www.inchem.org/documents/icsc/icsc/eics0247.htm
	EC	2008	Regulation (EC) 1272/2008.
4121	Griffithis, D	2008	Technical Deltamethrin: Acute Inhalation Toxicity (Nose only) Study in the rat. SafePharm Laboratories - Project Number: 1700/0063,GLP unpublished.
4129	Albrecht, A	2008	Acute Dermal Irritation / Corrosion with Technical Deltamethrin. BSL Report No. 071956, GLP unpublished.
4130	Albrecht, A	2008	Acute Eye Irritation/Corrosion with Technical Deltamethrin. BSL Report No. 071957, GLP unpublished.
4132	Albrecht, A	2008	Acute Oral Toxicity/Acute Toxic Class Method with Technical Deltamethrin. BSL Report No. 071958, GLP unpublished.
4133	Albrecht, A	2008	Acute Dermal Toxicity (Limit Test) Technical Deltamethrin. BSL Report No. 071959, GLP unpublished.
4134	Albrecht, A	2008	Test for Sensitization (Guinea Pig Maximisation Test) with Technical Deltamethrin. BSL Report No. 071960, GLP unpublished.

DELTAMETHRIN

FAO/WHO Evaluation Report 333/2008.2

Recommendations

The Meeting recommended the following.

The existing FAO and WHO specifications for deltamethrin EW should be revised as follows.

The clause for persistent foam should be changed to:
Maximum: 40 mL after 1 min.

Appraisal

The Meeting considered information submitted by Bayer CropScience concerning the foaming properties of the deltamethrin emulsion, oil in water formulation (EW). For one of the Bayer CropScience EW products, the company has slightly modified the composition of the formulation to achieve desired characteristics. Even though a new chemical was added at a level less than 1%, this led to an increase in persistent foam. This was noted by regulatory authorities in countries where the product was registered. The manufacturer proposed therefore to change the persistent foam maximum limit from 20 mL to 40 mL in order to align the specification with the quality of the product placed on the market. The Meeting found the proposal acceptable and agreed that the existing limit for persistent foam in both existing FAO and WHO specifications should be revised accordingly.

DELTAMETHRIN

FAO/WHO Evaluation Report 333/2008.1

Recommendations

The Meeting recommended the following.

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

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

Appraisal

The Meeting considered data and information submitted by Gharda Chemicals Limited (India) for extension of : (i) existing WHO specifications for deltamethrin TC, SC and EC (April 2005) and for deltamethrin WP and UL (September 2005); (ii) existing FAO specifications for deltamethrin TC, SC and EC (May 2005) and for deltamethrin WP and UL (April 2006). The data submitted by Gharda were generally in accordance with the requirements of the FAO/WHO Specifications Manual (Section 3.2).

The Meeting was provided by Gharda with commercially confidential data on the manufacturing process, the manufacturing specification and 5-batch analysis data for deltamethrin and all detectable impurities. The manufacturing process provided by Gharda is not exactly the same to this one from the reference process provided by Bayer CropScience but can be considered as quite similar as regards the list of potential impurities. The company stated also that the TC is manufactured on a commercial scale and on regular basis.

The 5-batch analysis study was performed according to GLP guidelines. HPLC was used for determination of deltamethrin (CIPAC method 333/TC/M3) and all impurities, except for one impurity where titration was used. All the analytical methods used were validated on their specificity, linearity of response, accuracy and repeatability. The company was questioned about the specificity of the titrimetric method used for becisthemic acid chloride. Gharda provided later a more specific method where becisthemic acid chloride is determined by GC-FID after dissolution into methanol containing diethyl phthalate as internal standard. Although the method used in routine is titrimetric, the results by both methods were found to be comparable.

The declared manufacturing QC limit for deltamethrin in the TC was minimum 980 g/kg, which is a little bit lower than the limit of the existing specification (985 g/kg). Moreover 2 out of the 5 batches analyzed showed deltamethrin content just below the specification limit. The manufacturer stated later that the Gharda product can comply with the current specification for deltamethrin TC with a minimum purity of

985 g/kg, and that the manufacturing QC limit will be revised accordingly. The Meeting agreed that this was acceptable and that no further batch data were needed.

Mass balances were high (≥ 98.6 – 99.4%), with no unknown detected, and similar to those of the reference profile of Bayer CropScience (≥ 98.6 – 99.5%). The manufacturing maximum limit for deltamethrin R-isomer [(*R*)-α-cyano-3-phenoxybenzyl (1*R*,3*R*)-3-(2,2-dibromovinyl)-2,2-dimethylcyclopropane carboxylate)] was 10 g/kg, but the 5-batch analysis data showed values ≤ 4 g/kg. Moreover the 2004 JMPS agreed that this is not a relevant impurity (FAO/WHO evaluation report 333/2004). The manufacturing maximum limits for other impurities are 2 – 5 g/kg depending on the impurity, but the 5-batch analysis data showed values lower than 0.5 g/kg. All these impurities were already evaluated by WHO/PCS who confirmed the non-relevance of these impurities (FAO/WHO evaluation reports 333/2004, 333/2005 and 333/2006.2).

Concerning the becisthemic acid chloride [(1*R*,3*R*)-3-(2,2-dibromovinyl)-2,2-dimethylcyclopropane carboxoyl chloride] which would be designed as a relevant impurity if it occurs at ≥ 1g/kg (of deltamethrin) according to the existing specification, Gharda proposed a manufacturing QC limit of 2 g/kg, but the 5-batch analysis showed levels < 0.5 g/kg. The manufacturer was asked by the Meeting to clarify the manufacturing QC limit for becisthemic acid chloride. The manufacturer stated that analysis of batches shows always that the level is < 1 g/kg and supplied certificates of analysis of 5 new batches supporting the statement (becisthemic acid chloride content of 0.2-0.6 g/kg). The company agreed also to revise the manufacturing QC limit accordingly. The Meeting agreed that becisthemic acid chloride should remain a non-relevant impurity.

The confidential information (manufacturing process, purity and impurity profile) submitted to FAO/WHO was confirmed by the Australian Pesticides and Veterinary Medicines Authority as being identical to that submitted for registration in Australia.

Gharda provided also data (supported by GLP studies) on the physico-chemical properties of pure deltamethrin. The results for vapour pressure, melting point, octanol / water partition coefficient, hydrolysis at pH 4 and 7 and/or dissociation characteristics can be considered as similar to those provided by previous proposers (Bayer CropScience, Tagros, Heranba). Nevertheless results for solubility in water, hydrolysis at pH 9 and photolysis characteristics are quite different. For water solubility the Gharda value is within the variation of the values given by previous proposers and the scientific literature and was accepted by the Meeting due to the very low water solubility of deltamethrin and due to the fact that solubility depends on the purity of the pure active ingredient. For hydrolysis at pH 9, the test was performed according to the OECD guideline 111. Preliminary test using half saturated solution of deltamethrin (purity : 98.0%) in pH 9 buffer at 50°C ± 1°C was kept for 5 days followed by analysis for deltamethrin content, which showed that less than 10% of deltamethrin had reacted. Hence full test was not performed and deltamethrin was considered hydrolytically stable at pH 9. For photolysis, Gharda has followed the US-EPA guideline CG-6000 of October 1983 “Photolysis of aqueous solution in sunlight”. As per this guideline preliminary screening test was carried out to detect an ability of deltamethrin to undergo direct phototransformation in water by running UV-visible spectrum. Since λ_{max} observed was 277.2 nm, i.e. below 290 nm, further experiment for full photolysis study was not conducted.

Gharda confirmed to FAO and WHO that the chemistry and toxicity data package was generated using Gharda deltamethrin complying with the declared impurity profile and composition.

The studies on acute toxicity, irritation and sensitization, submitted by Gharda and performed according to GLP guidelines, were considered by WHO/PCS (PCS 2008), who concluded to equivalence with the data supporting the reference profile. Gharda provided also data on mutagenicity and ecotoxicology profiles. These data were supported by GLP studies.

On basis of all data provided by Gharda (manufacturing process, impurity profile, 5-batch analysis data, physico-chemical properties of active ingredient, chemical composition of TC and toxicological summaries), the Meeting concluded that the Gharda deltamethrin TC should be considered as equivalent to that on which the existing specification is based (FAO/WHO evaluation reports 333/2004).

The Meeting was provided by Gharda with specifications for EC, WP, SC and UL formulations. The data were in accordance with the requirements of the FAO/WHO Specifications Manual (Section 5 to 9). The company stated also that the existing CIPAC methods for the determination of deltamethrin is appropriate for the analysis of the company's TC and formulations and that the existing CIPAC methods for the determination of physical properties are appropriate for their formulations. The Meeting concluded that the proposed specifications are in compliance with the existing FAO specifications for deltamethrin SC and EC (May 2005), and for deltamethrin WP and UL (April 2006), and the existing WHO specifications for deltamethrin SC and EC (April 2005) and for deltamethrin WP and UL (September 2005). The extensions of the existing FAO specifications for deltamethrin DP, WG, EW and EG, and of the existing WHO specifications for DP, WG, EW, LN and WT were neither proposed by the company nor considered by the Meeting, as part of evaluation 333/2008.1.

Supporting Information
for
Evaluation Report 333/2008.1

Physico-chemical properties of deltamethrin

Table 1. Physico-chemical properties of pure deltamethrin

Parameter	Value(s) and conditions	Purity %	Method	Reference
Vapour pressure	1.2 x 10^{-7} Pa (25°C)	98%	EEC A-4	1 C.DMO.003
Melting point	Melting point = 99-102 °C	98%	OECD 102	2 C.DMO.002
Solubility in water	90.7 μg/l at 25°C	98%	OECD 105	3 C.DMO.008
Octanol/water partition coefficient	log P_{OW} = 4.61 at 25 °C	98%	OECD 107	4 C.DMO.010
Hydrolysis characteristics	Stable at pH 4.0, 7.0 and 9.0	98%	OECD 111	5 C.DMO.019
Photolysis characteristics	Aqueous photolysis of Deltamethrin is not possible as the material do not absorb sunlight in the region of λ_{max} > 290 nm, observed λ_{max} = 277.20 nm	98%	EPA guidelines, "Photolysis of aqueous solution in sunlight", CG-6000	6 C.DMO.011
Dissociation characteristics	Does not dissociate	98%	OECD 112	7 C.DMO.020

Table 2. Chemical composition and properties of deltamethrin 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 98.6-99.4 %, with no unknowns.
Declared minimum deltamethrin content	985 g/kg
Relevant impurities ≥ 1 g/kg and maximum limits for them	None
Relevant impurities < 1 g/kg and maximum limits for them	None
Stabilizers or other additives and maximum limits for them	None
Melting range of the TC	99-102°C

Formulations

The main formulation types available are EC, WP, SC and UL. Gharda deltamethrin TC is registered and sold in Argentina, Australia, India, China, Taiwan; the EC formulation in Moldova, India, Malaysia, Nicaragua, Taiwan and Vietnam; the WP formulation in India and Nepal; the SC formulation in India.

