

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

PERMETHRIN

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

3-phenoxybenzyl (1*RS*,3*RS*;1*RS*,3*SR*)-3-(2,2-dichlorovinyl)-
2,2-dimethylcyclopropanecarboxylate



**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 1st edition of Manual for Development and Use of FAO and WHO Specifications for Pesticides (2002). 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 1st edition 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/>).

PART ONE

SPECIFICATIONS

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PERMETHRIN

INFORMATION

ISO common names

permethrin (E-ISO, BSI, ANSI, ESA, BAN)
perméthrine (F-ISO)

Synonyms

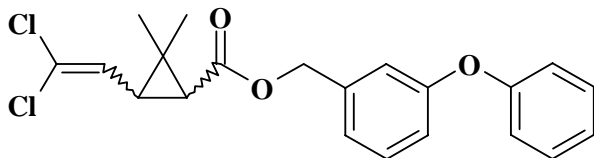
none

Chemical names

IUPAC 3-phenoxybenzyl (1*RS*,3*RS*;1*RS*,3*SR*)-3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropanecarboxylate

CA (3-phenoxyphenyl)methyl 3-(2,2-dichloroethenyl)-2,2-dimethylcyclopropanecarboxylate

Structural formula of one stereoisomer



Empirical formula

$C_{21}H_{20}Cl_2O_3$

Relative molecular mass

391.3

CAS Registry number

52645-53-1

CIPAC number

331

Identity tests

GC retention time; IR spectrum.

PERMETHRIN LONG-LASTING (INCORPORATED INTO FILAMENTS) INSECTICIDAL NET (LN)

Amended* WHO interim specification 331/LN (July 2006**)

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 (331/LN/2006). 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. The evaluation report 331/LN/2006, as PART TWO, forms an integral part of this publication.

1 Description

The product shall be formed from netting (Note 1), consisting of high density polyethylene mono-filament fibres containing technical permethrin complying with WHO specification WHO/SIT/28, together with any necessary stabilizers, plasticizers and other formulants. The product shall appear clean and shall be free from visible extraneous matter (Note 2), visible damage (such as splitting or tearing) and visible manufacturing defects (such as poorly made seams or a weave that is either not uniform or too loose to remain uniform in use). It shall be suitable for use as an insecticidal net with long-lasting activity (Notes 3 & 4).

2 Active ingredient (Note 5)

2.1 Identity tests (CIPAC Handbook, Note 6)

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 Permethrin content (CIPAC Handbook, Notes 6 & 7)

The permethrin content shall be declared (20 g/kg) and, when determined, the average content shall not differ from that declared by more than ± 3 g/kg.

2.3 Permethrin isomer ratio (CIPAC Handbook, Note 6)

The [1*RS*,3*RS*]:[1*RS*,3*SR*] (*cis:trans*) permethrin isomer ratio shall be in the range 50:50 to 30:70.

2.4 Permethrin release characteristics (Note 3)

When determined by the CIPAC tentative method (Note 8), the surface concentration of permethrin calculated from rinse 2 shall be in the range 0.15-0.60 g/kg and the permethrin release index shall be in the range 0.55 to 1.20 (Note 9).

* This amended interim specification replaces one which was published in 2002.

** 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 (Note 5)

3.1 Netting mesh size

When counted by the method given in Note 10, the average number of complete holes per 100 cm² shall be not less than 528 and the lowest value shall be not less than 500.

3.2 Dimensional stability to washing (ISO 5077 [1984], ISO 3795 [1984], ISO 6330 6A & flat dry [2000], Note 11)

Dimensional stability: not exceeding $\pm 10\%$ of the initial dimensions.

3.3 Bursting strength (ISO 13938-1 or -2 [1999]) (Note 12)

The minimum bursting strength of the fabric shall be declared (not less than 350 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 average for the fabric.

4 STORAGE STABILITY

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

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

- release index (2.4) ;
- dimensional stability (3.2);
- bursting strength (3.3);

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

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

Note 3 A long-lasting insecticidal net is expected to retain insecticidal activity during its life span and through a number of washes. The clause for permethrin release characteristics (2.4) is based on a model washing regime and compliance with the limit does not guarantee that activity will be retained through any particular number of washes performed according to local practice.

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

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

Note 5 Each net is expected to conform to the specification and, for the purposes of testing for compliance, material from two or more nets must not be mixed. Samples for testing should be taken in such a way as to be representative of the net or netting. Unless stated otherwise for the test, samples should be assembled from pieces taken from nets as shown in Figure 1. Samples from bulk netting should be assembled from similar pieces taken along a suitable diagonal across the netting. The sizes of pieces should be appropriate to the tests required and sufficient for both pre- and post-storage stability tests. Samples for chemical analysis

may be cut into 1-2cm squares and thoroughly mixed, to provide representative test portions (this is not appropriate for tests of some physical properties).

