

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

ALPHA-CYPERMETHRIN

**LONG-LASTING (COATED ONTO FILAMENTS)
INSECTICIDAL NET**

A racemic mixture of:

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



**World Health
Organization**

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Disclaimer¹

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

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

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

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

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

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

¹ This disclaimer applies to all specifications published by WHO.

INTRODUCTION

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

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

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

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

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

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

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

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

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SPECIFICATIONS

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WHO SPECIFICATIONS FOR PUBLIC HEALTH PESTICIDES

ALPHA-CYPERMETHRIN

INFORMATION

Common name

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

Synonyms

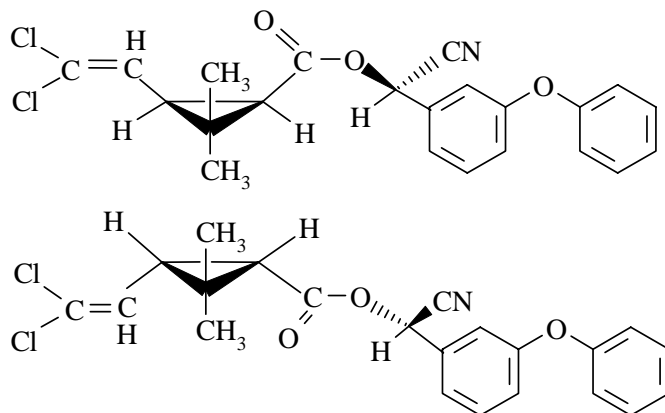
alphamethrin (rejected common name), alfoxylate

Chemical names

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

CA: [1 α (*S*^{*}), 3 α]-(\pm)-cyano(3-phenoxyphenyl)methyl 3-(2,2-dichloroethenyl)-2,2-dimethylcyclopropanecarboxylate

Structural formula



Empirical formula

$C_{22}H_{19}Cl_2NO_3$

Relative molecular mass

416.3

CAS Registry number

67375-30-8

CIPAC number

454

Identity tests

GC retention time, IR spectrum.

WHO SPECIFICATIONS FOR PUBLIC HEALTH PESTICIDES

ALPHA-CYPERMETHRIN LONG-LASTING (COATED ONTO FILAMENTS) INSECTICIDAL NET

WHO interim specification 454/LN/1 (October 2009*)

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 (454/2009.1). It should be applicable to relevant products of this manufacturer but it is not an endorsement of those products, nor a guarantee that they comply with the specification. The specification may not be appropriate for the products of other manufacturers, irrespective of the source of TC. The evaluation report (454/2009.1), 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 75 or 100 denier multi-filament (minimum 32 filaments) polyester fibres, treated with a formulation containing technical alpha-cypermethrin complying with the requirements of WHO specification 454/SC (April 2006), and a polymeric binder together with any necessary additives. 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). It shall be suitable for use as an insecticidal net with long-lasting activity (Notes 3 & 4).

2 Active ingredient

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

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

2.2 Alpha-cypermethrin content (454/LN/M/3.1, CIPAC Handbook M, p.40, 2009) (Notes 5 & 6)

The alpha-cypermethrin content shall be declared (6.7 g/kg for the 75 denier yarn and 5.0 g/kg for the 100 denier yarn) and, when determined, the average measured content shall not differ from that declared by more than $\pm 25\%$.

2.3 Alpha-cypermethrin retention index (Note 7)

The retention index of alpha-cypermethrin from the netting, when determined, shall be within the range 0.90 to 0.98.

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

3 Physical properties

3.1 Netting mesh size

When counted by the method given in Note 8, the netting shall have a minimum of 24 complete holes/cm².

3.2 Dimensional stability of netting to washing (Note 9)

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

3.3 Bursting strength (Note 10)

The minimum bursting strength of the fabric shall be declared (not less than 250 kPa for 75 denier fabric, not less than 405 kPa for 100 denier fabric) and, when determined, the average shall be not less than that declared.

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

4 Storage stability

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

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

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

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

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

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

Note 4 Flammability of the product is not part of the specification but it should be measured by the manufacturer, according to 16CFR Part 1610, and the result presented on the package.

