FAO SPECIFICATIONS AND EVALUATIONS
FOR AGRICULTURAL PESTICIDES

PYRAOXYSTROBIN

Methyl (2*E*)-2-(2-{[3-(4-chlorophenyl)-1-methylpyrazol-5-yl]oxymethyl}phenyl)-3-methoxyacrylate

FOOD AND AGRICULTURE ORGANIZATION *of* THE UNITED NATIONS

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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.

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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 FAO specifications follows the **New Procedure**, described in the 1st edition of the "Manual on 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. Evaluations bear the date (year) of the meeting at which the recommendations were made by the JMPS.

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

PART ONE

SPECIFICATIONS

PYRAOXYSTROBIN

INFORMATION

ISO common name

Pyraoxystrobin (ISO 1750, provisionally approved)

Chemical names

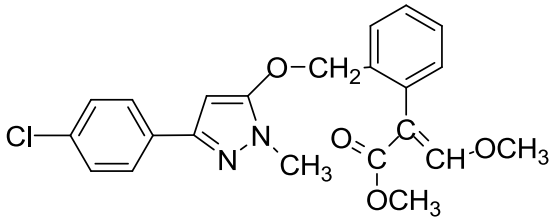
IUPAC methyl (2*E*)-2-(2-{[3-(4-chlorophenyl)-1-methylpyrazol-5-yl]oxymethyl} phenyl)-3-methoxyacrylate

CA methyl (*αE*)-2-[[[3-(4-chlorophenyl)-1-methyl-*1H*-pyrazol-5-yl]oxy]methyl] -*α*-(methoxymethylene)benzeneacetate

