

# FAO SPECIFICATIONS AND EVALUATIONS FOR AGRICULTURAL PESTICIDES

## FIPRONIL

(±)-5-amino-1-(2,6-dichloro- $\alpha,\alpha,\alpha$ -trifluoro-p-tolyl)-4-trifluoromethylsulfanylpyrazole-3-carbonitrile



FOOD AND AGRICULTURE ORGANIZATION *of* THE UNITED NATIONS

# TABLE OF CONTENTS

## FIPRONIL

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|   | Page |
|---|------|
| DISCLAIMER  |      |
| INTRODUCTION  | 1    |
| <b>PART ONE</b>   |      |
| SPECIFICATIONS FOR FIPRONIL   | 2    |
| FIPRONIL INFORMATION  | 3    |
| FIPRONIL TECHNICAL MATERIAL (AUGUST 2009)                                     | 5    |
| FIPRONIL WATER DISPERSIBLE GRANULES (JULY 2009)                               | 6    |
| FIPRONIL WATER BASED SUSPENSION CONCENTRATE<br>(AUGUST 2009)                  | 9    |
| FIPRONIL EMULSIFIABLE CONCENTRATE (JULY 2009)                                 | 12   |
| FIPRONIL WATER BASED SUSPENSION CONCENTRATE<br>FOR SEED TREATMENT (JULY 2009) | 14   |
| FIPRONIL ULTRA LOW VOLUME LIQUID (JULY 2009)                                  | 17   |
| FIPRONIL GRANULES (AUGUST 2009)   | 19   |
| <b>PART TWO</b>   |      |
| EVALUATIONS OF FIPRONIL   | 21   |
| 2009.2 FAO/WHO EVALUATION REPORT ON FIPRONIL                                  | 22   |
| SUPPORTING INFORMATION  | 24   |
| ANNEX 1: HAZARD SUMMARY PROVIDED BY THE PROPOSER                              | 27   |
| ANNEX 2: REFERENCES   | 30   |
| 2009.1 FAO/WHO EVALUATION REPORT ON FIPRONIL                                  | 31   |
| SUPPORTING INFORMATION  | 35   |
| ANNEX 1: HAZARD SUMMARY PROVIDED BY THE PROPOSER                              | 39   |
| ANNEX 2: REFERENCES   | 50   |

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## DISCLAIMER<sup>1</sup>

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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.

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<sup>1</sup> This disclaimer applies to all specifications published by FAO.

## INTRODUCTION

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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.

Since 1999 the development of FAO specifications follows the **New Procedure**, described in the 5<sup>th</sup> edition of the “Manual on the development and use of FAO specifications for plant protection products” (FAO Plant Production and Protection Page No. 149). 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 JMPS, rather than the JMPS.]

FAO Specifications now only apply to products for which the technical materials have been evaluated. Consequently from the year 2000 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 plant protection product in accordance with chapter 4, 5 and 6 of the 5<sup>th</sup> edition of the “Manual on the development and use of FAO specifications for plant protection products”.

**PART TWO: The Evaluation Report(s)** of the plant protection product reflecting the evaluation of the data package carried out by FAO and the JMPS. The data are to be provided by the manufacturer(s) according to the requirements of Appendix A, Annex 1 or 2 of the “Manual on the development and use of FAO specifications for plant protection products” 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 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. Dates of publication of the earlier versions, if any, are identified in a footnote. Evaluations bear the date (year) of the meeting at which the recommendations were made by the JMPS.**

\* NOTE: PUBLICATIONS ARE AVAILABLE ON THE INTERNET AT  
<http://www.fao.org/agriculture/crops/core-themes/theme/pests/pm/jmps/en/>

- OR IN HARDCOPY FROM THE PLANT PROTECTION INFORMATION OFFICER.

**PART ONE**

**SPECIFICATIONS**

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FIPRONIL

Page

**PART ONE**

|   |    |
|---|----|
| SPECIFICATIONS FOR FIPRONIL   | 2  |
| FIPRONIL INFORMATION  | 3  |
| FIPRONIL TECHNICAL MATERIAL (AUGUST 2009)                                     | 5  |
| FIPRONIL WATER DISPERSIBLE GRANULES (JULY 2009)                               | 6  |
| FIPRONIL WATER BASED SUSPENSION CONCENTRATE<br>(AUGUST 2009)                  | 9  |
| FIPRONIL EMULSIFIABLE CONCENTRATE (JULY 2009)                                 | 12 |
| FIPRONIL WATER BASED SUSPENSION CONCENTRATE<br>FOR SEED TREATMENT (JULY 2009) | 14 |
| FIPRONIL ULTRA LOW VOLUME LIQUID (JULY 2009)                                  | 17 |
| FIPRONIL GRANULES (AUGUST 2009)   | 19 |

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FIPRONIL

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INFORMATION

*ISO Common Name:*

Fipronil (ISO 1750 published)

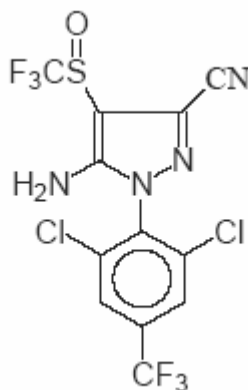
*Synonyms:*

None

*Chemical names*

IUPAC (±)-5-amino-1-(2,6-dichloro- $\alpha,\alpha,\alpha$ -trifluoro-p-tolyl)-4-trifluoromethylsulfinylpyrazole-3-carbonitrile  
CA 5-amino-[2,6-dichloro-4-(trifluoromethyl)phenyl]-4-[(1R,S)-(trifluoromethyl)sulfinyl]-1H-pyrazole-3-carbonitrile

*Structural formula:*



*Empirical formula*

C<sub>12</sub> H<sub>4</sub> Cl<sub>2</sub> F<sub>6</sub> N<sub>4</sub> OS

*Relative molecular mass*

437.15

*CAS Registry number*

120068-37-3

*CIPAC number*  
581

*Identity tests*  
HPLC retention time, IR spectrum.

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## FIPRONIL TECHNICAL MATERIAL

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### FAO specification 581/TC (August 2009<sup>\*</sup>)

*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 (581/2009.2 and 581/2009.1). 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 specifications. The specification may not be appropriate for the products of other manufacturers. The evaluation reports (581/2009.2 and 581/2009.1) as PART TWO form an integral part of this publication.*

#### 1. Description

The material shall consist of fipronil together with related manufacturing impurities and shall be a white to yellowish crystalline powder with moldy odor, free from visible extraneous matter and added modifying agents.

#### 2. Active ingredient

##### 2.1 Identity tests (581/TC/M/2, CIPAC J, p.60, 2000)

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 Fipronil content (581/TC/M/2, CIPAC J, p.60, 2000)

The fipronil content shall be declared (not less than 950 g/kg based on the dry active ingredient, Note 1) and, when determined, the average measured content shall not be lower than the declared minimum content.

Note 1 Fipronil TC may be a wet cake, as water can be added to the technical material to reduce its dustiness and the resulting risk of inhalation. For technical reasons (preparation of oil based formulations), the water content should not exceed 90g/kg. The water content can be measured using MT 30.5, CIPAC J, p. 120, 2000

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\* Specifications may be revised and/or additional evaluations may be undertaken. Ensure the use of current versions by checking at: <http://www.fao.org/agriculture/crops/core-themes/theme/pests/pm/jmps/ps/en/>.



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## FIPRONIL WATER DISPERSIBLE GRANULES

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FAO specification 581/WG (July 2009\*)

*This specification, which is PART ONE of this publication, is based on an evaluation of data submitted by the manufacturer whose name is listed in the evaluation report (581/2009.1). 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 specifications. The specification may not be appropriate for the products of other manufacturers. The evaluation report (581/2009.1) as PART TWO forms an integral part of this publication.*

### 1. Description

The material shall consist of a homogeneous mixture of technical fipronil, complying with the requirements of the FAO specification 581/TC (August 2009), together with carriers and any other necessary formulants. It shall be in the form of beige to brownish, irregularly shaped granules<sup>2</sup> 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 (581/WG/M/2 Note 1)

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 Fipronil content (581/WG/M/2 Note 1)

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

| Declared content in g/kg                       | Tolerance |
|--|-----------|
| above 250 up to 500                            | ± 5%      |
| above 500                                      | ± 25 g/kg |
| Note in each range the upper limit is included |           |

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\* Specifications may be revised and/or additional evaluations may be undertaken. Ensure the use of current versions by checking at: <http://www.fao.org/agriculture/crops/core-themes/theme/pests/pm/jmps/ps/en/>.

<sup>2</sup>granules with 95 % of the granules being of the size of 100 - 500 µm

### 3. Relevant impurity

#### 3.1 Water (MT 30.5, CIPAC J, p. 120, 2000)

Maximum: 20 g/kg.

### 4. Physical properties

#### 4.1 Wettability (MT 53.3, CIPAC F, p. 164, 1995)

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

#### 4.2 Wet sieve test (MT 185, CIPAC K, p. 149, 2003)

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

#### 4.3 Degree of dispersion (MT 174, CIPAC F; p. 435, 1995)

Dispersibility: minimum 85 % after 1 minute of stirring.

#### 4.4 Suspensibility (MT 168, CIPAC F, p. 417, 1995, MT 184, CIPAC K, p. 142, 2003) (Note 2 and 3)

A minimum of 70 % of the fipronil content found under 2.2 shall be in the suspension after 30 min in CIPAC Standard Water D at 30 + 2 °C (Note 2).

#### 4.5 Persistent foam (MT 47.2, CIPAC F, p. 152, 1995) (Note 4)

Maximum: 50 ml after 1 min.

#### 4.6 Dustiness (MT 171, CIPAC F, p. 425, 1995, gravimetric) (Note 5)

Essentially dust free.