Note 6 Methods for the identification and determination of permethrin content and permethrin isomer ratio in TC and LN were adopted by CIPAC in 2006, but the methods are not yet published in a Handbook. Prior to publication of the Handbook, copies of the methods for analysis of LN may be obtained through the CIPAC website, <http://www.cipac.org>.

Note 7 The permethrin content may be declared as both g/kg and mg/m² but, in cases of dispute, g/kg values shall be used. If the active ingredient content is also specified as mg/m² of netting, the actual value is calculated from the values for active ingredient content in g/kg and mass of net/m². Mass of net/m² should be determined according to ISO 3801 (1977).

Note 8 The test method for determination of permethrin release characteristics was adopted by CIPAC in 2006, with tentative status only, and is not published in a Handbook. Copies of the method may be obtained through the CIPAC website, <http://www.cipac.org>.

Note 9 The measured values for either surface concentration at rinse 2 or release index are more likely to approach the specification limits immediately after manufacture of the net but, from any particular net, results for both parameters are not expected to be at the limits of their range.

Note 10 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 or on which an accurately calibrated ($\pm 1\%$ in each dimension) square (e.g. 5 x 5 cm) has been cut or 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. If practicable, at least one edge of the square to be counted should be aligned with a row of complete holes in the fabric. Count 5 replicate squares in pieces selected according to Figure 1, below, calculate the average and note the lowest value.

Note 11 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 x 500 mm; mark off 350 x 350 mm within the test portion. Test a total of 4 replicate portions, duplicates washed in each of 2 separate loads. Type of washing machine: ISO type A (front loading). Washing programme: ISO type 6A (1 main wash, 3 rinses, 40°C). Fill the washer with dummy load (with fabric as per ISO standard) up to the standard of 2 to 4 kg. Each test portion should be washed in a bag, to avoid stretching of the fabric. Drying: flat drying.

Note 12 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.

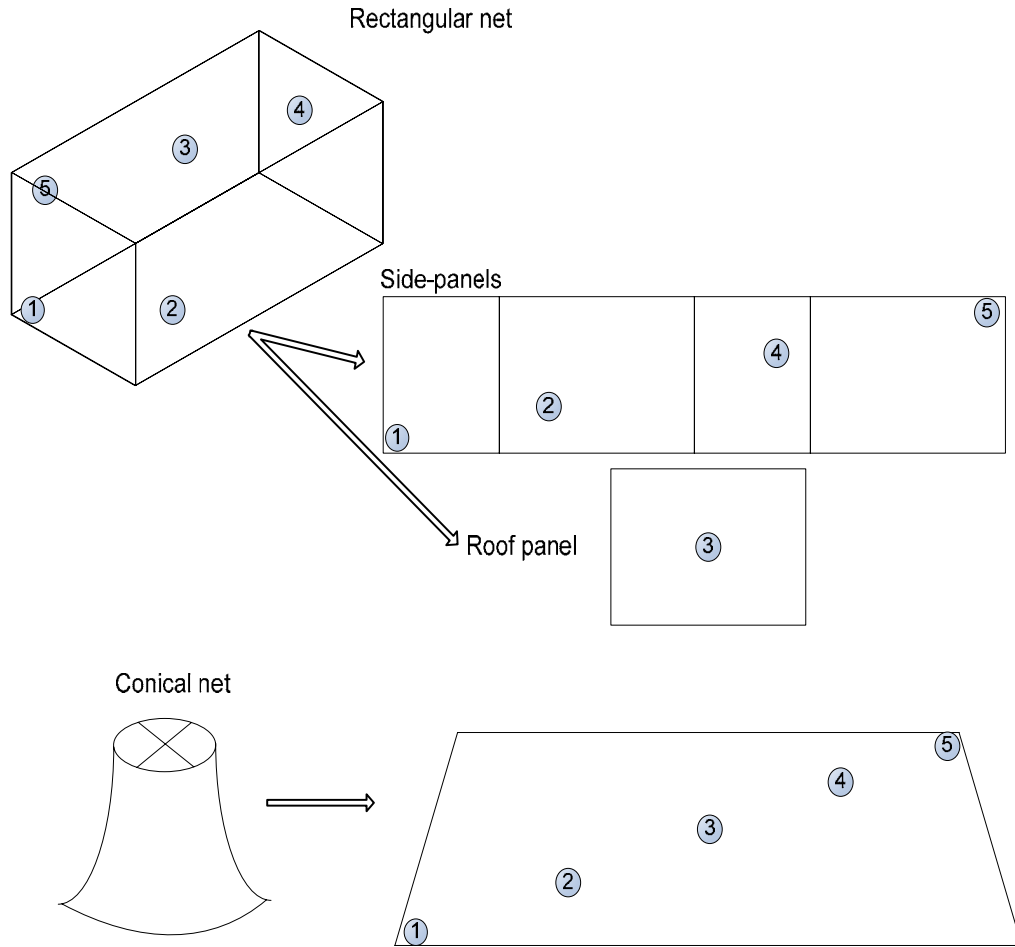
The method to test seam bursting strength is identical to that used to test the fabric, except that 5 replicate tests should be performed with a seam centred on the test head. Up to 5 seams may be tested, to provide the total of 5 measurements.