Methods of analysis and testing

Gharda confirmed that the existing CIPAC method for the determination of active ingredient content is appropriate for the analysis of their products. Test methods for determination of physico-chemical properties of the pure and technical active ingredient were based on OECD / EPA / EC / CIPAC, while those for the formulations were CIPAC, as indicated in the specifications.

Annex 1: Hazard Summary Provided by the Proposer

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

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

Species	Test	Duration and conditions or guideline adopted	Result	Reference
Rat (Wistar)	Acute oral	OECD 401 Purity: 98.5%	LD_{50} = 87.4 mg/kg bw	8 T.DMO.009
Rat (Wistar)	Acute dermal	OECD 402 Purity: 98.5%	LD_{50} > 2000 mg/kg bw	9 T.DMO.011
Rat (Wistar)	Acute Inhalation	OECD 403 Purity: 98%	LC_{50} = 0.232 mg/l	10 T.DMO.024
Rabbit, New Zealand white	Skin irritation	OECD 404 Purity: 98.5%	Non irritant	11 T.DMO.012
Rabbit, New Zealand white	Eye irritation	OECD 405 Purity: 98.5%	Mild irritant	12 T.DMO.013
Guinea pig	Skin sensitisation	OECD 406 Purity: 98.5%	Non sensitizer	13 T.DMO.017

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

Species	Test	Conditions and guideline	Result	Reference
Salomonella typhimurium TA 98, TA 100, TA 1535, TA 1537 and one tryptophan dependent auxotroph of Escherichia coli, strain CM891	Bacterial reverse mutation assay	The United Kingdom GLP requirement 1997, EEC 87/18, OECD Environment Monograph 45 Concentrations up to 5000 μg/plate. Purity: 98.5%	Non mutagenic	15 T.DMO.026
Mouse (bone marrow)	In vivo micro-nucleus test	Gaitonde Committee guideline, dosages 3, 10 and 30 mg/kg once orally for two consecutive days. Purity: 99.4%	Non clastogenic	16 T.DMO.028
Mouse (bone marrow)	In vivo cytogenetic test	Gaitonde Committee guideline, Dosages 3,10,30 mg/kg Once orally for two consecutive days Purity: 99.4%	Non clastogenic	17 T.DMO.029

Table C. Ecotoxicology profile of deltamethrin technical material

Species	Test	Duration and conditions	Result	Reference
Daphnia magna (water flea)	Acute toxicity	48 h flow through observations at 24 and 48 h OECD procedure 202 Purity: 98.5%	EC_{50} (48 hr) = 0.0753 μg/l	18 T.DMO.032
*Oncorhynchus mykiss (*Rainbow trout fish)	Acute toxicity	Under flow through exposure conditions for 96 hrs OECD procedure 203 Purity: 98.5%	LC_{50} (96 hr) = 0.688 μg/l	19 T.DMO.031
Lepomis macrochirus (Bluegill sunfish)	Acute toxicity	Under flow through exposure conditions for 96 hrs OECD procedure 203 Purity: 98.5%	LC_{50} (96 hr) = 0.727 μg/l NOEC = 0.289 μg/l	20 T.DMO.033
Apis mellifera (Honey bee)	Acute oral toxicity	Dosed and observed for 24, 48 h at 24-25°C United Kingdom Control of Pesticides Regulation 1986, EPA Pesticide Assessment Guidelines 1989 for non-target pests Purity: 98.5%	LD_{50} (48 hrs) = 0.049 µg/bee	22 T.DMO.023
Apis mellifera (Honey bee)	Acute contact toxicity	Topical application, observed at 24, 48 h at 24-25°C United Kingdom Control of Pesticides Regulation 1986, EPA Pesticide Assessment Guidelines 1989 for non-target pests Purity: 98.5%	LD_{50} (48 hrs) = 0.032 µg/bee	22 T.DMO.023
Colinus virginianus (Bobwhite quail)	Acute oral toxicity	Test levels, 0,500,1000,2000 mg/kg EPA guidelines, Series 71 – Avian and Mammalian Testing Purity: 98.5%	LD_{50} > 2000 mg/kg bw	23 T.DMO.018

Annex 2: References

Gharda document number or other references		Year	Title of report or publication details
1	C.DMO.003	1997	Physical & chemical characteristics of Determination - vapour pressure
2	C.DMO.002	1997	Physical & chemical characteristics of Determination - Melting point
3	C.DMO.008	1997	Physical & chemical characteristics of Deltamethrin - solubility in water
4	C.DMO.010	1997	Physical & chemical characteristics of Deltamethrin - n-Octanol/Water partition coefficient
5	C.DMO.019	1997	Physical & chemical characteristics of Deltamethrin - Hydrolysis as a function of pH
6	C.DMO.011	1997	Physical & chemical characteristics of Deltamethrin - Direct photo-transformation in water
7	C.DMO.020	1997	Physical & chemical characteristics of Deltamethrin - Determination of the dissociation constant
8	T.DMO.009	1997	Acute oral toxicity in Wistar rats
9	T.DMO.011	1997	Acute dermal toxicity study in Wistar rats
10	T.DMO.024	1997	Acute inhalation toxicity in Wistar rats
11	T.DMO.012	1997	Acute dermal irritation / corrosion study in New Zealand White Rabbits
12	T.DMO.013	1997	Acute eye irritation / corrosion study in New Zealand white rabbits
13	T.DMO.017	1997	Deltamethrin Technical - Skin sensitisation in the Guinea pig
14	Extoxnet	2006	Extension Toxicology Network, Pesticide Information Profiles
15	T.DMO.026	1997	Deltamethrin Tech. Bacterial Mutation Assay
16	T.DMO.028	1998	*In vivo* Micronucleus Test in Mouse Bone Marrow with Deltamethrin technical
17	T.DMO.029	1998	In vivo Mammalian Mouse Bone marrow Cytogenic Test with Deltamethrin technical
18	T.DMO.032	1998	Deltamethrin Technical : Acute toxicity to *Daphnia magna*
19	T.DMO.031	1998	Deltamethrin Technical : Acute toxicity to Rainbow Trout – Determination of 96 hour LC_{50}
20	T.DMO.033	1998	Deltamethrin Technical : Acute toxicity to bluegill sunfish – Determination of 96 hour LC_{50}
21	Pesticide Manual	1996	The Pesticide Manual 13th Edn. – Deltamethrin - Crop Protection Publication
22	T.DMO.023	1997	Deltamethrin Technical – Acute toxicity to honey bees (*Apis mellifera*)
23	T.DMO.018	1997	Deltamethrin Technical – Acute toxicity (LD_{50}) to Bobwhite quail
	PCS	2008	JMPS specifications for Gharda Chemicals Limited deltamethrin. Assessment prepared for PCS and submitted to WHOPES

DELTAMETHRIN

FAO/WHO Evaluation Report 333/2007

Recommendations

The Meeting recommended the following.

(i) The existing WHO specification for deltamethrin WG (333/WG, April 2005) and the existing FAO specification for deltamethrin WG (333/WG, May 2005) should be revised as follows.

The clause for acidity should be changed to:
Maximum acidity: 20 g/kg calculated as H_2SO_4.

(ii) The specification for deltamethrin WT proposed by Bayer CropScience, as amended, should be adopted by WHO.

Appraisal

The Meeting considered a proposed revision of the existing FAO and WHO specifications for deltamethrin water dispersible granules (WG) and a proposed new specification for deltamethrin water dispersible tablets (WT), provided by Bayer CropScience, together with supporting information.

Deltamethrin water dispersible granules (WG)

The manufacturer proposed that the existing limit for acidity (WHO 333/WG April 2005 and FAO 333/WG May 2005) should be revised from 5 g/kg to 20 g/kg. The existing limit had been reported in error to the JMPS in 2003/4. Data from recent tests on one batch were provided, showing results of 11.79 and 11.83 g/kg, and the limit of 20 g/kg was proposed as a more appropriate and acceptable quality criterion. The Meeting agreed that the existing limit in both the FAO and WHO specifications for WG should be revised accordingly.

Deltamethrin water dispersible tablets (WT)

The deltamethrin WT considered by the Meeting is a water-dispersible tablet formulation, intended for do-it-yourself treatment of mosquito nets after disintegration and dispersion in water, with stirring.

The tablets are individually packed in a blister pack as a ready-to-use product. Tablets are provided to users in the form of kits, each of which includes a blister-packed tablet, a pair of gloves and a leaflet explaining how to treat the mosquito net. Tablets are also supplied to aid agencies in boxes containing 200 tablets, individually blister-packed. One tablet is used to treat one mosquito net by disintegrating and dispersing the tablet in a bowl containing sufficient water to be absorbed by the net and by dipping the mosquito net in the resultant suspension.

The 2004 JMPS (FAO/WHO evaluation 333/2004) recommended that a proposed specification for deltamethrin WT should be reconsidered by the JMPS when the analytical and physical test method requirements and proposed limits had been

clarified and the test methods suitably validated. The 2005 JMPS (FAO/WHO evaluation 333/2005) noted that the development of a specification for deltamethrin WT could not be addressed until suitable methods became available for test tablet hardness and friability.

Supporting data, including information on test methods, together with a draft specification for deltamethrin WT, all provided by Bayer CropScience, were considered by the Meeting for the development of a new WHO specification.

Deltamethrin content clause

An analytical method for the determination of deltamethrin in tablet formulations, based on CIPAC method 333/WT/m/3 (CIPAC Handbook L, page 54), was adopted by CIPAC with provisional status in 2006 and as full CIPAC method in 2007.

Due to the specific intended use of the deltamethrin WT under consideration product, the Meeting agreed that the active ingredient content should be declared in g per tablet (0.4 g/tablet), with an appropriate tolerance applying to each tablet, instead of the usual form of expressing active ingredient content, as g/kg.

