

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

**S-BIOALLETHRIN* + PERMETHRIN
+ PIPERONYL BUTOXIDE**

OIL-IN-WATER EMULSION

(S)-3-allyl-2-methyl-4-oxocyclopent-2-enyl (1*R*,3*R*)-2,2-dimethyl-3-(2-methylprop-1-enyl)cyclopropanecarboxylate*

+

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

+

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



**World Health
Organization**

* S-bioallethrin is defined here, in the absence of an ISO common name, as a mixture of allethrin isomers which is predominantly comprised of the (S)(1*R*,3*R*) enantiomer.

TABLE OF CONTENTS

	PAGE
DISCLAIMER	3
INTRODUCTION	4
PART ONE	
SPECIFICATION FOR S-BIOALLETHRIN + PERMETHRIN + PIPERONYL BUTOXIDE	
S-BIOALLETHRIN INFORMATION	6
PERMETHRIN INFORMATION	7
PIPERONYL BUTOXIDE INFORMATION	8
S-BIOALLETHRIN + PERMETHRIN + PIPERONYL BUTOXIDE OIL-IN-WATER EMULSION (NOVEMBER 2006)	9
PART TWO	
2005 EVALUATION REPORT FOR S-BIOALLETHRIN + PERMETHRIN + PIPERONYL BUTOXIDE OIL-IN-WATER EMULSION	13
SUPPORTING INFORMATION	15
ANNEX 1: REFERENCES	17

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 has followed the **New Procedure**, described in the 1st edition of Manual for Development and Use of FAO and WHO Specifications for Pesticides (2002) and amended with the supplement of this manual (2006), which is available only on the internet through the FAO and WHO web sites. 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.

* The publications are available on the Internet under (<http://www.who.int/whopes/quality/en/>).

** Except in special cases for which the justification is presented in the associated evaluation reports.

PART ONE

SPECIFICATIONS

	PAGE
S-BIOALLETHRIN INFORMATION	6
PERMETHRIN INFORMATION	7
PIPERONYL BUTOXIDE INFORMATION	8
S-BIOALLETHRIN + PERMETHRIN + PIPERONYL BUTOXIDE OIL-IN-WATER EMULSION (OCTOBER 2006)	9

S-BIOALLETHRIN*

INFORMATION

ISO common name

none

Synonyms

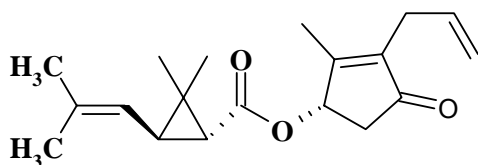
S-bioallethrin*; esdepalléthrine (France AFNOR); esbiol;
bioallethrin S-cyclopentenyl isomer

Chemical names

IUPAC (S)-3-allyl-2-methyl-4-oxocyclopent-2-enyl (1R,3R)-2,2-dimethyl-3-(2-methylprop-1-enyl)cyclopropanecarboxylate*

CA [1R-[1 α (S*),3 β]-2-methyl-4-oxo-3-(2-propenyl)-2-cyclopenten-1-yl 2,2-dimethyl-3-(2-methyl-1-propenyl)cyclopropanecarboxylate*

Structural formula*



Empirical formula

C₁₉H₂₆O₃

Relative molecular mass

302.4

CAS Registry number

28434-00-6

CIPAC number

750

Identity tests

Capillary GC-FID retention time; chiral HPLC retention time and peak pattern.

* S-bioallethrin is defined here, in the absence of an ISO common name, as a mixture of allethrin isomers which is predominantly comprised of the (S)(1R,3R) enantiomer.

PERMETHRIN

INFORMATION

ISO common names

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

Synonyms

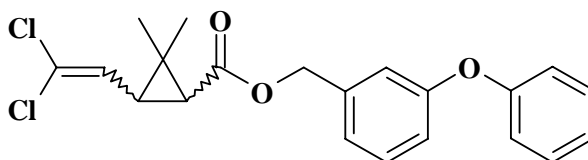
none

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



Empirical formula

C₂₁H₂₀Cl₂O₃

Relative molecular mass

391.3

CAS Registry number

52645-53-1

CIPAC number

331

Identity tests

GC retention time; IR and mass spectra.

PIPERONYL BUTOXIDE

INFORMATION

Common names

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

Synonyms

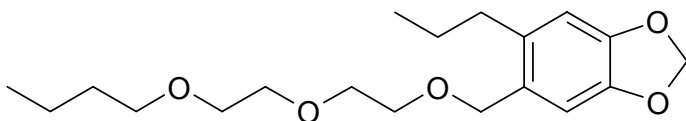
PBO

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.

