WHO SPECIFICATIONS AND EVALUATIONS FOR PUBLIC HEALTH PESTICIDES

IMIDACLOPRID + PRALLETHRIN

ULTRA LOW VOLUME LIQUID

(*E*)-1-(6-chloro-3-pyridylmethyl)-*N*-nitroimidazolidin-2-ylideneamine

+

(*S*)-2-methyl-4-oxo-3-prop-2-ynylcyclopent-2-enyl(1*R*)-*cis*,*trans*-2,2-dimethyl-3-(2-methylprop-1-enyl) cyclopropanecarboxylate

World Health Organization

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Disclaimer[1]

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.

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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

IMIDACLOPRID + PRALLETHRIN Page

IMIDACLOPRID

INFORMATION

ISO common name

Imidacloprid (BSI, E-ISO 1750, published)

Synonyms

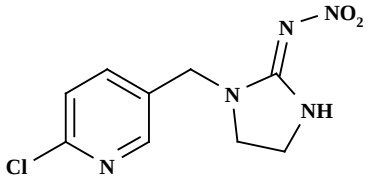
BAY NTN 33 893

Chemical names

IUPAC (*E*)-1-(6-chloro-3-pyridylmethyl)-*N*-nitroimidazolidin-2-ylideneamine

CA (2*E*)-1-[(6-chloro-3-pyridinyl)methyl]-*N*-nitro-2-imidazolidinimine

Structural formula



Empirical formula

$C_9H_{10}ClN_5O_2$

Relative molecular mass

255.7

CAS Registry number

138261-41-3

CIPAC number

582

Identity tests

Retention time in HPLC with UV-detection, IR, NMR

PRALLETHRIN

INFORMATION

ISO common name

Prallethrin* (ISO 1750, published) is the common name for the mixture of 8 stereoisomers

Chemical names

IUPAC (*RS*)-2-methyl-4-oxo-3-prop-2-ynylcyclopent-2-enyl (1*RS*)-cis-trans-2,2-dimethyl-3-(2-methylprop-1-enyl)cyclopropanecarboxylate

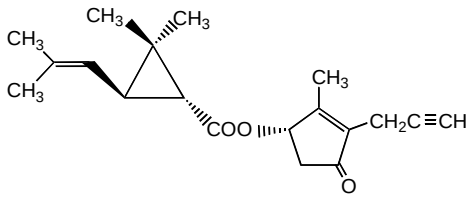
CA 2-methyl-4-oxo-3-(2-propyn-1-yl)-2-cyclopenten-1-yl-2,2-dimethyl-3-(2-methyl-1-propen-1-yl)cyclopropanecarboxylate

The mixture defined by the WHO specification 743/TC (November 2004) for the technical material is

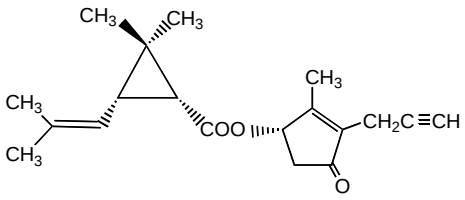
IUPAC (*S*)-2-methyl-4-oxo-3-prop-2-ynylcyclopent-2-enyl(1*R*)-*cis*,*trans*-2,2-dimethyl-3-(2-methylprop-1-enyl)cyclopropanecarboxylate

CA (*S*)-2-methyl-4-oxo-3-(2-propynyl)-2-cyclopent-1-yl (1*R*)-*cis*,*trans*-2,2-dimethyl-3-(2-methyl-1-propenyl)cyclopropanecarboxylate

Structural formula



1R,trans; S



1R,cis; S

prallethrin consists of [1R,trans; S] + [1R,cis; S] in approximate 4 : 1

Note: prallethrin, as defined in the accompanying specification, consists mainly of [1*R*,*trans*; *S*] and [1*R*,*cis*; *S*] isomers in a ratio of approximately 4:1. The E-ISO common name and CAS Registry number define prallethrin as the racemic mixture of the 8 possible stereoisomers implied by the structure. WHO recognizes that this use of the ISO common name is potentially confusing but, in the absence of an internationally accepted alternative, the name prallethrin is applied to the mixture defined by the WHO specification.

