

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

DELTAMETHRIN + PIPERONYL BUTOXIDE

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

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

+

5-[2-(2-butoxyethoxy)ethoxymethyl]-6-propyl-1,3-benzodioxole



**World Health
Organization**

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Disclaimer¹

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.

¹ 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

DELTAMETHRIN + PIPERONYL BUTOXIDE

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WHO SPECIFICATIONS FOR PUBLIC HEALTH PESTICIDES

DELTAMETHRIN

INFORMATION

ISO common names

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

Synonyms

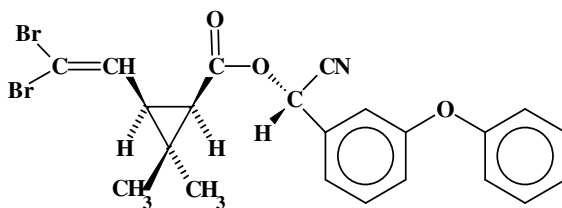
Decamethrin (rejected common name)

Chemical names

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

CA [1R-[1 α (S*),3 α]]-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

Identity tests

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

WHO SPECIFICATIONS FOR PUBLIC HEALTH PESTICIDES

PIPERONYL BUTOXIDE

INFORMATION

ISO common names

Piperonyl butoxide (BAN; accepted in lieu of a common name by BSI, E-ISO, ESA); piperonyl butoxyde (F-ISO)

Synonyms

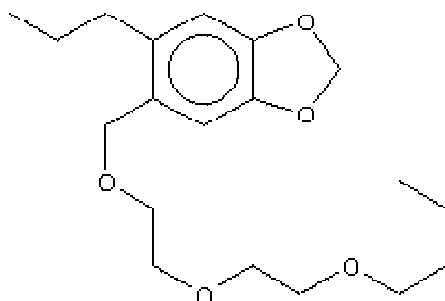
PBO

Chemical names

IUPAC 5-[2-(2-butoxyethoxy)ethoxymethyl]-6-propyl-1,3-benzodioxole

CA 5-[[2-(2-butoxyethoxy)ethoxy]methyl]-6-propyl-1,3-benzodioxole

Structural formula



Empirical formula

$C_{19}H_{30}O_5$

Relative molecular mass

338.4

CAS Registry number

51-03-6

CIPAC number

33

Identity tests

GC retention time, mass spectrum (from GC-MS)

WHO SPECIFICATIONS FOR PUBLIC HEALTH PESTICIDES

DELTAMETHRIN + PIPERONYL BUTOXIDE LONG-LASTING (INCORPORATED INTO FILAMENTS) INSECTICIDAL NETTING

WHO interim specification 333+33/LN (NETTING) (December 2010*)

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+33/2010). 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+33/2010), given in PART TWO, forms an integral part of this publication.

1 Description

The product shall be in the form of netting (Note 1), consisting of 100 denier knitted mono-filament polyethylene fibres, incorporating technical deltamethrin complying with the requirements of WHO specification 333/TC (April 2005), and technical piperonyl butoxide (synergist) complying with the requirements of WHO specification 33/TC (December 2010), together with any necessary other formulants. 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 (CIPAC/4673/m and CIPAC/4675/m) (Notes 5 & 6)

The active ingredient and synergist 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 (CIPAC/4673/m) (Notes 5, 6, 7 & 8)

The deltamethrin content shall be declared (4 g/kg) and, when determined, the average content shall not differ from that declared by more than $\pm 25\%$.

* This specification is applicable to the roof netting of long-lasting insecticidal nettings commercialized under the trade name PermaNet 3.0 produced by Vestergaard Frandsen. The question of the extension of specifications for LN has been discussed by the JMPS in 2009. The Meeting agreed that - in contrast to other formulations - an extension of a specification to nominally similar LN of other manufacturers was not possible with the data currently available and that the manufacturer and the product should be named in a footnote or in the specification.

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/>.

2.3 Deltamethrin retention index (Note 9)

The average retention index of deltamethrin per wash from the netting, when determined, shall be within the range 0.90 to 1.00.

