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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PART TWO

EVALUATIONS OF DELTAMETHRIN + PIPERONYL BUTOXIDE

Disclaimer[1]

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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.

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[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 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. 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. 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 the WHO Prequalification Team - Vector control products (PQT-VC) website.

PART ONE

SPECIFICATIONS

DELTAMETHRIN + PIPERONYL BUTOXIDE

DELTAMETHRIN

INFORMATION

ISO common names

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

Synonyms

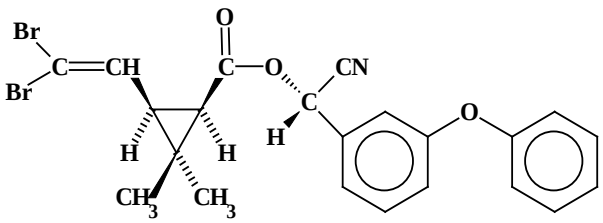
Decamethrin (rejected common name)

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

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

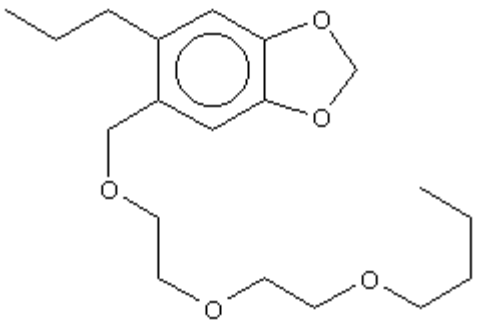
PBO

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)

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

WHO specification 333+33/LN/1 (NETTING) (April 2019*)

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 reports (333+33/2010, 333+33/2012, 333+33/2015, 333+33/2018.1, 333+33/2019). 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 reports (333+33/2010, 333+33/2012, 333+33/2015, 333+33/2018.1, 333+33/2019), 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 (Note 2) knitted mono-filament polyethylene fibres, incorporating technical deltamethrin complying with the requirements of WHO specification 333/TC (November 2017), and technical piperonyl butoxide complying with the requirements of WHO specification 33/TC (September 2018), together with any necessary other formulants. The product shall appear clean and shall be free from visible extraneous matter (Note 3), 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 4).

2 Active ingredients

2.1 **Identity tests** (333/LN/(M2)/2, CIPAC Handbook N, p.34, 2012 for deltamethrin, and 33/LN/(M)/2, CIPAC Handbook N, p.111, 2012 for piperonyl butoxide) (Note 5)

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

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* This specification is applicable to the roof netting of long-lasting insecticidal nettings commercialized under the trade name of PermaNet® 3.0 produced by Vestergaard. The subject 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 the WHO Prequalification Team - Vector control products (PQT-VC) website.

2.2 **Deltamethrin content** (333/LN/(M2)/3, CIPAC Handbook N, p.34, 2012) (Notes 5, 6 & 7)

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

2.3 **Deltamethrin wash resistance index** (MT 195, CIPAC Handbook O, p. 205, 2017) (Note 8)

The wash resistance index of deltamethrin from the netting, when determined, shall be within the range 88% to 100%.

2.4 **Piperonyl butoxide content** (33/LN/(M)/3, CIPAC Handbook N, p.111, 2012) (Notes 6 & 7)

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 ± 25%.

2.5 **Piperonyl butoxide wash resistance index** (MT 195, CIPAC Handbook O, p. 205, 2017) (Note 8)

The wash resistance index of piperonyl butoxide from the netting, when determined, shall be within the range 81% to 100%.

3 **Physical properties** (Notes 6 & 14)

3.1 **Fabric weight (mass per m²)** (ISO 3801 / EN 12127)

The mass per unit area shall be declared (30 g/m²), and when determined, shall not differ from that declared by more than ± 10 %.

3.2 **Netting mesh size**

When counted by the method given in Note 9, the minimum number of complete holes/cm² shall be not less than 15.5 holes/cm².

3.3 **Dimensional stability of netting to washing** (Note 10)

Not more than 10% shrinkage and not more than 5% expansion in both directions.

3.4 **Bursting strength** (ISO 13938:2) (Note 11)

The bursting strength of the fabric shall be declared (not less than 300 kPa) and, when determined, the average shall be not less than that declared.

3.5 **Flammability** (EN 1102) (Note 12)

Tested according to EN 1102 the following requirements should be achieved*:

After removing the ignition source the following fire phenomena should not occur:
- ignition
- propagation of the flame or glow.
- flaming debris
- ignition of the filter paper

*Fulfilling the requirements above the flame speed rate is 0 mm/s, i.e., no flame or glow achieves first and third marker threads.

Formation of holes is allowed provided that the burnt or melted width and length of the holes does not exceed 50 mm and 150 mm, respectively.

4 Storage stability

4.1 **Stability at elevated temperature** (MT 46.3.4, CIPAC Handbook O, p. 176, 2017)

After storage at 54 ± 2°C for 2 weeks, the determined total active ingredients content (measured individually) shall not be lower than 95%, relative to the average contents found before storage (Note 13) and the product shall continue to comply with the clauses for:

- wash resistance index (2.3 and 2.5);
- dimensional stability (3.3);
- 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 The linear density (denier) of the fibres cannot be measured in the netting or the manufactured bed net but it should be identified on the packaging.

Note 3 Occasional short lengths of loose thread present in finished nets are not considered to be extraneous matter.

Note 4 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 wash resistance index (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 5 For complete identification and good quantification, deltamethrin which is a single pyrethroid stereoisomer consisting of [α*S*,1*R*,3*R*]-isomer (also known as the *S*-isomer) must be separated from the [α*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. These diastereomers may be separated by non-chiral techniques as provided in the CIPAC method for deltamethrin.

Note 6 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 selvedges.

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 direct sunlight) or freezing, and analyzed/tested with minimum delay. Representative portions (sub-samples) for testing should be taken as described in each test method.

Note 7 The deltamethrin and piperonyl butoxide content may be declared as both g/kg and mg/m^2 but, in case of dispute, g/kg values shall be used. If the active ingredient content is also specified as mg/m^2 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/m^2. Mass of net/m^2 should be determined according to ISO 3801 / EN 12127.

Note 8 The content of deltamethrin in the net pieces before and after washing should be determined by the CIPAC method 333/LN/(M2)/3. The content of piperonyl butoxide in the net pieces before and after washing should be determined by the CIPAC method 33/LN/(M)/3.

Note 9 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. The number of holes per measured area is converted in holes/cm². Before counting, the fabric should be conditioned according to ISO 139 (4 h, 20ºC, 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 (±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 ≥ ½ are counted as complete holes, whereas those < ½ are not counted. Count 5 replicate squares selected according to Note 6, calculate the average and note the lowest value.

Another suitable method is the use of a stereomicroscope with an image analyser software, where the number of holes in a defined area is counted. In case of discrepancy between the mesh count using stereomicroscopic method and direct or indirect counting method, the stereomicroscopic method shall be the referee method.

Note 10 Method of preparation, marking and measuring: ISO 3759. Method of washing: ISO 6330. Method of calculation: ISO 5077. 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: 30ºC Mild programme. Fill the washer with fabrics and ballast Type III (polyester ballast) up to 2 kg (according to the ISO 6330 standard). Drying: flat drying.

Note 11 Test method: ISO 13938 part 2 with conditioning of the fabric as specified in the ISO standard. The declared bursting strength, and testing for compliance with it, should be based on tests of 7.3 cm^2 areas of fabric. 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 figure 1. 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 12 Flammability test according to EN 1102, using the surface ignition method (position the burner perpendicular to the surface of the specimen).

The following shall be reported: the after flame time, the afterglow time, the maximum burnt or damage width and length, whether or not flame reaches vertical edge of the specimen, whether or not a hole is burnt or melted in the specimen, whether or not any flaming debris falls below the bottom edge of the specimen and ignition of the filter paper.
Definitions according to ISO 4880:1997 (not included in EN 1102:1995 and EN ISO 6941: 1995):
- Ignition: initiation of combustion.
- Combustion: exothermic reaction of a combustible substance with an oxidizer, accompanied by flames and/or glowing and/or emission of smoke.

Procedure for measuring burnt or damage width and length dimensions of each specimen:

Remove the specimen from the specimen holder and place it on a flat horizontal surface. Place a rule on top of the test specimen along the line of maximum damage and parallel with the length side of the test specimen. Measure the maximum length in mm from the lowest point of burnt or damage to the end of the hole. To measure the burnt or damage width, proceed in the same way but with the ruler parallel to the width side of the test specimen. Proceed in the same way for the other 5 specimens.

Note 13 Samples of the netting taken before and after the storage stability test should be analyzed concurrently after the test in order to reduce the analytical error.

Note 14 Normative references for physical tests:

Currently the following standards are the latest versions of the documents to be used for physical tests. The updated version of the standard should always be used when available.

ISO 139:2005/Amd.1:2011 Textiles - Standard atmospheres for conditioning and testing.- Textiles - Standard atmospheres for conditioning and testing.

ISO 3801:1977 - Textiles - Woven fabrics - Determination of mass per unit length and mass per unit area.

