Food and Agriculture Organization
of the United Nations

FAO SPECIFICATIONS AND EVALUATIONS

FOR AGRICULTURAL PESTICIDES

CLOTHIANIDIN

(*E*)-1-(2-chloro-1,3-thiazol-5-ylmethyl)-3-methyl-2-nitroguanidine

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DISCLAIMER[1]

FAO 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.

FAO disclaims any and all liability for any injury, death, loss, damage or other prejudice of any kind that may 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, FAO 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.

FAO 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, FAO does not in any way warrant or represent that any pesticide claimed to comply with a FAO specification actually does so.

[1] This disclaimer applies to all specifications published by FAO.

INTRODUCTION

FAO establishes and publishes specifications* for technical material and related formulations of agricultural 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 1999 onward, the development of FAO specifications follows the **New Procedure**, described first in the 5th edition of the "Manual on the development and use of FAO specifications for plant protection products" and later in the 1st edition of "Manual for Development and Use of FAO and WHO Specifications for Pesticides" (2002) - currently available as the 2nd edition of the "Manual on development and use of FAO and WHO specifications for chemical pesticides (2022)"-, 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 FAO and the Experts of the FAO/WHO Joint Meeting on Pesticide Specifications (JMPS). [Note: prior to 2002, the Experts were of the FAO Panel of Experts on Pesticide Specifications, Registration Requirements, Application Standards and Prior Informed Consent, which now forms part of the JMPM, rather than the JMPS.]

FAO Specifications now only apply to products for which the technical materials have been evaluated. Consequently, from the year 1999 onwards the publication of FAO 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 8 of the "Manual on development and use of FAO and WHO specifications for chemical pesticides".

Part Two: The Evaluation Report(s) of the pesticide, reflecting the evaluation of the data package carried out by FAO 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.

FAO specifications developed 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. FAO 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.

* NOTE: PUBLICATIONS ARE AVAILABLE ON THE INTERNET AT http://www.fao.org/pest-and-pesticide-management/guidelines-standards/faowho-joint-meeting-on-pesticide-specifications-jmps/pesticide-specifications/pesticide-specifications-list/en/

PART ONE

SPECIFICATIONS

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CLOTHIANIDIN

INFORMATION

ISO common name

Clothianidin (ISO 1750 published)

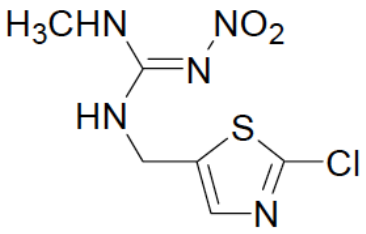
Chemical name

IUPAC (*E*)-1-(2-chloro-1,3-thiazol-5-ylmethyl)-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 g/mol

CAS Registry number

210880-92-5

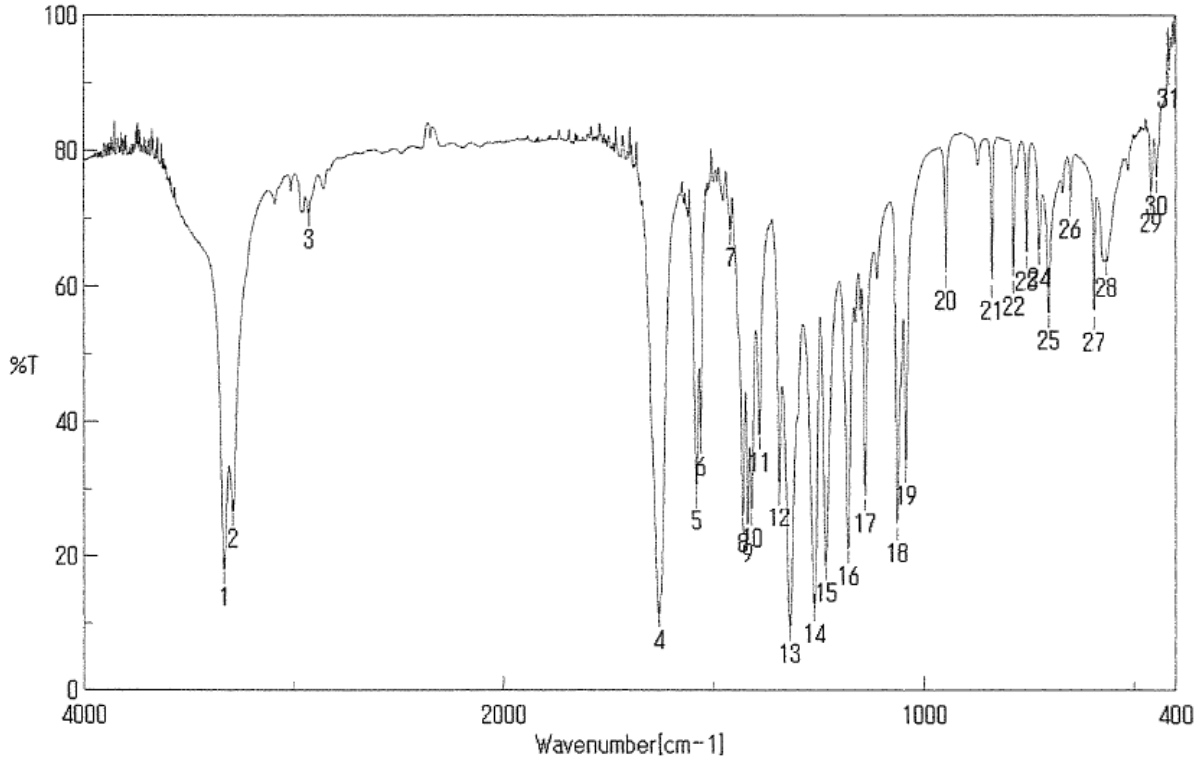
CIPAC number

738

Identity tests

Retention time in reversed phase HPLC, IR spectrum

Figure 1. IR spectrum of clothianidin



CLOTHIANIDIN TECHNICAL MATERIAL

FAO Specification 738 / TC (March 2022*)

This specification, which is PART ONE of this publication, is based on an evaluation of data submitted by the manufacturers whose names are listed in the evaluation reports (738/2009 & 738/2020). It should be applicable to relevant products of these manufacturers, 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 reports (738/2009 & 738/2020) as PART TWO forms an integral part of this publication

1 Description

The material shall consist of clothianidin together with related manufacturing impurities, and shall be white to pale yellow crystalline powder free from visible extraneous matter and added modifying agents.

2 Active ingredient

2.1 **Identity tests** (738/TC/M/2, CIPAC Handbook N, p.15, 2012)

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 **Clothianidin content** (738/TC/M/3, CIPAC Handbook N, p.15, 2012)

The clothianidin content shall be declared (not less than 960 g/kg) and, when determined, the average measured content shall not be lower than the declared minimum content.

* Specifications may be revised and/or additional evaluations may be undertaken. Ensure the use of current versions by checking at: https://www.fao.org/pest-and-pesticide-management/guidelines-standards/faowho-joint-meeting-on-pesticide-specifications-jmps/pesticide-specifications/en/

CLOTHIANIDIN SUSPENSION CONCENTRATE

FAO Specification 738 / SC (March 2022*)

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 (738/2009 & 738/2020). It 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 (738/2009 & 738/2020) as PART TWO, form an integral part of this publication.

1 Description

The material shall consist of a suspension of fine particles of technical clothianidin, complying with the requirements of FAO specification 738/TC (March 2022), in the form of a white or brown viscous liquid with faint characteristic odor, in an aqueous phase together with suitable formulants. After gentle agitation the material shall be homogeneous (Note1) and suitable for further dilution in water.

2 Active ingredient

2.1 Identity tests (738/SC/M/2, CIPAC Handbook N, p.19, 2012)

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 Clothianidin content (738/SC/M/3, CIPAC Handbook N, p.19, 2012) (Note 1)

The clothianidin content shall be declared (g/kg or g/l at 20 ± 2°C, Note 2) and, when determined, the average content measured shall not differ from that declared by more than the following tolerances:

Declared content in g/kg or g/l at 20 ± 2°C	Tolerance
above 100 up to 250	± 6 % or of the declared content
Note: The upper limit is included in the range	

3 Physical properties

3.1 Pourability (MT 148.1, CIPAC Handbook J, p.133, 2000)

Maximum "residue": 4 %.

* Specifications may be revised and/or additional evaluations may be undertaken. Ensure the use of current versions by checking at: https://www.fao.org/pest-and-pesticide-management/guidelines-standards/faowho-joint-meeting-on-pesticide-specifications-jmps/pesticide-specifications/en/

3.2 **Spontaneity of dispersion** (MT 160, CIPAC Handbook F, p.391, 1994) (Note 3)

A minimum of 90 % of the clothianidin content found under 2.2 shall be in suspension after 5 min in CIPAC Standard Water D at 30 ± 2°C.

3.3 **Suspensibility** (MT 184.1, CIPAC Handbook P, p.245, 2021) (Note 3)

A minimum of 95 % of the clothianidin content found under 2.2 shall be in suspension after 30 min in CIPAC Standard Water D at 30 ± 2°C.

3.4 **Wet sieve test** (MT 185, CIPAC Handbook K, p.149, 2003) (Note 4)

Maximum: 0.5 % of the formulation shall be retained on a 75 µm test sieve.

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

Maximum: 50 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 ± 2°C for 7 days, the formulation shall continue to comply with clauses for:

- suspensibility (3.3)
- wet sieve test (3.4)

4.2 **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 ingredient 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:

- pourability (3.1),
- spontaneity of dispersion (3.2),
- suspensibility (3.3).

Note 1 Before sampling to verify the formulation quality, inspect the commercial container carefully. On standing, suspension concentrates usually develop a concentration gradient from the top to the bottom of the container. This may even result in the appearance of a clear liquid on the top and/or of sediment on the bottom. Therefore, before sampling, homogenize the formulation 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. After this procedure, the container should not contain a sticky layer of non-dispersed matter at the bottom. A suitable and simple method of checking for a non-dispersed sticky layer "cake" is by probing with a glass rod or similar device adapted to the size and shape of the container. All the physical and chemical tests must be carried out on a laboratory sample taken after the recommended homogenization procedure

Note 2 Unless homogenization is carried out carefully, it is possible for the sample to become aerated. This can lead to errors in the determination of the mass per millilitre and in calculation of the active ingredient content (in g/l) if methods other than MT 3.3 are used. 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 3 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 4 This test detects coarse particles (e.g. caused by crystal growth) or agglomerates (crust formation) or extraneous materials which could cause blockage of spray nozzles or filters in the spray tank.

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

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

CLOTHIANIDIN WATER SOLUBLE GRANULES

FAO Specification 738 / SG (March 2022*)

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 (738/2009 & 738/2020). It 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 (738/2009 & 738/2020) as PART TWO, form an integral part of this publication.

1 Description

The material shall consist of granules containing technical clothianidin, complying with the requirements of the FAO specification 738/TC (March 2022), in the form of blue-green fine particle with faint characteristic odor, and suitable carriers and/or necessary formulants. It shall be homogeneous, free from visible extraneous matter and/or hard lumps, free flowing, and essentially non-dusty. The active ingredient shall be soluble in water. Insoluble carriers and formulants shall not interfere with compliance with 3.2.

2 Active ingredient

2.1 **Identity tests** (738/SG/M/2, CIPAC Handbook N, p.20, 2012)

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 **Clothianidin content** (738/SG/M/3, CIPAC Handbook N, p.20, 2012)

The clothianidin content shall be declared (g/kg) and, when determined, the average content measured shall not differ from that declared by more than the following tolerances:

Declared content in g/kg	Tolerance
above 100 up to 250	± 6 % or of the declared content
Note: The upper limit is included in the range	

* Specifications may be revised and/or additional evaluations may be undertaken. Ensure the use of current versions by checking at: https://www.fao.org/pest-and-pesticide-management/guidelines-standards/faowho-joint-meeting-on-pesticide-specifications-jmps/pesticide-specifications/en/

3 Physical properties

3.1 **Degree of dissolution and solution stability** (MT 179, CIPAC Handbook H, p.307, 1998)

Residue of formulation retained on a 75 µm test sieve after dissolution in CIPAC Standard Water D at 30 ± 2°C.

Maximum: 2 % after 5 min.
Maximum: 2 % after 18 hours.

3.2 **Persistent foam** (MT 47.3 CIPAC Handbook O, p. 177, 2017) (Note 1)

Maximum: 40 ml after 1 minute.

3.3 **Dustiness** (MT 171.1, CIPAC Handbook P, p. 235, 2021) (Note 2)

Essentially non-dusty.

3.4 **Attrition resistance** (MT 178.2, CIPAC Handbook H, p. 304, 1998)

Minimum: 98 % attrition resistance.

3.5 **Flowability** (MT 172.2, CIPAC Handbook P, p. 241, 2021)

At least 98 % of the formulation shall pass through a 5 mm test sieve after 20 drops of the sieve.

4 Storage stability

4.1 **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 ingredient content must not be lower that 95 % relative to the determined average content found before storage (Note 3) and the formulation shall continue to comply with the clauses for:

- Degree of dissolution and solution stability (3.1),
- dustiness (3.3),
- attrition resistance (3.4).

Note 1 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.

Note 2 Measurement of dustiness must be carried out on the sample "as received" and, where practicable, the sample should be taken from a newly opened container because changes in the water content of samples may influence dustiness significantly. The optical method of MT 171.1 usually shows good correlation with the gravimetric method and can, therefore, be used as an alternative where the equipment is available. Where the correlation is in doubt, it must be checked with the formulation to be tested. In case of dispute, the gravimetric method shall be used.