2.4 Piperonyl butoxide content (CIPAC/4675/m) (Notes 5, 6, 7 & 8)

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

2.5 Piperonyl butoxide retention index (Note 9)

The average retention index of piperonyl butoxide per wash from the netting, when determined, shall be within the range 0.85 to 0.99.

3 Physical properties

3.1 Netting mesh size

When counted by the method given in Note 10, the average number of complete holes/cm² shall be not less than 21 holes/cm² and the lowest value shall be not less than 20 holes/cm².

3.2 Dimensional stability of netting to washing (Note 11)

Not more than 5% shrinkage/expansion in both dimensions.

3.3 Bursting strength (Note 12)

The minimum bursting strength of the fabric shall be declared (not less than 400 kPa) and, when determined, the average shall be not less than that declared.

4 Storage stability

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

After storage at $54 \pm 2^\circ\text{C}$ for 2 weeks, the determined total active ingredient and synergist content must not be lower than 95% of the average content found before storage (Note 13) and the netting shall continue to comply with the clauses for:

- retention index (2.3 and 2.5);
- dimensional stability (3.2);
- bursting strength (3.3).

Note 1 The specification applies to bulk netting. The netting may be white or colored, for example, yellow, pink, khaki or light brown, blue or dark blue, green or dark green.

Note 2 Occasional short lengths of loose thread present in finished nets 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 standardized laboratory washes. The clauses for deltamethrin / piperonyl butoxide retention characteristics (2.3 and 2.5) are based on a model washing regime and compliance with the limit does not guarantee that activity will be retained through any particular number of washes performed according to local practice.

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 fibers cannot be measured in the netting or the manufactured net but it should be identified on the packaging.

Note 5 For complete identification and good quantification, deltamethrin (i.e. the [*S*,1*R*,3*R*]-isomer, otherwise known as the *S*-isomer) must be separated from the [*R*,1*R*,3*R*]-isomer (otherwise known as the *R*-isomer), which is not part of the active ingredient and not a relevant impurity. The isomers may be separated by non-chiral techniques as provided in the CIPAC method for deltamethrin.

Note 6 The extension of the CIPAC method 333/LN/(M)/3 (CIPAC/4673/m) for determination of deltamethrin incorporated into polyethylene LN and the extension of the AOAC-CIPAC method 32+33+345/TK/(M)/3 (CIPAC/4675/m) for determination of piperonyl butoxide incorporated into polyethylene LN were accepted as provisional CIPAC methods in 2009. Prior to their publication in a Handbook, copies of the methods may be obtained through the CIPAC website, <http://www.cipac.org/prepubme.htm>.

Note 7 Samples should be taken according to a convenient diagonal across the width of bulk material. Samples must be sufficiently large to conduct all tests required and representative of the netting. Except where seams are to be tested, do not test material within 10 cm of seams or selvages.

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.

Note 8 The deltamethrin and piperonyl butoxide content may be declared as both g/kg and mg/m² but, in case of dispute, g/kg values shall be used. If the active ingredient content is also specified as mg/m² of netting material, the actual content on this basis is calculated from the measured values for active ingredient content in g/kg and mass of net/m². Mass of net/m² should be determined according to ISO 3801 (1977).

Note 9 Currently (2010), 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 at least 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 10 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 of 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 $\geq \frac{1}{2}$ are counted as complete holes, whereas those $< \frac{1}{2}$ are not counted. Count 5 replicate squares selected according to Note 7, calculate the average and note the lowest value.

Note 11 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 mm x 500 mm; mark off 350 mm 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 programme: 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 12 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 cm² areas of fabric. Proposed specifications based on tests of 50 cm² area must be supported by data showing the suitability of the proposed value and its relationship to minimum of 400 kPa (which is based on 7.3 cm² area). Five replicate tests should be conducted on samples taken at approximately equal distances on a diagonal across the netting, taking no sample within 10 cm of a border or seam. In made up rectangular nets, the "diagonal" may correspond to one produced by conceptually arranging the panels end to end). 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 centred 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 13 Samples of the formulation taken before and after the storage stability test should be analyzed concurrently after the test in order to reduce the analytical error.