#### 4.7 Flowability (MT 172, CIPAC F, p. 430, 1995)

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

#### 4.8 Attrition resistance (MT 178.2)

Minimum: 96 % attrition resistance.

### 5. Storage stability

#### 5.1 Stability at elevated temperature (MT 46, CIPAC F, p.148, 1995)

After storage at 54 + 2 °C for 14 days (Note 6), 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

- wet sieve test (4.2),
- degree of dispersion (4.3),
- suspensibility (4.4),
- dustiness (4.6) and
- flowability (4.7), as required.

Note 1 Methods for the identification and determination of fipronil content in FS, SC and WG formulations were presented at the CIPAC Meeting in 2008 and provisionally adopted as CIPAC method. Prior to their publication in Handbook N, copies of the methods may be obtained through the CIPAC

website, <http://www.cipac.org/prepubme.htm>

- Note 2 The formulation should be tested at the highest and lowest rates of use recommended by the supplier, provided this does not exceed the conditions given in methods MT 168 and MT 184.
- 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, MT 168, 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 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 method, MT 171.2, usually shows good correlation with the gravimetric method, MT 171.1, 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 6 Unless other temperatures and/or times are specified.
- Note 7 Analysis of the formulation, before and after the storage stability test, should be carried out concurrently (i.e. after storage) to reduce analytical error.

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## FIPRONIL AQUEOUS SUSPENSION CONCENTRATE

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### FAO specification 581/SC (August 2009<sup>\*</sup>)

*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 (581/2009.2 and 581/2009.1). 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 specifications. The specification may not be appropriate for the products of other manufacturers. The evaluation reports (581/2009.2 and 581/2009.1) as PART TWO form an integral part of this publication.*

#### 1. Description

The material shall consist of a suspension of fine particles of technical fipronil, complying with the requirements of FAO specification 581/TC (August 2009), in an aqueous phase together with suitable formulants. After gentle agitation the material shall be homogeneous (Note 1) and suitable for further dilution in water.

#### 2. Active ingredient

##### 2.1 Identity tests (581/SC/M/2 Note 1)

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 Fipronil content (581/SC/M/2 Note 1)

The fipronil content shall be declared (g/kg or g/l at  $20 \pm 2^\circ\text{C}$ , Note 2) and, when determined, the average measured content shall not differ from that declared by more than the following tolerances:

| Declared content in g/kg or g/l at $20 \pm 2^\circ\text{C}$ | Tolerance                          |
|---|------------------------------------|
| above 25 up to 100  | $\pm 10\%$ of the declared content |
| above 100 up to 250   | $\pm 6\%$ of the declared content  |
| Note: in each range the upper limit is included.            |                                    |

#### 3. Physical properties

##### 3.1 pH range (MT 75.3, CIPAC J, p.131, 2000)

pH range: 5 to 7

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\* Specifications may be revised and/or additional evaluations may be undertaken. Ensure the use of current versions by checking at: <http://www.fao.org/agriculture/crops/core-themes/theme/pests/pm/jmps/ps/en/>.

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

Maximum "residue": 5%.

**3.3 Spontaneity of dispersion** (MT 160, CIPAC F, p.391, 1995) (Note 3)

A minimum of 80% of the fipronil content found under 2.2 shall be in the suspension after 5 min in CIPAC standard water D at  $30 \pm 2^\circ\text{C}$ .

**3.4 Suspensibility** (MT 184, CIPAC K, p.142, 2003) (Note 3)

A minimum of 70% of the fipronil content found under 2.2 shall be in the suspension after 30 min in CIPAC standard water D at  $30 \pm 2^\circ\text{C}$ .

**3.5 Wet sieve test** (MT185, CIPAC K, p.149, 2003) (Note 4)

Maximum: 2% of the formulation shall be retained on a 75  $\mu\text{m}$  test sieve.

**3.6 Persistent foam** (MT 47.2, CIPAC F, p. 152, 1995) (Note 5)

Maximum: 50 ml after 1 min.

**4. Storage stability**

**4.1 Stability at  $0^\circ\text{C}$**  (MT 39.3, CIPAC J, p.126, 2000)

After storage at  $0 \pm 2^\circ\text{C}$  for 7 days, the formulation shall continue to comply with the clauses for:

- suspensibility (3.4),
- wet sieve test (3.5).

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

After storage at  $54 \pm 2^\circ\text{C}$  for 14 days (Note 6), 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 product shall continue to comply with the clauses for:

- pH range (3.1),
- pourability (3.2),
- spontaneity of dispersion (3.3),
- suspensibility (3.4),
- wet sieve test (3.5).

**Note 1** Methods for the identification and determination of fipronil content in FS, SC, WG and GR formulations were presented at the CIPAC Meeting in 2008 and provisionally adopted as CIPAC method. Prior to their publication in Handbook N, copies of the methods may be obtained through the CIPAC website, <http://www.cipac.org/prepubme.htm>

**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 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 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 the 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 Chemical assay is the only fully reliable method to measure the mass of active ingredient still in suspension. However, simpler methods such as gravimetric and solvent extraction determination may be used on a routine basis provided that these methods have been shown to give results equal to those of the chemical assay method. In case of dispute, the chemical method shall be the referee method.

Note 5 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 6 The mass of sample to be used in the test should be at the application rate of use recommended by the supplier.

Note 7 Unless other temperatures and/or times are specified.

Note 8 Samples of the formulation taken before and after the storage stability test should be analyzed concurrently after the test in order to reduce the analytical error.

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## FIPRONIL EMULSIFIABLE CONCENTRATE

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### FAO specification 581/EC (July 2009\*)

*This specification, which is PART ONE of this publication, is based on an evaluation of data submitted by the manufacturer whose name is listed in the evaluation report (581/2009.1). 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 specifications. The specification may not be appropriate for the products of other manufacturers. The evaluation report (581/2009.1) as PART TWO forms an integral part of this publication.*

#### 1. Description

The material shall consist of technical fipronil, complying with the requirements of FAO specification 581/TC (August 2009) dissolved in suitable solvents together with any other necessary formulants. It shall be in the form of a stable homogeneous liquid, free from visible suspended matter and sediment, to be applied as an emulsion after dilution with water.

#### 2. Active ingredient

##### 2.1 Identity tests (581/EC/M/2, CIPAC J p.63, 2000)

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 Fipronil content (581/EC/M/3, CIPAC J, p.63, 2000)

The fipronil content shall be declared (g/kg or g/l at  $20 \pm 2^\circ\text{C}$ , Note 1) and, when determined, the average measured content shall not differ from that declared by more than the following tolerances:

| Declared content in g/kg or g/l at $20 \pm 2^\circ\text{C}$ | Tolerance                          |
|---|------------------------------------|
| up to 25  | $\pm 15\%$ of the declared content |
| above 25 up to 100  | $\pm 10\%$ of the declared content |
| Note: in each range the upper limit is included.            |                                    |

#### 3. Physical properties

##### 3.1 Emulsion stability and re-emulsification (MT 36.3; CIPAC K, p.137, 2003)

The formulation, when diluted at  $30 \pm 2^\circ\text{C}$  (Note 2) with CIPAC Standard Waters A and D, shall comply with the following:

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\* Specifications may be revised and/or additional evaluations may be undertaken. Ensure the use of current versions by checking at: <http://www.fao.org/agriculture/crops/core-themes/theme/pests/pm/jmps/ps/en/>.

|  |  |
|--|--|
| Time after dilution  | Limits of stability, MT 36.3                       |
| 0 h  | Initial emulsification complete                    |
| 0.5 h  | “Cream”, maximum: 2 ml                             |
| 2 h  | “Cream”, maximum: 2 ml “Free oil”, maximum: 0.2 ml |
| 24 h   | Re-emulsification complete                         |
| 24.5 h   | “Cream”, maximum: 2 ml “Free oil”, maximum: 0.2 ml |
| Note: tests after 24 h are required only where results at 2 hr are in doubt. |  |

### 3.2 Persistent foam (MT 47.2, CIPAC F, p.152, 1995) (Note 3)

Maximum: 50 ml after 1min.

## 4. Storage stability

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

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

### 4.2 Stability at elevated temperature (MT 46.3, CIPAC J, p.128, 2000)

After storage at  $54 \pm 2$  °C for 14 days (Note 4), the determined average active ingredient content must not be lower than 95% relative to the determined average content found before storage (Note 5) and the product shall continue to comply with the clauses for:

- emulsion stability and re-emulsification (3.1).

Note 1 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 2 Unless another temperature is specified.

Note 3 The test should be carried out at the highest application concentration.

Note 4 Unless other temperatures and/or times are specified.

Note 5 Samples of the formulation taken before and after the storage stability test should be analyzed concurrently after the test in order to reduce the analytical error.



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**FIPRONIL SUSPENSION CONCENTRATE FOR SEED TREATMENT**

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FAO specification 581/FS (July 2009<sup>\*</sup>) (Note 1)

*This specification, which is PART ONE of this publication, is based on an evaluation of data submitted by the manufacturer whose name is listed in the evaluation report (581/2009.1). 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 specifications. The specification may not be appropriate for the products of other manufacturers. The evaluation report (581/2009.1) as PART TWO forms an integral part of this publication.*

**1. Description**

The material shall consist of a suspension of fine particles of technical fipronil, complying with the requirements of FAO specification 581/TC (August 2009), in an aqueous phase together with suitable formulants (Note 1). After gentle agitation the material shall be homogeneous (Note 2) and suitable for further dilution in water.

**2. Active ingredient**

**2.1 Identity tests** (581/FS/M/2 Note 3)

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 Fipronil content** (581/FS/M/2 Note 3)

The fipronil content shall be declared (g/kg or g/l at 20 ± 2°C, Note 3) and, when determined, the average measured content 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 25 up to 100                               | ± 10% of the declared content |
| above 100 up to 250                              | ± 6% of the declared content  |
| above 250 up to 500                              | ± 5% of the declared content  |
| above 500  | ±25 g/kg or g/l               |
| Note: in each range the upper limit is included. |                               |

**3. Physical properties**

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

5 to 9.