Empirical formula

$C_{19}H_{24}O_3$

Relative molecular mass

300.4

CAS Registry number

23031-36-9 (established for a mixture of 8 isomers)

CIPAC number

743

Identity tests

GC retention time, IR spectrum, stereo-selective HPLC (stereoisomer composition)

IMIDACLOPRID + PRALLETHIN ULTRA LOW VOLUME LIQUID

WHO specification 582+743/UL (February 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 (582+743/2018). It should be applicable to relevant products of this manufacturer, and those of any other formulators who use only imidacloprid TC and prallethrin TC from the evaluated sources. 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 imidacloprid TC and prallethrin TC from other sources. The evaluation report (582+743/2018), as PART TWO, forms an integral part of this publication.

1 Description

The material shall consist of technical imidacloprid, complying with the requirements of WHO specification 582/TC (February 2019), and of technical prallethrin, complying with the requirements of WHO specification 743/TC (November 2004) in the form of an organic liquid together with any necessary formulants. It shall be in the form of a stable homogeneous liquid, free from visible suspended matter and sediment.

2 Active ingredients

2.1 **Identity tests** (582/TC/M2/2, CIPAC Handbook K, p.70, 2003 and CIPAC/5162 for imidacloprid (Note 1); CIPAC 743/LV/M/2, CIPAC Handbook L, p.117, 2006 and CIPAC/5164 for prallethrin (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 **Imidacloprid content** (CIPAC/5162) (Note 1)

The imidacloprid content shall be declared (30 g/kg) and, when determined, the average content measured shall not differ from that declared by more than ± 10% of the declared content.

2.3 **Prallethrin content** (CIPAC/5164) (Note 2)

The total prallethrin isomers content shall be declared (7.5 g/kg) and, when determined, the average content measured shall not differ from that declared by more than ± 15% of the declared content.

* 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.

3 Storage stability

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

After storage at 0 ± 2°C for 7 days, the volume of solid and/or liquid which separates shall not be more than 0.3 ml.

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

After storage at 54 ± 2°C for 14 days, the determined average active ingredients content must not be lower than 95% relative to the determined average content found before storage (Note 3).

Note 1 The extension of the scope (CIPAC/5162) of CIPAC method 582/TC/M2/ for the determination of the imidacloprid content in UL formulations, with the modification of the run time, was accepted as provisional CIPAC method in 2018. Prior to its publication in the next Handbook, copies of the method can be obtained through the CIPAC website, https://www.cipac.org/index.php/methods-publications/pre-published-methods

Note 2 The extension of the scope (CIPAC/5164) of CIPAC method 743/LV/M/ for the determination of the prallethrin content in UL formulations, with the modifications in the inlet and detector temperatures and use of standard addition for quantification, was accepted as provisional CIPAC method in 2018. Prior to its publication in the next Handbook, copies of the method can be obtained through the CIPAC website, https://www.cipac.org/index.php/methods-publications/pre-published-methods

Note 3 Samples of the formulation taken before and after the storage stability test may be analyzed concurrently after the test in order to reduce the analytical error.

PART TWO

EVALUATION REPORTS

IMIDACLOPRID + PRALLETHRIN

IMIDACLOPRID + PRALLETHRIN

FAO/WHO EVALUATION REPORT 582+743/2018

Recommendations

The Meeting recommended that the specification for imidacloprid + prallethrin UL, proposed by Clarke Mosquito Control Products, Inc., as amended, should be adopted by WHO.

Appraisal

The Meeting considered the information in support of a new WHO specification for an UL formulation containing a mixture of imidacloprid and prallethrin, based on the draft specification and the supporting data provided by Clarke Mosquito Control Products, Inc. in 2016.

A FAO specification for imidacloprid TC (582/TC) was developed under the new procedure in 2004 based on submission of data from Bayer CropScience AG. In 2013 the existing TC specification was extended to the technical material produced by Cheminova A/S and in 2017 to the technical material produced by United Phosphorus Limited [FAO 2018]. Bayer CropScience agreed to extend the imidacloprid FAO TC specification to WHO as well.

The existing WHO specification for prallethrin TC (743/TC) was published in November 2004. The prallethrin specification is referring to prallethrin, consisting mainly of [1R,trans; S] and [1R,cis; S] isomers in a ratio of approximately 4:1. The E-ISO common name and CAS Registry number define prallethrin as the mixture of the four enantiomeric pairs of diastereomers implied by the structure [WHO 2004]. WHO recognizes that this use of the ISO common name is potentially confusing but, in the absence of an internationally accepted alternative, the name prallethrin is applied to the mixture defined by the WHO specification.

