WHO SPECIFICATIONS AND EVALUATIONS FOR PUBLIC HEALTH PESTICIDES

CLOTHIANIDIN + DELTAMETHRIN

(*E*)-1-[(2-chloro-1,3-thiazol-5-yl)methyl]-3-methyl-2-nitroguanidine

+

(*S*)-α-cyano-3-phenoxybenzyl (1*R*,3*R*)-3-(2,2-dibromovinyl)-2,2-dimethylcyclopropanecarboxylate

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[2] 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. evaluation reports include 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 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.

[2] Publications available on the WHO Prequalification Unit – Vector Control Product Assessment Team (PQT/VCP) website, https://extranet.who.int/pqweb/vector-control-products

PART ONE: SPECIFICATIONS

Clothianidin Information

ISO common name

Clothianidin (ISO 1750 published)

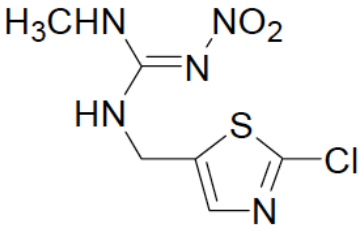
Chemical name

IUPAC (*E*)-1-[(2-chloro-1,3-thiazol-5-yl)methyl]-3-methyl-2-nitroguanidine

CA [*C*(*E*)]-*N*-[(2-chloro-5-thiazolyl)methyl]-*N′*-methyl-*N″*-nitroguanidine

Synonyms TI-435

Structural formula



Molecular formula

$C_6H_8ClN_5O_2S$

Relative molecular mass

249.7

CAS Registry number

210880-92-5

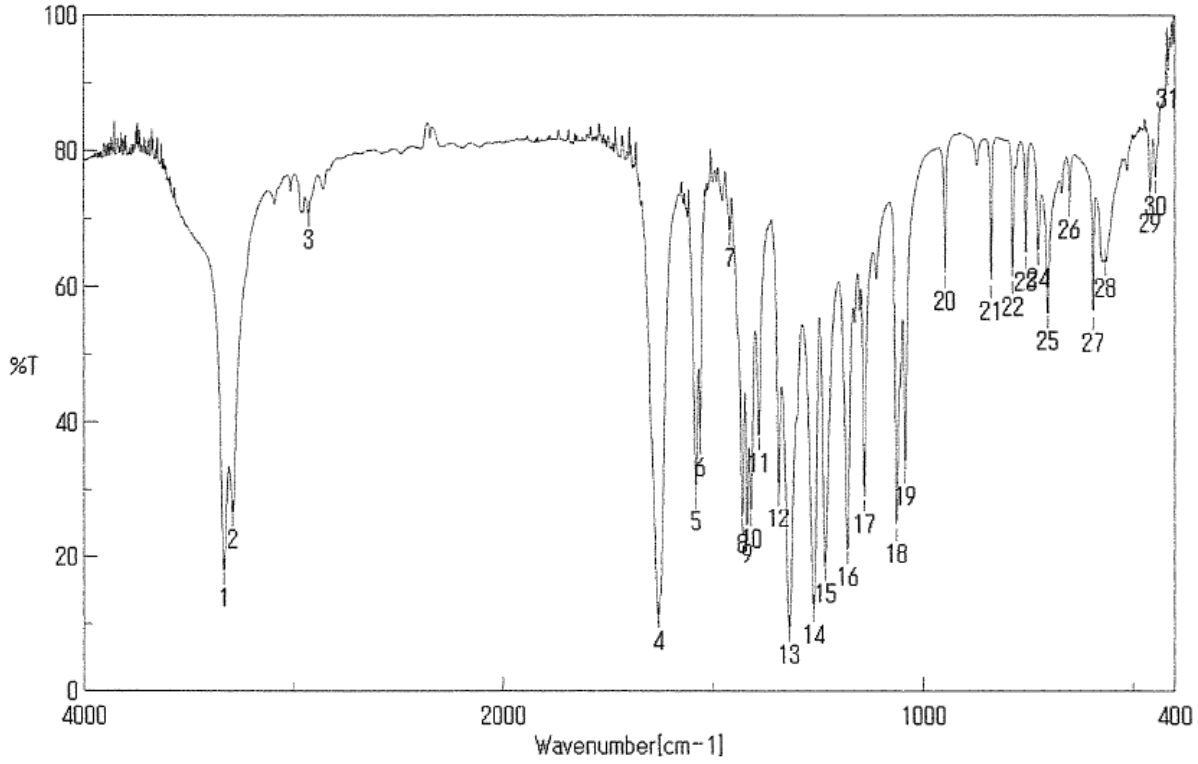
CIPAC number

738

Identity tests

Retention time in reversed phase HPLC, IR spectrum

Figure 1. IR spectrum of clothianidin



Deltamethrin Information

ISO common names

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

Synonyms

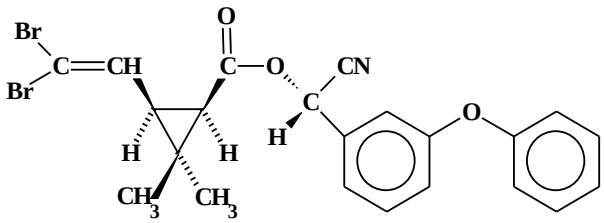
Decamethrin (rejected common name)

Chemical names

IUPAC (*S*)-α-cyano-3-phenoxybenzyl (1*R*,3*R*)-3-(2,2-dibromovinyl)-2,2-dimethylcyclopropanecarboxylate

CA [1*R*-[1α(*S**),3α]]-cyano(3-phenoxyphenyl)methyl 3-(2,2-dibromoethenyl)-2,2-dimethylcyclopropanecarboxylate

Structural formula



Empirical formula

$C_{22}H_{19}Br_2NO_3$

Relative molecular mass

505.2

CAS Registry number

52918-63-5

CIPAC number

333

EEC number

258-256-6

Identity tests

Retention time in reversed phase and enantioselective HPLC; TLC; IR, NMR and mass spectra

Clothianidin + Deltamethrin Wettable Powder

WHO specification 738+333/WP (September 2021*)

