Food and Agriculture Organization
of the United Nations

FAO SPECIFICATIONS AND EVALUATIONS
FOR AGRICULTURAL PESTICIDES

FLUPYRADIFURONE

4-[(6-chloro-3-pyridylmethyl)(2,2-difluoroethyl)
amino]furan-2(*5H*)-one

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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.

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

INTRODUCTION

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

From 2002, the development of WHO specifications follows the **New Procedure**, described in the 1st edition of "Manual for Development and Use of FAO and WHO Specifications for Pesticides" (2002) - currently available as 3rd revision of the 1st edition (2016) - , which is available only on the internet through the FAO and WHO web sites.

This **New Procedure** follows a formal and transparent evaluation process. It describes the minimum data package, the procedure and evaluation applied by FAO and the Experts of the FAO/WHO Joint Meeting on Pesticide Specifications (JMPS). [Note: prior to 2002, the Experts were of the FAO Panel of Experts on Pesticide Specifications, Registration Requirements, Application Standards and Prior Informed Consent, which now forms part of the JMPM, rather than the JMPS.]

FAO Specifications now only apply to products for which the technical materials have been evaluated. Consequently from the year 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 pesticide in accordance with chapters 4 to 9 of the "Manual on development and use of FAO and WHO specifications for pesticides".

Part Two: The Evaluation Report(s) of the pesticide, reflecting the evaluation of the data package carried out by FAO and the JMPS. The data are provided by the manufacturer(s) according to the requirements of chapter 3 of the "FAO/WHO Manual on Pesticide Specifications" and supported by other information sources. The Evaluation Report includes the name(s) of the manufacturer(s) whose technical material has been evaluated. Evaluation reports on specifications developed subsequently to the original set of specifications are added in a chronological order to this report.

FAO specifications developed under the **New Procedure** do not necessarily apply to nominally similar products of other manufacturer(s), nor to those where the active ingredient is produced by other routes of manufacture. FAO has the possibility to extend the scope of the specifications to similar products but only when the JMPS has been satisfied that the additional products are equivalent to that which formed the basis of the reference specification.

Specifications bear the date (month and year) of publication of the current version.

* NOTE: PUBLICATIONS ARE AVAILABLE ON THE INTERNET AT (http://www.fao.org/agriculture/crops/thematic-sitemap/theme/pests/jmps/ps-new/en/) OR IN HARDCOPY FROM THE PLANT PROTECTION INFORMATION OFFICER.

PART ONE

SPECIFICATIONS

FLUPYRADIFURONE

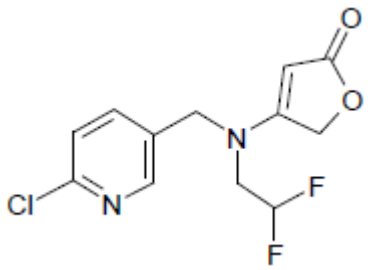
FLUPYRADIFURONE INFORMATION

ISO common name: (ISO 1750 provisionally approved) Flupyradifurone
Chemical name(s):
IUPAC: 4-[(6-chloro-3-pyridylmethyl)(2,2-difluoroethyl)amino]furan-2(*5H*)-one

CA: 4-[[(6-chloro-3-pyridinyl)methyl](2,2-difluoroethyl)amino]-2(*5H*)-furanone

Synonym: BYI 02960

Structural formula:



Molecular formula: $C_{12}H_{11}ClF_2N_2O_2$

Relative molecular mass: 288.68 g/mol

CAS Registry No.: 951659-40-8

CIPAC No.: 987

Identity tests: Retention time in HPLC-DAD

FLUPYRADIFURONE TECHNICAL MATERIAL

FAO Specification 987 / TC (Month 2017*)

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 (987/2017). It should be applicable to TC produced by this manufacturer but it is not an endorsement of those products, nor a guarantee that they comply with the specification. The specification may not be appropriate for TC produced by other manufacturers. The evaluation report (987/2017), as PART TWO, forms an integral part of this publication.

1 Description

The material shall consist of flupyradifurone together with related manufacturing impurities, in the form of a white to beige to pink powder, free from visible extraneous matter and added modifying agents.

2 Active ingredient

2.1 **Identity tests** (CIPAC 987/TC/M2) (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 **Flupyradifurone content** (CIPAC 987/TC/M3) (Note 1)

The flupyradifurone content shall be declared (not less than 980 g/kg) and, when determined, the average measured content shall not be lower than the declared minimum content.

Note 1 The results of the collaborative trial on identification and determination of flupyradifurone in TC, EC, EW, FS, SL, AL and WG based on reversed phase HPLC UV-detection were presented at the 61th CIPAC Meeting in June 2017 in Rome and provisionally adopted. Copies of the methods can be obtained through the CIPAC prepublishment scheme http://www.cipac.org/index.php/methods-publications/pre-published-methods

* 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/

FLUPYRADIFURONE EMULSIFIABLE CONCENTRATE

FAO Specification 987 / EC (Month 2017*)

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 (987/2017). It should be applicable to relevant products of this manufacturer, and those of any other formulators who use only TC from the evaluated source. The specification is not an endorsement of those products, nor a guarantee that they comply with the specification. The specification may not be appropriate for the products of manufacturers who use TC from other sources. The evaluation report (987/2017), as PART TWO, forms an integral part of this publication.

1 **Description**

The material shall consist of technical flupyradifurone, complying with the requirements of FAO specification 987 / TC (December 2017) 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 in water.

2 **Active ingredient**

2.1 **Identity tests** (CIPAC 987/EC/M2) (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 **Flupyradifurone content** (CIPAC 987/EC/M3)(Note 1)

The flupyradifurone content shall be declared in g/l at 20 ± 2ºC (Note 2) and, when determined, the average content measured shall not differ from that declared by more than the appropriate tolerance, given in the table of tolerances.

Declared content in g/l at 20 ± 2°C	Tolerance
up to 25	± 15% of the declared content
above 25 up to 100	± 10% of the declared content
above 100 up to 250	± 6% of the declared content
Note: the upper limit is included in each range	

.3 **Physical properties**

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

* 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/

The formulation, when diluted at 30 ± 2 °C (Note 3) with CIPAC Standard Waters A and D, shall comply with the following:

Time after dilution	Limits of stability, MT 36.3
0 h	initial emulsification complete
0.5 h	"cream", maximum: 1 ml
2.0 h	"cream", maximum: 1 ml "free oil", none
24 h	re-emulsification complete
24.5 h	"cream", maximum: 1 ml "free oil", maximum: none

Note: tests after 24 h are required only where results at 2 h are in doubt.

3.2 **Persistent foam** (MT 47.3, CIPAC Handbook O, p. 117, 2017) (Note 4)

Maximum: 40 ml after 1 min.

4 Storage stability

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

After storage at 0 ± 2°C for 7 days, the 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 Handbook 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 5) and the formulation shall continue to comply with the clauses for:

- emulsion stability and re-emulsification (3.1)

Note 1 The results of the collaborative trial on identification and determination of flupyradifurone in TC, EC, EW, FS, SL, AL and WG based on reversed phase HPLC UV-detection were presented at the 61th CIPAC Meeting in June 2017 in Rome and provisionally adopted. Copies of the methods can be obtained through the CIPAC prepublishment scheme http://www.cipac.org/index.php/methods-publications/pre-published-methods

Note 2 If the buyer requires both g/kg and g/l at 20 °C, then in case of dispute the analytical results shall be calculated as g/kg.

Note 3 As outlined in CIPAC MT 36.3, the test concentrations should be based on those in the recommended directions for use supplied with the product. Where several concentrations are recommended, the highest and lowest concentrations within the scope of the method should be used.

Note 4 The mass of sample to be used in the test should correspond to the highest rate of use recommended by the supplier. The test is to be conducted in CIPAC standard water D.

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

FLUPYRADIFURONE SUSPENSION CONCENTRATE FOR SEED TREATMENT

FAO Specification 987 / FS (December 2017*)

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 (987/2017). It should be applicable to relevant products of this manufacturer, and those of any other formulators who use only TC from the evaluated source. The specification is not an endorsement of those products, nor a guarantee that they comply with the specification. The specification may not be appropriate for the products of manufacturers who use TC from other sources. The evaluation report (987/2017), as PART TWO, forms an integral part of this publication.

1 **Description**

The material shall consist of a suspension of fine particles of technical flupyradifurone, complying with the requirements of FAO specification 987/TC (December 2017), in an aqueous phase together with suitable formulants, including colouring matter. After gentle stirring or shaking, the material shall be homogeneous (Note 1) and suitable for further dilution with water if necessary.

2 **Active ingredient**

2.1 **Identity tests** (CIPAC 987/FS/M2), (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 **Flupyradifurone content** (CIPAC 987/FS/M3) (Note 2)

The flupyradifurone content shall be declared (250 to 500 g/l at 20 ± 2ºC, Note 3) and, when determined, the average content measured shall not differ from that declared by more than ± 5% of the declared content.

3 **Physical properties**

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

Maximum "residue": 5 %.

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

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

3.3 **Persistent foam** (MT 47.3, CIPAC Handbook O, p. 177, 2017) (Note 4)

Maximum: 20 ml after 1 min

* 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/

3.4 **Adhesion to seeds** (MT 194, CIPAC Handbook N, p. 145, 2011)

Rape seeds: A minimum of 95% of the flupyradifurone shall remain on the seeds after the test.

4 Storage stability

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

After storage at 0 ± 2°C for 7 days, the formulation shall continue to comply with the clause for: wet sieve test (3.2).

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

After storage at 35 ± 2°C for 12 weeks, 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 formulation shall continue to comply with the clauses for:

- pourability (3.1),
- wet sieve test (3.2),
- adhesion to seeds (3.5)

Note 1 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 2 The results of the collaborative trial on identification and determination of flupyradifurone in TC, EC, EW, FS, SL, AL and WG based on reversed phase HPLC UV-detection were presented at the 61th CIPAC Meeting in June 2017 in Rome and provisionally adopted. Copies of the methods can be obtained through the CIPAC prepublishment scheme http://www.cipac.org/index.php/methods-publications/pre-published-methods

Note 3 Unless homogenization is carried out carefully, it is possible for the sample to become aerated. This can lead to errors in the determination of the mass per millilitre, and in calculation of the active ingredient content (in g/l) if methods other than MT 3.3 are used. If the buyer requires both g/kg and g/l at 20°C, then in case of dispute the analytical results shall be calculated as g/kg.

Note 4 The mass of sample to be used in the test should correspond to the highest rate of use recommended by the supplier. The test is to be conducted in CIPAC standard water D.

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

FLUPYRADIFURONE SOLUBLE CONCENTRATE

FAO Specification 987 / SL (Month 2017*)

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 (987/2017). It should be applicable to relevant products of this manufacturer, and those of any other formulators who use only TC from the evaluated source. The specification is not an endorsement of those products, nor a guarantee that they comply with the specification. The specification may not be appropriate for the products of manufacturers who use TC from other sources. The evaluation report (987/2017), as PART TWO, forms an integral part of this publication.

