

FAO SPECIFICATIONS AND EVALUATIONS FOR AGRICULTURAL PESTICIDES

PROCHLORAZ

N-propyl-*N*-[2-(2,4,6-trichlorophenoxy)ethyl]imidazole-1-carboxamide



FOOD AND AGRICULTURE ORGANIZATION *of* THE UNITED NATIONS

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DISCLAIMER¹

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

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

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

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

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

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¹This disclaimer applies to all specifications published by FAO

INTRODUCTION

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

From 1999, the development of FAO specifications has followed the **New Procedure**, described in the 1st edition of “Manual for Development and Use of FAO and WHO Specifications for Pesticides” (2002) and amended with the supplement of this manual (2006), 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 JMPS, rather than the JMPS.]

FAO Specifications now only apply to products for which the technical materials have been evaluated. Consequently from the year 2000 onwards the publication of FAO specifications under the **New Procedure** has changed. Every specification consists now of two parts namely the specifications and the evaluation report(s):

Part One: The Specification of the technical material and the related formulations of the 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 plant protection product reflecting the evaluation of the data package carried out by FAO and the JMPS. The data are to be provided by the manufacturer(s) according to the requirements of Appendix A, annex 1 or 2 of the “Manual on the development and use of FAO and WHO specifications for pesticides” 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. Dates of publication of the earlier versions, if any, are identified in a footnote. Evaluations bear the date (year) of the meeting at which the recommendations were made by the JMPS.

* NOTE: PUBLICATIONS ARE AVAILABLE ON THE INTERNET AT <http://www.fao.org/agriculture/crops/core-themes/theme/pests/pm/en/> OR IN HARDCOPY FROM THE PLANT PROTECTION INFORMATION OFFICER.

PART ONE

SPECIFICATIONS

PROCHLORAZ

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PROCHLORAZ

INFORMATION

ISO common name

Prochloraz (E-ISO, (m) F-ISO, BSI, ANSI)

Chemical name(s)

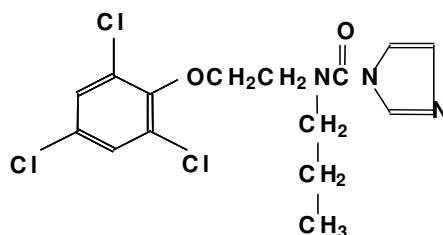
IUPAC: *N*-propyl-*N*-[2-(2,4,6-trichlorophenoxy)ethyl]imidazole-1-carboxamide

CA: *N*-propyl-*N*-[2-(2,4,6-trichlorophenoxy)ethyl]-1*H*-imidazole-1-carboxamide

Synonyms

None

Structural formula



Molecular formula

$C_{15}H_{16}Cl_3N_3O_2$

Relative molecular mass

376.7 g/mol

CAS Registry number

67747-09-5

CIPAC number

407

Identity tests

HPLC retention time; IR, UV, NMR and mass spectra.

PROCHLORAZ TECHNICAL MATERIAL

FAO specification 407/TC (April 2009*)

This specification, which is PART ONE of this publication, is based on an evaluation of data submitted by the manufacturer whose name is listed in the evaluation report (407/2007). 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 specifications. The specification may not be appropriate for TC produced by other manufacturers. The evaluation report (407/2007), as PART TWO, forms an integral part of this publication.

1 Description

The material shall consist of prochloraz together with related manufacturing impurities and shall be a brownish waxy solid, free from visible extraneous matter and added modifying agents.

2 Active ingredient

2.1 Identity tests (CIPAC 407/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 Prochloraz content (CIPAC 407/TC/M)

The prochloraz content shall be declared (not less than 970 g/kg) and, when determined, the average measured content shall not be lower than the declared minimum content.

3 Relevant impurities (Note 2)

Note 1 Methods for identification and determination of the content of active ingredient in prochloraz TC and EC were adopted by CIPAC in 2007 but are not yet published in a Handbook. Prior to publication of the Handbook, copies of the methods may be obtained through the CIPAC website, <http://www.cipac.org>.

Note 2 There are no relevant impurities to be controlled in products of the manufacturer identified in evaluation report 407/2007. However, dioxins can occur as a result of certain manufacturing processes. If 2,3,7,8-tetrachlorodibenzodioxin (2,3,7,8-TCDD) occurs at $\geq 0.1 \mu\text{g}/\text{kg}$ (of prochloraz) in the products of other manufacturers, it may be designated as a relevant impurity and a clause may be required to limit its concentration.