Letters of access were provided to Clarke Mosquito Control Products, Inc. from the manufacturers of the technical materials used in the UL formulation authorising the use of the information in those specifications in the scope of the evaluation of the ultra-low volume cold aerosol of Clarke Mosquito Control Products, Inc. [At. 4].

Supporting data on imidacloprid + prallethrin UL formulation were in accordance with the requirements of the third revision of the first edition of the Manual on development and use of FAO and WHO specifications for pesticides [FAO/WHO Manual] and supported the proposed specification.

The registration process of the UL formulation with the development code CMP123-004 is underway in a number of countries.

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 manufacturer 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. The Meeting

agreed that, exceptionally, a specification should be developed for the mixed formulation.

The proposed specification for UL was essentially in accordance with the requirements of the FAO/WHO Manual. It was confirmed that the clauses for pH and viscosity are not relevant for this formulation. Data were provided to support the clauses of the specification. The extension of the scope of CIPAC method 743/LV/M/ for the determination of the prallethrin content in UL formulations was accepted as provisional CIPAC method in 2018 [CIPAC/5164]. Since prallethrin isomer ratio is included in the TC specification, and isomer ratio will not change during storage of the formulation, a requirement for prallethrin isomer ratio was not included in the UL specification. The extension of the scope of CIPAC method 582/TC/M2/ for the determination of the imidacloprid content in UL formulations was accepted as provisional CIPAC method in 2018 [CIPAC/5162].

Test methods for determination of physico-chemical properties of the UL formulation were CIPAC, as indicated in the specification [CIPAC, J; CIPAC, K; CIPAC, L].

SUPPORTING INFORMATION

FOR

EVALUATION REPORT 582+743/2018

Uses

The mixed imidacloprid + prallethrin ultra-low volume (UL) formulation will primarily be applied directly (without dilution) using specialised cold fogging application equipment, hand held and vehicle mounted (indoor and outdoor applications).

Formulations

The UL formulation is under development and registration process is underway in a number of countries: Mexico, Brazil, Columbia, Malaysia, Indonesia, India, Thailand, Philippines, Saudi Arabia, Turkey, Egypt (and approximately 20-24 other countries).

The formulation does not contain any adjuvant or synergist.

Methods of analysis

The analytical method for identification and determination of imidacloprid in TC is a full CIPAC method. Full CIPAC methods are available for identification and determination of prallethrin in TC and LV formulations. The extensions of the methods for the determination of the content of the active ingredients to the UL formulation were adopted as provisional CIPAC methods in 2018.

Containers and packaging

The commercial formulation will be packed in either Fluorinated High Density Polythene (FHDPE) bottles for hand held application or in coated metal drums for truck mounted application.

Expression of the active ingredient

The active ingredients are expressed as imidacloprid and prallethrin and are to be quantified as such.

ANNEX 1: REFERENCES

Study number	Author(s)	Year	Study title. Study identification number. Report identification number. GLP [if GLP]. Company conducting the study
FAO, 2018		2018	http://www.fao.org/fileadmin/templates/agphome/documents/Pests_Pesticides/Specs/Imidacloprid_2018_05_21.pdf
WHO, 2004		2004	http://www.who.int/neglected_diseases/vector_ecology/pesticide-specifications/en/prallethrin_spec_eval_Nov_2004.pdf
At. 4		2016	Attachment#4 Sumitomo and UPL Letters of Access.pdf
FAO/WHO Manual		2016	Manual on development and use of FAO and WHO specifications for pesticides, First edition – third revision, FAO Plant Production and Protection Paper 228.
CIPAC, J	Martijn A and Dobrat W	2000	CIPAC Handbook Volume J. Analysis of Technical and Formulated Pesticides, p.126, 128.
CIPAC, K	Martijn A and Dobrat W	2003	CIPAC Handbook Volume K. Analysis of Technical and Formulated Pesticides, p.70.
CIPAC, L	Martijn A and Dobrat W	2006	CIPAC Handbook Volume L. Analysis of Technical and Formulated Pesticides, p.118.
CIPAC/5164		2018	Prallethrin 743/LV/M/- Method Extension for Prallethrin UL
CIPAC/5162		2018	Imidacloprid, 582/TC/M2/- Method Extension for Imidacloprid UL