1 **Description**

The material shall consist of technical flupyradifurone, complying with the requirements of FAO specification 987/TC (December 2017) dissolved in suitable solvents, together with any other necessary formulants. It shall be in the form of a clear or opalescent liquid, free from visible suspended matter and sediment, to be applied as a true solution of the active ingredient in water.

2 **Active ingredient**

2.1 **Identity tests** (CIPAC 987/SL/M2), (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 **Flupyradifurone content** (CIPAC 987/SL/M3), (Notes 1 & 2)

The flupyradifurone content shall be declared in g/l at 20 ± 2ºC and, when determined, the average content measured shall not differ from that declared by more than the appropriate tolerance, given in the table of tolerances.

Declared content in g/l at 20 ± 2°C	Tolerance
up to 25	± 15% of the declared content
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
Note: the upper limit is included in each range	

* 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**

3.1 **Solution stability** (MT 41.1, CIPAC Handbook O, p. 174, 2017)

The formulation, following dilution (Note 3) with CIPAC standard water D and standing at 30 ± 2°C for 24 h, shall give a clear or opalescent solution, free from more than a trace of sediment and visible solid particles. Any visible sediment or particles produced shall pass through a 75 µm test sieve.

3.2 **Persistent foam** (MT 47.3, CIPAC Handbook O, p. 177, 2017) (Note 4)

Maximum: 30 ml after 1 minute.

4 **Storage stability**

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

After storage at 0 ± 2°C for 7 days, the 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 Handbook 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 5) and the formulation shall continue to comply with the clauses for:

- solution stability (3.1),

Note 1 The results of the collaborative trial on identification and determination of flupyradifurone in TC, EC, EW, FS, SL, AL and WG based on reversed phase HPLC UV-detection were presented at the 61th CIPAC Meeting in June 2017 in Rome and provisionally adopted. Copies of the methods can be obtained through the CIPAC prepublishment scheme http://www.cipac.org/index.php/methods-publications/pre-published-methods

Note 2 If the buyer requires both g/kg and g/l at 20°C, then in case of dispute the analytical results shall be calculated as g/kg.

Note 3 The concentration used for the test should not be higher than the highest concentration recommended in the instructions for use.

Note 4 The mass of sample to be used in the test should correspond to the highest rate of use recommended by the supplier. The test is to be conducted in CIPAC standard water D.

Note 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.

PART TWO

EVALUATION REPORTS

FLUPYRADIFURONE

FLUPYRADIFURONE

FAO/WHO EVALUATION REPORT 987/2017

Recommendations

The Meeting recommended that

i the specifications for flupyradifurone TC, EC, EW, FS and SL, proposed by Bayer CropScience and as amended, should be adopted by FAO, subject to clarification of some points.

ii specifications for flupyradifurone TC and EW (in combination with transfluthrin) proposed by Bayer CropScience and as amended, should be adopted by WHO, subject to adoption of the collaborative validation of the analytical method by CIPAC, the clearance of the product by the WHO Prequalification (PQ) Scheme and clarification of some points.

Appraisal

The Meeting considered data on flupyradifurone submitted by Bayer CropScience (BCS), in support of new FAO specifications for TC, EC, EW, FS and SL and new WHO specifications for TC and an EW combination product of flupyradifurone with transfluthrin.

The ISO common name flupyradifurone designates a molecule consisting of a five-membered lactone ring attached to a chloronicotinyl moiety through a difluoroamin-bridge. The lactone moiety is called a butenolide. Flupyradifurone was developed after the lead compound, stemofoline, a plant alkaloid sharing the butenolide moiety as toxophore. Flupyradifurone is an insecticide and has a similar mode of action as the neonicotinoids - it acts reversibly as an agonist on the insect nicotinic acetylcholine receptors (nAChR). However, its chemical structure differs from those of the nitroguanidine neonicotinoids and thus it is a separate sub-class of IRAC Group 4.

Flupyradifurone has been evaluated for its toxicology and residues in 2015 (JMPR, 2015). An ADI of 0-0.08 mg/kg bw and an ARfD of 0.2 mg/kg bw were allocated in 2015 which were extended at subsequent meetings.

There is no IPCS hazard classification of flupyradifurone and no harmonised classification in accordance with Regulation (EC) No 1272/2008 on classification, labelling and packaging of substances and mixtures, is currently available.

The compound has a fairly low volatility and a melting point of 69 and 67 °C (pure compound and TC, respectively). As a medium polarity compound, it is soluble in water with 3.2 g/L and has an octanol/water partition coefficient (log Pow) of 1.2. It does not dissociate at pH of 1 to 12 and is stable to hydrolysis. It is interesting to note that flupyradifurone, due to its physical-chemical properties, is amenable to many different types of formulations like EC, EW, FS and SL.

The Meeting was provided with confidential information on the manufacturing process and specification limits for the technical material as manufactured. The minimum purity of the active ingredient and maximum impurity limits as proposed by the BCS were supported by 5 batch analysis data. Flupyradifurone is produced in a one-step synthesis. The minimum purity of 980 g/kg was justified by the 5-batch data. Mass balances were high (99.76 – 100.52 %). The analytical methods for the majority of organic impurities are based on HPLC and are

adequately validated and support the results in the 5-batch study. The limits of quantitation were determined as part of the validation.

The Meeting concluded that none of the impurities included in the manufacturing specification should be considered as relevant. A CIPAC method based on reversed phase HPLC has been developed for determination of flupyradifurone in TC, EC, EW, FS and SL formulations and was presented at the 2017 CIPAC Meeting in Rome. The method was provisionally adopted as CIPAC method and is available through the prepublishment scheme.

The proposed specification for TC, EC, EW, FS and SL were essentially in accordance with the requirements of the Manual (3rd revision of the 1st edition, FAO/WHO 2016). As flupyradifurone is hydrolytically stable independent of pH value, no clause for pH or acidity was proposed in any of the formulation specification. This was accepted by the Meeting.

The WHO product flupyradifurone coformulated with transfluthrin in an EW is intended for space spraying vector control and is currently under clearance by the WHO PQ Scheme.

Certain issues were identified in some formulation specifications as follows:

Emulsion, oil in water (EW)

The low temperature stability test (CIPAC MT 39.3) apparently leads to some crystallization of the active ingredient resulting in a turbid liquid with faint sedimentation. The company explained, that the turbidity of the formulation does not have an adverse effect on the use of the formulation in reality. Later on, the specification for the EW was withdrawn by the company - a new composition of the formulation currently under development should guarantee adequate low temperature stability.

Suspension concentrate for seed treatment (FS)

The formulation is intended to be used without or with minimal dilution only. The minimal dilution (e.g. 50 % concentration) is out of the scope of the test to determine suspensibility (MT 184) which is approximately 10 %. For that reason, the suspensibility clause was removed.

Adhesion to seed (FS): The proposed limit for adhesion to rapeseed was 90 %, a value that was considered as very low by the Meeting. Even though for the moment no general limits are given in the Manual, experience of last years with a number of FS formulations has shown that typical adhesion/seed retention values are around 95 % or higher. The Meeting challenged the 90 % on rape seed - in morphological terms these seeds are not more difficult to coat than cereal seed like maize. The company then proposed a higher value (95 %) that was accepted by the Meeting.

The Meeting noted the exceptionally low temperature proposed by the company to carry out the stability at elevated temperature test (MT 46.3). The company explained, that the formulation tends to solidify under higher temperature (54°C for 2 weeks) or to show a reduced pourability (storage at 40° for 8 weeks) so a temperature/time combination was chosen (35°C for 12 weeks) where no clear adverse effect could be observed. As the product shows appropriate stability when stored in original packaging at 25°C for two years, the Meeting considered the explanations as adequate and accepted the unusually low temperature in the accelerated storage test.

SUPPORTING INFORMATION
FOR
EVALUATION REPORT 987/2017

USES

Flupyradifurone is a butenolide insecticide acting by both contact and ingestion. Its mode of action is on the insect central nervous system (CNS) as a selective partial agonist of the postsynaptic nicotinic acetylcholine receptor (nAChR). Flupyradifurone belongs to the IRAC Class 4D Mode of Action Classification.

Flupyradifurone is intended to be used as an insecticide in agriculture on a wide range of crops such as vegetables, fruits, grapes, date palm, coffee, cocoa and ornementals as foliar spray or soil drench, and as a seed treatment product for arable crops, e.g. soybean.

Flupyradifurone is scheduled for submission for a public health space spray product supporting the control of mosquitos to prevent malaria and other vector transmitted diseases such as Zika or Dengue.

Flupyradifurone is a systemic insecticide, flexible in application and mainly intended for sucking pest control such as aphids, hoppers and whiteflies.

IDENTITY OF THE ACTIVE INGREDIENT

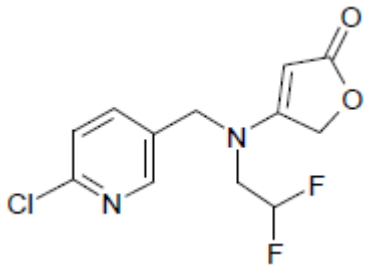
ISO common name:
Flupyradifurone

Chemical name(s):
IUPAC: 4-[(6-chloro-3-pyridylmethyl)(2,2-difluoroethyl)amino]furan-2(*5H*)-one

CA: 4-[[(6-chloro-3-pyridinyl)methyl](2,2-difluoroethyl)amino]-2(*5H*)-furanone

Synonym(s): Flupyradifurone TC, BYI 02960

Structural formula:



Molecular formula: $C_{12}H_{11}ClF_2N_2O_2$

Relative molecular mass: 288.68 g/mol

CAS Registry No.: 951659-40-8

CIPAC No.: 987

EC No.: not allocated

EU Index No.: not allocated

Identity tests: HPLC-DAD

METHODS OF ANALYSIS AND TESTING

The analytical method for determination of the content of the active ingredient in TC and formulated products (AL, EC, EW, FS, SL and WG formulations, CIPAC/5094), is a reversed phase HPLC method using UV detection at 280 nm and external standardization.

The methods for determination of impurities are based on HPLC using UV detection and and GC-FID.

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

FORMULATIONS AND CO-FORMULATED ACTIVE INGREDIENTS

The main formulation types available are SL, FS, WG and EW, but also AL, AE, GR and PR.

Flupyradifurone may be co-formulated with e.g. spiromesifen, deltamethrin and transfluthrin.

The SL formulation is the main formulation and is registered and sold in numerous countries globally. The registrations for the mixtures and the other straight formulations are ongoing.

CONTAINERS AND PACKAGING

No special requirements for containers and packaging have been identified.

EXPRESSION OF THE CONTENT OF THE ACTIVE INGREDIENT

The active ingredient is expressed and quantified as flupyradifurone.

