

**WHO SPECIFICATIONS AND EVALUATIONS  
FOR PUBLIC HEALTH PESTICIDES**

**ALPHA-CYPERMETHRIN**

**LONG-LASTING (INCORPORATED INTO  
FILAMENTS) INSECTICIDAL NET**

A racemic mixture of:

(*S*)- $\alpha$ -cyano-3-phenoxybenzyl-(1*R*,3*R*)-3-(2,2-dichlorovinyl)-  
2,2-dimethylcyclopropane-carboxylate and  
(*R*)- $\alpha$ -cyano-3-phenoxybenzyl-(1*S*,3*S*)-3-(2,2-dichlorovinyl)-  
2,2-dimethylcyclopropane-carboxylate



**World Health  
Organization**

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## Disclaimer<sup>1</sup>

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

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

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

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

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

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

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

## INTRODUCTION

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

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

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

**Part One:** The Specifications of the technical material and the related formulations of the pesticide in accordance with chapters 4 to 9 of the “FAO/WHO Manual on Pesticide Specifications.”

**Part Two:** The Evaluation Report(s) of the pesticide, reflecting the evaluation of the data package carried out by WHO and the JMPS. The data are provided by the manufacturer(s) according to the requirements of chapter 3 of the “FAO/WHO Manual on Pesticide Specifications” and supported by other information sources. The Evaluation Report includes the name(s) of the manufacturer(s) whose technical material has been evaluated. Evaluation reports on specifications developed subsequently to the original set of specifications are added in a chronological order to this report.

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

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

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

**PART ONE**  
**SPECIFICATIONS**

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# WHO SPECIFICATIONS FOR PUBLIC HEALTH PESTICIDES

## ALPHA-CYPERMETHRIN

### INFORMATION

#### Common name

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

#### Synonyms

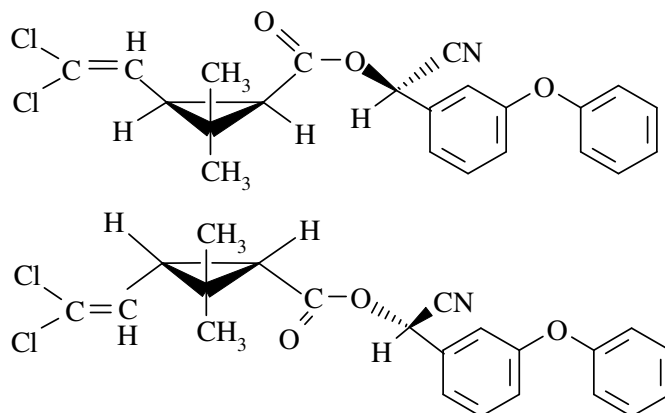
alphamethrin (rejected common name), alfoxylate

#### Chemical names

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

*CA*: [1 $\alpha$ (*S*\*), 3 $\alpha$ ]( $\pm$ )-cyano(3-phenoxyphenyl)methyl 3-(2,2-dichloroethenyl)-2,2-dimethylcyclopropanecarboxylate

#### Structural formula



#### Empirical formula

$C_{22}H_{19}Cl_2NO_3$

#### Relative molecular mass

416.3

#### CAS Registry number

67375-30-8

#### CIPAC number

454

#### Identity tests

GC retention time, IR spectrum.

## WHO SPECIFICATIONS FOR PUBLIC HEALTH PESTICIDES

### ALPHA-CYPERMETHRIN LONG-LASTING (INCORPORATED INTO FILAMENTS) INSECTICIDAL NET

WHO interim specification 454/LN/2 (July 2011\*)

*This specification, which is PART ONE of this publication, is based on an evaluation of data submitted by the manufacturers whose name are listed in the evaluation reports (454/2009.2, 454/2011.1, 454/2011.2). It should be applicable to relevant products of these manufacturers but it is not an endorsement of those products, nor a guarantee that they comply with the specification. The specification may not be appropriate for the products of other manufacturers, irrespective of the source of TC. The evaluation reports (454/2009.2, 454/2011.1, 454/2011.2), given in PART TWO, form an integral part of this publication.*

#### 1 Description

The product shall be in the form of netting (Note 1), consisting of 150 denier monofilament, high density polyethylene fibres, incorporating technical alpha-cypermethrin complying with the requirements of WHO specification 454/TC (April 2006). The product shall appear clean and shall be free from visible extraneous matter (Note 2), visible damage (such as splitting or tearing) and visible manufacturing defects (such as poorly made seams or a weave that is either not uniform or too loose to remain uniform in use), and shall be suitable for use as an insecticidal net with long-lasting activity (Notes 3 & 4).

#### 2 Active ingredient

##### 2.1 Identity tests (454/LN/M/2, CIPAC Handbook M, p.40, 2009)

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

##### 2.2 Alpha-cypermethrin content (454/LN/M/3.2, CIPAC Handbook M, p.40, 2009) (Notes 5 & 6)

The alpha-cypermethrin content shall be declared (5.8 g/kg) and, when determined, the average measured content shall not differ from that declared by more than  $\pm 25\%$ .

##### 2.3 Alpha-cypermethrin retention index (Note 5 & 7)

The retention index of alpha-cypermethrin from the netting, when determined, shall be within the range 0.95 to 0.99.