Synonyms

None

Structural formula



Molecular formula

$C_{22}H_{21}ClN_2O_4$

Relative molecular mass

412.9

CAS Registry number

862588-11-2

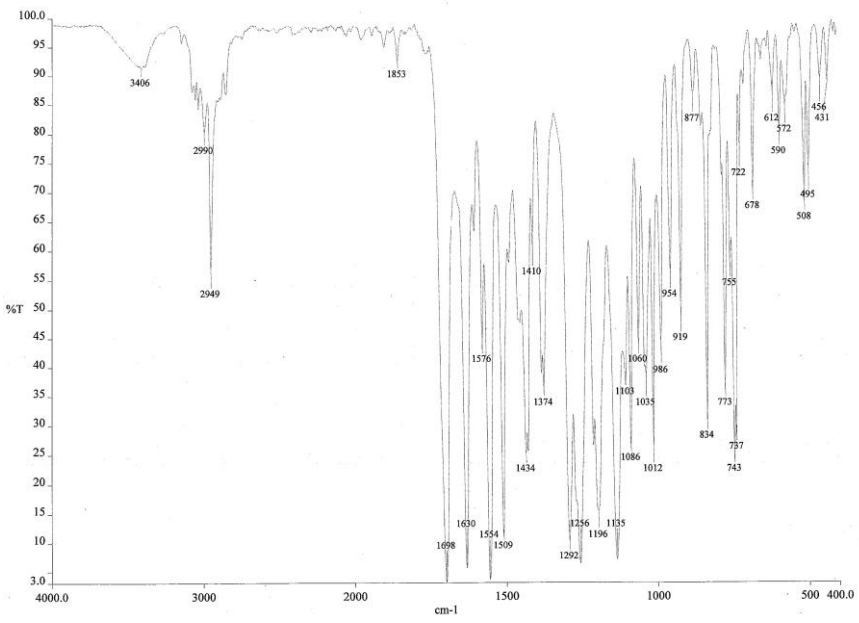
CIPAC number

964

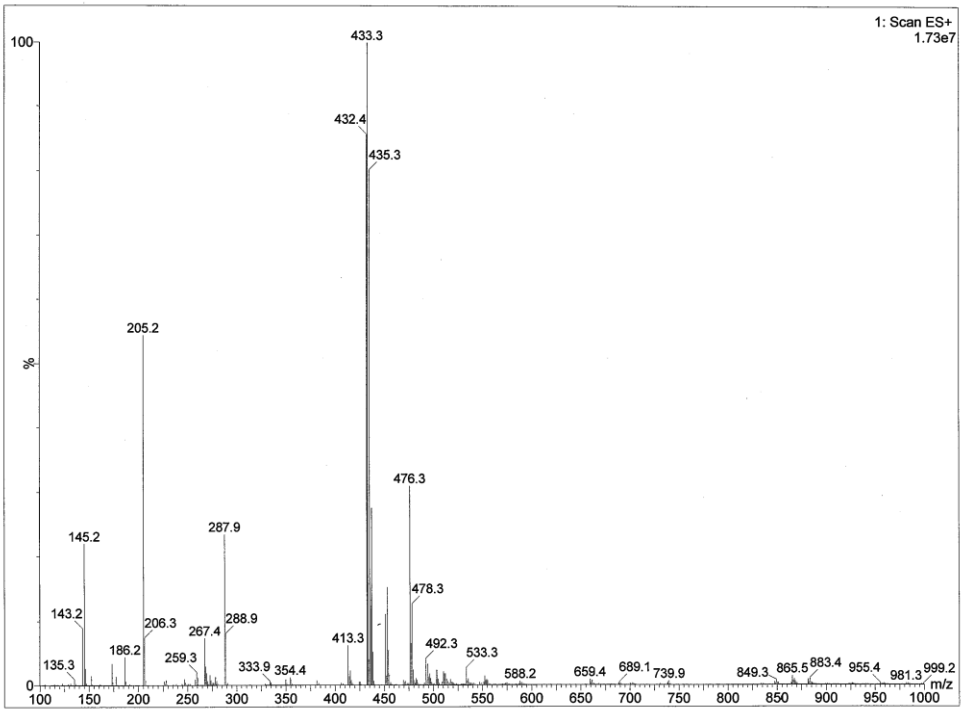
Identity tests

HPLC retention time, UV, IR, LC-MS spectrum and ^{1}H-NMR spectrum

Typical IR spectrum of pyraoxystrobin



Typical LC-MS spectrum of pyraoxystrobin



PYRAOXYSTROBIN TECHNICAL MATERIAL

FAO Specification 964 / TC (February 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 (964/2016). 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 (964/2016) as PART TWO forms an integral part of this publication.

1. Description

The material shall consist of pyraoxystrobin together with related manufacturing impurities, in the form of a white to cream-coloured solid, free from visible extraneous matter and added modifying agents.

2 Active ingredient

2.1 **Identity tests** (CIPAC/964/TC/M/-) (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 **Pyraoxystrobin content** (CIPAC/964/TC/M/-) (Note 1)

The pyraoxystrobin content shall be declared (not less than 950 g/kg) and, when determined, the average measured content shall not be lower than the declared minimum content.

Note 1 The methods for the identification and determination of pyraoxystrobin content in pyraoxystrobin TC and SC (CIPAC/4936) were adopted by CIPAC in 2015 but are not yet published in a CIPAC Handbook. Prior to publication in a next Handbook, copies of the methods may be obtained through the CIPAC website, 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/jmps/ps-new/en/

PYRAOXYSTROBIN SUSPENSION CONCENTRATE

FAO Specification 964 / SC (February 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 (964/2016). 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 other manufacturers who use TC from other sources. The evaluation report (964/2016) as PART TWO forms an integral part of this publication

1 Description

The material shall consist of a suspension of fine particles of technical pyraoxystrobin, complying with the requirements of FAO/WHO specification 964/TC (February 2017), 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 (CIPAC/964/SC/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 Pyraoxystrobin content (CIPAC/964/SC/M/-) (Note 2)

The pyraoxystrobin content shall be declared (g/kg or g/l at 20 ± 2ºC, Note 3) and, when determined, the average content measured shall not differ from that declared by more than the following tolerances:

Declared content in g/kg or g/L at 20 ± 2°C	Tolerance
above 100 up to 250 above 250 up to 500 above 500	± 6% or of the declared content ± 5% or of the declared content ± 25 g/kg or g/L of the declared content
Note: the upper limit is included in the range	

3 Physical properties

3.1 Pourability (MT 148.1, CIPAC Handbook F, p. 348, 1995)

Maximum "residue": 5%.

* 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/jmps/ps-new/en/

3.2 **Spontaneity of dispersion** (MT 160, CIPAC Handbook F, p. 391, 1995) (Note 4)

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

3.3 **Suspensibility** (MT 184, CIPAC Handbook K, p. 142, 2003) (Note 4)

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

3.4 **Wet sieve test** (MT 185, CIPAC Handbook K, p. 148, 2003) (Note 5)

Maximum: 2% of the formulation shall be retained on a 75 µm test sieve.

3.5 **Persistent foam** (MT 47.3) (Notes 6 & 7)

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 formulation shall continue to comply with clauses for:

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

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

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

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

Note 2 The methods for the identification and determination of pyraoxystrobin content in pyraoxystrobin TC and SC (CIPAC/4936) were adopted by CIPAC in 2015 but are not yet published in a CIPAC Handbook. Prior to publication in a next Handbook, copies of the methods may be obtained through the CIPAC website, 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 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 equal results 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 correspond to the highest rate of use recommended by the supplier. The test is to be conducted in CIPAC standard water D.

Note 7 MT 47.3 is a revised version of MT 47.2 using a standard measuring cylinder. This new method was accepted as a full CIPAC method in 2013. Prior to publication of the method in a Handbook, copies of the method may be obtained through the CIPAC website, http://www.cipac.org/index.php/methods-publications/pre-published-methods

Note 8 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.