Table 1. Physico-chemical properties of pure flupyradifurone

Parameter	Value(s) and Conditions	Purity (%)	Method Reference (and technique if the reference gives more than one)	Study number
Vapour pressure	9.1×10^{-7} Pa for 20 °C (extrapolated) 1.7×10^{-6} Pa for 25 °C (extrapolated) 2.6×10^{-5} Pa for 50 °C (extrapolated)	99.9	OECD 104 EC A.4 OPPTS 830.7950	M-309853-01-1
Melting point	69.0 °C (pure) 67.1 °C (technical)	99.4 97.6	OECD 102 EC A.1 OPPTS 830.7200	M-367370-01-1 M-414242-01-1
Temperature of decomposition	Pure flupyradifurone (BYI 02960), showed an exothermal decomposition in the temperature range 270 – 355 °C with a mean decomposition energy of 895 J/g. Flupyradifurone (BYI 02960), technical substance, showed an exothermal effect in the temperature range of 245 – 400 °C (245 – 355 °C respectively) with an energy of 836 to 938 J/g.	99.4 97.6	OECD 113	M-367370-01-1 M-414242-01-1
Solubility in water	pH 4 (buffer) 3.2 g/L at 20°C pH 9 (buffer) 3.0 g/L at 20°C In distilled water: pH 7 3.2 g/L at 20°C	99.4	OECD 105 EC A.6 flask method) OPPTS 830.7840	M-409513-01-1
Octanol/water partition coefficient	at 25 °C Pow log Pow pH 4 16 1.2 pH 7 16 1.2 pH 9 16 1.2	99.4	OECD 117 EC A.8 OPPTS 830.7570 (HPLC-method)	M-414485-01-1
Hydrolysis characteristics	BYI 02960 is hydrolytically stable at ambient temperature at pH 4, 7 and 9 under sterile and dark conditions	99.0	EPA, subdivision N § 161-1 (OECD 111) CAN PMRA, DACO 8.2.3.2 MAFF, 12 Nousan 8147	M-398952-01-1
Photolysis characteristics	in sterile phosphate buffer (pH 7): DT_{50} : 13.8 hrs	99.3	OPPTS 835.2240 CAN PMRA, DACO 8.3.3.2	M-418426-02-1

	Based on this experimental half-life, the half-life of BYI 02960 under environmental conditions is calculated to be 1.75 days in Phoenix, AZ (latitude 33.3°N). Therefore, based on the results of this study, BYI 02960 should rapidly degrade by aqueous photolysis in the environment.			
Dissociation characteristics	No dissociation of pure BYI 02960 occurs in aqueous solutions in the pH-range 1< pH <12. It is not possible to specify a pKa value for BYI 02960 in water.	99.4	OECD 112 OPPTS 830.7370	M-414102-01-1
Solubility in organic solvents	(g/L at 20 °C): methanol > 250 n-heptane 0.0005 toluene 3.7 dichloromethane > 250 acetone > 250 ethylacetate > 250 dimethyl sulfoxide > 250	99.4	OECD 105 (flask method) EC A.6 (flask method), OPPTS 830.7840	M-414064-01-1

Table 2. Chemical composition and properties of flupyradifurone technical material (TC)

Manufacturing process, maximum limits for impurities ≥ 1 g/kg, 5 batch analysis data	Confidential information supplied and held on file by FAO and WHO. Mass balances were 99.76 – 100.52 % and no unidentified impurities were reported.
Declared minimum flupyradifurone content	980 g/kg
Relevant impurities ≥ 1 g/kg and maximum limits for them	None
Relevant impurities **<** 1 g/kg and maximum limits for them:	None
Stabilisers or other additives and maximum limits for them:	None
Melting temperature range of the TC	(see Table 1)

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 flupyradifurone having impurity profiles similar to those referred to in the table 2 above.

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

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

Species	Test	Purity %	Guideline, duration, doses and conditions	Result	Study number
Rat (Wistar), female	oral	96.2%	OECD 423 (2001); EEC Directive 440/2008 Part B – Method B.1.tris; EPA Health Effects test Guidelines (OPPTS 870.1100) (1998)	Mortalities observed at 2000 mg/kg; none at 300 mg/kg LD_{50} cut off = 2000 mg/kg	M-349992-01-2
Rat (Wistar), male and female	dermal	96.2%	OECD 402 (1987); EEC Directive 440/2008 – Method B.3.;EPA Health Effects Test Guidelines (OPPTS 870.1200; 1998)	LD_{50} > 2 000 mg/kg	M-349995-01-2
Rat (Wistar), male and female	inhalation	96.2%	OECD 403 (1981); EEC Directive 92/69 Annex V - Method B.2. (1992); EPA Health Effects Test Guidelines (OPPTS 870.1300; 1998); Japan MAFF, Notification N° 12 Nousan-8147 (2000)	LC_{50} at 4 hours > 4671 mg/m^3	M-362791-01-2
Rabbit (NZW), female	skin irritation	96.2%	OECD 404 (2002); EEC Directive 440/2008; EPA Health Effects Test Guideline (OPPTS 870.2500; 1998)	Not irritating to skin	M-353761-01-2
Rabbit (NZW), female	eye irritation	96.2%	OECD 405 (2002); EEC Directive 440/2008; EPA Health Effects Test Guideline (OPPTS 870.2400; 1998)	Not irritating to eyes	M-361319-02-2
Mice (NMRI), female	skin sensitisation (modified Local Lymph Node Assay (IMDS))	96.2%	OECD 406 (1992) and 429 (2002); EEC Directive 2004/73/EC Annex V – Method B.6. (1996) and B42 (2001); EPA Health Effects Test Guideline (OPPTS 870.2600; 2003)	Not sensitizing	M-353715-01-2

Table 4. Toxicology profile of flupyradifurone technical material based on repeated administration (subacute to chronic)

Species	Test	Purity %	Guideline, duration, doses and conditions	Result	Study number
Rat (Wistar), male and female	28-days oral, gavage 0, 75, 200 & 350 mg/kg/day	98.3%	At the time of study conduct no guideline was in place (only preliminary and explorative study design)	NO(A)EL = 75 mg/kg/d LO(A)EL = 200 mg/kg/d Main findings observed at LO(A)EL: Changes in biochemical parameters, increased liver weight Liver: centrilobular hepatocellular hypertrophy, both sexes Thyroid: Minimal diffuse follicular cell hypertrophy in males only at 200 mg/kg/day	M-283421-02-2
Rat (Wistar), male	28-days oral, gavage 0, 500 & 5000 ppm	99.7%	At the time of study conduct no guideline was in place (only preliminary and explorative study design)	NO(A)EL = 500 ppm/33.6 mg/kg bw/d LO(A)EL = 5000 ppm/385 mg/kg bw/d Main findings observed at LO(A)EL: Liver: slight to moderate diffuse centrilobular hepatocellular hypertrophy Thyroid: Minimal to slight diffuse follicular cell hypertrophy Decreased T4, increased TSH, BROD and UDPGT inductions	M-297120-01-2
Mice (C57BL/6J), male and female	28-days oral, gavage 0, 300, 600 & 1200 ppm	99.7%	At the time of study conduct no guideline was in place (only preliminary and explorative study design)	NO(A)EL = 960 to 1080 ppm/166 to 186♂-192 to 216♀ mg/kg bw/d LO(A)EL = >960 to 1080 ppm/>166 to 186 mg/kg bw/d Main findings observed at LO(A)EL: Only slight body weight decrease	M-294820-01-2

Species	Test	Purity %	Guideline, duration, doses and conditions	Result	Study number
Dog (Beagle), male and female	28-day, oral, diet 0, 500, 2000 & 4000 ppm	99.5%	At the time of study conduct no guideline was in place (only preliminary and explorative study design)	NO(A)EL = 2000 ppm/62♂-77♀ mg/kg bw/d LO(A)EL = 4000 ppm/118♂-131♀ mg/kg bw/d Main findings observed at LO(A)EL: Liver: centrilobular glycogen accumulation decreased in incidence and/or severity	M-312461-01-3
Rat (Wistar), male and female	28-days dermal 50, 150, 500 mg/kg/d	96.2%	OECD 410 (1981); EPA Health Effects Test Guideline (OPPTS 870.3200; 1998)	NO(A)EL = 500 mg/kg/d LO(A)EL = >500 mg/kg/d Main findings observed at LO(A)EL: Non-adverse decreases in food consumption in females and mild decreases in absolute and relative liver weights in males	M-432336-01-1
Rat (Wistar), male and female	90-day, oral, diet 0, 100, 500 & 2500 ppm	99.5%	OECD 408 (1998); EEC Directive 2001/59/EC, Method B.26 (August, 2001),EPA Health Effects Test Guideline (OPPTS 870.3100; 1998); M.A.F.F. in Japan notification 12 Nousan N°8147 (2000) guidelines	NO(A)EL = 500 ppm/30♂-38♀mg/kg bw/d LO(A)EL = 2500 ppm/156♂-186♀ mg/kg bw/d Main findings observed at LO(A)EL: Changes in biochemical parameters, increased liver and thyroid weight Liver: centrilobular hepatocellular hypertrophy in both sexes Thyroid: follicular cell hypertrophy in males only	M-329048-03-2

Species	Test	Purity %	Guideline, duration, doses and conditions	Result	Study number
Mouse (C57BL/6J), male and female	90-day, oral, diet 0, 100, 500 & 2500 ppm	99.5%	OECD 408 (1998); EEC Directive 2001/59/EC, Method B.26 (August, 2001),EPA Health Effects Test Guideline (OPPTS 870.3100; 1998); M.A.F.F. in Japan notification 12 Nousan N°8147 (2000) guidelines.	NO(A)EL = 500 ppm/80.6♂-98.1♀ mg/kg bw/d LO(A)EL = 2500 ppm/407♂-473♀ mg/kg bw/d Main findings observed at LO(A)EL: Reduced body weight, changes in biochemical parameters, increased liver weight, decreased kidney weight Liver: increased diffuse hepatocellular vacuolations Kidney: decreased multifocal/diffuse Corticoepithelial vacuolation	M-328668-03-2
Dog (Beagle), male and female	90-day, oral, diet 0, 400, 1200 & 3600/2400 ppm	96.2%	OECD 409 (1998); EPA Health Effects Test Guideline (OPPTS 870.3150; 1998); M.A.F.F. in Japan notification 12 Nousan N°8147 (2000) guidelines.	NO(A)EL = 400 ppm/12♂-12♀ mg/kg bw/d LO(A)EL = 1200 ppm/31♂-41♀ mg/kg bw/d Main findings observed at LO(A)EL: Reduced body weight gain, changes in biochemical parameters Liver: increased absolute and relative weight in both sexes; brown pigment in Kupffer cells in females (high dose) Kidney: increased relative weights in both sexes Skeletal muscle: myofiber atrophy/degeneration in both sexes	M-369978-01-2

Species	Test	Purity %	Guideline, duration, doses and conditions	Result	Study number
Dog (Beagle), male and female	1-year, oral, diet 0, 150, 300, 1000 ppm	96.2%	OECD 452 (2009); EPA Health Effects Test Guideline (OPPTS 870.4100; 1998); M.A.F.F. in Japan notification 12 Nousan N°8147 (2000) guidelines.	NO(A)EL = 300 ppm/7.8♂-♀ mg/kg bw/d LO(A)EL = 1000 ppm/28.1♂-28.2♀ mg/kg bw/d Main findings observed at LO(A)EL: Minimal to slight degeneration of skeletal muscle (gastrocnemius and biceps femoris) in both sexes	M-425272-03-1