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<sup>\*</sup> Specifications may be revised and/or additional evaluations may be undertaken. Ensure the use of current versions by checking at: <http://www.fao.org/agriculture/crops/core-themes/theme/pests/pm/jmps/ps/en/>.

**3.2 Pourability (MT 148.1)**

Maximum "residue": 5%.

**3.3 Wet sieve test (MT185, CIPAC K, p.149, 2003) (Note 4)**

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

**3.4 Particle size distribution (MT 187, CIPAC Handbook K, p. 153, 2003)**

>50% of particles shall be in the range 0.1 µm to 4 µm (Note 5)

**4. Storage stability**

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

After storage at  $0 \pm 2^\circ\text{C}$  for 7 days, the volume of solid and/or liquid which separates shall not be more than 0.3 ml.

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

After storage at  $54 \pm 2^\circ\text{C}$  for 14 days (Note 6) 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 product shall continue to comply with the clause for:

- pH range (3.1),
- pourability (3.2)
- wet sieve test (3.3)

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. Treated seeds shall be colored. 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 Methods for the identification and determination of fipronil content in FS, SC, WG and GR formulations were presented at the CIPAC Meeting in 2008 and provisionally adopted as CIPAC method. Prior to their publication in Handbook N, copies of the methods may be obtained through the CIPAC website, <http://www.cipac.org/prepubme.htm>

Note 4 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  $20^\circ\text{C}$ , then in case of dispute the analytical results shall be calculated as g/kg.

Note 5 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 6 Percentages may be specified in one or more ranges, as appropriate to the product.

Note 7 Unless other temperatures and/or times are specified.

Note 8 Samples of the formulation taken before and after the storage stability test should be analyzed concurrently after the test in order to reduce the analytical error.

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## FIPRONIL ULTRA LOW VOLUME LIQUID

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### FAO specification 581/UL (August 2009)\*

*This specification, which is PART ONE of this publication, is based on an evaluation of data submitted by the manufacturer whose name is listed in the evaluation report (581/2009.1). 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 specifications. The specification may not be appropriate for the products of other manufacturers. The evaluation report (581/2009.1) as PART TWO forms an integral part of this publication*

#### 1. Description

The material shall consist of technical fipronil, complying with the requirements of FAO specification 581/TC (August 2009), in the form of an organic solution, together with any necessary formulants. It shall be in the form of a stable homogeneous liquid, free from visible suspended matter and sediment.

#### 2. Active ingredient

##### 2.1 Identity tests (581/UL/M/2, CIPAC J, p.63, 2000)

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 Fipronil content (581/UL/M/3, CIPAC J, p.63, 2000)

The fipronil content shall be declared (g/kg or g/l at  $20 \pm 2^\circ\text{C}$ , Note 1) and, when determined, the average measured content shall not differ from that declared by more than the following tolerances:

| Declared content in g/kg or g/l at $20 \pm 2^\circ\text{C}$ | Tolerance                          |
|---|------------------------------------|
| up to 25 g/l  | $\pm 15\%$ of the declared content |
| above 25 up to 100  | $\pm 10\%$ of the declared content |
| Note in each range the upper limit is included              |                                    |

#### 3. Relevant impurity

##### 3.1 Water (MT 30.5, CIPAC J; p. 120, 2000)

Maximum: 5 g/l.

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\* Specifications may be revised and/or additional evaluations may be undertaken. Ensure the use of current versions by checking at: <http://www.fao.org/agriculture/crops/core-themes/theme/pests/pm/jmps/ps/en/>.

#### 4. Physical properties (Note 2)

##### 4.1 Viscosity, (MT 192) (Note 3)

The viscosity shall be declared for individual formulations. It shall be in the range of 2 to 50 mPa.s.

#### 5. Storage stability

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

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

##### 5.2 Stability at elevated temperature (MT 46.3, CIPAC J, p.128, 2000)

After storage at  $54 \pm 2$  °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 4)

Note 1 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 2 A limit for the flash point of the formulation is not a standard clause under "Physical properties". However, as the UL is intended for application by aircraft, a minimum of 61° C unless defined otherwise by national regulation is proposed for safety reasons to control possible ignition of the solvent vapors of the UL on hot parts of the aircraft engine.

Note 3 MT 192 (Viscosity of Liquids by Rotational Viscometry) is designed for determination of the viscosity of Non-Newtonian Liquids, but can be used for measuring the viscosity of Newtonian liquids like UL as well.

Note 4 Samples of the formulation taken before and after the storage stability test should be analyzed concurrently

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## FIPRONIL GRANULES

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### FAO specification 581/GR (August 2009)\*

*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 (581/2009.2 and 581/2009.1). 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 specifications. The specification may not be appropriate for the products of other manufacturers. The evaluation reports (581/2009.2 and 581/2009.1) as PART TWO form an integral part of this publication.*

#### 1. Description

The material shall consist of fine granules containing technical fipronil, complying with the requirements of FAO specification 581/TC (August 2009), together with suitable carriers and any other necessary formulants, including coloring matter, if applicable (Note 1). 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 (581/GR/M, Note 2)

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 Fipronil content (581/GR, Note 2)

The fipronil content shall be declared (g/kg at  $20 \pm 2^\circ\text{C}$ ,) and, when determined, the average measured content shall not differ from that declared by more than the following tolerances:

| Declared content in g/kg at $20 \pm 2^\circ\text{C}$ | Tolerance                          |
|--|------------------------------------|
| up to 25 g/kg  | $\pm 25\%$ of the declared content |
| above 25 g/kg up to 100 g/kg                         | $\pm 10\%$ of the declared content |
| Note in each range the upper limit is included       |                                    |

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\* Specifications may be revised and/or additional evaluations may be undertaken. Ensure the use of current versions by checking at: <http://www.fao.org/agriculture/crops/core-themes/theme/pests/pm/jmps/ps/en/>.

### 3. Physical properties (Note 3)

#### 3.1 Dustiness (MT 171, CIPAC F, p. 425, 1995)

Essentially non-dusty (Note 4).

#### 3.2 Attrition resistance (MT178)

Minimum 98% attrition resistance.

### 4. Storage stability

#### 4.1 Stability at elevated temperature (MT 46.3, CIPAC J, p.128, 2000)

After storage at  $54^{\circ} \pm 2^{\circ}\text{C}$  for 14 days (Note 5) 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 product shall continue to comply with the clause for:

- dustiness (3.1)
- attrition resistance (3.2).

Note 1 The formulation may contain a dye or pigment that permanently colours the granule, when the main way of application in the country is manual.

Note 2 Methods for the identification and determination of fipronil content in FS, SC, WG and GR formulations were presented at the CIPAC Meeting in 2008 and provisionally adopted as CIPAC method. Prior to their publication in Handbook N, copies of the methods may be obtained through the CIPAC website, <http://www.cipac.org/prepubme.htm>

Note 3 The GR formulations of the reference and second manufacturer differ somewhat in nominal size ranges. The size range of BASF and BCS GR is described as "Not less than 850 g/kg of the formulation shall be within the nominal declared size range of 250 – 1000  $\mu\text{m}$ , whereas the GR of Gharda is "not less than 900 g/kg 500 to 1000  $\mu\text{m}$ "  
The method used is CIPAC MT 58, CIPAC Handbook F, p. 173, 1995.

Note 4 The optical method, MT 171.2, usually shows good correlation with the gravimetric method, MT 171.1, 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 5 Unless other temperatures and/or times are specified. Granules based on sand shall be stored at 30  $^{\circ}\text{C}$  for 18 weeks due to the surface activity of the carrier.

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

## PART TWO

### EVALUATION REPORTS

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#### FIPRONIL

|  | <b>Page</b> |
|--|-------------|
| <b>2009.2 FAO/WHO EVALUATION REPORT</b> based on a submission of data from Gharda Chemical Company (India)                 | 22          |
| <b>Supporting information</b>  | 24          |
| <b>Annex 1:</b> Hazard summary provided by the proposer  | 27          |
| <b>Annex 2:</b> References   | 30          |
| <br>   |             |
| <b>2009.1 FAO/WHO EVALUATION REPORT</b> based on a submission of data from BASF (Germany) and Bayer Crop Science (Germany) | 31          |
| <b>Supporting information</b>  | 35          |
| <b>Annex 1:</b> Hazard summary provided by the proposer  | 39          |
| <b>Annex 2:</b> References   | 50          |



## FIPRONIL

### FAO/WHO EVALUATION REPORT 548/2009.2

#### **Recommendation**

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The Meeting recommended that

(i) the existing FAO specifications for fipronil TC, SC and GR should be extended to encompass the products of Gharda Chemical Company

#### **Appraisal**

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The Meeting considered data on fipronil provided by Gharda Chemical Company (India) in support of specifications based on equivalence to existing FAO specifications (July 2009) for TC, SC and GR formulations. The data submitted were in accordance with the requirements of the FAO/WHO Manual, 1st edition (2006).

CIPAC methods for determination of fipronil in TC, EC and UL are published in Handbook J and method extensions for FS, SC and WG formulations were adopted by CIPAC in 2008 and available through the CIPAC website before publication in Handbook N. Fipronil is determined by high performance liquid chromatography on a reversed-phase column with UV detection using an external standard.

The Meeting was provided with confidential information on the manufacturing process for technical grade fipronil in India. Also included were the results for the analysis of five batches of the technical material and certified limits based on those analyses. The information on the batch analyses and the certified limits is identical to that provided to Australia.

The Meeting concluded that the Gharda manufacturing process leads to a technical material comparable to that of the existing FAO specification (2009). The minimum purity and the nature and limits of impurities declared are similar to those of the existing specification and none should be considered significant.