EN 12127:1997 - Textiles - Fabrics - Determination of mass per unit area using small samples.

ISO 3759:2011 - Textiles - Preparation, marking and measuring of fabric specimens and garments in tests for determination of dimensional change.

ISO 6330:2012 - Textiles - Domestic washing and drying procedures for textile testing.

ISO 5077:2007 - Textiles - Determination of dimensional change in washing and drying.

ISO 13938-2:1999 - Textiles - Bursting properties of fabrics - Part 2: Pneumatic method for determination of bursting strength and bursting distension

EN 1102:1995 - Textiles and textile products. Burning behaviour. Curtains and drapes. Detailed procedure to determine the flame spread of vertically oriented specimens.

DELTAMETHRIN LONG-LASTING (COATED ONTO FILAMENTS) INSECTICIDAL NET

COMBINED WITH

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

WHO specification 333+33/LN/1 (NET) (April 2019*)

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 reports (333+33/2010, 333+33/2012, 333+33/2015, 333+33/2018.1, 333+33/2019). 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 reports (333+33/2010, 333+33/2012, 333+33/2015, 333+33/2018.1, 333+33/2019), 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 fibers, incorporating technical deltamethrin and technical piperonyl butoxide (synergist), together with any necessary other formulants, complying with the requirements of WHO specification 333+33/LN/1 (NETTING) (April 2019). The side of the net shall be formed from multi-filament polyester fibres of 75 or 100 denier with or without a strengthened 70 cm lower border or 150 denier without a strengthened lower border treated with technical deltamethrin, together with any necessary other formulants, complying with the requirements of WHO specification 333/LN/1 (April 2019). 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).

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* This specification is applicable to long-lasting insecticidal nets commercialized under the trade name of PermaNet® 3.0 produced by Vestergaard. The subject 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 the WHO Prequalification Team - Vector control products (PQT-VC) website.

2 **Physical properties** (Note 3)

2.1 **Bursting strength** (ISO 13938:2) (Note 4)

The bursting strength of the fabric in the netting without strengthened border shall be declared (not less than 250 kPa, 350 kPa or 380 kPa, respectively, for fabric made of 75, 100 or 150 denier yarn) and, when determined, the average shall be not less than that declared.

The bursting strength of the fabric in the strengthened 70 cm lower border, shall be declared (not less than 280 kPa or 380 kPa, respectively for fabric made of 75 or 100 denier yarn) and, when determined, the average shall be not less than that declared.

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 selvedges. 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 direct sunlight) 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 2 with conditioning of the fabric as specified in the ISO standard. The declared bursting strength, and testing for compliance with it, should be based on tests of 7.3 cm^2 areas of fabric. Proposed specifications based on tests of 50 cm^2 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^2 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 figure 1. 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.

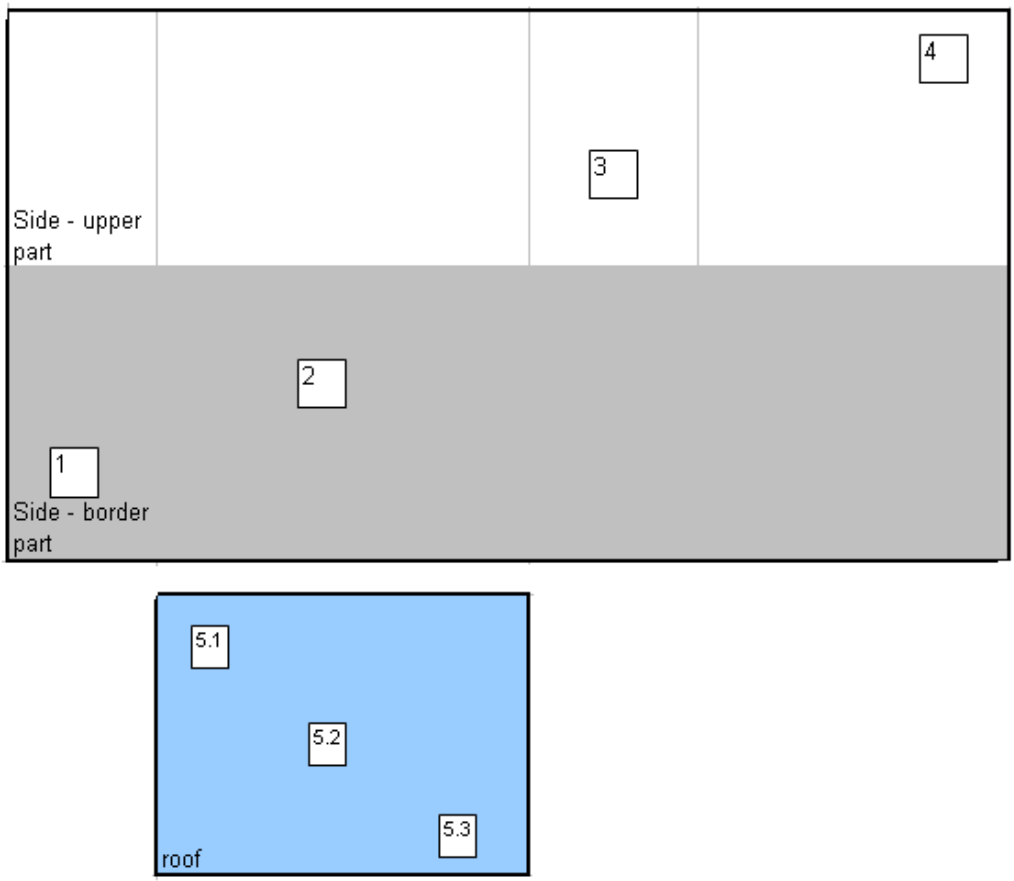
Figure 1 Method for sampling

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

Sampling for PermaNet 3.0 with a strengthened border

For determining deltamethrin content as g/kg in the side netting with a strengthened border, 4 pieces of net with area of 100 cm^2 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/m^2 can be calculated by multiplying the content in g/kg by the corresponding mass of net/m^2.

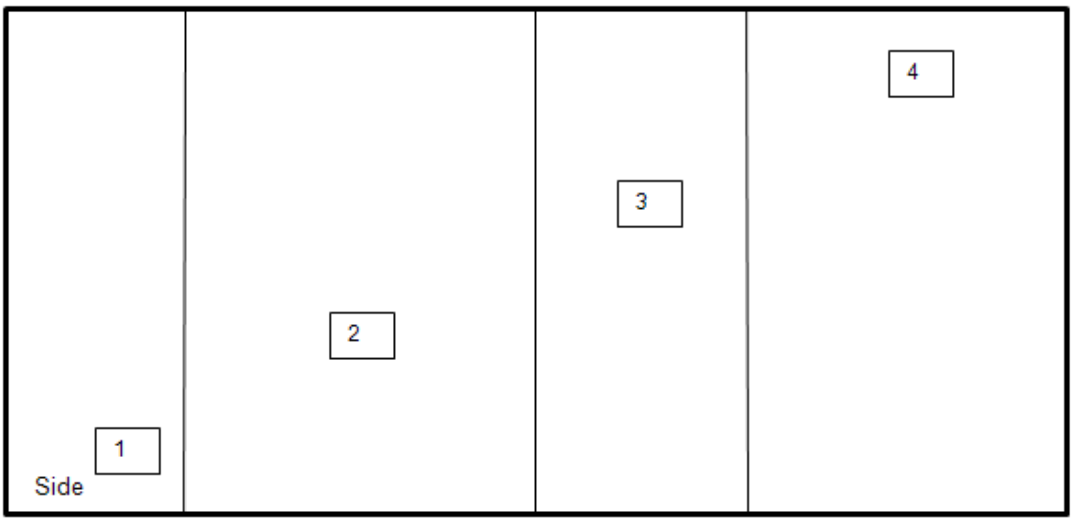
For determining deltamethrin and piperonyl butoxide content in the roof netting, 3 pieces of net with area of 100 cm^2 each are cut from position 5.1-5.3, and further cut into small pieces of less than 1 x 1cm and mixed well before taking the analytical portions.

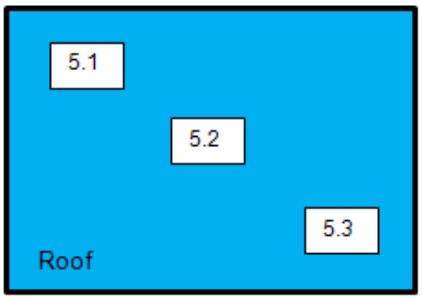


Sampling for PermaNet 3.0 without a strengthened border

For determining deltamethrin content as g/kg in the side netting without a strengthened border, 4 pieces of net with area of 100 cm^2 each minimum are cut from position 1-4. 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 side netting in mg/m^2 can be calculated by multiplying the content in g/kg by the corresponding mass of net/m^2.

For determining deltamethrin and piperonyl butoxide content in the roof netting, 3 pieces of net with area of 100 cm^2 each are cut from position 5.1-5.3, and further cut into small pieces of less than 1 x 1cm and mixed well before taking the analytical portions.