PART TWO

EVALUATION REPORTS

PYRAOXYSTROBIN

PYRAOXYSTROBIN

FAO/WHO EVALUATION REPORT 964/2016

Recommendation

The Meeting recommended that the specifications for pyraoxystrobin TC and SC, proposed by Shenyang Sciencreat Chemicals Co.,Ltd. and as amended, should be adopted by FAO.

Appraisal

The Meeting considered data and supporting information submitted in November 2015 by Shenyang Sciencreat Chemicals Co., Ltd. (Shenyang Sciencreat) for the development of new FAO specifications for pyraoxystrobin TC and SC. The data submitted were broadly in accordance with the requirements of the 'Manual on Development and Use of FAO and WHO specifications for Pesticides' (November 2010 2nd revision of the 1st edition) and supported the draft specifications for new FAO specifications.

Pyraoxystrobin is under patent in People's Republic of China, United States of America, Japan and Europe until 2025.

Pyraoxystrobin belongs to the strobilurin chemical class of fungicides. Pyraoxystrobin is the ISO common name of the compound referring to the *E*-isomer only. The main formulation type available are suspension concentrates (SC). Pyraoxystrobin is not co-formulated with other pesticides. Its formulations are registered and sold in China.

Pyraoxystrobin has not been evaluated by the WHO/IPCS and FAO/WHO JMPR or classified by ECHA.

Pyraoxystrobin is a white crystalline solid that decomposes at 222.1°C. The vapor pressure (1.22×10^{-8} Pa at room temperature) indicates that pyraoxystrobin has a low volatility. It is sparingly soluble in water (0.1 g/L at 20 °C) independent of pH. Pyraxoystrobin is readily soluble in medium polarity solvents like acetone, ethyl acetate, dichloromethane, toluene and methanol but only slightly soluble in apolar solvents like hexane (0.148 g/L). The octanol/water partition coefficient - log P_{OW} of 3.4 - indicates that the molecule is lipophilic. The Meeting requested the manufacturer to clarify if the material used for testing the physical-chemical properties is technical or pure active ingredient and the proposer clarified that the testing material is purified technical (98%) which is considered as pure active ingredient.

Pyraoxystrobin is hydrolytically stable at pH 4, 7 and 9 and its stability decreases as the pH value is increased. In alkaline pH (pH=9) the DT_{50} is 577 days at 25 °C (estimated by extrapolation).

The Meeting was provided with commercially confidential information on the manufacturing process and 5-batch analysis data on all impurities present below or above 1 g/kg and their manufacturing limits in the TC.

Mass balances ranged from 98.5 to 99.4 % in the five batches. The Meeting noted, that for some impurities included in the manufacturing specification the maximum limits for two of them were supported by the 5- batch analysis data and statistically justified. However, three other impurities detected at levels below 1g/kg were also included in the specifications with maximum content 1g/kg. The proposer was asked to justify these limits and to explain their possible relevance.

The proposer submitted *in vitro* mutagenicity studies (Ames test) with those impurities giving rise to structural alerts. The Meeting concluded, that based on the outcome of the *in vitro* mutagenicity studies none of these impurities under consideration should be considered as relevant. The proposer further explained that the formation of nitrosamines and polychlorinated dioxins and -furans in the manufacturing process can be ruled out based on the intermediates and reaction conditions used. The proposer declared the minimum purity of the pyraxystrobin TC as 950 g/kg which is statistically justified.

The manufacturing process and the 5 batch analysis results for pyraoxystrobin TC produced by Shenyang Sciencreat, submitted to JMPS are the same as those submitted to ICAMA in support of the registration in China (Chen T., 2015).

The identity of pyraoxystrobin was confirmed by HPLC retention time comparison, by UV, IR, LC-MS spectrum and ^{1}H-NMR. The analytical method for the determination of the active ingredient pyraoxystrobin in pyraoxystrobin technical is reversed phase HPLC with UV detection at 280 nm and external standardization. The method used for the analysis of technical material has been accepted as full CIPAC method in 2015 but has not been published yet, however it is available as a pre-published method [964]. A reversed phase HPLC method with UV detection at 254nm has been proposed for the determination of all the detected organic impurities. The method is validated with respect to specificity, linearity of response, precision, accuracy and limit of detection. The LOD for all organic impurities ranged from 0.08 mg/L to 0.2 mg/L. An appropriate LC-MS method was used for the confirmation of all impurities. Further data was presented to the Meeting to demonstrate that the *Z*-isomer could not be detected in the TC using several different analytical techniques and that synthesis of the *Z*-isomer was not possible.

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

Toxicity data were available for acute and sub-acute to chronic toxicity, including carcinogenicity, reproductive developmental toxicity/teratogenicity, genetic toxicity test, ecotoxicology derived from the technical grade active ingredient manufactured by the proposer.

