

FAO SPECIFICATIONS AND EVALUATIONS FOR AGRICULTURAL PESTICIDES

FIPRONIL

(±)-5-amino-1-(2,6-dichloro- α,α,α -trifluoro-p-tolyl)-4-trifluoromethylsulfinylpyrazole-3-carbonitrile

2009



Food and Agriculture Organization
of the United Nations

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DISCLAIMER¹

FAO specifications are developed with the basic objective of promoting, as far as practicable, the manufacture, distribution and use of pesticides that meet basic quality requirements.

Compliance with the specifications does not constitute an endorsement or warranty of the fitness of a particular pesticide for a particular purpose, including its suitability for the control of any given pest, or its suitability for use in a particular area. Owing to the complexity of the problems involved, the suitability of pesticides for a particular purpose and the content of the labelling instructions must be decided at the national or provincial level.

Furthermore, pesticides which are manufactured to comply with these specifications are not exempted from any safety regulation or other legal or administrative provision applicable to their manufacture, sale, transportation, storage, handling, preparation and/or use.

FAO disclaims any and all liability for any injury, death, loss, damage or other prejudice of any kind that may arise as a result of, or in connection with, the manufacture, sale, transportation, storage, handling, preparation and/or use of pesticides which are found, or are claimed, to have been manufactured to comply with these specifications.

Additionally, FAO wishes to alert users to the fact that improper storage, handling, preparation and/or use of pesticides can result in either a lowering or complete loss of safety and/or efficacy.

FAO is not responsible, and does not accept any liability, for the testing of pesticides for compliance with the specifications, nor for any methods recommended and/or used for testing compliance. As a result, FAO does not in any way warrant or represent that any pesticide claimed to comply with a FAO specification actually does so.

¹ This disclaimer applies to all specifications published by FAO.

INTRODUCTION

FAO establishes and publishes specifications* for technical material and related formulations of agricultural pesticides, with the objective that these specifications may be used to provide an international point of reference against which products can be judged either for regulatory purposes or in commercial dealings.

Since 1999 the development of FAO specifications follows the **New Procedure**, described in the 5th 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 5th 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/pest-and-pesticide-management/expert-bodies-conventions/faowho-joint-meeting-on-pesticide-specifications-jmps/pesticide-specifications/en/> OR IN HARDCOPY FROM THE PLANT PROTECTION INFORMATION OFFICER.

PART ONE

SPECIFICATIONS

FIPRONIL

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FIPRONIL

INFORMATION

ISO Common Name:

Fipronil (ISO 1750 published)

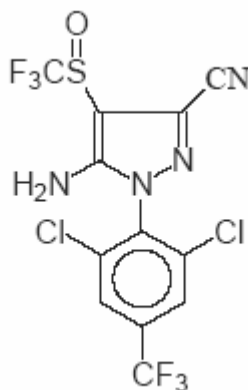
Synonyms:

None

Chemical names

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

Structural formula:



Empirical formula

C₁₂ H₄ Cl₂ F₆ N₄ OS

Relative molecular mass

437.15

CAS Registry number

120068-37-3

CIPAC number
581

Identity tests
HPLC retention time, IR spectrum.

FIPRONIL TECHNICAL MATERIAL

FAO specification 581/TC (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 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

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

FIPRONIL WATER DISPERSIBLE GRANULES

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 granules² 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	

* 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/>.

²granules 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.

FIPRONIL AQUEOUS SUSPENSION CONCENTRATE

FAO specification 581/SC (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 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

* Specifications may be revised and/or additional evaluations may be undertaken. Ensure the use of current versions by checking at: <http://www.fao.org/pest-and-pesticide-management/expert-bodies-conventions/fawho-joint-meeting-on-pesticide-specifications-jmps/pesticide-specifications/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 μm 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°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.