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 (738+333/2021). The specification should be applicable to relevant products of this manufacturer and those of any other formulators who use only 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 TC from other sources. The evaluation report (738+333/2021), as PART TWO, forms an integral part of this publication.

1 Description

The material shall consist of a homogeneous mixture of technical clothianidin, complying with the requirements of WHO specification 738/TC/1 or 738/TC/2 and technical deltamethrin, complying with the requirements of WHO Specification 333/TC, together with filler(s) and any other necessary formulants. It shall be in the form of a fine powder, free from visible extraneous matter and hard lumps.

2 Active ingredient

2.1 **Identity tests** (738/WP/M/2, CIPAC Handbook P, p.52, 2021 for clothianidin and 333/WP/(M)/2, CIPAC Handbook L, p.50, 2006 for deltamethrin)

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 **Clothianidin content** (738/WP/M/3, CIPAC Handbook P, p.52, 2021)

The clothianidin content shall be declared (500 g/kg) and, when determined, the average content measured shall not differ from that declared by more than ± 5%.

2.3 **Deltamethrin content** (333/WP/(M)/3, CIPAC Handbook L, p.50, 2006)

The deltamethrin content shall be declared (62.5 g/kg) and, when determined, the average content measured shall not differ from that declared by more than ± 10%.

3 Relevant impurities (Notes 1 & 2)

4 Physical properties

4.1 **pH range** (MT 75.3, CIPAC Handbook J, p. 131, 2000)

pH range: 3.0 to 6.0

* Specifications may be revised and/or additional evaluations may be undertaken. Ensure the use of current versions by checking at the WHO Prequalification Unit – Vector Control Product Assessment Team (PQT/VCP) website, https://extranet.who.int/pqweb/vector-control-products

4.2 **Wettability** (MT 53.3.1, CIPAC Handbook F, p.165, 1995)

The formulation shall be completely wetted in 1 minute without swirling.

4.3 **Wet sieve test** (MT 185, CIPAC Handbook K, p.149, 2003)

Maximum: 1% retained on a 75 µm test sieve.

4.4 **Suspensibility** (MT 184.1, CIPAC Handbook P, p.245, 2021) (Notes 3 & 4)

Suspensibility: minimum 70% after 30 minutes in CIPAC Standard Water D at 25 ± 5°C.

4.5 **Persistent foam** (MT 47.3, CIPAC Handbook O, p.177, 2017) (Note 5)

Maximum: 50 ml after 1 minute.