The Meeting recommended the adoption of the new FAO specification for TC and SC.

SUPPORTING INFORMATION

FOR

EVALUATION REPORT 964/2016

USES

Pyraoxystrobin is a strobilurin fungicide with broad spectrum fungicidal activity. It is used in agriculture to control diseases like wheat powdery mildew, rice blast, cucumber downy mildew, gray mold, watermelon anthracnose, and tomato blight.

IDENTITY OF THE ACTIVE INGREDIENT

ISO common name Pyraoxystrobin (ISO 1750, provisionally approved)

Chemical name(s)

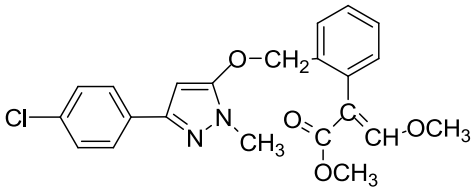
IUPAC Methyl (2*E*)-2-(2-{[3-(4-chlorophenyl)-1-methylpyrazol-5-yl]oxymethyl} phenyl)-3-methoxyacrylate

CA Methyl (α*E*)-2-[[[3-(4-chlorophenyl)-1-methyl-1*H*-pyrazol-5-yl]oxy]methyl] -α-(methoxymethylene)benzeneacetate

Synonyms

None

Structural formula



Molecular formula

$C_{22}H_{21}ClN_2O_4$

Relative molecular mass

412.9

CAS Registry number

862588-11-2

CIPAC number

964

Identity tests

IR spectroscopy for TC, UV spectrum, ^{1}H-NMR, Retention time HPLC, LC-MS spectrum.

Table 1. Physico-chemical properties of pure pyraoxystrobin

Parameter	Value(s) and conditions	Purity %	Method reference (and technique if the reference gives more than one)	Study number
Vapour pressure	1.22 x 10^{-8} Pa at 25 °C	98.0	EPA EPI Suite™ estimation software	H114100010
Melting point.	129.6 °C	98.0	OECD 102	H113900020
Temperature of decomposition	222.1 °C with loss of weight	98.0	US EPA Product Properties Test Guidelines OPPTS 830.6316 Explodability	2015LH001
Solubility in water	1.3x10^{-4}g/l at 20 °C at pH 6	98.0	OECD 105	E114200010
Octanol/water partition coefficient	log P_{OW} = 3.4 at 20 - 25 °C	98.0	OECD 117	E114300010
Hydrolysis characteristics	100.8 4% pyraoxystrobin remained at 50°C at pH 4.0 for 5 days. 90.2 3% pyraoxystrobin remained at 50°C at pH 7.0 for 5 days. Half-life: 578 days at 25 °C at pH 9.0 Half-life: 21.6 days at 50 °C at pH 9.0	96.0	Test Guidelines on environmental safety assessment for chemical pesticides Part 2: Hydrolysis as a function of pH	E114800030
Photolysis characteristics	A xenon lamp was used, the intensity of illumination ranged between 3990Lux and 4219Lux, the UV intensity was between 60.4μw/cm^2 and 62.7μw/cm^2.This study was performed at 25±2°C constant temperature condition. The photo-transformation half-life tested in water of pyraoxystrobin was 27.2 min.	96.0	Test Guidelines on enviromental safety assessment for chemical pesticides Part 3: Phototrans-formation	H114900150
Dissociation characteristics	Does not dissociate	98.0	OECD 112	2015LH001
Solubility in organic solvents	8.9 g/l methanol at 20 °C 101.4 g/l acetone at 20 °C 40-50 g/l ethyl acetate at 20 °C ＞250 g/l dichloromethane at 20 °C 0.148 g/l n-hexane at 20 °C 40-50 g/l toluene at 20 °C	98.0	CIPAC MT 181 “Solubility in Organic Solvents” Handbook H, 314.	2015LH001

Table 2. Chemical composition and properties of pyraoxystrobin 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. Mass balances were 98.5 – 99.4 % and percentages of unknowns were 0.6 – 1.5%.
Declared minimum pyraoxystrobin 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.
Stabilisers or other additives and maximum limits for them:	None.

Parameter	Value and conditions	Purity %	Method reference	Study number
Melting temperature range of the TC and/or TK	125.6 – 128.3 °C	96.0	OECD 102	H113900010

FORMULATIONS AND COFORMULATED ACTIVE INGREDIENTS

The main formulation type available for pyraoxystrobin is SC which is currently registered and sold in People's Republic of China.

Pyraoxystrobin is not co-formulated with other active ingredients.

METHODS OF ANALYSIS AND TESTING

The analytical method for the active ingredient (including identity tests) is CIPAC method 964. The pyraoxystrobin is determined by reversed phase high performance liquid chromatography using UV detection at 280 nm and external standardisation.

