FAO SPECIFICATIONS AND EVALUATIONS FOR AGRICULTURAL PESTICIDES

IPRODIONE

3-(3,5-dichlorophenyl)-*N*-isopropyl-2,4-dioxo-imidazolidine-1-carboxamide

FOOD AND AGRICULTURE ORGANIZATION *of* THE UNITED NATIONS

TABLE OF CONTENTS

IPRODIONE

DISCLAIMER[1]

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

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

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

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

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

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

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

INTRODUCTION

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

Since 1999 the development of FAO specifications follows the **New Procedure**, described in the 5th edition of the " Manual on the development and use of FAO specifications for plant protection products" (FAO Plant Production and Protection Page No. 149). This **New Procedure** follows a formal and transparent evaluation process. It describes the minimum data package, the procedure and evaluation applied by FAO and the Experts of the FAO/WHO Joint Meeting on Pesticide Specifications (JMPS). [Note: prior to 2002, the Experts were of the FAO Panel of Experts on Pesticide Specifications, Registration Requirements, Application Standards and Prior Informed Consent, which now forms part of the JMPS, rather than the JMPS.]

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

PART ONE: **The Specification** of the technical material and the related formulations of the plant protection product in accordance with chapter 4, 5 and 6 of the 5th edition of the "Manual on the development and use of FAO specifications for plant protection products".

PART TWO: **The Evaluation Report(s)** of the plant protection product reflecting the evaluation of the data package carried out by FAO and the JMPS. The data are to be provided by the manufacturer(s) according to the requirements of Appendix A, annex 1 or 2 of the "Manual on the development and use of FAO specifications for plant protection products" and supported by other information sources. The Evaluation Report includes the name(s) of the manufacturer(s) whose technical material has been evaluated. Evaluation reports on specifications developed subsequently to the original set of specifications are added in a chronological order to this report.

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

Specifications bear the date (month and year) of publication of the current version. Dates of publication of the earlier versions, if any, are identified in a footnote. Evaluations bear the date (year) of the meeting at which the recommendations were made by the JMPS.

* NOTE: PUBLICATIONS ARE AVAILABLE ON THE INTERNET AT (http://www.fao.org/ag/agp/agpp/pesticid/) OR IN HARDCOPY FROM THE PLANT PROTECTION INFORMATION OFFICER.

PART ONE

SPECIFICATIONS

IPRODIONE

PART ONE

IPRODIONE

INFORMATION

ISO common name

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

Synonyms

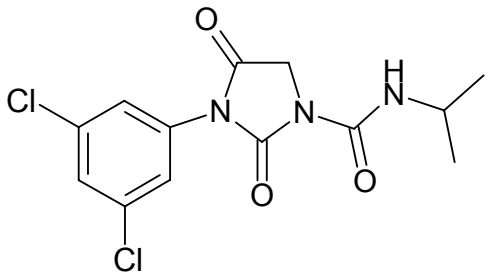
Glycophene (rejected common name proposal)

Chemical names

IUPAC 3-(3,5-dichlorophenyl)-*N*-isopropyl-2,4-dioxo-imidazolidine-1-carboxamide

CA 3-(3,5-dichlorophenyl)-*N*-(1-methylethyl)-2,4-dioxo-1-imidazolidinecarboxamide

Structural formula



Empirical formula

$C_{13}H_{13}Cl_2N_3O_3$

Relative molecular mass

330.2

CAS Registry number

36734-19-7

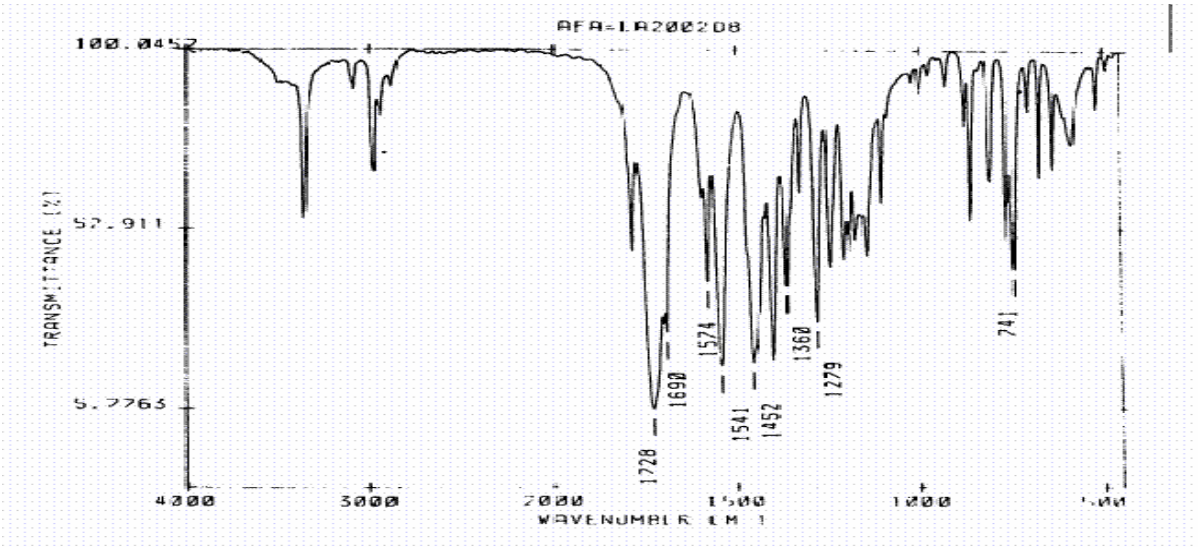
CIPAC number

278

Identity tests

HPLC retention time; IR spectrum (page 4)

IR spectrum of iprodione



IPRODIONE TECHNICAL MATERIAL

FAO specification 278/TC (July 2006*)

*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 (*278/2004*). It should be applicable to relevant products of these manufacturers but it is not an endorsement of those products, nor a guarantee that they comply with the specifications. The specification may not be appropriate for the products of other manufacturers. The evaluation report (*278/2004*) as PART TWO forms an integral part of this publication.*

1 Description

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

2 Active ingredient

2.1 **Identity tests** (CIPAC 278/TC/M/2, CIPAC Handbook G, p.99, 1995)

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 **Iprodione content** (CIPAC 278/TC/M/3, CIPAC Handbook G, p.99, 1995)

The iprodione content shall be declared (not less than 960 g/kg) and, when determined, the average measured content shall not be lower than the declared minimum content.