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

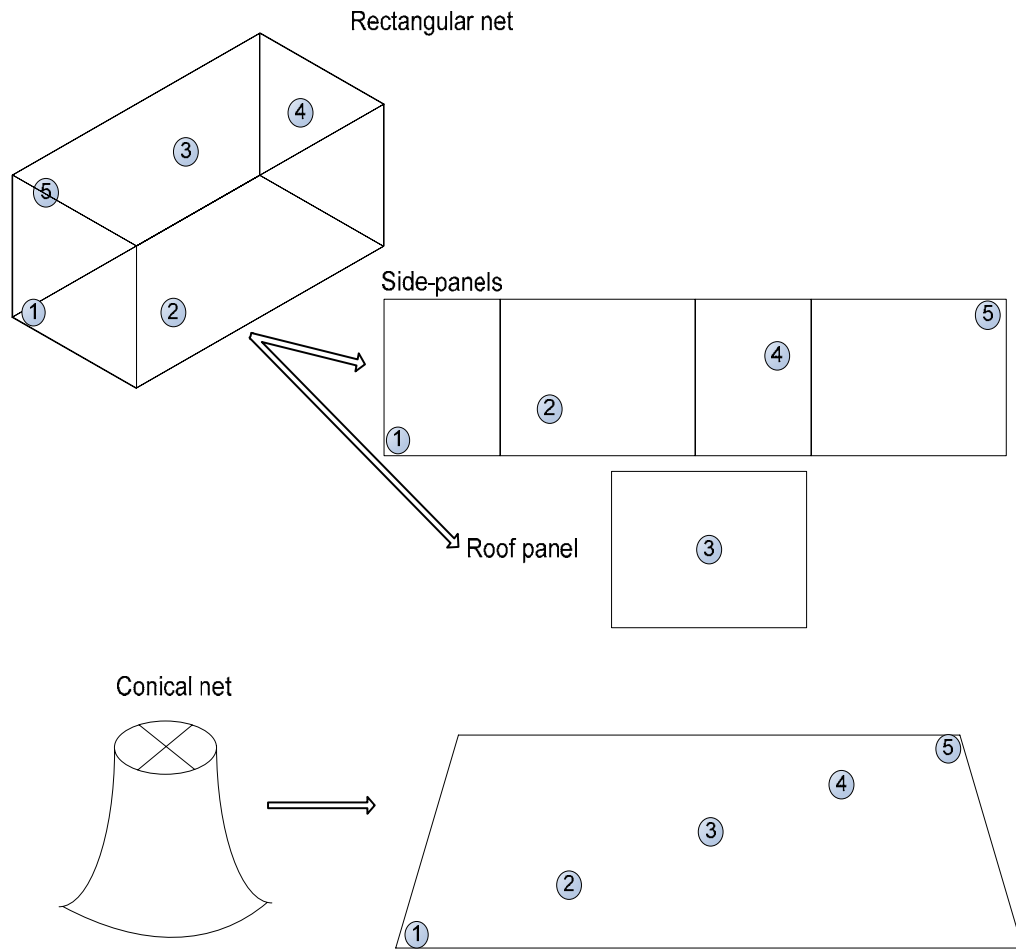
Use sharp scissors, or equivalent, to minimize damage to the fibres and fabric and thus avoid any consequential bias in the results of certain tests. Roll up the strips or squares and place them in labelled, new, clean aluminium foil prior to analysis. Samples should be kept cool, avoiding heat sources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

Test portion and replication requirements for physical test methods are defined in the methods or Notes referenced but, for determination of active ingredient content and retention index, each sample to be tested/analyzed should be comprised of 25 x 25 cm pieces.

- Note 6 The target content of alpha-cypermethrin of 6.7 and 5.0 g/kg for the 75 and 100 denier yarn netting or net, respectively, corresponds to 200 mg/m² in both cases with a tolerance of ± 50 mg/m². This value can be calculated from values for active ingredient content in g/kg and mass of net/m². Mass of net/m² should be determined according to ISO 3801 (1977). In cases of dispute, g/kg values shall be used.
- Note 7 Currently, CIPAC is developing a wash method for determination of the retention behaviour of long-lasting insecticidal mosquito nets. A draft method for determination of alpha-cypermethrin retention index is available through the CIPAC website, <http://www.cipac.org>. Washing should be conducted according to the method given 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 2 and 3 for total alpha-cypermethrin content and calculating the amount of insecticide remaining after the additional wash step by expressing the result as a fraction of the amount being present before. A retention index of 0.95 indicates that at least 95 % of the insecticide present in samples washed 2 times is still present after an additional wash step. The retention index applies to the average obtained from triplicate tests performed on samples removed from the same net or batch of netting.
- Note 8 In the absence of a simple or standard method to determine the size of holes, which may have complex shapes, in highly flexible fabrics, mesh size is determined by counting the number of holes in a square of the fabric. Counting may be done directly on the fabric or indirectly by scanning/photocopying the fabric. Indirect methods may ease counting and provide a permanent record. Before counting, the fabric should be conditioned according to ISO 139 (1973) (4 h, 20°C, 65% relative humidity).
- Use a template to define the square of netting, taking care not to stretch or distort the fabric. The template should be a rigid sheet, 1-2 mm thick, in/on which a calibrated (±1% in each dimension) square (e.g. 1 x 1 in or 2 x 2 cm) has been accurately cut/marked. If a template is not available and a ruler must be used, great care is required to ensure that the area counted is square. Where practicable, one edge of the square to be counted should be aligned with a row of complete holes in the fabric. Incomplete holes $\geq \frac{1}{2}$ are counted as complete holes, whereas those $< \frac{1}{2}$ are not counted. Count 5 replicate squares in pieces taken according to Note 5, calculate the average and note the lowest value.
- Note 9 Dimensional stability is determined as follows. Method of preparation: ISO 3759 (1995, under revision in 2006). Method of washing: ISO 6330 (2001). Method of calculation: ISO 5077 (1984). Size of test portions: 500 mm²; mark off 350 mm² within the test portion. Test a total of 4 replicate portions, 2 washed in each of 2 separate loads. Type of washing machine: ISO type A (front loading). Washing program: ISO type 8A (gentle cycle 30°C). Fill the washer with dummy load (with fabric as per ISO standard) up to the standard of 2 to 4 kg. Drying: flat drying.
- Note 10 Test method for bursting strength: ISO 13938 part 1 (1999) and ISO 13938 part 2 (1999), with conditioning of the fabric as specified in the ISO standard. Results should be based tests of 7.3 cm² areas of fabric. Five replicate tests should be conducted on samples taken according to Figure 1 and the average 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 to provide the total of 5 measurements.
- Note 11 Samples of the product taken before and after the storage stability test should be analyzed concurrently in order to reduce the analytical error.