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

Species	Test	Purity %	Guideline, duration, doses and conditions	Result	Study number
Salmonella typhimurium	Reverse mutation assay 'Ames test' in vitro	96.2%	OECD 471 (1997); EEC Directive 2000/32/EC Method B13/14 (2000); EPA Health Effects Test Guideline (OPPTS 870.5100; 1998) S. typh.: TA 98, TA 100, TA 102, TA 1535, TA 1537 16-5000 µg/plate (+/-S9 mix)	BYI 02960 is not mutagenic in the Ames test	M-354173-01-2
Salmonella typhimurium	Reverse mutation assay 'Ames test' in vitro	97.2%	OECD 471 (1997); EEC Directive 2000/32/EC Method B13/14 (2000); EPA Health Effects Test Guideline (OPPTS 870.5100; 1998) S. typh.: TA 98, TA 100, TA 102, TA 1535, TA 1537 3-5000 µg/plate (+/-S9 mix)	BYI 02960 is not mutagenic in the Ames test	M-420539-02-2
Chinese Hamster V79 cells	Chromosome aberration assay in vitro	96.2%	OECD 473 (1997); EEC Directive 2000/32/EC Method B10 (2000); EPA Health Effects Test Guideline (OPPTS 870.5375; 1998) -S9: 0, 500, 1000, 2000, 2500 and 3000 µg/mL (4 hours treatment, harvest 18 hours after the beginning of treatment) 0, 2000, 2500 and 3000 µg/mL (4 hours treatment, harvest 30 hours after the beginning of treatment)	BYI 02960 did not induce structural chromosome aberrations in V79 cells when tested up to and including cytotoxic concentrations. Based on the results of this test, BYI 02960 is considered not to be clastogenic for mammalian cells *in vitro*.	M-359746-01-2

Species	Test	Purity %	Guideline, duration, doses and conditions	Result	Study number
			0, 100, 200, 400, 600 and 800 µg/mL (18 hours treatment, harvest at the same time) +S9: 0, 500, 1000, 2000, 2500 and 3000 µg/mL (4 hours treatment, harvest 18 hours after the beginning of treatment) 0, 2000, 2500 and 3000 µg/mL (4 hours treatment, harvest 30 hours after the beginning of treatment)		
Chinese Hamster V79 cells	HPRT Test, gene mutation in vitro	96.2%	OECD 476 (1997); EEC Directive 2000/32/EC Method B17 (2000); EPA Health Effects Test Guideline (OPPTS 870.5300; 1998) -S9: 0, 46, 92, 184, 368, 736, 1472, 2944 µg/mL; +S9: 0, 46, 92, 184, 368, 736, 1472, 2944 µg/mL	BYI 02960 has no mutagenic potency in vitro in the CHO/HPRT assay. The test substance did not induce unscheduled DNA synthesis in mammalian cells	M-359743-01-2
Mouse (NMRI BR), male	Micronucleus Test	96.2%	OECD 474 (1997); EEC Directive 2000/32/EC Method B12 (2000); EPA Health Effects Test Guideline (OPPTS 870.5395; 1998) Two intraperitoneal injections separated by 24 hrs 10, 20 and 40 mg/kg bw	BYI 02960 has no potential to induce micronuclei in mouse bone marrow cells	M-353785-01-2

Species	Test	Purity %	Guideline, duration, doses and conditions	Result	Study number
Mouse (NMRI BR), female	Micronucleus Test	97.2%	OECD 474 (1997); EEC Directive 2000/32/EC Method B12 (2000); EPA Health Effects Test Guideline (OPPTS 870.5395; 1998) Two intraperitoneal injections separated by 24 hrs 12.5, 25 and 50 mg/kg bw	BYI 02960 has no potential to induce micronuclei in mouse bone marrow cells	M-420536-01-2

Table 6. Toxicology profile of flupyradifurone BYI 02960 technical material based on repeated administration (chronic)

Species	Test	Purity %	Guideline, duration, doses and conditions	Result	Study number
long-term toxicity/carcinogenicity					
Rat (Wistar), male and female	104-week, oral, diet Oncogenicity	96.2%	OECD 453 (1981); EEC Directive 88/302/EEC – Annex V - Method B.33. (1987); EPA Health Effects Test Guideline (OPPTS 870.4300; 1998); M.A.F.F. in Japan notification 12 Nousan N°8147 (2000) guidelines. 0, 80, 400 & 2000 ppm	NO(A)EL = 400 ppm/ 15.8♂-22.5♀ mg/kg bw/d LO(A)EL = 2000ppm/ 80.8♂-120♀ mg/kg bw/d Main findings observed in target organs liver & thyroid either sex; lung in females: No tumors. Only slight body weight decrease	M-428257-01-1
Mouse (C57BL/6J), male and female	78-week, oral, diet Oncogenicity	96.2%	OECD 453 (1981); EEC Directive 88/302/EEC – Annex V - Method B.33. (1987); EPA Health Effects Test Guideline (OPPTS 870.4300; 1998); M.A.F.F. in Japan notification 12 Nousan N°8147 (2000) guidelines. 0, 70, 300 or 1500 ppm	NO(A)EL = 300ppm = 43♂-53♀ mg/kg bw/d LO(A)EL = 1500ppm = 224♂-263♀mg/kg bw/d Main findings observed in target organs: liver both sex; kidney in males: No tumours.	M-428257-01-1
long-term toxicity/ Reproduction and development					
Rat (Wistar), male and female	Reproduction 1-generation	96.2%	No guidelines - pilot study. pre-mating 10 weeks 0, 80, 400 & 2000 ppm	Parent: NO(A)EL = 50.1♂-17.5♀ mg/kg bw/d LO(A)EL = 147.5♂-60♀ mg/kg bw/d Main findings observed at LO(A)EL: ♂:Slight declines in BWG - ♀:Decreased BW and /or BWG (premating, gestation, and	M-394208-01-2

Species	Test	Purity %	Guideline, duration, doses and conditions	Result	Study number
				lactation) Reproduction: NO(A)EL = 147.5♂-168.9♀ mg/kg bw/d LO(A)EL = >147.5♂-168.9♀ mg/kg bw/d Main findings observed at LO(A)EL: No effects Offspring: NO(A)EL = 17.5 mg/kg bw/d LO(A)EL = 60.9 mg/kg bw/d Main findings observed at LO(A)EL: Decreased BWG and brain weight	
Rat (Wistar), male and female	Reproduction 2-generation	96.2%	OPPTS Guideline Number: 870.3800 Reproduction and Fertility Effects EU Guidelines on Reproductive Toxicity Studies 91/414/EEC; OECD 416 Two-Generation Reproduction Toxicity Study; JMAFF 12 Nousan No. 8147 Health Canada, Guideline on Reproduction Toxicity Studies pre-mating 10 weeks 0, 100, 500, 1800 ppm	Parent: NO(A)EL = 500♂-100♀ ppm = 32.3♂-7.8♀ mg/kg bw/d LO(A)EL = 1800♂-500♀ ppm = 119.8♂-39.2♀ mg/kg bw/d Main findings observed at LO(A)EL: ♂: Increased liver weights (P). Increased thyroid weights (P). Increased incidence of centrilobular hypertro-phy (minimal – P). ♀: Decreased BW (premating, gestation, and lactation; F_1) Decreased BWG (premating; P and F_1) Decreased terminal body weights (P & F_1)	M-417665-01-2

Species	Test	Purity %	Guideline, duration, doses and conditions	Result	Study number
				Reproduction: NO(A)EL = 500♂♀ ppm = 32.3♂-39.2♀ mg/kg bw/d LO(A)EL = 1800♂♀ ppm = 119.8♂-140.2♀ mg/kg bw/d Main findings observed at LO(A)EL: Decreased cycle number (F1), litter size (F1), and number of implants (F1) Offspring: NO(A)EL = 100 ppm = 7.8 mg/kg bw/d LO(A)EL 500 ppm = 39.8 mg/kg bw/d Main findings observed at LO(A)EL: Decreased BW and BWG (F2); with Secondary to BW decreases: organ weight changes in brain, thymus, and spleen EFSA conclusion: NOAEL 6.4 mg/kg bw/d (parental and offspring toxicity)	
Rat (Sprague Dawley), female	Teratogenicity study	96.2%	OECD 414 (2001); EPA Health Effects Test Guideline (OPPTS 870.3700; 1998); M.A.F.F. in Japan notification 12 Nousan N°8147 (2000) guidelines. gestation days 6-20 0, 15, 50, 150 mg/kg/d	Dams: NO(A)EL = 50 mg/kg bw/d (Maternal) LO(A)EL = 150 mg/kg bw/d Main findings observed at LO(A)EL: Decreased mean BWG and food consumption (FC). Increased liver weight Fetuses:	M-363938-01-2

Species	Test	Purity %	Guideline, duration, doses and conditions	Result	Study number
				NO(A)EL = 50 mg/kg bw/d (Develop.) LO(A)EL = 150 mg/kg bw/d Main findings observed at LO(A)EL: Decreased fetal BW; Reduced ossification of a few skull bones	
Rat (Sprague Dawley), female	Maternal tolerability studyComplementary study	96.2%	Not guidelines applicable; complementary study on maternal toxicity. gestation days 6-20 0, 20, 30 mg/kg/d	Dams: NO(A)EL = 30 mg/kg bw/d (Maternal) LO(A)EL = >30 mg/kg bw/d Main findings observed at LO(A)EL: No maternal toxicity	M-425810-01-2
Rabbit (NZW), female	Teratogenicity study	96.2%	OECD 414 (2001); EPA Health Effects Test Guideline (OPPTS 870.3700; 1998); M.A.F.F. in Japan notification 12 Nousan N°8147 (2000) guidelines. gestation days 6-28 0, 7.5, 15, 40 mg/kg/d	Dams: NO(A)EL = 40 mg/kg bw/d (Maternal) LO(A)EL = 40 mg/kg bw/d Main findings observed at LO(A)EL: Decreased BW, BWG, corrected BWG, and FC (GD6-10) Fetuses: NO(A)EL = 40 mg/kg bw/d (Develop.) LO(A)EL = >40 mg/kg bw/d Main findings observed at LO(A)EL: No treatment-related effects	M-423559-01-1
Neurotoxicity					
Rat (Wistar), male and female	Acute neurotoxicity feeding	96.2%	OECD 424 (1997); EPA Health Effects Test Guideline (OPPTS 870.6200; 1998); M.A.F.F. in Japan	NO(A)EL = 35♂♀ mg/kg bw/d LO(A)EL = 50♂♀ mg/kg bw/d Main findings observed in target organs: Piloerection and dilated	M-415408-01-2