3 Relevant impurities

3.1 **Loss on drying** (MT 17.2, CIPAC Handbook F, p.56, 1995)

Maximum: 10 g/kg.

* 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/.

IPRODIONE WETTABLE POWDER

FAO specification 278/WP (July 2006*)

*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 (*278/2004*). It should be applicable to relevant products of these manufacturers but it is not an endorsement of those products, nor a guarantee that they comply with the specifications. The specification may not be appropriate for the products of other manufacturers. The evaluation report (*278/2004*) as PART TWO forms an integral part of this publication.*

1 Description

The material shall consist of an homogeneous mixture of technical iprodione complying with the requirements of FAO specification 278/TC (July 2006). It shall be in the form of a fine powder free from visible extraneous matter and hard lumps.

2 Active ingredient

2.1 **Identity tests** (CIPAC 278/WP/M/2, CIPAC Handbook G, p.102, 1995)

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 **Iprodione content** (CIPAC 278/WP/M/3, CIPAC Handbook G, p.102, 1995)

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

Declared content, g/kg	Tolerance
above 100 up to 250	± 6% of the declared content
above 250 up to 500	± 5% of the declared content
above 500	± 25 g/kg
Note: in each range the upper limit is included.	

3 Relevant impurities

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

Maximum: 20 g/kg.

4 Physical properties

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

pH range: 4 to 6.

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

Maximum: 1% retained on a 75 µm test sieve.

---

* 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/.

4.3 **Suspensibility** (MT 184, CIPAC Handbook K, p.142, 2003) (Notes 1 & 2)

A minimum of 70% of the iprodione content found under 2.2 shall be in suspension after 30 min in CIPAC standard water D at 30 ± 2°C (Note 3).

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

Maximum: 50 ml after 1 min.

4.5 **Wettability** (MT 53.3.1, CIPAC Handbook F, p.165, 1995)

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

5 Storage stability

5.1 **Stability 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 97%, relative to the determined average content found before storage (Note 5), and the formulation shall continue to comply with the clauses for:

- pH range (4.1),
- wet sieve test (4.2),
- suspensibility (4.3),
- wettability (4.5).

Note 1 The formulation should be tested at the highest and lowest rates of use recommended by the supplier.

Note 2 This test will normally only be carried out after the heat stability test, 5.1.

Note 3 Chemical assay is the only fully reliable method to measure the mass of active ingredient still in suspension. However, simpler methods such as gravimetric and solvent extraction determination may be used on a routine basis provided that these methods have been shown to give results which are in agreement to those of the chemical assay method. In case of dispute, the chemical method shall be the referee method.

Note 4 The mass of sample to be used in the test should be at the highest rate of use recommended by the supplier.

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.

IPRODIONE WATER DISPERSIBLE GRANULES

FAO specification 278/WG (July 2006*)

*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 (*278/2004*). It should be applicable to relevant products of these manufacturers but it is not an endorsement of those products, nor a guarantee that they comply with the specifications. The specification may not be appropriate for the products of other manufacturers. The evaluation report (*278/2004*) as PART TWO forms an integral part of this publication.*

1 Description

The material shall consist of an homogeneous mixture of technical iprodione, complying with the requirements of the FAO specification 278/TC (July 2006), together with carriers and any other necessary formulants. It shall be in the form of granules for application after disintegration and dispersion in water. The formulation shall be dry, free-flowing, essentially non-dusty, and free from visible extraneous matter and hard lumps.

2 Active ingredient

2.1 **Identity tests** (CIPAC 278/WP/M/2, CIPAC Handbook G, p.102, 1995, 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 **Iprodione content** (CIPAC 278/WP/M/3, CIPAC Handbook G, p.102, 1995, Note 1)

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

Declared content, g/kg	Tolerance
above 250 up to 500 above 500 Note: the upper limit is included in the range	± 5% of the declared content ± 25 g/kg

3 Relevant impurities

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

Maximum: 8 g/kg.

* 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/.

4 Physical properties

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

pH range: 8.9 to 9.9.

4.2 **Wettability** (MT 53.3.1, CIPAC Handbook F, p.165, 1995)

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

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

Maximum: 1% retained on a 75 µm test sieve.

4.4 **Degree of dispersion** (MT 174, CIPAC Handbook F, p.435, 1995)

Dispersibility: minimum 90% after 2 min stirring.

4.5 **Suspensibility** (MT 184, CIPAC Handbook K, p.142, 2003. Note 2)

A minimum of 70% shall be in suspension after 30 min in CIPAC standard water D at 30 ± 2°C.

4.6 **Persistent foam** (MT 47.2, CIPAC Handbook F, p.152, 1995) (Note 3)

Maximum: 50 ml after 1 min.

4.7 **Dustiness** (MT 171, CIPAC Handbook F, p.425, 1995) (Note 4)

Essentially non-dusty.

4.8 **Flowability** (MT 172, CIPAC Handbook F, p.430, 1995)

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

5 Storage stability

5.1 **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 that 97% relative to the determined average content found before storage (Note 5) and the formulation shall continue to comply with the clauses for:

- pH range (4.1),
- wet sieve test (4.3),
- degree of dispersion (4.4),
- suspensibility (4.5),
- dustiness (4.7),
- flowability (4.8).

Note 1 The CIPAC method for determination of iprodione in wettable powders (WP) is also applicable to water dispersible granules (WG). However, prior to analysis, samples of the granules should be ground to a powder.

Note 2 Chemical assay is the only fully reliable method to measure the mass of active ingredient still in suspension. However, the simpler gravimetric method, MT 168, may be used on a routine basis provided that it has been shown to give equal results to those of chemical assay. In case of dispute, chemical assay shall be the "referee method".

Note 3 The mass of sample to be used in the test should be at the highest application rate of use recommended by the supplier.