S-BIOALLETHRIN + PERMETHRIN + PIPERONYL BUTOXIDE OIL-IN-WATER EMULSION

WHO specification 750+331+33/EW (November 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 reports (750+331+33/2005). It should be applicable to relevant products of this manufacturer, and those of any other formulators who use only S-bioallethrin TC from the evaluated source. The specification 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 who use S-bioallethrin TC from other sources. The evaluation reports (750+331+33/2005), as PART TWO, form an integral part of this publication.

1 Description

The formulation shall consist of an emulsion of technical S-bioallethrin, complying with the requirements of WHO specification 750/TC (April 2006); technical permethrin, complying with the requirements of WHO specification WHO/SIT/28.R1 (10 December 1999); and technical piperonyl butoxide; in an aqueous phase together with suitable formulators. After gentle agitation, the formulation shall be homogeneous (Note 1) and suitable for dilution in water.

2 Active ingredients

- 2.1 **Identity tests** (750/EW/M/2 for S-bioallethrin [Note 2]; 331/EW/M/2 for permethrin, CIPAC Handbook [Note 2]; 33/EW/M/2, CIPAC Handbook 1C, p.2190, 1985, for piperonyl butoxide [Note 2])

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

- 2.2 **S-bioallethrin content** (750/EW/M/3, CIPAC Handbook, Note 2 and 3)

The S-bioallethrin content shall be declared (1.4 g/kg or g/l at $20 \pm 2^\circ\text{C}$, Note 4) and, when determined, the average measured content shall not differ from that declared by more than $\pm 15\%$.

- 2.3 **S-bioallethrin isomer composition** (750/TC/M/3, CIPAC Handbook L, Notes 2 and 3)

The proportion of *trans*-isomer in the active ingredient shall be declared (not less than 98.0%) and, when determined, the average measured *trans*-isomer proportion shall not be lower than the declared minimum.

The proportion of 1*R*-isomer content in the acid moiety of the active ingredient shall be declared (not less than 98.0%) and, when determined, the average measured 1*R*-isomer proportion shall not be lower than the declared minimum.

The proportion of S-isomer content in the alcohol moiety of the active ingredient shall be declared (not less than 96.0%) and, when determined, the

* 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/>.

average measured S-isomer proportion shall not be lower than the declared minimum.

2.4 Permethrin content (331/EW/M/3, CIPAC Handbook, Note 2)

The permethrin content shall be declared (103 g/kg or g/l at 20 ± 2°C, Note 4) and, when determined, the average measured content shall not differ from that declared by more than ± 6%.

2.5 Permethrin *cis/trans* isomer ratio (331/EW/M/3, CIPAC Handbook, Note 2)

The [1*RS*,3*RS*]:[1*RS*,3*SR*] (*cis:trans*) permethrin isomer ratio shall be in the range 35:65 to 15:85.

2.6 Piperonyl butoxide content (33/TC/M/3, CIPAC Handbook 1C, p.2190, 1985, Note 2)

The piperonyl butoxide content shall be declared (98 g/kg or g/l at 20 ± 2°C, Note 4) and, when determined, the average measured content shall be not less than 88 g/kg or g/l at 20 ± 2°C.

3 Physical properties

3.1 pH range (MT 75.3, CIPAC Handbook J, p.131, 2000) (Note 5)

pH range of a 1% aqueous solution: 4.0 to 7.0.

3.2 Pourability (MT 148, CIPAC Handbook F p.348, 1995)

Maximum "residue": 5%.

3.3 Emulsion stability and re-emulsification (MT 36.3, CIPAC Handbook K p.137, 2003) (Note 6)

The formulation, when diluted (Note 7) at 30 ± 2°C with CIPAC standard waters A and D, shall comply with the following:

Time after dilution	Limits of stability, MT 36.3
0 h	Initial emulsification complete
0.5 h	"Cream": maximum 2 ml
2.0 h	"Cream", maximum 2 ml "Free oil", maximum 0 ml
24 h	Re-emulsification complete
24.5 h	"Cream", maximum 2 ml "Free oil", maximum 0 ml
<u>Note:</u> tests after 24 h are required only where results at 2 h are in doubt	

3.4 Persistent foam (MT 47.2, CIPAC Handbook F p.152, 1995) (Note 8)

Maximum: 60 ml after 1 min.

4 Storage stability

4.1 Stability at 0°C (MT 39.3, CIPAC Handbook J p. 126, 2000)

After storage at $0 \pm 2^\circ\text{C}$ for 7 days, no separation of particulate or oily matter shall be visible after gentle agitation.