FIPRONIL EMULSIFIABLE CONCENTRATE

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:

* Specifications may be revised and/or additional evaluations may be undertaken. Ensure the use of current versions by checking at: <http://www.fao.org/pest-and-pesticide-management/expert-bodies-conventions/faowho-joint-meeting-on-pesticide-specifications-jmps/pesticide-specifications/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 $0 \pm 2^\circ\text{C}$ 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 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.

FIPRONIL SUSPENSION CONCENTRATE FOR SEED TREATMENT

FAO specification 581/FS (July 2009^{*}) (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.

^{*} Specifications may be revised and/or additional evaluations may be undertaken. Ensure the use of current versions by checking at: <http://www.fao.org/pest-and-pesticide-management/expert-bodies-conventions/fawho-joint-meeting-on-pesticide-specifications-jmps/pesticide-specifications/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 ± 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 ± 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 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 °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.

FIPRONIL ULTRA LOW VOLUME LIQUID

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.

* Specifications may be revised and/or additional evaluations may be undertaken. Ensure the use of current versions by checking at: <http://www.fao.org/pest-and-pesticide-management/expert-bodies-conventions/fawho-joint-meeting-on-pesticide-specifications-jmps/pesticide-specifications/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 ± 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 ± 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

FIPRONIL GRANULES

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	

* Specifications may be revised and/or additional evaluations may be undertaken. Ensure the use of current versions by checking at: <http://www.fao.org/pest-and-pesticide-management/expert-bodies-covventions/faowho-joint-meeting-on-pesticide-specifications-jmps/pesticide-specifications/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 μm , whereas the GR of Gharda is "not less than 900 g/kg 500 to 1000 μm "
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

FIPRONIL

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FIPRONIL

FAO/WHO EVALUATION REPORT 548/2009.2

Recommendation

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

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**

PHYSICO-CHEMICAL PROPERTIES OF FIPRONIL

Table 1 : Physico-chemical properties of technical grade fipronil

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

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

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

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

No special requirements for containers and packaging have been identified.

EXPRESSION OF THE ACTIVE INGREDIENT

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 (Sprague dawley) 5 M ; 5 F	Acute oral	OECD 401	95.5	LD ₅₀ : 66 mg/kg b.wt.	2 <u>T.FPO.002</u> <u>T.FPO.002A</u>
Mice (Swiss albino) 5 M ; 5 F	Acute oral	OECD 401	95.5	LD ₅₀ : 74 mg/kg b.wt.	3 <u>T.FPO.001</u>
Rat (Sprague dawley) 5 M ; 5 F	Acute dermal	OECD 402	95.5	LD ₅₀ : >2000 mg/kg b.wt.	4 <u>T.FPO.003</u> <u>T.FPO.003A</u>
Rat (Sprague dawley) 5 M ; 5 F	Acute Inhalation	OECD 403	95.5	LC ₅₀ : 0.98 mg/lit	5 <u>T.FPO.004</u> <u>T.FPO.004A</u>
Rabbit (New Zealand white) 3 M ; 3 F	Skin irritation	OECD.404	95.5	Non irritant	6 <u>T.FPO.005</u>
Rabbit, (New Zealand white) 6 F	Eye irritation	OECD 405	95.5	Non irritant	7 <u>T.FPO.006</u>
Guinea pig (Dunkan Hartly) M&F : 15	Skin sensitisation	OECD 406	98.2	Non sensitizer	8 <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 TA 1535,TA 1537, TA 98 and TA 100.	Bacterial reverse mutation assay	95.5	Gaitonde Committee Guidelines Dosages: 5000, 1500, 500, 150, 50 and 15 µg/plate.	non-mutagenic	10 <u>T.FPO.007</u>

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

Table 5. Ecotoxicology profile of technical fipronil

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

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

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.