Note 4 Measurement of dustiness must be carried out on the sample "as received" and, where practicable, the sample should be taken from a newly opened container, because changes in the water content of samples may influence dustiness significantly. The optical method, MT 171.2, usually shows good correlation with the gravimetric method, MT 171.1, and can, therefore, be used as an alternative where the equipment is available. Where the correlation is in doubt, it must be checked with the formulation to be tested. In case of dispute the gravimetric method shall be used.

Note 5 Analysis of the formulation, before and after the storage stability test, should be carried out concurrently (i.e. after storage) to reduce analytical error.

IPRODIONE AQUEOUS SUSPENSION CONCENTRATE

FAO specification 278/SC (July 2006*)

*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 (*278/2004*). It should be applicable to relevant products of these manufacturers but it is not an endorsement of those products, nor a guarantee that they comply with the specifications. The specification may not be appropriate for the products of other manufacturers. The evaluation report (*278/2004*) as PART TWO forms an integral part of this publication.*

1 Description

The material shall consist of a suspension of fine particles of technical iprodione, complying with the requirements of FAO specification 278/TC (July 2006), 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 278/SC/M/2, CIPAC Handbook G, p.104, 1995)

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 **Iprodione content** (CIPAC 278/SC/M/3, CIPAC Handbook G, p.104, 1995)

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

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

3 Physical properties

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

pH range: 4.0 to 6.0.

3.2 **Pourability** (MT 148, CIPAC Handbook F, p.348, 1995)

Maximum residue: 5%.

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

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

---

* 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/.

3.4 **Suspensibility** (MT 184, CIPAC Handbook K, p.142, 2003) (Notes 3 & 4)

A minimum of 70% of the iprodione content found under 2.2 shall be in suspension after 30 min in CIPAC standard water D at 30 ± 2°C.

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

Maximum: 1% of the formulation shall be retained on a 75 µm test sieve.

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

Maximum: 25 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 the clauses for:

- spontaneity of dispersion (3.3),
- suspensibility (3.4),
- wet sieve test (3.5).

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 97%, relative to the determined average content found before storage (Note 6), and the formulation shall continue to comply with the clauses for:

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

Note 1 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 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 Chemical assay is the only fully reliable method to measure the mass of active ingredient still in suspension. However, simpler methods such as gravimetric and solvent extraction determination may be used on a routine basis provided that these methods have been shown to give results which are in agreement to those of the chemical assay method. In case of dispute, the chemical method shall be the referee method.

Note 4 This test will normally only be carried out after the heat stability test: 4.2.

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

Note 6 Analysis of the formulation, before and after the storage stability test, should be carried out concurrently to reduce analytical error.

PART TWO

EVALUATION REPORTS

IPRODIONE

IPRODIONE

FAO/WHO EVALUATION REPORT 278/2004

Recommendations

The Meeting recommended that:

(i) the existing FAO specifications for iprodione TC, WP and SC should be withdrawn;

(ii) the specifications for iprodione TC, WP, WG and SC proposed by Bayer CropScience and BASF, as amended, should be adopted by FAO.

Appraisal

The Meeting considered data on iprodione, submitted by Bayer CropScience and BASF, for review of existing (1999) FAO specifications for TC, WP and SC and a proposed new specification for WG.

Iprodione is a non-systemic fungicide, widely used in agriculture. It is not under patent.

Iprodione is a solid (m.p. 133ºC) of low vapour pressure (5×10^{-7} at Pa 25^0C), with log P Kow of 3.0. It is slowly hydrolyzed at pH 5 and progressively more rapidly at higher pH values. It is degraded only slowly by photolysis. Its water solubility is not pH dependent and iprodione has no acidic or basic properties.

Iprodione has been evaluated for toxicology and residues by the JMPR on a number of occasions and has been reviewed by the US EPA and the EU. The Meeting asked the manufacturer to provide evidence to whether or not cataracts may be induced by iprodione (certain other dicarboximides present this hazard). The manufacturer stated (M-267118-01-1) that iprodione does not induce cataracts and referred to 7 unpublished studies which addressed this issue (M-211475-01-1, M-211414-01-1, M-213190-01-2, M-213364-01-1, M-160902-01-1, M-210816-01-1 and M-210652-01-1).

The Meeting was provided with confidential information on the manufacturing process and the manufacturing specifications for all impurities ≥1 g/kg, which were supported by 5 batch analyses. Mass balances were high, in the range 997 to 1001 g/kg. These data were confirmed as identical to those submitted in support of registration of iprodione in The Netherlands. Information was provided on the methods of analysis used for determination of all impurities.

The Meeting questioned whether one of the impurities, 3,5-dichloroaniline (which is also a metabolite of iprodione), should be considered relevant for specifications purposes. Information relating to the toxicity of 3,5-dichloroaniline (M-213979-01-1, 1997/1002678, Rashid *et al*. 1987, Yoshimi 1988, Valentovic *et al*. 1997, Rankin *et al.* 1986 and Lo *et al*. 1990) was provided by the manufacturer (M-267118-01-1) to WHO/PCS. After reviewing the data, the PCS secretariat concluded (PCS 2005) that (i) 3,5-dichloroaniline does not show toxicity that is qualitatively different from iprodione; (ii) the irritation characteristics of the impurity are not reflected in iprodione

TC; and (iii), in the improbable worst-case scenario of 3,5-dichloroaniline occurring at 40 g/kg in iprodione TC (minimum purity 960 g/kg), it would not contribute significantly to the acute toxicity of the TC. WHO/PCS therefore concluded that 3,5-dichloroaniline does not constitute a relevant impurity and the Meeting agreed. No other impurities were considered to be relevant.

Analytical methods for the TC, WP and SC are full CIPAC methods. The manufacturer stated that, after grinding, the WG is effectively in the form of a WP and provided an in-house validation study showing that the CIPAC method for WP was appropriate for analysis of the WG. The Meeting accepted the evidence presented.

Test methods for physical properties of the formulations, referenced in the specifications, are all full CIPAC methods.

The Meeting considered the proposed specifications for TC, WP, WG and SC.

TC. The Meeting welcomed the proposed lower limit for iprodione content of 960 g/kg, which was higher than the 940 g/kg in the existing specification.