The Meeting concluded that the toxicological profile of the Gharda Chemical Company fipronil TC, based on acute oral, dermal and inhalation toxicity, skin and eye irritation, and skin sensitization, showed the same endpoints (within a factor of 2) as the profile of the reference TC.

The Meeting concluded that the Gharda GR and SC formulation have specifications broadly similar to the existing specifications for BCS and BASF GR and SC formulations (July 2009).

However, the Meeting noted several minor differences between the reference specifications and the specifications proposed by Gharda which required an extension or modification of the existing specification to accommodate the specifications for fipronil TC and formulations produced by Gharda. These are

**TC:**

The TC produced by Gharda may contain residual water, which is carried forward from the last step in the manufacturing process. The company proposed a limit of 20 g/kg. This is different from the situation in the reference profile TC, where both a dry material and a wet cake is produced. In the wet cake, which is used to formulate solid formulations like WG and GR or water based formulations like FS or SC the water content is limited to 90 g/kg. The reason of the wet cake is to reduce dust formation when the formulations are produced.

In summary two different limits for water content in fipronil were proposed: one for the TC intended for formulation of oil-based formulations like EC and UL with 20 g/kg and one for the "wet cake" for solid or water based formulations with 90 g/kg. The meeting concluded that the 90 g/kg for the wet cake was still acceptable and that this limit was also compatible with the water limits in solid formulations and oil-based formulations, as these formulations contain rather low content of fipronil.

**Physical and chemical properties:** the melting point of pure fipronil is 203 °C, whereas that of the TC produced by Gharda shows a melting range of 196 to 203 °C which is explained by the presence of two crystal modifications in the actual sample of the technical material having a purity of 930 g/kg. The melting range of the reference TC is given as 195 to 203 °C.

**SC**

**pH range:** The necessity for a pH range in the specification for the SC was discussed by the meeting. The justification provided was that the pH clause is necessary for the stability of the formulation. The pH range in the reference profile is pH 4 to 8.5, whereas that of Gharda was pH 5 to 7. The Meeting concluded that the narrower range proposed by Gharda was acceptable.

**Spontaneity of dispersion and suspensibility:** the limits proposed by Gharda were 90 % for both parameters, whereas those of the reference are 80 and 70 %, respectively. The Meeting agreed to keep the 80 and 70 % limits for the spontaneity of dispersion and suspensibility for both formulations, as they had been found acceptable.

**GR**

**Particle size range:** The particle size range in the reference is "Not less than 850 g/kg of the formulation shall be within the nominal declared size range of 250 – 1000 microns", whereas the formulation produced by Gharda is described by the size range "not less than 900 g/kg of the formulation shall be in the size range 500 to 1000 microns" The Meeting concluded that the size ranges of both formulations should be given in a footnote to the specification.

**SUPPORTING INFORMATION  
FOR  
EVALUATION REPORT 571/2009.2**

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## PHYSICO-CHEMICAL PROPERTIES OF FIPRONIL

**Table 1 : Physico-chemical properties of technical grade fipronil**

| Parameter  | Value   | Purity % | Method                             | Reference              |
|--|---|----------|------------------------------------|------------------------|
| Vapour pressure  | $2.702 \times 10^{-7}$ Pa at 25°C   | 93%      | OECD 104                           | 18<br><u>C.FPO.010</u> |
| Melting point, boiling point and/or temperature of decomposition | Melting point :199.6 to 200.7°C   | 93%      | OECD 102                           | 19<br><u>C.FPO.011</u> |
| Solubility in water  | 1.61 mg/L at 20°C ± 0.5°C   | 93%      | OECD 105                           | 20<br><u>C.FPO.009</u> |
| Octanol/water partition coefficient                              | $\log_{10} P_{OW} = 3.62$ at 24± 1°C  | 93%      | OECD 107                           | 21<br><u>C.FPO.007</u> |
| Hydrolysis characteristics                                       | Hydrolytically stable at pH 4 and 7.<br>At pH= 9<br>Rate constant $k_{obs}$ : $1.3237 \times 10^{-3}$ /hr<br>$t_{1/2}$ : 523.5 hr at 25°C (22 days)<br>Compound formed by hydrolysis:<br>product : fipronil amide | 93%      | OECD 111                           | 22<br><u>C.FPO.012</u> |
| Photolysis characteristics                                       | Quantum yield : 0.520<br>Rate constant $K_p$ : 7.07 days <sup>-1</sup><br>$t_{1/2}$ (summer) : 0.098 days<br>Rate constant $K_p$ : 3.0 days <sup>-1</sup><br>$t_{1/2}$ (winter) : 0.231 days                      | 97.1%    | US EPA guideline<br>OPPTS 835.2210 | 23<br><u>C.FPO.013</u> |
| Dissociation characteristics                                     | Does not dissociate in water  | 93%      | OECD 112                           | 24<br><u>C.FPO.008</u> |

**Table 2: Chemical Composition and properties of fipronil technical material (TC)**

|  |  |   |
|--|--|---|
| Manufacturing process, maximum limits for impurities ≥ 1 g/kg, 5 batch analysis data | Mass balances were between 995 g/kg to 1007 g/kg | Confidential information supplied by Gharda Chemical Co. and held on file by FAO. |
| Declared minimum Fipronil content  | 950 g/kg   |   |
| Relevant impurities ≥ 1 g/kg and maximum limits for them.                            | None   |   |

|   |               |  |
|---|---------------|--|
| Relevant impurities <1 g/kg and maximum limits for them:    | None          |  |
| Stabilizers or other additives and maximum limits for them: | None          |  |
| Melting or boiling temperature range                        | 195° – 203° C |  |

## **FORMULATIONS**

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The main formulation types produced are EC, FS; GR, SC, UL and WG. These formulations are registered and sold in more than 60 countries for agricultural, non-agricultural and veterinary uses. Fipronil is formulated either alone or co-formulated with fungicides like triticonazole, azoxystrobin, probenazole and insecticides like aldicarb, carbosulfan and other.

## **PHYSICAL PROPERTIES OF FIPRONIL FORMULATIONS**

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The physical properties, the methods for testing them and the limits proposed for the SC and WG formulations, comply with the requirements of the FAO Manual (FAO, 2006).

## **METHODS OF ANALYSIS AND TESTING**

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

## **CONTAINERS AND PACKAGING**

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No special requirements for containers and packaging have been identified.

## **EXPRESSION OF THE ACTIVE INGREDIENT**

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The fipronil active ingredient content is expressed as fipronil

**ANNEX 1**

**HAZARD SUMMARY PROVIDED BY THE PROPOSER**

Note: Gharda provided written confirmation that the toxicological data included in the following summary were derived from fipronil having impurity profiles similar to those referred to in table 2, above

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

| Species                                    | Test               | Guideline adopted | Purity % | Result                               | Reference                                  |
|--|--------------------|-------------------|----------|--------------------------------------|--|
| Rat<br>(Sprague dawley)<br>5 M ; 5 F       | Acute oral         | OECD 401          | 95.5     | LD <sub>50</sub> : 66 mg/kg b.wt.    | 2<br><u>T.FPO.002</u><br><u>T.FPO.002A</u> |
| Mice<br>(Swiss albino)<br>5 M ; 5 F        | Acute oral         | OECD 401          | 95.5     | LD <sub>50</sub> : 74 mg/kg b.wt.    | 3<br><u>T.FPO.001</u>                      |
| Rat<br>(Sprague dawley)<br>5 M ; 5 F       | Acute dermal       | OECD 402          | 95.5     | LD <sub>50</sub> : >2000 mg/kg b.wt. | 4<br><u>T.FPO.003</u><br><u>T.FPO.003A</u> |
| Rat<br>(Sprague dawley)<br>5 M ; 5 F       | Acute Inhalation   | OECD 403          | 95.5     | LC <sub>50</sub> : 0.98 mg/lit       | 5<br><u>T.FPO.004</u><br><u>T.FPO.004A</u> |
| Rabbit<br>(New Zealand white)<br>3 M ; 3 F | Skin irritation    | OECD.404          | 95.5     | Non irritant                         | 6<br><u>T.FPO.005</u>                      |
| Rabbit,<br>(New Zealand white)<br>6 F      | Eye irritation     | OECD 405          | 95.5     | Non irritant                         | 7<br><u>T.FPO.006</u>                      |
| Guinea pig<br>(Dunkan Hartly)<br>M&F : 15  | Skin sensitisation | OECD 406          | 98.2     | Non sensitizer                       | 8<br><u>T.FPO.013</u>                      |

**Table 4. Mutagenicity profile of technical fipronil based on in vitro and in vivo tests**

| Species  | Test                             | Purity % | Duration and Conditions   | Result        | Reference              |
|--|----------------------------------|----------|---|---------------|------------------------|
| Salomonella typhimurium<br>TA 1535,TA 1537,<br>TA 98 and TA 100. | Bacterial reverse mutation assay | 95.5     | Gaitonde Committee Guidelines<br><br>Dosages: 5000, 1500, 500, 150, 50 and 15 µg/plate. | non-mutagenic | 10<br><u>T.FPO.007</u> |

| Species  | Test                        | Purity % | Duration and Conditions  | Result        | Reference                  |
|--|-----------------------------|----------|--|---------------|----------------------------|
| Swiss Albino Mice<br>(Bone marrow cytogenetic )<br><br>2M ; 2F | Chromosomal aberration test | 95.5     | Gaitonde Committee Guideline.<br><br>Dosages : 4, 8 and 16 mg/kg                       | Non mutagenic | 11<br><br><u>T.FPO.008</u> |
| Swiss Albino Mice<br>(Bone marrow)<br><br>3M ; 3F              | In vivo Micronuclei test    | 95.5     | Gaitonde Committee Guideline,<br><br>Dosages 4, 8 and 16 mg/kg                         | Non mutagenic | 12<br><br><u>T.FPO.009</u> |
| Swiss Albino Mice<br>(Bone marrow)<br><br>10 M                 | Dominant Lethal Test        | 95.5     | Gaitonde Committee Guideline.<br>Dosages 8 mg/kg & 16 mg/kg<br><br>8 consecutive weeks | Non mutagenic | 13<br><br><u>T.FPO.010</u> |