The Meeting noted that the standard tolerance (±25%) for active ingredient in heterogeneous formulations with low active ingredient content (Manual on the development and use of FAO and WHO specifications for pesticides, 2006) would be inappropriate in this case, partly because the tolerance applies to g/kg (or g/l) concentrations and partly because the Meeting considered that a ±25% tablet-to tablet range would be too wide to ensure uniform efficacy of a product where only one tablet is used in each application.

The manufacturer provided a report on 6 batches of deltamethrin WT25 (K-O TAB®) (10 individual tablets from 5 batches and 5 individual tablets from 1 batch), giving information on tablet-to-tablet variability and batch-to-batch variability. Results from the 55 tablets showed that the deltamethrin/tablet average content ±3 SD encompassed the range 0.349-0.444 g, with a batch-to-batch relative standard deviation of ±2.5%. The manufacturer therefore proposed a specification tolerance of ±12.5%, implying a deltamethrin content per tablet within the range 0.350 to 0.450 g, and this was considered acceptable by the Meeting.

pH clause

The manufacturer proposed that the acceptable pH range should be 4.1 to 7.5. The Meeting questioned the suitability of a minimum pH of 4.1, because a rounded value of 4.0 or 4.5 appeared to be more appropriate. The manufacturer stated that the minimum pH of 4.1 arose from an EU registration requirement to perform a test for acidity if the pH range extended to ≤4. The Meeting considered this to be a regulatory issue, not directly related to the quality of the product. Moreover, the manufacturer stated that the measured pH of deltamethrin WT is always between 4.0-4.5. The Meeting and the manufacturer thus agreed that, for the purposes of the WHO specification, the limits for the pH range should be 4.0 to 7.5.

Disintegration time, wet sieve test and suspensibility clauses

The Meeting queried the need for test of disintegration time test (normally required for effervescent tablets) and the absence of clauses for wet sieve test and suspensibility test (normally required for WT).

The manufacturer explained that disintegration time is important because the tablet is to be dispersed in a small volume of water, into which a mosquito net will be dipped. An effervescent system could increase user risks but, without it, a combination of the hardness required for tablet integrity and low affinity of deltamethrin for water means that tablets tend to disperse relatively slowly. The Meeting agreed that a clause for disintegration time is required.

The manufacturer explained that the slurry in the bowl, produced when the tablet is dispersed in water by the user, is taken up by the net dipped in it and is not intended to be sprayed. Thus there is no possibility of blocking filters or sprayer nozzles and a wet sieve test, though it might indicate the acceptability of tablet disintegration, is not appropriate for this particular application. The same considerations apply to suspensibility: the dispersion does not remain in a tank before spraying but is stirred in a bowl before dipping the bednet, which is also a form of agitation.

The test method for disintegration time has been published by the European Pharmacopoeia (2.9.1, disintegration of tablets and capsules). As published, the method states that the test should be conducted at 37°C, reflecting human body temperature appropriate for disintegration of pharmaceutical tablets. However, tests for compliance with FAO and WHO specifications for pesticides are generally based on a harmonized temperature of 30 ± 2°C and this was used by the manufacturer to derive the proposed limit of 2½ minutes. The water to be used is CIPAC standard water D, which is the normal requirement in FAO and WHO specifications for tests involving hard water. The Meeting noted that the test requires equipment that may not be widely available in pesticide formulation testing laboratories, though it is widely used in pharmaceutical laboratories.

Tablet integrity and tablet hardness clauses

A clause of maximum 1% broken tablets was proposed by the manufacturer. As the FAO/WHO specification guideline for WT formulations indicates that there should be no broken tablets, the manufacturer was asked for clarification. The manufacturer stated that during the study of variability in active ingredient content, a single 200-tablet pack was found to contain one broken tablet and the proposed clause was based on this information. The manufacturer added that the tablets are always packaged in blister packs, so that if a tablet is found to be broken, it can still be used and there will be no contact with the user. On the basis that even the occasional broken tablet does not increase user risks, the Meeting accepted that a zero tolerance was unnecessarily stringent in this case.

The proposed limit of 1% broken tablets implied that at least 100 tablets would have to be removed from the blister packaging, in order to test for compliance. However, assuming a random distribution of broken tablets within the packs, inspection of 100 tablets would give only about 87% probability of detecting a 2% incidence of broken tablets (a 2-fold exceedance of the proposed limit). To achieve the more usually acceptable 95% probability of detecting the same level of non-compliance, about 150 tablets would have to be assessed. The blister packs being completely opaque, an unacceptably large number of tablets would therefore have to be removed from the packaging for testing compliance with a 1% limit. The alternative of adopting a higher limit, solely to reduce the numbers of tablets to be inspected, was considered equally unacceptable.

However, tablet integrity and hardness are closely related. The manufacturer had proposed a clause and limits for hardness, referencing a standard European Pharmacopoeia method (2.9.8, resistance to crushing of tablets) and testing 10 tablets. Broken tablets, or those likely to break within the blister pack, would fail the test of tablet hardness. The Meeting therefore agreed with the manufacturer that the proposed clause for tablet integrity should be deleted and reliance placed on the clause and limits for tablet hardness. The Meeting noted that tablet hardness testing machines may not be widely available in pesticide formulation testing laboratories but are widely used in pharmaceutical laboratories.

Persistent foam clause

Due to the specific application of this type of product (treatment of mosquito nets after disintegration and dispersion in water following stirring process), the Meeting considered that persistent foam was not appropriate in this case and that it was unnecessary to include a clause in the specification.

Degree of attrition clause

CIPAC method MT 193 (friability of tablets) for determination of the attrition resistance of non-coated tablets was published in CIPAC Handbook L, p. 147. In 2006, CIPAC agreed to modify the title of the method to “attrition resistance”. Therefore the Meeting agreed that the specification clause and limit should be expressed in the form of “attrition resistance: minimum 95%” instead of “degree of attrition: maximum 5%”.

Embittering agent

The manufacturer provided commercially confidential information on the embittering agent added into the product. The identity and exact concentration of the embittering agent were not considered by the manufacturer to be critical for product quality, although the presence of such a component makes an important contribution to user safety. The Meeting agreed that it was not necessary to include a clause for control of the embittering agent, nor to append to the specification a suitable peer-validated analytical method for its determination. The Meeting agreed that the description clause should state that the product contains an embittering agent.

DELTAMETHRIN

FAO/WHO Evaluation Report 333/2006.2

Recommendations

The Meeting recommended the following.

(i) The existing WHO specifications for deltamethrin TC, DP, SC, EC WG, WP, UL and EW should be extended to encompass the products of Heranba Industries Ltd*.

(ii) The existing FAO specifications for deltamethrin TC, DP, WP, SC, EC, UL, WG, EG and EW should be extended to encompass the products of Heranba Industries Ltd.

Appraisal

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

The Meeting was provided by Heranba with commercially confidential information on the manufacturing process, the manufacturing specification and 5-batch analysis data for all detectable impurities. The batch data were derived from analyses conducted in two different laboratories on the same 5 batches. Data from the 1st laboratory addressed the content of active ingredient and all impurities with manufacturing specifications ≥1 g/kg. Data from the 2nd laboratory primarily addressed the content of deltamethrin. Although there was an apparent slight bias between the two series of data for deltamethrin content (988, 983 g/kg averages), the differences (-3.5 to -5.9 g/kg) were within the reproducibility (R = 17 g/kg at 998 g/kg) expected from the current CIPAC method (CIPAC L). The manufacturer proposed that the deltamethrin data from the 2nd laboratory should be utilized in the equivalence determination. Although these values were slightly lower than those from the first laboratory, mass balances were ≥99.4% with no unknowns detected. The confidential information was confirmed as being similar to that submitted for registration in Taiwan.

The manufacturing specification indicated non-equivalence with the reference profile of impurities, with respect to bicisthemic acid anhydride [(1R,3R)-3-(2,2-dibromovinyl)-2,2-dimethylcyclopropane carboxylic anhydride]. A similar issue had been considered by the 2005 JMPS (FAO/WHO evaluation report 333/2005, below) and WHO had advised that the impurity should not be considered relevant. Bicisthemic acid chloride [(1R,3R)-3-(2,2-dibromovinyl)-2,2-dimethylcyclopropane carboxoyl chloride] was also present in the Heranba profile but, as the levels were

* Note: extension of the existing WHO specification for deltamethrin LN was neither proposed by the company nor considered by the Meeting, as part of evaluation 333/2006.2.

<1 g/kg, it remained a non-relevant impurity, on the same basis as that decided by the 2005 JMPS. The studies on acute toxicology, submitted by Heranba, were considered by WHO/PCS (PCS 2006) to indicate equivalence of toxicology (FAO/WHO 2006) with the data supporting the reference profile. The Meeting therefore concluded that Heranba deltamethrin TC should be considered equivalent to that on which the existing specifications are based (FAO/WHO evaluation report 333/2004, below).

Heranba confirmed that the deltamethrin TC and formulations produced by the company comply with existing FAO and WHO specifications. The company also stated that existing CIPAC methods for identification and determination of deltamethrin were appropriate for the analysis of the company's TC and formulations.

Heranba proposed a specification for deltamethrin WT. A specification for WT had been proposed in 2004 by Bayer CropScience (see evaluation report 333/2004) but was not adopted, due to the lack of a suitably validated analytical method and unresolved problems regarding physical characteristics and the corresponding test methods. These issues were finally resolved by Bayer CropScience when an analytical method for deltamethrin in WT was adopted by CIPAC in 2006. A revised specification for WT is scheduled for JMPS evaluation in 2007 and a decision on the 2006 Heranba proposal for extension of the WT specification was therefore deferred.

Supporting Information
for
Evaluation Report 333/2006.2

Physico-chemical properties of deltamethrin

Table 1. Physico-chemical properties of pure deltamethrin

Parameter	Value(s) and conditions	Purity %	Method	Reference
Vapour pressure	1.24×10^{-5} mPa at 25°C	98	OECD 104	HIL/D12/02
Melting point	100°C	98	CIPAC MT 2	HIL/D12/03
Temperature of decomposition	>270°C	98	CIPAC MT 2	HIL/D12/03
Solubility in water	<0.1 mg/l at 25°C, pH not stated	98	CIPAC MT 157.2	HIL/D12/04

Table 2. Chemical composition and properties of technical deltamethrin (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 99.81-99.84%, with no unknowns.
Declared minimum deltamethrin content	985 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
Melting temperature of the TC	98-101°C

Formulations

Heranba deltamethrin formulations are registered and sold in Malaysia, Taiwan and Thailand.