WHO SPECIFICATIONS FOR PUBLIC HEALTH PESTICIDES

DELTAMETHRIN LONG-LASTING (COATED ONTO FILAMENTS) INSECTICIDAL NET

COMBINED WITH

DELTAMETHRIN + PIPERONYL BUTOXIDE LONG-LASTING (INCORPORATED INTO POLYETHYLENE) INSECTICIDAL NET

WHO interim specification 333+33/LN (NET) (December 2010^{*})

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+33/2010). 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+33/2010), given in PART TWO, forms an integral part of this publication.

1 Description

The product shall be in the form of a finished net (Note 1), as illustrated in the Figure 1. The roof of the net shall be formed from 100 denier knitted mono-filament polyethylene fibres, incorporating technical deltamethrin and technical piperonyl butoxide (synergist), together with any necessary other formulants, complying with the requirements of WHO specification 333+33/LN (netting) (December 2010). The side of the net shall be formed from 75 or 100 denier multi-filament polyester fibres with a strengthened 70 cm border, treated with technical deltamethrin, together with any necessary other formulants, complying with the requirements of WHO specification 333/LN/1 (netting) (September 2010). 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 (Note 3).

^{*} This specification is applicable to long-lasting insecticidal nets commercialized under the trade name PermaNet 3.0 produced by Vestergaard Frandsen. The question of the extension of specifications for LN has been discussed by the JMPS in 2009. The Meeting agreed that - in contrast to other formulations - an extension of a specification to nominally similar LN of other manufacturers was not possible with the data currently available and that the manufacturer and the product should be named in a footnote or in the specification.

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/>.

2 Physical properties

2.1 Bursting strength (Note 4)

The average bursting strength of seams shall be not less than the measured average for the weaker fabric of the two (when considering a seam connecting two different nettings), or not less than the stated value for the fabric (when considering a seam connecting a given fabric to itself).

Note 1 The specification applies to rectangular finished bed nets. The nets may be white or colored, for example, yellow, pink, khaki or light brown, blue or dark blue, green or dark green.

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

Note 3 Samples should be taken according to Figure 1. Samples must be sufficiently large to conduct all tests required and representative of the net. Except where seams are to be tested, do not test material within 10 cm of seams or selvages. 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.

Note 4 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 cm² areas of fabric. Proposed specifications based on tests of 50 cm² 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 cm² area). Five replicate tests should be conducted on samples taken at approximately equal distances on a diagonal across the netting, taking no sample within 10 cm of a border or seam. In made up rectangular nets, the "diagonal" may correspond to one produced by conceptually arranging the panels end to end). The average of the 5 measurements is calculated.