Species	Test	Purity %	Guideline, duration, doses and conditions	Result	Study number
			notification 12 Nousan N°8147 (2000) guidelines. 0, 20, 35, 50, 200 and 800 mg/kg bw	pupils - At high dose levels: lower muscle tone, rapid respiration, gait incoordination, tremors, reduced motor activity, impaired righting reflex, impaired flexor and tail pinch responses	
Rat (Wistar), male and female	90-day Sub-chronic neurotoxicity feeding	96.2%	OECD 424 (1997); EPA Health Effects Test Guideline (OPPTS 870.6200; 1998); M.A.F.F. in Japan notification 12 Nousan N°8147 (2000) guidelines. 0, 100, 500,2500 ppm	NO(A)EL = 143♂-173♀ mg/kg bw/d LO(A)EL = >143♂->173♀ mg/kg bw/d Main findings observed in target organs: none	M-410022-01-2
Rat (Wistar), male and female	Developmen-tal neurotoxicity feeding	96.2%	OECD 426 (2007); EPA Health Effects Test Guideline (OPPTS 870.6300; 1998) 0, 120, 500, 1200 ppm from gestation Day (GD) 6 through lactation Day (LD) 21	NO(A)EL = 500 ppm = 42.4 mg/kg bw/d LO(A)EL = 1200 ppm = 102 mg/kg bw/d Main findings observed in target organs: Maternal : decreased body weight and body weight gain Offspring: decreased body weight gain in pups Increase Startle amplitude (females only) on PND 60. Increase motor and locomotor activity on PND 13 (males only).	M-434203-01-1

Table 7. Ecotoxicology profile of the technical material

Species	Test	Purity %	Guideline, duration, doses and conditions	Result	Study number
BYI 02960 Birds toxicity					
Bobwhite Quail (*Colinus virginianus)*	acute, oral	96.2%	OPPTS 850.2100 OECD Guideline 223 Birds received 25, 50, 100, 200 and 400 mg a.i./kg body weight via gelatine capsule and were observed over a period of 14 days	LD_{50} 232 mg a.i./kg bw	M-386036-01-1
Canary (*Serinus canaria*)	acute, oral	96.2%	OPPTS 850.2100 OECD Guideline 223 Birds received 44, 88, 175, 350 and 700 mg a.i./kg b.w, via gelatine capsule and were observed over a period of 14 days	LD_{50} 330 mg a.i./kg bw	M-408514-01-1
chicken *(Gallus gallus domesticus)*	acute, oral	96.2%	OECD Guideline 223 Five birds (treatment group) were orally administered with gelatine capsules containing 2000 mg a.i./kg b.w. and were observed for a period of 28 days	LD_{50} >2000 mg a.i./kg bw	M-420519-01-2
Mallard Duck *(Anas platyrhynchos)*	5-day-feeding	96.2%	OECD Guideline No. 205 OPPTS 850.2200 Nominal concentrations in feed were 313, 625, 1250, 2500 and 5000 ppm corresponding to 66, 129, 272, 459 and 825 mg a.i./kg body weight/day . Birds were exposed to treated feed during a period of 5 days and observed thereafter for another 3 days	LC_{50} >4741 mg a.i./kg diet ≡ >825 mg a.i./kg bw/d NOEL 2238 mg a.i./kg diet ≡ 459 mg a.i./kg bw/d	M-388718-01-1

Species	Test	Purity %	Guideline, duration, doses and conditions	Result	Study number
Bobwhite Quail *(Colinus virginianus)*	5-day-feeding	96.2%	OECD Guideline No. 205 OPPTS 850.2200 Nominal concentrations in feed were 313, 625, 1250, 2500 and 5000 ppm corresponding to 48, 99, 170, 262 and 470 mg a.i./kg body weight/day. Birds were exposed to treated feed during a period of 5 days and observed thereafter for another 3 days	LC_{50} >4876 mg a.i./kg diet ≡ >470 mg a.i./kg bw/d NOEL 1133 mg a.i./kg diet ≡ 170 mg a.i./kg bw/d	M-394535-01-1
Mallard Duck *(Anas platyrhynchos)*	20-week feeding chronic, reproduction	96.2%	OECD Guideline No. 206 OPPTS 850.2300 FIFRA Guideline 71-4 Nominal concentrations in feed were 111, 333 and 1000 ppm corresponding to 9, 28 and 81 mg a.i./kg body weight/day. Birds were exposed to treated feed during a period of approximately 20 weeks	NOAEL ≥845 mg a.i./kg diet ≡ ≥81 mg a.i./kg bw/d	M-412917-02-1
Bobwhite Quail *(Colinus virginanus)*	23-week feeding chronic, reproduction	96.2%	OECD Guideline No. 206 OPPTS 850.2300 FIFRA Guideline 71-4 Nominal concentrations in feed were 111, 333 and 1000 ppm corresponding to 14, 40 and 154 mg a.i./kg body weight/day Birds were exposed to treated feed during a period of 23 weeks	NOAEL 302 mg a.i./kg diet ≡ 40 mg a.i./kg bw/d	M-424704-01-2
BYI 02960 Fish toxicity					
Rainbow Trout *(Oncorhynchus mykiss)*	acute, 96 h	96.2%	OECD Test Guideline 203 EPA-FIFRA § 72-1 OPPTS 850.1075	LC_{50} > 74.2 mg a.i./L (mm) NOEC ≥ 74.2 mg a.i./L (mm)	M-390611-01-1

Species	Test	Purity %	Guideline, duration, doses and conditions	Result	Study number
			Nominal (mean measured) concentrations in feed were 5.00 (3.52), 10.0 (8.31), 20.0 (19.0), 40.0 (35.1) and 80.0 (74.2) mg a.i./L. Fishes were exposed under static conditions over a period of 96 hours		
Fathead Minnow *(Pimephales promelas)*	acute, 96 h	96.2%	OECD Test Guideline 203 EPA-FIFRA § 72-1 OPPTS 850.1075 Nominal (mean measured) concentrations in feed were 5.00 (4.29), 10.0 (9.00), 20.0 (19.4), 40.0 (34.3) and 80.0 (70.5) mg a.i./L. Fishes were exposed under static conditions over a period of 96 hours	LC_{50} > 70.5 mg a.i./L (mm) NOEC ≥ 70.5 mg a.i./L (mm)	M-392560-01-1
Carp *(Cyprinus carpio)*	acute, 96 h	96.2%	OECD Test Guideline No. 203; EU Directive 92/69/EEC, C.1 (1992) EPA-FIFRA § 72-1; OPPTS 850.1075 JMAFF, 12 Nousan No. 8147 Nominal concentrations in feed was 100 mg a.i./L. Fishes were exposed under static conditions over a period of 96 hours	LC_{50} > 100 mg a.i./L (mm) NOEC ≥ 100 mg a.i./L (mm)	M-420407-01-2
Fathead Minnow *(Pimephales promelas)*	Chronic, early life stage (ELS), 35d	96.2%	OECD Guideline 210 (1992(EPA-FIFRA Guideline 72-4 (a), 1982 OPPTS 850.1400 (1996 draft) Fishes were exposed in a flow-through system over a period of 35 days to nominal concentrations of 0.625, 1.25, 2.50, 5.00 and 10.0 mg a.i./L (corresponding to mean measured concentrations of 0.619, 1.11, 2.05, 4.41 and 8.40 mg a.i./L)	NOEC 4.41 mg a.i./L (mm) LOEC 8.41 mg a.i./L (mm)	M-409339-01-1

Species	Test	Purity %	Guideline, duration, doses and conditions	Result	Study number
BYI 02960 Amphibians toxicity					
African clawed frog tadpoles *(Xenopus laevis)*	acute, 48 h		USEPA, OPPTS Guideline 850.1075 USEPA-FIFRA, 40 CFR, Part 158, Guideline No. 72-1 OECD Guideline 203 Tadpoles were exposed in a static system over a period of 48 hours to a nominal concentration of 80 mg a.i./L corresponding to a measured concentration of 74 mg a.i./L)	LC_{50} > 73.8 mg a.i./L (mm) NOEC ≥ 73.8 mg a.i./L (mm)	M-417822-01-1
BYI 02960 Aquatic Invertebrates toxicity					
waterflea *(Daphnia magna)*	acute, 48 h	96.2%	OECD Guideline 202 EPA OPP 72-2 EPA OPPTS 850.1010 *Daphnia magna* ((6 replicates of 5) <24 hour old neonates) were exposed in a static system over a period of 48 hours to nominal concentrations of 80 mg a.i./L (corresponding to analytically verified concentrations of 77.6 mg a.i./L).	EC_{50} > 77.6 mg a.i./L (mm) NOEC ≥ 77.6 mg a.i./L (mm)	M-357476-01-1
waterflea *(Daphnia magna)*	chronic, static renewal, 21 d	96.2%	OECD-Guideline No. 211 EC Council Regulation No 440/2008, Method C.20 U.S. FIFRA72-4 (1982) U.S. EPA- OPPTS Guideline 850.1300 *Daphnia magna* (<24 hour old neonates, 10 animals per study group) were exposed in a static-renewal system over a period of 21 days to nominal concentrations of 0.8, 1.6, 3.2, 6.4, 12.8 and 25.6 mg a.i./L.	NOEC 3.2 mg a.i./L (nom) LOEC 6.4 mg a.i./L (nom)	M-414066-01-2

Species	Test	Purity %	Guideline, duration, doses and conditions	Result	Study number
Chironomus riparius	acute, 48 h	96.2%	No specified guideline; study is performed according to general aspects of OECD Guideline No. 202 *Chironomus riparius* (first instars, less than 2 to 3 days old, 40 per test concentration) were exposed in a static system over a period of 48 hours to nominal concentrations of 3.125, 6.25, 12.5, 25.0, 50.0 and 100 µg a.i./L.	EC_{50} 0.062 mg a.i./L (nom) NOEC 0.025 mg a.i./L (nom)	M-414739-01-2
Chironomus riparius	chronic, spiked water, 28 d	96.2%	OECD Guideline 219 Midge larvae of *Chironomus riparius* (1st instar larvae, 2-3 days old, 4 replicates of 20 per treatment and control) were exposed in a static water sediment system (spiked-water exposure) over a period of 28 days to nominal concentrations of 1.25, 2.50, 5.00, 10.0, 20.0 and 40.0 µg a.i. /L.	NOEC 0.0105 mg a.i./L (mi) LOEC 0.0213 mg a.i./L (mi) EC_{50} 0.0353 mg a.i./L (mi) EC_{15} 0.0219 mg a.i./L (mi)	M-401792-01-2
BYI 02960 Marine organisms toxicity					
sheepshead minnow *(Cyprinodon variegatus)*	static acute, 96 h	96.2%	OECD Test Guideline 203: EPA-FIFRA § 72-3 OPPTS 850.1075 Cyprinodon variegatus (10 fish per treatment level) were exposed in a static system over a period of 96 hours to nominal concentrations of 5.00, 10.0, 20.0, 40.0 and 80.0 mg a.i./L (corresponding to analytically verified concentrations of 5.6, 10.4, 21.0, 40.4 and 83.9 mg a.i./L; 101 to 112% of nominal)	LC_{50} > 83.9 mg a.i./L (mm) NOEC 83.9 mg a.i./L (mm)	M-357479-01-1