**Table 5. Ecotoxicology profile of technical fipronil**

| Species                              | Test           | Purity % | Duration and conditions   | Result                         | Reference                  |
|--------------------------------------|----------------|----------|---|--------------------------------|----------------------------|
| Fish, Guppy<br>(Poecilia Reticulata) | Acute toxicity | 98.2     | Litchfield & Wilcoxon's method (1949)<br><br>Duration : 96 hours<br>Temp: 21°C ± 3°C<br><br>OECD guidelines 203                           | LC <sub>50</sub> : 0.165 mg/l  | 14<br><br><u>T.FPO.011</u> |
| Daphnia magna                        | Acute toxicity | 98.2     | Litchfield & Wilcoxon's method (1949)<br><br>Duration: 48 hours<br>Conc. 0, 1, 0.5, 0.25, 0.125 and 0.0625 mg/l<br><br>OECD guideline 202 | EC <sub>50</sub> : 0.25 mg/lit | 15<br><br><u>T.FPO.012</u> |



**ANNEX 2: REFERENCES**

| Reference Number | Gharda or Other Reference Number | Year and Title or Publication Details  |
|------------------|----------------------------------|--|
| 1                | <i>Pesticide Manual</i>          | Physico chemical properties  |
| 2                | T.FPO.002                        | 2002 Acute oral toxicity to rat  |
| 3                | T.FPO.001                        | 2002 Acute oral toxicity to mice   |
| 4                | T.FPO.015                        | 2008 Acute dermal toxicity study in rat  |
|                  | T.FPO.004                        | 2002 Acute inhalation toxicity to rat  |
| 6                | T.FPO.005                        | 2002 Acute skin irritation study in rabbit                                       |
| 7                | T.FPO.006                        | 2002 Acute mucous membrane irritation study in rabbit                            |
| 8                | T.FPO.013                        | 2004 Skin sensitisation test in Guinea pig                                       |
| 9                | FAO Repository                   | 2007 FAO Corporate Document Repository – Fipronil                                |
| 10               | T.FPO.007                        | 2002 Bacterial Mutation Assay  |
| 11               | T.FPO.008                        | 2002 Mutagenicity studies –Cytogenetic Test                                      |
| 12               | T.FPO.009                        | 2002 Mutagenicity studies – Micronucleus test                                    |
| 13               | T.FPO.010                        | 2003 Dominant Lethal Test in Swiss Albino Mice                                   |
| 14               | T.FPO.011                        | 2004 Acute toxicity test to Fish, Guppy ( <i>Poecilia Reticulata</i> )           |
| 15               | T.FPO.012                        | 2004 Acute immobilization test in <i>Daphnia magna</i>                           |
| 16               | PAN UK                           | 2000 Briefing paper “Health & Environmental Effects of Fipronil”                 |
| 17               | IPCS INCHEM                      | 1997 Pesticide Residues in Food 1997 & Toxicological & Environmental Evaluations |
| 18               | CFPO.10                          | 2007, Vapour Pressure  |
| 19               | CFPO.11                          | 2007, Melting Point  |
| 20               | CFPO.9                           | 2007, Solubility in Water  |
| 21               | CFPO.7                           | 2007, n-Octanol/Water Partition Coefficient                                      |
| 22               | CFPO.12                          | 2007, Hydrolysis as a Function of pH   |
| 23               | CFPO.13                          | 2007, Direct Photolysis in Water and Natural Sunlight                            |
| 24               | CFPO.8                           | 2007, Dissociation Constant  |
| 25               | FAO/WHO                          | 2001, 2005, , Report of the Joint Meeting on Pesticide Residues                  |
| 27               | IPCS                             | 2004, WHO Recommended Classification of Pesticides by Hazard                     |

## FIPRONIL

### FAO/WHO EVALUATION REPORT 548/2009.1

#### Recommendation

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The Meeting recommended that

- i) the specifications for fipronil TC, WG, SC, EC, FS, UL, and GR formulations, proposed by BASF (Germany) and Bayer Crop Science (Germany), as amended, should be adopted by FAO
- ii) the specifications under old procedure for fipronil TC, should be withdrawn

#### Appraisal

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The Meeting considered data on fipronil, provided by BASF (Germany) and Bayer CropScience (Germany), in support of proposed new specifications for TC, WG, SC, EC, FS, UL, and GR formulations. The data submitted were broadly in accordance with the requirements of the "Manual on development and use of FAO and WHO specifications for pesticides, March 2006 revision of the First edition.

The patent situation of fipronil is described as: "Patents covering the active ingredient fipronil itself will have expired in most countries in mid of 2010 (except Argentina) but a number of additional patents related to manufacturing or using the insecticide fipronil will still be applicable beyond this date".

The data packages are similar as those submitted to the UK (BASF) and the USA (BCS, BASF).

Fipronil was evaluated for the first time by the JMPR in 1997 and again in 2000 - 2001. The JMPR established an ADI of 0.0002 mg/kg body weight and an Acute RfD of 0.003 mg/kg body weight (1997/JMPR; 2000/JMPR; 2001/JMPR). The WHO IPCS hazard class for fipronil technical active ingredient is Class II, or moderately hazardous (2004/INCHEM).

Fipronil is a systemic insecticide acting agonistically on the GABA gated chloride channel in target pests. The TC is a white powdered solid that melts at 203 °C. It has a rather low vapor pressure and a low water solubility. It does not ionize at environmentally relevant pHs and undergoes rapid photolysis. This and the octanol/water partition coefficient (log 3.6) indicate a certain lipophilicity.

The molecular structure of fipronil shows an asymmetrically substituted sulfur atom (the sulfinyl moiety being substituted with a trifluoromethyl group, an oxygen and the heterocycle) which together with the non-bonding electron pair at the sulfur leads to a center of asymmetry. The ISO common name refers to the racemate as the active ingredient.

Fipronil is determined by high performance liquid chromatography on a reversed-phase column with UV detection using external standardization and was collaboratively validated by CIPAC.

The main method is published in Handbook J, validated for TC, EC and UL-formulations). A method extension for WG, FS, SC and GR was presented at the 2008 CIPAC meeting and provisionally adopted as CIPAC methods.

The Meeting was provided with confidential information on the manufacturing process for technical grade fipronil in France (BASF) and in China (Bayer Crop Science). Also included were the results for the analysis of five batches of the technical material from both locations.

Mass balances were in the range of 98.9 – 99.6% (w/w) for the BASF material and 99.6 – 100.5% (w/w) for the BCS material. Limits for minimum purity were supported by data on five typical batches for both BASF and BCS.

The Meeting concluded that the two sites use the same manufacturing process, that they produce comparable technical materials, and that none of the impurities should be considered relevant. The Meeting confirmed that the minimum limit for fipronil and the maximum limits for impurities in the TC are the same as submitted to the UK (BASF) and to the USA (BASF, BCS).

The Meeting concluded that the BASF source (1997) is the reference profile, as the toxicity data were generated on this profile.

The following issues were addressed by the Meeting (2008):

**General:**

A confirmation that the specification/data for the BCS material had been evaluated by a competent national authority was required. Confirmation was in progress with China at the time of the 2008 Meeting. However, this process could not be completed, and BCS subsequently provided a letter of authorization to the confidential information held by registration authorities in the USA. The confirmation process was then successfully completed.

**Issues relating to TC only**

The TC may be present as “wet cake”, as water is added to reduce formation of dust in handling for preparation of formulations. A limit of 90 g water /kg is proposed.

Nevertheless, the material is a TC and not a TK as proposed.

The companies agreed and modified the description as follows: “Water can be added to the technical material to reduce its dustiness and the resulting risk of inhalation.” This remark was added in a footnote: 1 The water content should not exceed 90g/kg. The water content can be measured using MT 30.5, CIPAC J, p. 120, 2000

### **Issues relating to EC only**

For emulsion stability, the Meeting considered a cream value of 4 ml as high given that the a.i. is oil soluble.

The companies proposed an amended value of 2 ml, which was accepted by the Meeting.

### **Issues relating to WG only**

The Meeting noted that the required property attrition resistance was missing in the draft specification. .

The companies then proposed: Attrition resistance (MT 178.2): Minimum: 96 % attrition resistance, which was accepted by the Meeting.

The Meeting noted that the clause acidity alkalinity/pH range is not normally necessary. The companies agreed to remove the clause.

The Meeting noted that the size description information was non-standard. Size description should be a visual process, but the specification as presented would require a test. If necessary, the additional information could be placed in a footnote.

BASF/BCS agreed to the Meeting proposal and reduced the size description to « irregular particles, » with the addition of the following footnote : « 1 granules with 95 % of the granules being of the size of 100 - 500 µm”

### **Issues relating to FS only**

The Meeting noted that a persistent foam clause is not needed as fluids for seed treatments are generally not diluted.

The companies agreed to remove the clause.

The Meeting noted that the particle size distribution stated that 50% of the particles shall be <4 µm, which is not a range.

The companies then proposed to amend the clause to: “>50% of particles shall be in the range 0.1 µm to 4 µm”. They further noted that the clause is needed to (1) ensure a high formulation stability due to less sedimentation, and to (2) ensure a good efficacy and distribution of the product on the seeds. The clause and its limits was therefore retained.

The Meeting questioned the need for a pH clause.

BASF/BCS explained that if the pH is too low there can be irritation/corrosive properties and if the pH is too high there can be hydrolysis. The Meeting agreed to retain the clause.