*Specifications may be revised and/or additional evaluations may be undertaken. Ensure the use of current versions by checking at: <http://www.fao.org/ag/agp/agpp/pesticid/>.

PROCHLORAZ EMULSIFIABLE CONCENTRATE

FAO specification 407/EC (April 2009*)

This specification, which is PART ONE of this publication, is based on an evaluation of data submitted by the manufacturer whose names is listed in the evaluation report (407/2007). 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 (407/2007), as PART TWO, forms an integral part of this publication.

1 Description

The material shall consist of technical prochloraz, complying with the requirements of FAO specification 407/TC (March 2009), dissolved in suitable solvents, together with any other necessary formulants. It shall be in the form of a stable homogeneous liquid, free from visible suspended matter and sediment, to be applied as an emulsion after dilution in water.

2 Active Ingredient

2.1 Identity tests (CIPAC 407/EC/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 Prochloraz content (CIPAC 407/EC/M, Note 1)

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

Declared content in g/kg or g/l at $20 \pm 2^\circ\text{C}$	Tolerance
Above 250 up to 500	$\pm 5\%$ of the declared content
<u>Note</u> : the upper limit is included in the range	

3 Relevant impurities (Note 3)

* 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/en/>

4 Physical Properties

4.1 Acidity (MT 191, CIPAC Handbook L, p.143, 2006)

Maximum: 1 g/kg calculated as H₂SO₄.

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

The formulation, when diluted at 30 ± 2°C with CIPAC standard waters A and D, shall comply with the following:

Time after dilution	Limits of stability
0 h	Initial emulsification complete
0.5 h	"Cream", maximum: 0 ml
2.0 h	"Cream", maximum: 2 ml "Free oil", maximum: 0.2 ml
24 h	Re-emulsification complete
24.5 h	"Cream", maximum: 2 ml "Free oil", maximum: 0.2 ml
Note: tests after 24 h are required only where results at 2 h are in doubt	

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

Maximum: 25 ml after 1 min.

5 Storage stability

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

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

5.2 Stability at elevated temperature (MT 46.3 CIPAC 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:

- acidity (3.1)
- emulsion stability and re-emulsification (3.2)

Note 1 Methods for identification and determination of the content of active ingredient in prochloraz TC and EC were adopted by CIPAC in 2007 but are not yet published in a Handbook. Prior to publication of the Handbook, copies of the methods may be obtained through the CIPAC website, <http://www.cipac.org>.

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 There are no relevant impurities to be controlled in products of the manufacturer identified in evaluation report 407/2007. However, dioxins could occur as a result of certain manufacturing processes. If 2,3,7,8-tetrachlorodibenzodioxin (2,3,7,8-TCDD) occurs at

≥0.1 µg/kg (of prochloraz) in the products of other manufacturers, it may be designated as a relevant impurity and a clause may be required to limit its concentration.

Note 4 The mass of the sample to be used in the test should be specified at 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

PROCHLORAZ

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PROCHLORAZ

FAO/WHO EVALUATION REPORT 407/2007

Recommendations

The Meeting recommended the following.

- (i) The specifications for prochloraz TC and EC, proposed by Makhteshim and as amended, should be adopted by FAO.
- (ii) The specifications for prochloraz TK and SC, proposed by Makhteshim and as amended, should be adopted by FAO, subject to acceptable validation and adoption by CIPAC (or equivalent) of an analytical method for determination of the active ingredient content in products that contain prochloraz as its zinc complex.

Appraisal

Data provided by Makhteshim Chemical Works were evaluated in support of proposed new FAO specifications for prochloraz TC, TK, EC and SC. Data were first evaluated by the 2004 JMPS, which required additional information on (i) analytical methods for determination of prochloraz, (ii) identification of the zinc complex of prochloraz and (iii) potentially relevant impurities. The additional information was considered by the 2007 JMPS.

Prochloraz is not under patent.

Prochloraz is a solid of rather low melting point, volatility and water solubility. It is hydrolyzed slowly at pH 9 and very slowly at pH 5 and 7. It is subject to slow photolysis and is subject to thermal decomposition at about 220°C. It is a weak base, becoming protonated in acidic conditions (pKa 3.8, Tomlin 2000). Prochloraz forms stable complexes with certain metal ions, such as Zn²⁺.