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\* This specification is applicable to long-lasting (incorporated into filaments) insecticidal nets. It is not applicable to long-lasting (coated onto filaments) insecticidal nets. The extension number to the specification code permit to distinguish between these two net types. Specifications may be revised and/or additional evaluations may be undertaken. Ensure the use of current versions by checking at: <http://www.who.int/whopes/quality/en/>.

### 3 Physical properties

#### 3.1 Netting mesh size

When counted by the method given in Note 8, the average number of complete holes/cm<sup>2</sup> shall be not less than 20 holes/cm<sup>2</sup> and the lowest value shall be not less than 20 holes/cm<sup>2</sup>.

#### 3.2 Dimensional stability of netting to washing (Note 9)

Not more than 10% shrinkage/expansion in both dimensions.

#### 3.3 Bursting strength (Note 10)

The minimum bursting strength of the fabric shall be declared (not less than 500 kPa) and, when determined, the average shall be not less than that declared.

If seams are present, their average bursting strength shall be not less than the measured average for the fabric.

### 4 Storage stability

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

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

- retention index (2.3);
- dimensional stability (3.2);
- bursting strength (3.3).

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Note 1 The specification applies to manufactured nets and bulk netting.

Note 2 Occasional short lengths of loose thread present in the netting are not considered to be extraneous matter.

Note 3 Long-lasting insecticidal netting is expected to retain its insecticidal activity during its life span and through a number of washes.

Note 4 Flammability of the product is not part of the specification but it should be measured by the manufacturer, according to 16CFR Part 1610, and the result presented on the package. The linear density (denier) of the fibres cannot be measured in the manufactured net, but should be identified on the packaging.

Note 5 Samples should be taken according to Figure 1 or on a convenient diagonal across the width of bulk material. Samples must be sufficiently large to conduct all tests required and representative of the net or netting. Except where seams are to be tested, do not test material within 10 cm of seams or selvages. Where a final product is made from more than one type of netting, each type of netting should be sampled and tested separately.

Use sharp scissors, or equivalent, to minimize damage to the fibres and fabric and thus avoid any consequential bias in the results of certain tests. Roll up the strips or squares and place them in labelled, new, clean aluminium foil prior to analysis. Samples should be kept cool, avoiding heat sources (including sun heat) or freezing, and analyzed/tested with minimum delay. Representative portions (sub-samples) for testing should be taken as described in each test method.

Test portion and replication requirements for physical test methods are defined in the methods or Notes referenced.

**Note 6** The declared value for alpha-cypermethrin content in g/kg - 5.8 - is equivalent to 261 mg/m<sup>2</sup>. The alpha-cypermethrin content may be declared as both g/kg and mg/m<sup>2</sup> but, in cases of dispute, g/kg values shall be used. If the active ingredient content is also specified as mg/m<sup>2</sup> of netting, the actual content on this basis is calculated from the measured values for active ingredient content in g/kg and mass of net/m<sup>2</sup>. Mass of net/m<sup>2</sup> should be determined according to ISO 3801 (1977).

**Note 7** Currently (2011), CIPAC is developing a wash method for determination of the retention behaviour of long-lasting insecticidal mosquito nets. Prior to the publication in a Handbook, copies of the method may be obtained through the CIPAC website, <http://www.cipac.org>. This method is a standardisation of the WHO washing method published in the "WHO Guidelines for laboratory and field testing of long-lasting insecticidal mosquito nets", document WHO/CDS/WHOPES/GCDPP/2005.11, World Health Organization, Geneva, 2005. Briefly, the retention index is determined by analyzing net samples in triplicate representing wash points 0 and 4 for total active ingredient content and calculating the average retention index per wash using the equation for a free migration stage behaviour. A retention index per wash of 0.95 indicates that 95 % of the insecticide present in samples washed 1 to 3 times is still present after an additional wash step. The retention index applies to the average obtained from triplicate tests performed on samples removed side by side in the length direction from the same net or batch of netting.

**Note 8** In the absence of a simple or standard method to determine the size of holes, which may have complex shapes, in highly flexible fabrics, mesh size is determined by counting the number of holes in a square of the fabric. Counting may be done directly on the fabric or indirectly by taking a picture/photocopy the fabric. Indirect methods may ease counting and provide a permanent record. Before counting, the fabric should be conditioned according to ISO 139 (1973) (4 h, 20°C, 65% relative humidity).

Use a template to define the square of netting, taking care not to stretch or distort the fabric. The template should be a 1-2 mm thick rigid sheet, in/on which an accurately calibrated ( $\pm 1\%$  in each dimension) square (e.g. 1 x 1 in or 5 x 5 cm) has been cut/marked. If a template is not available and a ruler must be used, great care is required to ensure that the area counted is square. Where practicable, one edge of the square to be counted should be aligned with a row of complete holes in the fabric. Incomplete holes  $\geq 1/2$  are counted as complete holes, whereas those  $< 1/2$  are not counted. Count 5 replicate squares in pieces taken according to Note 5, calculate the average and note the lowest value.