5 Storage stability

5.1 **Stability at elevated temperature** (MT 46.4, CIPAC Handbook P, p.232, 2021)

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 6), and the formulation shall continue to comply with the clauses for:

- pH range (4.1);
- wettability (4.2);
- wet sieve test (4.3);
- suspensibility (4.4);
- persistent foam (4.5).

Note 1 There are no relevant impurities to be controlled in the clothianidin products of the manufacturer identified in the evaluation reports 738+333/2016 and 738+333/2021. However, a compound (TI triazan, IUPAC name: (Z)-5-benzyl-1-methyl-N-nitro-1,3,5-triazinan-2-imine, CAS-Nr. 141856-57-7) may occur as a result of certain manufacturing processes. If this impurity could occur at > 3 g/kg (of clothianidin) in the products of other manufacturers, it would be designated as a relevant impurity, and a clause would be required to limit its concentration.

Note 2 There are no relevant impurities to be controlled in deltamethrin products of the manufacturers identified in evaluation reports 738+333/2016 and 738+333/2021. However, becisthemic acid chloride [(1*R*,3*R*)-3-(2,2-dibromovinyl)-2,2-dimethylcyclopropane carboxoyl chloride], sometimes spelt bicisthemic acid chloride, can occur as a result of certain manufacturing processes. If this impurity could occur at ≥1 g/kg (of deltamethrin) in the products of other manufacturers, it would be designated as a relevant impurity, and a clause would be required to limit its concentration.

Note 3 The formulation should be tested at the highest and lowest rates of use recommended by the supplier, provided this does not exceed the conditions given in method MT 184.1.

Note 4 Chemical assay is the only fully reliable method to measure the mass of active ingredient still in suspension. However, the simpler gravimetric method may be used on a routine basis provided that it has been shown to give equal results to those of chemical assay. In case of dispute, chemical assay shall be the referee method.

Note 5 The mass of sample to be used in the test should be at the highest rate of use recommended by the supplier. The test is to be conducted in CIPAC standard water D at 25 ± 5°C.

Note 6 Samples of the formulation taken before and after the accelerated storage stability test may be analyzed concurrently after the test in order to reduce the analytical error.

Clothianidin + Deltamethrin Wettable Powder
In Sealed Water Soluble Bag

WHO specification 738+333/WP-SB (September 2021*)

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 (738+333/2016, 738/2020.1, 738+333/2021). The specification should be applicable to relevant products of this manufacturer and those of any other formulators who use only 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 TC from other sources. The evaluation reports (738+333/2016, 738.2020.1, 738+333/2020.1), as PART TWO, form an integral part of this publication.

1 Description

The material shall consist of a defined quantity of a homogeneous mixture of technical clothianidin, complying with the requirements of WHO specification 738/TC/1 or 738/TC/2 and technical deltamethrin, complying with the requirements of WHO specification 333/TC, together with filler(s) and any other necessary formulants. It shall be in the form of a fine powder, free from visible extraneous matter and hard lumps, contained in a sealed water soluble bag.

2 Active ingredient

2.1 **Identity tests** (738/WP/M/2, CIPAC Handbook P, p.52, 2021 for clothianidin and 333/WP/(M)/2, CIPAC Handbook L, p.50, 2006 for deltamethrin)

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 **Clothianidin content** (738/WP/M/3, CIPAC Handbook P, p.52, 2021)

The clothianidin content shall be declared (500 g/kg) and, when determined, the average content measured shall not differ from that declared by more than ± 5 %.

2.3 **Deltamethrin content** (333/WP/(M)/3, CIPAC Handbook L, p.50, 2006)

The deltamethrin content shall be declared (62.5 g/kg) and, when determined, the average content measured shall not differ from that declared by more than ± 10 %.

3 Relevant impurities (Notes 1 & 2)

4 Physical properties (Note 3)

4.1 **pH range** (MT 75.3, CIPAC Handbook J, p.131, 2000)

* Specifications may be revised and/or additional evaluations may be undertaken. Ensure the use of current versions by checking at the WHO Prequalification Unit – Vector Control Product Assessment Team (PQT/VCP) website, https://extranet.who.int/pqweb/vector-control-products

pH range: 3.0 to 6.0

4.2 **Wettability** (MT 53.3.1, CIPAC Handbook F, p.165, 1995)

The formulation shall be completely wetted in 1 minute without swirling.

4.3 **Wet sieve test** (MT 185, CIPAC Handbook K, p.149, 2003)

Maximum: 1% retained on a 75 µm test sieve.