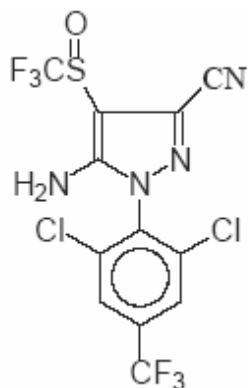
Identity of the active ingredient

ISO common name
Fipronil

Synonyms
None

Chemical names
IUPAC
(±)-5-amino-1-(2,6-dichloro- α,α,α -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
C₁₂ H₄ Cl₂ F₆ N₄ 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 ⁻⁶ 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 Boiling point: none, decomposition before boiling Decomposition temperature: ca. 230 °C	99.3 %	OECD 102, R010170/1996
Solubility in water	3.78 x 10 ⁻³ 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 log POW= 4.0at 20 °C (shake flask method)	99.9 % 99.3 %	EEC A8 by extrapolation, R010185/1997 OECD 107, R010078/1991
Hydrolysis characteristics	Half-life = stable at 25 °C at pH 5 (>97.6% of applied radioactivity at 30 days) Half-life = nearly stable at 25 °C at pH 7 (>97.6% of applied radioactivity at 30 days) Half-life = 28 days at 25 °C at pH 9 (30 day study, pseudo-first order kinetics) (25° C, dark)	98.6 % radio-chemical 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 ≥ 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 ≥ 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

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

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

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

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

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

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

No special requirements for containers and packaging have been identified.

EXPRESSION OF THE ACTIVE INGREDIENT

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 ₅₀ = 97 mg/kg bw	1988/1000897
Mouse (m,f)	Acute oral toxicity	95.3	14d Not stated but complies with EEC 92/69/EEC, B.1 (1992)	LD ₅₀ = 95 mg/kg bw	1995/1001721
Rat (m,f)	Acute percutaneous toxicity	93	14d OECD 402 (1987)	LD ₅₀ > 2000 mg/kg bw	1988/1000898
Rabbit (m,f)	Acute percutaneous Toxicity	96.7	28d USEPA (=EPA) FIFRA 81-2 (1984)	LD ₅₀ = 354 mg/kg bw	1993/1001210
Rat (m,f)	Acute inhalation toxicity	95.4	14d USEPA (=EPA) 81-3 (1984)	LC ₅₀ = 0.682 mg/l	1990/1001127
Rat (m,f)	Acute inhalation toxicity	96.72	14d USEPA (=EPA) 81-3 (1984) OECD 403 (1981)	LC ₅₀ = 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 (m,f)	Skin sensitization (Buehler)	95.4	35d OECD 406 (1981)	Not a sensitizer*	1990/1001128
Guinea pig (m,f)	Skin sensitization (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) 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) 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) 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 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 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 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 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 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 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)		
			0 - 7.5 - 15 - 22.5 and 30 µg/ml (24-and/or 48-hour exposures) With S9 mix		
Chinese hamster lung V79 cells	In vitro Gene mutation in mammalian cells	97.2	0 - 15 - 30 and 60 µg/ml (6-hour exposure)	Negative (slight toxicity observed in second test at 100 and 500 µg/ml)	1993/1001185
			0 - 0.8 - 4 - 20 - 100 and 500 µg/ml with and without S9 mix		
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 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 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 USEPA (=EPA) FIFRA 122-2 USEPA (=EPA) FIFRA123-2	EC50> 140 µg a.i./l	1993/1001234
Anabaena flos-aquae	Chronic toxicity	96.1	120h USEPA (=EPA) FIFRA 122-2 USEPA (=EPA) FIFRA123-2	EC50> 170 µg a.i./l	1993/1001233
Navicula pelliculosa	Chronic toxicity	96.1	120h USEPA (=EPA) FIFRA 122-2 USEPA (=EPA) FIFRA123-2	EC50> 120 µg a.i./l	1993/1001235
			14d		