Methods of analysis and testing

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

Annex 1: Hazard Summary Provided by the Proposer

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

Table A. Toxicology profile of Heranba deltamethrin technical material, based on acute toxicity, irritation and sensitization

Species	Test	Duration and conditions	Result	Reference
Rat (m,f)	Oral	OECD 401 Purity 98.5%	LD_{50} (m) = 324 (305-343) mg/kg bw LD_{50} (f) = 341 (309-372) mg/kg bw	8400
Rat (m,f)	Dermal	OECD 402 Purity 98.5%	LD_{50} >2000 mg/kg bw	8402
Rat (m,f)	Inhalation	OECD 403 Purity 98.5%	LC_{50} = 3.1 (2.3-4.2) mg a.i./l	8517
Rabbit (m,f)	Skin irritation	OECD 404 Purity 98.5%	Non-irritant	8403
Rabbit (m,f)	Eye irritation	OECD 405 Purity 98.5%	Not irritant	8404
Guinea pig (m)	Skin sensitization	OECD 406 Purity 98.5%	Non-sensitizer	8484

Table B. Mutagenicity profile of Heranba deltamethrin technical material, based on *in vitro* and *in vivo* studies

Species	Test	Duration and conditions	Result	Reference
Salmonella typhimurium	Ames test, reverse mutation assay (*in vitro)*	OECD 471; ±S9 metabolic activation; 0.5,5,50 and 5000 µg/plate mixed in DMSO. Deltamethrin purity 98.5%	Non-mutagenic	8525
Saccharomyces cerevisiae	Gene mutation	OECD 480; ±S9 metabolic activation; up to 5000 µg/plate. Deltamethrin purity 98.5%	Non-mutagenic	8528
Mus musculus (Swiss albino)	Mouse bone marrow cytogenetic assay (chromosomal aberration)	OECD 475; 10, 5, 2.5 mg/kg b.w. triethylenemelamine (TEM) dose at 1.0 mg/kg b.w. via split-dose i.p. injection. Deltamethrin purity 98.5%	Non-mutagenic	8527

Table C. Ecotoxicology profile of Heranba deltamethrin technical material

Species	Test	Duration and conditions	Result	Reference
Water flea, *Daphnia magna*	Acute immobilization test	24 h. OECD 202, purity 98.5%	EC_{50} = 0.45 µg/l	8436
Freshwater fish, *Poecilia reticulata*	Acute toxicity	24-96 h. OECD 203, purity 98.5%	LC_{50} (24 h) >1.6 µg/l LC_{50} (48 h) >1.6 µg/l LC_{50} (72 h) = 1.17 µg/l LC_{50} (96 h) 0.56 µg/l	8433
Japanese quail, *Coturnix coturnix japonica*	Acute dietary toxicity	8 days, OECD 205, purity 98.5%	LC_{50} = 545.51 ppm	8435

Annex 2. References

Heranba document number	Year and title of report or publication details
8400	2001. Acute oral toxicity study in Wistar rats.
8402	2001. Acute dermal toxicity study in Wistar rats.
8403	2001. Study on Primary skin irritation in Himalayan albino Rabbits.
8404	2001. Study on irritation to mucous membrane* in Himalayan albino Rabbits.
8433	2001. Acute toxicity to freshwater fish.
8435	2001. Acute dietary toxicity study in Japanese quail.
8436	2001. Acute immobilization test with deltamethrin technical in Daphnia magna.
8484	2001. Skin sensitization potential in guinea pig.
8517	2001. Acute inhalation study in Wistar rats.
8525	2001. Mutagenicity evaluation by Ames *Salmonella typhimurium*-Reverse Mutation assay.
8527	2001. Mutagenicity evaluation by mouse bone marrow cytogenetic assay Chromosomal aberration.
8528	2001. Mutagenicity evaluation: Induction of gene mutation in Yeast –*Saccharomyces cerevisiae*.
CIPAC L	Collaborative International Pesticides Analytical Council (CIPAC). Deltamethrin. Handbook L, p. 45. Harpenden, U.K., 2006.
FAO/WHO 2006	Manual on development and use of FAO and WHO specifications for Pesticides. March 2006 revision, published in the internet at http://www.fao.org/ag/agp/agpp/pesticid/ and http://www.who.int/quality/en/.
HIL/D12/02	2002. Study on vapor pressure of deltamethrin technical.
HIL/D12/03	2003. Study on melting point of deltamethrin technical.
HIL/D12/04	2003. Study on solubility in water of deltamethrin technical.
PCS 2006	2006. JMPS specification for Heranba Industries deltamethrin. Assessment prepared for PCS and submitted to WHOPES on 8 September, 2006.

* Refers to the eye.

DELTAMETHRIN

FAO/WHO Evaluation Report 333/2005

Recommendations

The Meeting recommended the following.

(i) The existing (April 2005) WHO specifications for deltamethrin TC, DP, SC, EC WG, and existing (September 2005) WHO specifications for deltamethrin WP, UL, together with the previously unpublished specification for deltamethrin EW (all originally based upon data submitted by Bayer CropScience) should be amended to include a footnote regarding the potentially relevant impurity, becisthemic acid chloride, and extended to encompass the products of Tagros (India) and Argos (South Africa). WHOPES evaluation of the EW having been completed satisfactorily, this specification should now be adopted by WHO.

(ii) The existing (May 2005) FAO specifications for deltamethrin TC, DP, SC, EC and WG, together with the previously unpublished specifications for deltamethrin EW, EG, WP and UL (all based upon data submitted by Bayer CropScience) should be amended to include a footnote regarding the potentially relevant impurity, becisthemic acid chloride1, and extended to encompass the products of Tagros (India) and Argos (South Africa). Analytical methods for determination of deltamethrin in EW, EG, WP and UL having been adopted by CIPAC, these specifications should now be adopted by FAO.

Appraisal

The Meeting considered data and information submitted by Tagros (India) and Argos (South Africa), for extension of: (i) existing FAO specifications for deltamethrin TC, DP, SC, EC and WG (May 2005); (ii) existing WHO specifications for TC, DP, SC, EC, WG (April 2005); (iii) existing WHO specifications for WP and UL (September 2005); (iv) pending FAO specifications for EG, EW, UL and WP; and (v) a pending WHO specification for EW.

Argos provided written confirmation that their products (currently WP only) contain only deltamethrin sourced from Tagros and therefore the Meeting agreed that decisions and recommendations relating to Tagros would apply also to Argos.

The Meeting was provided by Tagros with commercially confidential information on the manufacturing process and batch analysis data on all detectable impurities. Mass balances were very high (99.91–100.10%), with no unknowns detected. The UK Health & Safety Executive (HSE) confirmed that there were no significant differences between the data submitted to FAO/WHO and those submitted for registration in the UK.

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[1] The name “becisthemic” is sometimes spelt “bicisthemic” but the common spelling is used here.

In evaluating the equivalence of Tagros and Bayer TCs, the Meeting considered two potentially relevant impurities, becisthemic acid anhydride [(1*R*,3*R*)-3-(2,2-dibromovinyl)-2,2-dimethylcyclopropane carboxylic anhydride] and becisthemic acid chloride [(1*R*,3*R*)-3-(2,2-dibromovinyl)-2,2-dimethylcyclopropane carboxoyl chloride]. Neither impurity occurred in the Bayer TC ≥1 g/kg but, initially, the Tagros manufacturing limits were 10 g/kg and 2 g/kg, respectively. The acute toxicology data submitted by Tagros suggested that these higher limits might be reflected in the classification of the company's TC as a mild irritant of eyes. The data for the acid anhydride were complicated by the fact that the analytical method did not distinguish between the anhydride and becisthemic acid and the analytical method used for determination of becisthemic acid chloride was based on titration and appeared to lack specificity.

WHO/PCS secretariat assessed the results of eye irritation studies conducted (to GLP and according to OECD guidelines 404 and 405) by Tagros and concluded that, as defined by GHS (GHS 2003), the Tagros TC should not be classified as an eye irritant (PCS 2005a). WHO/PCS also concluded that, on the basis of toxicology, the Tagros TC should be considered equivalent to that of Bayer and the Meeting agreed.

No information was available on the toxicity of becisthemic anhydride but WHO/PCS concluded that it should not be considered a relevant impurity (PCS 2005a) . Limited experimental data had indicated that a structural analogue of it, namely chrysanthemic anhydride, is sensitizing to the skin and, applying the precautionary principle, JMPS had previously concluded that the analogue should be considered a relevant impurity in *d*-allethrin (JMPS 2002). However, when assessing the relevance of a chlorine analogue of becisthemic anhydride (namely 2,2-dimethyl-3-(2,2'-dichlorovinyl) cyclopropane carboxylic acid anhydride), it was considered that there was no justification for declaring it a relevant impurity. That is, the structure-activity relationship was not considered to be strong enough to extend the weak data for sensitization from the non-halogenated chrysanthemic anhydride to the dichloro analogue of becisthemic acid anhydride (PCS 2005b). In keeping with this rationale, PCS considered that the structural relationship between chrysanthemic anhydride and becisthemic anhydride does not justify the classification of becisthemic anhydride as sensitizing. The conclusion was supported by the fact that Tagros deltamethrin TC was not sensitizing to the skin of Guinea pigs (studies performed according to the OECD guideline and GLP). The Meeting therefore agreed that becisthemic anhydride is not a relevant impurity in deltamethrin TC.

As in the case of the anhydride, no information was available on the toxicity of becisthemic acid chloride but WHO/PCS secretariat concluded that it should be considered a relevant impurity (PCS 2005a), if it occurred at ≥1 g/kg in the TC. WHO/PCS advised that, based on its chemical structure, becisthemic acid chloride is likely to be irritating (several acid chlorides are corrosive). WHO/PCS noted that, in the GHS classification, substances for which structure-activity or structure-response assessments indicate that they may be corrrosive/irritant, should be classified as corrosive/irritant, in the absence of human or experimental data (GHS 2003). WHO/PCS thus recommended that becisthemic acid chloride should be considered as a relevant impurity. GHS guidelines (GHS 2003) indicate that when classifying a mixture, the data used should be derived primarily from studies on the mixture itself. As Tagros deltamethrin, apparently containing the becisthemic acid chloride at ≤2g/kg, (also and becisthemic acid and anhydride at a sum concentration of ≤10 g/kg), was not irritating, WHO/PCS concluded that this limit could be accepted as the

specification limit for becisthemic acid chloride. WHO/PCS noted that the conclusion is the same if the GHS second tier approach, classification by the concentration of the impurity, is applied: a mixture is classified as corrosive if the sum concentration of corrosive components is ≥5% and as an irritant if it is ≥1 but <5%.