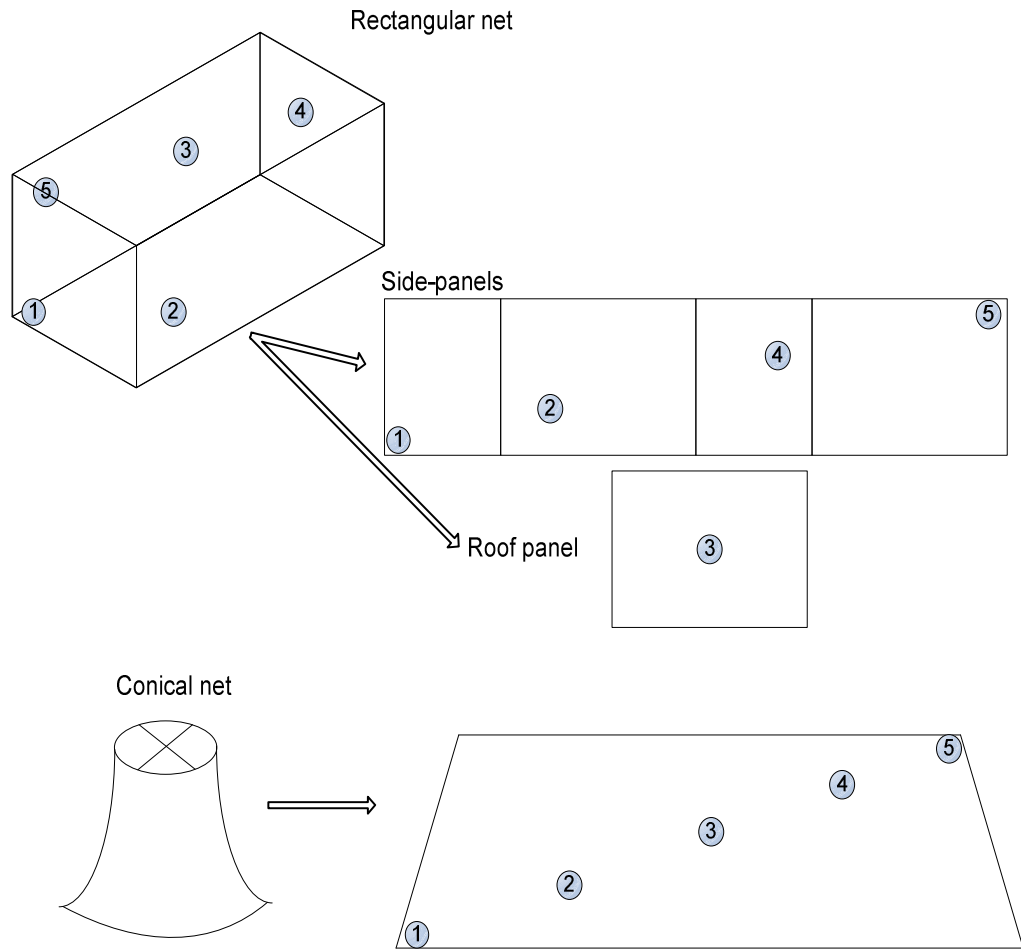
**Note 9** Method of preparation, marking and measuring: ISO 3759 (2007). Method of washing: ISO 6330 (2001). Method of calculation: ISO 5077 (1984). Size of test portions: 500 x 500 mm; mark off 350 x 350 mm within each test portion. Test a total of 4 replicate portions, 2 washed in each of 2 separate loads. Type of washing machine: ISO type A (front loading). Washing program: ISO type 8A (gentle cycle 30°C). Fill the washer with dummy load (with fabric as per ISO standard) up to the standard of 2 to 4 kg. Drying: flat drying.

**Note 10** Test method: ISO 13938 part 1 (1999) and ISO 13938 part 2 (1999), with conditioning of the fabric as specified in the ISO standard. The declared minimum bursting strength, and testing for compliance with it, should be based on tests of 7.3 cm<sup>2</sup> areas of fabric. Proposed specifications based on tests of 50 cm<sup>2</sup> area must be supported by data showing the suitability of the proposed value and its relationship to minimum of 250 kPa (which is based on 7.3 cm<sup>2</sup> area). Five replicate tests should be conducted on samples taken as described in Note 5. The average of the 5 measurements is calculated.

The method to test seam bursting strength is identical to that used to test the fabric, except that 5 replicate tests should be made, with the seam centered on the test head. Up to 5 seams may be tested but, if there are  $< 5$  seams, replicate measurements should be made on 1 or more seams, to provide a total of 5 measurements.

**Note 11** Samples of the product taken before and after the storage stability test should be analyzed concurrently in order to reduce the analytical error.

Figure 1 Recommended positions from which 5 pieces of netting should be taken from a made up bed net and combined to form a representative sample.



**PART TWO**  
**EVALUATION REPORTS**

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**ALPHA-CYPERMETHRIN**

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## WHO SPECIFICATIONS FOR PUBLIC HEALTH PESTICIDES

### ALPHA-CYPERMETHRIN

#### FAO/WHO EVALUATION REPORT 454/2011.2

#### **Recommendations**

The Meeting recommended the following.

The existing WHO interim specification 454/LN/2 for alpha-cypermethrin (incorporated into filaments) LN should be extended to encompass the corresponding product of Disease Control Technologies LLC.

#### **Appraisal**

Supporting data and information for alpha-cypermethrin long-lasting (incorporated into filaments) insecticidal net (LN), provided by Disease Control Technologies LLC, were considered by the Meeting for extension of the existing WHO interim specification 454/LN/2 (October 2009).