Lemna gibba	Chronic toxicity	96.1	USEPA (=EPA) FIFRA 122-2 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 (m,f)	Acute oral toxicity	95	21d USEPA (=EPA) FIFRA, E, 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, 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, 71-1	LD50> 2150 mg a.i./kg bw	1990/1001137
Mallard duck	Short-term dietary toxicity	95	22d USEPA (=EPA) FIFRA, E, 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 (m,f)	Acute oral toxicity	96.7	14d USEPA (=EPA) FIFRA, E, 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 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 Acute contact toxicity	95.4	48h USEPA L, 141-1	LD50oral= 0.00417 µg a.i./bee LD50contact = 0.00593 µg a.i./bee	1991/1001380
Earthworms (Eisenia fetida)	Acute toxicity	> 95	14d OECD 207 (1984)	LC50> 1000 mg a.i./kg	1991/1001379
Earthworms (Eisenia fetida)	Subchronic and reproductive toxicity	96	56d ISO 11268 part II (draft), BBA VI-2-2 (1994)	NOEC = 1000 mg a.i./kg	1999/1007002

Annex 2: References

BASF Document number	Year and title of report or publication details
C018246	2001. Measurement of Vapour Pressure of Fipronil
R010170	1996. Fipronil active ingredient- Suitability for use as an analytical standard reference material
C018248	2001. Measurement of water solubility of Fipronil
R010185	1997. Fipronil active ingredient n-octanol/water partition coefficient.
R010078	1991. MB 46030-Octanol/Water Partition Coefficient at 20°C.
R010574	1992.14C-MB 46030-Hydrolysis at 25°C
R010090	1992. 14C-MB46030 Aqueous photolysis
C011803	2001. Statement on the dissociation constant
1988/1000897	1988. Acute oral toxicity to rats of M&B 46,030
1995/1001721	1995. MB 46030 - Acute oral LD50 in the mouse
1988/1000898	1988. Acute dermal toxicity to rats of M&B 46,030
1993/1001210	1993. MB 46030 (technical): Cutaneous irritancy study in the rabbit
1990/1001127	1990. M&B 46030: Acute inhalation toxicity study in the rat
1995/1001719	1995. Fipronil: Acute nose-only dust inhalation toxicity study in rats
1988/1000899	1988. Irritant effects on rabbit skin of M&B 46030
1993/1001210	1993. MB 46030 (technical): Cutaneous irritancy study in the rabbit
1988/1000900	1988. Irritant effects on the rabbit eye of M&B 46030
1993/1001209	1993. MB 46030 (technical): Ocular irritancy study in the rabbit
1990/1001128	1990. M&B 46030: Dermal sensitisation study in guinea-pigs
1993/1001198	1993. M&B 46030: Delayed contact hypersensitivity study in guinea-pigs
1990/1001129	1990. M&B 46030 - Toxicity to rats by dietary administration for 4 weeks

BASF Document number	Year and title of report or publication details
1991/1001348	1991. M&B 46030: Preliminary toxicity study by oral (capsule) administration to beagle dogs for four weeks - Amended final report
1991/1001350	1991. M&B 46030: Toxicity study by dietary administration to CD rats for 13 weeks - Final report
1991/1001355	1991. M&B 46030: Toxicity study by oral (capsule) administration to beagle dogs for 13 weeks - Final report
1992/1001142	1992. M&B 46030: Toxicity study by administration to beagle dogs for 52 oral (capsule) weeks
1993/1001213	1993. M&B 46030: Toxicity study by dietary administration to beagle dogs for 52 weeks
1993/1001201	1993. M&B 46030: Twenty-one day repeated cutaneous dose toxicity study in New Zealand white rabbits #2
1993/1001199	1993. M&B 46030: Combined oncogenicity and toxicity study by dietary administration to CD rats for 104 weeks including a 13 week reversibility period on completion of 52 weeks of treatment
1992/1001140	1992. M&B 46030: Oncogenicity study by dietary administration to CD-1 mice for 78 weeks - Interim report after 53 weeks of treatment - Volume 1
1992/1001138	1992. M&B 46030: Reproductive performance study in rats treated continuously through two successive generations
1991/1001352	1991. The effect of M&B 46030 on pregnancy of the rat
1990/1001134	1990. M&B 46030: Teratology study in the rabbit
1993/1001200	1993. M&B 46030: Single exposure neurotoxicity study in Sprague Dawley rats peroral (gavage)
1997/1002133	1997. Fipronil: Neurotoxicity to rats by acute administration (including a time to peak effect oral study)
1993/1001208	1993. M&B 46030: Ninety-day dietary neurotoxicity study in Sprague Dawley rats
1995/1001734	1995. A developmental neurotoxicity study of Fipronil in the rat via dietary administration
1988/1000901	1988. Study to determine the ability of M&B 46030 to induce mutation in four histidine-requiring strains of Salmonella typhimurium

