FAO SPECIFICATIONS AND EVALUATIONS

FOR PLANT PROTECTION PRODUCTS

PROCYMIDONE

N-(3,5-Dichlorophenyl)-1,2-dimethylcyclopropane-1,2-dicarboximide

2001

Food and Agriculture Organization
of the United Nations

TABLE OF CONTENTS

PROCYMIDONE

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INTRODUCTION

FAO establishes and publishes specifications* for technical material and related formulations of plant protection products 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 Panel of Experts on Pesticide Specifications, Registration Requirements, Application Standards and Prior Informed Consent."
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 Panel of Experts. 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 methods of synthesis. FAO has the possibility to extend the scope of the specifications to similar products, but only when the Panel of Experts has been satisfied that the additional products are equivalent to those which formed the basis of the reference specification.

* Footnote: The publications are available on the Internet under (http://www.fao.org/pest-and-pesticide-management/en) or as hardcopy from the Plant Protection Information Officer.

PART ONE

SPECIFICATIONS

PROCYMIDONE

FAO SPECIFICATIONS AND EVALUATIONS FOR
PLANT PROTECTION PRODUCTS

PROCYMIDONE

INFORMATION

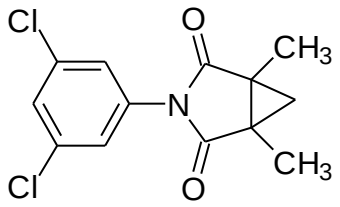
ISO common name
procymidone (E-ISO, F-ISO [f])

Synonyms
S-7131 (Sumitomo)

Chemical names
IUPAC N-(3,5-Dichlorophenyl)-1,2-dimethylcyclopropane-1,2-dicarboximide

CA 3-(3,5-Dichlorophenyl)-1,5-dimethyl-3-azabicyclo[3.1.0]hexane-2,4-dione

Structural formula



Molecular formula
$C_{13}H_{11}Cl_2NO_2$

Relative molecular mass
284.1

CAS Registry number
32809-16-8

CIPAC number
383

EEC number
251-233-1 (EINECS)

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PROCYMIDONE TECHNICAL MATERIAL

FAO Specification 383/TC (2001)

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 (383/2001). It should be applicable to relevant products of 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 the products of other manufacturers. The evaluation report (383/2001) as PART TWO forms an integral part of this publication.

1 Description

The material shall consist of procymidone together with related manufacturing impurities and shall be off-white to light brown granular crystals or powder, free from visible extraneous matter and added modifying agents.

2 Active ingredient

2.1 **Identity tests** (383/TC/M/2, CIPAC)

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 **Procymidone content** (383/TC/M/3, CIPAC)

The procymidone content shall be declared (not less than 985 g/kg) and, when determined, the mean measured content shall not be lower than the declared minimum content.

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PROCYMIDONE WETTABLE POWDER

FAO Specification 383/WP(2001)

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 (383/2001). It should be applicable to relevant products of 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 the products of other manufacturers. The evaluation report (383/2001) as PART TWO forms an integral part of this publication.

1 Description

The material shall consist of an homogeneous mixture of technical procymidone, complying with the requirements of FAO specification 383/TC, together with fillers and any other necessary formulants. 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** (383/WP/M/2, CIPAC)

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 **Procymidone content** (383/WP/M/3, CIPAC)

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

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

3 Physical properties

3.1 **pH range** (MT 75, CIPAC F, p.205)

pH range: 4 to 8.

3.2 **Wet sieve test** (MT 59.3, CIPAC F, p.179)

Maximum: 2% retained on a 75µm test sieve.

3.3 **Suspensibility** (MT 15.1, CIPAC F, p.45) (Notes 1 and 2)

A minimum of 60% of the procymidone content found under 2.2 shall be in suspension after 30 min in CIPAC Standard Water D at 30 ± 2°C (Notes 3 & 4).