The Meeting questioned the requirement for a clause for “loss on drying”, which also appeared in the existing specification (though with a new limit of 20 g/kg instead of 10 g/kg). The manufacturer explained that the clause was primarily intended to control the water content (and hence to limit potential hydrolysis of active ingredient) but provided a faster and cheaper method than direct measurement of water. The Meeting agreed to the proposed clause.

WP. The Meeting noted that the proposed specification was broadly similar to the existing specification, with some limits having been changed slightly. The manufacturer stated that the clauses to restrict water content and pH are essential to maintain quality of the formulation and avoid loss of active ingredient.

WG. The Meeting noted that the clauses in this proposed new specification were in accordance with the WG guideline in the manual (FAO/WHO 2002) but questioned the limits (8.9-9.9) given for pH range, because the hydrolysis half-life of iprodione is only 27 min at pH 9. Although the water content of the WG is limited to 8 g/kg, it appeared possible that degradation could occur during storage or use (the corresponding limits proposed for WP and SC were pH 4 to 6). The manufacturer provided a report (M-210100-01-1) to show that storage stability of the WG is satisfactory. The pH of diluted WG suspensions (at concentrations corresponding to normal use) decreased very rapidly after initial dispersion. Over a 3 h period, the pH declined from 8.9 to 7 in CIPAC water A and from 8.0 to 7.8 in CIPAC water D. During the following 3 days, the pH in CIPAC water A remained unchanged but there was a small decrease to pH 7.4 in CIPAC water D. Over the 3-day period, the iprodione content had declined by only 3% in both waters. Thus the initial pH of the dispersed WG is not indicative of potential hydrolysis. The manufacturer stated that while it was known that formulation quality is maintained in the proposed pH range, no information was available to show whether or not adverse effects occur at higher or lower pH. In the absence of such information, the Meeting agreed that the proposed clause and limits should be adopted on a precautionary basis.

SC. The Meeting accepted that the clause to restrict pH is essential to avoid loss of active ingredient but questioned whether the rearrangement of iprodione (to an isomer with low fungicidal activity), known to occur in alcoholic solution (Cooke *et al*. 1979), could occur in the SC. The manufacturer indicated that compliance with the clause for stability at elevated temperature showed that the rearrangement did not

occur.

SUPPORTING INFORMATION
FOR
EVALUATION REPORT 278/2004

Uses

Iprodione is non-systemic dicarboxamide fungicide, with both protectant and eradicant properties. It is active against both spores and mycelium of a number of parasitic fungi. It is used in as a selective contact fungicide to control diseases in a wide range of fruit, vines, vegetable crops, cereals, oilseed rape, sunflower, ornamental plants and turf.

Identity of the active ingredient

ISO common name

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

Synonyms

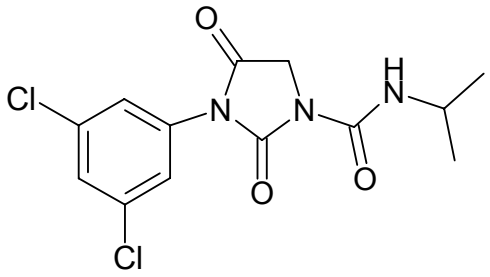
Glycophene (rejected common name proposal)

Chemical names

IUPAC 3-(3,5-dichlorophenyl)-*N*-isopropyl-2,4-dioxo-imidazolidine-1-carboxamide

CA 3-(3,5-dichlorophenyl)-*N*-(1-methylethyl)-2,4-dioxo-1-imidazolidinecarboxamide

Structural formula



Empirical formula

$C_{13}H_{13}Cl_2N_3O_3$

Relative molecular mass

330.2

CAS Registry number

36734-19-7

CIPAC number

278

Identity tests

HPLC retention time; IR spectrum

Physico-chemical properties of iprodione

Table 1. Physico-chemical properties of pure iprodione

Parameter	Value(s) and conditions	Purity %	Method	Reference
Vapour pressure	5×10^{-7} Pa at 25°C 2×10^{-8} Pa at 35°C 4×10^{-5} Pa at 51°C	99.7	OECD104	M-189561-01-1
Melting point, boiling point and/or temperature of decomposition	Melting point: 133.4°C Boiling point: undetermined Decomposition point: 164.5°C	99.7	OECD 102, ECA1 OECD 103, ECA2 OECD 103, ECA2	M-189622-01-1
Solubility in water	12.2 mg/l at 20°C at pH 7 No dissociation in water, so no other pH measurement	96.1	EPA series 63-8, EEC A6	M-209773-01-1
Solubility in organic solvents (g/l at 20°C)	acetone: 342 hexane: 0.59 acetonitrile: 168 dichloromethane: 450 ethyl acetate: 225 toluene: 147 octanol: 10.0	96.1	EPA 63-8, EEC A6	M-209773-01-1
Octanol/water partition coefficient (at 25°C)	log P K_{OW} = 2.99 at pH 3 log P K_{OW} = 3.00 at pH 5 log P K_{OW} is independent of pH	99.7	EPA series 63-11, EEC A8	M-209810-01-1
Hydrolysis characteristics	Half-life = 130.7 d at pH 5 Half-life = 6.4 d at pH 7 Half-life = 27.2 min. at pH 9 At 20-25°C in the dark, iprodione is stable at pH ≤ 5. It is increasingly unstable at pH ≥ 6.	98.0	EPA series 161-1	M-189558-01-1
Photolysis characteristics	In pH 5 buffer, the half live was about 67 d of the equivalent of summer sunlight in Florida. No reaction products accounted for >10%.	99.3	EPA series 161-2	M-189545-01-1
Dissociation characteristics	Iprodione does not dissociate.	-	OECD 112 Assessment	M-189579-01-1

Table 2 Chemical composition and properties of technical iprodione (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 99.6-100.1% and no unknowns were reported
Declared minimum iprodione content	960 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 or boiling temperature range of the TC	128-130°C decomposition occurs at 153°C

Hazard summary

Iprodione has been evaluated by the FAO/WHO JMPR (JMPR 1977, 1980, 1992a, 1992b, 1994a, 1994b, 1995a, 1995b, 2001). The JMPR (JMPR 1995a, 1995b) allocated an ADI of 0-0.06 mg/kg bw/d, based on an NOAEL of 6 mg/kg bw per day derived from a 2-year study of carcinogenicity in rats and a safety factor of 100. It was also concluded that the intake of residues of Iprodione, resulting from its uses considered by the JMPR, is unlikely to present a public health concern (JMPR 1995a, 1995b).