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.

CLOTHIANIDIN GRANULES

FAO Specification 738 / GR (March 2022*)

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 (738/2009 & 738/2020). It 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 (738/2009 & 738/2020) as PART TWO, form an integral part of this publication.

1 Description

The material shall consist of granules containing technical clothianidin, complying with the requirements of FAO specification 738/TC (March 2022), in the form of grey or red spheroidal granules with faint characteristic odor, together with suitable carriers and any other necessary formulants. It shall be dry, free from visible extraneous matter and hard lumps, free-flowing, essentially non-dusty and intended for application by machine.

2 Active ingredient

2.1 **Identity tests** (738/GR/M/2, CIPAC Handbook N, p.19, 2012)

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 **Clothianidin content** (738/GR/M/3, CIPAC Handbook N, p.19, 2012)

Declared content in g/kg	Tolerance
up to 25	± 25 % of the declared content
Note: The upper limit is included in the range	

3 Physical properties

3.1 **Nominal size range** (MT 58, CIPAC Handbook F, p.173, 1994) (Note 1)

Not less than 950 g/kg of the formulation shall be within the size range 200 to 2000 µm.

3.2 **Dustiness** (MT 171.1, CIPAC Handbook P, p. 235, 2021)

Nearly dust-free (Note 2).

3.3 **Attrition resistance** (MT178, CIPAC Handbook H, p.304, 1998)

Minimum 99 % attrition resistance.

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4 Storage stability

4.1 **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 ingredient content must not be lower than 95 % relative to the determined average content found before storage (Note 3) and the formulation shall continue to comply with the clauses for:

- nominal size range (3.1),
- dustiness (3.2),
- attrition resistance (3.3).

Note 1 Higher ratios increase the risk of segregation and adverse effects on the flow rate. This should be checked with the machine to be used. The purchaser should check that the nominal size range is suitable for his requirements, since different size ranges may affect biological activity.

Note 2 Measurement of dustiness must be carried out on the sample "as received" and, where practicable, the sample should be taken from a newly opened container because changes in the water content of samples may influence dustiness significantly. The optical method of MT 171.1 usually shows good correlation with the gravimetric method and can, therefore, be used as an alternative where the equipment is available. Where the correlation is in doubt, it must be checked with the formulation to be tested. In case of dispute, the gravimetric method shall be used.

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

CLOTHIANIDIN FLOWABLE CONCENTRATE FOR SEED TREATMENT

(Note 1)

FAO Specification 738 / FS (March 2022*)

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 (738/2009, 738/2010 & 738/2020). It 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 (738/2009, 738/ 2010 & 738/2020) as PART TWO, form an integral part of this publication.

1 Description

The material shall consist of a suspension of fine particles of technical clothianidin, complying with the requirements of FAO specification 738/TC (March 2022), in the form of white to off-white opaque slightly viscous liquid or dark pink to reddish opaque slightly viscous liquid with faint characteristic odour, in an aqueous phase together with suitable formulants, including colouring matter (Note 1). After gentle stirring or shaking, the material shall be a homogeneous uncoloured or coloured slightly viscous liquid, depending on the colour stated on the label (Note 2) and suitable for further dilution with water if necessary.

2 Active ingredient

2.1 **Identity tests** (738/FS/M/2, CIPAC Handbook N, p.20, 2012)

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 **Clothianidin content** (738/FS/M/3, CIPAC Handbook N, p.20, 2012)

The clothianidin content shall be declared (g/kg or g/l at 20 ± 2°C, Note 3) and, when determined, the average content measured shall not differ from that declared by more than the appropriate tolerances.

Declared content in g/kg or g/L at 20 ± 2°C	Tolerance
above 250 up to 500	± 5% or of the declared content
above 500	± 25 g/kg or g/L of the declared content
Note: In each range the upper limit is included	

* Specifications may be revised and/or additional evaluations may be undertaken. Ensure the use of current versions by checking at: https://www.fao.org/pest-and-pesticide-management/guidelines-standards/faowho-joint-meeting-on-pesticide-specifications-jmps/pesticide-specifications/en/

3 Physical properties

3.1 **Pourability** (MT 148.1, CIPAC Handbook J, p.133, 2000)

Maximum "residue": 4 %.

3.2 **Wet sieve test** (MT 185, CIPAC Handbook K, p.149, 2003) (Note 4)

Maximum: 0.5 % retained on a 75 µm test sieve.

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

If the product is intended to be used after dilution, persistent foam is to be measured at a 50 % dilution. In those conditions, the maximum is 60 mL after 1 min. This clause is not applicable where the product is used without dilution.

3.4 **Suspensibility** (MT 184.1, CIPAC Handbook P, p. 245, 2021) (Note 6)

If the product is intended to be used after dilution, suspensibility is to be measured at a 50 % dilution. In those conditions, a minimum of 90 % of the clothianidin content found under 2.2 shall be in suspension after 30 min in CIPAC Standard Water D at 30 ± 2°C. This clause is not applicable where the product is used without dilution.

4. Storage stability

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

After storage at 0 ± 2°C for 7 days, the formulation shall continue to comply with the clause for:

- wet sieve test (3.2).

5.2 **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 ingredient content must not be lower than 95 % relative to the determined average content found before storage (Note 7) and the formulation shall continue to comply with the clauses for:

- pourability (3.1),
- wet sieve test (3.2),
- suspensibility (3.4),

Note 1 The influence of treatment on germination is of major importance but it is not the subject of a specification clause because no test method is applicable to all types of seeds. To avoid adverse effects, users should apply the formulation strictly according to the recommendations of the manufacturer and should not treat seeds for which effect on germination is not known. Treated seeds should be stored in a suitable container and should be protected from excessive temperature and moisture.

The formulation shall contain a dye or pigment that permanently colours the seed after treatment (red is recommended). In some countries, there may be a legal requirement that a specific colour shall be used. The same colour must not be used for denaturing seeds intended for use as livestock feeding stuffs.

Note 2 Before sampling to verify the formulation quality, inspect the commercial container carefully. On standing, suspension concentrates usually develop a concentration gradient from the top to the bottom of the container. This may even result in the appearance of a clear liquid on the top and/or sediment on the bottom. Therefore, before sampling, homogenize the formulation according to the instructions given by the manufacturer or, in the absence of such instructions, gently shake the commercial container (for example by inverting the closed container several times, large containers must be opened and stirred adequately). After this procedure, the container should not contain a sticky layer of non-dispersed matter at the bottom. A suitable and simple method of checking for a non-dispersed sticky layer ("cake") is by probing with a glass rod or similar device adapted to the size and shape of the container. All the physical and chemical tests must be carried out on a laboratory sample taken after the recommended homogenization procedure.

Note 3 Unless homogenization is carried out carefully, it is possible for the sample to become aerated. This can lead to errors in the determination of the mass per millilitre, and in calculation of the active ingredient content (in g/l) if methods other than MT 3.3 are used. 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 4 This test should detect coarse particles (e.g. caused by crystal growth) or extraneous materials which could cause blockage of spray nozzles or filters of the application equipment.

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

Note 6 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 7 Samples of the formulation taken before and after the accelerated storage stability test may be analysed concurrently after the test in order to reduce the analytical error.

CLOTHIANIDIN WATER DISPERSIBLE GRANULES

FAO Specification FAO 738 / WG (March 2022*)

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 (738/2013 & 738/2020). It 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/ 2013 & 738/2020) as PART TWO, form an integral part of this publication.

1 Description

The material shall consist of an homogeneous mixture of technical clothianidin, complying with the requirements of the FAO specification 738/TC (March 2022), in the form of off-white to brown granules with faint characteristic odour, together with carriers and any other necessary formulants. It shall be in the form of granules for application after disintegration and dispersion in water. The formulation shall be dry, free-flowing, essentially non-dusty, and free from visible extraneous matter and hard lumps.

2 Active ingredient

2.1 **Identity tests** (738/WG/M/2, CIPAC Handbook N, p.17, 2012)

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 **Clothianidin content** (738/WG/M/3, CIPAC Handbook N, p.17, 2012) (Note 1)

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

Declared content in g/kg	Tolerance
above 500	± 25 g/kg of the declared content
Note: the upper limit is included in the range	

3 Physical properties

3.1 **Wettability** (MT 53.3, CIPAC Handbook F, p.164, 1994)

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

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

Maximum: 2 % retained on a 75 µm test sieve.

* Specifications may be revised and/or additional evaluations may be undertaken. Ensure the use of current versions by checking at: https://www.fao.org/pest-and-pesticide-management/guidelines-standards/faowho-joint-meeting-on-pesticide-specifications-jmps/pesticide-specifications/en/

3.3 **Dispersibility** (MT 174, CIPAC Handbook F, p.435, 1994)

Dispersibility: minimum 80 % after 1 minute of stirring.

3.4 **Suspensibility** (MT 184.1, CIPAC Handbook O, p.245, 2021) (Notes 2 & 3)

A minimum of 60 % shall be in suspension after 30 min in CIPAC Standard Water D at 30 ± 2°C.

3.5 **Persistent foam** (MT 47.2, CIPAC Handbook F, p.152, 1995) (Note 4)

Maximum: 60 ml after 1 minute.

3.6 **Dustiness** (MT 171.1, CIPAC Handbook P, p.235, 2021) (Note 5)

The formulation shall have a maximum collected dust of 30 mg by the gravimetric method.

3.7 **Flowability** (MT 172.2, CIPAC Handbook P, p.241, 2021)

At least 99 % of the formulation shall pass through a 5 mm test sieve after 20 drops of the sieve.

3.8 **Attrition resistance** (MT178.2, CIPAC Handbook K, p.140, 2003)

Minimum: 98 % attrition resistance.

4 Storage stability

4.1 **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 ingredient content must not be lower that 95 % relative to the determined average content found before storage (Note 6) and the formulation shall continue to comply with the clauses for:

- wet sieve test (3.2),
- dispersibility (3.3),
- suspensibility (3.4),
- dustiness (3.6),
- attrition resistance (3.8),
- suspensibility (3.4).

Note 1 The sonication time may be increased, if necessary.

Note 2 The formulation should be tested at the highest (0.05 %) and lowest rates (0.02 %) of use recommended by the supplier, provided this does not exceed the conditions given in a method MT 184.1.

Note 3 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 4 The mass of sample to be used in the test should be specified at the highest rate (0.05 %) recommended by the supplier. The test is to be conducted in CIPAC standard water D.

Note 5 Measurement of dustiness must be carried out on the sample "as received" and, where practicable, the sample should be taken from a newly opened container, because changes in the water content of samples may influence dustiness significantly. The optical submethod of MT 171.1 usually shows good correlation with the gravimetric submethod, and can, therefore, be used as an alternative where the equipment is available. Where the correlation is in doubt, it must be checked with the formulation to be tested. In cases of dispute the gravimetric method shall be used.

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

PART TWO

EVALUATION REPORTS

CLOTHIANIDIN

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CLOTHIANIDIN

FAO/WHO EVALUATION REPORT 738/2020

Recommendations

The Meeting recommended the following:

(i) The clothianidin TC proposed by Tagros Chemicals India Private Limited should be accepted as equivalent to the clothianidin reference profile of Sumitomo.

(ii) The existing FAO specification 738/TC/1 for clothianidin TC should be extended to the technical material produced by Tagros Chemicals India Private Limited.

(iii) The existing WHO specification 738/TC/1 for clothianidin TC should be extended to the technical material produced by Tagros Chemicals India Private Limited.

Appraisal

The Meeting considered data and supporting information submitted in 2019 by Tagros Chemicals India Private Limited (Tagros) for the determination of the equivalence of their clothianidin TC with the Sumitomo reference profile (FAO/WHO specification 738/TC/1) (WHO, 2018). 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). The reference specification and supporting data for clothianidin TC had been provided by Sumitomo.

The Meeting was provided with commercially confidential information on the manufacturing process and five batch analysis data on clothianidin and all impurities present at or above 1 g/kg and their manufacturing limits in the TC.

The confidential information (manufacturing process, purity and impurity profile) submitted to FAO/WHO was confirmed by the Australian authorities (APVMA) as being identical to that submitted for registration in Australia (Margerison, 2020).

The manufacturing process, impurity profile and five batch analyses were compared with the data of the reference profile of Sumitomo. The manufacturing process of Tagros is different than that used by the first source of Sumitomo, considered as the reference source. However, it is somewhat similar to the process of the second source of Sumitomo, considered equivalent to the first one. The Tagros process leads to a reduced amount of impurities and higher purity of the technical clothianidin produced. The proposer declared the minimum active ingredient content of their clothianidin TC as 980 g/kg, which is higher than the purity of the existing FAO/WHO specification 738/TC/1 for the clothianidin TC from Sumitomo (960 g/kg). Mass balances ranged from 992.0 to 995.2 g/kg in the five batch data. The maximum limits for the impurities were supported by the five batch data and were statistically justified.

The analytical method for the active ingredient content was reversed-phase HPLC with UV detection, similar to CIPAC method 738/TC/M/3. The organic impurities were determined by HPLC with UV detection and GC-MS, and Karl Fischer coulometric titration was used to determine residual water.

The impurity profiles of the clothianidin TC of Tagros and Sumitomo are different, with that produced by Tagros containing less impurities. Comparing the Tagros clothianidin TC profile with the Sumitomo reference profile, there is one common impurity and two new impurities, one being a residual solvent.