3.4 **Persistent foam** (MT 47.2, CIPAC F, p.152) (Note 5)

Maximum: 60 ml after 1 min.

3.5 **Wettability** (MT 53.3.1, CIPAC F, p.164)

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

4 Storage stability

4.1 **Stability at elevated temperature** (MT 46, CIPAC F, p.148)

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), wet sieve test (3.2), suspensibility (3.3) and wettability (3.5).

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Note 1 The formulation should be tested at the highest and lowest rates of use recommended by the supplier, provided this dose not exceed the conditions given in method MT 15.1.

Note 2 This test will normally only be carried out after the heat stability test 4.1.

Note 3 Unless another temperature is specified.

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. In case of dispute, chemical assay shall be the "referee method".

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

Note 6 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.

PROCYMIDONE WATER DISPERSIBLE GRANULES

FAO Specification 383/WG(2001)

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 (383/2001). It should be applicable to relevant products of 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 the products of other manufacturers. The evaluation report (383/2001) as PART TWO forms an integral part of this publication.

1 Description

The material shall consist of an homogeneous mixture of technical procymidone, complying with the requirements of FAO specification 383/TC, 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** (383/WG/M/2, CIPAC)

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 **Procymidone content** (383/WG/M/3, CIPAC)

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

Declared content in 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 Physical properties

3.1 **pH range** (MT 75, CIPAC F, p.205)

pH range: 5 to 9.

3.2 **Wettability** (MT 53.3.1, CIPAC F, p.164)

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

3.3 **Wet sieve test** (MT 167, CIPAC F, p.416)

Maximum: 2% retained on a 75µm test sieve.

3.4 **Degree of dispersion** (MT 174, CIPAC F, p.435)

Dispersibility: minimum 70% after 1 min of stirring.

3.5 **Suspensibility** (MT 168, CIPAC F, p.417) (Notes 1 and 2)

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

3.6 **Persistent foam** (MT 47.2, CIPAC F, p.152) (Note 4)

Maximum: 60 ml after 1 min.

3.7 **Dustiness** (MT 171, CIPAC F, p.425) (Note 5)

Nearly dust-free.

3.8 **Flowability** (MT 172, CIPAC F, p.430)

100% of the formulation shall pass through a 5 mm test sieve after 20 drops of the sieve.

4 Storage stability

4.1 **Stability at elevated temperature** (MT 46, CIPAC F, p.148)

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), wet sieve test (3.3), degree of dispersion (3.4), suspensibility (3.5) and dustiness (3.7).

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Note 1 The formulation should be tested at the highest and lowest rates of use recommended by the supplier, provided this dose not exceed the conditions given in method MT 168.

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, MT168, may be used on a routine basis provided that it has been shown to give equal results to those of the chemical assay. In case of dispute, chemical assay shall be the "referee method".

Note 3 Unless another temperature is specified.

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

Note 5 Measurement of dustiness must be carried out on the sample "as received" and, where practicable, the sample should be taken from a newly opened container, because changes in the water content of samples may influence dustiness significantly. The optical method, MT 171, usually shows good correlation with the gravimetric method and can, therefore, be used as an alternative where the equipment is available. Where the correlation is in doubt, it must be checked with the formulation to be tested. In case of dispute the gravimetric method shall be used.

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

PROCYMIDONE AQUEOUS SUSPENSION CONCENTRATE

FAO Specification 383/SC(2001)

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 (383/2001). It should be applicable to relevant products of 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 the products of other manufacturers. The evaluation report (383/2001) as PART TWO forms an integral part of this publication.

1 Description

The material shall consist of a suspension of fine particles of technical procymidone, complying with the requirements of FAO specification 383/TC, 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** (383/SC/M/2, CIPAC)

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 **Procymidone content** (383/SC/M/3, CIPAC)

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

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

3 Physical properties

3.1 **Mass per millilitre at 20°C** (MT 3.3, CIPAC F, p.18)

If required, the range of the mass per millilitre (g/ml) at 20 ± 2°C shall be declared.