The method used for the determination of impurities is a reversed phase HPLC method with external standardization and UV detection at 254nm.

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

PHYSICAL PROPERTIES OF PYRAOXYSTROBIN FORMULATIONS

The physical properties, the methods for testing them and the limits proposed for the SC formulations, comply with the requirements of the FAO/WHO Manual (2010 edition) as indicated in the specifications.

CONTAINERS AND PACKAGING

No special requirements for containers and packaging have been identified.

EXPRESSION OF THE ACTIVE INGREDIENT

The active ingredient is expressed as pyraoxystrobin.

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 pyraoxystrobin having impurity profiles similar to those referred to in the table above.
(ii) The conclusions expressed in the summary below are those of the proposer, unless otherwise specified.

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

Species	Test	Purity % Note[2]	Guideline, duration, doses and conditions	Result	Study number
Rat female	Oral	96.0%	OECD 401(2001); Two groups of 3 female rats were dosed at 2000 mg/kg bw and 2 groups of 3 female rats were dosed at 300 mg/kg bw. Test item was formulated in 0.5% sodium carboxymethyl cellulose and every animal was dosed once.	LD_{50} >1000 mg/kg bw	S110110090
Rat male/female	Dermal	96.0%	OECD 402; 24 h, limit dose level of 2000 mg/kg bw, semi-occlusive conditions	LD_{50} > 2000 mg/kg bw	S110210030
Rat male/female	Inhalation	96.0%	OECD 403; 4 h exposure, 2000mg/m^3、1000mg/m^3、500mg/m^3、100mg/m^3、20mg/m^3,only-nose exposure	Male:LC_{50} = 137 mg/m^3 Female :LC_{50} =195mg/m^3	S110510030
Guinea pig	Skin sensitization	96.0%	OECD 406; 0.2g test item per animal was selected as induction dose and challenge dose. On day 1, 8, 15 animals of the treatment group were induced three times, on day 29 was challenged once,semi-occlusive conditions	Non-sensitizing	S110640020
Rabbit male	Eye irritation	96.0%	OECD 405;24 h exposure,100mg per animal	Slightly acute ocular irritant and fully reversible (Category 2B)	S110330020
Rabbit male	Skin irritation	96.0%	OECD 404; 4 h exposure, 0.5g per animal	Non-irritating	S110430020

[2] Note: Purity is the content of pure active ingredient in the technical material, expressed as a percentage.

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

Species	Test	Purity % Note[3]	Guideline, duration, doses and conditions	Result	Study number
Rat male/female	Sub-chronic feeding	96.0%	OECD 408, dosing for 90 days, recovery period 28 days, 0ppm, 10ppm, 50ppm and 250ppm equivalent to: 0.0±0.0\0.7±0.0\3.7±0.2\19.6±1.4 mg/kg bw/d (male) 0.0±0.0\0.8±0.0\4.1±0.4\21.6±1.3mg/kg bw/d (female)	NOAEL =3.7±0.2mg/kg bw(Male)/4.1±0.4mg/kg bw(Female) LOEL =19.6±1.4mg/kg bw(Male)/21.6±1.3mg/kg bw(Female) Body weight gain in 250ppm dose group was affected, and food consumption was inhibited during the treatment,total protein and the albumin was significantly lower.	S111210010
Rat male/female	Chronic oncogenicity feeding	96.0%	OECD 453; 104 weeks 0ppm, 10ppm, 50ppm and 150ppm equivalent to: 0.0±0.0\0.5±0.0\2.3±0.2\7.5±0.8 mg/kg bw/d (male) 0.0±0.0\0.6±0.1\3.1±0.4\10.9±1.8mg/kg bw/d (female)	NOAEL =2.3±0.2mg/kg bw(Male)/ 0.6±0.1mg/kg bw(Female) LOEL =7.5±0.8mg/kg bw(Male)/ 3.1±0.4mg/kg bw(Female) not carcinogenic	S111910010
Rat male/female	Reproduction 2-generation,feeding	96.0%	China national standard GB 15670-1995 "Test method for pesticide registration toxicology" (part 16: two generation propagation test); 0ppm, 15ppm, 50ppm and 150ppm equivalent to F0: 0.0±0.0,1.2±0.1,3.9±0.4,13.4±2.6(male) 0.0±0.0,1.5±0.2,5.2±0.9,17.7±3.1(female) F1: 0.0±0.0,1.6±0.2,5.8±0.9,19.3±3.3(male) 0.0±0.0,2.0±0.3,6.9±1.3,25.2±3.2(female)	NOEL:Male F_0 1.2±0.1 mg/kg/day, F_1 1.6±0.2 mg/kg/day; Female F_0 5.2±0.9mg/kg/day, F_1 6.9±1.3 mg/kg/day; LOEL:Male F_0 3.9±0.4 mg/kg/day, F_1 5.8±0.9 mg/kg/day; Female F_0 17.7±3.1mg/kg/day, F_1 25.2±3.2 mg/kg/day; Non reproductive and developmental toxicity	S111610010

[3] Note: Purity is the content of pure active ingredient in the technical material, expressed as a percentage.