4.2 Stability at elevated temperature (MT 46.3, CIPAC Handbook J p.149, 2000)

After storage $54 \pm 2^\circ\text{C}$ for 14 days, the determined average active ingredient content must not be lower than 95%, relative to the determined average content found before storage (Note 9), and the formulation shall continue to comply with the clauses for:

- pH range (3.1),
- emulsion stability and re-emulsification (3.3).

Note 1 All physical and chemical tests listed in this specification are to be performed with a laboratory sample taken after the recommended homogenisation procedure. Before sampling to verify the formulation quality, the commercial container must be inspected carefully. On standing, emulsions may develop a concentration gradient which could even result in the appearance of a clear liquid on the top (sedimentation of the emulsion) or on the bottom (creaming up of the emulsion). Therefore, before sampling, the formulation must be homogenised according to the instructions given by the manufacturer or, in the absence of such instructions, by gentle shaking of the commercial container (for example, by inverting the closed container several times). Large containers must be opened and stirred adequately.

Note 2 Extensions of the methods for the identification and determination *S*-bioallethrin, permethrin and piperonyl butoxide to the analysis of EW formulations were adopted by CIPAC in 2006 but are not yet published in a Handbook. Prior to publication of the Handbook, copies of the methods may be obtained through the CIPAC website, <http://www.cipac.org/prepubme.htm>.

Note 3 *S*-bioallethrin is quantified as a mixture of allethrin isomers, though predominantly comprised of the (*S*)(1*R*,3*R*) enantiomer. Identification of the active ingredient as *S*-bioallethrin requires compliance with clause 2.3.

Note 4 If the buyer requires both g/kg and g/l at 20°C, then in case of dispute the analytical results shall be calculated as g/kg.

Note 5 In case of drifting pH values, the reading on the pH-meter is taken as constant and valid if the deviation in value is less than 0.1 pH unit over a period of 10 min (without stirring).

Note 6 This test will normally be carried out only after the test of stability at elevated temperature (4.2).

Note 7 The formulation should be tested at the highest (10%) and lowest (1%) rates of use recommended by the supplier.

Note 8 The test should be carried out at the highest application concentration (10%), in CIPAC standard water D.

Note 9 Samples of the formulation taken before and after the storage stability test should be analyzed concurrently after the test in order to reduce the analytical error.

PART TWO
EVALUATION REPORTS

S-BIOALLETHRIN + PERMETHRIN OIL-IN-WATER EMULSION

Page

2005	Evaluation report based on submission of data from Bayer	
	CropScience (EW)	13
	Supporting information	15
	Annex 1: references	17

WHO SPECIFICATIONS AND EVALUATIONS FOR
PUBLIC HEALTH PESTICIDES

S-BIOALLETHRIN + PERMETHRIN OIL-IN-WATER EMULSION

EVALUATION REPORT 750+331+33/2005

Recommendations

The Meeting recommended that:

- (i) the specification for S-bioallethrin + permethrin + piperonyl butoxide EW, proposed by Bayer CropScience, should be adopted by WHO, subject to CIPAC adoption of extensions of the analytical methods for S-bioallethrin and permethrin to EW and the peer-validated method for determination of piperonyl butoxide in EW*.
- (ii) the cross-reference to permethrin TC in the EW specification should be updated, as and when a revised specification for permethrin TC is published.

Appraisal

The Meeting considered information in support of a new WHO specification for an EW formulation containing a mixture of S-bioallethrin, permethrin (*cis/trans* nominal ratio 25:75) and piperonyl butoxide. Piperonyl butoxide is widely used as a synergist in formulations of pyrethrins and pyrethroids, as it inhibits the natural detoxification systems of insects and thus increases the efficacy of these pesticides.

Information supporting the proposed specification was provided by Bayer CropScience in 2004. The EW is registered and sold in many countries including: Bosnia, Cambodia, Croatia, Cuba, Czech Republic, Guatemala, Honduras, Iraq, Kingdom of Saudi Arabia, Lebanon, Macedonia, Malaysia, Mexico, North Cyprus, Oman, Philippines, Romania, Serbia, Slovakia, Slovenia, Sudan, Syria, Thailand, United Arab Emirates, the U.K. and Vietnam.

A WHO specification for S-bioallethrin TC (750/TC) was developed under the new procedure in 2005. The existing WHO specification for permethrin TC (WHO/SIT/28.R1), which encompasses both 25:75 and 40:60 *cis/trans* ratios, was developed under the old procedure in 1999. Permethrin specifications are scheduled for review by the JMPS in 2006 and the Meeting noted that EW specification should be updated to refer to the new TC specification, when this is published. As a synergist, piperonyl butoxide TC is not subject to WHO specifications.