The Meeting considered the possible relevance of these two new impurities.

- The QSAR analysis of impurities provided by Tagros showed that the toxicity of impurities is comparable with this of the active ingredient. The *in-vitro* reverse mutation study with clothianidin TC did not indicate a positive response. A dermal sensitization study (Local Lymph Node Assay) done with one of the technical materials from the five batch analysis was also provided. The study was conducted in compliance with GLP and according to OECD Test Guideline 429. Clothianidin TC did not demonstrate dermal sensitization potential in the mouse LLNA.
- Tagros had initially specified a manufacturing limit of 2 g/kg for the residual solvent. A maximum acceptable concentration of 2 g/kg was calculated by the Meeting taking into account the worst-case-possible hazard, which in the present case is acute oral toxicity, the reference dose for oral exposure derived by the US EPA, and the hazard classification by ECHA and UN GHS for this residual solvent. At the request of the Meeting, the proposer provided additional quality control data showing that the content of this potentially relevant impurity was lower than 1 g/kg in their clothianidin TC. The Meeting therefore concluded that this impurity was not relevant in the technical material of Tagros.

The Meeting concluded that the clothianidin TC of Tagros Chemicals India Private Limited should be accepted as equivalent to the reference profile of Sumitomo clothianidin TC based on Tier-1 and Tier-2 data.

In addition, the Meeting noted that the clothianidin FAO specifications for SC, GR and FS needed some editorial updates. With the appearance of the CropLife Monograph 2 in 2017, the name of "aqueous suspension concentrate" (SC) was changed to "suspension concentrate" only. The title of the SC specification was adapted accordingly

Certain CIPAC physical-chemical test methods had been revised to better reflect progress in science and technology, and the newer versions are deemed to provide equivalent results as compared to the older versions. Where possible and justified, the specifications were editorially updated while no limits had been changed. These methods include i.a.

- Flowability of granular preparations: MT 172.2 replaces MT 172.1.
- Dustiness: the corrected version, MT 171.1 is now referenced.
- Suspensibility: MT 184.1 replaces MT 184, but the temperature range of MT 184 has been kept (30 ± 2°C) as the supporting data had been elaborated using that temperature range and the range in MT 184.1 is valid for new submissions.
- Accelerated storage: the harmonised version MT 46.4 replaces MT 46.3.
- In the specification for the WG, the reference to persistent foam was intentionally kept with MT 47.2, as the proposer and holder of the reference specification (Sumitomo) had shown for this particular product MT 47.2 is better suited (see Evaluation report 738/2013).

SUPPORTING INFORMATION

FOR

EVALUATION REPORT 738/2020

Table 1. Chemical composition and properties of clothianidin technical material (TC)

Manufacturing process, maximum limits for impurities ≥ 1 g/kg, 5 batch analysis data	Confidential information supplied and held on file by FAO and WHO. Mass balances were 99.20-99.52% and percentages of unknowns were 0.48-0.80%.			
Declared minimum clothianidin content	980 g/kg			
Relevant impurities ≥ 1 g/kg and maximum limits for them	None			
Relevant impurities < 1 g/kg and maximum limits for them	None			
Stabilisers or other additives and maximum limits for them	None			
Parameter	Value and conditions	Purity %	Method reference	Study number
Melting temperature range of the TC	174 - 176°C	98.62	-	-

METHODS OF ANALYSIS AND TESTING

The analytical method for the active ingredient was reversed-phase HPLC with UV detection, similar to CIPAC method 738/TC/M/3.

The methods for determination of organic impurities are based on analysis by reverse phase liquid chromatography using UV detection and quantification by external standard calibration and gas chromatography with mass spectrometry detection (GC-MS).

FORMULATIONS AND CO-FORMULATED ACTIVE INGREDIENTS

The present application is for determination of equivalence of clothianidin technical.

CONTAINERS AND PACKAGING

No special requirements for containers and packaging have been identified.

EXPRESSION OF THE ACTIVE INGREDIENT

The active ingredient is expressed as clothianidin.

ANNEX 1

HAZARD SUMMARY PROVIDED BY THE PROPOSER

Notes.

(i) The proposer confirmed that the toxicological data included in the summary below were derived from clothianidin having impurity profiles similar to those referred to in the table above.

(ii) The conclusions expressed in the summary below are those of the proposer unless otherwise specified.

Table 2. Mutagenicity profile of clothianidin technical material based on *in vitro* tests

Species	Test	Purity %	Guideline, duration, doses and conditions	Results	References
Salmonella typhimurium TA1535, TA98, TA100 and TA1537 *Escherichia coli* WP2uvrA (pKM101)	Bacterial reverse mutation test	98.40	OECD 471 The bacterial tester strains were exposed to clothianidin technical in triplicate at 50, 158, 500, 1581 and 5000 µg/plate using the direct plate incorporation mode of exposure in the initial mutation assay and using the pre-incubation mode of exposure in the confirmatory mutation assay in the presence and absence of metabolic activation system (S9 fraction prepared from Aroclor 1254 induced rat liver).	Negative Clothianidin technical was not mutagenic in this Bacterial Reverse Mutation Assay up to the highest OECD 471 recommended dose of 5000 µg/plate, under the conditions of testing employed.	G18447

Table 3. *In vivo* Local Lymph Node Assay (LLNA, OECD Guideline 429) sensitization test data of clothianidin technical material

Species	Test	Purity %	Guideline, duration, doses and conditions	Results	References
Local lymph node assay (LLNA) in CBA/Ca mice	Dermal sensitization study	98.62	OECD Guideline for Testing of Chemicals, Test Guideline No. 429, Skin Sensitization: Local Lymph Node Assay. 22 July 2010	The test item clothianidin technical did not demonstrate dermal sensitization potential in the mouse LLNA, as the lymph nodes draining the area of topical application did not elicit a proliferative response greater than the 3X threshold.	G19423

ANNEX 2

REFERENCES

Study number	Author(s)	Year	Study title. Study identification number. Report identification number. GLP [if GLP]. Company conducting the study.
WHO 2018		2018	WHO specifications for clothianidin https://extranet.who.int/pqweb/vector-control-product/document/clothianidin-2018
FAO/WHO Manual, 2016		2016	Manual on development and use of FAO and WHO specifications for pesticides, First edition - third revision https://extranet.who.int/pqweb/vector-control-products/manual-amendments
Margerison, 2020		2020	Notice of approval of an active constituent, Agricultural and Veterinary Chemicals Code (Agvet Code), as set out in the Schedule to the Agricultural and Veterinary Chemicals Code Act 1994, No. 122206.
ECHA			https://echa.europa.eu/information-on-chemicals/cl-inventory-database/-/discli/details/37212
CIPAC N	Martijn A and Dobrat W	2012	CIPAC Handbook Volume N. Analysis of Technical and Formulated Pesticides, p.18, 2012.
G18231	Ravikanth Gogineni	2019	Five Batch Analysis of Clothianidin Technical. Study Number G18231, Eurofins Advinus Limited, GLP, Unpublished.
G18447	Divyashree K	2019	Clothianidin Technical: Bacterial Reverse Mutation Test. Study Number G18447, Eurofins Advinus Limited, GLP, Unpublished.
G19423	Kammar, Umesh	2020	Clothianidin Technical: local lymph node assay (LLNA) in CBA/Ca mice, OECD Guideline for Testing of Chemicals, Test Guideline No. 429 (2010): Skin Sensitization: Local Lymph Node Assay, GLP, Unpublished.

CLOTHIANIDIN

FAO/WHO EVALUATION REPORT 738/2013

Recommendation

The Meeting recommended that the specification for clothianidin WG proposed by Sumitomo Chemical Company, as amended, should be adopted by FAO.

Appraisal

The Meeting considered data on clothianidin submitted by Sumitomo Chemical Company., Ltd. (SCC), in support of a new FAO specification for water dispersible granules (WG).

The FAO specifications for clothianidin TC, SC, GR, SG and FS were published in 2011 based on a submission by SCC as well [FAO 2011]

The meeting was provided with a draft specification for clothianidin water dispersible granules. The proposed specification for the WG was essentially in accordance with the requirements of the Manual [FAO/WHO Manual].

The analytical method for the active ingredient was reversed-phase HPLC with UV detection, according to CIPAC method 738/WG/M/3. [CHC, CIPAC N]

Physical-chemical properties data were provided for clothianidin WG formulations for wettability, wet sieve test, degree of dispersion, suspensibility, persistent foam, dustiness, flowability and attrition resistance.

The Meeting noted that the persistent foam determination was carried out at a concentration of 0.05 % formulation and asked for confirmatory data to demonstrate that the limit is also met at the highest used concentration. The company explained that the CIPAC MT47.2 does not provide a concentration limit and range, and since they have a range of products covering many application conditions, 0.05% was chosen as a representative concentration. The company was asked to clarify whether the formulation is indeed a WG and not rather a SG. The company explained, that the intended use of the WG was somewhat different in application rate and concentration of the product in the spray solution, leading to the conclusion that the majority of the active ingredient is dispersed and not dissolved. The Meeting accepted the explanation and concluded, that the clauses and limits of the WG formulation were in agreement with the requirements of the FAO and WHO Manual for WG formulations.

The analytical method used for the determination of the active ingredient content in the formulated product was based on the CIPAC method 738/WG/M/3. The Meeting noted that a slightly different type of column was used. The CIPAC Method for clothianidin recommends a certain column type but allows for equivalent columns provided that the chromatographic signal produced by the active ingredient is symmetrical. The Meeting accepted this justification.

Furthermore, some editorial changes were initially introduced like the references to the clothianidin methods meanwhile published in Handbook N and some updated physical-chemical methods as the method for determination of persistent foam, MT 47.3. However, the company provided some preliminary results that, according to their data, some

clothianidin formulations intended to be used after dilution with water may produce slightly higher volumes of foam when MT 47.3 instead of MT 47.2 is used. These formulations would therefore not comply with the limits set with the use of MT 47.2. For these reasons, the reference to MT 47.2 and the appropriate limits were retained in the specifications for formulated products where persistent foam is to be tested.

SUPPORTING INFORMATION

FOR

EVALUATION REPORT 738/2013

METHODS OF ANALYSIS AND TESTING

The analytical method for the active ingredient in WG is HPLC using UV detection at 269 nm, according to the CIPAC method 783/WG/M/3.

Test methods for determination of physical-chemical properties of the formulation were CIPAC, as indicated in the specification. [CIPAC F, CIPAC J, CIPAC K]

FORMULATIONS AND CO-FORMULATED ACTIVE INGREDIENTS

The main formulation types available are SC, GR, SG, FS and WG.

CONTAINERS AND PACKAGING

No special requirements for containers and packaging have been identified.

EXPRESSION OF THE ACTIVE INGREDIENT

The active ingredient is expressed as clothianidin.

ANNEX 2. REFERENCES

Study number	Author(s)	year	Study title. Study identification number. Report identification number. GLP [if GLP]. Company conducting the study.
FAO 2011		2011	http://www.fao.org/fileadmin/templates/agphome/documents/Pests_Pesticides/Specs/Clothianidin2011.pdf
FAO/WHO Manual		2010	Manual on development and use of FAO and WHO specifications for pesticides, JANUARY 2010 second revision of the first edition http://www.fao.org/fileadmin/templates/agphome/documents/Pests_Pesticides/PestSpecsManual2010.pdf
CHC		2013	Kozuki, Y., Physico-chemical properties of clothianidin water dispersible granules, Sumitomo Chemical, Study report, 2013, Unpublished
CIPAC N	Martijn A and Dobrat W	2012	CIPAC Handbook Volume N. Analysis of Technical and Formulated Pesticides, p.18, 2012
CIPAC F	Martijn A and Dobrat W	1995	CIPAC Handbook Volume F. Physico-chemical Methods for Technical and Formulated Pesticides
CIPAC J	Martijn A and Dobrat W	2000	CIPAC Handbook Volume K. Analysis of Technical and Formulated Pesticides
CIPAC K	Martijn A and Dobrat W	2003	CIPAC Handbook Volume K. Analysis of Technical and Formulated Pesticides

CLOTHIANIDIN

FAO/WHO EVALUATION REPORT 738/2010

Recommendation

The Meeting recommended that the specification for clothianidin FS proposed by Sumitomo Chemical Company, as amended, should be adopted by FAO.

Appraisal

The meeting considered data on clothianidin submitted by Sumitomo Chemical Co., Ltd., in support of a new FAO specification for FS.

The meeting was provided with a proposed specification for a clothianidin suspension concentrate for seed treatment (FS). The Meeting idendified several issues with the draft specification.

Clauses for physical properties: persistent foam and suspensibility:
The Meeting noted that these clauses were conditional "when diluted with water". The company explained that four different FS with clothianidin are manufactured and some are used undiluted, some after dilution with water. The specification is intended to cover both types. This explication was accepted by the Meeting.

Clause for storage stability:
The draft specification included a clause on particle size distribution to be determined after the accelerated storage test. This is one of the clauses where the inclusion is "where required". The company explained that they had no objection to remove the subclause.

Clause for seed adhesion:
The clause was not included in the draft specification. The company explained, that reasonable limits for FS in general could not yet be set. Adhesion is not only a quality criterion of the FS under evaluation, but also depending on type of seeds and conditioning prior to treatment. This explanantion was accepted by the Meeting.