Tagros then replaced the company's non-specific titrimetric procedure with an HPLC method, which was more specific for the determination of becisthemic acid chloride and which had a limit of quantification of 0.1 g/kg (Tagros 2006a, 2006b). In consequence, the manufacturer reported that levels of this impurity did not occur at up to 2 g/kg, as previously stated, but were actually <1 g/kg. The Tagros manufacturing specification for this impurity was consequently lowered to <1 g/kg. Although the stability of the impurity during analysis was not reported, the HPLC method did not seem likely to under-estimate the concentration of becisthemic acid chloride and the change in manufacturing specification from 2 to <1 g/kg effectively changed the designation of this impurity to non-relevant. Consequently, there was no requirement for a specification clause to control its concentration. The new data had not been considered by a national registration authority.

The Meeting agreed that a cautionary footnote should be added to specifications, to indicate that becisthemic acid chloride could be a relevant impurity in the products of other manufacturers, if it occurred at ≥1 g/kg deltamethrin.

Overall, Tagros deltamethrin complied with the existing specification for TC but the becisthemic acid anhydride (not becisthemic acid chloride) indicated non-equivalence of the impurity profiles. However, the PCS assessment of this impurity and the available hazard data for Tagros deltamethrin TC showed no evidence to suggest that the Tagros TC presents greater or additional hazards compared with Bayer deltamethrin TC. Thus the Meeting concluded that the two TCs should be considered equivalent.

Tagros and Argos stated their products otherwise complied with the existing (September 2005) FAO and/or WHO specifications for TC, WP, EC and SC. The Meeting noted that development of the specifications for WT, proposed by Bayer and Tagros, cannot be addressed until suitable methods become available to test tablet hardness and friability.

CIPAC methods are available for identification and determination of deltamethrin in the TC and formulations, with the exception of WT for which the CIPAC method status is tentative. A more acceptable method is therefore required to support the proposed specification for WT.

The Meeting noted that WHOPES trials of deltamethrin EW had been successfully completed (WHO 2006).

Supporting Information
for
Evaluation Report 333/2005

Physico-chemical properties of deltamethrin

Table 1. Physico-chemical properties of pure deltamethrin (Tagros)

Parameter	Value(s) and conditions	Purity %	Method	References
Vapour pressure	1.24 X 10^{-8} Pa at 20°C	98.0	EEC A4	10803
Melting point	98-101°C	98.0	EEC A1, A2	10761
Temperature of decomposition	>300°C	98.0	EEC A1, A2	10761
Solubility in water, at 20ºC	0.16 x 10^{-6} g/l at 20°C	98.0	OECD 105	10760
Octanol/water partition coefficient, at 23ºC	log P K_{OW} = 4.61 at 25 ± 1°C	98.0	EEC A8	10806
Hydrolysis characteristics, at 25ºC	Negligible hydrolysis at 50°C, pH 4.0 & 7.0 Half-life = 1.75 d at 40°C, pH 9.0 Half-life = 1.85 d at 30°C, pH 9.0	98.0	OECD 111	12430

Table 2. Chemical composition and properties of technical deltamethrin (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 99.91-100.10%, with no unknowns.
Declared minimum deltamethrin content	985 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
Melting temperature of the TC	98-101°C

Formulations

Tagros deltamethrin TC is registered and sold in Taiwan, China, Korea, Australia South Africa, Ecuador and Spain; the EC formulation in Taiwan, Saudi Arabia, Azerbaijan, Kyrgystan, Cambodia, Turkmenistan, Sri Lanka and Romania; the SC formulation in Taiwan; the WP formulation in Sri Lanka, Azerbaijan and Sudan; and the ULV formulation in Lebanon.. Argos formulations are registered and sold in South Africa.

Methods of analysis and testing

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

Annex 1: Hazard Summary Provided by the Proposer

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

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

Species	Test	Duration and conditions	Result	References
Rat, Wistar, m	Acute oral	14 d obs., dose: 0, 500, 750 & 1000 mg/kg bw, vehicle vegetable oil, OECD 401, 99.2% purity	(i) LD_{50} = 612 mg/kg bw (ii) LD_{50} = 782 mg/kg bw	7719
Mouse Swiss albino, m & f	Acute oral	14 d obs., dose 0, 50, 100 & 150 mg/kg bw, vehicle vegetable oil, OECD 401, 99.2% purity	LD_{50} = 86 mg/kg bw (m) LD_{50} = 130 mg/kg bw (f)	7720
Rat, Wistar, m & f	Acute dermal	14 d obs., dose 0 & 2000 mg/kg bw OECD 402, 99.2% purity	LD_{50} >2000 mg/kg bw (m,f)	7721
Rat, Wistar, m & f	Acute inhalation	14 d obs., dose 0, 1.63, 3.11 & 4.39 mg/l, OECD 403, 99.2% purity	LC_{50} = 3.16 mg/l	8205
Rabbit	Skin irritation	Observation 1, 24, 48 & 72 h after treatment, dose: 500 mg (4 hours), OECD 404, 99.2% purity	non-irritant	7722
Rabbit	Eye irritation	Observation: 1, 24, 48 & 72 h after treatment, dose: 69 mg, OECD 405, 99.2% purity	mild irritant	7723
Guinea pig, Hartley	Skin sensitization	Observation: 28 d, dose 25 mg, OECD 406, 99.2% purity	non-sensitizer	7724

Deltamethrin has moderate to high acute toxicity when administered orally to the rat or mouse. Dullness, lethargy, mild tremor, salivation, diarrhoea and paralysis were observed in both male and female rats 2 h after treatment and persisted up to 24 h. In the rat, deltamethrin is less toxic by the dermal route but is highly toxic by inhalation. Deltamethrin is a mild-irritant to eye and non-irritant to skin of rabbits. It is not a skin sensitizer in the Guinea pig.

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

Species	Test	Duration and conditions	Result	References
Rat	90 day oral	90 d, dose 0, 25, 50 & 75 mg/kg bw/d, OECD 408, purity 98%	NOAEL = 50 mg/kg bw/day	10380

Table C. Mutagenicity profile of Tagros deltamethrin technical material, based on *in vitro* and *in vivo* studies

Species	Test	Duration and conditions	Result	References
Salmonella typhimurium (TA 98, TA100, TA1535, TA1537)	Bacterial reverse mutation assay	Gaitonde Committee guideline 6.3.0 (1); dosage 0.5–5000 µg/plate, purity 98.65%	Negative	11270
TK6 human lymphoblastoid cells	Mammalian cell gene mutation test	Dosage 0.005, 0.01, 0.04 & 0.06 mM with S-9 mix; 0.005, 0.01, 0.02 & 0.04 mM without S-9 mix; OECD 476, purity 98.65%	Negative	10401
Human lymphocytes	DNA damage and repair	OECD 482; dosage 250, 500, & 1000 µg/plate, purity 98.65%	Negative	8181
Chinese hamster ovary (CHO) cells	Chromosomal aberration assay	Dosage 6, 7, & 8 µM with S-9 mix, 2, 4 & 6 µM without S-9 mix, OECD 473, purity 98.65%	Negative	10399
Mouse, Swiss Albino (m,f)	Mouse micronucleus assay	Gaitonde Committee guideline 6.3.0.2 (A), dosage 0,7.5,15,30 mg/kg, once or twice orally – 24h apart, purity 98.65%	Negative	11271
Mouse, Swiss Albino bone-marrow cells	Chromosomal aberration	Gaitonde Committee Guideline 6.3.0 (1), dosage: 0, 7.5, 15, 30 mg/kg b.w., once orally, purity 98.65%	Negative	11272
Mouse Swiss Albino (m, germinal cells)	Dominant lethal mutation	Gaitonde Committee Guideline 6.3.0.2 (A), dosage 0, 1.25, 2.5, 5 mg/kg b.w, once orally, purity 98.65%	Negative	11273

Table D. Ecotoxicology profile of Tagros deltamethrin technical material

Species	Test	Duration and conditions	Result	References
Daphnia magna (water flea)	Acute immobilization	Dosage: 1, 2, 4, 8 and 16 µg/l, 24 h, OECD 202, 99.2% purity	EC_{50} = 4.14 µg/l	7739
Poecilia immobiliza (freshwater fish)	Acute toxicity	Dosage: 0, 0.75, 1.13, 1.68, 2.53 and 3.79 µg/l, 96 h, OECD 203, 99.2% purity	LC_{50} = 1.74 µg/l	7737
Chlorella vulgaris (green algae)	Growth	72 h, OECD 201, 98.65% purity	EC_{50} = 22.77 µg/l	11442
Lampito mauritii (earthworm)	Acute toxicity	Dosage 150–1000 mg/kg dry soil, 14 d, OECD No.207, 99.2% purity	LC_{50} >1000 mg/kg dry soil	8321
Apis cerana indica (honey bee)	Acute contact toxicity	Dosage 0.05–1.20 ppm, 24 h, EPPO 170, 99.2% purity	LC_{50} = 0.52 ppm	8320
Coturnix coturnix japonica (Japanese quail)	Dietary toxicity	Dosage 1000, 2000, 3000, 4000 or 5000 ppm, 5 d, OECD 205, 99.2% purity	LC_{50} >5000 ppm	7738

Under laboratory conditions, deltamethrin is highly toxic for fish, aquatic arthropods, and honeybees. However, under field conditions, lasting adverse effects are not likely to occur under recommended conditions of use.