Species	Test	Purity % Note[3]	Guideline, duration, doses and conditions	Result	Study number
Rat female	Developmental toxicity/ teratogenicity	96.0%	OECD 414; gestation days 6-19, 0mg/kg, 5mg/kg,15mg/kg,45mg/kg bw/d,	Maternal NOEL = 5 mg/kg bw/d LOEL = 15 mg/kg bw/d Developmental LOEL = 5 mg/kg bw/d, at 5,15 and 45 mg/kg bw/d fetal rats' weight loss not teratogenic	S111510010

Pyraoxystrobin has not been evaluated by the FAO/WHO JMPR or IPCS and there is no WHO classification available

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

Species	Test	Purity % Note[4]	Guideline, duration, doses and conditions	Result	Study number
Salmonella typhimurium	Reverse mutation assay 'Ames test' in vitro	96.0%	OECD 471; S. typhimurium: TA97a, TA 98, TA 100, TA 102, TA 1535, 0-128-320-800-2000-5000µg/plate/tube (+/-S9 mix)	Negative	S110800020
Chinese hamster lung (CHL) cells	Chromosome aberration assay *in vitro*	96.0%	OECD 473; 3-6hrs exposure 0-11-33-100-300-900µg/mL (- S9 mix), 0-0.4-1.2-3.7-11-33µg/mL (+ S9 mix); 24hrs exposure:0-3.7-11-33-100-300µg/mL (- S9 mix)	Negative	S112500010
Mouse lymphoma cells	Gene mutation in mammalian cells *in vitro*	96.0%	OECD 476; 0-1.1-3.3-10-30µg/mL (+/-S9 mix),positive control MMS and Cyclophosphamide (CP), L1578Y cell	Negative	S112800050
Mouse bone marrow cells	Chromosome aberration assay Micronucleus test *in vivo*	96.0%	OECD 474;0-500-1000-2000mg/kg bw, CP 50mg/kgbw, oral route,2 dosing, 24 hours interval	Negative	S110920060

[4] Note: Purity is the content of pure active ingredient in the technical material, expressed as a percentage.

Table 6. Ecotoxicology profile of pyraoxystrobin technical material

Species	Test	Purity % Note[5]	Guideline, duration, doses and conditions	Result	Study number
Zebrafish *Danio rerio*	acute toxicity	96.0%	OECD 203, "Fish, Acute Toxicity Test" (Adopted: 17th July 1992), 96h, semi-static, 0,3.0,4.1,5.5,7.4 ,10 µg/L	LC_{50}(96h)：8.43 (7.70 - 9.24) µg/L	E113420020
Water flea *Daphnia magna*	acute toxicity	96.0%	OECD 202, "*Daphnia* sp., Acute Immobilisation Test" (Adopted: 13 April 2004), 48h, static, 0, 1.25, 2.5, 5.0, 10 and 20µg/L	EC_{50}：3.72(2.31- 5.99) µg/L	E115570020
Green alga *Desmodesmus subspicatus*	acute toxicity	96.0%	OECD 201, "Freshwater Alga and Cyanobacteria, Growth Inhibition Test" (Adopted: 23 March 2006; Annex 5 corrected: 28 July 2011), 72h, static, 0, 1.0, 2.3, 5.5, 13 and 30 µg/L	EyC_{50}(72h)：6.0(4.3-8.4) µg/L ErC_{50}(72h)：29.2(15.9-53.7) µg/L	E115680020
Earthworm *Eisenia fetida*	acute toxicity	96.0%	OECD: 207; "Earthworm, Acute Toxicity Tests",14days exposure, 0, 20, 25, 32, 40, 50mg/kg dw	LC_{50}(14d)：27.8 (26.4 - 29.4) mg/kg dw dry soil	H113460500
Honeybees *Apis mellifera*	acute contact	96.0%	OECD 214, "Honeybee, Acute Contact Toxicity Test" (Adopted 21st September 1998) 48h,100 µg a.i./bee	LD_{50} >100 µg/bee	E113230020
Honeybees *Apis mellifera*	acute oral	96.0%	OECD 213, "Honeybees, Acute Oral Toxicity Test" (Adopted 21st September 1998), 48h, 10 µg a.i./bee	LD_{50} >10 µg/bee	E113130020

[5] Note: Purity is the content of pure active ingredient in the technical material, expressed as a percentage.