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

WHO specification 333+33/LN/2 (NETTING) (January 2019*)

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+33/2017). 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+33/2017), 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 130 denier (Note 2) knitted mono-filament polyethylene fibres, incorporating technical deltamethrin complying with the requirements of WHO specification 333/TC (November 2017), and technical piperonyl butoxide complying with the requirements of WHO specification 33/TC (September 2018), together with any necessary other formulants (Note 3). The product shall appear clean and shall be free from visible extraneous matter (Note 4), 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 5).

2 Active ingredients

2.1 **Identity tests** (333/LN/(M2)/2, CIPAC Handbook N, p.34, 2012 for deltamethrin and 33/LN/(M)/2, CIPAC Handbook N, p.111, 2012 for piperonyl butoxide) (Note 6)

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

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* This specification is applicable to long-lasting insecticidal nettings and nets produced by Tana Netting Co., Ltd. (NRS International Group) and commercialized under the trade names of DawaPlus 4.0 and DawaPlus 3.0 (roof). The subject 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 the WHO Prequalification Team - Vector control products (PQT-VC) website.

2.2 **Deltamethrin content** (333/LN/(M2)/3, CIPAC Handbook N, p.34, 2012) (Notes 6 & 7)

The deltamethrin content shall be declared (3.0 g/kg) and, when determined, the average content shall not differ from that declared by more than ± 25%.

2.3 **Deltamethrin wash resistance index** (MT 195, CIPAC Handbook O, p.205, 2017) (Note 8)

The wash resistance index of deltamethrin from the netting, when determined, shall be within the range 93% to 100%.

2.4 **Piperonyl butoxide content** (33/LN/(M)/3, CIPAC Handbook N, p.111, 2012) (Note 7)

The piperonyl butoxide content shall be declared (11.0 g/kg) and, when determined, the average content shall not differ from that declared by more than ± 25%.

2.5 **Piperonyl butoxide wash resistance index** (MT 195, CIPAC Handbook O, p.205, 2017) (Note 8)

The wash resistance index of piperonyl butoxide from the netting, when determined, shall be within the range 90% to 100%.

3 **Physical properties** (Note 7 & 14)

3.1 **Fabric weight (mass per m²)** (ISO 3801 / EN 12127)

The mass per unit area shall be declared (40 g/m²), and when determined, shall not differ from that declared by more than ± 10 %.

3.2 **Netting mesh size**

When counted by the method given in Note 9, the average number of complete holes/cm² shall be not less than 17 holes/cm² and the lowest value shall be not less than 16 holes/cm².

3.3 **Dimensional stability of netting to washing** (Note 10)

Not more than 10% shrinkage and not more than 5% expansion in both directions.

3.4 **Bursting strength** (ISO 13938:2) (Note 11)

The 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.

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

3.5 **Flammability** (EN 1102) (Note 12)

Tested according to EN 1102 the following requirements should be achieved*:

After removing the ignition source the following fire phenomena should not occur:
- ignition
- propagation of the flame or glow.
- flaming debris

- ignition of the filter paper

*Fulfilling the requirements above means that the flame speed rate is 0 mm/s, i.e., no flame or glow achieves first and third marker threads.

Formation of holes is allowed provided that the burnt or melted width and length of the holes does not exceed 50 mm and 150 mm, respectively.

4 Storage stability

4.1 **Stability at elevated temperature** (MT 46.3.4, CIPAC Handbook O, p.176, 2017)

After storage at 54 ± 2°C for 2 weeks, the determined active ingredient and synergist content (measured individually) shall not be lower than 95%, relative to the average contents found before storage (Note 13) and the product shall continue to comply with the clauses for:

- wash resistance index (2.3 and 2.5);
- dimensional stability (3.3);
- bursting strength (3.4).

Note 1 The specification applies to netting, in bulk, and to finished bed nets, which may be rectangular or conical in design.

Note 2 The linear density (denier) of the fibres cannot be measured in the manufactured net but it should be identified on the packaging.

Note 3 Two different master batches of polyethylene are used for the mixture net - one with deltamethrin and the other one with piperonyl butoxide. The active ingredient and synergist are incorporated together with the knitting pattern.

Note 4 Occasional short lengths of loose thread present in the netting are not considered to be extraneous matter.

Note 5 Long-lasting insecticidal netting is expected to retain its insecticidal activity during its life span and through a number of washes.

Note 6 For complete identification and good quantification, deltamethrin which is a single pyrethroid stereoisomer consisting of [α*S*,1*R*,3*R*]-isomer (also known as the *S*-isomer) must be separated from the [α*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. These diastereomers may be separated by non-chiral techniques as provided in the CIPAC method for deltamethrin.

Note 7 Samples should be taken according to Figure 1 or 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 selvedges.

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 direct sunlight) 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 content of deltamethrin in the net pieces before and after washing should be determined by the method 333/LN/(M2)/3, CIPAC Handbook N, p.34, 2012. The content of piperonyl butoxide in the net pieces before and after washing should be determined by the method 33/LN/(M)/3, CIPAC Handbook N, p.111, 2012.

Note 9 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. The number of holes per measured area is converted in holes/cm². Before counting, the fabric should be conditioned according to ISO 139 (4 h, 20ºC, 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 (±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 ≥ ½ are counted as complete holes, whereas those < ½ are not counted. Count 5 replicate squares selected according to Note 6, calculate the average and note the lowest value.

Another suitable method is the use of a stereomicroscope with an image analyser software, where the number of holes in a defined area is counted. In case of discrepancy between the mesh count using stereomicroscopic method and direct or indirect counting method, the stereomicroscopic method shall be the referee method.

Note 10 Method of preparation, marking and measuring: ISO 3759. Method of washing: ISO 6330. Method of calculation: ISO 5077. 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: 30ºC Mild programme. Fill the washer with fabrics and ballast Type III (polyester ballast) up to 2 kg (according to the ISO 6330 standard). Drying: flat drying.

Note 11 Test method: ISO 13938 part 2 with conditioning of the fabric as specified in the ISO standard. The declared bursting strength, and testing for compliance with it, should be based on tests of 7.3 cm^2 areas of fabric. 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 figure 1. 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 12 Flammability test according to EN 1102, using the surface ignition method (position the burner perpendicular to the surface of the specimen).

The following shall be reported: the after flame time, the afterglow time, the maximum burnt or damage width and length, whether or not flame reaches vertical edge of the specimen, whether or not a hole is burnt or melted in the specimen, whether or not any flaming debris falls below the bottom edge of the specimen and ignition of the filter paper.
Definitions according to ISO 4880:1997 (not included in EN 1102:1995 and EN ISO 6941: 1995):
- Ignition: initiation of combustion.
- Combustion: exothermic reaction of a combustible substance with an oxidizer, accompanied by flames and/or glowing and/or emission of smoke.

Procedure for measuring burnt or damage width and length dimensions of each specimen:

Remove the specimen from the specimen holder and place it on a flat horizontal surface. Place a rule on top of the test specimen along the line of maximum damage and parallel with the length side of the test specimen. Measure the maximum length in mm from the lowest point of burnt or damage to the end of the hole. To measure the burnt or damage width, proceed in the same way but with the ruler parallel to the width side of the test specimen. Proceed in the same way for the other 5 specimens.

Note 13 Samples of the product taken before and after the storage stability test should be analyzed concurrently after the test in order to reduce the analytical error.

Note 14 Normative references for physical tests:

Currently the following standards are the latest versions of the documents to be used for physical tests. The updated version of the standard should always be used when available.

ISO 139:2005/Amd.1:2011 Textiles - Standard atmospheres for conditioning and testing.- Textiles - Standard atmospheres for conditioning and testing.

ISO 3801:1977 - Textiles - Woven fabrics - Determination of mass per unit length and mass per unit area.

EN 12127:1997 - Textiles - Fabrics - Determination of mass per unit area using small samples.

ISO 3759:2011 - Textiles - Preparation, marking and measuring of fabric specimens and garments in tests for determination of dimensional change.