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

The sample should consist of 5 pieces, taken approximately according to the pattern shown in the diagram below. Sufficient material should be taken for all tests and thus the pattern indicated is intended only for general guidance. For most tests, pieces should be taken at least 15 cm from seams or selvages, avoiding folded and creased areas, so as to represent the netting material as fully as possible. To test the bursting strength of seams (clause 3.3), up to 5 seams may be tested, avoiding intersections, to provide a total of 5 measurements.



PART TWO
EVALUATION REPORTS

ALPHA-CYPERMETHRIN

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2009.1 **FAO/WHO evaluation report** based on data submitted
by BASF (LN)

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Annex 1: References

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WHO SPECIFICATIONS FOR PUBLIC HEALTH PESTICIDES

ALPHA-CYPERMETHRIN

FAO/WHO EVALUATION REPORT 454/2009.1

Recommendations

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

Appraisal

Supporting data and draft specifications for alpha-cypermethrin long-lasting (coated onto filaments) insecticidal net (LN), were provided by BASF in 2005 and additional studies were submitted in following years. The documents were considered by the Meeting for development of a new WHO specification. Appropriate clauses, limits and methods of testing for certain parameters of this new type of formulation were also developed by the company over this period.

The alpha-cypermethrin (coated onto filaments) LN produced by this manufacturer was tested/evaluated under the auspices of WHOPEs and an interim recommendation for their use in malaria prevention and control was issued in 2007 (WHO 2007).

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

The LN under consideration is a warp-knitted fabric with the active ingredient, alpha-cypermethrin, coated onto the polyester netting after the knitting process. The yarn used to produce the netting is a polyester polyfilament type which is subsequently coated with a formulated alpha-cypermethrin (SC) from a source compliant with the existing WHO specification for this active ingredient (BASF).

Description clause

The Meeting agreed that the specification should apply to white or coloured warp-knitted fabrics made from 75 or 100 denier multi-filament (minimum 32 filaments) polyester fibres and that it should apply equally to made up, ready-to-use nets (rectangular and circular) or to netting in bulk.

Active ingredient content clause

The target doses of alpha-cypermethrin (6.7 g/kg for the 75 denier yarn, and 5.0 g/kg for 100 denier yarn) is related to the technology, in order to achieve a satisfactory biological activity over the expected lifetime of the net. The Meeting agreed that the declared and tolerance values should be based on g/kg, with the corresponding mg/m² value (200 mg/m² for both yarns) being defined in a Note to the specification.

The Meeting observed that random variations in the distribution of alpha-cypermethrin may influence the variation in measured values for g/kg. The manufacturer provided between- and within-batch data, based on analysis of single pieces of 25 x 25 cm and variations in alpha-cypermethrin content following the sampling procedure as detailed in the LN guideline in the Manual, and demonstrated acceptable to good precision with two batches of net distributed and analyzed in three different laboratories (RSD < 3% with one batch, approx. 7 % with another batch).

The analytical method for determination of the alpha-cypermethrin content in LN coated type was validated as an extension of the existing CIPAC method for alpha-cypermethrin in other formulations and adopted as provisional method by CIPAC in 2007 and is published as a full method in Handbook M (August 2009).