In the EU, it is listed in the Annex I of directive 91/414/EC (EU 2003). With respect to wildlife, the EU concluded that use of iprodione is unlikely to pose a significant risk to birds but that it should be classified as very toxic to aquatic organisms (Commission Directive 2001/59/EC, 6 July 2001).

The U.S. EPA considered that registered uses of iprodione will not cause unreasonable risk to humans (EPA 1991).

The WHO classification of iprodione is U: unlikely to cause acute hazard in normal use (WHO 2002).

Formulations

The main formulation types are WP, WG and SC. These formulations are registered and sold in about 90 countries, in all continents. Iprodione may be co-formulated with other fungicides, such as carbendazim, thiophanate-methyl, diniconazole or bromuconazole.

Methods of analysis and testing

The analytical method for determination of the active ingredient (including identity tests) is a full CIPAC method. Iprodione is determined by reversed-phase HPLC, utilising internal standardization with propiophenone and UV detection at 220 nm. Although the method was validated by CIPAC for analysis of WP and SC, not WG, grinding the WG produces (for analytical purposes) material similar to WP and the CIPAC method for WP may then be used to analyze the powdered material (M-203801-02-1). Identification is by HPLC retention time and IR spectrum.

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

Physical properties

The physical properties, the methods for testing them and the limits proposed for the WP, SC and WG formulations, comply with the requirements of the FAO/WHO manual, 1st edition (FAO/WHO 2002).

Containers and packaging

No special requirements for containers and packaging have been identified.

Expression of the active ingredient

The active ingredient is expressed as iprodione (g/kg in WP and WG; g/kg or g/l in SC).

ANNEX 1

HAZARD SUMMARY PROVIDED BY THE PROPOSER

Note: Bayer CropScience provided written confirmation that the toxicological and ecotoxicological data included in the following summary were derived from iprodione having impurity profiles similar to those referred to in Table 2, above.

Table A. Toxicology profile of iprodione technical material, based on acute toxicity, irritation and sensitization

Species	Test	Duration and conditions or guideline adopted	Purity %	Result	Reference
Rat, Sprague Dawley	Oral	Gavage, guideline not stated. Observed 14 d.	97.9	LD_{50} >2000 mg/kg bw	M-210407-01-1
Dog, beagle	Oral	Gavage, guideline not stated. 1000 and 2000 mg/kg. Observed 14 d.	Not known	LD_{50} >2000 mg/kg bw	M-210404-01-1
Rabbit	Dermal	24-h exposure. Observed 14 d post-treatment, guideline not stated.	95.8	LD_{50} >2000 mg/kg bw	M-210415-01-2
Rat, Sprague Dawley	Inhalation	4-h whole body exposure, guideline not stated.	96.0	LC_{50} >5.16 mg/l	M-189593-01-2
Rabbit, New Zealand white	Skin irritation	4-h exposure (abraded and intact skin). Skin evaluated at 72 h post-treatment, guideline not stated.	96.2	Non irritating	M-189547-01-2
Rabbit, New Zealand white	Eye irritation	Eyes evaluated at 1, 24, 72 h and day 7, guideline not stated.	96.2	Non irritating*	M-189546-01-1
Guinea pig, Hartley albino	Skin sensitization	9 topical induction applications, 2 weeks later a challenge treatment, followed 1 week later by a 2nd challenge treatment (Buehler)	95.8	Non sensitizer	M-210418-01-1

* Technical iprodione caused mild and transient eye irritation without eye washing, whereas it is not irritant to the rabbit eye when instillation is followed by eye washing.

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

Species	Test	Duration and conditions or guideline adopted	Purity %	Result	Reference
Rabbit, New Zealand White (m,f)	Dermal study	21-d, guideline not stated. 0, 100, 500 and 1000 mg/kg/day	96.2	NOEL = 1000 mg/kg bw/d. No critical effects	M-213195-01-1
Rat, Crl/CD (m,f)	Sub-chronic dietary study	90-d, guideline not stated. 0, 250, 500, 800, 3000 ppm	97.1	NOEL = 500 ppm or 33.3 mg/kg bw/d. No critical effects. Effects at 800 ppm: decreased body weight gain and increased incidence and severity of corticocellular vacuolation of the adrenals	M-189655-01-1

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

Species	Test	Duration and conditions or guideline adopted	Purity %	Result	Reference
Dog, beagle (m,f)	90-d dietary study	90-d, guideline not stated. 0, 800, 2400, and 7200 ppm	100	NOEL = 2400 ppm or 60-76 mg/kg bw/d. No critical effects. Effects at 7200 ppm: slight hepatomegaly and increase in alkaline phosphatase activity	M-247665-01-2
Dog, beagle (m,f)	1-year dietary studies	1st study: 0, 100, 600 and 3,600 ppm, guideline not stated.	96.5	NOEL = 100 ppm or 4.2 mg/kg bw/d. No critical effects. Effects at 600 ppm: transient increase in Heinz bodies, lower prostate weight, slight adrenals and kidney microscopic changes	M-211475-01-1
		2nd study: 0, 200, 300, 400 and 600 ppm., guideline not stated	96.1	NOEL = 400 ppm or 18 mg/kg bw/d. No critical effects. Effects at 600 ppm (NOAEL): slight and occasional significant reduction in RBC, Hb and Ht	M-211465-02-1
Rat, Sprague Dawley (m,f)	Oncogenicity, chronic toxicity study	0, 150, 300 and 1600 ppm, guideline not stated	Not stated	NOEL = 150 ppm or 6.1 and 8.4 mg/kg/day (m & f respectively), mean = 7.25 mg/kg/day No critical effects*	M-189567-02-1