Note 13 The test should be conducted on samples without the presence of packaging material.

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

Figure 1 General method for sampling rectangular and conical nets

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 15cm 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

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

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WHO SPECIFICATIONS AND EVALUATIONS FOR
PUBLIC HEALTH PESTICIDES

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

EVALUATION REPORT 331LN/2006

Recommendations

The Meeting recommended the following.

- (i) The existing (2002) WHO interim specification for permethrin LN should be withdrawn.
- (ii) The specification for permethrin LN proposed by Sumitomo, as amended, should be adopted by WHO with interim status.
- (iii) The new interim specification for permethrin LN should be promoted to the status of a full WHO specification, subject to:
 - (a) satisfactory validation and CIPAC adoption of the test method for determination of the release characteristics;
 - (b) development of a WHO full specification for permethrin TC under the new procedure; and
 - (c) confirmation by the manufacturer that the permethrin incorporated into the LN complies with the new full specification for TC.
- (iv) Future proposals for extension of this specification (at interim or full status) to apparently equivalent LN formulations should be supported by evidence to show whether or not the test method and limit for active ingredient release characteristics are appropriate for the additional products.

Appraisal

Information and a proposed revised specification were provided by Sumitomo in 2005, for review of the existing (2002) interim WHO specification for an LN containing permethrin (nominal *cis/trans* ratio 40:60). The Meeting considered only revision of the technical aspects of the specification, not its interim status. The Meeting noted that subsequent promotion from interim to full specification status would be automatic, subject to fulfilment of the criteria given in the recommendations (above).

Existing FAO and WHO specifications for permethrin TC were developed, separately, under the old procedure and are awaiting review by the JMPS. The existing WHO specification for permethrin TC (WHO/SIT/28.R1), which encompasses both 25:75 and 40:60 *cis/trans* permethrin ratios, was published in 1999.

The existing and proposed specifications are for warp-knitted mono-filament fabric, in which the active ingredient is incorporated into the filaments.

The proposed LN specification had been amended in accordance with the newly published interim guideline specification for LN (FAO/WHO 2006), which reflected improvements in knowledge about various LN products that had occurred since WHO published its first interim guideline for LN specifications. Among the consequential changes, perhaps most significant was in the method and clause for testing the release characteristics of the LN.

Unlike coated-filament fabrics, in which adequate retention of active ingredient during washing is an important criterion (indicating whether or not there is an appropriate quantity or quality of coating polymer), in fabrics where the active ingredient is incorporated into the filaments it is important to ensure adequate but not excessive release of the active ingredient after washing. This is partly because re-equilibration throughout the filament by diffusion takes longer than it does in a thin coating and partly because slow mechanical/conformational changes are also involved¹. Where the active ingredient is incorporated into filaments, rapid total loss of active ingredient is not likely to occur during washing but, if redistribution to the surface is too slow, the product may be ineffective for an unacceptable period after washing. Alternatively, if the redistribution is too rapid, the surface concentration could become higher than expected, leading to higher losses of active ingredient during washing and possibly increased user exposure to the active ingredient.

The manufacturer had shown that macro-scale distribution of total permethrin is very uniform within the LN (<2% RSD, measured in single 2 g samples withdrawn from material cut into 5-10 mm squares and mixed) (Sumitomo 2005a). The 2 g samples corresponded to approximately 0.04 m² but, being well mixed, they were representative of a much larger quantity of netting. A similar cutting, mixing and sub-sampling procedure cannot be used for the determination of release index. The release characteristics (measurements of “surface concentrations²” at rinses 2 and 3) are determined as the average result obtained from three separate 5 cm square pieces (a total of 0.0075 m² or 0.375 g) of netting and the results tend to be much less uniform than measurements of total active ingredient content. Analysis of these smaller samples increases the (statistical) sampling error and contributes to the variation in measured release characteristics but the manufacturer concluded that the results were fit for purpose (Sumitomo 2005b).