For most purposes, WHO and FAO specifications for individual active ingredients are expected to apply equally to solo and co-formulated products. However, in the present case, the manufacturers stated that a combination of optimal efficacy, minimization of active ingredient use, and avoidance of target pest resistance could be achieved only by utilizing the specified mixture of active ingredients

* 2006 footnote: extensions of the analytical methods for determination of S-bioallethrin, permethrin and piperonyl butoxide in EW formulations were adopted by CIPAC in 2006.

(BCS/GRA/BAJ/050137). The Meeting agreed that, exceptionally, a specification should be developed for the mixed formulation. The manufacturer also stated that efficacy had been optimized using permethrin with a *cis/trans* ratio of 25:75 (BCS/GRA/BAJ/050137) and the Meeting therefore accepted that an appropriate clause should be included in the specification.

The manufacturer stated that the requirement for piperonyl butoxide content of the mixture is that it must exceed the minimum threshold required for inhibition of the detoxification pathway (BCS/GRA/BAJ/050137). The Meeting therefore noted that the specification requires only a minimum value for the content of piperonyl butoxide.

The Meeting questioned the proposed limits for emulsion stability, which appeared to be relatively poor for an EW. The manufacturer stated that it had not been possible to improve this characteristic and that the emulsions are sufficiently stable for use in practice (BCS/GRA/BAJ/050137). It was stated that operator movements (hand-held foggers) or in-built recirculation systems (vehicle-mounted foggers) are sufficient to maintain homogeneity of the emulsion. The Meeting accepted the explanation and noted that careful re-emulsification may be more important after storage of the undiluted EW than after its subsequent dilution for use.

All other clauses and limits were in accordance with the requirements of the manual (FAO/WHO 2002).

The manufacturer stated that extensions to the CIPAC analytical methods for identification and determination of *S*-bioallethrin, permethrin and piperonyl butoxide in EW will be validated and presented to CIPAC in 2006*.

* 2006 footnote: extensions of the analytical methods for determination of *S*-bioallethrin, permethrin and piperonyl butoxide in EW formulations were adopted by CIPAC in 2006.

**SUPPORTING INFORMATION
FOR
EVALUATION REPORT 750+331+33/EW/2005**

Uses

The mixed S-bioallethrin + permethrin + piperonyl butoxide EW formulation, for which a specification was proposed by Bayer CropScience, is used for space spraying and outdoor ground application by aerial or vehicle-mounted ULV equipment, thermal fogging (hand-held fogging machines) or misting techniques. It contains an anti-evaporant to help maintain droplet size during application and thus aid accurate deposition, especially in hot climates.

Formulations

The EW is registered and sold in many countries including: Bosnia, Cambodia, Croatia, Cuba, Czech Republic, Guatemala, Honduras, Iraq, Kingdom of Saudi Arabia, Lebanon, Macedonia, Malaysia, Mexico, North Cyprus, Oman, Philippines, Romania, Serbia, Slovakia, Slovenia, Sudan, Syria, Thailand, United Arab Emirates, the U.K. and Vietnam.

Methods of analysis

The analytical method for identification and determination of S-bioallethrin in TC is a full CIPAC method. The manufacturer is in process of validating extension of the method to EW and the results will be presented to CIPAC in 2006*.

Full CIPAC methods were available for identification** and determination*** of permethrin in TC but the techniques involved were essentially obsolete. New methods are being validated and the results will be presented to CIPAC in 2006. The manufacturer will present validation data in support of an extension of these methods to EW to CIPAC, also in 2006*.

The manufacturer provided methods for identification of piperonyl butoxide and is in process of peer validating a method for the determination of this synergist in the EW. The results will be presented to CIPAC in 2006*.

* 2006 footnote: extensions of the analytical methods for determination of S-bioallethrin, permethrin and piperonyl butoxide in EW formulations were adopted by CIPAC in 2006.

** MT 163, CIPAC Handbook F, p.404, 1995.

*** 331/TC/M/3, CIPAC Handbook 1C, p.2173, 1985.

ANNEX 1. REFERENCES

Bayer CropScience document number, or other reference	Year and title of report, or publication details
BCS/GRA/BAJ/050137	2005. Aqua-Reslin Super – WHO specifications: answers to the WHO expert questions asked during 2005 FAO/WHO Utrecht meeting.
FAO/WHO 2002	Manual on the development and use of FAO and WHO specifications for pesticides, 1 st edition. FAO plant production and protection paper 173. FAO, Rome, 2002.