* Effects observed at 300 ppm: Increased liver weight, slight centrilobular hepatocyte enlargement, atrophy or reduced activity of male accessory sexual glands, vacuolation of the *"zona reticularis* " (male) in adrenals and interstitial cell hyperplasia in testes. Effects observed at 1600 ppm: similar lesions plus generalized vacuolation of the "*zona fasciculata*" and "*zona reticularis*" in adrenals (males) and significantly increased testes weight related to increased incidence of interstitial cell tumours in testes with cell hyperplasia and atrophy of seminiferous tubules. Leydig cell tumours arose only at a high dose level (≥MTD, 1600 ppm). A clear NOEL (150 ppm) and a clear threshold for oncogenic effects (300 ppm) were determined. Iprodione was shown to act via a disruption of testosterone biosynthesis from interstitial cells which in turn causes perturbation in the hypothalamic-pituitary gonadal axis. The overproduction of LH results in the overstimulation of leydig cells and tumours may then further develop in sensitive species, such as the rat, due to persistent hyperplasia. Mechanistic studies have demonstrated the existence of a clear threshold for these effects on testosterone and LH biosynthesis. Iprodione was shown to be non genotoxic. Hence the tumours observed in Leydig cells of rats receiving high doses of iprodione (10-fold higher than the NOEL of the 2-year rat carcinogenicity study) are considered to be of limited concern.

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

Species	Test	Duration and conditions or guideline adopted	Purity %	Result	Reference
Mouse, CD-1 (m,f)	Oncogenicity study	0, 160, 800 and 4000 ppm, guideline not stated	97.5	NOEL = 160 ppm or 23 and 27 mg/kg bw/d (m & f respectively), mean value of 25 mg/kg/day. No critical effects**	M-211435-04-1
Rat, Sprague-Dawley (m,f)	2-generation reproduction	Dietary administration, 0, 300, 1,000 and 3,000 ppm, guideline not stated.	96.2	NOEL = 300 ppm or 20 mg/kg bw/d. No critical effects observed. Effects at 1000 and 3000 ppm: depression of body weight gain in F0 and F1, lower food consumption in F0 and F, lower number of live pups/litter and lower pup weight, poor health of pups	M-211460-01-1
Rat, Sprague-Dawley (f)	Developmental toxicity study	Gavage, 0, 40, 90 and 200 mg/kg bw/d, guideline not stated	94.2	NOEL = 90 mg/kg bw/d. No teratogenic effects	M-214215-02-1
Rabbit, New Zealand White (f)	Developmental toxicity study	Gavage 0, 20, 60 and 200 mg/kg bw/d, guideline not stated	95	NOEL = 20 mg/kg bw/d No teratogenic effects	M-231159-01-1

Table C. Mutagenicity profile of iprodione technical material based on *in vitro* and *in vivo* tests

Species	Test	Conditions	Purity %	Result	Reference
Salmonella typhimurium, strains TA98, TA100, TA1535, TA1537 and TA1538.	Bacterial reverse mutation assay (Ames), *in vitro*	10-5000 µg/plate with activation, 1-250µg/plate without activation	95 to 99.3	Negative	M-214044-01-1, M-214045-01-1, M-214052-01-2, M-208976-01-1, M-242402-01-2

** Centrilobular hypertrophy enlargement (female), vacuolation and hypertrophy of interstitial cells in testes, hyperkeratosis of non-glandular stomach. Effects observed at 4000 ppm: increased liver weight, decreased uterus weight, increased incidence of benign and malignant liver cell tumors and slight increase of luteomas in females ovaries, vacuolation and hypertrophy of interstitial cells in testes, hyperkeratosis of non-glandular stomach, heamosiderosis in spleen, amyloidosis and cortical scarring in kidneys (female). Liver tumours arose only at a high dose level which were at or exceeded the MTD (4000 ppm). A clear NOEL (160 ppm) and threshold for oncogenic effects (800 ppm) were determined. Iprodione was shown to act via a phenobarbital-like mechanism, which is widely considered to be non relevant to humans. Iprodione was shown to be non genotoxic. Hence the tumours observed in the liver of mice receiving high dose of iprodione (25-fold higher than the NOEL of the mice oncogenicity study) are considered to be of limited concern.

Table C. Mutagenicity profile of iprodione technical material based on *in vitro* and *in vivo* tests

Species	Test	Conditions	Purity %	Result	Reference
E. coli, po/A$^{+/-}$	DNA repair assay, *in vitro*	12.5-200 µg/plate, with and without S9 activation	95.1 & 99.3	Negative	M-214044-01-1, M-214045-01-1
CHO/HGPRT	Mammalian cell gene mutation	5-100 µg/ml (without activation), 100-1500 µg/ml with activation	Not known	Negative	M-214055-01-1
Mouse (CD-1), (m,f)	Micronucleus formation assay, *in vivo*	1 dose by gavage at equivalent to 0-3000 mg/kg iprodione	96.1	Negative	M-189578-01-1
Chinese hamster ovary cells	sister chromatid exchange, *in vitro*	5-100 µg/ml without activation, 5-400 µg/ml with activation	Not known	Negative	M-209011-01-1
Chinese hamster ovary cells	Chromosome aberrations in CHO cells *in vitro*	15-150 µg/ml without activation, 40-400 µg/ml with activation	Not known	Negative	M-214057-01-1
Bacillus subtilis, 19-strains M45(rec-) and H17(rec+) strains	Recombination assay, *in vitro*	20.6, 61.9, 185.6, 556.7 and 1670 µg/disc	96.8	Positive response at 20.6, 61.9 and 1670 µg/disc but not at 185.6 and 556.7*	M-214041-01-1

* These results were considered by the manufacturer to be of doubtful significance, due to several deficiencies in the testing method.