Relevant impurities

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

Alpha-cypermethrin retention index clause

An adequate amount of active ingredient must be present on the surface of the LN, for efficacy, but the majority must reside within the coating of the fibres of the LN, to avoid excessive losses during washing and to provide a reservoir from which the surface is replenished with active ingredient. The nature of the coating and binding material – a polymer which provides adequate protection for the reservoir of the insecticide – strongly influences the migration of alpha-cypermethrin to the surface when the LN is subjected to repeated washing. The Meeting agreed that also for coated types of LN, the retention index is the appropriate expression of the depletion and replenishment of the active ingredient on the surface of the multifilament fibre.

The manufacturer provided experimental data showing that approximately constant proportions of the remaining alpha-cypermethrin are removed from the surface of the filament by successive washings with aqueous detergent. The manufacturer proposed a range for the retention index of 0.90 as the minimum and a maximum of 0.98, which was agreed by the Meeting. When agreeing on limits in a specification, the sampling and analytical methods need to be properly validated so these limits can be checked and enforced by quality control laboratories if necessary. The upper limit of 0.98 was chosen for practicability reasons: the default precision requirement for content determination is $\leq 5\%$.

Sampling of alpha-cypermethrin (coated into filaments) LN was done by cutting a total of 6 pieces for analysis. Six pieces of net (25 x 25 cm) were cut and washed for a specified number of washes using the WHO washing method (WHO 2005). After drying, the samples were again analyzed for alpha-cypermethrin content. The recommended positions from which the pieces of netting should be taken from a made up bed net are similar to those given in the manual (FAO/WHO 2006), as shown in figure 1, appended to the specification. The manufacturer's results showed certain small but measurable decrease of alpha-cypermethrin content with each washing step, with more than 90% of total alpha-cypermethrin remaining after each wash step. Using bioassays, the regeneration time required for diffusion to restore the surface concentration to full biological activity after washing was shown to be one day.

Physical property clauses

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

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

The $\pm 5\%$ tolerance on dimensional stability to washing was in agreement with the standard 5% given in the LN guideline (FAO/WHO 2006) and was supported by test results.

Storage stability clause

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

ANNEX 1. REFERENCES

BASF document or other reference No.	Full reference
2005/1025927	M. Siebecker, 2005. Quantitative determination of alpha-cypermethrin: total contents and adherent contents on the surface of fibers of long-lasting insecticidal nets (LNs). BASF document 2005/1025927.
2005/1031627	J. Fries, 2005. Long lasting insecticidal nets (LNs): determination of the release or retention index of alpha-cypermethrin, final report. BASF document 2005/1031627 [a revision of BASF document 2005/1026842].
2006/1006722	Reply: Proposed WHO specification for alpha-cypermethrin LN. E-mail sent by T. Maurer to A. Hill and M. Zaim (WHO) on 19/01/06.
CIPAC H	Alpha-cypermethrin. CIPAC Handbook H, pp.14-21, Collaborative International Pesticides Analytical Council, Harpenden, U.K., 1998.
FAO/WHO 2002	Manual on development and use of FAO and WHO specifications for pesticides, 1 st edition. FAO Plant production and protection paper 173. FAO, Rome, 2002.
FAO/WHO 2006	Manual on development and use of FAO and WHO specifications for pesticides. FAO, Rome, March 2006 (internet publication).
LIN/06/05	J. Bonnet, S. Duchon & V. Corbel, 2005. Wash resistance and efficacy of long lasting insecticide nets from BASF against susceptible mosquitoes of <i>Anopheles gambiae</i> , final report. BASF document DOC/LIN/06/05.
LIN/IRD/O1/05	J. Bonnet, S. Duchon & V. Corbel, 2005. WHOPES phase I study on LLINs from BASF (TSA V2 181 345), final report. BASF document DOC/LIN/IRD/01/05.
WHO 2005	Guidelines for laboratory and field testing of long-lasting insecticidal mosquito nets. Document WHO/CDS/WHOPES/GCDPP/2005.11. World Health Organization, Geneva, 2005.
WHO 2005	Technical consultation on specifications and quality control of netting materials for mosquito nets (untreated and treated). 29 November–02 December 2005. WHO Headquarters, Geneva, Switzerland.
WHO 2007	Report of the Tenth WHOPES Working Group Meeting, WHO/HQ, Geneva, 11-14 December 2006. Geneva, World Health Organization, document WHO/CDS/NTD/WHOPES/2007.1
WHO 2008	Report of the Eleventh WHOPES Working Group Meeting, WHO/HQ, Geneva, 10-13 December 2007. Geneva, World Health Organization, document WHO/HTM/NTD/WHOPES/2008.1.