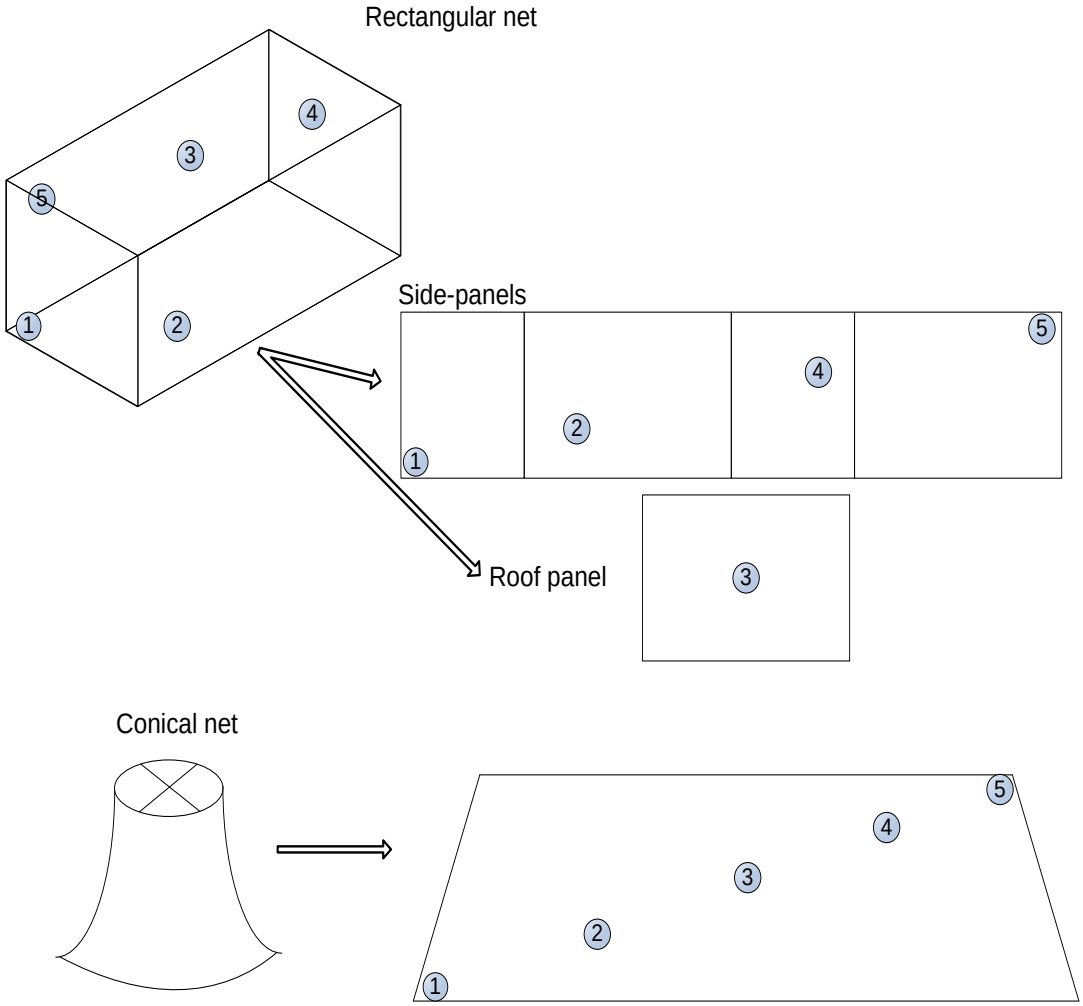
ISO 6330:2012 - Textiles - Domestic washing and drying procedures for textile testing.

ISO 5077:2007 - Textiles - Determination of dimensional change in washing and drying.

ISO 13938-2:1999 - Textiles - Bursting properties of fabrics - Part 2: Pneumatic method for determination of bursting strength and bursting distension

EN 1102:1995 - Textiles and textile products. Burning behaviour. Curtains and drapes. Detailed procedure to determine the flame spread of vertically oriented specimens.

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.



DELTAMETHRIN LONG-LASTING (COATED ONTO FILAMENTS) INSECTICIDAL NET

COMBINED WITH

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

WHO specification 333+33/LN/2 (NET) (January 2019*)

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+33/2017). 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 reports (333+33/2017), 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 130 denier (Note 2) 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/2 (NETTING) (January 2019) (Note 3). The sides of the net shall be formed from multi-filament polyester fibres of 100 denier, treated with formulated deltamethrin complying with the requirements of WHO specification 333/LN/2 (January 2019). The product shall appear clean and shall be free from visible extraneous matter (Note 4), 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 5).

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* This specification is applicable to long-lasting insecticidal nets produced by Tana Netting Co., Ltd. (NRS International Group) and commercialized under the trade name of DawaPlus 3.0. The subject 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 the WHO Prequalification Team - Vector control products (PQT-VC) website.

2 **Physical properties** (Note 6)

2.1 **Bursting strength** (ISO 13938:2) (Note 7)

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.

Note 2 The linear density (denier) of the fibres cannot be measured in the manufactured net but it should be identified on the packaging.

Note 3 Two different master batches of fibre are used for the mixture net - one with deltamethrin and the other one with piperonyl butoxide. The active ingredient and synergist are incorporated together with the knitting pattern.

Note 4 Occasional short lengths of loose thread present in the netting are not considered to be extraneous matter.

Note 5 Long-lasting insecticidal netting is expected to retain its insecticidal activity during its life span and through a number of washes.

Note 6 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 selvedges. 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 direct sunlight) or freezing, and analyzed/tested with minimum delay. Representative portions (sub-samples) for testing should be taken as described in each test method.

Note 7 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.

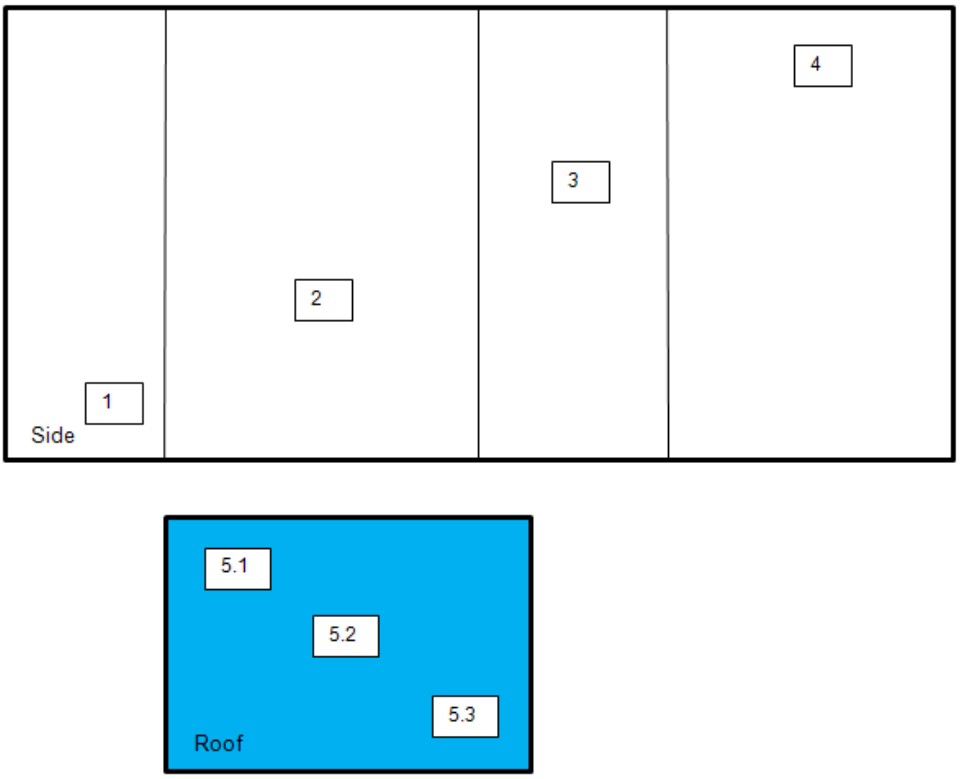
Figure 1 Method for sampling

Recommended positions from which pieces of netting should be taken from a finished bed net and combined to form a representative sample.

Sampling for DawaPlus 3.0

For determining deltamethrin content as g/kg in the side netting, 4 pieces of net with area of 100 cm^2 each minimum are cut from position 1-4. 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 side netting in mg/m^2 can be calculated by multiplying the content in g/kg by the corresponding mass of net/m^2.

For determining deltamethrin and piperonyl butoxide content in the roof netting, 3 pieces of net with area of 100 cm^2 each are cut from position 5.1-5.3, and further cut into small pieces of less than 1 x 1cm and mixed well before taking the analytical portions.



PART TWO

EVALUATION REPORTS

DELTAMETHRIN + PIPERONYL BUTOXIDE

DELTAMETHRIN + PIPERONYL BUTOXIDE

FAO/WHO EVALUATION REPORT 333+33/2019

Recommendations

The Meeting recommended the following:

(i) The existing WHO specification 333/LN/1 for deltamethrin long-lasting (coated onto filaments) insecticidal net should be extended to encompass the 150 denier products of Vestergaard (PermaNet® 2.0 and PermaNet® 3.0 side panels), and revised as proposed by Vestergaard and as amended by the Meeting.

(ii) The existing WHO specifications 333+33/LN/1 (netting and net) for deltamethrin + piperonyl butoxide long-lasting (incorporated into filaments) insecticidal netting and net should be revised as proposed by Vestergaard and as amended by the Meeting.

Appraisal

PermaNet® 2.0 and PermaNet® 3.0 side panels, 150 denier

A draft revised specification and supporting data, provided by Vestergaard, were considered by the Meeting for the extension of the existing WHO specification 333/LN/1 (January 2019) to the 150 denier yarn products (PermaNet® 2.0 and PermaNet® 3.0 side panels).

The nominal deltamethrin content of this 150 denier yarn product is 1.4 g/kg with a fabric weight of 40 g/m². Vestergaard proposed to specify 12.4 holes/cm² as the minimum average number and 10.6 holes/cm² as the minimum lowest value, and 380 kPa as minimum bursting strength. The company also proposed to revise the tolerance for dimensional stability to washing from not more than 5% shrinkage/expansion in both directions to not more than 10% shrinkage and not more than 5% expansion in both directions, to be in line with the tolerance currently recommended in the FAO/WHO Manual on pesticide specifications.