Table D. Ecotoxicology profile of iprodione technical material

Species	Test	Duration and conditions	Purity %	Result	Reference
Daphnia magna (water flea)	Acute toxicity	48-h flow-through, observed at 24 and 48 h. 48-h static	96.2 97.3	EC_{50} = 0.25 mg/l EC_{50} = 0.66 mg/l	M-189543-01-1 M-211781-01-1
Lepomis macrochirus (bluegill sunfish)	Acute toxicity	96-h, flow-through, 20°C	96.2	LC_{50} = 3.7 mg/l	M-189541-01-1
Oncorhynchus mykiss (rainbow trout)	Acute toxicity	96-h, static, 12°C	96.2	LC_{50} = 4.1 mg/l	M-211742-01-1
*Selenastrum capricornutum (*green algae)	Effect on growth	FIFRA guidelines 122-2 and 123-2, 120 h	96.2	EC_{50} = 1.9 mg/l	M-189542-01-1
Eisenia foetida (earthworm)	Acute toxicity	14 d, artificial soil	96.1	LC_{50} >1000 mg/kg soil (dry weight)	M-189556-01-1
Apis mellifera (honey bee)	Acute contact toxicity	Topical application, observed at 24 and 48h, 24°C	97.1	LD_{50} >200 µg/bee	M-189653-01-1
Apis mellifera (honey bee)	Oral toxicity (normal feeding)	Dosed and observed for 24 and 48 h, 24°C	97.1	LD_{50} >25 µg/bee	M-189654-01-1

Table D. Ecotoxicology profile of iprodione technical material

Species	Test	Duration and conditions	Purity %	Result	Reference
Anas platyrhynchos (Mallard duck)	Acute oral toxicity	Administered orally, as 2% cellulose gum (CMC) suspension, or in gelatine capsules, up to 10400 mg/kg bw	Not known	LD_{50} >10400 mg/kg bw	M-210594-01-1
Colinus virginianus (Bobwhite quail)	Acute oral toxicity	Single dose administered in corn oil. Observed 14 d post-treatment	96.2	LD_{50} >2000 mg/kg bw	M-211328-01-1
Anas platyrhynchos (Mallard duck)	Dietary sub-acute toxicity	8-day (5-day exposure, 3-day observation), up to 5620 ppm	96.2	LC_{50} >5620 ppm	M-211322-01-1
Colinus virginianus (Bobwhite quail)	Dietary sub-acute toxicity	8-day (5-day exposure, 3-day observation), up to 5620 ppm	96.2	LC_{50} >5,620 ppm	M-211319-01-1

ANNEX 2. REFERENCES

Bayer CropScience document number or other reference	Year and title of report or publication details
1997/1002678	1997. Salmonella typhimurium reverse mutation assay with Norharman on 3,5-dichloroaniline and 4-chloroaniline.
Cooke *et al*. 1979	Cooke X. *et al*.1979. The structural rearrangement of iprodione in ethanolic solution. *Pesticide Science*, **10**, 393-398, 1979.
EPA 1991	U.S. EPA, 1991. Integrated Risk Information System (IRIS). Iprodione (Rovral).
EU 2003	Directive 203/31/EC, Official Journal of the European Communities, L101/3, 23 April 2003.
FAO/WHO 2002	Manual on the development and use of FAO and WHO specifications for pesticides, 1st edition, FAO Plant production and protection paper 173, FAO, Rome, 2002.
JMPR 1977	Pesticide residues in food: 1977 evaluations. FAO Plant Production and Protection Paper 10 Sup. FAO, Rome, 1977.
JMPR 1980	Pesticide residues in food: 1980 evaluations. FAO Plant Production and Protection Paper 26 Sup. FAO, Rome, 1980.
JMPR 1992a	Pesticide residues in food: 1992 Report. FAO Plant Production and Protection Paper 116. FAO, Rome, 1992.
JMPR 1992b	Pesticide residues in food – 1989. Report of the Joint Meeting of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Expert Group on Pesticide Residues. WHO/PCS/93.34, 1992.
JMPR 1994a	Pesticide residues in food – 1994. Report of the Joint Meeting of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Expert Group on Pesticide Residues. FAO Plant Production and Protection Paper 127. FAO, Rome, 1992.
JMPR 1994b	Pesticide residues in food – 1994. Evaluations 1994, part I-residues, Volume 1, FAO Plant Production and Protection Paper 131/1. FAO, Rome, 1992.
JMPR 1995a	Pesticide residues in food – 1995. Report. FAO Plant Production and Protection Paper 133. FAO, Rome, 1992.
JMPR 1995b	Pesticide residues in food – 1995, Evaluations 1995. WHO/PCS/96.48.
JMPR 2001	Pesticide residues in food – 2001 Report 2001. FAO Plant Production and Protection Paper 167. FAO, Rome, 2001.
Lo *et al*. 1990	Lo, H.H. *et al*., 1990. Acute nephrotoxicity induced by isomeric dichloroanilines in Fisher 344 rat. *Toxicology*, **63** (2): 215-231, 1990.
M-160902-01-1	1991. EXP1861-Acute eye irritation test in rabbits.
M-189541-01-1	1990. Iprodione technical - acute toxicity to bluegill sunfish (Lepomis macrochirus) under flow-through conditions.
M-189542-01-1	1990. Iprodione technical - toxicity to the freshwater green alga Selenastrum capricornutum.
M-189543-01-1	1990. Iprodione technical - acute toxicity to daphnids (Daphnia magna) during a 48-hour flow-through exposure.
M-189545-01-1	1991. 14C, Iprodione aqueous photolysis.
M-189546-01-1	1991. Primary eye irritation study in rabbits with iprodione (EPA-FIFRA) final report.
M-189547-01-2	1991. Primary skin irritation study in rabbits with iprodione (EPA-FIFRA) final report.
M-189556-01-1	1992. The acute toxicity of iprodione to earthworms (Eisenia foetida).
M-189558-01-1	1990. Hydrolysis of iprodione in aqueous solutions buffered at pH 5,7 and 9.
M-189561-01-1	1992. The Vapour pressure of Iprodione.
M-189567-02-1	1999. Iprodione potential tumorigenic and toxic effects in prolonged dietary administration to rats.
M-189578-01-1	1994. Iprodione mouse micronucleus test. Bayer CropScience.
M-189579-01-1	1994. Iprodione-Dissociation constant, dissociation.
M-189593-01-2	1993. Iprodione: Acute Dust Inhalation Toxicity Study in Rats.
M-189622-01-1	2000. Iprodione- melting, boiling point and decomposition point..