Analytical Method:
A CIPAC method based on reversed phase HPLC has been developed for determination of clothianidin in TC, SC, GR and SG formulations and was presented at the 2009 CIPAC Meeting in El Salvador. An extension of the CIPAC Method for clothianidin FS was presented at the CIPAC Meeting 2010 in Slovenia and provisionally adopted.

CLOTHIANIDIN

FAO/WHO EVALUATION REPORT 738/2009

Recommendation

The Meeting recommended that the specifications for clothianidin TC, SC, GR and SG proposed by Sumitomo Chemical Company, as amended, should be adopted by FAO.

Appraisal

The meeting considered data on clothianidin submitted by Sumitomo Chemical Co., Ltd., (SCC) in support of new FAO specifications for TC, SC, GR and SG.

Clothianidin is a white to pale yellow coloured crystalline powder. It has a low volatility and has a melting point of 176.8 °C. It is slightly soluble in water at 0.33 g/L at 20°C. It is not fat soluble and is not likely to bioaccumulate with a log P_{ow} of circa 0.9. It is considered to be stable to hydrolysis at all environmentally relevant pH's. It undergoes rapid photolysis with a half life of 3.3 hours at pH 7 at 25°C. Clothianidin is a strong base with a pK_a of 11.

The meeting was provided with confidential information on the manufacturing process and limits for minimum purity and for impurities, which were supported by 5 batch analysis data. Mass balances were 99.1 – 99.5 %. The minimum purity at 960 g/kg was questioned but it was confirmed by Sumitomo that this is necessary as production has not yet stabilised. A statement was provided by the Belgian regulatory authority confirming that the confidential data on the manufacturing process and declaration of composition submitted to the FAO were the same as those submitted to the national regulatory authority. The meeting considered that none of the impurities are relevant. A CIPAC method based on reversed phase HPLC has been developed for determination of clothianidin in TC, SC, GR and SG formulations and was presented at the 2009 CIPAC Meeting in El Salvador. The method was adopted as provisional CIPAC method.

The proposed specification for TC, SC, GR and SG were essentially in accordance with the requirements of the manual (FAO/WHO 2006). For the TC the melting point provided was for purified material and not the TC. SCC were asked if data for the TC was available and they have now stated that this is not available. Finally it was considered as a minor issue and the melting point for the pure material was accepted.

In the specifications for the SC, GR and SG the meeting requested that the descriptions of the formulations should be more specific. The company have addressed this and revised specifications were provided. For these specifications the company were also asked why the after storage minimum active content was higher at 97 % than the standard 95 %. The company explained that clothianidin is very stable and their products will meet the higher percentage value. In the end the company were happy to accept the 95 % as standard. For these specifications it was agreed that the method footnotes could be deleted as the CIPAC methods are presented in 2009, this has been done in the revised specification.

The draft specifications for SG and GR formulations, respectively, contained a clause for control of pH range. As clothianidin is not sensitive to hydrolysis in the pH range 5 to 9, the necessity of the clause was questioned by the meeting. It was confirmed that this is not needed and it has been removed from the specifications.

SUPPORTING INFORMATION

FOR

EVALUATION REPORT 738/2009

HISTORY

Clothianidin was developed by Takeda Chemical Industries in Japan in the 1990. This is also reflected in the development code number allocated to that compound - TI-435, with TI standing for Takeda Industries. Takeda was later incorporated into Sumitomo, and clothianidin was further developed jointly by Sumitomo Chemical Company (SCC) and Bayer CropScience (BCS). Therefore, some of the nonpublished studies referenced in the hazard summary are owned by SCC, some by BCS, and some by both companies.

USES

Clothianidin is a systemic insecticide which acts as acute contact and stomach poison. Clothianidin belongs to the chemical class of insecticides known as neonicotinoids and is classified by the Insecticide Resistance Action Committee (IRAC) as "nicotinic Acetylcholine receptor agonist / antagonist".

Clothianidin has a broad spectrum of activity, particularly against sucking insects such as aphids, leaf hoppers, thrips and white flies. Furthermore, various species of beetles (e.g. *Atomaria* spp., *Agriotes lineatus*, *Diabrotica* spp.) and some species of flies (e.g. *Oscinella* frit and *Pegomyia* spp.) and cut worm (e.g. *Agrotis* spp.) are effectively controlled. Clothanidin shows no efficacy against spider mites and nematodes. Products containing clothianidin are used as foliar and soil applications as well as seed treatments.

Table 1. **Physico-chemical properties of pure clothianidin**

Parameter	**Value(s) and conditions**	**Purity %**	**Method reference (and technique if the reference gives more than one) and company report number/date**
Vapour pressure	1.3×10^{-10} Pa at 25°C 3.8×10^{-11} Pa at 20°C (extrapolated)	99.7 %	OECD 104 EC A.4 [101]
Melting point, boiling point and/or temperature of decomposition	Melting point: 176.8°C Boiling point: decompose before boiling Decomposition temperature: 242 °C	99.7 %	OECD 102 EC A.1 (DSC) [102]
Solubility in water	pH 7: 0.327 g/L at 20 °C determined in deionized water (resistivity > 17 MΩ)	99.7 %	OECD 105 (equivalent to EEC A.6, flask method) [103]
Octanol/water partition coefficient	pH 4 log P_{OW} = 0.893 at 25 °C pH 7 log P_{OW} = 0.905 at 25 °C pH 10 log P_{OW} = 0.873 at 25 °C	99.7 %	EEC A8 [104]
Hydrolysis characteristics	Half-life = 14.4 days at 50 °C at pH 9 Half-life = 3.7 days at 62 °C at pH 9 Half-life = 0.7 days at 74 °C at pH 9 Stable at 50 °C at pH 4 and 7 (<10% degradation after 5 days) Stable at 25°C at pH 5, 7 and 9 (<5% degradation after 33 days)	>98 %	EPA Series 161-1 EEC method C.7 [105]
Photolysis characteristics	Half-life 3.3 hours in sterile buffer pH 7 at 25°C Equivalent to 0.6 days of summer solar exposure at Phoenix, Arizona, US (40° latitude) using a Xenon lamp with UV cut-off filter at 290 nm. Intensity (300-800 nm) = 1027 W/m^2 by radiometry. Photon flow density = 125.86 X 1014 s^{-1} cm^{-2}. Quantum yield (Φ) = 0.014	>99%	EPA Series 161-2 SETAC [106] [107]
Dissociation characteristics	pK_a = 11.09 (at 20°C)	99.7%	OECD 112 (spectrophotometric method) [103]

Table 2. **Chemical composition and properties of clothianidin technical materials**

Manufacturing process, maximum limits for impurities ≥ 1 g/kg, 5 batch analysis data	Confidential information supplied and held on file by FAO. Mass balances were 99.1 – 99.5 %.
Declared minimum clothianidin content	960 g/kg
Relevant impurities ≥ 1 g/kg and maximum limits for them	None
Relevant impurities **<** 1 g/kg and maximum limits for them:	None
Stabilisers or other additives and maximum limits for them:	None
Melting or boiling temperature range of the TC and/or TK	176.8 °C The value given is for pure material, a measurement for the TC is not available.

HAZARD SUMMARY

Clothianidin has not been evaluated by the WHO IPCS or by the FAO/WHO JMPR.

In EU the classification process is not yet finalized (but Annex I listing is already done). The classification has been discussed between the notifiers and the rapporteur member state and the proposal is reported as such in the draft assessment report:

FORMULATIONS AND CO-FORMULATED ACTIVE INGREDIENTS

The main formulation types available are SG, SC and GR.

Clothianidin is used alone or co-formulated with probenazole, cartap, validamycin, diclocymet, ferimzone, phthalide.

These formulations are registered and sold in many countries in Europe, Northern and Southern America, Africa, Asia and Australia.

METHODS OF ANALYSIS AND TESTING

The analytical method for determination of the active ingredient content is determined by reversed-phase HPLC with UV detection at 269 nm and external standardization.

The collaborative study for TC, SG, SC, and GR formulations were presented at the 2009 CIPAC meeting in El Salvador and were provisionally adopted as CIPAC Methods.

The methods for determination of impurities are based on HPLC- method using UV detection and internal standardization

Test methods for determination of physical and chemical properties of the technical active ingredient were OECD, EPA, and/or EC as indicated, while those for the formulations were CIPAC, as indicated in the specifications.

PHYSICAL PROPERTIES

The physical properties, the methods for testing them and the limits proposed for the SG, SC and GR formulations, comply with the requirements of the FAO/WHO Manual (1st edition, 2006).

CONTAINERS AND PACKAGING

No special requirements for containers and packaging have been identified

EXPRESSION OF THE ACTIVE INGREDIENT

The active ingredient is expressed as clothianidin and is to be quantified as such.

ANNEX 1

HAZARD SUMMARY PROVIDED BY THE PROPOSER

Notes.

(i) The proposer confirmed that the toxicological and ecotoxicological data included in the summary below were derived from clothianidin having impurity profiles similar to those referred to in the table above.

(ii) The conclusions expressed in the summary below are those of the proposer, unless otherwise specified.

Table 3. **Toxicology profile of clothianidin technical material, based on acute toxicity, irritation and sensitization**

Species	Test	Duration and conditions or guideline adopted	Result	Reference
Rat male/female	Oral	JMAFF 59 NohSan No 4200; JMAFF 63-44; OECD 401; Directive 92/69/EC Method B.I.; Directive 92/18/EEC, L97; US-EPA Section 81-1; OPPTS 870. 1100 Purity: 96.0%	LD_{50} = > 5000 mg/kg bw	[201]
Rat male/female	Acute neurotoxicity gavage	US-EPA-FIFRA, Guideline 81-8(SS); US-EPA OPPTS 870.6200 0-100-200-400 mg/kg bw/d Purity: 95.2-96.0%	NOELs (male / female) Overall = > 60 / 100 mg/kg bw Neurotoxicity = > 400 mg/kg bw/d not neurotoxic	[202]
Mouse male/female	Oral	OECD 401; Directive 92/69/EC, Method B. 1.; Directive 92/18/EEC, L97; US-EPA Section 81-1; US-EPA OPPTS 870.1100 Purity: 96.0%	LD_{50} = 389 mg/kg bw (m) 465 mg/kg bw (f)	[203]
Rat male/female	Dermal	JMAFF 59 NohSan No 4200; JMAFF 63-44; OECD 402; Directive 92/69/EC, Method B.3.; Directive 92/18/EEC, L97; US-EPA Section 81-2; US-EPA OPPTS 870.1200 24 h semi-occlusive conditions Purity: 96.0%	LD_{50} = > 2000 mg/kg bw	[204]
Rat male/female	Inhalation	JMAFF 59 NohSan No 4200; JMAFF 63-44; OECD 403; Directive 92/69/EC, Method B.2.; Directive 92/18/EEC, OJEC, L97; USA-EPA Section 81-3; US-EPA OPPTS 870.1330 4.5 h exposure Purity: 96.0%	LC_{50} = > 6.141 mg/L	[205]

Rabbit male/female	Skin irritation	JMAFF 59 NohSan No 4200; JMAFF 63-44; OECD 404; Directive 92/69/EC, Method B.4.; Directive 92/18/EEC L97; US-EPA Section 81-5; US-EPA OPPTS 870.2500 4 h exposure Purity: 96.0%	Non-irritating	[201]
Rabbit male	Eye irritation	OECD 405; Directive 92/69/EC, Method B.5.; Directive 92/18/EEC L97; US-EPA Section 81-4; US-EPA OPPTS 870.2400 24 h exposure Purity: 96.0%	Non-irritating	[202]
Guinea pig	Skin sensitization	OECD 406; Directive 92/69/EC, Method B.6.; Directive 92/18/EEC L97; US-EPA Section 81-6; US-EPA OPPTS 870.2600 Purity: 96.0%	Non-sensitizing	[203]

Table 4. **Toxicology profile of technical clothianidin based on repeated administration (sub-acute to chronic)**

Species	Test	Duration and conditions or guideline adopted	Result	Reference
Rat male/female	Oral	JMAFF 59 NohSan No 4200; JMAFF 63-44; OECD 401; Directive 92/69/EC Method B.I.; Directive 92/18/EEC, L97; US-EPA Section 81-1; OPPTS 870. 1100 Purity: 96.0%	LD50 = > 5000 mg/kg bw	[206]
Rat male/female	Acute neurotoxicity gavage	US-EPA-FIFRA, Guideline 81-8(SS); US-EPA OPPTS 870.6200 0-100-200-400 mg/kg bw/d Purity: 95.2-96.0%	NOELs (male / female) Overall = > 60 / 100 mg/kg bw Neurotoxicity = > 400 mg/kg bw/d not neurotoxic	[207]
Mouse male/female	Oral	OECD 401; Directive 92/69/EC, Method B. 1.; Directive 92/18/EEC, L97; US-EPA Section 81-1; US-EPA OPPTS 870.1100 Purity: 96.0%	LD50 = 389 mg/kg bw (m) 465 mg/kg bw (f)	[208]
Rat male/female	Dermal	JMAFF 59 NohSan No 4200; JMAFF 63-44; OECD 402; Directive 92/69/EC, Method B.3.; Directive 92/18/EEC, L97; US-EPA Section 81-2; US-EPA OPPTS 870.1200 24 h semi-occlusive conditions Purity: 96.0%	LD50 = > 2000 mg/kg bw	[209]
Rat male/female	Inhalation	JMAFF 59 NohSan No 4200; JMAFF 63-44; OECD 403; Directive 92/69/EC, Method B.2.; Directive 92/18/EEC, OJEC, L97; USA-EPA Section 81-3; US-EPA OPPTS 870.1330 4.5 h exposure Purity: 96.0%	LC50 = > 6.141 mg/L	[210]