4.4 **Suspensibility** (MT 184.1, CIPAC Handbook P, p.245, 2021) (Notes 3, 4, 5 & 6)

The suspensibility shall be tested on a suspension containing the WP and the bag material in the actual ratio of application, prepared according to the procedure described in Note 6.

Suspensibility: minimum 70% after 30 minutes in CIPAC Standard Water D at 25 ± 5°C.

4.5 **Persistent foam** (MT 47.3, CIPAC Handbook O, p.177, 2017) (Notes 3, 6 & 7)

The persistent foam shall be tested on a suspension containing the WP and the bag material in the actual ratio of application in CIPAC Standard Water D, prepared according to the procedure described in Note 6.

Maximum: 50 ml after 12 minutes.

4.6 **Dissolution of the bag** (MT 176, CIPAC Handbook F, p.440, 1995) (Notes 3 & 8)

The dissolution of the bag shall be tested on a sample of the emptied and cleaned bag together with an appropriate proportion of the WP in CIPAC Standard Water D taken according to the procedure described in Note 9.

Flow time of the suspension: maximum 30 seconds.

5 Storage stability

5.1 **Stability at elevated temperature** (MT 46.4, CIPAC Handbook P, p.232, 2021)

The package should be enclosed in a watertight sachet, box or any other container at 54°C ± 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 9), and the formulation shall continue to comply with the clauses for:

- pH range (4.1);
- wettability (4.2);
- wet sieve test (4.3);
- suspensibility (4.4);
- persistent foam (4.5);
- dissolution of the bag (4.6)

None of the bags tested should show signs of leakage or rupture during normal handling, before and after storage.

Note 1 There are no relevant impurities to be controlled in the clothianidin products of the manufacturer identified in the evaluation reports 738+333/2016 and 738+333/2021. However, a compound (TI triazan, IUPAC name: (Z)-5-benzyl-1-methyl-N-nitro-1,3,5-triazinan-2-imine,

CAS-Nr. 141856-57-7) may occur as a result of certain manufacturing processes. If this impurity would occur at > 3 g/kg (of clothianidin) in the products of other manufacturers, it would be designated as a relevant impurity, and a clause would be required to limit its concentration.

Note 2 There are no relevant impurities to be controlled in deltamethrin products of the manufacturers identified in evaluation reports 738+333/2016 and 738+333/2021. However, becisthemic acid chloride [(1*R*,3*R*)-3-(2,2-dibromovinyl)-2,2-dimethylcyclopropane carboxoyl chloride], sometimes spelt bicisthemic acid chloride, may occur as a result of certain manufacturing processes. If this impurity would occur at ≥1 g/kg (of deltamethrin) in the products of other manufacturers, it would be designated as a relevant impurity, and a clause would be required to limit its concentration.

Note 3 Sub-sampling

Lay the bag on a bench and carefully open one side of the bag with a cutter, taking care not to damage the seals. Transfer the contents of the bag into a suitable flask. This material shall be used to carry out the tests for:

- active ingredients identity (2.1),
- active ingredients content (2.2 & 2.3),
- pH range (4.1),
- wettability (4.2),
- wet sieve test (4.3),
- suspensibility (4.4),
- persistent foam (4.5),
- dissolution of the bag (4.6).

The bag is then opened on three sides, completely cleaned from adhering powder by brushing or suction, and weighed to the nearest 0.01 g. Aliquots of an aqueous solution of the bag material shall be used in the suspensibility (4.4) and persistent foam (4.5) tests.

In the case of delay of the above tests, the bag shall be stored in a watertight container (glass bottle or equivalent) to avoid any change in its properties.

Note 4 The formulation should be tested at the highest and lowest rates of use recommended by the supplier, provided this does not exceed the conditions given in method MT 184.1.

Note 5 Chemical assay is the only fully reliable method to measure the mass of active ingredient still in suspension. However, the simpler gravimetric method may be used on a routine basis provided that it has been shown to give equal results to those of chemical assay. In case of dispute, chemical assay shall be the referee method.

Note 6 The procedure for adding the bag material to the solution for the suspensibility and persistent foam tests should be as follows:

Prepare a stock solution of the bag material (1 mg/ml) by weighing a sample (n mg) of the bag (excluding sealed parts). Dissolve this sample by stirring in the standard water used for the tests to give a final volume of n ml. Store the stock solution in a stoppered bottle before use.