BASF Document number	Year and title of report or publication details
1988/1000902	1988. Study to evaluate the chromosome damaging potential of M&B 46030 by its effects on cultured human lymphocytes using an in vitro cytogenetics assay
1995/1001736	1995. Fipronil: Chromosome aberration test in CHL cells in vitro
1993/1001185	1993. M&B 46030: Investigation of mutagenic activity at the HGPRT locus in a chinese hamster V79 cell mutation system - Amended final report
1993/1001184	1993. M&B 46030: Assessment of clastogenic action on bone marrow erythrocytes in the micronucleus test -Amended final report
1995/1001720	1995. M&B 46030: Mouse micronucleus test to comply with O.E.C.D. guideline 474 (1983)
2005/1011567	2005. Escherichia coli reverse mutation assay (standard plate test and preincubation test) with BAS 350 I (Fipronil)
2004/1021187	2004. In vivo unscheduled DNA synthesis (UDS) assay with BAS 350 I (Fipronil) in rat hepatocytes - single oral administration
2005/1027930	2005. Amendment No. 1 to the report: In vivo unscheduled DNA synthesis (UDS) assay with BAS 350 I (Fipronil) in rat hepatocytes - Single oral administration
1990/1001141	1990. (M&B 46030) - Acute toxicity to daphnids (<i>Daphnia magna</i>) during a 48-hour flow-through exposure
1990/1001142	1990. The chronic toxicity of M&B 46030 to <i>Daphnia magna</i> under flow-through conditions
1991/1001378	1991. The algistatic activity of M&B 46030
1993/1001234	1993. MB 46030 - Toxicity to the freshwater green alga, <i>Selenastrum capricornutum</i>
1993/1001233	1993. MB 46030 - Toxicity to the freshwater blue-green alga, <i>Anabaena flos-aquae</i>
1993/1001235	1993. MB 46030 - Toxicity to the freshwater diatom, <i>Navicula pelliculosa</i>
1993/1001232	1993. MB 46030 - Toxicity to duckweed, <i>Lemna gibba</i>
1993/1001236	1993. MB 46030 -Skeletonema Toxicity to the marine diatom, <i>costatum</i>
1991/1001372	1991. M&B 46030: Acute toxicity to rainbow trout, <i>Oncorhynchus mykiss</i> , under flow-through test conditions

BASF Document number	Year and title of report or publication details
1992/1001149	1992. (M&B 46030) -The toxicity to rainbow trout (<i>Oncorhynchus mykiss</i>) during an early life-stage exposure
1991/1001371	1991. M&B 46030: Acute toxicity to bluegill, <i>Lepomis macrochirus</i> , under flow-through test conditions
1991/1001373	1991. The acute toxicity of M&B 46030 to common carp (<i>Cyprinus carpio</i>)
1997/1002146	1997. Fipronil technical - Acute toxicity to channel catfish (<i>Ictalurus punctatus</i>) under flow-through conditions
1990/1001138	1990. M&B 46030 technical: 21-day acute oral LD50 study in bobwhite quail
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