The manufacturer provided the Meeting with quality control data on several samples of PermaNet® 2.0, 150 denier. These data showed that all the samples fully comply with the proposed specification tolerances for deltamethrin content and wash resistance index, fabric weight, netting mesh size, dimensional stability of netting to washing and bursting strength. The deltamethrin content and wash resistance index after storage at 40°C for 8 weeks also complied with the specification tolerances.

PermaNet® 3.0 roof

Draft revised specifications and supporting data, provided by Vestergaard, were considered by the Meeting for the revision of the existing WHO specifications 333+33/LN/1 (netting and net) (January 2019) in order to specify a larger mesh size for the roof of PermaNet® 3.0.

Vestergaard proposed to specify 15.5 holes/cm² as the minimum number of holes/cm² instead of 21 holes/cm² as the minimum average number and 20 holes/cm² as the minimum lowest value in the current specification, and 300 kPa as minimum bursting strength. Consequently, the specification tolerance for fabric weight was changed from 36 g/m² ± 10% to 30 g/m² ± 10%. The company also proposed to revise the tolerance for dimensional stability to washing from not more than 5% shrinkage/expansion in both directions to not more than 10% shrinkage and not more than 5% expansion in both directions to be in line with the tolerance currently recommended in the FAO/WHO Manual on pesticide specifications.

The manufacturer provided the Meeting with quality control data on several samples of PermaNet® 3.0 roof. These data showed that all the samples fully comply with the proposed specification tolerances for deltamethrin and piperonyl butoxide content and wash resistance index, fabric weight, netting mesh size, dimensional stability of netting to washing and bursting strength. The deltamethrin and piperonyl butoxide content, the wash resistance index, the dimensional stability to washing and the bursting strength after storage at 54°C for 2 weeks also complied with the specification tolerances.

ANNEX 1: 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. Third revision of the first edition. FAO, Rome and WHO, Geneva, March 2016 (internet publications).
	Melinda Hadi	2018	Draft revised specification 333/LN/1 for deltamethrin long-lasting (coated onto filaments) insecticidal net submitted to WHO PQT-VC on December 2018.
	Melinda Hadi	2018	Summary of the new proposed specification for PermaNet® 2.0, 150 denier. Document submitted to WHO PQT-VC on December 2018.
SLA000478	Linh Vu	2018	PermaNet® 2.0 - 150 denier. Quality evaluation. Test report SLA000478. ISO 17025. Vestergaard, June 6, 2018.
	Melinda Hadi	2018	Draft revised specifications 333+33/LN (netting and net) for deltamethrin + piperonyl butoxide long-lasting (incorporated into filaments) insecticidal net submitted to WHO PQT-VC on December 2018.
	Melinda Hadi	2018	Summary of the new proposed specification for PermaNet® 3.0, 150 denier for side panels. Document submitted to WHO PQT-VC on December 2018.
SLA000484.1	Linh Vu	2018	PermaNet® 3.0 - Roof 30 GSM. Quality evaluation. Test report SLA000484.1. ISO 17025. Vestergaard, June 6, 2018.
VNVL.18.001	Rebecca Pwalia	2018	WHO tunnel tests on new PermaNet® 3.0 specification. Vestergaard - NMIMR Vector labs and Noguchi Memorial Institute for Medical Research, Ghana. July 30, 2018.

DELTAMETHRIN + PIPERONYL BUTOXIDE

FAO/WHO EVALUATION REPORT 333+33/2018.1

Recommendations

The Meeting recommended the following:

The existing WHO specifications 333/LN/1 for deltamethrin long-lasting (coated onto filaments) insecticidal net and 333+33/LN/1 (netting and net) for deltamethrin + piperonyl butoxide long-lasting (incorporated into filaments) insecticidal netting should be revised as proposed by Vestergaard and as amended by the Meeting.

Appraisal

The Meeting was requested by Vestergaard to revise the WHO specification 333/LN/1 for deltamethrin long-lasting (coated onto filaments) LN in order to include the deltamethrin content in the side panels of PermaNet 3.0. This clause was omitted in the current version of the specification when this specification was revised in October 2015 to withdrawn PermaNet 2.0 Extra. The Meeting agreed with the proposal of the manufacturer to specify 2.8 and 2.1 g/kg with a tolerance of ± 25%, respectively for 75 and 100 denier yarn.

The Meeting requested also Vestergaard to provide, for the WHO specifications 333/LN/1 and 333+33/LN/1 (netting), specification tolerances with supporting data for fabric weight (mass of net per m^2) and flammability, which are currently requested in the third version (March 2016) of the first edition of the FO/WHO Manual on pesticide specifications.

The manufacturer provided the Meeting with quality control data for fabric weight on 871 samples of PermaNet 2.0, 75 denier and 5881 samples of PermaNet 2.0, 100 denier produced in 2015, 2016 and 2017. These data showed that the tolerance of 30 g/m^2 ± 10 % for 75 denier yarn and 40 g/m^2 ± 10 % for 100 denier yarn was slightly exceeded for some net samples. At the request of the Meeting, the manufacturer provided later additional quality control data for fabric weight on 127 samples of PermaNet 2.0, 75 denier and 1337 samples of PermaNet 2.0, 100 denier produced from January to September 2018 showing that all samples comply with the tolerance limit.

The manufacturer proposed a minimum limit of 30 g/m^2 for the roof panel of PermaNet 3.0 and provided quality control data for fabric weight on 436 samples of PermaNet 3.0 (roof panel) produced in 2015, 2016 and 2017. At the request of the Meeting, the manufacturer proposed a tolerance of 36 g/m^2 ± 10 % and provided later additional quality control data for fabric weight on 253 samples of PermaNet 3.0 (roof panel) produced from January to September 2018 showing that all samples comply with the tolerance limit.

The manufacturer provided also the Meeting with a test report on the flammability of one sample of PermaNet 2.0 and one sample of PermaNet 3.0, showing that the nets did not ignite. Nevertheless, the test method used was the CFR Part 1610

which is not recommended anymore by WHO. At the request of the Meeting, the manufacturer provided later additional flammability data according to the test method EN 1102 showing that no fire phenomena occur in PermaNet 2.0 and PermaNet 3.0 (roof panel).

The Meeting also proposed :

- in the description clause of the specifications 333/LN/1, 333/LN/5, 333+33/LN/1 (netting) and 333+33/LN/2 (netting), to refer to the updated specification 333/TC for deltamethrin TC (November 2017).
- in the description clause of the specifications 333/LN/2, to refer to the updated specification 333/SC for deltamethrin SC (November 2017).
- in the specifications 333/LN/1, 333/LN/5 and 333+33/LN/1 (netting) to updated the references to the CIPAC methods MT 195 for wash resistance index and MT 46.3.4 for stability at elevated temperature which are now published in the Handbook O.
- in the specifications 333/LN/1, 333/LN/5, 333+33/LN/1 and 333+33/LN/2 (netting and net) to updated the footnotes for the physical tests according to the third version (March 2016) of the first edition of the FO/WHO Manual on pesticide specifications.

ANNEX 1: REFERENCES

Study number	Author(s)	Year	Study title. Study identification number. Report identification number. GLP [if GLP]. Company conducting the study
	FAO/WHO	2006	Manual on development and use of FAO and WHO specifications for pesticides. March 2006 third revision of the first edition. FAO, Rome and WHO, Geneva, March 2006 (internet publications).
R148. GSM	Linh Vu	2017	Determination of mass per square meter of PermaNet 2.0. Vestergaard Vector Control Laboratories, September 21, 2017.
R177. GSM	Linh Vu	2017	Determination of mass per square meter of PermaNet 3.0. Vestergaard Vector Control Laboratories, September 21, 2017.
R148. GSM	Linh Vu	2018	Determination of mass per square meter of PermaNet 2.0. Vestergaard Vector Control Laboratories, October 08, 2018.
R177. GSM	Linh Vu	2018	Determination of mass per square meter of PermaNet 3.0. Vestergaard Vector Control Laboratories, October 08, 2018.
71911877669-EEC18/01-CSL	Shareen Chan	2018	Flammability testing of PermaNet 2.0 & PermaNet 3.0 side. Test report 7191187669-EEC18/01-CSL of TÜV SÜD PSB Singapore for Vestergaard, June 19, 2018.
71911877669-EEC18/02-CSL	Shareen Chan	2018	Flammability testing of PermaNet 3.0 Roof. Test report 7191187669-EEC18/02-CSL of TÜV SÜD PSB Singapore for Vestergaard, June 19, 2018.
275-24-01-12/ITV-1	Tran Van Doan	2012	Flammability of PermaNet 2.0. Test report 275-24-04-12/TNV-1 of the Textile Research Institute, Vietnam for Vestergaard, May 07, 2012.
274-24-01-12/ITV-2	Tran Van Doan	2012	Flammability of PermaNet 3.0. Test report 274-24-04-12/TNV-2 of the Textile Research Institute, Vietnam for Vestergaard, May 07, 2012.