3.2 **pH range** (MT 75, CIPAC F, p.205)

pH range: 6 to 9.

3.3 **Pourability** (MT 148, CIPAC F, p.348)

Maximum "residue": 8%.

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

A minimum of 70% of the procymidone content found under 2.2 shall be in suspension after 5 min in CIPAC Standard Water D at 30 ± 2°C (Note 4).

3.5 **Suspensibility** (MT 161, CIPAC F, p.394) (Note 3)

A minimum of 70% of the procymidone content found under 2.2 shall be in suspension after 30 min in CIPAC Standard Water D at 30 ± 2°C (Note 4).

3.6 **Wet sieve test** (MT 59.3, CIPAC F, p.179)

Maximum: 0.5% of the formulation shall be retained on a 75µm test sieve.

3.7 **Persistent foam** (MT 47.2, CIPAC F, p.152) (Note 5)

Maximum: 60 ml after 1 min.

4 Storage stability

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

After storage at 0 ± 2°C for 7 days, the formulation shall continue to comply with the clauses for suspensibility (3.5) and wet sieve test (3.6).

4.2 **Stability at elevated temperature** (MT 46, CIPAC F, p.148)

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 (3.2), pourability (3.3), spontaneity of dispersion (3.4), suspensibility (3.5) and wet sieve test (3.6).

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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 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 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 equal results to those of the chemical assay method. In case of dispute the chemical method shall be the referee method.

Note 4 Unless other temperatures and/or times are specified.

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

Note 6 Samples of the formulation taken before and after the storage stability test should be analyzed concurrently after the test in order to reduce analytical error.

PART TWO

EVALUATION REPORT(S)

PROCYMIDONE

FAO SPECIFICATIONS AND EVALUATIONS FOR

PLANT PROTECTION PRODUCTS

PROCYMIDONE

EVALATION REPORT 383/2001

Explanation

The data for procymidone were evaluated in support of new FAO specifications.

Procymidone was evaluated by the FAO/WHO JMPR in 1981, 1989, 1990, 1993 and 1998. It was evaluated by US EPA in 1994, by the Pest Management Regulatory Agency of Canada in 1997 and is currently under evaluation by the European Commission.

The draft specification and the supporting data were provided by Sumitomo Chemical Company, Limited in 2000.

Uses

Procymidone is a dicarboximide fungicide with moderate systemic activity. Although most uses involve foliar application, absorption though roots occurs with translocation to leaves and flowers. Procymidone inhibits spore germination, mycelial growth and triglyceride synthesis in fungi. It is used in agriculture, horticulture and viticulture against *Botrytis sp., Sclerotinia sp., Monilia sp., Alternaria sp., Fusarium sp. and Rhizoctonia sp*.

Identity of the active ingredient

ISO common name

Procymidone (ISO, BSI)

Chemical name(s)

IUPAC

N-(3,5-Dichlorophenyl)-1,2-dimethylcyclopropane-1,2-dicarboximide

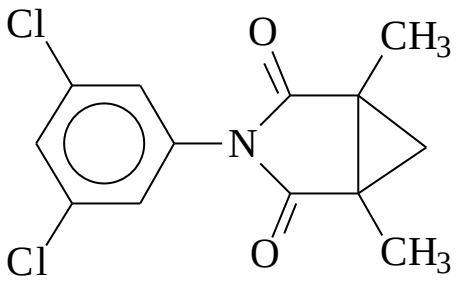
CA

3-(3,5-Dichlorophenyl)-1,5-dimethyl-3-azabicyclo[3.1.0]hexane-2,4-dione

Synonyms

S-7131 (Sumitomo)

Structural formula



Molecular formula

$C_{13}H_{11}Cl_2NO_2$

Relative molecular mass

284.1

CAS Registry number

32809-16-8

CIPAC number

383

EEC number

251-233-1 (EINECS)