The LN under consideration (Royal Sentry) is a warp knitted fabric netting material made from 150 denier monofilament yarn composed of high density polyethylene containing technical alpha-cypermethrin. The manufacturer confirmed that the active ingredient incorporated into the LN is from a source compliant with the existing WHO specification for alpha-cypermethrin TC (Tagros).

Royal Sentry was tested and evaluated by WHOPES who concluded that the bio-efficacy and wash resistance is comparable to the reference product (DuraNet). WHOPES recommended also the extension of the WHO specifications for alpha-cypermethrin (incorporated into filaments) LN to Royal Sentry, subject to satisfactory assessment of the physical and chemical properties of the product by JMPS (WHO 2011).

#### Description clause

The Meeting concluded that the description of Royal Sentry consisting of 150 denier monofilament, high density polyethylene fibres, incorporating technical alpha-cypermethrin complies with the existing WHO interim specification 454/LN/2.

#### Active ingredient identity and content clauses

The declared alpha-cypermethrin content is 5.8 g/kg. Data provided by the manufacturer and generated by an independent laboratory on 3 nets showed that the measured active ingredient content complies with the existing WHO interim specification 454/LN/2.

Special attention needs to be paid to control random variations in the distribution of the insecticide within the net and between nets. The spatial variation data provided by the manufacturer and generated by an independent laboratory (active ingredient content on 5 individual net pieces taken according to the Figure 1 of the specification) showed a good homogeneity of the active ingredient content within the net (within-net RSD = 2.15%, n = 5).

WHOPES Phase I data showed that alpha-cypermethrin content in Royal Sentry complies with the target dose of 5.8 g/kg ( $\pm 25\%$ ) and that the between-net variation of alpha-cypermethrin content is very low (RSD = 2.5-4.2%, n = 4) (WHO 2011).

The CIPAC method 454/LN/M/3.2 (alpha-cypermethrin incorporated into filaments) published in the CIPAC Handbook M and involving extraction by heating under reflux for 30 minutes with xylene in presence of citric acid, addition of dioctyl phthalate as internal standard, and determination by gas chromatography with flame ionization detection (GC-FID), was used for the studies and is fully applicable for Royal Sentry.

#### Alpha-cypermethrin retention index clause

An adequate amount of active ingredient must be present at the surface of the LN, for efficacy, whereas the majority must reside within the LN, to avoid excessive losses during washing and to provide a reservoir from which the surface is replenished with active ingredient. Depletion of total active ingredient content by washing (retention index) is accomplished by analyzing separate washed and unwashed pieces of the same fabric. As the diffusion processes in solid materials are significantly slower than in solution, a certain time period is necessary to re-establish the equilibrium level of the active ingredient at the surface of polymer.

Currently (2011), CIPAC is developing a wash method for the determination of the retention behavior of long-lasting insecticidal mosquito nets. This method is a further standardization of the WHO washing method published in the "WHO Guidelines for laboratory and field testing of long-lasting insecticidal mosquito nets", document WHO/CDS/WHOPES/GCDPP/2005.11, World Health Organization, Geneva, 2005. Briefly, the retention index is determined by analyzing net samples in triplicate representing wash points 0 and 4 for total active ingredient content and calculating the average retention index using the equation for a free migration stage behavior.

The WHOPES Phase I study performed according to the WHO washing method (using Marseille soap at 2 g/L) showed that decreasing proportions of the remaining alpha-cypermethrin are removed from the polymer by successive washings with aqueous soap (free-migration stage behavior), with an average retention index per wash in the range 0.99 to 1.00 for wash cycles 1 up to 25, and that the wash curve is similar to this one of the reference product (DuraNet).

The manufacturer also provided data generated by an independent laboratory on 3 nets washed 1, 3 and 5 times (according to the draft CIPAC washing method using ECE-A non-phosphate reference detergent at 2 g/L) showing an average alpha-cypermethrin retention index per wash in the range 0.96 to 0.99.

On basis of these data, the Meeting concluded that the alpha-cypermethrin retention index of Royal Sentry complies with the clause of the existing WHO interim specification 454/LN/2 (0.95 to 0.99).

#### Physical properties clauses

The manufacturer provided study reports generated by an independent laboratory showing that Royal Sentry fully complies with the clauses of the existing WHO interim specification 454/LN/2 for netting mesh size, dimensional stability of netting to washing and bursting strength.

### Storage stability clause

The manufacturer provided data generated by an independent laboratory after storage at 54°C for 2 weeks and after storage at 40°C for 8 weeks showing that the loss of alpha-cypermethrin is less than 5% (2% and 5% respectively) and that the retention index remains unchanged (average alpha-cypermethrin retention index per wash for wash cycles 1 to 5 in the range 0.96 to 0.99 and in the range 0.98 to 0.99, respectively). The manufacturer also provided data showing that the netting mesh size, the dimensional stability of netting to washing and the bursting strength remains unchanged after storage at 54°C for 2 weeks and after storage at 40°C for 8 weeks. The Meeting agreed to keep the storage clause of 54°C for 2 weeks in the specification and concluded that Royal Sentry complies with the existing WHO interim specification 454/LN/2.

The Meeting agreed also to update some notes of the existing specification relating to the linear density, retention index and dimensional stability to washing to be in line with the draft guideline for LN of the November 2010 – second revision of the first edition of the FAO/WHO Manual.