Species	Test	Purity %	Guideline, duration, doses and conditions	Result	Study number
Eastern Oyster *(Crassostrea virginica)*	acute, flow-through, 96 h	96.2%	OPPTS 850.1025 Oysters (mean valve height of 35.1 ± 2.7 mm; range: 30.2 to 40.1 mm, 20 per treatment level) were exposed in a flow through system over a period of 96 hours to nominal concentrations of 0.94, 1.9, 3.8, 7.5, 15 and 30 mg a.i./L (corresponding to analytically verified concentrations of 0.90, 1.8, 3.6, 7.3, 15 and 29 mg a.i./L; 95 to 97% of nominal)	EC_{50} > 29 mg a.i./L (mm) NOEC ≥ 29 mg a.i./L (mm)	M-361668-01-1
Saltwater Mysid *(Americamysis bahia)*	static acute, 96 h	96.2%	EPA OPP 72-3(b) EPA OPPTS 850.1035 Juvenile *Americamysis bahia* (< 24 hours old, 20 per treatment level) were exposed in a static system over a period of 96 hours to nominal concentrations of 0.13, 0.22, 0.36, 0.60 and 1.0 mg a.i./L (corresponding to analytically verified concentrations of 0.12, 0.21, 0.35, 0.58 and 0.98 mg a.i./L)	EC_{50} 0.26 mg a.i./L (mm) NOEC 0.12 mg a.i./L (mm)	M-364620-01-1
Saltwater Mysid *(Americamysis bahia)*	life cycle, flow-through, 28 d	96.2%	OPPTS Number 850.1350: Mysid Chronic Toxicity Test ASTM Standard E 1191-03a: Standard Guide for Conducting Life-Cycle Toxicity Tests with Saltwater Mysid Fifteen neonates (<24 h old) of *Americamysis bahia* per replicate were exposed in a flow-through system over a period of 28 days to nominal concentrations of 4.6, 8.0, 13.9, 24.2 and 42 µg a.i./L	NOEC 0.0132 mg a.i./L (mm) LOEC 0.0236 mg a.i./L (mm)	M-420783-01-1

Species	Test	Purity %	Guideline, duration, doses and conditions	Result	Study number
			(corresponding to analytically verified concentrations of 4.2, 7.8, 13.2, 23.6 and 40 µg a.i./L)		
BYI 02960 Algae and Aquatic plants toxicity					
Green Alga *Pseudokirchneriella subcapitata*	growth inhibition, 96 h	96.2%	EPA OPPTS 850.5400 OECD Guideline 201 FIFRA 123-2 Cultures of *Pseudokirchneriella subcapitata* with an initial cell density of 10000 cells/mL were exposed in a static system over a period of 96 hours to nominal concentrations of 5.0, 10, 20, 40 and 80 mg a.i./L (corresponding to analytically verified concentrations of 5.9,11, 23, 47 and 95 mg a.i./L)	ErC_{50} > 80 mg a.i./L (nom) NOErC ≥ 80 mg a.i./L (nom)	M-397552-01-1
Duckweed (*Lemna gibba* G3)	growth inhibition, 7 d	96.2%	OECD Test Guideline 221: FIFRA Guideline 123-2 OPPTS 850.4400 Cultures of *Lemna gibba* with an initial density of 12 fronds per vessel were exposed in a static renewal (one renewal at day 3) system over a period of 7 days to nominal concentrations of 5.0, 10, 20, 40 and 80 mg a.i./L (corresponding to analytically verified concentrations of 4.02, 8.17, 16.0, 34.2 and 67.7 mg a.i./L)	EbC_{50} (frond no.) > 67.7 mg a.i./L (mm) ErC_{50} (frond no) > 67.7 mg a.i./L (mm) NOEC (frond no) 34.2 mg a.i./L (mm)	M-398376-01-1
BYI 02960 Honeybees toxicity					
Honey Bees *(Apis mellifera L.)*	Acute contact & oral	99.5%	OECD Guideline 213 OECD Guideline 214	LD_{50} contact, 96 h 122.8 µg a.i./bee	M-308904-02-2

Species	Test	Purity %	Guideline, duration, doses and conditions	Result	Study number
			In the oral dose response test 30 adult worker honey bees were exposed for 48 hours to doses of 2.8, 2.1, 1.3, 0.68, 0.34 and 0.17 µg a.i. per bee by feeding (values based on the actual intake of the test item). For the contact dose response test 30 honey bees were exposed for 96 hours to doses of 200.0, 100.0, 50.0, 25.0 and 12.5 µg a.i. per bee by topical application.	LD_{50} oral, 48 h 1.2 µg a.i./bee	
Honey Bees *(Apis mellifera L.)*	Chronic effects: 10 d continuous feeding (laboratory), adult honeybees	96.2%	No specific guideline available Over a period of 10 days, honey bees were exposed to 50% (w/v) sucrose solution, containing nominally 100, 300, 1000, 3000 and 10000 µg a.i./L of the test item BYI 02960 by continuous and *ad libitum* feeding	No adverse effects (mortality & behavior); LC_{50} = 61100 µg/kg 1.83 µg a.s/bee.d	M-462475-01-1
Honey Bees *(Apis mellifera L.)* larvae	Chronic effects: 10 d continuous feeding (laboratory), adult honeybees	96.2%	No validated guideline available. Study design according to the recommendations of the INRA (Institut National de la Recherche Agronomique) - method for testing pesticide toxicity to honeybee brood in laboratory conditions (January, 2008) and the recommendations of the honeybee larvae laboratory ring-test group, organized by ICPBR (Aupinel et al., 2009) Over a period of 22 days, honey bee larvae were exposed to BYI 02960 (tech.) incorporated into the artificial exposure diet at the nominal test	No adverse effects; NOEC = 10000 µg a.i./L	M-406645-01-3

Species	Test	Purity %	Guideline, duration, doses and conditions	Result	Study number
			concentrations of 150, 600, 2500 and 10000 µg a.i./kg diet		

BYI 02960 Non-target arthropods toxicity					
Parasitoid wasp *Aphidius rhopalosiphi*	Laboratory, glass plates	17.0%	Mead-Briggs & al. (2000), Candolfi & al. (2001) The test item was applied on glass plates at nominal rates of 10, 20, 40, 80 and 160 g a.i./ha, respectively, and effects on 60 adults (4 replicates with 15 wasps per test group) of the parasitoid wasp *Aphidius rhopalosiphi* were assessed during 24 h after exposure	LR_{50} < 0.5 g a.i./ha	M-366965-01-3
Predatory mite *Typhlodromus pyri*	Laboratory, glass plates	17,0%	Mead-Briggs & al. (2000), Candolfi & al. (2001) The test item was tested under laboratory conditions via residual contact exposure of protonymphs of the predatory mite *Typhlodromus pyri* to spray residues with rates of 2, 4, 9, 19 and 40 g a.i./ha, respectively in 200 L deionized water/ha applied on glass plates.	LR_{50} 17.3 g a.i./ha	M-366957-01-2
BYI 02960 Soil organisms toxicity					
Earthworms *(Eisenia fetida)*	acute, 14 d (10% peat in test soil)	96.2%	OECD-Guideline No. 207 Adult earthworms (more than two months old, four replicates of 10) were exposed in an artificial soil system with peat content of 10% over a period of 14 days to concentrations of 5.6, 10, 18, 32, 56, 100 mg test item / kg dry soil (1st run) and 178, 316, 562 and 1000 mg test item / kg dry soil (2nd run).	LC_{50} 192.9 mg a.i./kg dry weight soil	M-363742-01-2

BYI 02960 SL 200 Soil organisms toxicity					
Earthworms *(Eisenia fetida)*	reproduction, 56 d (10% peat in test soil)	17,0%	ISO 11268-2, 1998 (E) and OECD 222 (2004) Earthworms (approximately 7 month old, 8 x 10 animals for the control group and 4 x 10 animals per test concentration of the treatment group) were exposed in an artificial soil system over a period of 56 days to nominal concentrations of 8.9, 15.8, 28.1, 50.0 and 89.0 mg product/kg dry weight soil	NOEC 8.9 mg prod./kg dry weight soil	M-392964-01-2
Collembola Species *Folsomia candida*	chronic, 28 d (5% peat in test soil)	17,0%	ISO 11267 (1999) Ten springtails (10 to 12 days old) per replicate (5 replicates per treatment group) were exposed in an artificial soil system with a peat content of 5 % over a period of 14 days to nominal concentrations of 8.8, 13.2, 19.9, 29.8 and 44.6 mg test item/kg artificial soil dry weight corresponding to 1.5, 2.3, 3.4, 5.1 and 7.6 mg a.i./kg dry weight soil in the 1st run and 5.88, 7.06 and 8.47 mg test item/kg dry weight soil, corresponding to1.00, 1.20 and 1.44 mg a.i./kg dry weight soil in the 2nd run	NOEC 8.47 mg prod./kg dry weight soil	M-359728-01-2
Soil mite *Hypoaspis aculeifer*	chronic, 14 d (5% peat in test soil)	17,0%	OECD Guideline No. 226 (2008) Ten mites (28 days old, after start of egg-laying) per replicate (4 replicates per treatment group and 8 control replicates) were exposed in an artificial soil system with a peat content of 5% over a period of 14 days to nominal concentrations of	NOEC ≥1000 mg prod./kg dry weight soil	M-358752-01-2

			100, 178, 316, 562 and 1000 mg test item/kg artificial soil dry weight		
BYI 02960 SL 200 Organic matter breakdown					
Soil litter degradation	217 d, spraying	17.1%	Guidance Document on the Breakdown of Organic Matter in Litter Bags (OECD Series on Testing and Assessment, Number 56, 2006) The test item was applied twice by spraying at a rate of 150 g a.i./ha, 1st to represent the plateau concentration and 2nd to represent the yearly application rate on six plots on a field in Germany (Bayer Experimental Farm Höfchen, Burscheid).	No influence on organic matter breakdown 217 days after application	M-413408-01-2
BYI 02960 SL 200 & FS 480 Organic matter breakdown					
Soil litter degradation	217 d, seed treatment	17.1%	OECD No. 56, 2006 (OECD Series on Testing and Assessment) The test item was applied twice. First by spraying at a rate of 150 g a.i./ha, represent the plateau concentration (as would occur after multi-year use) and second, as seed treatment at a rate of 265 g a.i./ha to represent the annual application rate. The study was performed on six plots on a field in Germany (Bayer Experimental Farm Höfchen, Burscheid).	No influence on organic matter breakdown 217 days after application	M-413416-01-2
BYI 02960 Soil micro-organisms toxicity					
N-cycle	28 d	96.2%	OECD guideline 216, 2000 Rates of 0.3 and 3.0 mg/kg a.i./ha (corresponding to 0.4 and 4.0 mg a.i./ kg dry weight soil) were applied on loamy sand soil. After the amendment with Lucerne-grass-green meal the	no influence to the nitrogen turnover of soil microflora	M-359803-01-2

			nitrogen turnover was measured at day 0, and after 7, 14 and 28 days of incubation.		
C-cycle	28 d	96.2%	OECD guideline 217, 2000 Rates of 0.3 and 3 kg a.i./ha (corresponding to 0.4 and 4.0 mg a.i./kg soil dry weight) were applied on sandy loam (USDA nomenclature). After the amendment of 2000 mg glucose/kg dry weight to soil subsamples at day 0, and after 7, 14 and 28 days of incubation the carbon turnover was measured during a period of at least 12 hours.	no influence to the carbon turnover of soil microflora	M-417194-01-2
BYI 02960 SL 200 Non-target terrestrial plants toxicity					
11 plant species	Vegetative vigour test,	17.0%	OPPTS 850.4150 (1996); OECD Guideline 227 (2006) vegetative vigour of eleven non-target terrestrial plant species was tested following a post-emergence 410 g a.i./ha application onto the foliage of plants	No adverse effects >25% on survival, visual phytotoxicity, growth, shoot length and shoot dry weight	M-397734-01-2
11 plant species	Seedling emergence test,	17.0%	OPPTS 850.4150 (1996); OECD Guideline 227 (2006) seedling emergence and growth of eleven non-target terrestrial plant species was tested following a pre-emergence application of the product onto the soil surface at a rate of 410 g a.i./ha	No adverse effects >25% on emergence, survival, visual phytotoxicity, growth, shoot length and shoot dry weight	M-397727-01-2