Species	Test	Purity % Note[5]	Guideline, duration, doses and conditions	Result	Study number
Silkworm *Bombyx mori*	acute toxicity	96.0%	Test guidelines on environmental safety assessment for chemical pesticides—Part 11: Silkworm acute toxicity test (2010)[6] , 96h, 0,1.0,1.8,3.2,5.6,10 mg/L	LC_{50}(96h)： 2.49 (2.39-2.59) mg/L	H113840880
Japanese quail *(Coturnix coturnix japonica)*	acute oral	96.0%	Test guidelines on environmental safety assessment for chemical pesticides—Part 9: Avian acute toxicity test (2010)[7].14d, 1500 mg/kg·bw	LD_{50}＞1500 mg/kg·bw	H113110480
Japanese quail *(Coturnix coturnix japonica)*	dietary	96.0%	Test guidelines on environmental safety assessment for chemical pesticides—Part 9: Avian acute toxicity test (2010)[7].. 5 days exposure, 3days recovery, 2000 mg/kg diet	LC_{50} > 2000 mg/kg diet	H113310130
Trichogramma *Trichogramma oscriniae*	acute contact	96.0%	Test guidelines on environmental safety assessment for chemical pesticides—Part 17:Trichogramma acute toxicity test (2010)[8] 1h, 1.0×10^{-2} mg/cm^2	LR_{50}＞1.0×10^{-2} mg/cm^2	H113890890

[6] GB/T 31270.11-2014 accessible through http://webstore.spc.net.cn/produce/search.asp or http://www.spc.org.cn/gb168/ (February 2017)
[7] GB/T 31270.9-2014
[8] GB/T 31270.17-2014

Species	Test	Purity % Note[5]	Guideline, duration, doses and conditions	Result	Study number
Amphibian *Xenopus laevis*	acute toxicity	96.0%	Test guidelines on environmental safety assessment for chemical pesticides—Part 18: Amphibian acute toxicity test(2010)[9];48 hrs; 0.0030,0.0041,0.0055,0.0074,0.010 mg/L	LC_{50}(48h)：4.0(3.8- 4.3) μg/L	H113850900
Soil microorganism		96.0%	Test guidelines on environmental safety assessment for chemical pesticides—Part 16: Soil microorganism toxicity test (2010)[10],15days; 0,0.07,0.7,7mg/kg dw; China Northeast Black Soil and cinnamon soil.	No significant effects	H113800910

[9]GB/T 31270.18-2014
[10] Draft guidance of GB/T 31270.16-2014

ANNEX 2

REFERENCES

(sorted by study number)

Study number	Author(s)	year	Study title. Study identification number. Report identification number. GLP [if GLP]. Company conducting the study.
	FAO/WHO	2010	Manual on development and use of FAO and WHO specifications for pesticides. November 2010 – second revision of the First Edition. FAO Plant Production and Protection Paper. Revised.
2015LH001		2015	Solubility in organic solvents Test of Pyraoxystrobin Technical. Study Number: 2015LH001; Report Number: 2015LH001-01; Non-GLP. Owner: Shenyang Sciencreat Chemicals Co., Ltd. Unpublished.
2015LH001		2015	Dissociation Constants in water Test of Pyraoxystrobin Technical. Study Number: 2015LH001; Report Number: 2015LH001-02; Non-GLP. Owner: Shenyang Sciencreat Chemicals Co., Ltd. Unpublished.
2015LH001		2015	Thermal Decomposition Test of Pyraoxystrobin Technical. Study Number: 2015LH001; Report Number: 2015LH001-03; Non-GLP. Owner: Shenyang Sciencreat Chemicals Co., Ltd. Unpublished.
2015LH001		2015	Solubility in organic solvents Test of Pyraoxystrobin Technical. Study Number: 2015LH001; Report Number: 2015LH001-04; Non-GLP. Owner: Shenyang Sciencreat Chemicals Co., Ltd. Unpublished.
H113110480		2011	Pyraoxystrobin TC: Avian acute oral toxicity test Study Number: H113110480; Non-GLP. Owner: Shenyang Sciencreat Chemicals Co., Ltd. Unpublished.
E113230020		2014	Pyraoxystrobin TC: Honeybee, Acute Contact Toxicity Test Study Number: E113230020; GLP. Owner: Shenyang Sciencreat Chemicals Co., Ltd. Unpublished.
H113310130		2012	Pyraoxystrobin TC: Avian dietary toxicity test Study Number: H113310130; non-GLP. Owner: Shenyang Sciencreat Chemicals Co., Ltd. Unpublished.
E113420020		2014	Pyraoxystrobin TC: Fish, Acute Toxicity Test. Study Number: E113420020; GLP. Owner: Shenyang Sciencreat Chemicals Co., Ltd. Unpublished.
H113460500		2012	Pyraoxystrobin TC: Earthworm, Acute Toxicity Test Study Number: H113460500; non-GLP. Owner: Shenyang Sciencreat Chemicals Co., Ltd. Unpublished.
H113800910		2011	Pyraoxystrobin TC: Soil microorganism toxicity test Study Number: H113800910 ; non-GLP. Owner: Shenyang Sciencreat Chemicals Co., Ltd. Unpublished.