Annex 2. References

Tagros document number or other reference	Year and title of report or publication details
7719	2000. Acute oral toxicity study with deltamethrin technical in Wistar rat.
7720	2000. Acute oral toxicity study with deltamethrin technical in Swiss albino mice.
7721	2000. Acute Dermal toxicity study with deltamethrin technical in Wistar rat.
7722	2000. A study on primary skin irritation of deltamethrin technical in Himalayan albino rabbits.
7723	2000. A study on irritation on mucous membrane of deltamethrin technical in Himalayan albino rabbits.
7724	2000. Skin sensitization potential of deltamethrin technical in Guinea pigs.
7737	2000. Acute toxicity of deltamethrin technical to freshwater fish, *Poecilia immobiliza*.
7738	2000. Dietary toxicity study with deltamethrin technical in Japanese quails.
7739	2000. Acute immobilization test with deltamethrin technical in *Daphnia magna*.
8181	2000. Mutagenicity evaluation of deltamethrin technical in human lymphocytes (DNA damage and repair – unscheduled synthesis).
8205	2000. Acute inhalation toxicity study with deltamethrin technical in Wistar rats.
8320	2001. Toxicity of deltamethrin technical to honey bee, *Apis indica.*
8321	2001. Toxicity of deltamethrin technical to earthworm, *Lampito mauritii.*
10380	2002. Sub-acute oral toxicity study with deltamethrin technical in Wistar rats.
10399	2002. Mutagenicity evaluation of deltamethrin technical – *in vitro* chromosomal aberration assay.
10401	2002. Mutagenicity evaluation of deltamethrin technical – *in vitro* mammalian cell gene mutation test.
10760	2002. Study on solubility of deltamethrin technical in water.
10761	2002. Study report on melting point, boiling point and relative density of deltamethrin technical.
10803	2002. Study report on vapour pressure of deltamethrin technical.
10806	2002. Study on partition co-efficient (*n*-octanol/water) of deltamethrin technical.
11270	2002. Mutagenicity evaluation of deltamethrin technical by Ames *Salmonella typhimurium* – reverse mutation assay.
11271	2002. Mutagenicity evaluation of deltamethrin technical – in vivo mouse micronucleus assay.
11272	2002. Mutagenicity evaluation of deltamethrin technical – in vivo by mouse bone marrow cytogenetic assay (chromosomal aberration)
11273	2002. Mutagenicity evaluation of deltamethrin technical – in vivo by dominant lethal test in mouse.
11442	2002. Effect of deltamethrin technical on the growth of green alga (*Chlorella vulgaris*).
12430	2002. Study on hydrolysis (abiotic) of deltamethrin technical.
GHS 2003	The Globally Harmonized System of Classification and Labelling of Chemicals (GHS) at: http://www.unece.org/trans/danger/publi/ghs/ghs_rev00/English/GHS-PART-3e.pdf , accessed on 9 September, 2005.
JMPS 2002	WHO Specifications and evaluations for public health pesticides. *d*-Allethrin. accessed at http://www.who.int/whopes/quality/en/dAllethrin_spec_eval_March_04.pdf on 12 September, 2005.
PCS 2005a	14 September 2005. Relevance of impurities in deltamethrin, and equivalence of two deltamethrin products.
PCS 2005b	11 January 2005. Dermal irritation and sensitization of permethrin.
Tagros 2006a	Method of analysis for the determination of bicisthemic acid content corresponding to deltamethrin content in deltamethrin technical. Tagros report on study No. 05063. E-mail sent to M. Zaim (WHO) and G Vaagt (FAO) on 24 February 2006.

Tagros document number or other reference	Year and title of report or publication details
Tagros 2006b	ReRe: Deltamethrin specifications E-mail sent to M. Zaim (WHO) and G Vaagt (FAO) on 01 March 2006.
WHO 2006	Report of the Ninth WHOPES Working Group Meeting. Geneva, World Health Organization, 2006 (WHO/CDS/NTD/WHOPES/2006.2).

DELTAMETHRIN

FAO/WHO Evaluation Report 333/2004

Explanation

The data for deltamethrin were evaluated for a review of existing FAO specifications for TC, WP, EC, DP, UL (AGP: CP/243-1991) and WHO specifications for TC (WHO/SIT/24/R2–1999), WP (WHO/SIF/42/R2–1999), EC (WHO/SIF/43/R2–1999), DP (WHO/SIF/44/R2–1999), UL (WHO/SIF/46/R1–1999), SC (WHO/SIF/64/R2–1999), interim WHO specifications for WT (WHO/IS/00.1–1999) and to support proposed new FAO specifications for EG, EW, WG and a new WHO specification for EW.

Deltamethrin is a single stereoisomer pyrethroid and is not under patent.

Deltamethrin was first evaluated by the FAO/WHO JMPR in 1980. Subsequent JMPR reviews were undertaken in 1984-1988, 1990 and 1992. Residues resulting from veterinary uses of deltamethrin were evaluated by the FAO/WHO Expert Committee on Food Additives (JECFA) in 1999. It was evaluated/reviewed by the European Commission (List 1) under Directive 91/414/EEC and is included in Annex 1, meaning that formulations may be registered in EU countries.

The draft specifications and the supporting data were provided by Bayer Crop Science in 2003, for evaluation in 2004.

Uses

Deltamethrin is a synthetic insecticide belonging to the pyrethroid family. It is widely registered and used in agriculture and in public and animal health as a broad spectrum insecticide against noxious insects belonging to groups such as Orthoptera, Thysanoptera, Heteroptera, Homoptera, Diptera, Coleoptera, Lepidoptera and Hymenoptera, and against ticks and mites. Main uses in agriculture are in top fruits, grapes, a wide range of vegetables, oilseed rape, cotton, cereals and maize. It is also recommended for use against locusts, indoor insects and pests of stored grain and timber. Deltamethrin is also widely used as an acaricide/insecticide for the control of ticks, mites and insect pests of livestock. Deltamethrin is non-systemic with contact and stomach action.

Identity

ISO common names

Deltamethrin (BSI, draft E-ISO), deltaméthrine ((f) draft F-ISO)

Synonyms

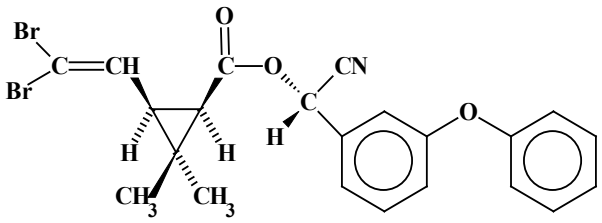
Decamethrin (rejected common name)

Chemical names

IUPAC (*S*)-α-cyano-3-phenoxybenzyl (1*R*,3*R*)-3-(2,2-dibromovinyl)-2,2-dimethylcyclopropane carboxylate

CA [1*R*-[1α(*S**),3α]]-cyano(3-phenoxyphenyl)methyl 3-(2,2-dibromoethenyl)-2,2-dimethylcyclopropanecarboxylate

Structural formula



deltamethrin is one of the eight possible stereoisomers having the structure shown.

Empirical formula

$C_{22}H_{19}Br_2NO_3$

Relative molecular mass

505.2 g/mol

CAS Registry number

52918-63-5

CIPAC number

333

Identity tests

HPLC retention time; TLC; IR, NMR and mass spectra.

Physical and chemical properties

Table 1. Physicochemical properties of pure deltamethrin

Characteristic	Value	Purity, %	Method	Reference
Vapour pressure	1.25 x 18^{-8} Pa at 25°C 4.13 x10^{-8} Pa at 35°C 1.98 x 10^{-7} Pa at 45°C	99.7	US EPA 63-9, equivalent to 92/69/EC A6 or OECD 104, gas sat. method	A47916
Melting point	100-102°C	99.7	OECD 102, US EPA 63-9	A70753
Boiling point	decomposes below boiling point	99.7	OECD 103 & 92/69/EC A2	A38362
Decomposition temperature	270°C	99.7	OECD 103 & 92/69/EC A2	A38362
Solubility in water	2 x 10^{-7} g/l, 25ºC; not pH-dependent but determined at pH 7.49-7.85. <5 x 10^{-6} g/l, 20ºC by column elution method, pH 6.2	99.6	US EPA 63-8 (A45109) 92/69/EC A6 & OECD 105	C009221
Solubility in organic solvents at 20ºC	acetone: 300-600 g/l dimethylsulfoxide: 200-300 g/l acetonitrile: 60-75 g/l at 1,2 dichloroethane: >600 g/l ethyl acetate: 200-300 g/l xylene: 150-200 g/l methanol: 8.15 g/l *n*-heptane 2.47 g/l	98.6	Similar to CIPAC MT181	C009220

Table 1. Physicochemical properties of pure deltamethrin

Characteristic	Value	Purity, %	Method	Reference
Octanol:water partition coefficient	P_{OW} = 40200 at 25°C logP (Kow) = 4.6 P_{OW} is not pH dependent	99.3	USEPA 63-11	A47915
Hydrolysis	Negligible hydrolysis at 25°C at pH 5 Negligible hydrolysis at 25°C at pH 7 Half-life = 2.5 days at 25°C at pH 9	98.0	US EPA 161-1	A45079
Photolysis	Deltamethrin is directly photo-transformed, DT_{50} = 48 days, and indirectly photo-transformed, DT_{50} = 4 days. A 6000 W xenon arc light system was used, reportedly of intensity corresponding to one half of the intensity of the sun (wavelength 310-740 nm, 25 ± 1°C). *Trans*-deltamethrin was found as a photolysis product but ≤ 2.0%.	99.3	US EPA 161-2	A41919
Dissociation characteristics	Does not dissociate.	-	-	-

Table 2. Chemical composition and properties of deltamethrin 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 98.6–99.5%. No unidentified impurities were reported.
Declared minimum deltamethrin content:	985 g/kg
Relevant impurities ≥ 1 g/kg and maximum limits for them:	None
Relevant impurities **<** 1 g/kg and maximum limits for them:	None
Stabilizers or other additives and maximum limits for them:	None
Melting or boiling temperature range	100-102°C

Hazard summary

Notes.

(i) The proposers provided written confirmation that the toxicological and ecotoxicological data included in the summary below were derived from deltamethrin having impurity profiles similar to those referred to in the table above.