BYI 02960 Sewage treatment					
Activated sludge	Respiration inhibition test	96.2%	EC No. 440/2008 method C.11 (2008) OECD 209 (1984) Activated sludge was exposed to BYI 02960 at nominal concentrations of 100, 180, 320, 560 and 1000 mg a.i./L, respectively. The respiration rate of each mixture was determined after aeration periods of 3 hours.	EC_{50} >1000 mg a.i./L EC_{10} 472.5 mg a.i./L	M-377311-01-1

ANNEX 2
REFERENCES

(sorted by study number)

Study number	Author(s)	Year	Study title. Company conducting the study. Report identification number. Date GLP yes/no
M-283421-02-2		2007	BYI 02960 - Exploratory 28-day toxicity study in the rat by gavage, Report No.: SA 06075, EPA MRID No.: 48844149 Date: 2007-02-02, Amended: 2009-02-24 GLP/GEP: no, unpublished
M-294820-01-2		2007	BYI 02960 : Preliminary 28-day toxicity study in the mouse by dietary administration Report No.: SA 07013, EPA MRID No.: 48844151 Date: 2007-11-23 GLP/GEP: no, unpublished
M-297120-01-2		2008	BYI 02960 - Exploratory 28-day toxicity study in the rat by dietary administration Report No.: SA 07047, EPA MRID No.: 48844150 Date: 2008-02-01 GLP/GEP: no, unpublished
M-308904-02-2		2008	Revised final report no.: 1 - Effects of BYI 02960 (acute contact and oral) on honey bees (Apis mellifera L.) in the laboratory Bayer CropScience, Report No.: 41121035, EPA MRID No.: 48843722 Date: 2008-08-20 Amended: 2012-03-22 GLP/GEP: yes, unpublished
M-309853-01-1		2008	BYI 02960, pure substance: Vapour pressure - Final report Bayer CropScience, Report No.: 20080615.01, Date: 2008-10-10 GLP/GEP: Yes, unpublished
M-312461-01-3		2008	Preliminary 28-day toxicity study in the dog by dietary administration

			Report No.: SA07290, EPA MRID No.: 48844152 Date: 2008-12-09 GLP/GEP: no, unpublished
M-328668-03-2		2009	BYI 02960 - 90-day toxicity study in the mouse by dietary administration - Amendment no.2 Report No.: SA 07295, EPA MRID No.: 48844112 Date: 2009-02-06, Amended: 2012-03-22 GLP/GEP: yes, unpublished
M-329048-03-2		2009	BYI 02960 - 90-day toxicity study in the rat by dietary administration - Amendment no.2 Report No.: SA 07294, EPA MRID No.: 48844111 Date: 2009-02-10, Amended: 2012-03-21 GLP/GEP: yes, unpublished
M-349992-01-2		2009	BYI 02960 - Acute toxicity in the rat after oral administration Report No.: AT05287, EPA MRID No.: 48844101 Date: 2009-06-08 GLP/GEP: yes, unpublished
M-349995-01-2		2009	BYI 02960 - Acute toxicity in the rat after dermal administration Report No.: AT05288, EPA MRID No.: 48844104 Date: 2009-06-08 GLP/GEP: yes, unpublished
M-353715-01-2		2009	BYI 02960 - Local lymph node assay in mice (LLNA/IMDS) Report No.: AT05334, EPA MRID No.: 48844108 Date: 2009-06-29 GLP/GEP: yes, unpublished
M-353761-01-2		2009	BYI 02960 - Acute skin irritation/corrosion on rabbits Report No.: AT05342, EPA MRID No.: 48844107 Date: 2009-07-08 GLP/GEP: yes, unpublished
M-353785-01-2	.	2009	BYI 02960 - Micronucleus-test on the male mouse Report No.: AT05350, EPA MRID No.: 48844134 Date: 2009-07-09 GLP/GEP: yes, unpublished

M-354173-01-2		2009	BYI 02960 (tested as BYI 02960 technical) (project: BYI 02960) - Salmonella/microsome test plate incorporation and preincubation method Report No.: AT05387, EPA MRID No.: 48844124 Date: 2009-07-24 GLP/GEP: yes, unpublished
M-357476-01-1	Banman, C. S.; Lam, C. V.	2009	Acute toxicity of BYI 02960 to *Daphnia magna* under static conditions Report No.: EBRVP032, EPA MRID No.: 48843701 Date: 2009-10-14 GLP/GEP: yes, unpublished
M-357479-01-1	Banman, C. S.; Lam, C. V.	2009	Acute toxicity of BYI 02960 technical to the sheepshead minnow *(Cyprinodon variegatus)* under static conditions Report No.: EBRVP034, EPA MRID No.: 48843710 Date: 2009-10-14 GLP/GEP: yes, unpublished
M-358752-01-2	Kratz, M.-A.	2009	BYI 02960 SL 200 G: Influence on mortality and reproduction on the soil mite species Hypoaspis aculeifer tested in artificial soil with 5 % peat Report No.: KRA-HR-19/09, EPA MRID No.: 48843758 Date: 2009-11-10 GLP/GEP: yes, unpublished
M-359728-01-2	Frommholz, U.	2009	BYI 02960 SL 200 G: Influence on the reproduction of the collembola species *Folsomia candida* tested in artificial soil with 5 % peat Report No.: FRM-COLL-75/09, EPA MRID No.: 48843755 Date: 2009-12-02 GLP/GEP: yes, unpublished
M-359743-01-2		2009	BYI 02960 (tested as BYI 02960 technical) (project: BYI 02960) - V79/HPRT test in vitro for the detection of induced forward mutations Bayer Schering Pharma AG, Wuppertal, Germany Bayer CropScience, Report No.: AT05625, EPA MRID No.: 48844128 Date: 2009-10-29 GLP/GEP: yes, unpublished
M-359746-01-2		2009	BYI 02960 (tested as BYI 02960 technical) - *In vitro* chromosome aberration test with chinese hamster V79

			cells Bayer CropScience, Report No.: AT05626, EPA MRID No.: 48844131 Date: 2009-11-11 GLP/GEP: yes, unpublished
M-359803-01-2		2009	BYI 02960 a.s.: Determination of effects on nitrogen transformation in soil Bayer CropScience, Report No.: FRM-N-130/09, Date: 2009-12-03 GLP/GEP: yes, unpublished
M-360693-04-1	FAO and WHO	2016	Manual on development and use of FAO and WHO specifications for pesticides - third revision of the first edition Date: 2016-06-30
M-361319-02-2		2009	BYI 02960 - Acute eye irritation on rabbits Report No.: AT05341 A, EPA MRID No.: 48844106 Date: 2009-07-08, Amended: 2009-10-29 GLP/GEP: yes, unpublished
M-361668-01-1		2009	BYI 02960: A 96-hour shell deposition test with the eastern oyster *(Crassostrea virginica)* Report No.: EBRVP023, EPA MRID No.: 48843703 Date: 2009-12-01 GLP/GEP: yes, unpublished
M-362791-01-2		2010	BYI 02960 - Activity ID TXRVP033 - Acute inhalation toxicity in rats Report No.: AT05727, EPA MRID No.: 48844105 Date: 2010-01-07 GLP/GEP: yes, unpublished
M-363742-01-2		2010	BYI 02960 (tech.): Acute toxicity to earthworms *(Eisenia fetida)* tested in artificial soil Report No.: LRT/RG-A-131/09, EPA MRID No.: 48843746 Date: 2010-02-18 GLP/GEP: yes, unpublished
M-363938-01-2		2010	BYI 02960: Developmental toxicity study in the rat by gavage Bayer CropScience, Report No.: SA 08347, Date: 2010-02-22

			GLP/GEP: yes, unpublished
M-364620-01-1		2009	BYI 02960: A 96-hour static acute toxicity test with the saltwater mysid *(Americamysis bahia)* Report No.: 149A-236, EPA MRID No.: 48843704 Date: 2009-12-08 GLP/GEP: yes, unpublished
M-366957-01-2		2010	Toxicity to the predatory mite *Typhlodromus pyri* SCHEUTEN *(Acari, Phytoseiidae)* using a laboratory test; BYI 02960 SL 200 g/L Report No.: CW09/073, EPA MRID No.: 48843745 Date: 2010-04-15 GLP/GEP: yes, unpublished
M-366965-01-3		2010	Toxicity to the parasitoid wasp *Aphidius rhopalosiphi* (DESTEPHANI-PEREZ) *(Hymenoptera: Braconidae)* using a laboratory test; BYI 02960 SL 200 g/L Report No.: CW09/079, EPA MRID No.: 48843744 Date: 2010-04-15 GLP/GEP: yes, unpublished
M-367370-01-1		2010	BYI 02960, pure substance: Melting point, boiling point, thermal stability Report No.: 20090051.01, Date: 2010-03-25 GLP/GEP: Y, unpublished
M-369978-01-2		2010	A 90-day toxicity feeding study in the beagle dog with technical grade BYi 02960 Report No.: 09-S76-QQ, EPA MRID No.: 48844114 Date: 2010-04-22 GLP/GEP: yes, unpublished
M-377311-01-1		2010	Activated sludge, respiration inhibition test with BYI 02960 (tech.) Report No.: 2010/0089/01, Date: 2010-06-21 GLP/GEP: yes, unpublished
M-386036-01-1		2010	Toxicity of BYI 02960 technical during an acute oral LD50 with the northern bobwhite quail *(Colinus virginianus)* Report No.: EBRVP022, EPA MRID No.: 48843715 Date: 2010-07-14 GLP/GEP: yes, unpublished