Rabbit male/female	Skin irritation	JMAFF 59 NohSan No 4200; JMAFF 63-44; OECD 404; Directive 92/69/EC, Method B.4.; Directive 92/18/EEC L97; US-EPA Section 81-5; US-EPA OPPTS 870.2500 4 h exposure Purity: 96.0%	Non-irritating	[211]
Rabbit male	Eye irritation	OECD 405; Directive 92/69/EC, Method B.5.; Directive 92/18/EEC L97; US-EPA Section 81-4; US-EPA OPPTS 870.2400 24 h exposure Purity: 96.0%	Non-irritating	[201]
Guinea pig	Skin sensitization	OECD 406; Directive 92/69/EC, Method B.6.; Directive 92/18/EEC L97; US-EPA Section 81-6; US-EPA OPPTS 870.2600 Purity: 96.0%	Non-sensitizing	[202]
Rat male/female	Sub-acute feeding	OECD 407; Directive 92/69/EEC (OJ No. L383A, 29.12.92), Part B, Method B.7.; EPA Guideline in Subdivision F. Hazard Evaluation: Human and Domestic Animals, JANUARY 1984; JMAFF 59 Nohsan No. 4200 4 weeks 0-1250-2500-5000-7500 ppm (equivalent to: 0-120-249-475-602 mg/kg bw/d (male), 0-137-228-454-689 mg/kg bw/d (female)) Purity: 97.5%	NOAEL = 120 / 137 mg/kg bw/d LOEL = 249 / 228 mg/kg bw/d	[203]
Mouse male/female	Sub-acute feeding	OECD 407; Directive 92/69/EEC (OJ No. L383A, 29.12.92), Part B, Method B.7.: EPA Guideline in Subdivision F. Hazard Evaluation: Human and Domestic Animals; JMAFF Nohsan No. 4200 deviation: duration 4 weeks 0-500-1000-2000-4000 ppm (equivalent to: 0-90-190-383-683 mg/kg bw/d (male) 0-122-248-491-619 mg/kg bw/d (female)) Purity: 97.5%	NOAEL = 190 / 248 mg/kg bw/d LOEL = 383 / 491 mg/kg bw/d	[204]

Dog female	Dose-range finding (palatability) feeding	Exposure to increasing dose levels 0 (for 11 days) - 3000 / 4000 / 5000 ppm (days 1-3 / 4-8 / 9-11) (equivalent to: 0- 51.1/50.8/51.8 mg/kg bw/d) Purity: 95.2%	NOEL = 51.8 mg/kg bw/d	[205]
Dog male/female	Dose-range finding feeding	Directive 88/302/EEC, Method B.27; US-EPA FIFRA Subdivision F, Section 82-1; US-EPA 870.3150; JMAFF 59 Nohsan No. 4200; mainly in accordance to OECD 409 4 weeks, 3 animals/sex/group 0-1250-2500-5000 ppm (equivalent to: 0-36.3-35.8-62.4 mg/kg bw/d (male) 0-35.6-52.3-57.4 mg/kg bw/d (female)) Purity: 95.2%	NOAEL = 36.3 / 35.6 mg/kg bw/d LOEL = 35.8 / 52.3 mg/kg bw/d	[206]
Rat male/female	Sub-acute dermal	US-EPA OPPTS 870.3200; JMAFF 59 Nohsan No. 4200; Directive 88/302/EEC (OJEC No. L 133/27) Part B; OECD 410 6 hrs/day, 28 days 0-100-300-1000 mg/kg bw/d Purity: 95.2%	NOEL = > 1000 mg/kg bw/d	[207]
Rat male/female	Sub-chronic feeding	FIFRA 82-1; TSCA 798.2650; US-EPA OPPTS 870.3100, OECD 408; JMAFF 59 NohSan No. 4200; Directive 87/302/EEC, part B 97 days 0-150-500-3000 ppm (equivalent to: 0-9.0-27.9-202 mg/kg bw/d (male) 0-10.9-34.0-254 mg/kg bw/d (female)) Purity: 95.3%	NOAEL = 27.9 / 34.0 mg/kg bw/d LOEL = 202 / 254 mg/kg bw/d	[208]

Dog male/female	Sub-chronic feeding	US-EPA-FTFRA Section. 82-1; US-EPA-OPPTS OPPTS 870.3150; OECD 409; JMAFF 59 Nohsan No. 4200; Directive 88/302/EEC (OJEC No. L 133/12), Part B 13 weeks 0-325-650-1500-2250 ppm (equivalent to: 0-9.2-19.3-40.9-58.2 mg/kg bw/d (male) 0-9.6-21.2- 42.1-61.8 mg/kg bw/d (female)) Purity: 95.2%	NOAEL = 19.3 / 21.2 mg/kg bw/d LOEL = 40.9 / 42.1 mg/kg bw/d	[209]
Dog male/female	Sub-chronic feeding	EPA-FIFRA Guideline 83-1; EPA-OPPTS Guideline Section 870.4100; OECD 452; JMAFF 59 Nohsan No. 4200, Directive 88/302/EEC, Part B 52 weeks 0-325-650-1500-2000ppm (equivalent to: 0-7.8-16.6-36.3-46.4 mg/kg bw/d (male) 0-8.5-15.0-40.1-52.9 mg/kg bw/d (female)) Purity: 95.2%	NOAEL = 36.3 / 40.1 mg/kg bw/d LOEL = 46.4 / 52.9 mg/kg bw/d	[210]
Rat male/female	Chronic oncogenicity feeding	JMAFF 59 NohSan No. 4200; OECD 453; EEC 88/302/EEC; FIFRA F, 83-5; OPPTS 870.4300 104 weeks 0-150-500-1500-3000 ppm (equivalent to: 0-8.1-27.4-82-157 mg/kg bw/d (male) 0-9.7-32.5-97.8-193 mg/kg bw/d (female)) Purity: 95.2-95.5%	NOAEL = 27.4 / 9.7 mg/kg bw/d LOEL = 82 / 32.5 mg/kg bw/d not carcinogenic	[211]
Mouse male/female	Oncogenicity feeding	JMAFF 59 NohSan No. 4200; OECD 451; EEC 88/302/EEC; FIFRA F, 83-2; OPPTS 870.4200 78 weeks 0-100-350-700/2000/2500/2000/1800 (week 1-4/ 5-10/ 11-34/ 35-termination 2000 ppm (m)/ 1800 ppm (f)) -1250 ppm (equivalent to: 0-13.5-47.2-171.4-251.9 mg/kg bw/d (male) 0-17.0-65.1-215.9-281.1 mg/kg bw/d (female)) Purity: 95.2%	NOAEL = 47.2 / 65.1 mg/kg bw/d LOEL = 171.4 / 215.9 mg/kg bw/d not carcinogenic	[212]

Rat male/female	Pilot reproduction one generation	US-EPA-FIFRA, Section 158.340, No. 83-4: US-EPA-TSCA, 40 CFR Section 798.4700: Guideline 87/302/EEC; OECD 416; J MAFF, 59 NohSan No. 4200 pre-mating 8 weeks 0-50-100-500-1000 ppm (equivalent during pre-mating to: 3.2-3.5 / 5.9-6.8 / 31.7-36.4 / 66.6 - 70.8 mg/kg bw/d) Purity: 95.2-96.0%	NOEL repro. = > 66.6 mg/kg bw/d	[213]
Rat male/female	Reproduction 2-generation	US-EPA, OPPTS 870.3800; Directive 91/414/EEC; OECD 416; JMAFF, 59 NohSan No. 4200 0-150-500-2500 ppm (equivalent to both generations combined: 0-10.2-32.7-179.6 mg/kg bw/d (male) 0-11.8-37.9-212.9 mg/kg bw/d (female) Purity: 95.3-96.0%	Parental NOEL = 32.7/11.8 mg/kg bw/d LOEL = 179.6/37.9 mg/kg bw/d Reproductive NOEL = >179.6/ >212.9 mg/kg bw/d Offspring NOEL = 10.2/11.8 mg/kg bw/d LOEL = 32.7/37.9 mg/kg bw/d	[214]
Rat female	Dose-range finding developmental toxicity	US-EPA OPPTS 870.3700 gestation days 6-19 0-125-250-500-1000 mg/kg bw/d Purity: 96.0%	Maternal NOAEL = not established LOEL = 125 mg/kg bw/d Developmental NOAEL = 125 mg/kg bw/d LOEL = 250 mg/kg bw/d	[215]
Rat female	Developmental toxicity	Guideline 88/302/EEC; OECD 414; US-EPA OPPTS 870.3700; JMAFF 59 NohSan no. 4200 gestation days 6-19 0-10-40-125 mg/kg bw/d Purity: 95.2%	Maternal NOEL = 10 mg/kg bw/d LOEL = 40 mg/kg bw/d Developmental NOAEL = 125 mg/kg bw/d LOEL = > 125 mg/kg bw/d not teratogenic	[216]
Rabbit female	Dose-range finding developmental toxicity	US-EPA OPPTS 870.3700 gestation days 6-28 0-62.5-125-250-500 mg/kg bw/d Purity: 96.0%	Maternal NOAEL = 62.5 mg/kg bw/d MTD < 125 mg/kg bw/d Developmental NOAEL > 62.5 mg/kg bw/d	[217]

Rabbit female	Developmental toxicity	Guideline 88/302/EEC, OECD 414; US-EPA OPPTS 870.3700; JMAFF 59 NohSan no. 4200 gestation days 6-28 0-10-25-75-100 mg/kg bw/d Purity: 95.2-95.5%	Maternal NOEL = 10 mg/kg bw/d LOEL = 25 mg/kg bw/d Developmental NOAEL = 75 mg/kg bw/d LOEL = 100 mg/kg bw/d not teratogenic	[218]
Rat male/female	Sub-chronic neurotoxicity feeding	US-EPA-FIFRA, Guideline 82-5(b); US-EPA OPPTS 870.6200 0-150-1000-3000 ppm equivalent to: 0-9.2-60-177 mg/kg bw/d (male) 0-10.6-71-200 mg/kg bw/d (female) Purity: 95.3-96.0%	NOELs (male / female) Overall = 60 / 71 mg/kg bw d Neurotoxicity = >177 / >200 mg/kg bw/d not neurotoxic	[219]
Rat male/female	Developmental neurotoxicity feeding	US-EPA OPPTS 870.6300; US-EPA Guideline 83-3; US-EPA Pesticide Assessment Guidelines, Subdivision F, addendum 10, neurotoxicity day 0 of gestation until 22 days post partum 0-150-500-1750 ppm (equivalent to: 0-12.9-42.9-142 mg/kg bw/d (gestation) 0-27.3-90.0-299 mg/kg bw/d (lactation) Purity: 95.5-95.9%	NOELs (gestation / lactation) Maternal = 42.9 / 90.0 mg/kg bw/d Developmental = 12.9 / 27.3 mg/kg bw/d Developmental neurobehavioral effects > 142 / > 299 mg/kg bw/d	[220]
Rat male/female	Oral	JMAFF 59 NohSan No 4200; JMAFF 63-44; OECD 401; Directive 92/69/EC Method B.I.; Directive 92/18/EEC, L97; US-EPA Section 81-1; OPPTS 870. 1100 Purity: 96.0%	LD50 = > 5000 mg/kg bw	[221]
Rat male/female	Acute neurotoxicity gavage	US-EPA-FIFRA, Guideline 81-8(SS); US-EPA OPPTS 870.6200 0-100-200-400 mg/kg bw/d Purity: 95.2-96.0%	NOELs (male / female) Overall = > 60 / 100 mg/kg bw Neurotoxicity = > 400 mg/kg bw/d not neurotoxic	[222]
Mouse male/female	Oral	OECD 401; Directive 92/69/EC, Method B. 1.; Directive 92/18/EEC, L97; US-EPA Section 81-1; US-EPA OPPTS 870.1100 Purity: 96.0%	LD50 = 389 mg/kg bw (m) 465 mg/kg bw (f)	[223]

Rat male/female	Dermal	JMAFF 59 NohSan No 4200; JMAFF 63-44; OECD 402; Directive 92/69/EC, Method B.3.; Directive 92/18/EEC, L97; US-EPA Section 81-2; US-EPA OPPTS 870.1200 24 h semi-occlusive conditions Purity: 96.0%	LD50 = > 2000 mg/kg bw	[224]
Rat male/female	Inhalation	JMAFF 59 NohSan No 4200; JMAFF 63-44; OECD 403; Directive 92/69/EC, Method B.2.; Directive 92/18/EEC, OJEC, L97; USA-EPA Section 81-3; US-EPA OPPTS 870.1330 4.5 h exposure Purity: 96.0%	LC50 = > 6.141 mg/L	[225]
Rabbit male/female	Skin irritation	JMAFF 59 NohSan No 4200; JMAFF 63-44; OECD 404; Directive 92/69/EC, Method B.4.; Directive 92/18/EEC L97; US-EPA Section 81-5; US-EPA OPPTS 870.2500 4 h exposure Purity: 96.0%	Non-irritating	[226]
Rat male/female	Oral	JMAFF 59 NohSan No 4200; JMAFF 63-44; OECD 401; Directive 92/69/EC Method B.I.; Directive 92/18/EEC, L97; US-EPA Section 81-1; OPPTS 870. 1100 Purity: 96.0%	LD50 = > 5000 mg/kg bw	[227]
Rat male/female	Acute neurotoxicity gavage	US-EPA-FIFRA, Guideline 81-8(SS); US-EPA OPPTS 870.6200 0-100-200-400 mg/kg bw/d Purity: 95.2-96.0%	NOELs (male / female) Overall = > 60 / 100 mg/kg bw Neurotoxicity = > 400 mg/kg bw/d not neurotoxic	[228]
Mouse male/female	Oral	OECD 401; Directive 92/69/EC, Method B. 1.; Directive 92/18/EEC, L97; US-EPA Section 81-1; US-EPA OPPTS 870.1100 Purity: 96.0%	LD50 = 389 mg/kg bw (m) 465 mg/kg bw (f)	[229]