Identity tests

GC retention time and IR

Physico-chemical properties of pure procymidone (*Table 1*)

Parameter	Value(s) and conditions	Purity %	Method reference (and technique if the reference gives more than one)
Vapour pressure	2.30×10^{-5} Pa at 25°C. 1.29×10^{-4} Pa at 35°C. 5.41×10^{-4} Pa at 45°C.	100.0	gas saturation method comparable to EC A4
Melting point, boiling point and/or temperature of decomposition	Melting point: 163-164.5 °C Decomposition temperature: 360 °C	99.5 99.9	EEC A1, metal block method OECD 113
Solubility in water (distilled)	1.47×10^{-3} g/l at 10 °C 2.46×10^{-3} g/l at 20 °C 3.07×10^{-3} g/l at 30 °C	99.5	EEC A6
Octanol/water partition coefficient	log P_{OW} = 3.30 at 25 °C (pH 6.0-6.1)	100.0	EEC A8
Hydrolysis characteristics	Half-life (days, hours or minutes) at: pH 15°C 30°C 45°C 2.0 619.5 d 120.4 d 33.9 d 7.1 31.5 d 3.8 d 20 h 9.0 12.7 h 1.9 h 28.4 min	> 99.0	German BBA Method
Photolysis characteristics	DT_{50} = 8 days under sunlight	> 99.0 radio-chemical purity	EPA Guidelines
Dissociation characteristics	No pKa value pH 2-12 at 20°C, decomposition at pH >8	100.0	OECD 112

Chemical composition and properties of procymidone technical materials (TC) (*Table 2*)

Manufacturing process, maximum limits for impurities [3] 1 g/kg, 5 batch analysis data	Confidential information supplied and held on file by FAO. Mass balances were 98.9-99.8 % and percentages of unknowns were 0.2-1.1 %.
Declared minimum procymidone content	985 g/kg
Relevant impurities [3] 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

The FAO/WHO JMPR did not identify any impurities as toxicologically relevant.

Hazard summary

Notes.
(i) The proposer confirmed that the toxicological and ecotoxicological data included in the summary below were derived from procymidone 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 theprocymidone technical material, based on acute toxicity, irritation and sensitization.

Species	Test	Duration and conditions or guideline adopted	Result
mice, male and female	oral	method in general agreement with Directive 92/69/EEC Part B	LD_{50} > 5000 mg/kg bw
rat, male and female	oral	method in general agreement with Directive 92/69/EEC Part B	LD_{50} > 5000 mg/kg bw
mice, male and female	dermal	24 hours, method in general agreement with Directive 92/69/EEC Part B	LD_{50} > 5000 mg/kg bw
rat, male and female	dermal	24 hours, method in general agreement with Directive 92/69/EEC Part B	LD_{50} > 5000 mg/kg bw
rat, male and female	inhalation	4 hours, 1.5 x 10^{-3} mg/m^3 is the highest concentration technically possible, method in agreement with Directive 92/69/EEC Part B	LC_{50} > 15 00 mg/m^3
rabbit, male	skin irritation	moistened, shaved backs of 5 rabbits for 4 hours, method in agreement with Directive 92/69/EEC	non irritant
rabbit, male	eye irritation	5 minutes and 24 hours, method in agreement with Directive 92/69/EEC Part B	non irritant
Guinea-pig, male	skin sensitisation	2 studies, one according to the method of Magnusson and Kligman	non-sensitising