M-388718-01-1		2010	Toxicity of BYI 02960 technical during an acute dietary LC50 with the mallard duck (*Anas platyrhynchos*) Report No.: EBRVP020, EPA MRID No.: 48843719 Date: 2010-08-26 GLP/GEP: yes, unpublished
M-390611-01-1		2010	Acute toxicity of BYI 02960 technical to the rainbow trout *(Oncorhynchus mykiss)* under static conditions Report No.: EBRVP041, EPA MRID No.: 48843705 Date: 2010-09-27 GLP/GEP: yes, unpublished
M-392560-01-1		2010	Acute toxicity of BYI 02960 technical to the fathead minnow *(Pimephales promelas)* under static conditions Report No.: EBRVP035, EPA MRID No.: 48843706 Date: 2010-10-21 GLP/GEP: yes, unpublished
M-392964-01-2		2010	BYI 02960 SL 200 G: Effects on survival, growth and reproduction on the earthworm *Eisenia fetida* tested in artificial soil Bayer CropScience, Report No.: LRT-RG-R-76/09, Date: 2010-10-21 GLP/GEP: yes, unpublished
M-394208-01-2		2012	Technical grade BYI 02960: A dose range-finding reproductive toxicity study in the Wistar rat Report No.: 09-P72-RB, Date: 2012-05-31 GLP/GEP: yes, unpublished
M-394535-01-1		2010	Toxicity of BYI 02960 technical during an acute dietary LC50 with the northern bobwhite quail *(Colinus virginianus)* Report No.: EBRVP021, EPA MRID No.: 48843718 Date: 2010-11-10 GLP/GEP: yes, unpublished
M-397552-01-1		2010	Toxicity of BYI 02960 technical to the green alga *Pseudokirchneriella subcapitata* Report No.: EBRVP030, EPA MRID No.: 48843732 Date: 2010-12-10 GLP/GEP: yes, unpublished
M-397727-01-2		2010	BYI 02960 SL 200 g/L - Effects on the seedling

			emergence and growth of eleven species of non-target terrestrial plants (Tier 1) Report No.: SE10/001, EPA MRID No.: 48843729 Date: 2010-12-14 GLP/GEP: yes, unpublished
M-397734-01-2		2010	BYI 02960 SL 200 g/L - Effects on the vegetative vigour of eleven species of non-target terrestrial plants (Tier 1) Report No.: VV 10/002, EPA MRID No.: 48843730 Date: 2010-12-14 GLP/GEP: yes, unpublished
M-398376-01-1		2010	Toxicity of BYI 02960 technical to duckweed *(Lemna gibba G3)* under static-renewal conditions Report No.: EBRVP043, EPA MRID No.: 48843731 Date: 2010-12-21 GLP/GEP: yes, unpublished
M-398952-01-1		2011	BYI-02960: Hydrolytic degradation Report No.: MERVP019, Date: 2011-01-07 GLP/GEP: Y, unpublished
M-401792-01-2		2011	*Chironomus riparius* 28-day chronic toxicity test with BYI 02960 (tech.) in a water-sediment system using spiked water Report No.: EBRVP025, Date: 2011-02-14 GLP/GEP: yes, unpublished ...also filed: KIIA 8.3.2.2 /01
M-406645-01-3		2011	BYI 02960 tech.: Effects of exposure to spiked diet on honeybee larvae *(Apis mellifera carnica)* in an *in vitro* laboratory testing design Report No.: E 318 3897-9, EPA MRID No.: 48843768 Date: 2011-05-02 GLP/GEP: yes, unpublished
M-408514-01-1		2011	Toxicity of BYI 02960 technical during an acute oral LD50 with the canary *(Serinus canaria)* Report No.: EBRVP036, EPA MRID No.: 48843716 Date: 2011-05-25 GLP/GEP: yes, unpublished
M-409339-01-1		2011	Early life stage toxicity of BYI 02960 technical to the Fathead minnow *(Pimephales promelas)* under flow-

			through conditions Report No.: EBRVP033, EPA MRID No.: 48843714 Date: 2011-06-14 GLP/GEP: yes, unpublished
M-409513-01-1		2011	BYI 02960, pure substance: Solubility in distilled water (pH 7), at pH 4 and pH 9 (flask method) Report No.: PA09/003, Date: 2011-06-17 GLP/GEP: Y, unpublished
M-410022-01-2		2011	BYI 02960 - 90-day neurotoxicity study in the rat by dietary administration Report No.: SA 09283, Date: 2011-06-28 GLP/GEP: yes, unpublished
M-412917-02-1		2011	Toxicity of BYI 02960 technical on reproduction to the mallard duck *(Anas platyrhynchos)* Report No.: EBRVP018-1, EPA MRID No.: 48843721 Date: 2011-08-25, Amended: 2012-03-19 GLP/GEP: yes, unpublished
M-413408-01-2		2011	BYI 02960: Effects on soil litter degradation after spray application Report No.: LRT-SLD-45/11, Date: 2011-09-06 GLP/GEP: yes, unpublished
M-413416-01-2		2011	BYI 02960: Effects on soil litter degradation if applied as seed treatment Report No.: LRT-SLD-46/11, Date: 2011-09-06 GLP/GEP: yes, unpublished
M-414064-01-1		2011	Flupyradifurone (BYI 02960): Solubility in organic solvents Report No.: PA09/005, Date: 2011-09-16 GLP/GEP: Y, unpublished
M-414066-01-2	Riebsch-laeger, T.	2011	Effects of BYI 02960 (techn.) on development and reproductive output of the waterflea *Daphnia magna* in a static-renewal laboratory test system Report No.: EBRVP209, EPA MRID No.: 48843711 Date: 2011-09-15 GLP/GEP: yes, unpublished
M-414102-01-1		2011	Flupyradifurone (BYI 02960), pure substance :

			Dissociation constant in water Report No.: PA10/048, Date: 2011-09-16 GLP/GEP: Y, unpublished
M-414242-01-1	Smeykal, H.	2011	Flupyradifurone (BYl 02960), technical substance: Melting point, boiling point, thermal stability Report No.: 20110197.01, Date: 2011-09-16 GLP/GEP: Y, unpublished
M-414485-01-1		2011	Flupyradifurone (BYI 02960), pure substance: Partition coefficient 1-octanol / water at pH 4, pH 7 and pH 9 (HPLC-method) Report No.: PA09/004, Date: 2011-09-26 GLP/GEP: Y, unpublished
M-414739-01-2		2011	Acute toxicity of BYI 02960 (tech.) to larvae of *Chironomus riparius* in a 48 h static laboratory test system Report No.: EBRVP026, Date: 2011-09-26 GLP/GEP: yes, unpublished ...also filed: KIIA 8.3.1.2 /01
M-415408-01-2		2011	BYI 02960 An acute neurotoxicity study in the rat by oral administration Bayer CropScience, Report No.: SA 10096, Date: 2011-09-30 GLP/GEP: yes, unpublished
M-417194-01-2		2011	BYI 02960 a.s.: Effects on the activity of soil microflora (carbon transformation test) Report No.: 11 10 48 058 C, EPA MRID No.: 48843754 Date: 2011-11-11 GLP/GEP: yes, unpublished
M-417665-01-2		2012	Technical grade BYF 02960: A two-generation reproductive toxicity study in the Wistar rat Bayer CropScience, Report No.: 09-R72-SA, Date: 2012-05-22 GLP/GEP: yes, unpublished
M-417822-01-1		2011	Acute toxicity of BYI 02960 to *Xenopus laevis* under flow-through conditions Report No.: EBRVP187, EPA MRID No.: 48843737

			Date: 2011-11-18 GLP/GEP: yes, unpublished
M-418426-02-1		2011	Phototransformation of [14C]BYI 02960 in aqueous pH 7 buffer - amended report Report No.: MERVP042-1, Date: 2011-11-28. Amended: 2012-03-05 GLP/GEP: Y, unpublished
M-420407-01-2		2011	Acute toxicity of BYI 02960 (tech.) to fish *(Cyprinus carpio)* under static conditions (limit test) Report No.: EBRVP186, Date: 2011-12-19 GLP/GEP: yes, unpublished
M-420519-01-2		2011	Acute oral toxicity of chicken *(Gallus gallus domesticus)* with BYI 2960 (tech.), according to OECD 223 - limit test- Report No.: BAR/LD 141, Date: 2011-12-19 GLP/GEP: yes, unpublished
M-420536-01-2		2011	Micronucleus assay in bone marrow cells of the mouse with BYI 02960-a.i. Report No.: 1425801, EPA MRID No.: 48844135 Date: 2011-11-10 GLP/GEP: yes, unpublished
M-420539-02-2		2011	1st amendment to report *Salmonella typhimurium* reverse mutation assay with BYI 02960 Bayer CropScience, Report No.: 1425802, EPA MRID No.: 48844125 Date: 2011-09-23 ...Amended: 2011-10-17 GLP/GEP: yes, unpublished
M-420783-01-2		2011	BYI 02960: A flow-through life-cycle toxicity test with the saltwater mysid *(Americanysis bahia)* Report No.: EBRVP038, EPA MRID No.: 48843713 Date: 2011-09-08 GLP/GEP: yes, unpublished
M-423559-01-1		2012	BYI 02960 - Developmental toxicity study in the rabbit by gavage Report No.: SA 10314, Date: 2012-01-26 GLP/GEP: yes, unpublished
M-424704-01-2		2012	Toxicity of BYI 02960 technical on reproduction to the

			northern bobwhite quail *(Colinus virginianus)* Report No.: EBRVP019, EPA MRID No.: 48843720 Date: 2012-02-09 GLP/GEP: yes, unpublished
M-425272-03-1	Cada, A.	2013	A chronic toxicity feeding study in the Beagle dog with technical grade BYI 02960 Report No.: 09-C76-RZ, EPA MRID No.: 48844121 Date: 2013-04-24 GLP/GEP: yes, unpublished
M-425810-01-2		2012	BYI 02960 - Complementary maternal tolerability study in the pregnant Sprague-Dawley rat by gavage Bayer CropScience, Report No.: SA 11140, Date: 2012-02-21 GLP/GEP: yes, unpublished
M-428257-01-1		2012	BYI 02960 - Chronic toxicity and carcinogenicity study in the Wistar rat by dietary administration Date: 2012-03-05 GLP/GEP: yes, unpublished
M-432336-01-1		2012	A subacute dermal toxicity study in rats with BYI 02960 Report No.: 11-S22-US, EPA MRID No.: 48844115 Date: 2012-06-05 GLP/GEP: yes, unpublished
M-434203-01-1		2012	A developmental neurotoxicity study with technical grade BYI 02960 in Wistar rats Report No.: 11-D72-UW, EPA MRID No.: 48844140 Date: 2012-07-09 GLP/GEP: yes, unpublished
M-462475-01-1		2013	Assessment of chronic effects of BYI 02960 tech. to the honey bee, *Apis mellifera L*., in a 10 days continuous laboratory feeding test Report No.: E 318 4561-8, Date: 2013-08-26 GLP/GEP: yes, unpublished