Rat male/female	Dermal	JMAFF 59 NohSan No 4200; JMAFF 63-44; OECD 402; Directive 92/69/EC, Method B.3.; Directive 92/18/EEC, L97; US-EPA Section 81-2; US-EPA OPPTS 870.1200 24 h semi-occlusive conditions Purity: 96.0%	LD50 = > 2000 mg/kg bw	[230]
Rat male/female	Inhalation	JMAFF 59 NohSan No 4200; JMAFF 63-44; OECD 403; Directive 92/69/EC, Method B.2.; Directive 92/18/EEC, OJEC, L97; USA-EPA Section 81-3; US-EPA OPPTS 870.1330 4.5 h exposure Purity: 96.0%	LC50 = > 6.141 mg/L	[231]
Rabbit male/female	Skin irritation	JMAFF 59 NohSan No 4200; JMAFF 63-44; OECD 404; Directive 92/69/EC, Method B.4.; Directive 92/18/EEC L97; US-EPA Section 81-5; US-EPA OPPTS 870.2500 4 h exposure Purity: 96.0%	Non-irritating	[232]
Rabbit male	Eye irritation	OECD 405; Directive 92/69/EC, Method B.5.; Directive 92/18/EEC L97; US-EPA Section 81-4; US-EPA OPPTS 870.2400 24 h exposure Purity: 96.0%	Non-irritating	[233]
Guinea pig	Skin sensitization	OECD 406; Directive 92/69/EC, Method B.6.; Directive 92/18/EEC L97; US-EPA Section 81-6; US-EPA OPPTS 870.2600 Purity: 96.0%	Non-sensitizing	[234]

Rat male/female	Sub-acute feeding	OECD 407; Directive 92/69/EEC (OJ No. L383A, 29.12.92), Part B, Method B.7.; EPA Guideline in Subdivision F. Hazard Evaluation: Human and Domestic Animals, JANUARY 1984; JMAFF 59 Nohsan No. 4200 4 weeks 0-1250-2500-5000-7500 ppm (equivalent to: 0-120-249-475-602 mg/kg bw/d (male), 0-137-228-454-689 mg/kg bw/d (female)) Purity: 97.5%	NOAEL = 120 / 137 mg/kg bw/d LOEL = 249 / 228 mg/kg bw/d	[235]
Mouse male/female	Sub-acute feeding	OECD 407; Directive 92/69/EEC (OJ No. L383A, 29.12.92), Part B, Method B.7.: EPA Guideline in Subdivision F. Hazard Evaluation: Human and Domestic Animals; JMAFF Nohsan No. 4200 deviation: duration 4 weeks 0-500-1000-2000-4000 ppm (equivalent to: 0-90-190-383-683 mg/kg bw/d (male) 0-122-248-491-619 mg/kg bw/d (female)) Purity: 97.5%	NOAEL = 190 / 248 mg/kg bw/d LOEL = 383 / 491 mg/kg bw/d	[236]
Dog female	Dose-range finding (palatability) feeding	Exposure to increasing dose levels 0 (for 11 days) - 3000 / 4000 / 5000 ppm (days 1-3 / 4-8 / 9-11) (equivalent to: 0- 51.1/50.8/51.8 mg/kg bw/d) Purity: 95.2%	NOEL = 51.8 mg/kg bw/d	[237]
Dog male/female	Dose-range finding feeding	Directive 88/302/EEC, Method B.27; US-EPA FIFRA Subdivision F, Section 82-1; US-EPA 870.3150; JMAFF 59 Nohsan No. 4200; mainly in accordance to OECD 409 4 weeks, 3 animals/sex/group 0-1250-2500-5000 ppm (equivalent to: 0-36.3-35.8-62.4 mg/kg bw/d (male) 0-35.6-52.3-57.4 mg/kg bw/d (female)) Purity: 95.2%	NOAEL = 36.3 / 35.6 mg/kg bw/d LOEL = 35.8 / 52.3 mg/kg bw/d	[238]

Rat male/female	Sub-acute dermal	US-EPA OPPTS 870.3200; JMAFF 59 Nohsan No. 4200; Directive 88/302/EEC (OJEC No. L 133/27) Part B; OECD 410 6 hrs/day, 28 days 0-100-300-1000 mg/kg bw/d Purity: 95.2%	NOEL = > 1000 mg/kg bw/d	[239]
Rat male/female	Sub-chronic feeding	FIFRA 82-1; TSCA 798.2650; US-EPA OPPTS 870.3100, OECD 408; JMAFF 59 NohSan No. 4200; Directive 87/302/EEC, part B 97 days 0-150-500-3000 ppm (equivalent to: 0-9.0-27.9-202 mg/kg bw/d (male) 0-10.9-34.0-254 mg/kg bw/d (female)) Purity: 95.3%	NOAEL = 27.9 / 34.0 mg/kg bw/d LOEL = 202 / 254 mg/kg bw/d	[240]
Dog male/female	Sub-chronic feeding	US-EPA-FTFRA Section. 82-1; US-EPA-OPPTS OPPTS 870.3150; OECD 409; JMAFF 59 Nohsan No. 4200; Directive 88/302/EEC (OJEC No. L 133/12), Part B 13 weeks 0-325-650-1500-2250 ppm (equivalent to: 0-9.2-19.3-40.9-58.2 mg/kg bw/d (male) 0-9.6-21.2- 42.1-61.8 mg/kg bw/d (female)) Purity: 95.2%	NOAEL = 19.3 / 21.2 mg/kg bw/d LOEL = 40.9 / 42.1 mg/kg bw/d	[241]
Dog male/female	Sub-chronic feeding	EPA-FIFRA Guideline 83-1; EPA-OPPTS Guideline Section 870.4100; OECD 452; JMAFF 59 Nohsan No. 4200, Directive 88/302/EEC, Part B 52 weeks 0-325-650-1500-2000ppm (equivalent to: 0-7.8-16.6-36.3-46.4 mg/kg bw/d (male) 0-8.5-15.0-40.1-52.9 mg/kg bw/d (female)) Purity: 95.2%	NOAEL = 36.3 / 40.1 mg/kg bw/d LOEL = 46.4 / 52.9 mg/kg bw/d	[242]

Rat male/female	Chronic oncogenicity feeding	JMAFF 59 NohSan No. 4200; OECD 453; EEC 88/302/EEC; FIFRA F, 83-5; OPPTS 870.4300 104 weeks 0-150-500-1500-3000 ppm (equivalent to: 0-8.1-27.4-82-157 mg/kg bw/d (male) 0-9.7-32.5-97.8-193 mg/kg bw/d (female)) Purity: 95.2-95.5%	NOAEL = 27.4 / 9.7 mg/kg bw/d LOEL = 82 / 32.5 mg/kg bw/d not carcinogenic	[243]
Mouse male/female	Oncogenicity feeding	JMAFF 59 NohSan No. 4200; OECD 451; EEC 88/302/EEC; FIFRA F, 83-2; OPPTS 870.4200 78 weeks 0-100-350-700/2000/2500/2000/1800 (week 1-4/ 5-10/ 11-34/ 35-termination 2000 ppm (m)/ 1800 ppm (f)) -1250 ppm (equivalent to: 0-13.5-47.2-171.4-251.9 mg/kg bw/d (male) 0-17.0-65.1-215.9-281.1 mg/kg bw/d (female)) Purity: 95.2%	NOAEL = 47.2 / 65.1 mg/kg bw/d LOEL = 171.4 / 215.9 mg/kg bw/d not carcinogenic	[244]
Rat male/female	Pilot reproduction one generation	US-EPA-FIFRA, Section 158.340, No. 83-4: US-EPA-TSCA, 40 CFR Section 798.4700: Guideline 87/302/EEC; OECD 416; J MAFF, 59 NohSan No. 4200 pre-mating 8 weeks 0-50-100-500-1000 ppm (equivalent during pre-mating to: 3.2-3.5 / 5.9-6.8 / 31.7-36.4 / 66.6 - 70.8 mg/kg bw/d) Purity: 95.2-96.0%	NOEL repro. = > 66.6 mg/kg bw/d	[245]
Rat male/female	Reproduction 2-generation	US-EPA, OPPTS 870.3800; Directive 91/414/EEC; OECD 416; JMAFF, 59 NohSan No. 4200 0-150-500-2500 ppm (equivalent to both generations combined: 0-10.2-32.7-179.6 mg/kg bw/d (male) 0-11.8-37.9-212.9 mg/kg bw/d (female) Purity: 95.3-96.0%	Parental NOEL = 32.7/11.8 mg/kg bw/d LOEL = 179.6/37.9 mg/kg bw/d Reproductive NOEL = >179.6/ >212.9 mg/kg bw/d Offspring NOEL = 10.2/11.8 mg/kg bw/d LOEL = 32.7/37.9 mg/kg bw/d	[246]

Rat female	Dose-range finding developmental toxicity	US-EPA OPPTS 870.3700 gestation days 6-19 0-125-250-500-1000 mg/kg bw/d Purity: 96.0%	Maternal NOAEL = not established LOEL = 125 mg/kg bw/d Developmental NOAEL = 125 mg/kg bw/d LOEL = 250 mg/kg bw/d	[247]
Rat female	Developmental toxicity	Guideline 88/302/EEC; OECD 414; US-EPA OPPTS 870.3700; JMAFF 59 NohSan no. 4200 gestation days 6-19 0-10-40-125 mg/kg bw/d Purity: 95.2%	Maternal NOEL = 10 mg/kg bw/d LOEL = 40 mg/kg bw/d Developmental NOAEL = 125 mg/kg bw/d LOEL = > 125 mg/kg bw/d not teratogenic	[248]
Rabbit female	Dose-range finding developmental toxicity	US-EPA OPPTS 870.3700 gestation days 6-28 0-62.5-125-250-500 mg/kg bw/d Purity: 96.0%	Maternal NOAEL = 62.5 mg/kg bw/d MTD < 125 mg/kg bw/d Developmental NOAEL > 62.5 mg/kg bw/d	[249]
Rabbit female	Developmental toxicity	Guideline 88/302/EEC, OECD 414; US-EPA OPPTS 870.3700; JMAFF 59 NohSan no. 4200 gestation days 6-28 0-10-25-75-100 mg/kg bw/d Purity: 95.2-95.5%	Maternal NOEL = 10 mg/kg bw/d LOEL = 25 mg/kg bw/d Developmental NOAEL = 75 mg/kg bw/d LOEL = 100 mg/kg bw/d not teratogenic	[250]
Rat male/female	Sub-chronic neurotoxicity feeding	US-EPA-FIFRA, Guideline 82-5(b); US-EPA OPPTS 870.6200 0-150-1000-3000 ppm equivalent to: 0-9.2-60-177 mg/kg bw/d (male) 0-10.6-71-200 mg/kg bw/d (female) Purity: 95.3-96.0%	NOELs (male / female) Overall = 60 / 71 mg/kg bw d Neurotoxicity = >177 / >200 mg/kg bw/d not neurotoxic	[251]

Rat male/female	Developmental neurotoxicity feeding	US-EPA OPPTS 870.6300; US-EPA Guideline 83-3; US-EPA Pesticide Assessment Guidelines, Subdivision F, addendum 10, neurotoxicity day 0 of gestation until 22 days post partum 0-150-500-1750 ppm (equivalent to: 0-12.9-42.9-142 mg/kg bw/d (gestation) 0-27.3-90.0-299 mg/kg bw/d (lactation) Purity: 95.5-95.9%	NOELs (gestation / lactation) Maternal = 42.9 / 90.0 mg/kg bw/d Developmental = 12.9 / 27.3 mg/kg bw/d Developmental neurobehavioral effects > 142 / > 299 mg/kg bw/d	[252]

Table 5. **Mutagenicity profile of technical clothianidin based on in vitro and in vivo tests**