The manufacturer provided supporting QC data (Sumitomo 2006a) for surface concentration at rinse 2 and release index and stated that the limits (0.15-0.60 and 0.55-1.2, respectively) were based on the average \pm 3 S.D. The Meeting questioned whether the proposed limits for release characteristics would really distinguish between good and bad materials. The product should contain 17-23 g/kg permethrin. In a theoretical worst-case scenario, at 17 g/kg and with a surface concentration at rinse 2 of 0.6 g/kg and a release index of 1.2, the fabric could be exhausted in about 22 washes, which was considered to be an acceptable number. Again theoretically, with surface concentration of 0.15 g/kg and release index of 0.55, although it may

¹ The filament is not a simple solid solution of active ingredient. The mechanical/conformational changes are slow but more or less irreversible and produce an effect which may be thought of as “sweating/bleeding”. This effect can lead to surface concentrations higher than would be produced by simple diffusion alone.

² “Surface concentrations” measured for the determination of release index should not be confused with the initial surface concentration. What is measured is broadly similar in concept (though difficult to define physically) in both cases but in the former case it is under experimental control, whereas in the latter case it is uncontrolled.

take about 200 washes to exhaust the fabric, the surface concentration may not be high enough for good efficacy. The manufacturer provided data (Sumitomo 2003) showing that good efficacy requires a minimum surface concentration of about 0.15 g/kg. Thus a surface concentration of 0.15 g/kg at rinse 2 would be just sufficient but a release index of 0.55 would imply that lower surface concentrations could occur. The manufacturer stated (Sumitomo 2005c) that combinations of extreme high + high or extreme low + low values for surface concentration at the 2nd wash and release index do not occur in practice and also that the dispersion of results for both parameters decreases with time after manufacture. Thus, in practice, the surface concentration does not decline below levels required for acceptable efficacy until the active ingredient content is becoming exhausted.

The manufacturer provided supporting QC data for permethrin surface concentration and retention index (Sumitomo 2006b), obtained before and after storage of samples at 54°C for 2 weeks, and stated that the proposed limits were based on the average ± 3 S.D. The data indicated what is achievable in manufacturing practice using the current test method, and the Meeting therefore accepted the proposed limits.

The proposed limit for dimensional stability ($\pm 10\%$) exceeded the standard $\pm 5\%$ in the current LN specification guideline (FAO/WHO 2006). The manufacturer stated (Sumitomo 2006c) that any shrinkage can be addressed by stretching the product, which is not harmed in the process. The manufacturer also stated that no complaints had been received from users or buyers. Therefore Meeting accepted the proposed limit.

New CIPAC analytical methods for identification and for the determination of permethrin content and isomer ratio in TC and LN were adopted in 2006, with provisional status, and are thus acceptable for support of a WHO full specification. However, the method for determination permethrin release characteristics was adopted by CIPAC in 2006 with tentative status only, which is not sufficient for support of a WHO full specification.

**SUPPORTING INFORMATION
FOR
EVALUATION REPORT 331LN/2006**

Uses

The LN is used in the form of bed nets to protect users against flying biting insects, especially mosquitoes which may serve as vectors for diseases such as malaria.

The LN is registered and sold in Colombia, Dominican Republic, Honduras, Indonesia, Kenya, Malaysia, Myanmar, Peru, Philippines, Singapore, Sri Lanka, Thailand, Tanzania, and Trinidad.

Formulations

Permethrin is not co-formulated with other pesticides in the LN.

Methods of analysis and testing

New analytical methods for identification and for the determination of permethrin content and isomer ratio in TC and LN were validated by collaborative study (organized by the company under the auspices of CIPAC) and were adopted by CIPAC in 2006, with provisional status.

The method for determination permethrin release characteristics was also the subject of a CIPAC collaborative study (organized by the company under the auspices of CIPAC) and was adopted by CIPAC in 2006, with tentative status.

The test method for storage stability is a full CIPAC method.

As indicated in the specification, the methods for testing physical properties are ISO standards, with the exception of mesh size which involves only measurement with a ruler or grid.

ANNEX 1. REFERENCES

Reference	Year and title of report/communication or publication details
FAO/WHO 2006	Supplement to the Manual on the development and use of FAO and WHO specifications for pesticides. Published on FAO and WHO websites, February 2006.
Sumitomo 2003	2003. Justification for new proposal of specification of Olyset net.
Sumitomo 2005a	2005. Distribution of permethrin.xls. Sampling method for permethrin LLIN.
Sumitomo 2005b	2005. Amended Interim Specification for Olyset Net WHO/IS/NI/331/2005.
Sumitomo 2005c	2005. RE: Amended Interim Specification for Olyset Net WHO/IS/NI/331/2005.
Sumitomo 2006a	2006. SC data.060531xls.xls. Revised interim specification for permethrin LN.
Sumitomo 2006b	2006. RI SC data.xls. Revised WHO interim specification for permethrin LN.
Sumitomo 2006c	2006. FW: Revised interim specification for permethrin LN.