### **Issues relating to SC only**

The Meeting noted that the viscosity clause was usually not needed.

The companies replied that there was not need to retain the clause and it was removed..

The Meeting also questioned the need for the pH clause.

BASF/BCS responded that the clause is essential. If the pH is too low there can be irritation/corrosive properties and if the pH is too high there can be hydrolysis. The Meeting agreed to retention of the clause.

The Meeting noted that a particle size distribution clause was usually not needed.

BASF/BCS responded that they agreed to remove the clause.

**Issues relating to GR only**

The Meeting noted that the declared tolerance for the a.i. content up to 25 g/kg should be corrected to be consistent with the Manual tolerance limits.

BASF/BCS agreed and proposed: “ ± 25 % of the declared content.”, which was agreed by the Meeting.

The Meeting stated that a pour/tap density is not needed.

The companies agreed to remove the clause.

**Issues relating to UL only**

The Meeting requested that the clause for flash point be removed as it is not standard. BASF/BCS responded that they consider it relevant because the product can be applied from aerial equipment and flash point is important from a safety perspective. It was agreed to enter flashpoint without a clause performance but with a footnote: “Minimum 61o C unless defined otherwise by national regulation.”

The Meeting noted that viscosity was tested by the dynamic procedure MT 192, but the kinematic method MT 22 is the preferred test. The company was asked to justify the use of MT 192.

The companies responded that MT 192 is acceptable and is in fact the recommended method in the Manual (7.4.4.2) for UL formulations. Modern viscosimeters used for CIPAC MT 192 are also suitable for Newtonian liquids. Calibration is performed with a standard oil of Newtonian character. MT 192 is suitable to check this specification for the UL in compliance with the latest guidance. The value shall be in the range of 2 to 50 mPa.s. MT 22 is in fact less accurate and cannot be run at different temperatures.

**Supporting Information  
For  
Evaluation Report 581/2009.1**

**Explanation**

Fipronil was developed by Rhône-Poulenc at Ongar Research Center in England in 1987. In 1997 Fipronil production started in FRANCE in the Elbeuf plant by Bayer CropScience (BCS), predecessor company Rhône-Poulenc Agro.

In 2002 Fipronil production started in CHINA Hangzhou by Bayer CropScience (BCS) predecessor company Aventis CropScience (formed by Rhône-Poulenc and AgrEvo Hoechst Schering).

Bayer Crop Science divested most products containing Fipronil worldwide. BASF acquired the business and registration data package of Fipronil in March of 2003 including the Fipronil manufacturing plant in Elbeuf / FRANCE. The exception is CHINA, where business, registrations and the Hangzhou / CHINA manufacturing site were left to Bayer Crop Science.

The data for fipronil were evaluated in support of the review of new as well as of existing FAO Specification 581/TC/EC/UL(1998). Fipronil is currently registered for multiple uses in several countries in Europe, North and South America and Asia . The draft specifications and the supporting data were provided by BASF AG and Bayer Crop Science.

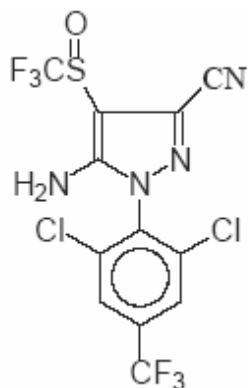
**Identity of the active ingredient**

ISO common name  
Fipronil

Synonyms  
None

Chemical names  
IUPAC  
(±)-5-amino-1-(2,6-dichloro- $\alpha,\alpha,\alpha$ -trifluoro-p-tolyl)-4-trifluoromethylsulfinylpyrazole-3-carbonitrile  
CA  
5-amino-[2,6-dichloro-4-(trifluoromethyl)phenyl]-4-[(1R,S)-(trifluoromethyl)sulfinyl]-1H-pyrazole-3-carbonitrile

Structural formula



Molecular formula  
C<sub>12</sub> H<sub>4</sub> Cl<sub>2</sub> F<sub>6</sub> N<sub>4</sub> OS

Relative molecular mass  
437.15

CAS Registry number  
120068-37-3

### Uses

Fipronil is an insecticide used in agriculture, horticulture, animal health, house protection/household markets and locust control. In agriculture, Fipronil offers low-dose insect control against a broad range of economically important pests. Registered crops range from row crops such as rice, corn, potatoes and small grains to several specialty crops.

Fipronil affects the nervous system of insects. It has both contact and ingestion activity. It is particularly effective by way of ingestion. It causes excitation and convulsions in insects and, at sufficient doses, death by disrupting the nervous system. Fipronil binds to three types of calcium-channels on the membranes of neurons, preventing calcium ion influx into the cell. One of these types of channels is mediated by the neurotransmitter gamma-aminobutyric acid (GABA) and the other two are mediated by glutamate.

**Table 1: Physico-chemical properties of pure fipronil**

| Parameter  | Value(s) and conditions  | Purity %                            | Method reference (and technique if the reference gives more than one) and company report number/date |
|--|--|-------------------------------------|--|
| Vapour pressure  | 2.0 x 10 <sup>-6</sup> Pa at 25 °C   | 99.8%                               | OECD 104, by extrapolation", C018246/2001  |
| Melting point, boiling point and/or temperature of decomposition | Melting point: 203 °C<br><br>Boiling point: none, decomposition before boiling<br><br>Decomposition temperature: ca. 230 °C  | 99.3 %                              | OECD 102, R010170/1996   |
| Solubility in water  | 3.78 x 10 <sup>-3</sup> g/l at 20 °C at pH 6.6   | 99.8 %                              | EEC A6, C018248/2001   |
| Octanol/water partition coefficient                              | log POW= 3.5at 20 °C<br><br>log POW= 4.0at 20 °C (shake flask method)  | 99.9 %<br><br>99.3 %                | EEC A8 by extrapolation, R010185/1997<br><br>OECD 107, R010078/1991                                  |
| Hydrolysis characteristics                                       | Half-life = stable at 25 °C at pH 5 (>97.6% of applied radioactivity at 30 days)<br><br>Half-life = nearly stable at 25 °C at pH 7 (>97.6% of applied radioactivity at 30 days)<br><br>Half-life = 28 days at 25 °C at pH 9 (30 day study, pseudo-first order kinetics)<br><br>(25° C, dark) | 98.6 % radio-chemical<br><br>purity | EEC C.7, OECD 111, R010574/1992  |
| Photolysis characteristics                                       | Irradiation with artificial sunlight in a buffered solution (pH 5) at 25 °C: the half-life was determined to be 0.33 days.   | >97.5 % radio-chemical purity       | EPA OPPTS 835.2210, 95/36/EEC; 94/37/EEC, R010090/1992   |
| Dissociation characteristics                                     | Does not dissociate.   | 99.3 %                              | OECD 112, titration method, spectrophotometric method, conductometric method, C011803/2001           |



**Table 2: Physico-chemical properties of fipronil technical materials (TC)**

|   |   |
|---|---|
| Manufacturing process, maximum limits for impurities $\geq 1$ g/kg, 5 batch analysis data | Confidential information supplied and held on file by FAO. Mass balances were 98.9 – 99.6%(BASF) and 99.6 – 100.5 % (Bayer CropScience). Percentages of unknowns were less than 0.1%. |
| Declared minimum Fipronil content   | 950g/kg (dry active ingredient; BASF & BayerCropScience )   |
| Relevant impurities $\geq 1$ 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.                               | Water can be added up to 90 g/kg* .   |
| Melting or boiling temperature range of the TC.   | 195-203°C (TC)  |

\* Water can be added to the technical material to reduce its dustiness and the resulting risk of inhalation.

## 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 fipronil having impurity profiles similar to those referred to in the table above.
- (ii) The conclusions expressed in the summary below (including Tables 3 – 7) are those of the proposer, unless otherwise specified.

#### SUMMARY

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Adverse effects in the short term studies are observed in the central nervous system for all species and in the liver and thyroid for the rat.

No genotoxic or carcinogenic potential is demonstrated. The mechanism for induction of thyroid tumours observed only in rats was discussed by several experts and considered specific to the rat and not relevant to humans. Neither reproductive nor developmental toxicity is observed. In specific neurotoxicity studies, no histopathological findings are observed in the nervous system.

Fipronil is of low acute toxicity to many avian species but appears to be selectively toxic to the galliform family. In field conditions, the potential risk for sensitive species is reduced by the low palatability of fipronil. There is no adverse impact on bird reproduction.

Based upon laboratory studies, fipronil is classified highly toxic to very highly toxic to fish and aquatic species as well as honey bees. However, the properties of the molecule, the low use rates as well as the recommended method and timing of application mitigate the level of toxicity and no unacceptable effect on the environment is expected from registered uses. Fipronil is non toxic to several environmental species such as earthworms and soil microflora.

Fipronil was evaluated by the FAO JMPR in 1997, 2000, and 2001. It was concluded that the short-term and long intake of residues of fipronil, when used in ways that have been considered, is unlikely to present a public health concern (1997/JMPR, 2000/JMPR, 2001/JMPR) . The IPCS hazard classification of Fipronil is “Moderately hazardous”, class II (2004/INCHEM).

The WHO IPCS hazard class for Fipronil technical active ingredient is Class II , or moderately hazardous. Fipronil was evaluated for the first time by the FAO JMPR in 2000 - 2001. The JMPR established an ADI of 0 - 0.0002 mg/kg body weight and an Acute RfD of 0.003 mg/kg body weight.

## **FORMULATIONS AND CO-FORMULATED ACTIVE INGREDIENTS**

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The main formulation types available are WG, SC, EC, FS, UL and GR for the use in agriculture. Fipronil may be formulated alone or co-formulated with other fungicides or insecticides, such as triticonazole, guazatine (BASF) and acephate, deltamethrin or triazaphos (Bayer CropScience)

These formulations are registered and sold in many countries all over the world (Europe, Asia, North- and South America, Africa, Australia).