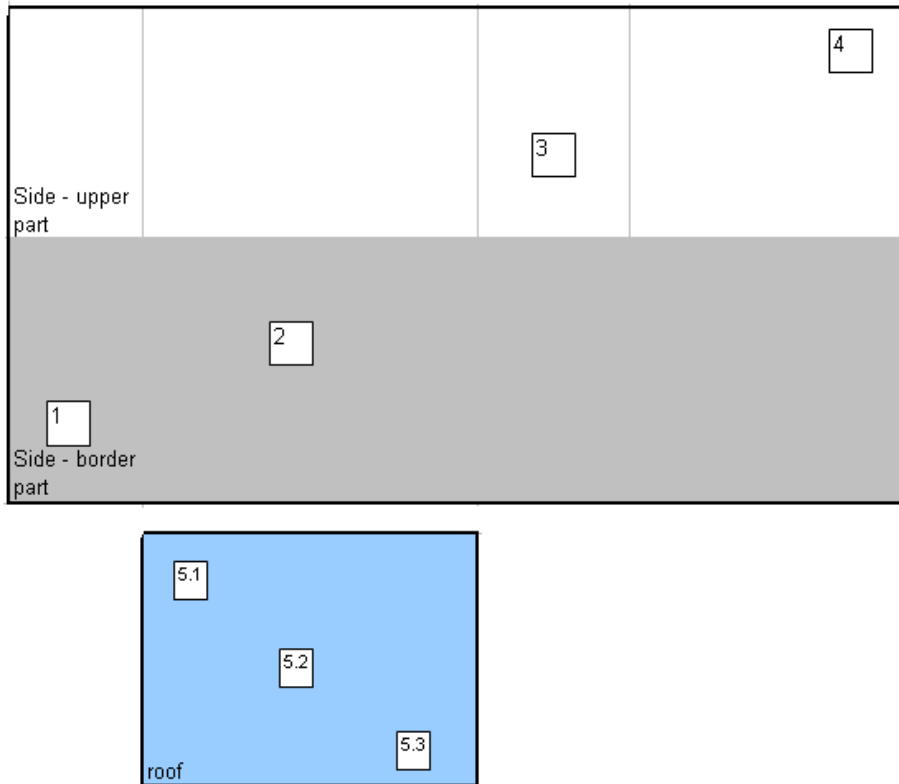
The method to test seam bursting strength is identical to that used to test the fabric, except that 5 replicate tests should be made, with the seam centred on the test head. Up to 5 seams may be tested but, if there are <5 seams, replicate measurements should be made on 1 or more seams, to provide a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

Figure 1 Method for sampling

The samples should be taken according to the pattern shown in the diagram below. Sufficient material should be taken for all tests and thus the pattern indicated is intended only for general guidance. For most tests, pieces should be taken at least 15 cm from seams or selvages, avoiding folded and creased areas, so as to represent the netting material as fully as possible.

For determining deltamethrin content as g/kg in the side netting, 4 pieces of net with area of 100 cm² each minimum are cut from position 1-4. Position 1 and 2 belong to the strengthened border and position 3-4 belong to the upper part of the side. All 4 positions are cut into small pieces of less than 1 x 1 cm and mixed well before taking the analytical portions. The deltamethrin content of the border and upper part in mg/m² can be calculated by multiplying the content in g/kg by the corresponding mass of net/m².

For determining deltamethrin and piperonyl butoxide content in the roof netting, 3 pieces of net with area of 100 cm² each are cut from position 5.1-5.3, and further cut into small pieces of less than 1 x 1 cm and mixed well before taking the analytical portions.



PART TWO

EVALUATION REPORTS

DELTAMETHRIN + PIPERONYL BUTOXIDE

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WHO SPECIFICATIONS FOR PUBLIC HEALTH PESTICIDES

DELTAMETHRIN + PIPERONYL BUTOXIDE

FAO/WHO EVALUATION REPORT 333+33/2010

Recommendations

The Meeting recommended the following.

- (i) Time-limited interim specifications (until December 2013) for deltamethrin + piperonyl butoxide (incorporated into filaments) LN (NETTING) and for deltamethrin (coated onto filaments) LN combined with deltamethrin + piperonyl butoxide (incorporated into filaments) LN (NET) proposed by Vestergaard Frandsen, as amended, should be adopted by WHO.
- (ii) Future proposals for extension of these specifications to apparently equivalent LN formulations should be supported by evidence to show whether or not the test method and limit for active ingredient retention characteristics are appropriate for the additional products.

Appraisal

Supporting data and draft specifications for deltamethrin + piperonyl butoxide (incorporated into filaments) LN, provided by Vestergaard Frandsen, were considered by the Meeting in 2009 and 2010 for development of new WHO specifications. Appropriate clauses, limits and methods of testing for certain parameters of this new type of formulation were also developed by the company and scientific institutes.