## ANNEX 1. REFERENCES

Study number	Author(s)	Year	Study title. Study identification number. Report identification number. GLP [if GLP]. Company conducting the study
	Butenhoff A.	2010	Royal Sentry®. JMPS Submission Dossier for World Health Organization Approval by Extension of Specification. Disease Control Technologies, October 4, 2010.
22324-2	CRA-W	2010	Determination of alpha-cypermethrin in Royal Sentry and DuraNet [alpha-cypermethrin long-lasting (incorporated into filaments) insecticidal net (LN)]. Report WHO / RE 22324 / 2010 / 2 of the Walloon Agricultural Research Centre, Gembloux, Belgium for WHO, September 28, 2010.
	FAO/WHO	2006	Manual on development and use of FAO and WHO specifications for pesticides. March 2006 revision of the 1 <sup>st</sup> edition. FAO, Rome and WHO, Geneva, March 2006 (internet publications).
	FAO/WHO	2010	Manual on development and use of FAO and WHO specifications for pesticides. Second revision of the 1 <sup>st</sup> edition. FAO, Rome and WHO, Geneva, November 2010 (internet publications).
	TÜV SÜD PSB Singapore	2010	Testing of mosquito nets submitted by Disease Control Technologies LLC. Test reports No. 719180595-MEC10/01-OJD, 719180595-MEC10/02-OJD, 719180595-MEC10/07-OJD, 719180595-CHM10-02-CSY-CR1, 719180595-CHM10-03-CSY-CR1, 719180595-CHM10-05-CSY-CR3, 719180406-CHM10-01-CSY-CR1, 719180595-MEC10/03-OJD-CR01, 719180595-MEC10/05-OJD, 719180595-MEC10/06-OJD, 719180595-CHM10-04-CSY-CR1, 719180595-CHM10-06-CSY-CR3, 719180595-MEC10/09-OJD, 719180595-MEC10/08-OJD-CR01, 719180595-MEC10/10-OJD, 719180595-CHM10-07-CSY, 719180595-CHM10-08-CSY, 719180595-MEC10/12-OJD, 719180595-MEC10/11-OJD and 719180595-MEC10/11-OJD for Disease Control Technologies, August – September 2010.
	WHO	2005	Guidelines for laboratory and field testing of long-lasting insecticidal mosquito nets. Document WHO/CDS/WHOPES/GCDPP/2005.11. WHO, Geneva, 2005.
	WHO	2005	Technical consultation on specifications and quality control of netting materials for mosquito nets (untreated and treated). 29 November – 02 December 2005. WHO Headquarters, Geneva, Switzerland.
	WHO	2008	Report of the Eleventh WHOPES Working Group Meeting, WHO/HQ, Geneva, 10-13 December 2007. WHO, Geneva, document WHO/HTM/NTD/WHOPES/2008.1.
	WHO	2011	Report of the Fourteen WHOPES Working Group Meeting, WHO/HQ, Geneva, 11-15 April 2011. WHO, Geneva, document to press.

# WHO SPECIFICATIONS FOR PUBLIC HEALTH PESTICIDES

## ALPHA-CYPERMETHRIN

### FAO/WHO EVALUATION REPORT 454/2011.1

#### **Recommendations**

The Meeting recommended the following.

The existing WHO interim specification 454/LN/2 for alpha-cypermethrin (incorporated into filaments) LN should be extended to encompass the corresponding product of V.K.A. Polymers Pvt. Ltd.

#### **Appraisal**

Supporting data and information for alpha-cypermethrin long-lasting (incorporated into filaments) insecticidal net (LN), provided by V.K.A. Polymers Pvt. Ltd., were considered by the Meeting for extension of the existing WHO interim specification 454/LN/2 (October 2009).

The LN under consideration (MAGNet) is a warp knitted fabric netting material made from 150 denier monofilament yarn composed of high density polyethylene containing technical alpha-cypermethrin. The manufacturer confirmed that the active ingredient incorporated into the LN is from a source compliant with the existing WHO specification for alpha-cypermethrin TC (Gharda Chemicals Limited).

MAGNet was tested and evaluated by WHOPES who concluded that the bio-efficacy and wash resistance is comparable to the reference product (DuraNet). WHOPES recommended also the extension of the WHO specifications for alpha-cypermethrin (incorporated into filaments) LN to MAGNet, subject to satisfactory assessment of the physical and chemical properties of the product by JMPS (WHO 2011).

#### Description clause

The Meeting concluded that the description of MAGNet consisting of 150 denier monofilament, high density polyethylene fibres, incorporating technical alpha-cypermethrin complies with the existing WHO interim specification 454/LN/2.

#### Active ingredient identity and content clauses

The declared alpha-cypermethrin content is 5.8 g/kg. Data from three different laboratories (two manufacturer laboratories and one independent laboratory) showed that the measured active ingredient content complies with the existing WHO interim specification 454/LN/2.

Special attention needs to be paid to control random variations in the distribution of the insecticide within the net and between nets. The spatial variation data provided by the manufacturer from three laboratories (active ingredient content on 5 individual net pieces taken according to the Figure 1 of the specification) showed a good homogeneity of the active ingredient content within the net (within-net RSD = 1.27-2.01%, n = 5).