DELTAMETHRIN + PIPERONYL BUTOXIDE

FAO/WHO EVALUATION REPORT 333+33/2017

Recommendations

The Meeting recommended the following.

The specifications for deltamethrin + piperonyl butoxide long-lasting (incorporated into filaments) insecticidal netting and for deltamethrin (coated onto filament) insecticidal net combined with deltamethrin + piperonyl butoxide long-lasting (incorporated into filaments) insecticidal netting, proposed by Tana Netting Co. Ltd. (NRS International Group), and as amended, should be adopted by WHO.

Appraisal

Draft specifications and supporting data, provided by Tana Netting Co. Ltd. (NRS International Group), were considered by the Meeting for development of new WHO specifications for :

- deltamethrin + piperonyl butoxide long-lasting (incorporated into filaments) insecticidal netting (DawaPlus 4.0).
- deltamethrin (coated onto filament) insecticidal net combined with deltamethrin + piperonyl butoxide long-lasting (incorporated filaments) insecticidal netting (DawaPlus 3.0).

The data and test reports provided by the manufacturer to support these specifications were generated by independent laboratories. The proposed specifications were in agreement with the LN specification guideline of the FAO/WHO Manual on pesticides specifications (FAO/WHO 2016).

The manufacturer confirmed that the active ingredient (deltamethrin) and the synergist (piperonyl butoxide) incorporated into the LNs are from sources compliant with the existing WHO specification 333/TC (January 2015) for deltamethrin TC (Bayer) and the existing WHO specification 33/TC (September 2011) for piperonyl butoxide TC (Endura) respectively.

DawaPlus 3.0 and DawaPlus 4.0 produced by Tana Netting were tested and evaluated by WHOPES and a time-limited interim recommendation for their use in malaria prevention and control was issued in 2017 (WHO 2017).

Description

The DawaPlus 4.0 is a knitted fabric in which technical deltamethrin and technical piperonyl butoxide (as synergist) are incorporated into mono-filament polyethylene fibres of 130 denier at the target dose of 3 g deltamethrin and 11 g piperonyl butoxide per kg of netting material. The Meeting was informed by the manufacturer that two different master batches of polyethylene are used for the mixture net - one with deltamethrin and the other one with piperonyl butoxide. The active ingredient and synergist are incorporated together with the knitting pattern. The Meeting and the manufacturer agreed to reflect this information in a footnote of the specification.

The roof of DawaPlus 3.0 contains the same netting material as DawaPlus 4.0, but the side panels consist of 100 denier multi-filament polyester fibres coated with deltamethrin at the target dose of 2.5 g/kg of netting material. The manufacturer and the Meeting agreed to develop a specification for the mixture LN (DawaPlus 4.0 and roof of DawaPlus 3.0) and to refer to the specification 333/LN/2 (deltamethrin coated onto filaments LN) for the side panels of DawaPlus 3.0. They also agreed to develop a short specification for the final combination net (DawaPlus 3.0) referring to the individual nettings which is produced from, and including some selected physical properties like bursting strength of the seams which belong to the final product and not the net parts.

Active ingredient and synergist content

The nominal content of deltamethrin and piperonyl butoxide of DawaPlus 4.0 and DawaPlus 3.0 roof is 3.0 and 11.0 g/kg respectively with a tolerance of ± 25%.

Data provided by the manufacturer on one batch of DawaPlus 4.0 showed that the product complies with the specification limits of 3.0 g/kg ± 25% for deltamethrin and 11.0 g/kg ± 25% for piperonyl butoxide A spatial variation study provided by the manufacturer on one sample of DawaPlus 4.0 (deltamethrin and piperonyl butoxide content on 5 individual net pieces taken from each side and roof of the net) showed an acceptable homogeneity of the distribution of the active ingredient and synergist within the net (within-net RSD of 5.3% and 2.3% respectively).

The WHOPES Phase I testing and evaluation of DawaPlus 4.0 showed that deltamethrin and piperonyl butoxide content in unwashed nets complies with the target dose of 3.0 g/kg (± 25%) and 11.0 g/kg (± 25%) respectively, and an acceptable homogeneity of the active ingredient and synergist distribution within and between the nets. The within-net variation, expressed as the relative standard deviation (RSD) of the deltamethrin and piperonyl butoxide content found on the 5 pieces taken from each side and roof of the same net ranged from 0.8% to 1.9% for deltamethrin and from 3.4% to 8.6% for piperonyl butoxide. The between-net variation, expressed as the relative standard deviation (RSD) of the deltamethrin and piperonyl butoxide content found on 4 different nets, is 0.9% for deltamethrin and 1.8% for piperonyl butoxide (CRA-W 2017, WHO 2017).

The WHOPES Phase II trials conducted in India, Burkina Faso and Tanzania showed that the deltamethrin and piperonyl butoxide content in all unwashed nets of DawaPlus 4.0 complies with the target dose of 3.0 g/kg (± 25%) and 11.0 g/kg (± 25%) respectively and an acceptable within-net homogeneity. Nevertheless, the nets of DawaPlus 3.0 roof from India and Tanzania were slightly underdosed. The within-net variation, expressed as the relative standard deviation (RSD) of the deltamethrin and piperonyl butoxide content found on 5 different net pieces cut from each DawaPlus 4.0 net ranged from 0.8% to 5.8% and from 3% to 13% respectively (CRA-W 2017, WHO 2017).

In the study provided by the manufacturer and in the WHOPES studies, the deltamethrin content was determined using a method comparable to the CIPAC method 333/LN/(M2)/3 published in Handbook N. This method involves extraction of deltamethrin by refluxing with xylene in presence of dicyclohexyl phthalate as internal standard, solvent exchange to the mobile phase and determination by high performance liquid chromatography with UV diode array detection (HPLC-DAD). The piperonyl butoxide content was determined using a method comparable to the

CIPAC method 33/LN/(M)/3 published in Handbook N. This method involves extraction of piperonyl butoxide by refluxing with xylene in presence of octadecane as internal standard and determination by high performance liquid chromatography with UV diode array detection (HPLC-DAD).

Active ingredient and synergist wash resistance index

An adequate amount of the active ingredient and synergist must be present at the surface of the LN, for efficacy reasons, 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. Depletion of total active ingredient and synergist content by washing (wash resistance index) is accomplished by analyzing separate washed and unwashed pieces of the same fabric.

Where the active ingredient and synergist are incorporated into filaments, rapid loss of molecules is not likely to occur during washing but, if re-equilibration to the surface is too slow, the product may be ineffective for an unacceptable period of time after washing. Alternatively, if the re-equilibration is too rapid, the surface concentration could become higher than expected, leading to higher losses of active ingredient and synergist during washing and possibly increased user exposure to the active ingredient.

A net like DawaPlus 4.0 containing an active ingredient and a synergist poses additional complexity in matching the wash resistances of the two molecules in order to maintain the ratio of the active ingredient and the synergist in a similar range.

The manufacturer provided data on two batches of DawaPlus 4.0 unwashed and washed 4 times according to the CIPAC method MT 195. The wash resistance index ranged from 98.8% to 100.4% for deltamethrin and from 96.2% to 98.2% for piperonyl butoxide.

The WHOPES Phase I testing results on deltamethrin and piperonyl butoxide content and associated biological efficacy of DawaPlus 4.0 washed up to 25 times (according to the WHO washing procedure) showed an exponential decay of the deltamethrin and piperonyl butoxide content in function of the number of washes (free-migration stage behaviour). The overall deltamethrin and piperonyl butoxide retention after 20 washes was 95.8% and 77.0% respectively, corresponding to an average retention index per wash of 99.8% and 99.0% respectively, as estimated by the exponential regression curve (CRA-W 2017, WHO 2017).

The manufacturer initially proposed to specify a range of 90% to 100% for both deltamethrin and piperonyl butoxide. The Meeting proposed to the company to specify a higher wash resistance index for deltamethrin compared to piperonyl butoxide to better reflect the release properties of the active ingredient and the synergist. The manufacturer finally proposed 93% to 100% for deltamethrin and 90% to 100% for piperonyl butoxide, and it was agreed by the Meeting. The manufacturer informed nevertheless the Meeting that the 1-day wash interval used for deltamethrin in the WHOPES phase I study supports a minimum criterion for the wash resistance index for quality control purposes while ensuring an acceptable bioefficacy, but it does not allow to really measure the absolute wash resistance index which should be based on a complete regeneration of the active ingredient.

Relevant impurities

There are no relevant impurities identified in the existing WHO specification for deltamethrin TC. During the manufacturing process, storage and use of deltamethrin LN, heat and base-catalyzed epimerization of deltamethrin to the (insecticidally inactive) *R*-alpha isomer may occur. This conversion must be kept at a minimum by the manufacturer to avoid significant losses of active ingredient. Data provided by the manufacturer as well as WHOPES Phase I testing and evaluation of DawaPlus 4.0 showed that the content of deltamethrin *R*-alpha isomer in DawaPlus 4.0 is lower than 5% of the deltamethrin content and that this amount does not increase in the LN washed up to 25 times (CRA-W 2017, WHOPES 2017).