Calculate the volume (V ml) of the stock solution of the bag to be added to the test suspension of the water dispersible granule according to the following equation:

$$V(\text{ml}) = X \times \frac{1000B}{W}$$

Where: B (g) = weight of the emptied and cleaned bag
W (g) = nominal weight of the WP contained in the bag
X (g) = weight of the WP sample used in the test

Note 7 The mass of sample to be used in the test should be specified at the highest rate recommended by the supplier. The test is to be conducted in CIPAC standard water D at 25 ± 5 °C.

Note 8 The sampling of the bag for the dissolution test should be as follows:

Lay the empty cleaned bag in its original configuration (double layer). Delineate and then cut up a test sample including part of the upper seal (5 cm) and symmetrically including the vertical seal (10 cm). If the size of the bag is less than this dimension, use the whole bag.

Carry out the dissolution test immediately to avoid any modification of the sample.

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

PART TWO: EVALUATION REPORTS

CLOTHIANIDIN + DELTAMETHRIN

CLOTHIANIDIN + DELTAMETHRIN

WHO Evaluation Report 738+333/2021

WHO Assessment Report

A change application was submitted by Bayer CropScience in 2020 to WHO PQT/VCP in relation to the prequalified product Fludora Fusion (PQ Ref #008-006) for the inclusion of an alternate form of the co-formulated clothianidin and deltamethrin (500 + 62.5 g/kg) product. The proposed change was to make available the same WP formulation without the water soluble bag packaging.

WHO assessed the submitted information. The assessment supported the establishment of the WP specification, including the proposed clauses. Based on the information submitted, the pH clause for the WP-SB specification was amended from 3.0 - 7.0 to 3.0 - 6.0.

WHO conducted a human health risk assessment to evaluate the potential impacts of the change in packaging to occupational exposure and risk. The proposed change did not result in any unacceptable risks.

Annex 1: References

Study number	Author(s)	Year	Study title. Study identification number. Report identification number. GLP [if GLP]. Company conducting the study
M-778247-01-1	Hutin P.	2021	Justification of the proposed WHO specifications for Clothianidin + Deltamethrin Wettable Powder regarding pH range and persistent foaming. Bayer S.A.S. Division CropScience, France

CLOTHIANIDIN

CLOTHIANIDIN + DELTAMETHRIN

FAO/WHO Evaluation Report 738/2020.1

Recommendations

The Meeting recommended the following:

(i) The change of manufacturer of the FAO reference specifications for clothianidin TC and FS from Bayer CropScience to BASF SE should be noted by FAO.

(ii) The editorially updated specifications for clothianidin TC and FS should be adopted by FAO.

(iii) The change of manufacturer of the WHO reference specification for clothianidin TC from Bayer CropScience to BASF SE should be noted by WHO.

(iv) The editorially updated specifications for clothianidin TC and clothianidin + deltamethrin WP-SB should be adopted by WHO.

Appraisal

The Meeting noted that in a press release dated April 26, 2018[1], BASF SE, Germany (BASF) announced the acquisition of clothianidin TC and certain formulated products from Bayer CropScience (BCS). Before then, BCS was the holder of one of the reference FAO and WHO specifications for clothianidin TC and the FAO specification for clothianidin FS (FAO/WHO evaluation reports 738/2015).

Later on, FAO and WHO were contacted by BCS in an official letter dated October 31, 2019, and in an e-mail dated December 10, 2019, stating the following:

- The intellectual property rights for clothianidin TC and certain formulations used in agriculture from BCS had been acquired by BASF.
- The manufacturing of clothianidin TC and certain formulations used in agriculture which are now under control of BASF continue to comply with all specifications clauses and limits as per the data package in support of clothianidin that had been evaluated by JMPS in 2015.
- BASF assures the continued support and stewardship for clothianidin TC and certain formulations acquired from BCS.
- The clothianidin + deltamethrin WP-SB formulation used in public health remains the property of BCS.

The Meeting therefore concluded that both the manufacturing sites and processes for manufacturing clothianidin TC and certain formulated products used in agriculture were not affected by the transition from BCS to BASF.

The Meeting also noted that the specifications for clothianidin FS and clothianidin + deltamethrin WP-SB needed some editorial updates to reflect the latest versions of certain physical-chemical test methods (suspensibility: MT 184.1 instead of MT 184, stability at elevated temperature: MT 46.4 instead of MT 46.3, both considered to provide equivalent results with the previous versions).