The Meeting was provided with details of the manufacturing process, 5 batch analysis data, and manufacturing limits for purity and all impurities ≥1 g/kg. Mass balances were high (98.45–99.15%), no unknowns were detected and the minimum prochloraz content of the TC was 970 g/kg. These data were confirmed as identical to those submitted for registration in the UK. The Meeting agreed that none of the impurities occurring ≥1 g/kg should be designated as relevant for the purposes of FAO specifications.

The structure of prochloraz indicates the possibility of dioxin impurity formation (particularly 2,3,7,8-tetrachlorodibenzodioxin or 2,3,7,8-TCDD, the most hazardous of the dioxins) during synthesis of the active ingredient. The Meeting therefore requested data on the dioxin content of prochloraz produced by the proposer. The manufacturer provided evidence showing that dioxins were not detectable (LOQ for 2,3,7,8-TCDD = 0.1 µg/kg of prochloraz) in the products. The Meeting therefore agreed that dioxins should not be designated as relevant impurities in the products of this manufacturer but that an appropriate cautionary note should be inserted into the specifications, alerting users to the possibility that dioxins could occur in the products of other manufacturers, at levels at which they would be considered relevant.

Reversed-phase HPLC-UV methods for the determination of prochloraz in the TC and EC were adopted in 2008 as full CIPAC methods. Various spectroscopic techniques are suitable for confirmation of the identity of prochloraz. The manufacturer provided an ICP-OES method for identification of the prochloraz-zinc complex in TK and SC, measuring the zinc content and based on the 1:2 stoichiometry of the Zn^{2+} :prochloraz complex. An analytical method for the determination of prochloraz in the TK and SC (in which prochloraz is present as the zinc complex) was adopted by CIPAC in 2007, with tentative¹ status only, which is not sufficient to support FAO specifications for these products.

The Meeting considered the proposed specifications for TC, TK, EC and SC, which were broadly in accordance with the requirements of the manual (FAO/WHO 2002, 2006). In addition to the issues already identified above, requiring the insertion of appropriate footnotes, the following issues were considered.

EC and SC. The Meeting questioned the need for control of acidity in the EC and for control of pH (specified limits, 6-8) in the SC, as prochloraz is relatively stable under neutral to acidic conditions. The manufacturer stated that prochloraz is unstable under more extreme conditions and that crystallization (or crystal growth in the SC) can occur under more extreme conditions in the formulations. The Meeting accepted the need for the clauses and limits.

¹ The "Summary of decisions...2008" (document CIPAC/4651/P, accessed at <http://www.cipac.org> on 10 March 2009) indicates that the method for determination of prochloraz in the TK and SC has "provisional" status, whereas the "Summary of decisions....2007" (document CIPAC/4598/P on the same website) indicates that the method was originally allocated "tentative" status only. The current "tentative" status of the method has been confirmed by CIPAC (CIPAC 2009).

**SUPPORTING INFORMATION
FOR
EVALUATION REPORT 407/2007**

Uses

Prochloraz is a non-systemic imidazole fungicide, an ergosterol biosynthesis inhibitor with contact and translaminar, protectant and eradicant activity. It is used in agriculture and horticulture against various plant diseases, especially Ascomycetes and Fungi Imperfecti. It is used to control foliar diseases of cereals (*Pseudocercospora*, *Pyrenophora*, *Rhynchosporium* and *Septoria spp.*), field crops (such as *Alternaria*, *Botrytis*, *Pyrenopeziza* and *Sclerotinia* in oilseed rape, *Ascochyta* and *Botrytis* in legumes, *Pyricularia* in rice), fruit (blossom blight) and vegetables (anthracnose).

Identity of the active ingredient

ISO common name

Prochloraz (E-ISO, (m) F-ISO, BSI, ANSI)

Chemical name(s)

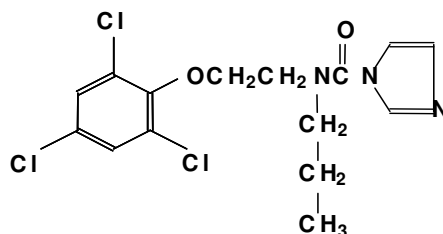
IUPAC: *N*-propyl-*N*-[2-(2,4,6-trichlorophenoxy)ethyl]imidazole-1-carboxamide

CA: *N*-propyl-*N*-[2-(2,4,6-trichlorophenoxy)ethyl]-1*H*-imidazole-1-carboxamide

Synonyms

None

Structural formula



Molecular formula

C₁₅H₁₆Cl₃N₃O₂

Relative molecular mass

376.7 g/mol

CAS Registry number

67747-09-5

CIPAC number

407

Identity tests

HPLC retention time; IR, UV, NMR and mass spectra.