Species	Test	Duration and Conditions	Result	Reference
Salmonella typhimurium / escherichia coli	Reverse mutation assay 'Ames test' in vitro	Guideline 92/69/EEC, Method B.I4.; OECD 471, US-EPA FIFRA section 84-2; JMAFF 59 NohSan no. 4200; Japan Ministry of Labour No. 77 S. typhimurium: TA 98, TA 100, TA 1535, TA 1537; E. coli: WP2uvrA$^-$ 0-50-150-500-1500-5000 µg/plate (+/- S9 mix) Purity: 95.2-96.0%	Positive (+S9 mix in TA 1535 only)	[201]
Salmonella typhimurium / escherichia coli	Reverse mutation assay 'Ames test' in vitro	Guideline 92/69/EEC, Method B.14.; JMAFF 59 NohSan no. 4200 S. typhimurium: TA 98, TA 100, TA 1535, TA 1537; E. coli: WP2uvrA$^-$ 0-313-625-1250-2500-5000 µg/plate (+/-S9 mix) Purity: ≥ 99%	Negative	[202]
Salmonella typhimurium	Reverse mutation assay 'Ames test' in vitro	Directive 92/69/EEC, Method B.14.; OECD 471; US-EPA 712-C-96-219, OPPTS 870.5265 S. typhimurium: TA 98, TA 100, TA 102, TA 1535, TA 1537 0-16-50-158-500-1581-5000 µg/plate/tube (+/-S9 mix) TA 102: 0-16-32-48-64-80-96-112 µg/plate (+/-S9 mix) Purity: 95.2%	Negative	[203]
Salmonella typhimurium	Reverse mutation assay 'Ames test' in vitro	Directive 92/69/EEC, Method B.14.; OECD 471; US- EPA 712-C-96-219, OPPTS 870.5265 S. typhimurium: TA 1535 Batch NLL 6100-3: 0-1000-2000-3000-4000-5000 µg/plate, Batch 30034708: 3000-5000-7000 µg/plate, 0-1000-2000-4000-6000-8000 µg/tube each batch +/- S9 mix, pre-incubation technique Purity: 98.6% (batch NLL 6100-3), 96.2% (batch 30034708)	Negative	[204]

Species	Test	Duration and Conditions	Result	Reference
Salmonella typhimurium / escherichia coli	Reverse mutation assay 'Ames test' in vitro	Guideline 92/69/EEC, Method B.I4.; OECD 471, US-EPA FIFRA section 84-2; JMAFF 59 NohSan no. 4200; Japan Ministry of Labour No. 77 S. typhimurium: TA 98, TA 100, TA 1535, TA 1537; E. coli: WP2uvrA$^-$ 0-50-150-500-1500-5000 µg/plate (+/- S9 mix) Purity: 95.2-96.0%	Positive (+S9 mix in TA 1535 only)	[205]
Salmonella typhimurium / escherichia coli	Reverse mutation assay 'Ames test' in vitro	Guideline 92/69/EEC, Method B.14.; JMAFF 59 NohSan no. 4200 S. typhimurium: TA 98, TA 100, TA 1535, TA 1537; E. coli: WP2uvrA$^-$ 0-313-625-1250-2500-5000 µg/plate (+/-S9 mix) Purity: ≥ 99%	Negative	[206]
Salmonella typhimurium	Reverse mutation assay 'Ames test' in vitro	Directive 92/69/EEC, Method B.14.; OECD 471; US-EPA 712-C-96-219, OPPTS 870.5265 S. typhimurium: TA 98, TA 100, TA 102, TA 1535, TA 1537 0-16-50-158-500-1581-5000 µg/plate/tube (+/-S9 mix) TA 102: 0-16-32-48-64-80-96-112 µg/plate (+/-S9 mix) Purity: 95.2%	Negative	[207]
Salmonella typhimurium	Reverse mutation assay 'Ames test' in vitro	Directive 92/69/EEC, Method B.14.; OECD 471; US- EPA 712-C-96-219, OPPTS 870.5265 S. typhimurium: TA 1535 Batch NLL 6100-3: 0-1000-2000-3000-4000-5000 µg/plate, Batch 30034708: 3000-5000-7000 µg/plate, 0-1000-2000-4000-6000-8000 µg/tube each batch +/- S9 mix, pre-incubation technique Purity: 98.6% (batch NLL 6100-3), 96.2% (batch 30034708)	Negative	[208]
Bacillus subtilis	DNA repair assay in vitro	JMAFF 59 Nohsan No. 4200 0-375-750-1500-3000-6000 µg/disc (+/- S9 mix) Purity: ≥ 99%	Negative	[209]

Chinese hamster lung (CHL) cells	Chromosome aberration assay in vitro	OECD 473; Directive 92/69/EEC, Annex V, Part B, Method B.10.; US-EPA FIFRA section 84-2 ; JMAFF 59 Nohsan No 4200 1st assay: 0-156.25-312.5-625-937.5-1250-1875 µg/mL 2nd assay: 0- 39 to 1875 µg/mL exposure 4 – 48 hrs, recovery 0 – 18 hrs, +/- S9 mix Purity: 96.0%	Positive (+/- S9 mix)	[210]
Mouse lymphoma cells	Gene mutation in mammalian cells in vitro	OECD 476; Directive 87/303/EEC no. LI 33, Method B. 14.; EPA FIFRA section 84-2; JMAFF 59 Nohsan No 4200 0-312.5-625-1250-1667-2500 µg/mL (+/-S9 mix) 0-300-600-1200-1600-2000 µg/mL (-S9 mix) 0-600-1200-1600-2000-2400 µg/mL (+S9 mix) Purity: 96.0%	Positive	[211]
Chinese hamster lung V79 cells	Gene mutation in mammalian cells in vitro	Directive 88/302/EEC; OECD 476; US-EPA712-C-96-221, OPPTS 870.5300 0-156-313-625-1250-2500-5000 µg/mL (+/- S9 mix) Purity: 95.2%	Negative	[212]
Mouse bone marrow cells	Chromosome aberration assay Micronucleus test in vivo	OECD 474; Directive 92/69/EEC, no. L383A, Method B.12.; EPA section 84-2; JMAFF 59 NohSan No. 4200 0-25-50-100 mg/kg bw (oral) Purity: 96.0%	Negative	[213]
Rat hepatocytes	Unscheduled DNA synthesis in vivo	In accordance with OECD draft guideline ‘OECD Guidelines for Testing of Chemicals, Proposal for a New Guideline, "Genetic Toxicology: DNA Damage and Repair/ Unscheduled DNA Synthesis (UDS) Test with Mammalian Liver Cells In Vivo’ and in addition Directive 88/302/EEC; OECD 482; US-EPA PB 84-233295 0-2500-5000 mg/kg bw (oral) Purity: 95.2-96.2%	Negative	[214]

Table 6. **Ecotoxicology profile of technical clothianidin**

Species	Test	Duration and conditions	Result	
Bobwhite quail *(Colinus virginianus)*	Acute oral	14d, US EPA Subdivision E, Guideline 71-1 (1982)	LD50 > 2000 mg /kg bw	[301]
Japanese quail *(Coturnix coturnix japonica)*	Acute oral	14d, US EPA Subdivision E, Guideline 71-1 (1982)	LD50 = 430 mg /kg bw	[302]
Bobwhite quail *(Colinus virginianus)*	dietary	8d, OECD 205 (1984)	LC50 > 5200 mg/kg diet	[303]
Mallard duck *(Anas platyrhynchos)*	dietary	8d, OECD 205 (1984)	LC50 > 5200 mg/kg diet	[304]
Bobwhite quail *(Colinus virginianus)*	Reproduction	20 weeks, OECD 206	NOEC = 500 mg/kg diet	[305]
Mallard duck *(Anas platyrhynchos*	Reproduction	20 weeks, OECD 206	NOEC = 500 mg/kg diet	[306]
Rainbow trout *(Oncorhynchus mykiss)*	acute	96h, static, limit test, OECD 203	LC50 > 100 mg/l	[307]
Bluegill *(Lepomis macrochirus)*	acute	96h, static, limit test, OECD 203	LC50 > 120 mg/l	[308]
Fathead minnow *(Pimephales promelas)*	Chronic, ELS	33d, flow-through, US EPA Subdivision E, Guideline 72-4 (1982), US EPA OPPTS draft guideline 850.1400 (1996)	NOEC = 20 mg/l	[309]

Sheepshead minnow *(Cyprinodon variegatus)*	acute	96h, static, OECD 203	LC50 > 102.5mg/l	[310]
water flea *(Daphnia magna*)	acute toxicity	48h, static, OECD 202	EC_{50} > 120 mg/l	[311]
water flea *(Daphnia magna*)	Chronic toxicity	21d, semi-static, OECD 211	NOEC = 0.120 mg/l	[312]
Mysid shrimp (Mysidopsis bahia)	acute	96h, flow-through	LC50 = 0.053 mg/l	[313]
Mysid shrimp (Mysidopsis bahia)	Chronic, life cycle	39d, flow-though, OPPTS 850.1350	NOEC = 0.0097 mg/l	[314]
Oyster (*Crassostrea virginica*)	acute	96h, flow-through; OPPTS 850.1025	EC50 > 129.1 mg/l	[315]
Green alga *(Scenedesmus subspicatus)*	Chronic toxicity	72h, static, OECD 201	ErC50 > 270 mg/l	[316]
Green alga *(Selenastrum capricornutum)*	Chronic toxicity	72h, static, OECD 201	ErC50 > 120 mg/l	[317]
Sediment dwelling invertebrates *(Chironomus riparius)*	acute	48h, static	EC50 = 0.029 mg/l	[318]
Sediment dwelling invertebrates *(Chironomus riparius)*	chronic	28d, static, BBA	EC15 = 0.00072 mg/l	[319]

Duckweed *(Lemna gibba)*	chronic	14d, static renewal, US EPA OPPTS guideline 850.4400 (1996)	EC50 > 121 mg/l	[320]
Honeybee (*Apis mellifera*)	Acute oral Acute contact	48h, EPPO guideline n° 170 (1992)	Oral LD50 = 0.004 µg/bee Contact LD50 = 0.044 µg/bee	[321]
Parasitoid (*Aphidius rhopalosiphi*)	Laboratory	48h, tested as formulated product WG 500 g/kg SETAC (1994)	100 % mortality at 60 g a.s./ha	[322]
Predatory mite (*Typhlodromus pyri*)	Laboratory	14d, tested as formulated product WG 500 g/kg SETAC (1994)	69 % mortality at 60 g a.s./ha 97 % effect on reproduction at 60 g a.s./ha	[323]
Ground dwelling predatory species (*Aleochara bilineata*)	Laboratory	28d, tested as formulated product WG 500 g/kg SETAC (1994)	89 % corrected mortality at 75 g a.s./ha	[324]
Foliage dwelling predatory species (*Chrysoperla carnea*)	Laboratory	28d, tested as formulated product WG 500 g/kg SETAC (1994)	97 % corrected mortality at 60 g a.s./ha	[325]
Earthworm (*Eisenia fetida*)	acute	14d, OECD 207	LC50 = 13.2 mg/kg soil	[326]
Nitrogen transformation Soil respiration		28d, OECD 216 and 217	No significant effects (<25%) at 750 g a.s./ha (equivalent to 1 mg a.s./kg soil)	[327]
Terrestrial plants (10 species)	Seedling emergence	14d, OPPTS 850.4100 and 850.4225	NOEC = 225 g a.s./ha	[328]
Terrestrial plants (10 species)	Vegetative vigour	14d, OPPTS 850.4150	NOEC = 225 g a.s./ha	[329]

ANNEX 2. REFERENCES

Reference Number	Year Title Published / Unpublished SCC report No BCS doc. ID	Owner
[101]	Year: 2000 Title: Vapor Pressure of TI-435, Pure Active Ingredient Unpublished SCC report No: THP-0026 BCS doc ID: M-026219-03-2	SCC
[102]	Year: 2000 Title: Determination of melting point/melting range of TI-435 pure active ingredient (PAI) Unpublished SCC report No: THP-0018 BCS doc ID: M-025309-02-1	SCC
[103]	Year: 2000 Title: Determination of Dissociation Constant and Physical-chemical Properties of TI-435 Pure Active Ingredient (PAI) (Density, Solubility, Octanol/Water Partition Coefficient, and Dissociation Constant) Unpublished SCC report No: THP-0013 BCS doc ID: M-026209-04-1	SCC
[104]	Year: 2001 Title:TI-435 (Pure Active Ingredient, PAI): Determination of the Effect of pH on Water Solubility and Partition Coefficient Unpublished SCC report No:not registered yet BCS doc ID: M-041740-01-1	
[105]	Year: 2000 Title: (14C)-TI-435: Hydrolytic stability Unpublished SCC report No: THP-0024 BCS doc ID: M-048047-01-1	SCC
[106]	Year: 2000 Title: Photolysis of [nitroimino-14C]TI-435 and [thiazolyl-2-14C]TI-435 in sterile aqueous buffer solution Unpublished SCC report No: THM-0013 BCS doc ID: M-023549-02-1	SCC
[107]	Year: 1999 Title: Determination of the quantum yield and assessment of the environmental half-life of the direct photodegradation of TI-435 in water Unpublished SCC report No: THP-0023 BCS doc ID: M-010153-02-1	SCC
[108]	Year: 2001 Title: Analytical method for analysis of TI-435 technical grade active ingredient (TGAI) Unpublished SCC report No: THA-0012 BCS doc ID: not registered	SCC
[201]	Year: 1997 Title: TI-435 - Acute oral toxicity study in the rat Unpublished	SCC