H11384 0880	2012	Pyraoxystrobin TC: Silkworm acute toxicity test Study Number: H113840880; non-GLP. Owner: Shenyang Sciencreat Chemicals Co., Ltd. Unpublished.
H11385 0900	2011	Pyraoxystrobin TC: Amphibian acute toxicity test Study Number: H113850900 ; non-GLP. Owner: Shenyang Sciencreat Chemicals Co., Ltd. Unpublished.
H11389 0890	2011	Pyraoxystrobin TC: Trichogramma acute toxicity test Study Number: H113890890; non-GLP. Owner: Shenyang Sciencreat Chemicals Co., Ltd. Unpublished.
H11390 0020	2011	Melting Point Test of Pyraoxystrobin TC. Study Number: H113900020; Report Number: H113900020; Non-GLP. Owner: Shenyang Sciencreat Chemicals Co., Ltd. Unpublished.
H11410 0010	2011	Vapor Pressure Test of Pyraoxystrobin TC. Study Number: H114100010; Report Number: H114100010; Non-GLP. Owner: Shenyang Sciencreat Chemicals Co., Ltd. Unpublished.
E11420 0010	2013	Water Solubility Test of Pyraoxystrobin TC. Study Number: E114200010; Report Number: E114200010; GLP. Owner: Shenyang Sciencreat Chemicals Co., Ltd.Unpublished.
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S11021 0030	2012	An Acute Dermal Toxicity Study with Pyraoxystrobin TC in Sprague Dawley Rats Study Number: S110210030; GLP. Owner: Shenyang Sciencreat Chemicals Co., Ltd. Unpublished.
S11033 0020	2012	An acute eye irritation study with Pyraoxystrobin TC in the rabbits Study Number: S110330020; GLP. Owner: Shenyang Sciencreat Chemicals Co., Ltd. Unpublished.
S11043 0020	2012	An Acute Dermal Irritation Study with Pyraoxystrobin TC Study Number: S110430020; GLP. Owner: Shenyang Sciencreat Chemicals Co., Ltd. Unpublished.
S11051 0030	2012	An Acute Inhalation Toxicity Study with Pyraoxystrobin TC in Sprague Dawley Rats Study Number: S110510030; GLP. Owner: Shenyang Sciencreat Chemicals Co., Ltd. Unpublished.
S11064 0020	2012	Skin Sensitization Toxicity Study of Pyraoxystrobin TC in Guinea Pigs Study Number: S110640020; GLP. Owner: Shenyang Sciencreat Chemicals Co., Ltd. Unpublished.

S11080 0020		2013	Bacterial Reverse Mutation Test of Pyraoxystrobin TC Study Number: S110800020; GLP. Owner: Shenyang Sciencreat Chemicals Co., Ltd. Unpublished.
S11121 0010		2013	Repeated Dose 90-day Oral Toxicity Study of Pyraoxystrobin TC in Sprague Dawley Rats Study Number: S111210010; GLP. Owner: Shenyang Sciencreat Chemicals Co., Ltd. Unpublished.
S11151 0010		2015	Prenatal Developmental Toxicity of Pyraoxystrobin TC in Sprague Dawley Rats Study Number: S111510010; GLP. Owner: Shenyang Sciencreat Chemicals Co., Ltd. Unpublished.
S11161 0010		2015	Two Generation Reproductive Toxicity Study of Pyraoxystrobin TC in Sprague Dawley Rats Study Number: S111910010; GLP. Owner: Shenyang Sciencreat Chemicals Co., Ltd. Unpublished.
S11191 0010		2015	104-week Dietary Combined Chronic Toxicity and Carcinogenicity Study of Pyraoxystrobin TC in Sprague Dawley Rats Study Number: S111910010; GLP. Owner: Shenyang Sciencreat Chemicals Co., Ltd. Unpublished.
S11092 0060		2013	Mammalian Erythocyte Micronucleus Test t of Pyraoxystrobin TC. Study Number: S110920060 ; GLP. Owner: Shenyang Sciencreat Chemicals Co., Ltd. Unpublished.
S11250 0010	Zhiqin Wang	2014	Pyraoxystrobin TC *in vitro* Mammalian Chromosome Aberration Test Study Number: S112500010 ; GLP. Owner: Shenyang Sciencreat Chemicals Co., Ltd. Unpublished.
S11280 0050	Zhiqin Wang	2014	Pyraoxystrobin TC in vitro Mammalian Cell Gene Mutation Test Study Number: S112800050 ; GLP. Owner: Shenyang Sciencreat Chemicals Co., Ltd. Unpublished.