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

Species	Test	Duration and conditions or guideline adopted	Result
mice, male and female	oral, short term toxicity	3-month, method in general agreement with Directive 87/307/EEC Part B	NOEL (male) 22 mg/kg bw/d NOEL (female) 84 mg/kg bw/d
mice, male and female	oral, short term toxicity	3-month, method in general agreement with Directive 87/307/EEC Part B	NOEL (male) 19 mg/kg bw/d NOEL (female) 31 mg/kgbw/d
mice, male and female	oral, short term toxicity	6-month, method in general agreement with Directive 87/307/EEC Part B	NOEL (male) 20 mg/kg bw/d NOEL (female) 24 mg/kg bw/d
mice, male	oral, short term toxicity	6-month, additional study to determine the NOEL for testicular atrophy observed in the 6-month study	NOEL (male) 43 mg/kg bw/d
rat, male and female	oral, short term toxicity	6/9-month, method in general agreement with Directive 87/302/EEC Part B	NOEL 150 ppm (no data available on equivalent concentration)
beagle dog, male and female	oral, short term toxicity	26-week, method in general agreement with Directive 87/302/EEC Part B	NOEL 100 mg/kg bw/d
beagle dog, male and female	oral, short term toxicity	1-year, US EPA 83-1, 1984, method in general agreement with Directive 87/302/EEC Part B	NOEL 100 mg/kg bw/d NOAEL 500 mg/kg bw/d
rat, male and female	feeding, carcinogenicity	2-year, method in general agreement with Directive 87/302/EEC Part B	NOAEL (male) 14 mg/kg bw/d NOAEL (female) 18 mg/kg bw/d
mice, male and female	feeding, carcinogenicity	2-year, method in general agreement with Directive 87/302/EEC Part B	NOAEL (male) 15 mg/kg bw/d NOAEL (female) 23 mg/kg bw/d
rat, male and female	feeding, 2-generation reproduction	2-generation, bodyweight, food intake, mortality, fertility, rearing capacity and the development of the progeny in 2 successive generations	NOEL (parental) 2.5 mg/kg bw/d NOEL (reproduction) 12.5 mg/kg bw/d
rat, male and female	feeding, 1-generation reproduction, supplementary study to the 2-generation study	1-generation, performed to provide information on reproductive organs of F1 males at 5 weeks of age and at sexual maturity (10 week of age)	NOEL (parental) 2.5 mg/kg bw/d NOEL (reproduction) 12.5 mg/kg bw/d

Species	Test	Duration and conditions or guideline adopted	Result
rat, female	teratogenicity and developmental toxicity	oral gavage on days 6 to 15 of gestation. Dams sacrified at day 20, method in general agreement with Directive 87/302/EEC Part B	NOEL (dams and foetuses) 300 mg/kg bw/d
rat, female	teratogenicity and developmental toxicity	modified teratogenicity study - offspring reared to day 45 post-partum, method in general agreement with Directive 87/302/EEC Part B	NOEL (dams, foetuses and offspring) 12.5 mg/kg bw/d
rabbit, female	teratogenicity and developmental toxicity	oral gavage on days 7 to 19 of gestation. Dams sacrified at day 30, method in agreement with Directive 87/302/EEC Part B, US EPA, Japan MAFF	no teratogenicity or embryotoxicity at 1000 mg/kg bw/d

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

Species	Test	Conditions	Result
Salmonella typhymurium	Point mutation assay *in vitro*	Bacterial mutation assay	negative
E. coli	Point mutation assay *in vitro*	Bacterial mutation assay	negative
Salmonella typhymurium	Point mutation assay *in vitro*	Host mediated assay	negative
Chinese hamster V79 cells	Point mutation assay *in vitro*	Mammalian cell mutation assay	negative
Chinese hamster ovary cells (CHO-K1)	Chromosome aberration assay *in vitro*	Cytogenetic study	negative
Bacillus subtilis	DNA damage in *vitro*	Rec assay	negative
Primary cultures from ICR mouse embryos	DNA damage in *vitro*	Sister chromatic assay	negative
Primary rat hepatocytes	DNA damage in *vitro*	Unscheduled DNA synthesis assay	negative
Male ddY mice, bone marrow cells	Chromosome aberration assay in *vivo*	Cytogenetic study	negative

Summary of the toxicological effects

A low acute toxicity was found in the species examined. In sub-chronic studies in mice, rats and dogs, the main effects were increased liver weight and hepatocellular hyperplasia.