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

Table 3. Toxicology profile of the deltamethrin technical material, based on acute toxicity, irritation and sensitization

Species	Test	Duration and conditions	Result
Rat, Sprague-Dawley	Oral	Deltamethrin (purity 98%) in corn oil administered by gavage as a single dose to 5 groups of 5 male and five female non-fasted rats. Observation period 14 d.	LD_{50} = 87 mg/kg bw/day
Rat (Wistar ICO:WI (IOPS AF/Han))	Dermal	Deltamethrin (purity 98.6%) in corn oil, topically administered to intact shaved skin of 5 males and 5 females. Administered dose 2000 mg/kg bw. Observation period 14 d.	LD_{50} >2000 mg/kg bw
Rat, Sprague-Dawley	Inhalation	Groups of 7 males and 7 females exposed whole body for a single 6-h period to dust particulate aerosol atmospheres of deltamethrin (purity not specified) at concentrations of 0 (air only) 0.049, 0.430, 0.540 and 0.720 mg/l air.	LC_{50} = 0.6 mg/l
Rabbit, New Zealand White	Skin irritation	24-h exposure (abraded and intact skin). Skin evaluated at 48 h post-treatment. Deltamethrin purity 98%.	Non irritating
Rabbit, New Zealand White	Eye irritation	Eyes evaluated at 1, 24, 72 h & 7 d in accordance with Draize method. Deltamethrin purity 99.2%.	Non irritating
Guinea pig, albino	Skin sensitization	M & K, Buehler. Deltamethrin purity 99.2%.	Non sensitizing

Table 4. Toxicology profile of deltamethrin technical material based on repeated administration (sub-acute to chronic)

Species	Test	Duration and conditions	Result
Mouse, male/female, CD& Crl	90 day dietary sub-chronic study	OECD Guideline 408. Dosage: 0, 6, 62, 600 and 1300 mg/kg bw/day for males and 0, 8, 77, 740 and 1400 mg/kg bw/day for females. Deltamethrin (purity 99.7%) administered in diet.	NOAEL = 62 mg/kg bw/day based on clonic contractions and clinical signs of poor condition at 600 mg/kg bw/day.
Rat, Male/female, CD	14 day inhalation toxicity study	Study performed prior to GLP regulations. Dosage: 3, 10 and 56 mg/m^3. Deltamethrin administered by inhalation, whole body exposure for 6 h/day, 5 days/week for 2 weeks and 4 days on the 3rd week (total 14 exposures).	NOAEC = 9.6 mg/m^3 corresponding to 2.6 mg/kg bw per exposure based on neurological signs.
Rat, Male/female, SD	21 day dermal toxicity study	OECD Guideline 410. Dosage: 0, 100, 300, 1000 mg/kg bw/day. Deltamethrin (purity, 99.6%) mixed with PEG 400 administered dermally for 6 h on 21 consecutive days.	NOAEL = 1000 mg/kg bw/day for systemic toxicity.

Table 4. Toxicology profile of deltamethrin technical material based on repeated administration (sub-acute to chronic)

Species	Test	Duration and conditions	Result
Rat, male/ female, Crl/CD	90 day dietary sub-chronic study	Study performed prior to GLP regulations. Dosage: 0, 0.1, 1.0, 2.5 and 10 mg/kg/day. Deltamethrin administered by oral gavage as solution in PEG 200	NOEL = 1.0 mg/kg/day LOEL = 2.5 mg/kg/day, depression of body weight.
Dog, male/female, beagle	90 day dietary sub-chronic study	OECD Guideline 409. Dosage: 0, 2, 10 and 50 mg/kg bw/day. Deltamethrin (purity 98.9%) administered orally in gelatine capsules.	NOAEL = 10 mg/kg bw/day based on neurological disturbances and reduced food intake and body-weight gain at 50 mg/kg bw/day.
Dog, male/ female, beagle	1-year dietary study	OECD Guideline 452. EPA/FIFRA Guideline 83-1. Dosages: control 4 M + 4 F; 1 mg/kg/day 4 M + 4 F; 10 mg/kg/day 4 M + 4 F; 50 mg/kg/day 4 M + 4 F. Deltamethrin (purity 98.9%) administered orally in gelatine capsules.	NOAEL = 1 mg/kg/day.
Rat, male/ female , Charles River CD strain	Two year oral toxicity and carcinogenicity study in rats	Study performed prior to GLP regulations. Dosages :0, 2, 20 and 50 ppm. Deltamethrin (purity 98%) concentration adjusted for each dosage level to give 2.5 g corn oil/kg basal diet for each group. Control rats received 2.5 g corn oil/kg basal diet.	NOEL = 25 ppm, i.e. 1 mg/kg/day. 50 ppm (LEL) produced consistent decrease in body weight gain in the males. No oncogenic effects were noted at up to and including 50 ppm (HDT).
Mouse, Male/ female, Charles River CD - 1.	Two-year oral toxicity and carcinogenicity study in mice	Study performed prior to GLP regulations. Dosages:0, 1, 5, 25 and 100 ppm. Deltamethrin (purity 98%) concentration adjusted for each dosage to give 5 g corn oil/kg basal diet for each dosage. Control mice received 5 g corn oil/kg of basal diet.	No adverse effects observed at highest dose tested. Therefore NOEL = 100 ppm, i.e. 12 mg/kg/day in male and 15 mg/kg/day in female. No oncogenic effects observed up to and including 100 ppm (HDT)
Rat, male/ female , Charles River, Crl:CD® BR VAF/Plus®	Two-generation reproduction	EPA - FIFRA Guidelines 83-4; 0ECD Guidelines section 4, No.416. 30 M + 30 F per treatment group (5 groups receiving, 0, 5, 20, 80 and 320 ppm deltamethrin in daily diet, deltamethrin purity 99.7%.	Parental toxicity NOEL = 80 ppm = 4.2 to 12.4 mg/kg bw/day. Offspring toxicity NOEL = 80 ppm = 10.6 to 26.4 mg/kg bw/day. Reproduction toxicity NOEL = 320 ppm = 18.3 to 43.8 mg/kg bw/day.

Table 5. Mutagenicity profile of deltamethrin technical material based on in vitro and in vivo tests

Species	Test	Conditions	Result
Salmonella typhimurum, strains TA98, TA100, TA1535, TA1537 *and E. Coli* WP2uvrA	Bacterial reverse mutation assay (Ames assay), *in vitro*	± S9 metabolic activation. Concentrations up to 5000 µg/plate. Deltamethrin purity 96%.	Negative
CHO/HGPRT	Mammalian cell gene mutation	Tested at 5 to 100 µg/ml without activation and 100 to 1500 µg/ml with activation.	Negative
Mouse (CD-1), males and females	Micronucleus formation assay, *in vivo*	Deltamethrin (purity 99.9%) dissolved in PEG 200 administered orally as a single dose to 5 to 8-week old mice at 500, 1000 and 2000 mg/kg bw. Each group was 5 animals/sex.	Negative
Chinese hamster ovary cells	Chromosome aberration assay	EPA/FIFRA 84-2 (b). Doses: 19, 38, 75, 150 µg/ml. TEM dose 0.5 µg/ml, CP dose 50 µg/ml. Metabolic activation S9. Deltamethrin purity 99.2%.	Negative
Rat primary hepatocyte	Unscheduled DNA synthesis	EPA/FIFRA 84-4. Doses: 4200, 1300, 420, 130, 42, 13, 4.2 µg/ml. Doses of DMBA 10 and 5 µg/ml. Deltamethrin purity 92%.	Negative
Male mouse strains	Dominant lethal assay	EPA 84-2, A.J. Bateman (1973) method.	Negative

Table 6. Ecotoxicology profile of deltamethrin technical material

Species	Test	Duration and conditions	Result
Daphnia magna (water flea)	Acute toxicity	48 h flow-through, observations at 24 and 48 h.	24 h EC_{50} >1.3 mg/l 48 h EC_{50} = 0.56 mg/l
Oncorhynchus mykiss (rainbow trout)	Acute toxicity		96 h LC50 = 0.26 µg/l
Lepomis macrochirus (bluegill sunfish)	Acute toxicity	FIFRA 72-1 96 h. Nominal concentrations: 0, 0.20, 0.41, 0.81, 1.6, 3.2 µg/l	96 h LC_{50} = 1.40 µg/l NOEC = 0.41 µg/l
*Selenastrum capricornutum (*green algae)	Effect on growth	OECD 201-1984. 96 h duration, 9.1 mg/l.	At the dose tested, no reduction in average growth occurred (deltamethrin partially degraded during test). E_bC_{50} uncertain but deltamethrin is not toxic to algae, because the initial and final test concentrations exceeded the water solubility of deltamethrin.
Eisenia fetida (earthworm)	Acute toxicity	OECD 207 14 days, artificial soil. Nominal concentrations: 167, 279, 465, 776 and 1290 ppm (dry soil).	LC_{50} >1290 mg/kg
Apis mellifera (honey bee)	Acute contact toxicity	Topical application, observed at 24 and 48 h, at 24°C.	LD_{50} (48 h) 1.5 ng/bee
Apis mellifera (honey bee)	Oral toxicity (normal feeding)	Dosed and observed for 24 and 48 h, at 24°C	LD_{50} 79 ng/bee

Table 6. Ecotoxicology profile of deltamethrin technical material

Species	Test	Duration and conditions	Result
Anas platyrhynchos (mallard duck)	Acute oral toxicity	FIFRA 71-1. Test levels: 215, 464, 1000, 2150, 4640 mg/kg.	LD_{50} >4640 mg/kg bw
Colinus virginianus (bobwhite quail)	Acute oral toxicity	FIFRA 71-1. Test levels 292, 486, 810, 1350, 2250 mg/kg.	LD_{50} >2250 mg/kg bw
Anas platyrhynchos (mallard duck)	Dietary toxicity	FIFRA 71-2. Test levels: 562, 1000, 1780, 3160, 5620 ppm	LC_{50} = 8039 ppm
Colinus virginianus (bobwhite quail)	Dietary toxicity	FIFRA 71-2. Test levels: 562, 1000, 1780, 3160, 5620 ppm	LC_{50} >5620 ppm

Deltamethrin was evaluated by the FAO/WHO JMPR in 1977, 1980, 1992, 1994, 1995 and 2000. On the basis of residues data from a wide range of crops, the JMPR concluded that intake of residues of deltamethrin is unlikely to present a public health concern (JMPR 1995). In 2000, the JMPR set an ADI of 0.01mg/kg bw and an acute RfD of 0.05 mg/kg bw.

The U.S. EPA considered that registered uses of deltamethrin will not cause unreasonable risk to humans.

The WHO hazard classification of deltamethrin is Class II, moderately hazardous.

Formulations

The main formulations type are DP, WP, EC, UL, SC and WT, with additional formulations now being produced (EG, EW, WG). These formulations are registered and sold in 90 countries throughout the world. Deltamethrin may be co-formulated with other pesticides, such as abamectin, azaconazole, buprofezin, chlorpyrifos, dichlorvos, difethialone, diflubenzuron, dimethoate, endosulfan, esbiothrin, fenitrothion, imidacloprid, pirimicarb, S-bioallethrin, tetramethrin, thiacloprid and triazophos.

Methods of analysis and testing

A full CIPAC method for determination of deltamethrin in TC, WP, EC, UL and DP was adopted in 1985 (CIPAC D). The method was based on normal-phase HPLC (silica column eluted with *iso*-octane/dioxan), with external standardization and UV detection at 254 nm. Identification of deltamethrin was by HPLC retention time (two techniques), with additional tests involving TLC, IR, NMR and MS.