[1] https://www.basf.com/global/en/media/news-releases/2018/04/p-18-182.html

For these reasons, the Meeting recommended that BASF should be noted as the new holder of the reference specifications for clothianidin TC previously owned by BCS and formulated products used in agriculture, and that these specifications should be considered as the new reference specifications.

CLOTHIANIDIN + DELTAMETHRIN

FAO/WHO Evaluation Report 738+333/2020.2

Recommendations

The Meeting recommended that the existing WHO specification for clothianidin + deltamethrin 500 + 62.5 g/kg wettable powder in sealed water soluble bag (WP-SB) should be extended to encompass the corresponding product of Tagros Chemicals India Limited.

Appraisal

The Meeting considered data and information submitted in 2019 by Tagros Chemicals India Limited (Tagros), to support the extension of the existing WHO specification 738+333/WP-SB for clothianidin and deltamethrin wettable powder in sealed water soluble bag (WP-SB). The data submitted were in accordance with the requirements of the Manual on development and use of FAO and WHO specifications for pesticides (2016, third revision of the first edition).

An FAO/WHO specification for deltamethrin TC (333/TC) was developed in 2004 based on submission of data from Bayer CropScience and extended in 2005 to the technical material produced by Tagros. The reference specification for deltamethrin TC was revised in 2016, and consequently, the deltamethrin TC produced by Tagros was re-evaluated based on the submission of new data and accepted in 2017 as equivalent to the deltamethrin TC revised reference specification. The source of deltamethrin TC in their WP-SB formulation is from Tagros. The clothianidin TC of Tagros was accepted in 2020 as equivalent to the reference profile of Sumitomo clothianidin TC based on Tier-1 and Tier-2 data. The source of clothianidin TC in their WP-SB formulation is from Tagros. The reference specification and supporting data for clothianidin + deltamethrin WP-SB had been provided by Bayer CropScience.

Tagros provided a GLP study on determination of physical-chemical properties of their clothianidin 50% + deltamethrin 6.25% WP-SB formulation including active ingredients content, pH, wettability, wet sieve test, suspensibility for clothianidin and deltamethrin, persistent foam, dissolution rate of water soluble bags and stability after storage at 54 ± 2°C for 14 days, for a single batch of WP-SB. The data submitted supported the clauses and the proposed limits for clothianidin + deltamethrin 500 + 62.5 g/kg WP-SB. The proposer indicated that the specification is representative of the quality of their WP-SB and confirmed this statement by providing historical QC data (10 different batches) for active ingredients content and all physical-chemical properties before and after accelerated storage. The data submitted by Tagros complied with the existing specification for clothianidin + deltamethrin WP-SB.

Tagros tested their clothianidin + deltamethrin WP-SB for all the physical-chemical properties using the most recent CIPAC methods. Tagros used the CIPAC method 333/WP/M/3 published in Handbook L for determination of deltamethrin content (before and after storage). Deltamethrin was determined by normal phase HPLC using external standardization and UV detection at 230 nm. Tagros used the CIPAC method 738//WP/M/3 published in Handbook P for determination of clothianidin content (before and after storage). Clothianidin was determined by a reversed phase HPLC using external standardization and UV detection at 269 nm.

The stability of the WP-SB formulation in the accelerated storage test MT 46.4 was demonstrated to be acceptable, and no significant deterioration was observed in terms of active ingredients content, suspensibility, residues after sieving, pH, persistent foam, wettability and dissolution rate of water soluble bags.

Additional Action proposed by the Meeting:

The Meeting recommended to reference in the specifications for the WP and WP-SB the extended CIPAC methods 738/WP/M/2 and 738/WP/M/3 for clothianidin identity and content, as currently published in the CIPAC Handbook P. The Meeting also recommended to update the CIPAC methods for suspensibility (MT 184.1 instead of MT 184) and stability at elevated temperature (MT 46.4 instead of MT 46.3). These updated methods published in CIPAC Handbook P are considered to provide equivalent results with the previous versions.

CLOTHIANIDIN + DELTAMETHRIN

FAO/WHO Evaluation Report 738+333/2016

Recommendations

The Meeting recommended that the specifications for clothianidin TC and clothianidin + deltamethrin 500 + 62.5 g/kg WP-SB, proposed by Bayer CropScience, as amended, should be adopted by WHO.