The impurity dihydrosafrole (DHS) which is specified as a relevant impurity in the WHO specification 33/TC for piperonyl butoxide TC at a maximum limit of 0.1 g/kg becomes a non relevant impurity in the net formulation containing a quite low synergist content (11 g/kg). Even assuming 100% dermal absorption for DHS, the cumulative life-time exposure for DawaPlus 4.0 is predicted (WHO 2012) to remain below 2×10^{-5} mg/kg bw, and the cumulative cancer risk as extrapolated from the TD_{50} (Gold *et al* 1984) is lower than 0.5×10^{-8}. The value is even lower, probably 1/10 of this, for DawaPlus 3.0 as PBO is only present in the roof part.

Physical properties

Data provided by the manufacturer on DawaPlus 4.0 showed:

- a fabric weight (mass per unit area) in agreement with the specified limit of 40 g/m² ± 10 %.
- an average and minimum number of complete holes/cm² in agreement with the specified minimum limit of 17 and 16 respectively.
- a dimensional stability to washing in agreement with the specified limit of not more than 10% shrinkage and not more than 5% expansion in both directions.
- a bursting strength (net and seams) higher than the minimum specified limit of 400 kPa.
- that no fire phenomena occurred and therefore that the product complies with the tolerance for flammability.

Storage stability

The manufacturer provided data showing that after storage at 54°C for 2 weeks, the average deltamethrin and piperonyl butoxide content (measured individually) are higher than 95% of the average content found before storage, and that the net still complies with the limits set for wash resistance index, dimensional stability to washing and bursting strength.

ANNEX 1: REFERENCES

Study number	Author(s)	Year	Study title. Study identification number. Report identification number. GLP [if GLP]. Company conducting the study
6200/2016-1	CITEVE	2016	Physical properties of DawaPlus 3.0 side panels and DawaPlus 4.0. Report 6200/2016-1 of CITEVE, Portugal for Tana Neting, June 24, 2016.
7648/2016-1	CITEVE	2016	Flammability of DawaPlus 3.0 side panels and DawaPlus 4.0. Report 7648/2016-1 of CITEVE, Portugal for Tana Neting, July 28, 2016.
RE/16/U10/ 24305	CRA-W	2017	Physical-chemical properties of DawPlus 4.0. Report RE/16/U10/243052 of the Walloon Agricultural Research Centre, Gembloux, Belgium for Tana Netting, January 13, 2017.
RE/16/U10/ 24353	CRA-W	2017	WHOPES Phase I testing and evaluation of DawaPlus 3.0 and DawaPlus 4.0. Chemical analysis of nets. Test report RE/16/U10/24353 of the Walloon Agricultural Research Centre, Gembloux, Belgium for WHO, February 03, 2017.
RE/17/U10/ 24417/1	CRA-W	2017	WHOPES Phase II testing and evaluation of DawaPlus 3.0 and DawaPlus 4.0 in India. Chemical analysis of nets. Test report RE/17/U10/24417/1 of the Walloon Agricultural Research Centre, Gembloux, Belgium for WHO, March 15, 2017.
RE/17/U10/ 24417/2	CRA-W	2017	WHOPES Phase II testing and evaluation of DawaPlus 3.0 and DawaPlus 4.0 in Burkina Faso. Chemical analysis of nets. Test report RE/17/U10/24417/2 of the Walloon Agricultural Research Centre, Gembloux, Belgium for WHO, March 15, 2017.
RE/17/U10/ 24484	CRA-W	2017	WHOPES Phase II testing and evaluation of DawaPlus 3.0 and DawaPlus 4.0 in Tanzania. Chemical analysis of nets. Test report RE/17/U10/24417/2 of the Walloon Agricultural Research Centre, Gembloux, Belgium for WHO, July 26, 2017.
	Milan Ivic	2017	Draft specification and supporting data for DawaPlus 3.0 and DawaPlus 4.0. JMPS data package. Tana Netting, February 17, 2017.
2016-10CH/VVL	VEGRO	2016	Wash resistance index of DawaPlus 4.0. Report 2016-10CH/VVL of VEGRO, Denmark for Tana Netting, June 28, 2016.
	WHO	2012	A generic risk assessment model for insecticide-treated nets, revised edition. Ref: ISBN 978 92 4 150341 9 and WHO/HTM/NTD/WHOPES/2012.3. Available at : http://apps.who.int/iris/bitstream/10665/44862/1/9789241503419_eng.pdf
	WHO	2017	Report of the 20th WHOPES Working Group Meeting, WHO/HQ, Geneva, 20-24 March 2017. Available at : http://apps.who.int/iris/bitstream/10665/258921/1/WHO-HTM-NTD-WHOPES-2017.04-eng.pdf

DELTAMETHRIN + PIPERONIL BUTOXIDE

FAO/WHO EVALUATION REPORT 333+33/2015

Recommendations

The Meeting recommended the following.

(i) The existing WHO interim specifications 333+33/LN (NETTING) for deltamethrin + piperonyl butoxide long-lasting (incorporated into filaments) insecticidal netting and the existing WHO interim specification 333+33/LN (NET) for deltamethrin long-lasting (coated onto filaments) insecticidal net combined with deltamethrin + piperonyl butoxide long-lasting (incorporated into filaments) insecticidal net should be revised as proposed by Vestergaard and as amended by the Meeting.

(ii) The revised specifications should get the status of full WHO specifications.

(iii) The existing WHO specification for deltamethrin long-lasting (coated onto filaments) insecticidal net with a strengthened border (PermaNet 2.0 Extra) should be withdrawn, as proposed by Vestergaard. Consequently the existing WHO specification 333/LN/1 (NET) should be withdrawn and the existing WHO specification 333/LN/1 (NETTING) should be revised as proposed by the Meeting.

Appraisal

Wash resistance index

The method MT 195 for determination of wash resistance index of LN was adopted as full CIPAC MT method in 2013. 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, WHO, Geneva, 2005 (WHO 2005). Briefly, the wash resistance index is determined by analyzing net samples in triplicate representing wash points 0 and 4 for total active ingredient content and calculating the average wash resistance index per wash using the equation for free migration stage behaviour. A wash resistance index per wash of 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 wash resistance index applies to the average obtained from triplicate tests performed on individual net pieces collected from the same net or batch of netting (CIPAC 2012 and 2013).

The Meeting requested Vestergaard, producing deltamethrin long-lasting (coated onto filaments) insecticidal net combined with deltamethrin + piperonyl butoxide long-lasting (incorporated into filaments) insecticidal net (PermaNet 3.0), to generate wash resistance index data using the new CIPAC washing method MT 195 and to propose a revised wash resistance index range based on these data.

The manufacturer provided the Meeting with quality control data (55 PermaNet 3.0 nets manufactured from 2012 to 2014) on the wash resistance index of deltamethrin and piperonyl butoxide in the polyethylene roof using the CIPAC method MT 195.

The wash resistance index ranged from 92% to 99% with a mean of 96% for deltamethrin and from 88% to 95% with a mean of 91% for piperonyl butoxide. Based on the mean and standard deviation of the results obtained from this study and considering the potential inter-laboratory variation in the measurement of the wash resistance index, the manufacturer proposed to specify a range of 88% to 100% for deltamethrin and a range of 81% to 100% for piperonyl butoxide. The data generated by another laboratory on 3 samples of PermaNet 3.0 confirmed that the ranges proposed for deltamethrin and piperonyl butoxide wash resistance index are acceptable (98.7% to 99.4% and 84.7% to 88.2% respectively) (CRA-W 2013). The Meeting agreed therefore with this proposal.

The manufacturer provided also wash resistance index data for the side of PermaNet 3.0 (75 denier with strengthened border and 100 denier without strengthened border) and proposed to specify a wash resistance index range of 85% to 100%. Nevertheless, the specification 333/LN/1 (netting) was already revised in 2012 to specify a range of 80% to 98% according to the new CIPAC washing method, as proposed by Vestergaard (FAO/WHO evaluation report 333/2012.3). Vestergaard finally confirmed that a wash resistance index of 80% to 98% should be specified.

The manufacturer informed the Meeting that PermaNet 2.5 or PermaNet 2.0 Extra is no longer produced and should be removed from the WHO specifications. The Meeting agreed therefore to withdrawn the existing WHO specification 333/LN/1 (NET) and to revise the existing WHO specification 333/LN/1 (NETTING).

The Meeting considered also data and information submitted by Vestergaard to support their request to revise the WHO interim specification 333+33/LN (NET) (November 2012) for deltamethrin long-lasting (coated onto filaments) insecticidal net combined with deltamethrin + piperonyl butoxide long-lasting (incorporated into filaments) insecticidal net (PermaNet 3.0) for the following parameters.