Reference Number	Year Title Published / Unpublished SCC report No BCS doc. ID	Owner
	SCC report No: THT-0047 BCS doc. ID: M-027393-01-1	
[202]	Year: 2000 Title: An acute oral neurotoxicity screening study with technical grade TI-435 in Fischer 344 rats Unpublished SCC report No: THT-0011 BCS doc. ID: M-027750-03-1	SCC
[203]	Year: 1997 Title: TI-435 - Acute oral toxicity study in the mouse Unpublished SCC report No: THT-0048 BCS doc. ID: M-027394-01-1	SCC
[204]	Year: 1997 Title: TI-435 - Acute dermal toxicity study in the rat Unpublished SCC report No: THT-0049 BCS doc. ID: M-027396-01-1	SCC
[205]	Year: 1998 Title: TI-435 - Single dose inhalation (head-only) toxicity study in the rat Unpublished SCC report No: THT-0070 BCS doc. M-027390-01-1	SCC
[206]	Year: 1997 Title: TI-435 - Skin irritation study in the rabbit Unpublished SCC report No: THT-0051 BCS doc. M-027402-01-1	SCC
[207]	Year: 1997 Title: TI-435 - Eye irritation study in the rabbit Unpublished SCC report No: THT-0050 BCS doc. M-027400-01-1	SCC
[208]	Year: 1997 Title: TI-435 - Skin sensitisation study in the guinea pig Unpublished SCC report No: THT-0065 BCS doc. M-027406-01-1	SCC
[209]	Year: 1997 Title: TI-435 - Toxicity to rats by dietary administration for 4 weeks Unpublished SCC report No: THT-0040 BCS doc. M-027408-01-1	SCC
[210]	Year: 1997 Title: TI-435 - Toxicity to mice by dietary administration for 4 weeks Unpublished SCC report No: THT-0041 BCS doc. M-027413-01-1	SCC
[211]	Year: 1998 Title: Palatability pilot study for dietary concentrations of TI-435 in dogs Unpublished SCC report No: THT-0078 BCS doc. M-027385-01-1	SCC

Reference Number	Year Title Published / Unpublished SCC report No BCS doc. ID	Owner
[212]	Year: 2000 Title: 4-week dietary toxicity study with TI-435 in dogs Unpublished SCC report No: THT-0069 BCS doc. M-027342-01-1	SCC
[213]	Year: 2000 Title: 28-day dermal toxicity study with TI-435 in rats Unpublished SCC report No: THT-0071 BCS doc. M-027480-01-1	SCC
[214]	Year: 2000 Title: Technical grade TI 435 - A subchronic toxicity testing study in the rat Unpublished SCC report No: THT-0045 BCS doc. M-027268-01-1	SCC
[215]	Year: 2000 Title: 13-Week dietary toxicity study with TI-435 in dogs Unpublished SCC report No: THT-0003 BCS doc. M-036499-02-1	SCC
[216]	Year: 2000 Title: 52-week dietary chronic toxicity study with TI-435 in dogs Unpublished SCC report No: THT-0004 BCS doc. M-036542-01-1	SCC
[217]	Year: 2000 Title: 104-week dietary combined chronic toxicity and carcinogenicity study with TI-435 in rats Unpublished SCC report No: THT-0038 BCS doc. M-031986-02-1	SCC
[218]	Year: 2000 Title: 78-week dietary carcinogenicity study with TI-435 in mice Unpublished SCC report No: THT-0005 BCS doc. M-032363-02-1	SCC
[219]	Year: 2000 Title: A pilot reproductive toxicity study with TI-435 in the Sprague-Dawley rat Unpublished SCC report No: THT-0001 BCS doc. M-027255-01-1	SCC
[220]	Year: 2000 Title: A two generation reproductive toxicity study with TI-435 in the Sprague-Dawley rat Unpublished SCC report No: THT-0046 BCS doc. M-031280-02-1	SCC
[221]	Year: 1998 Title: Oral (gavage) dosage-range developmental toxicity study of TI-435 in rats Unpublished SCC report No: THT-0062	SCC

Reference Number	Year Title Published / Unpublished SCC report No BCS doc. ID	Owner
	BCS doc. M-027430-02-1	
[222]	Year: 1998 Title: Oral (gavage) developmental toxicity study of TI-435 in rats Unpublished SCC report No: THT-0061 BCS doc. M-027416-01-1	SCC
[223]	Year: 1998 Title: Oral (stomach tube) dosage-range developmental toxicity study of TI-435 in rabbits Unpublished SCC report No: THT-0060 BCS doc. M-027436-02-1	SCC
[224]	Year: 1998 Title: Oral (stomach tube) developmental toxicity study of TI-435 in rabbits Unpublished SCC report No: THT-0059 BCS doc. M-027442-01-1	SCC
[225]	Year: 2000 Title: A subchronic neurotoxicity screening study with technical grade TI-435 in Fischer 344 rats Unpublished SCC report No: THT-0067 BCS doc. M-027986-01-1	SCC
[226]	Year: 2000 Title: Developmental neurotoxicity study of TI-435 administered orally via diet to CRL:CD BR VAF/PLUS presumed pregnant rats Unpublished SCC report No: THT-0068 BCS doc. M-027178-02-1	SCC
[227]	Year: 2000 Title: TI-435 - Reverse mutation assay 'Ames test' using *Salmonella typhimurium* and *Escherichia coli* Unpublished SCC report No: THT-0086 BCS doc. M-036520-01-1	SCC
[228]	Year: 1990 Title: Bacterial reverse mutation test of TIR-435 Unpublished SCC report No: THT-0087 BCS doc. M-036420-02-1	SCC
[229]	Year: 1997 Title: TI 435 - Salmonella/microsome test plate incorporation and preincubation method - revised version of Bayer report 26584, first revision - Unpublished SCC report No: THT-0079 BCS doc. M-009777-02-1	SCC
[230]	Year: 1996 Title: Special study - TI 435 - Salmonella/microsome test using *Salmonella typhimurium* TA 1535 plate incorporation and preincubation method - revised version of Bayer report 25739 - first revision Unpublished SCC report No: THT-0080 BCS doc. M-009769-02-1	SCC

Reference Number	Year Title Published / Unpublished SCC report No BCS doc. ID	Owner
[231]	Year: 1990 Title: DNA repair test of TIR-435 in *Bacillus subtilis* Unpublished SCC report No: THT-0097 BCS doc. M-036407-02-1	SCC
[232]	Year: 2000 Title: TI-435 - Chromosome aberration test in CHL cells in vitro Unpublished SCC report No: THT-0096 BCS doc. M-036479-02-1	SCC
[233]	Year: 2000 Title: TI-435 - L5178Y TK +/- mouse lymphoma assay Unpublished SCC report No: THT-0099 BCS doc. M-036462-02-1	SCC
[234]	Year: 1997 Title: TI 435 - Mutagenicity study for the detection of induced forward mutations in the V79-HPRT assay in vitro - revised version of Bayer report 26437, first revision - Unpublished SCC report No: THT-0095 BCS doc. M-009761-02-1	SCC
[235]	Year: 2000 Title: TI-435 - Micronucleus test in the mouse Unpublished SCC report No: THT-0098 BCS doc. M-036435-02-1	SCC
[236]	Year: 1997 Title: TI 435 - Test on unscheduled DNA synthesis with rat liver cells in vivo - revised version of Bayer report 26915, first revision - Unpublished SCC report No: THT-0100 BCS doc. M-009751-03-1	SCC
[301]	Year: 1998 Title: TI-435 technical - Acute oral toxicity (LD50) to bobwhite quail Unpublished SCC report No: THW-0119 BCS doc. M-027064-01-1	SCC
[302]	Year: 2000 Title: TI-435 technical: An acute oral toxicity study with the japanese quail Unpublished SCC report No: THW-0118 BCS doc. M-027285-01-1	SCC
[303]	Year: 1998 Title: TI-435 technical - Dietary LC50 to the bobwhite quail Unpublished SCC report No: THW-0120 BCS doc. M-027059-01-1	SCC
[304]	Year: 1998 Title: TI-435 technical - Dietary LC50 to the mallard duck Unpublished SCC report No: THW-0121 BCS doc. M-027068-01-1	SCC

Reference Number	Year Title Published / Unpublished SCC report No BCS doc. ID	Owner
[305]	Year: 2000 Title: TI-435 technical: A reproduction study with the northern bobwhite (*Colinus virginianus*) Unpublished SCC report No: THW-0116 BCS doc. M-027293-01-1	SCC
[306]	Year: 2000 Title: TI-435 technical: A reproduction study with the mallard (*Anas platyrhynchos*) Unpublished SCC report No: THW-0117 BCS doc. M-027289-01-1	SCC
[307]	Year: 1998 Title: TI-435 technical - Fish (rainbow trout), acute toxicity test, 96 h, limit test Unpublished SCC report No: THW-0029 BCS doc. M-027029-02-1	SCC
[308]	2000 Year: Title: TI-435 technical - A 96-hour static acute toxicity test with the bluegill (*Lepomis macrochirus*) Unpublished SCC report No: THW-0027 BCS doc. M-031285-01-1	BCS, SCC
[309]	Year: 2000 Title: TI-435 technical: An early life-stage toxicity test with the fathead minnow (*Pimephales promelas*) Unpublished SCC report No: THW-0026 BCS doc. M-031516-01-1	BCS, SCC
[310]	Year: 1999 Title: TI-435 technical - Fish (Sheepshead minnow), acute toxicity test, limit test, 96 h, semi-static Unpublished SCC report No: THW-0028 BCS doc. M-027244-01-1	SCC
[311]	Year: 2000 Title: TI-435 technical - A 48-hour static acute toxicity test with the cladoceran (*Daphnia magna*) Unpublished SCC report No: THW-0043 BCS doc. M-031283-01-1	BCS, SCC
[312]	Year: 1998 Title: TI-435 technical - Daphnia magna reproduction test (21 d) Unpublished SCC report No: THW-0049 BCS doc. M-027071-02-1	SCC
[313]	Year: 2000 Title: TI-435 technical: A 96-hour flow-through acute toxicity test with the saltwater mysid (*Mysidopsis bahia*) - final report Unpublished SCC report No: THW-0057	SCC

Reference Number	Year Title Published / Unpublished SCC report No BCS doc. ID	Owner
	BCS doc. M-019551-01-1	
[314]	Year: 2000 Title: TI-435 technical: A flow-through life-cycle toxicity test with the salwater mysid (*Mysidopsis bahia*) Unpublished SCC report No: THW-0058 BCS doc. M-026384-01-1	SCC
[315]	Year: 1999 Title: TI-435 technical - Oyster, acute toxicity test (shell deposition), limit test, flow-through, 96 h Unpublished SCC report No: THW-0059 BCS doc. M-028515-01-1	SCC
[316]	Year: 1998 Title: TI-435 technical - Alga, growth inhibition test (120 (h)) (*Scenedesmus subspicatus*) Unpublished SCC report No: THW-0040 BCS doc. M-027041-02-1	SCC
[317]	Year: 2000 Title: TI-435 technical - A 5-day toxicity test with the freshwater alga (*Selenastrum capricornutum*) Unpublished SCC report No: THW-0041 BCS doc. M-026366-01-1	SCC
[318]	Year: 2001 Title: TI-435: Comparative acute toxicity of *Chironomus riparius* with TZMU, MU, TZNG and MNG Unpublished SCC report No: THW-0051 BCS doc. M-032142-01-1	SCC
[319]	Year: 1999 Title: Infuence of TI 435 technical on development and emergence of larvae of *Chironomus riparius* in a water-sediment system Unpublished SCC report No: THW-0052 BCS doc. M-011874-01-1	SCC
[320]	Year: 2000 Title: TI-435 technical - A 14-day static-renewal toxicity test with duckweed (*Lemna gibba* G3) Unpublished SCC report No: THW-0042 BCS doc. M-031279-01-1	BCS, SCC
[321]	Year: 1998 Title: Final report - TI-435 technical: Acute contact and oral toxicity to honeybees Unpublished SCC report No: THW-0104 BCS doc. M-027051-01-1	SCC
[322]	Year: 1999 Title: Final report - TI-435: Tier I standard laboratory bioassay of the effects of fresh residues on Aphidius rhopalosiphi (Hymenoptera, Braconidae) Unpublished	SCC

Reference Number	**Year** **Title** **Published / Unpublished** **SCC report No** **BCS doc. ID**	**Owner**
	SCC report No: THW-0125 BCS doc. M-027182-01-1	
[323]	Year: 1999 Title: Final report - TI-435: Tier I standard laboratory bioassay of the effects of fresh residues on *Typhlodromus pyri* (Acari, Phytoseiidae) Unpublished SCC report No: THW-0132 BCS doc. M-027179-01-1	SCC
[324]	Year: 1999 Title: A laboratory evaluation of the effects of TI-435 50% WDG on adults of the staphylinid beetle, *Aleochara bilineata* *Unpublished* SCC report No: THW-0131 BCS doc. M-027200-01-1	SCC
[325]	Year: 1999 Title: Final report - TI-435: Tier I standard laboratory bioassay of the effects of fresh residues on *Chrysoperla carnea* (Neuroptera, Chrysopidae) Unpublished SCC report No: THW-0129 BCS doc. M-027198-01-1	SCC
[326]	Year: 1998 Title: Final report - TI-435 technical: Acute toxicity to the earthworm *Eisenia foetida* Unpublished SCC report No: THW-0065 BCS doc. M-027046-01-1	SCC
[327]	Year: 1999 Title: The effect of TI-435 50 % WDG on soil microflora (OECD guidelines 216 and 217 for the testing of chemicals. Revised draft documents, January 1999) Unpublished SCC report No: THW-0020 BCS doc. M-027297-01-1	SCC
[328]	Year: 2000 Title: TI-435 50 % WDG: A toxicity test to determine the effects of the test substance on seedling emergence of ten species of plants Unpublished SCC report No: THW-0002 BCS doc. M-026377-01-1	SCC
[329]	Year: 2000 Title: TI-435 50 % WDG: A toxicity test to determine the effects of the test substance on vegetative vigour of ten species of plants Unpublished SCC report No: THW-0015 BCS doc. M-026381-01-1	SCC