Appraisal

A draft specification for clothianidin and deltamethrin co-formulated as 500 + 62.5 g/kg WP-SB, provided by Bayer CropScience, was received in 2015 and considered by the Meeting for development of a new WHO specification. A data package on physical-chemical properties of the formulation in the water soluble bag was also received (Mo5190, 2015) and supported the clauses and the proposed limits. Both compounds have first been developed independently as mosquito adulticides for indoor residual spraying (IRS) by Sumitomo and Bayer, respectively, and the specification, therefore, is limited to WHO. Bayer CropScience has proposed this WP-SB product for use as indoor residual spraying. The product is intended to complement the existing WHO specifications for the single active ingredient formulations for controlling pyrethroid resistant vectors.

The active ingredient clothianidin is one of the rare examples, where nominally the same active ingredient has been proposed for FAO and WHO reference specifications by two different companies (see a brief outline of the development history of clothianidin in the 2015 evaluation report). The source of clothianidin in the formulated product is from Bayer, which is relevant to know as the two TC specifications are similar but not identical. FAO specifications for clothianidin TC and FS, based on the data package submitted by Bayer CropScience, were published in October 2016. The Meeting therefore agreed to publish also a WHO specification for clothianidin TC, based on the specification published by FAO.

The proposed specification for clothianidin + deltamethrin 500 + 62.5 g/kg WP-SB was broadly in agreement with the guidelines given in the Manual (FAO/WHO 2010) and the new guideline for WP packed in water soluble bags.

Formulation type, description, content of active ingredients and analytical methods

The two active ingredients are co-formulated as a wettable powder packed in a water soluble bag. The amount of formulation in a single sachet is 80 or 100 g. The whole content including sachet is dispersed in a final volume of 8 or 10 L (for the 80 and 100 g sachet, respectively) in a pressurized sprayer. The proposed application concentration is therefore always 1 %.

One of the active ingredients (clothianidin) is currently (January 2018) under WHO evaluation as a product for IRS (Sumishield WG, containing 500 g/kg clothianidin). Deltamethrin (in the form of a 25 % WG-SB) has received WHOPES recommendation for IRS in 2002. The WHO specifications for clothianidin TC and WG proposed by Sumitomo were published in September 2017. In the case of the current product, the Meeting proposed to jointly publish the specification for clothianidin TC produced by Bayer together with that for the WP-SB. The appraisal of the evaluation of the TC however refers to the initial proposition of the FAO

specifications for the TC and FS formulation and has been adopted as such from the FAO specification (FAO, 2016).

The extension of the analytical methods for confirmation of the identity and determination of clothianidin content to WP formulations have been presented at the CIPAC Meeting in 2016 and was adopted as full CIPAC method in 2017. The method for deltamethrin is a full CIPAC method published in Handbook L.

Physical-chemical properties, storage stability

In certain tests to be carried out to assess the physical-chemical parameters of the WB-SB, the neat formulation is used (e.g., in pH range, wet sieve test and wettability). The results of the studies show that the formulation complies with the specified limits.

Whereas both active ingredients in the formulation are expected to be fairly stable at 54°C for two weeks, the water soluble polymer material used for the bag may deterioriate and have an impact on the limits of certain clauses like dissolution of the bag and wet sieve test. The test results of samples before and after storage at 54°C for two weeks showed that the physical-chemical parameters were not adversely affected after storage at 54°C.

The Meeting questioned the necessity of specifying both a pH range (3.0 to 7.0) and acidity (10 g/kg). The company responded that pH-range was deemed sufficient to ensure the quality of the product and the clause for acidity was removed.

The clauses and limits in the physical-chemical subsection were essentially in agreement with the requirement of the Manual. In addition to standard clauses for a WP-SB formulation, the persistent foam after storage was included in agreement with the latest amendments of the Manual. After accelerated storage at 54°C for 2 weeks, the products still complies with the clauses for pH, wettability, wet sieve test, suspensibility, persistent foam and dissolution of the bag.

Annex 1: References

Study number	Author(s)	Year	Study title. Study identification number. Report identification number. GLP [if GLP]. Company conducting the study
Mo5190	Brux A.	2015	Determination of physico-chemical Properties and Storage Stability Tests for CTD+DLT WP-SB 50+6,25 in Composite Film Bags, BioGenius, Germany. GLP.