Physico-chemical properties of prochloraz

Table 1. Physico-chemical properties of pure prochloraz (a) and prochloraz zinc complex (b)

Parameter	Value(s) and conditions	Purity %	Method	Reference
Vapour pressure	3.5x10 ⁻⁶ Pa at 20°C	99.3 (a)	OECD 104, EEC A4 and EPA guideline subdivision D, 63-9	R-7280
	<8.8 x 10 ⁻⁵ Pa at 25°C	99.7 (b)	EC method A4, OECD 104	R-17277
Melting point	48.0-51.0°C	99.3 (a)	EPA guideline 63-5	R-7278
	102.5-105.0°C	99.7 (b)	EC method A1, OECD 102	R-17277
Temperature of decomposition	222°C	98.9(a)	Differential scanning calorimetry	R-17276
Solubility in water	0.0276 g/l at 20°C at pH 5 0.0249 g/l at 20°C at pH 7 0.0236 g/l at 20°C at pH 9 0.0265 g/l at 20°C (purified water)	99.3(a)	CIPAC MT 157, OECD 105, EEC A6, EPA guidelines subdivision D, 63-8	R-7281
Partition coefficient	log P _{ow} = 4.06 at 25°C at pH 7	98.2(a)	EPA guideline 63-11	R-5424
Hydrolysis characteristics	Half-life = 61.7 days at 25°C at pH 9 <20% of prochloraz degraded during 35 days at pH 5 and 7	98.2(a)	EPA guideline 161.1	R-6150
Photolysis characteristics	half-life = 11.4 days at 25°C (artificial light by xenon arc lamp, 12 h light/12 h dark)	98.9(a)	EPA guideline 161-2	R-6144
Relative density	1.413	99.3(a)	EC method A3,	R-7279
	1.475	99.7(b)	OECD 109	R-17277

Table 2. Chemical composition and properties of technical prochloraz (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 98.45-99.15%, with no unknowns ≥1 g/kg.
Declared minimum prochloraz content	970 g/kg
Relevant impurities ≥ 1 g/kg and maximum limits for them	None
Relevant impurities < 1 g/kg and maximum limits for them	None
Stabilizers or other additives and maximum limits for them	None
Melting temperature range	48.0-51.0°C

Hazard summary

Prochloraz was evaluated by the FAO/WHO JMPR in 1983, 1985, 1987, 1988, 1989, 1990, 1991, 1992 and 2001. The 2001 JMPR confirmed the ADI of 0-0.01 mg/kg bw/d set originally by the 1983 JMPR and set an acute reference dose of 0.1 mg/kg bw (JMPR 2001).

The WHO hazard classification of prochloraz is class III, slightly hazardous (WHO 2002).

Classification and labelling of prochloraz according to the EU council directive (67/548/EEC) is as follows.

Hazard symbols: Xn (harmful), N (dangerous for the environment)

Risk phrases: R22 (harmful if swallowed), R50 (very toxic to aquatic organisms), R53 (may cause long-term effects in the aquatic environment).

Safety phrases: S2 (keep out of reach of children), S60 (this material and its container must be disposed of as hazardous waste), S61 (avoid release to the environment).

Formulations and co-formulated active ingredients

The main formulation types available are emulsifiable concentrates (EC) and aqueous suspension concentrates (SC), used as agricultural fungicides. These formulations are registered and sold in many countries in Europe and South America.

Prochloraz may be co-formulated with other pesticides.

Methods of analysis and testing

Reversed-phase HPLC-UV methods for the determination of prochloraz in the TC and EC were adopted in 2008 as full CIPAC method. IR, UV, NMR and mass spectral techniques are suitable for confirmation of the identity of prochloraz and representative spectra were provided to FAO. Identification of the prochloraz-zinc complex in TK and SC is by means of the manufacturer's in-house ICP-OES method, measuring the zinc content, and is based on the 1:2 stoichiometry of the Zn^{2+} :prochloraz complex. An analytical method for the determination of prochloraz in the TK and SC (in which prochloraz is present as the zinc complex) was adopted by CIPAC in 2008, with "tentative" status¹.

The method(s) for determination of impurities are based on reversed-phase HPLC with UV detection at 240 nm and external standardization.