Deltamethrin (as insecticide) together with piperonyl butoxide (as synergist) long-lasting (incorporated into filaments) insecticidal nets (LN) were tested and evaluated by WHOPES and a time-limited interim recommendation for their use in malaria prevention and control was issued (WHO 2009). As with other slow release technologies like CS formulations, the apparent diversity of LN technologies currently requires specification clauses and limits to be tailored to individual products or type of products, as efficacy is strongly dependent on retention / release characteristics of the product. The LN under consideration is a warp-knitted fabric in which deltamethrin and piperonyl butoxide are incorporated into mono-filament polyethylene fibres of 100 denier at the target dosage of 4 g deltamethrin and 25 g piperonyl butoxide per kg of netting material.

The manufacturer confirmed that the active ingredient (deltamethrin) and the synergist (piperonyl butoxide) incorporated into the LN was from sources compliant with the existing WHO specifications for deltamethrin TC and piperonyl butoxide TC respectively.

Description clause

The Meeting and manufacturer agreed that the specification for deltamethrin + piperonyl butoxide (incorporated into filaments) LN should be applied to white or coloured fabrics made from 100 denier mono-filament polyethylene yarn and that it should apply to netting in bulk. The LN under consideration is only a part (roof) of a finished ready-to-use net (PermaNet 3.0). The Meeting agreed on a position statement on WHO specifications for "combination LNs". Combination LNs are long-lasting insecticidal nets and finished products which combine two or more different nets based on different types of fabric, insecticide with or without a synergist. In principle, an almost unlimited amount of combinations of yarns, insecticides and coating/incorporation technologies seems possible. In order to keep WHO specifications as straightforward as possible, separate WHO specifications have to be developed for each part of the net which in itself is of the same composition. Noting that the physico-chemical characteristics of the different nettings have bearings on safety and efficacy of the final product, a specification need also to be developed for the final product. This specification is a very short one, including a description of the final net with reference to the individual nettings it is produced from and some selected physical properties like bursting strength of the seams which belong to the final product and not to the net parts it is composed of. The Meeting agreed to develop a brief separate specification for the final product (PermaNet 3.0) including a description of the final rectangular net with reference to individual nettings.

The manufacturer provided the Meeting with a sub-sampling scheme as illustrated in the Figure 1 of the specification for the finished net. Supporting data demonstrated that the proposed sampling scheme provides an acceptable repeatability (RSD < 2.5%) for deltamethrin and piperonyl butoxide content (expressed as g/kg) and is representative of the combination net.

Active ingredient and synergist content clauses

The target dose of deltamethrin and piperonyl butoxide is 4 g/kg and 25 g/kg respectively with a tolerance of $\pm 25\%$.

The extension of the CIPAC method 333/LN/(M)/3 (CIPAC/4673/m) for determination of deltamethrin in incorporated into polyethylene LN by high performance liquid chromatography with UV detection (HPLC-UV) was accepted as a provisional CIPAC method in 2009. The extension of the AOAC-CIPAC method 32+33+345/TK/(M)/3 (CIPAC/4675/m) for determination of piperonyl butoxide in incorporated into polyethylene LN by capillary gas chromatography with flame ionisation detection (GC-FID) was accepted as a provisional CIPAC method in 2009. The manufacturer provided also the Meeting with an identity test of piperonyl butoxide in PermaNet 3.0 by gas chromatography with mass spectrometry detection (GC-MS).

A new validated method (CIPAC/4682/m) for determination of both deltamethrin and piperonyl butoxide in a single method by GC-FID was also presented at the CIPAC technical meeting in 2009 and recommended for a small scale collaborative trial. The method involves extraction of both deltamethrin and piperonyl butoxide from net samples by heating under reflux with xylene and determination by capillary gas chromatography with flame ionisation detection (GC-FID) using the internal standard calibration.

Special attention needs to be paid to describe and control random variations in the distribution of the insecticide and synergist in the net. The spatial variation study performed by the manufacturer showed an acceptable within-net homogeneity (n = 5, RSD = 2.2 % for deltamethrin and 4.2 % for piperonyl butoxide). The analysis of 5 different batches in a study and of 9 different nets randomly taken from several batches in another study indicated that the deltamethrin and piperonyl butoxide content is within the proposed tolerance ($\pm 25\%$). The WOPES Phase II testing of PermaNet 3.0 showed also that, except for some outliers, the active ingredient and synergist content comply with the target doses (WHO 2009).