## **METHODS OF ANALYSIS AND TESTING**

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The analytical method for the active ingredient (including identity tests) is a full CIPAC method (CIPAC Handbook J, p. 63, 2000) for the analysis of TC, EC and UL. The existing analytical CIPAC method will be extended for the determination of fipronil in WG, FS, SC and GR preparations. The method extension is currently being peer validated and the extensions will be presented in the CIPAC meeting in June 2008. The fipronil is determined by reversed phase HPLC, using UV detection at 280 nm and external standardisation.

Impurities in fipronil are determined by HPLC-UV methods, typically with detection at 220 nm.

Test methods for determination of physico-chemical properties of the technical active ingredient are OECD, EPA, or EEC, while those for the formulations are CIPAC water determination, MT 30.5; pH range, MT 75; wettability, MT 53.3; accelerated storage stability, MT 46; low temperature stability, MT 39.3; wet sieve test, MT 185; dispersibility, MT 174; suspensibility, MT 168, MT 184; wettability, MT 53.3.2; persistent foam MT 47.2; dustiness, MT 171; particle size distribution, MT 187; nominal size range, MT 58; attrition resistance, MT 178 and MT 178.2; flowability, MT 172; pourability, MT 148; spontaneity of dispersion, MT 160; emulsion stability and reemulsification, MT 36.3; viscosity, MT 192; flash point, MT 12, as indicated in the appropriate specification.

## **PHYSICAL PROPERTIES**

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The physical properties, the methods for testing them and the limits proposed for the WG, SC, EC, FS, UL and GR formulations, comply with the requirements of the FAO manual (2nd edition, 2006). Water has been specified for UL and WG formulations, because a higher water content would have adverse effects on the stability of the formulations. For UL formulations the flash point and the viscosity have been specified because of the application by aircraft.

## **METHODS OF ANALYSIS AND TESTING**

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The analytical method for the active ingredient Fipronil is based on reversed-phase HPLC, with UV detection and external standardisation. The method was adopted by CIPAC.

The method for determination of impurities is based on reversed-phase HPLC with UV detection at 220 nm and external standardization.

Test methods for determination of physico-chemical properties of the technical active ingredient were OECD, EEC, and EPA, while those for the formulations were CIPAC.

### **PHYSICAL PROPERTIES OF FIPRONIL FORMULATIONS**

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The physical properties, the methods for testing them, and the limits proposed for the WG, SC, EC, FS, UL, and GR formulations comply with the requirements of the FAO Manual (1st edition).

### **CONTAINERS AND PACKAGING**

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No special requirements for containers and packaging have been identified.

### **EXPRESSION OF THE ACTIVE INGREDIENT**

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The fipronil active ingredient content is expressed as fipronil

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

| Species      | Test                        | Purity % | Duration and conditions or guideline adopted                     | Result                           | Reference (BASF Doc ID) |
|--------------|-----------------------------|----------|--|----------------------------------|-------------------------|
| Rat (m,f)    | Acute oral toxicity         | 93       | 14d OECD 401 (1987)  | LD <sub>50</sub> = 97 mg/kg bw   | 1988/1000897            |
| Mouse (m,f)  | Acute oral toxicity         | 95.3     | 14d<br>Not stated but complies with<br>EEC 92/69/EEC, B.1 (1992) | LD <sub>50</sub> = 95 mg/kg bw   | 1995/1001721            |
| Rat (m,f)    | Acute percutaneous toxicity | 93       | 14d OECD 402 (1987)  | LD <sub>50</sub> > 2000 mg/kg bw | 1988/1000898            |
| Rabbit (m,f) | Acute percutaneous Toxicity | 96.7     | 28d<br>USEPA (=EPA) FIFRA 81-2<br>(1984)                         | LD <sub>50</sub> = 354 mg/kg bw  | 1993/1001210            |
| Rat (m,f)    | Acute inhalation toxicity   | 95.4     | 14d USEPA (=EPA) 81-3 (1984)                                     | LC <sub>50</sub> = 0.682 mg/l    | 1990/1001127            |
| Rat (m,f)    | Acute inhalation toxicity   | 96.72    | 14d USEPA (=EPA) 81-3 (1984)<br>OECD 403 (1981)                  | LC <sub>50</sub> = 0.39 mg/l     | 1995/1001719            |
| Rabbit (m)   | Skin irritation             | 93       | 4d OECD 404 (1987)   | Not irritant*                    | 1988/1000899            |
| Rabbit (m,f) | Skin irritation             | 96.7     | 7d USEPA (=EPA) 81-5 (1984)                                      | Not irritant*                    | 1993/1001210            |
| Rabbit (m)   | Eye irritation              | 93       | 7d OECD 405 (1987)   | Not irritant*                    | 1988/1000900            |
| Rabbit (m,f) | Eye irritation              | 96.7     | 14d USEPA (=EPA) 81-4 (1984)                                     | Not irritant*                    | 1993/1001209            |

|                     |                                   |      |                     |                   |              |
|---------------------|-----------------------------------|------|---------------------|-------------------|--------------|
| Guinea pig<br>(m,f) | Skin sensitization<br>(Buehler)   | 95.4 | 35d OECD 406 (1981) | Not a sensitizer* | 1990/1001128 |
| Guinea pig<br>(m,f) | Skin sensitization<br>(Magnusson- | 95.4 | 24d OECD 406 (1981) | Not a sensitizer* | 1993/1001198 |

\* according to the EU and GHS classification criteria

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

| Species      | Test   | Purity % | Duration and conditions or guideline adopted                                   | Result                           | Reference (BASF DocID) |
|--------------|--|----------|--|----------------------------------|------------------------|
| Rat (m,f)    | Toxicity by dietary administration                                 | 93       | 28d EU 92/69/EEC, B.7 (1992)   | NOEL = <3.4 - 3.5 mg/kg bw/d     | 1990/1001129           |
| Dog (m,f)    | Toxicity by oral (capsule) administration                          | 97.2     | 28d No specific guidelines exist for such non-rodent range finding studies     | NOAEL = 1 mg/kg bw/d             | 1991/1001348           |
| Rat (m,f)    | Oral toxicity  | 95.4     | 90d USEPA (=EPA) 82-1 (1984)<br>Also compliant with EU 88/302/EEC, B.26 (1988) | NOAEL = 0.33 - 0.37 mg/kg/d      | 1991/1001350           |
| Dog (m,f)    | Dietary subchronic toxicity  | 95.4     | 90d USEPA (=EPA) 82-1 (1984)<br>Also compliant with EU 88/302/EEC, B.27 (1988) | NOEL = 0.5 mg/kg bw/d            | 1991/1001355           |
| Dog (m,f)    | Toxicity by oral (capsule) administration                          | 96.8     | 1 year USEPA (=EPA) 82-1 (1984)  | NOAEL = 0.2 mg/kg/d              | 1992/1001142           |
| Dog (m,f)    | Toxicity by dietary administration                                 | 95.7     | 1 year USEPA (=EPA) 82-1 (1984)  | NOEL = 0.3 mg/kg bw/d            | 1993/1001213           |
| Rabbit (m,f) | Cutaneous toxicity   | 96.7     | 21d US EPA (=EPA) 82-2 Also compliant with OECD 410 (1981)                     | NOEL = 5 mg/kg bw/d              | 1993/1001201           |
| Rat (m,f)    | Combined oncogenicity and toxicity study by dietary administration | 95.4     | 2-year USEPA (=EPA) 83-5 (1984)<br>Dose: 0 - 0.5 - 1.5 - 30 and 300 ppm        | NOAEL = 0.019 - 0.025 mg/kg bw/d | 1993/1001199           |

| Species       | Test   | Purity % | Duration and conditions or guideline adopted   | Result  | Reference (BASF DocID) |
|---------------|--|----------|--|---|------------------------|
| Mouse (m,f)   | Combined oncogenicity and toxicity study by dietary administration | 95.4     | 78-week USEPA (=EPA) 83-5 (1984) Dose: 0 - 0.1 - 0.5 - 10 - 30 and 60 ppm  | NOEL = 0.055 - 0.063 mg/kg bw/d<br>No evidence of carcinogenicity                         | 1992/1001140           |
| Rat (m,f)     | 2-generation reproduction  | 95.4     | USEPA (=EPA) 83-4 (1984) Dose: 0 - 3 - 30 and 300 ppm  | NOEL (parental) = 0.25 - 0.27 mg/kg bw/d<br>NOEL (developmental) = 2.53 - 2.74 mg/kg bw/d | 1992/1001138           |
| Rat (m,f)     | Teratogenicity   | 93       | Not stated but compliant with EU 88/302/EEC (1988), OECD 414 (1981) and USEPA (=EPA) 83.3 (1984) Dose: 0 - 1 - 4 and 20 mg/kg bw/d | NOAEL (parental) = 4 mg/kg bw/d<br>NOEL (developmental) = 20 mg/kg bw/d                   | 1991/1001352           |
| Rabbit (m, f) | Developmental toxicity   | 95.4     | USEPA (=EPA) 83-3 (1984) Also compliant with EU 88/302/EEC (1988) and OECD 414 (1981) Dose: 0 - 0.1 - 0.2 - 0.5 and 1.0 mg/kg bw/d | NOAEL (parental) = 0.2 mg/kg bw/day<br>NOEL (developmental) = 1.0 mg/kg bw/d              | 1990/1001134           |
| Rat (m,f)     | Acute oral neurotoxicity   | 96.7     | USEPA (=EPA) 81-8 (1991) Dose: 0 - 0.5 - 5 and 50 mg/kg/d  | NOEL = 0.5 mg/kg  | 1993/1001200           |
| Rat (m,f)     | Acute oral neurotoxicity   | 97.9     | USEPA (=EPA) 81-8 (1991) Dose: 0 - 2.5 - 7.5 and 25 mg/kg/d  | NOEL = 2.5 mg/kg  | 1997/1002133           |
| Rat (m,f)     | Dietary neurotoxicity  | 96.7     | USEPA (=EPA) 82-5 (b) (1991) Dose: 0 - 0.5 - 5.0 - 150 ppm   | NOEL (neurotoxicity) = 150 ppm<br>NOAEL (general toxicity) = 5 ppm                        | 1993/1001208           |
| Rat (f)       | Developmental neurotoxicity  | 96.1     | USEPA (=EPA) 83-6 (1995) Dose: 0 - 0.5 - 10 and 200 ppm  | NOEL (neurotoxicity) = 10 ppm<br>NOAEL (general toxicity) = 5 ppm                         | 1995/1001734           |