A new analytical method for determination of deltamethrin in TC, DP, SC, EC and WG was adopted by CIPAC, with provisional status, in 2004. This method also involved HPLC but used a cyano-column and detection at 230 nm. The new method was also collaboratively studied for analysis of WT but the results were not within the normally acceptable range and CIPAC agreed that the method for WT should be given only tentative status. In 2005, the manufacturer is conducting a validation study for extension (according to CIPAC requirements) of the new method to the

analysis of WP, EG, EW and UL, and this will include a re-validation of the method for WT*. The original identity tests (CIPAC D) remain valid.

Test methods for determination of physico-chemical properties of the pure and technical active ingredient were EC, USEPA, OECD, CIPAC while those for the formulations were CIPAC, as indicated in the specifications. Methods for the determination of tablet hardness and disintegration time of WT are being validated under the auspices of CIPAC, for completion in 2005.

Physical properties

The physical properties, and the methods for testing and the limits proposed for them, of the DP, WP, SC, EC, UL, EG, EW, WT and WG formulations, comply with the requirements of the Manual (FAO/WHO 2002).

Containers and packaging

No special requirements for containers and packaging have been identified.

Expression of active ingredient

The active ingredient is expressed as deltamethrin, in g/kg in solid formulations, and in g/kg or g/l at 20 ± 2C in liquid formulations.

Appraisal

The Meeting considered data on deltamethrin for the review of (i) existing FAO full specifications for TC, WP, EC, DP, UL; (ii) of existing WHO full specifications for TC, WP, EC, DP, UL, SC; (iii) of an existing WHO interim specification for WT; and for the development of proposed new FAO specifications for EG, EW, WG and a new WHO specification for EW. The data submitted by Bayer CropScience were in accordance with the requirements of the FAO/WHO Manual and supported the proposed specifications, which were largely in accordance with the requirements of the FAO/WHO manual.

Deltamethrin is a pyrethroid insecticide which is both very widely used and has a very wide range of applications in agriculture, animal health and public health. It is out of patent.

Deltamethrin consists of a single stereoisomer ((*S*)-α-cyano-3-phenoxybenzyl (1*R*,3*R*)-3-(2,2-dibromovinyl)-2,2-dimethylcyclopropane carboxylate), being one of the eight possible stereoisomers of the same structure.

Deltamethrin does not dissociate in water and it has extremely low water solubility and low volatility. The octanol/water partition coefficient is high, indicating fat solubility and partition into soil organic matter. Bioaccumulation does not occur

* Extensions of the analytical method to EG, EW and WP were adopted by CIPAC in 2005 (CIPAC 2005a) but the status of the method for WT remained only tentative. The manufacturer explained that, for analytical purposes, the UL is analogous to the EC and CIPAC agreed that the method validation accepted in 2004 for analysis of EC could also encompass the UL (CIPAC 2005b).

because it is fairly rapidly metabolized and in soil it is neither mobile nor of long persistence.

Deltamethrin is stable to hydrolysis at pH 4-7 but is rather slowly hydrolyzed at pH 9. Direct and indirect photolysis can occur in solution and products, other, less insecticidally active, stereoisomers can be produced, along with other degradation products.

The WHO hazard classification is Class II, moderately hazardous and the FAO/WHO JMPR has allocated an ADI of 0.01 mg/kg bw and the acute RfD of 0.05 mg/kg bw. The JMPR concluded that intake of residues of deltamethrin is unlikely to present a public health concern and USEPA concluded that registered uses of deltamethrin will not cause unreasonable risk to humans. Deltamethrin is not a skin/eye irritant, nor a skin sensitizer, and there is no evidence of genotoxic, carcinogenic, mutagenic, teratogenic or reproductive effects. Like many other pyrethroids used as insecticides, deltamethrin is very highly toxic to fish, daphnids and non-target insects, such as honeybees.

The Meeting was provided with commercially confidential information on the manufacturing process and batch analysis data on all detectable impurities. None of the impurities was present at or above 1 g/kg. Mass balances were high (98.6–99.5%). The data were confirmed as identical to those evaluated for the registration of deltamethrin in Belgium.

The Meeting considered the relevance of impurities.

The existing FAO and WHO specifications included clauses to limit the concentrations of various impurities. The existing specifications for TC limited the concentration of “deltamethrin *R*-isomer” ((*R*)-α-cyano-3-phenoxybenzyl (1*R*,3*R*)-3-(2,2-dibromovinyl)-2,2-dimethylcyclopropane carboxylate) to 10 g/kg; “deltamethrin acid chloride” ((1*R*,3*R*)-3-(2,2-dibromovinyl)-2,2-dimethylcyclopropane carboxy chloride) to 2 g/kg; and the sum of “deltamethrin acid” ((1*R*,3*R*)-3-(2,2-dibromovinyl)-2,2-dimethylcyclopropane carboxylic acid) and “deltamethrin acid anhydride” (the anhydride of (1*R*,3*R*)-3-(2,2-dibromovinyl)-2,2-dimethylcyclopropane carboxylic acid) to 10 g/kg. The existing specifications for the formulations included clauses to limit “deltamethrin *R*-isomer” and water.

The manufacturer and the Meeting agreed that “deltamethrin acid” is not a relevant impurity and that it was not necessary to specify the maximum water content of formulations, partly because deltamethrin has extremely low affinity for water and partly because the water content is adequately controlled indirectly through clauses for physical properties. There was also agreement that, because the concentrations of “deltamethrin acid chloride” and “deltamethrin acid anhydride” do not approach 1 g/kg, that these should not be specified as relevant impurities.

The manufacturer proposed that “deltamethrin *R*-isomer” should be identified as a relevant manufacturing impurity. The manufacturer had validated an analytical method for the determination of this isomer. It has lower insecticidal activity than deltamethrin, it is also less hazardous to humans and the environment than deltamethrin and it has no other properties which would make relevant according to the criteria given in the FAO/WHO manual. The Meeting therefore agreed that it should not be identified as a relevant impurity. Its concentration will be controlled indirectly by the clause limiting the minimum content of the active ingredient, in the

same way as any other non-relevant impurities, including those produced during storage.

A new analytical method for the determination of deltamethrin TC, SC, EC, DP and WG was adopted by CIPAC in 2004, with provisional status, which is sufficient to support the proposed specifications. However, the method did not give acceptable results for the analysis of WT and CIPAC allocated it a tentative status, which is not sufficient to support of the proposed specification for WT.

The manufacturer stated that validation of extensions of the new CIPAC method is in progress for the analysis of EG, EW, UL, WP and WT. These method extensions have to be adopted by CIPAC, with provisional status, to provide appropriate support for the specifications proposed for these formulations*.

Apart from the issue of relevant impurities, the proposed specifications were in accordance with the requirements of the FAO/WHO manual.

The existing specifications for deltamethrin formulations included various limits for pH range and acidity/alkalinity but the manufacturer rationalised these in the proposed specifications, specifying the same pH range (4-7.5) in all cases except WG. In the case of WG, the formulants produce a pH of 3.5-3.6 and the Meeting and manufacturer agreed that it is more appropriate to limit the measured concentration of acid than the pH range in this case.

In accordance with the guideline given in the manual, the existing WHO interim and proposed specifications for WT incorporated a clause for disintegration time. The manufacturer stated that the test method would be validated under the auspices of CIPAC in 2005 but a specification limit was not proposed. An acceptable clause and limit for degree of attrition (CIPAC MT 193 “Friability”) was provided under the heading of “tablet integrity” but the manufacturer disputed the need to specify “no broken tablets”. Both were specified in the existing interim WHO specification. The manufacturer proposed inclusion of a clause for tablet hardness and stated that the test method would be validated under the auspices of CIPAC in 2005 but specification limits were not proposed. Tablet hardness was not specified in the existing WHO interim specification. The Meeting agreed that the WT specification should then be reconsidered when the requirements and limits have been clarified.

Recommendations

The Meeting recommended the following.

(i) Existing FAO specifications for deltamethrin TC, WP, EC, DP and UL should be withdrawn.

(ii) Existing WHO full specifications for deltamethrin TC, WP, EC, DP, UL and SC, and the existing WHO interim specification for deltamethrin WT, should be withdrawn.

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* Extensions of the analytical method to EG, EW and WP were adopted by CIPAC in 2005 (CIPAC 2005a) but the status of the method for WT remained only tentative. The manufacturer explained that, for analytical purposes, the UL is analogous to the EC and CIPAC agreed that the method validation accepted in 2004 for analysis of EC could also encompass the UL (CIPAC 2005b).

(iii) The proposed specifications for deltamethrin TC, DP, SC, EC and WG, amended as described in the appraisal above, should be adopted by FAO and WHO.

(iv) The proposed specifications for deltamethrin EG and EW, amended as described in the appraisal above, should be adopted by FAO, subject to CIPAC adoption* of the analytical method extensions to these formulations.

(v) The proposed specifications for deltamethrin EW, amended as described in the appraisal above, should be adopted by WHO, subject to CIPAC adoption* of the analytical method extensions to these formulations and WHOPES testing/evaluation of the product for public health use.

(vi) The proposed specification for deltamethrin UL and WP, amended as described in the appraisal above, should be adopted by FAO and WHO, subject to CIPAC adoption* of the analytical method extensions to these formulations.

(vii) The proposed specification for deltamethrin WT should be reconsidered the JMPS when the physical test requirements, methods and proposed limits have been clarified and the test methods suitably validated; and that adoption of the specification should be subject to satisfactory validation of a method for analysis of this formulation type, by CIPAC.

(viii) Although specifications for DP, SC, EC, WG, EW, UL and WP used in agriculture and public health are identical, users must adhere to label recommendations and not use the products interchangeably.

References

Bayer Crop Science document No. or other reference	Year and title or publication details
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CIPAC D	A. Martijn and W. Dobrat, eds., 1988. CIPAC Handbook volume D, pp. 57-66. Collaborative International Pesticides Analytical Council Ltd., Harpenden, UK.
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C009221	2000. Deltamethrin A.I. - solubility in water at 20°C.
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A70753	1990. Deltamethrin A.I. – determination of melting point.

* Extensions of the analytical method to EG, EW and WP were adopted by CIPAC in 2005 (CIPAC 2005a) but the status of the method for WT remained only tentative. The manufacturer explained that, for analytical purposes, the UL is analogous to the EC and CIPAC agreed that the method validation accepted in 2004 for analysis of EC could also encompass the UL (CIPAC 2005b).

Bayer Crop Science document No. or other reference	Year and title or publication details
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