Active ingredient and synergist retention index clauses

An adequate amount of active ingredient and synergist 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 and synergist. The manufacturer provided data showing that decreasing proportions of the remaining deltamethrin and piperonyl butoxide are removed from the polymer by successive washings with aqueous detergent (free-migration stage behaviour). 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.

Depletion of total active ingredient content by washing (retention index) is accomplished by analyzing separate washed and unwashed pieces of the same fabric. Currently (2010), CIPAC is developing a wash method for the determination of the retention behaviour of long-lasting insecticidal mosquito nets. 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 using the equation for a free migration stage behaviour.

The manufacturer initially proposed a minimum retention index of 85% for both deltamethrin and piperonyl butoxide based on the wash 0-1. The meeting did not accept this clause as WHOPES data have shown that the first wash always eliminate more active ingredient than the following washes, and is therefore not representative of the retention characteristics of LNs.

Currently (2010), 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. This method is a standardisation of the WHO washing method and involves the determination of the retention index 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 (WHO 2008).

The data provided by the manufacturer showed that a minimal retention index per wash of 90% and 85% is adequately supported for deltamethrin and PBO respectively. WHOPES Phase I data confirmed also these clauses. Moreover the PBO retention after washing was slightly lower than that of the deltamethrin, and a range of 0.85 to 0.99 as average retention index per wash could be proposed. PBO retention increases with the number of washes and after 15 washes no release of PBO seems to occur (WHO 2009).

Relevant impurities clause

There are no relevant impurities identified in the existing WHO specifications for deltamethrin TC and piperonyl butoxide TC. During the manufacturing process of deltamethrin LN, epimerization of deltamethrin to the (insecticidally inactive) α R-isomer may occur. This conversion must be controlled by the manufacturer to avoid losses of active ingredient. WHOPES data showed that deltamethrin α R-isomer content can reach up to 20% of deltamethrin content. In the meantime the manufacturer has improved the manufacturing process to reduce the epimerization. The manufacturer provided additional data on PermaNet 3.0 during production and storage over time (11 months) showing that the deltamethrin α R-isomer content is less than 2% of the deltamethrin content.

This conversion can also occur if the LN is exposed to excessive heat during storage or use. The Meeting agreed that the α R-isomer should remain designated as a non-relevant impurity and hence remain excluded from the specification. It is however indirectly specified by the content clause in the accelerated storage test, where at least 95% of deltamethrin is still present after the test thus limiting the epimerization to a maximum of 5%.

Physical properties clauses

The clauses for physical properties are based on ISO methods, with the exception of netting mesh size which do not require standardisation and deltamethrin and piperonyl butoxide retention index, which relates to the active ingredient and synergist.

The 5% tolerance for dimensional stability to washing is in agreement with the standard of 5% given in the LN guideline (FAO/WHO 2006).

Storage stability clause

Although deltamethrin in bulk is stable over a very wide temperature range and has very low volatility, in the LN it apparently behaves differently. The manufacturer initially provided data after storage at 40°C for 8 weeks showing that no loss of deltamethrin and piperonyl butoxide occurs and that the physical properties of the fabric are maintained. The manufacturer initially stated that deltamethrin in the LN has better stability at 40°C than at 54°C and its concentration remains almost unchanged after 2 years at 40°C. Above 80°C, deltamethrin is rapidly and completely lost from the LN, apparently due to volatilization. The manufacturer provided additional data on PermaNet 3.0 stored at 40°C for 8 weeks, 45°C for 6 weeks and 54°C for 2 weeks. At 54°C for 2 weeks, the loss of deltamethrin and piperonyl butoxide was less than 5% and the manufacturer and the Meeting finally agreed to include in the specification for the netting the standard testing of 54°C for 2 weeks.