**Table 5. Mutagenicity profile of technical fipronil based on in vitro and in vivo test**

| Species   | Test  | Purity % | Conditions  | Result   | Reference BASF Doc ID |
|---|---|----------|---|--|-----------------------|
| Salmonella typhimurium TA 1535, TA 1537, TA 98 and TA 100 | In vitro Bacterial reverse mutation (Ames test) | 95-97    | 0 - 0.8 - 4 - 20 - 100 and 500µg/plate (test 1) 0 - 25 - 50 - 100 - 200 and 400 µg/plate (test 2)                           | negative (toxicity observed at 400µg/plate and above)                              | 1988/1000901          |
| E.coli strain WP2 uvrA                                    | Bacterial reverse mutation (Ames test)          | 98.9     | 0 - 20 - 100 - 500 - 2500 - 5000 µg/plate   | Negative (toxicity observed at 2500 µg/plate)                                      | 2005/1011567          |
| Human lymphocytes   | In vitro Chromosome aberrations                 | 95-97    | 0 - 75 - 150 and 300µg/ml with and without S9 mix   | negative (300µg/ml was limit of solubility)  | 1988/1000902          |
| Chinese hamster lung                                      | In vitro Chromosome aberrations                 | 98.3     | Without S9 mix  | Positive at 6-hour exposure with and without S9 mix at toxic dose levels (60µg/ml) | 1995/1001736          |
|   |   |          | 0 - 30 - 45 and 60 µg/ml (6-hour exposure)<br>0 - 7.5 - 15 - 22.5 and 30 µg/ml (24-and/or 48-hour exposures)<br>With S9 mix |  |                       |
|   |   |          | 0 - 15 - 30 and 60 µg/ml (6-hour exposure)  |  |                       |
| Chinese hamster lung V79 cells                            | In vitro Gene mutation in mammalian cells       | 97.2     | 0 - 0.8 - 4 - 20 - 100 and 500 µg/ml with and without S9 mix  | Negative (slight toxicity observed in second test at 100 and 500 µg/ml)            | 1993/1001185          |
| CD-1 mice   | In vivo   | 97.2     | 0 - 1 - 5 and 25 mg/kg  | Negative (no toxicity to bone)   | 1993/1001184          |

|   |                            |      |                            |   |                              |
|---|----------------------------|------|----------------------------|---|------------------------------|
| erythrocyte bone marrow cells           | Mouse micronucleus         |      |                            | marrow cells)                               |                              |
| CD-1 mice erythrocyte bone marrow cells | In vivo Mouse micronucleus | 96.2 | 0 - 12.5 - 25 and 50 mg/kg | Negative (no toxicity to bone marrow cells) | 1995/1001720                 |
| Rat primary hepatocytes                 | Unscheduled DNA synthesis  | 91.7 | 0 - 12.5 - 25 - 50 mg/kg   | Negative                                    | 2004/1021187<br>2005/1027930 |

**Table 6. Ecotoxicology profile of technical Fipronil on some species**

| Species                   | Test             | Purity % | Duration and conditions                                     | Result   | Reference (BASF Doc ID) |
|---------------------------|------------------|----------|---|--|-------------------------|
| Daphnia magna             | Acute toxicity   | 100      | 48h USEPA (=EPA) FIFRA 72-2                                 | EC50= 190 µg a.i./l  | 1990/1001141            |
| Daphnia magna             | Chronic toxicity | 100      | 21d OECD 202  | NOEC (growth) = 9.8 µg a.i./l<br>NOEC (repro) = 20 µg a.i./l | 1990/1001142            |
| Scenedesmus subspicatus   | Chronic toxicity | >95      | 24h, 48h, 96h OECD 201, (1984)                              | 96h EbC50= 68 µg a.i./l 24-48 h ErC50= 74 µg a.i./l          | 1991/1001378            |
| Selenastrum capricornutum | Chronic toxicity | 96.1     | 120h<br>USEPA (=EPA) FIFRA 122-2<br>USEPA (=EPA) FIFRA123-2 | EC50> 140 µg a.i./l  | 1993/1001234            |
| Anabaena flos-aquae       | Chronic toxicity | 96.1     | 120h<br>USEPA (=EPA) FIFRA 122-2<br>USEPA (=EPA) FIFRA123-2 | EC50> 170 µg a.i./l  | 1993/1001233            |
| Navicula pelliculosa      | Chronic toxicity | 96.1     | 120h<br>USEPA (=EPA) FIFRA 122-2<br>USEPA (=EPA) FIFRA123-2 | EC50> 120 µg a.i./l  | 1993/1001235            |
|                           |                  |          | 14d   |  |                         |

|                         |                     |       |   |                          |              |
|-------------------------|---------------------|-------|---|--------------------------|--------------|
| Lemna gibba             | Chronic toxicity    | 96.1  | USEPA (=EPA) FIFRA 122-2<br>USEPA (=EPA) FIFRA123-2 | EC50> 160 µg a.i./l      | 1993/1001232 |
| Rainbow trout           | Acute toxicity      | 95.4  | 96h USEPA (=EPA) FIFRA 72-1                         | LC50= 248 µg a.i./l      | 1991/1001372 |
| Rainbow trout           | Chronic toxicity    | 96.7  | 90d USEPA (=EPA) FIFRA 72-4                         | NOEC = 15 µg a.i./l      | 1992/1001149 |
| Bluegill sunfish        | Acute toxicity      | 95.4  | 96h USEPA (=EPA) FIFRA 72-1                         | LC50= 85.2 µg a.i./l     | 1991/1001371 |
| Common carp             | Acute toxicity      | 95    | 96h OECD 203 (1984)                                 | LC50= 430 µg a.i./l      | 1991/1001373 |
| Channel catfish         | Acute toxicity      | 97.08 | 96h USEPA (=EPA) FIFRA 72-1                         | LC50= 560 µg a.i./l      | 1997/1002146 |
| Bobwhite quail<br>(m,f) | Acute oral toxicity | 95    | 21d USEPA (=EPA) FIFRA, E,<br>71-1                  | LD50= 11.3 mg a.i./kg bw | 1990/1001138 |

| Species                       | Test                          | Purity % | Duration and conditions            | Result                     | Reference (BASF DocID) |
|-------------------------------|-------------------------------|----------|------------------------------------|----------------------------|------------------------|
| Bobwhite quail                | Short-term dietary toxicity   | 95       | 22d USEPA (=EPA) FIFRA, E,<br>71-2 | LC50= 48 mg a.i./kg diet   | 1990/1001139           |
| Bobwhite quail                | Chronic/reproduction toxicity | 96.7%    | USEPA (=EPA) FIFRA, E, 71-4        | NOEC= 10 mg a.i./kg diet   | 1992/1001146           |
| Mallard duck (m,f)            | Acute oral toxicity           | 95       | 21d USEPA (=EPA) FIFRA, E,<br>71-1 | LD50> 2150 mg a.i./kg bw   | 1990/1001137           |
| Mallard duck                  | Short-term dietary toxicity   | 95       | 22d USEPA (=EPA) FIFRA, E,<br>71-2 | LC50> 5000 mg a.i./kg diet | 1990/1001140           |
| Mallard duck                  | Chronic/reproduction toxicity | 96.7%    | USEPA (=EPA) E, 71-4(b)            | NOEC= 1000 mg a.i./kg diet | 1993/1001231           |
| House sparrow<br>(m,f)        | Acute oral toxicity           | 96.7     | 14d USEPA (=EPA) FIFRA, E,<br>71-1 | LD50= 1120 mg a.i./kg bw   | 1991/1001369           |
| Pheasant (m,f)                | Acute oral toxicity           | 95.4     | 35d USEPA (=EPA) FIFRA 71-1        | LD50= 31 mg a.i./kg bw     | 1992/1001144           |
| Red-legged<br>partridge (m,f) | Acute oral toxicity           | 95.4     | 21d USEPA (=EPA) FIFRA 71-1        | LD50= 34 mg a.i./kg bw     | 1992/1001145           |

|                                |   |      |   |  |              |
|--------------------------------|---|------|---|--|--------------|
| Pigeon (m,f)                   | Acute oral toxicity                           | 97.7 | 14d USEPA (=EPA) FIFRA 71-1                         | LD50> 2000 mg a.i./kg bw   | 1991/1001370 |
| Honey bee                      | Acute oral toxicity<br>Acute contact toxicity | 95.4 | 48h USEPA L, 141-1                                  | LD50oral= 0.00417 µg a.i./bee<br>LD50contact = 0.00593 µg a.i./bee | 1991/1001380 |
| Earthworms<br>(Eisenia fetida) | Acute toxicity                                | > 95 | 14d OECD 207 (1984)                                 | LC50> 1000 mg a.i./kg  | 1991/1001379 |
| Earthworms<br>(Eisenia fetida) | Subchronic and<br>reproductive toxicity       | 96   | 56d ISO 11268 part II (draft), BBA<br>VI-2-2 (1994) | NOEC = 1000 mg a.i./kg   | 1999/1007002 |

## Annex 2: References

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