Bayer CropScience document number or other reference	Year and title of report or publication details
M-189653-01-1	1995. A laboratory determination of the topical and oral LD50s for honey bees exposed to technical-grade iprodione.
M-189654-01-1	1995. A laboratory determination of the topical and oral LD50s for honey bees exposed to technical-grade iprodione.
M-189655-01-1	1997. Iprodione 90-day toxicity study in the rat by dietary administration.
M-203801-02-1	2000. EXP10887C – Determination of physico-chemical characteristics and storage stability.
M-208976-01-1	1980. Supplementary studies of mutagenesis in microorganisms Iprodione (26019R.P).
M-209011-01-1	1985. In vitro sister chromatid exchange in Chinese hamster ovary cells (CHO) Iprodione.
M-209773-01-1	1991. Iprodione technical grade-Solubility at 200C.
M-209810-01-1	1992. Determination of the Octanol/water partition coefficient of iprodione.
M-210100-01-1	2002. EXP10887C (WG) – Chemical stability of iprodione in CIPAC A & D water.
M-210404-01-1	1974. Acute toxicity and local tolerance.
M-210407-01-1	1989. Iprodione: Acute oral toxicity study in the rat.
M-210415-01-2	1987. Acute dermal limit test in the rabbit Iprodione (technical).
M-210418-01-1	1987. Dermal sensitization test in the guinea pig (Buehler method) Iprodione (technical).
M-210594-01-1	1994. The determination of the acute oral LD50 in mallard duck for 26019RP.
M-210652-01-1	2002. EXP10887C-Acute eye irritation in the rabbits.
M-210816-01-1	1991. EXP1862F-Acute eye irritation test in rabbits
M-211319-01-1	1990. Iprodione technical: A dietary LC50 study with the Northern bobwhite.
M-211322-01-1	1990. Iprodione technical: A dietary LC50 study with the mallard.
M-211328-01-1	1990. An acute oral toxicity study with the Northern bobwhite Iprodione.
M-211414-01-1	1978. Chronic toxicologic and carcinogenic study with RP26019 in rats (24 month).
M-211435-04-1	1999. Iprodione - Potential tumorigenic effects in prolonged dietary adminstration to mice.
M-211460-01-1	1991. Two generation reproduction study with iprodione technical in rats.
M-211465-02-1	1995. A 52 week dietary toxicity study of iprodione in the beagle dog.
M-211475-01-1	1984. Iprodione: 52-week toxicity study in dietary administration to beagle dogs.
M-211742-01-1	1990. Iprodione technical - Acute toxicity to rainbow trout (Oncorhynchus mykiss) under flow-through conditions.
M-211781-01-1	1997. Acute toxicity (48 hours) to Daphnids (Daphnia magna) under semi-static conditions.
M-213190-01-2	1977. Histological examination of ocular toxicity in, dog after three months treatment.
M-213195-01-1	1991. 21-day dermal toxicity study in rabbits with iprodione technical.
M-213364-01-1	1999. EXP1671H-Acute eye irritation study of Rovral fungicide in albino rabbits.
M-213979-01-1	1974. Intermediate of the manufacture of RP 26019: RP 32596 and RP 32597 – Acute toxicity & local cutaneous tolerance.
M-214041-01-1	1985. DNA damage in Bacillus subtilis with iprodione technical.
M-214044-01-1	1982. Iprodione (26 019 R.P.) technical grade compound in vitro mutagenesis in microorganisms.
M-214045-01-1	1980. Iprodione (26 019 R.P.) - Supplementary studies of mutagenesis in microorganisms.
M-214052-01-2	1990. Mutagenicity test on iprodione (technical) in the Salmonella/mammalian-microsome reverse mutation assay (Ames test) with confirmatory assay.
M-214055-01-1	1985. CHO/HGPRT - Mammalian cell forward gene mutation assay Iprodione.
M-214057-01-1	1985. CHO metaphase analysis In vitro chromosome aberration analysis in Chinese hamster ovary cells (CHO) Iprodione.
M-214215-02-1	1987. Iprodione (technical grade): Teratology study in the rat.
M-231159-01-1	1985. A teratology study in rabbits with iprodione.

Bayer CropScience document number or other reference	Year and title of report or publication details
M-242402-01-2	1979. Iprodione (26 019 R.P.) - In-vitro mutagenicity study in Salmonella typhimurium (Ames' strains) and in Saccharomyces cerevisae (Zimmermann's strain D7).
M-247665-01-2	1973. 3 month study of toxicity of 26,019 RP orally in the dog.
M-267118-01-1	2003. FAO Specifications: answer to the FAO/WHO expert questions asked during the FAO/WHO Bucharest meeting (Iprodione_Answers to the last FAO questions.pdf). Bayer letter to G. Vaagt (FAO), dated 12 November 2003. Ref: BCS/GRA/BAJ/03027. Unpublished. BCS Doc ID: M-267118-01-1.
PCS 2005	The relevance of the impurity 3,5-dichloroaniline in iprodione. WHO/PCS, 20 September 2005. Unpublished report. Attachment to e-mail sent by A. Aitio (WHO/PCS) to M. Zaim (WHOPES) and G Vaagt, (FAO), 7 October, 2005.
Rankin *et al.* 1986	Rankin, G.O. *et al*., 1986. 3,5-dichloroaniline-induced nephrotoxicity in the Sprague Dawley rat. *Toxicol. Lett*., **30**: 173-179, 1986.
Rashid *et al*. 1987	Rashid, K.A. *et al*., 1987. Mutagenicity of chloroanilin / lignin metabolites in the salmonella/microsome assay. *J. Environ. Sci. Health*, Part B, **B 22** (6): 721-729.
Valentovic *et al*. 1997	Valentovic, *et al*., 1997. Characterisation of methemoglobin formation induced by 3,5-dichloroaniline, 4-amino-2,6-dichlorophenol and 3,5-dichlorophenylhydroxylamine. *Toxicology*, **118** (1): 23-36, 1997.
WHO 2002	The WHO recommended classification of pesticides by hazard and guidelines to classification 2000-2002. WHO, Geneva, 2002.
Yoshimi 1988	Yoshimi, N., 1988. The genotoxicity of a variety of aniline derivatives in a DNA repair test with primary cultured rat hematocytes. *Mutat. Res*., **206**: 183-191, 1988.