WHOPES Phase I data showed that alpha-cypermethrin content in MAGNet complies with the target dose of 5.8 g/kg ( $\pm 25\%$ ) and that the between-net variation of alpha-cypermethrin content is very low (RSD = 1.9-2.5%, n = 4).

The CIPAC method 454/LN/M/3.2 (alpha-cypermethrin incorporated into filaments) published in the CIPAC Handbook M and involving extraction by heating under reflux for 30 minutes with xylene in presence of citric acid, addition of dioctyl phthalate as internal standard, and determination by gas chromatography with flame ionization detection (GC-FID), was used in these studies and is fully applicable for MAGNet. Gas chromatography with mass spectrometry detection (GC-MS) was also used in studies from one laboratory of the manufacturer and was found to give equivalent results than GC-FID.

#### Alpha-cypermethrin retention index clause

An adequate amount of active ingredient must be present at the surface of the LN, for efficacy, whereas the majority must reside within the LN, to avoid excessive losses during washing and to provide a reservoir from which the surface is replenished with active ingredient. Depletion of total active ingredient content by washing (retention index) is accomplished by analyzing separate washed and unwashed pieces of the same fabric. As the diffusion processes in solid materials are significantly slower than in solution, a certain time period is necessary to re-establish the equilibrium level of the active ingredient at the surface of polymer.

Currently (2011), CIPAC is developing a wash method for the determination of the retention behavior of long-lasting insecticidal mosquito nets. This method is a further standardization of the WHO washing method published in the "WHO Guidelines for laboratory and field testing of long-lasting insecticidal mosquito nets", document WHO/CDS/WHOPES/GCDPP/2005.11, World Health Organization, Geneva, 2005. Briefly, the retention index is determined by analyzing net samples in triplicate representing wash points 0 and 4 for total active ingredient content and calculating the average retention index using the equation for a free migration stage behavior.

The WHOPES Phase I study performed according to the WHO washing method (using Marseille soap at 2 g/L) showed that decreasing proportions of the remaining alpha-cypermethrin are removed from the polymer by successive washings with aqueous soap (free-migration stage behavior), with an average retention index per wash of 0.99 for wash cycles 1 up to 25, and that the wash curve is similar to this one of the reference product (DuraNet).

The manufacturer also provided data generated by three laboratories (two manufacturer laboratories and one independent laboratory) on net samples washed 1, 2, 3, 5, 10, 15, 20 and 25 times (according to the draft CIPAC washing method using IEC-A\* reference detergent without phosphate at 2.5 g/L) showing an average alpha-cypermethrin retention index per wash in the range 0.97 to 0.99.

On basis of all these data, the Meeting concluded that the alpha-cypermethrin retention index of MAGNet complies with the clause of the existing WHO interim specification 454/LN/2 (0.95 to 0.99).

### Physical properties clauses

The manufacturer provided study reports generated by three laboratories (one manufacturer laboratory and two independent laboratories) showing that MAGNet fully complies with the clauses of the existing WHO interim specification 454/LN/2 for netting mesh size, dimensional stability of netting to washing and bursting strength.

### Storage stability clause

The manufacturer provided data generated by three laboratories (one manufacturer laboratory and two independent laboratories) after storage at 54°C for 2 weeks showing that the loss of alpha-cypermethrin is less than 5% (2-5%). One study showed that the retention index after accelerated storage is lower compared to the values before storage (average alpha-cypermethrin retention index per wash in the range 0.93 to 0.95 for wash cycles 3 up to 5). The lower retention index after accelerated storage was confirmed by an increase of the alpha-cypermethrin surface concentration of 283% after storage (regeneration study). Additional studies provided by the manufacturer and generated by an independent laboratory showed that the retention index, for wash cycles 3 up to 5, is in the range 0.95 to 0.97 after storage at 54°C for 2 weeks and in the range 0.97 to 0.98 after storage at 40°C for 8 weeks, and is therefore compliant with the clause of the existing specification. The manufacturer also provided data showing that the netting mesh size, the dimensional stability of netting to washing and the bursting strength remains unchanged after storage at 54°C for 2 weeks.

The Meeting and the manufacturer agreed to keep the storage clause of 54°C for 2 weeks in the specification and the Meeting concluded that MAGNet complies with the existing WHO interim specification 454/LN/2.

The Meeting agreed also to update some notes of the existing specification relating to the linear density, retention index and dimensional stability to washing to be in line with the draft guideline for LN of the November 2010 – second revision of the first edition of the FAO/WHO Manual.