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

Physical properties

¹ The "Summary of decisions...2008" (document CIPAC/4651/P, accessed at <http://www.cipac.org> on 10 March 2009) indicates that the method for determination of prochloraz in the TK and SC has "provisional" status, whereas the "Summary of decisions....2007" (document CIPAC/4598/P on the same website) indicates that the method was originally allocated "tentative" status only. The current "tentative" status of the method has been confirmed by CIPAC (CIPAC 2009).

The physical properties, the methods for testing them and the limits proposed for the EC and SC formulations, complied with the requirements of the FAO/WHO manual (FAO/WHO 2002, 2006).

Containers and packaging

No special requirements for containers and packaging have been identified.

Expression of the active ingredient

The active ingredient is expressed as prochloraz (in g/kg or g/l at $20 \pm 2^{\circ}\text{C}$) whether present as free prochloraz or its zinc complex.

ANNEX 1
HAZARD SUMMARY PROVIDED BY THE PROPOSER

Note. The proposer confirmed that most of the toxicological and ecotoxicological data included in the summary below were derived from prochloraz having impurity profiles similar to those referred to in the table above but there are some exceptions. The acute toxicity studies and the short-term toxicity (rat) and teratogenicity (rabbit) studies were conducted with lower purity prochloraz technical (93.4-95.4%) and thus represented worst-case scenarios with respect to impurity hazards.

Table A. Toxicology profile of prochloraz technical material (TC), based on acute toxicity, irritation and sensitization

Species	Test	Duration and conditions	Result	Reference
Rat, Sprague-Dawley (m,f)	Acute oral	Single dose administered as solution in maize oil, followed by 14-d observation. OECD 401. Purity 94.6%	LD ₅₀ = 1204 mg/kg bw	R-5306
Rat (m,f)	Acute dermal	Single dermal application in place 24 h, 14-d observation. OECD 402. Purity 94.6%	LD ₅₀ >2000 mg/kg bw	R-5307
Rat (m,f)	Acute inhalation	4-h exposure followed by 14-d observation. Complied with OECD 403. Purity 94.6%	LC ₅₀ >2.41 mg/l	R-5420
Rabbit	Skin irritation	Single 4-h exposure followed by 8 d observation. OECD 404, EPA FIFRA guideline, subdivision F 81-5. Purity 94.6%	Mild irritant	R-5308
Rabbit	Eye irritation	Single dose followed by 72-h observation. OECD 405, EPA FIFRA guideline subdivision F 81-4. Purity 94.6%	Non irritant	R-5309
Guinea pig	Skin sensitization	Buehler method. OECD 406, EPA FIFRA guideline subdivision F 81-6. Purity 94.6%	Non sensitizing	R-5310

Table B. Toxicology profile of prochloraz technical material (TC), based on repeated administration (sub-acute to chronic)

Species	Test	Duration and conditions	Result	Reference
Rat (m)	Oral, short-term	13 weeks, dietary administration. OECD 408, EPA FIFRA guidelines, subdivision F 82-1. Purity 93.4%	NOAEL = 50 ppm ≅ 4.4 mg/kg bw/d (m)	R-5312
Rat (m,f)	Carcinogenicity	104 weeks, dietary administration. OECD 456, EPA FIFRA guideline subdivision F 83-5. Purity 97.4%	NOAEL = 40 ppm ≅ 1.7 mg/kg bw/d (m) LOEL = 220 ppm ≅ 8.4 mg/kg bw/d(m) Not carcinogenic	R-5924
Mouse (m,f)	Carcinogenicity	78 weeks, dietary administration. OECD 451, EPA FIFRA guideline subdivision F 83-5. Purity 97.4%	NOAEL = 40 ppm ≅ 4.7 mg/kg bw/d (m) LOEL = 220 ppm ≅ 26.3 mg/kg bw/d(m) Not carcinogenic	R-5926
Rat (m,f)	Reproduction	F0 generation, 14 weeks; F1 generation, 14 weeks; and F2 generation, 10 weeks; dietary administration. OECD 416, EPA FIFRA guideline subdivision F 83-4, Japanese MAFF. Purity 97.5%	Reproductive NOAEL = 50 ppm (F0, F1, F2) ≅ 3.7 mg/kg bw/d (m F0) LOEL = 150 ppm (F0, F1, F2) ≅ 11.1 mg/kg bw/d (m F0)	R-5928
Rat (f)	Teratogenicity	Gavage administration (day 6 to day 15 of gestation inclusive). EPA FIFRA guideline, subdivision F 83-3 and complied with OECD 414. Purity 97.5%	NOAEL (maternal) = 120 mg/kg/ bw/d NOAEL (foetal) = 30 mg/kg/ bw/d LOEL (foetal) = 60 mg/kg/ bw/d Not teratogenic	R-5930
Rabbit (f)	Teratogenicity	Gavage administration (day 7 to day 19 post-coitum). OECD 414, EPA FIFRA guideline subdivision F 83-3, (1981). Purity 95.4%	NOAEL (maternal) = 40 mg/kg/ bw/d NOAEL (foetal) = 40 mg/kg/ bw/d Not teratogenic	R-5315

No evidence of delayed neurotoxicity observed in acute, sub-chronic and chronic studies.