100 denier sides with strengthened border

The manufacturer requested the Meeting to include in the specifications the option of 100 denier sides with strengthened border in order to improve the strength of the most vulnerable part of the net. The manufacturer provided quality control data on several samples of PermaNet 3.0, 100 denier side with strengthened border, including chemical properties (deltamethrin content and wash resistance index before and after accelerated storage at 40°C for 8 weeks) and physical properties (netting mesh size, bursting strength, dimensional stability to washing). These data showed that the new optional product fully comply with the clauses of the existing specifications. The data generated by another laboratory on 5 samples of PermaNet 3.0, 100 denier side with strengthened border, confirmed that the new optional product fully comply with the specification for deltamethrin content and wash resistance index (CRA-W 2015).

Bursting strength

The manufacturer requested the Meeting to reduce the limit for bursting strength in the border of 75 denier sides of PermaNet 3.0 to “not lower than 280 kPa” instead of “not lower than 320 kPa”. The company stated that the original limit proposed in the specification was based on a too small data set that did not reveal the wider variation in production. The manufacturer provided the Meeting with quality control data on 415 samples of PermaNet 3.0, 75 denier side with strengthened border manufactured from 2011 to 2014 to support this change. He provided also data from

inter-laboratory studies between different quality control laboratories that fully supported the proposed reduction of the bursting strength limit for the PermaNet 3.0, 75 denier side with strengthened border.

Vestergaard confirmed also a bursting strength of minimum 380 kPa for PermaNet 3.0 side of 100 denier with strengthened border and 350 kPa for PermaNet 3.0 side of 100 denier without border.

Supplementary information to the Note for accelerated storage stability

The manufacturer requested the Meeting to clarify the note on the storage stability test in order to further clarify on how this test should be conducted in order to minimise the impact of sample heterogeneity on the repeatability of the test.

He proposed to add the following sentence : “Samples of the formulation shall be well homogenized by cutting the sub-sampling patches into small pieces of less than 1 x 1cm each; mixing well, taking 2 equivalent portions, one for before storage stability, the other for being stored in the chosen condition as per CIPAC MT 46.3.4”. The Meeting did not accept this deviation to the newly adopted CIPAC method MT 46.3.4 (requiring 5 net pieces of 25 cm x 25 cm in a glass bottle to be exposed to the standard combination of temperature and time) because it is unlikely that the method would not be applicable for their products.

The Meeting agreed also:

- to update into the specification 333+33/LN (NETTING) the methods for deltamethrin and piperonyl butoxide identity and content as well as some footnotes of the specification to be in line with the current CIPAC methods.
- to refer only to the standard pneumatic method (EN ISO 13938-2) for bursting strength, as recommended in the report of the WHO consultation of August 2014 on fabric strength of LNs.
- to refer to the method MT 46.3.4 adopted as full CIPAC MT method in 2015 for accelerated storage procedure.

ANNEX 1: REFERENCES

Study number	Author(s)	Year	Study title. Study identification number. Report identification number. GLP [if GLP]. Company conducting the study
	CIPAC	2012	MT 19X. Wash resistance index of LN, CIPAC method 4827/m.
	CIPAC	2012	MT 19X. Wash resistance index of LN, small scale collaborative trial, CIPAC report 4828/R.
	CIPAC	2013	MT 195. Wash resistance index of LN, available at http://www.cipac.org/cipacpub.htm
4909/R	CIPAC	2013	Wash resistance index of LN - Validation of the new CIPAC Washing Method, CIPAC report 4909/R.
RE/13/U10/ 23187	CRA-W	2013	Deltamethrin and piperonyl butoxide wash resistance index of PermaNet 3.0 (roof). Report RE/13/U10/23187 of the Walloon Agricultural Research Centre, Gembloux, Belgium for Vestergaard Frandsen, July 01, 2013.
RE/15/U10/ 23898	CRA-W	2015	Deltamethrin content and wash resistance index of PermaNet 3.0 side, 100 denier border. Report RE/15/U10/23898 of the Walloon Agricultural Research Centre, Gembloux, Belgium for Vestergaard, May 13, 2015.
L-14-083	Le Nam & Phan Chi	2014	Determination of wash resistance index in PermaNet 3.0. Vestergaard, May 16, 2014.
SLA000131	Duong Thom & Phan Chi	2014	Bursting strenght of PermaNet 3.0 - 75D with strengthened border. Vestergaard, December 05, 2014.
SLA000161	Le Nam & Phan Chi	2015	Quality characteristics of PermaNet® 3.0 by Vestergaard, 100 denier with strengthened border - side panel, deltamethrin coated polyester netting. Vestergaard, January 14, 2015.
P3-SP-58.1	Pates Helen	2015	Product specification – PermaNet® 3.0 by Vestergaard side 100D with strengthened border. June 05, 2015.
	WHO	2015	Determination of fabric strength of long-lasting insecticidal nets. Report of a WHO consultation, Geneva, 20-22 August 2014. WHO, Geneva, document WHO/HTM/NTD/WHOPES/2015.1.

DELTAMETHRIN + PIPERONIL BUTOXIDE

FAO/WHO EVALUATION REPORT 333+33/2012

Recommendations

The Meeting recommended the following.

(i) The existing WHO interim specifications 333+33/LN (NETTING and NET) for deltamethrin + piperonyl butoxide long-lasting (incorporated into filaments) and deltamethrin long-lasting (coated onto filaments) insecticidal net combined with deltamethrin + piperonyl butoxide long-lasting (incorporated into filaments) insecticidal net should be revised as proposed by Vestergaard Frandsen and as amended by the Meeting.

(ii) The existing WHO interim specifications 333/LN/1 (NETTING and NET) for deltamethrin long-lasting (coated onto filaments) insecticidal netting and net should also be revised as proposed by the Meeting.

Appraisal

The Meeting considered data and information submitted by Vestergaard Frandsen to support the revision of the WHO interim specification 333+33/LN (NET) for deltamethrin long-lasting (coated onto filaments) insecticidal net combined with deltamethrin + piperonyl butoxide long-lasting (incorporated into filaments) insecticidal net regarding the description clause.

The company required the Meeting to change the description clause of the WHO interim specification 333+33/LN (NET) (PermaNet 3.0) in relation to the side netting to include the phrase 75 denier with a strengthened 70 cm border or 100 denier without a strengthened 70 cm border, in order to enable countries to choose between both options and to allow countries to maintain their requirement of minimum 100 denier.

The Meeting expressed their concern to the company regarding the bursting strength which is related to the durability of the net. The company provided the Meeting with a test report from an accredited laboratory comparing the bursting strength, the tensile strength and the tear strength of the 75 denier border and the 100 denier nettings. This report concluded that the 100 denier netting without the strengthened border shows equal or higher mechanical strength properties than the 75 denier with the strengthened border. The company provided also the Meeting with adapted sampling methods and figures.

The Meeting agreed that it was also necessary to revise the description and bursting strength clauses of the WHO interim specification 333/LN/1 (NET) (PermaNet 2.0, PermaNet 2.0 Extra and Yorkool LN) to ensure consistency with the request. The Meeting agreed also to include in the WHO interim specifications 333/LN/1 (NET) for the finished net the relevant sampling method and figure.

The Meeting discussed also the impurity dihydrosafrole (DHS) which is specified as a relevant impurity in the new WHO specification 33/TC for piperonyl butoxide TC

(September 2011) at a maximum limit of 0.1 g/kg. Assuming that a TC complying with the WHO specification is used, the net complies with the WHO specification, and that contact with the roof (treated with PBO) of the net is the 1/10 of that with the walls (not treated with PBO), the life-time average daily exposure to DHS of people using the net can be estimated not to exceed 1.1×10^{-10} g/kg/d (WHO 2012) and the cumulative cancer incidence from exposure to DHS is 1.3×10^{-9} (Gold et al 1984). The Meeting thus concluded that dihydrosafrole is not a relevant impurity in this formulation.

The Meeting proposed also to adapt the footnotes of the actual specification for flammability, net sampling, wash resistance index, netting mesh size, dimensional stability to washing and bursting strength according to the recommendations of the draft LN guideline of the FAO/WHO Manual (November 2010 – second revision of the first edition).

ANNEX 1: REFERENCES

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. Second revision of the 1st edition. FAO, Rome and WHO, Geneva, November 2010 (internet publications).
	Gold LS *et al.*	1984	A carcinogenic potency database of the standardized results of animal bioassays. Environ Health Perspect 58: 9-319. Available at: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1569423/?tool=pubmed
	Pates Jamet H.	2011	Request to revise the specification 333+33/LN (NET) for PermaNet 3.0. Vestergaard Frandsen, 1 November 2011.
	Käse S. & Tausif M.	2011	Accredited Testing of PermaNet structures. Report of NIRI for Vestergaard Frandsen, October 10, 2011.
	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	2012	A generic risk assessment model for insecticide-treated nets. Revised edition. Available at:http://whqlibdoc.who.int/publications/2012/9789241503419_eng.pdf

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 ± 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 (± 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) αR-isomer may occur. This conversion must be controlled by the manufacturer to avoid losses of active ingredient. WHOPES data showed that deltamethrin αR-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 αR-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 αR-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 54ºC 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 1st 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 *et al.*	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 *et al.*	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.