## ANNEX 1. REFERENCES

Study number	Author(s)	Year	Study title. Study identification number. Report identification number. GLP [if GLP]. Company conducting the study
	CITEVE	2010	Physical tests on MAGNet. Reports No. 6335/2009-1 and 7510/2009-1 for V.K.A. Polymers Pvt. Ltd., October - November 2009.
22069	CRA-W	2010	Physical and chemical properties and accelerated storage stability for MAGNet [alpha-cypermethrin long-lasting (incorporated into polyethylene) insecticidal mosquito net (LN)]. Report V.K.A. Polymers / RE 22069 / 2009 of the Walloon Agricultural Research Centre, Gembloux, Belgium for V.K.A. Polymers Pvt. Ltd., January 11, 2010.
22151	CRA-W	2010	Accelerated storage stability study for MAGNet [alpha-cypermethrin long-lasting (incorporated into polyethylene) insecticidal mosquito net (LN)]. Report V.K.A. Polymers / RE 22151 / 2009 of the Walloon Agricultural Research Centre, Gembloux, Belgium for V.K.A. Polymers Pvt. Ltd., March 31, 2010.
22157	CRA-W	2010	Accelerated storage stability study for MAGNet – batch MN-1005 [alpha-cypermethrin long-lasting (incorporated into polyethylene) insecticidal mosquito net (LN)]. Report V.K.A. Polymers / RE 22157 / 2010 of the Walloon Agricultural Research Centre, Gembloux, Belgium for V.K.A. Polymers Pvt. Ltd., May 11, 2010.
22324-1	CRA-W	2010	Determination of alpha-cypermethrin in MAGNet and DuraNet [alpha-cypermethrin long-lasting (incorporated into filaments) insecticidal net (LN)]. Report WHO / RE 22324 / 2010 / 1 of the Walloon Agricultural Research Centre, Gembloux, Belgium for WHO, September 28, 2010.
	FAO/WHO	2006	Manual on development and use of FAO and WHO specifications for pesticides. March 2006 revision of the 1 <sup>st</sup> edition. FAO, Rome and WHO, Geneva, March 2006 (internet publications).
	FAO/WHO	2010	Manual on development and use of FAO and WHO specifications for pesticides. Second revision of the 1 <sup>st</sup> edition. FAO, Rome and WHO, Geneva, November 2010 (internet publications).
	Ramanathan N. & Samiappan A.	2010	Physical and chemical properties, accelerated and extended storage stabilities for MAGNet™ (alpha-cypermethrin incorporated into polyethylene) long-lasting insecticidal mosquito net. Report submitted to World Health Organization Pesticide Evaluation Scheme (WHOPES). V.K.A. Polymers Pvt. Ltd., August 2010.
	TÜV SÜD PSB Singapore	2009	Testing of mosquito nets submitted by V.K.A. Polymers Pvt. Ltd. Test reports No. S09MEC05349/JL/CORR2 and S09MEC05349-CSY-CORR03 for V.K.A. Polymers Pvt. Ltd., September 2009.
	WHO	2005	Guidelines for laboratory and field testing of long-lasting insecticidal mosquito nets. Document WHO/CDS/WHOPES/GCDPP/2005.11. WHO, Geneva, 2005.
	WHO	2005	Technical consultation on specifications and quality control of netting materials for mosquito nets (untreated and treated). 29 November – 02 December 2005. WHO Headquarters, Geneva, Switzerland.

Study number	Author(s)	Year	Study title. Study identification number. Report identification number. GLP [if GLP]. Company conducting the study
	WHO	2008	Report of the Eleventh WHOPES Working Group Meeting, WHO/HQ, Geneva, 10-13 December 2007. WHO, Geneva, document WHO/HTM/NTD/WHOPES/2008.1.
	WHO	2011	Report of the Fourteen WHOPES Working Group Meeting, WHO/HQ, Geneva, 11-15 April 2011. WHO, Geneva, document to press.

# WHO SPECIFICATIONS FOR PUBLIC HEALTH PESTICIDES

## ALPHA-CYPERMETHRIN

### FAO/WHO EVALUATION REPORT 454/2009.2

#### **Recommendations**

The Meeting recommended that a time-limited interim specification (until October 2012) for alpha-cypermethrin long-lasting (incorporated into filaments) insecticidal net proposed by Clarke Mosquito Control, as amended, should be adopted by WHO.

#### **Appraisal**

Supporting data and draft specifications for alpha-cypermethrin long-lasting (incorporated into filaments) insecticidal net (LN), provided by Clarke Mosquito Control Inc., were considered by the Meeting for development of a new WHO specification. Appropriate clauses, limits and methods of testing for certain parameters of this new type of formulation were also developed by the company over this period.

The alpha-cypermethrin (incorporated into filaments) LN produced by this manufacturer was tested/evaluated under the auspices of WHOPES and an interim recommendation for their use in malaria prevention and control was issued in 2008 (WHO 2008).

A provisional specification guideline for LN formulations was accepted by the JMPS in 2004 and published by WHO. The guideline for LN was subsequently amended, taking into account the recommendations of a WHO consultation on mosquito nets (WHO 2005) and published in the revised manual (FAO/WHO 2006). However, the apparent diversity of LN technologies currently requires specification clauses and limits to be tailored to individual products.

The LN under consideration is a warp-knitted fabric in which the active ingredient, alpha-cypermethrin, is incorporated into the polymer prior to the spinning process. The yarn is a high-density polyethylene monofilament. The manufacturer confirmed that the active ingredient incorporated into the LN is from a source compliant with the existing WHO specification for alpha-cypermethrin (Tagros).

#### Description clause

The Meeting agreed that the specification should be applied to white or coloured warp-knitted fabrics made from 150 denier monofilament high-density polyethylene yarn and that it should apply equally to made up, ready-to-use nets (rectangular and circular) or to netting in bulk.

#### Active ingredient content clause

The target dose of alpha-cypermethrin (5.8 g/kg) is related to the technology, in order to achieve a satisfactory biological activity. The target dose on a fabric area basis (261 mg/m<sup>2</sup>) is calculated from measurements of g/kg and fabric density in g/m<sup>2</sup>. The Meeting agreed that the declared and tolerance values should be based on g/kg, with the corresponding mg/m<sup>2</sup> value being defined in a Note to the specification.