Table C. Mutagenicity profile of prochloraz technical material (TC), based on *in vitro* and *in vivo* tests

Species	Test	Duration and conditions	Result	Reference
<i>Salmonella typhimurium</i> (TA-1535, TA-100, TA-1538, TA-98 and TA-1537)	Reverse mutation test for bacteria, <i>in vitro</i>	2.5-260 µg/plate ±S-9 mix. Complied with OECD 471 (1983). Purity not stated	Negative	R-5400
Human lymphocytes	Cytogenetic test, <i>in vitro</i>	5-40 µg/ml, without S-9 10-150 µg/ml, with S-9 OECD 473. Purity 94.6%	Negative Positive Some evidence of clastogenic potential with metabolic activation.	R-5438
Mouse bone marrow cells (m,f)	Micronucleus test, <i>in vivo</i>	Doses 12-300 mg/kg OECD 474 (1983). Purity 94.6%	Negative	R-5439
Rat hepatocytes	Unscheduled DNA synthesis, <i>in vivo</i>	Doses 40-400 mg/kg. Methods based on: Mirsalis and Butterworth (1980); Mirsalis <i>et al.</i> (1982); Ashby <i>et al.</i> (1985); Butterworth <i>et al.</i> (1987). Complied with OECD 486. Purity 97.9%	Negative	R-6646

Table D. Ecotoxicology profile of prochloraz technical material (TC)

Species	Test	Duration and conditions	Result	Reference
<i>Daphnia magna</i> (water flea)	Acute toxicity	Static, 48-h, 19°C. OECD 202 (1984). Purity 99%	EC ₅₀ = 0.85 mg/l	R-5934
<i>Oncorhynchus mykiss</i> (rainbow trout)	Acute toxicity	Flow-through, 96-h, 14.9°C. OECD 203 (1984). Purity 99%	LC ₅₀ = 1.43 mg/l	R-5932
<i>Selenastrum capricornutum</i> (green alga)	Effect on growth	96-h, 20.0-22.8°C. OECD 201. Purity 99%	E _b C ₅₀ = 0.28 mg/l E _r C ₅₀ = 1.19 mg/l	R-5931
<i>Eisenia foetida</i> (earthworm)	Acute toxicity	Artificial soil system, 14-d, 20.5-22.0°C. OECD 207. Purity 97.5%	LC ₅₀ >1000 mg/kg dry soil	R-6352
<i>Apis mellifera</i> (honey bee)	Acute oral and contact toxicity	48-h. Guideline: Laboratory testing for toxicity to honey bees, working document 7/3; MAFF, UK. Purity 97.5%	LD ₅₀ (oral) = 684.03 µg/bee LD ₅₀ (contact) = 14.89 µg/bee	R-6211
<i>Anas platyrhynchos</i> (mallard duck)	Acute toxicity	14 days, single oral dose. Guideline: EPA-FIFRA, Subdivision E, No. 71-1. EPA-TOSCA, Subdivision E, wildlife and aquatic organisms, paragraph 797.2175. Purity 97.5%	LD ₅₀ >2000 mg/kg bw NOEC = 2000 mg/kg bw	R-6010

ANNEX 2. References

Makhteshim document number or other reference	Year and title of report or publication details
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R-6144	1994. Mirage: Photodegradation in water.
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R-6211	1991. Laboratory testing for oral and contact toxicity of Mirage technical to honey bees, <i>Apis mellifera</i> L.
R-6352	1991. Acute toxicity (LC50) study of Mirage technical to earthworms.
R-6646	1992. Mirage: Induction of unscheduled DNA synthesis (UDS) in rat hepatocytes.
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R-7280	1994. Mirage (pure): Determination of the vapour pressure.
R-7281	1994. Mirage (pure): Determination of the water solubility.
R-17276	2004. Prochloraz (pure grade) - Boiling temperature.
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