ANNEX 1: REFERENCES

Study number	Author(s)	Year	Study title. Study identification number. Report identification number. GLP [if GLP]. Company conducting the study
R59.26	Chi Phan	2010	Proposal on sub-sampling for PermaNet 3.0 combination net. Report R59.26 of Vestergaard Frandsen Laboratories, Vietnam, August 2010.
R59.27	Chi Phan	2010	Supporting data for PermaNet 3.0 combination net sub-sampling recommended by WHO panel. Report R59.27 of Vestergaard Frandsen Laboratories, Vietnam, August 2010.
CIPAC/4682/m	CRA-W	2009	Determination of deltamethrin and/or piperonyl butoxide in Long-Lasting (incorporated into polyethylene) Insecticidal Mosquito Nets. Analytical method by GC-FID. 2009 CIPAC Technical Meeting, CIPAC Document 4682/m.
CIPAC/4683/R	CRA-W	2009	Determination of deltamethrin and/or piperonyl butoxide in Long-Lasting (incorporated into polyethylene) Insecticidal Mosquito Nets. Validation and performance verification of the analytical method by GC-FID. 2009 CIPAC Technical Meeting, CIPAC Document 4683/R.
	FAO/WHO	2006	Manual on development and use of FAO and WHO specifications for pesticides. March 2006 revision of the 1 st edition. FAO, Rome and WHO, Geneva, March 2006 (internet publications).
R50	Nam Le	2008	PermaNet 3.0 information and data requirement. Report R50 of Vestergaard Frandsen Laboratories, Vietnam, October 2008.
CIPAC/4674/R	Quynh Chi Phan <i>et al.</i>	2009	Deltamethrin 333/LN. Method extension for polyethylene LN (PermaNet 3.0 roof netting), Validation Data and Statistics. 2009 CIPAC Technical Meeting, CIPAC Document 4674/R.
CIPAC/4676/R	Quynh Chi Phan <i>et al.</i>	2009	Piperonyl butoxide 32+33+345/TK/. Method extension for polyethylene LN (PermaNet 3.0 roof netting), Validation Data and Statistics. 2009 CIPAC Technical Meeting, CIPAC Document 4676/R.
R59.18	Thom Duong	2010	Review on R-isomerisation of Deltamethrin in PermaNet 3.0 roof 2009 production data. Report R59.18 of Vestergaard Frandsen Laboratories, Vietnam, February 2010.
R59 (10)	TNT	2009	PermaNet 3.0 roof. Bursting strength data package supporting to WHO specification. Report R59 (10) of Vestergaard Frandsen Laboratories, Vietnam, June 2009.
R59.20	Trung Tran	2010	Review on accelerated storage stability of DM and PBO in PN 3.0 roof. Report R59.20 of Vestergaard Frandsen Laboratories, Vietnam, March 2010.
R112.6	Trung Tran	2010	Identity test of piperonyl butoxide in PermaNet 3.0 by gas chromatography – mass spectrometry. Report R112.6 of Vestergaard Frandsen Laboratories, Vietnam, August 2010.
	Vestergaard	2008	Draft specifications for PermaNet 3.0, October 2008.
	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	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.

Study number	Author(s)	Year	Study title. Study identification number. Report identification number. GLP [if GLP]. Company conducting the study
	WHO	2009	Report of the Twelfth WHOPES Working Group Meeting, WHO/HQ, Geneva, 8-11 December 2008. Geneva, World Health Organization, document WHO/HTM/NTD/WHOPES/2009.1.
CIPAC/4673/m	Zellweger M.	2009	Method extension of CIPAC 333/LN. Determination of deltamethrin in PE by high performance liquid chromatography. 2009 CIPAC Technical Meeting, CIPAC document 4673/m.
CIPAC/4675/m	Zellweger M.	2009	Method extension of CIPAC 32+33+345/TK/M. Determination of Piperonyl butoxide in polyethylene matrix by GC-FID. 2009 CIPAC Technical Meeting, CIPAC Document 4675/m.