The Meeting observed that random variations in the distribution of alpha-cypermethrin may influence the variation in measured values for g/kg. The manufacturer provided between- and within-batch data, based on analysis of single 225 cm<sup>2</sup> pieces (15 cm x 15 cm) and variations in alpha-cypermethrin content following the sampling procedure as detailed in the LN guideline in the Manual, and demonstrated good precision (RSD < 5% in one experiment).

The analytical method for determination of the alpha-cypermethrin content in LN incorporated type was validated as an extension of the existing CIPAC method for alpha-cypermethrin (coated type) and adopted as full method by CIPAC in 2008 and is published in Handbook M (August 2009).

#### Relevant impurities

There are no relevant impurities identified in the existing WHO specification for alpha-cypermethrin TC proposed by Tagros. The clause has therefore been omitted.

#### Alpha-cypermethrin retention index clause

An adequate amount of active ingredient must be present on the surface of the LN, for efficacy, but the majority must reside within the fibres of the LN, to avoid excessive losses during washing and to provide a reservoir from which the surface is replenished with active ingredient. The nature of the fibre material – a high density polyethylene with a typical crystallinity of 60% – strongly influences the migration of alpha-cypermethrin to the surface when the LN is subjected to repeated washing. The Meeting agreed that also for incorporated types of LN, the retention index is the appropriate expression of the depletion and replenishment of the active ingredient on the surface of the monofilament fibre.

The manufacturer provided both theoretical considerations on the migration behaviour of the insecticide to the surface and experimental data showing that approximately constant proportions of the remaining alpha-cypermethrin are removed from the surface of the filament by successive washings with aqueous detergent. The manufacturer proposed a minimum retention index of 0.95 and a maximum of 0.99, which was agreed by the Meeting. When agreeing on limits in a specification, the sampling and analytical methods need to be properly validated so these limits can be checked and enforced by quality control laboratories if necessary. The upper limit of 0.99 was chosen for practicability reasons: the default precision requirement for content determination is ≤ 5%. Therefore, the upper limit of the retention index is lower but close to 1.0, as the WHOPES Phase I laboratory studies with good efficacy after each wash step clearly show. The errors in sampling and analytical method prevent to define a closer range of the retention index.

Sampling of alpha-cypermethrin (incorporated into filaments) LN was done by cutting a total of 5 pieces for analysis. Five pieces of net (15 x 15 cm) were cut and washed for a specified number of washes using the WHO washing method (WHO 2005). After drying, the samples were again analyzed for alpha-cypermethrin content. The recommended positions from which 5 pieces of netting were taken from a made up bed net are similar to those given in the manual (FAO/WHO 2006), as shown in figure 1, appended to the specification. The manufacturer's results showed a small decrease of alpha-cypermethrin content with each washing step, with more than 95% of total alpha-cypermethrin remaining after each wash step. As the range for the retention index is defined by the minimum of 0.95 and the maximum is close but distinctly lower than 1.0, the Meeting agreed to consider the lower limit of 0.95 and

the upper limit of 0.99 as acceptable. Using bioassays, the regeneration time required for diffusion to restore the surface concentration to full biological activity after washing was shown to be one day.

Physical property clauses

The clauses for dimensional stability to washing and bursting strength specify ISO methods. The test method for netting mesh size does not require standardization.

The Meeting accepted the manufacturer's explanation that the test for bursting strength obviated the need for a separate clause for tearing strength.

The  $\pm 10\%$  tolerance on dimensional stability to washing was higher than the standard 5% given in the LN guideline (FAO/WHO 2006) but was supported by test results. The actual measurements showed a significantly better performance than 5% in most cases, with one exception.

Storage stability clause

The incorporated alpha-cypermethrin is stable over a very wide temperature range and has low volatility, providing additional protection to the active ingredient. At 54°C for 2 weeks, the loss of alpha-cypermethrin was minimal (approximately 1%) and the physical properties of the fabric were maintained. The physical tests as well as the determination of the release index met the general requirements of the Manual (FAO/WHO 2006).

## ANNEX 1. REFERENCES

Reference and year	Title of report or publication details
FAO/WHO 2006	Manual on development and use of FAO and WHO specifications for pesticides, March 2006 revision of the 1 <sup>st</sup> edition. FAO, Rome, March 2006; WHO, Geneva, March 2006 (internet publications).
WHO 2005	Technical consultation on specifications and quality control of netting materials for mosquito nets (untreated and treated). 29 November–02 December 2005. WHO Headquarters, Geneva, Switzerland.
WHO 2005	Guidelines for laboratory and field testing of long-lasting insecticidal mosquito nets. Document WHO/CDS/WHOPES/GCDPP/2005.11. World Health Organization, Geneva, 2005.
WHO 2007	Report of the Tenth WHOPES Working Group Meeting, WHO/HQ, Geneva, 11-14 December 2006. Geneva, World Health Organization, document WHO/CDS/NTD/WHOPES/2007.1
WHO 2008	Report of the Eleventh WHOPES Working Group Meeting, WHO/HQ, Geneva, 10-14 December 2007. Geneva, World Health Organization, document WHO/HTM/NTD/WHOPES/2008.1.