In a long-term feeding study, a slightly increased incidence in liver tumours was reported in mice; in rats, decreased weight gain was observed at 1000 and 2000 ppm. At these doses, testicular interstitial cell and ovarian stromal hyperplasia, and an increased incidence of testicular interstitial cell tumours, were observed.

In a 2-generation study in rats, infertility and abnormalites of the male sexual organs were observed in adults and in pups at the highest dose level of 750 ppm.

In teratogenicity studies with rats and rabbits no embryotoxic or teratogenic effects were found. No mutagenic properties were found in various test systems (*in vivo* and *in vitro*). The effects on reproduction and the induction of testicular tumours in the long-term rat study can be explained by the effects of procymidone on the endrocine system.

Table 6. Ecotoxicology profile of the technical material

Species	Test	Duration and conditions	Result
Daphnia magna (water flea)	acute toxicity	48 hours, OECD 202	EC_{50} >1.8 x 10^{-3} g/l
Daphnia magna (water flea)	acute toxicity	48 hours, OECD 202	EC_{50} >4.2 x 10^{-3} g/l
Daphnia magna (water flea)	acute toxicity	48 hours, conducted with the sodium salt of the acid metabolite of procymidone, PCM-NH-COONa (99.9% purity), OECD 202	EC_{50} >95 x 10^{-3} g/l
Daphnia pulex (water flea)	acute toxicity	24 hours, static conditions, in-house method	EC_{50} 10.0 x 10^{-3} g/l
Lepomis macrochirus (bluegill sunfish)	acute toxicity, flow-through	96 hours, US EPA	LC_{50} 10.3 x 10^{-3} g/l
Oncorhynchus mykiss (rainbow trout)	acute toxicity, flow-through	96 hours, US EPA	LC_{50} 7.2 x 10^{-3} g/l
Oryzius latipes (killifish)	acute toxicity, static conditions	72 hours, in-house method	LC_{50} >10 x 10^{-3} g/l
Cyprinus carpio (carp)	acute toxicity, static conditions	72 hours, in-house method	LC_{50} > 10 x 10^{-3} g/l
Oncorhynchus mykiss (rainbow trout)	early life stage test, flow-through	test initiated with newly fertilised eggs (< 24 hours old) and lasted 88 days (60 days post-hatch), OECD 210	NOEC (length and weight) = 0.5 x 10^{-3} g/l NOEC (other parameters) = 1.0 x 10^{-3} g/l LOEC = 1.0 x 10^{-3} g/l
Cyprinus carpio (carp)	bioconcentration in fish	nominal water concentrations of 0.1 ppm and 0.01 ppm, method in "The Japanese Control Law"	After transferring the treated fish to procymidone-free water, procymidone was eliminated quickly from fish tissue, with a half-life of <3 days for each exposure concentration. BCF = 100
Scenedesmus subspicatus (green alga)	effect on growth static water	96 hours, Netherlands Standards Institute (ISO/SC5/WG5 N 74 of 2.3.83)	EC_{50} 4.7 x 10^{-3} g/l NOEC <1.0 x 10^{-3} g/l
Scenedesmus pannonicus (green alga)	effect on growth static water	96 hours, OECD 201	EC_{50} 2.6 x 10^{-3} g/l NOEC 0.32 x 10^{-3} g/l

Table 6. Ecotoxicology profile of the technical material, continued

Species	Test	Duration and conditions	Result
Pseudokirchneriella subcapitata (green alga)	effect on biomass and growth, static water of the sodium salt of the acid metabolite of procymidone, PCM-NH-COONa (99.9% purity) - Method OECD 201	72 hours, OECD 201	E_bC_{50} 21 x 10^{-3} g/l NOEC(biomass) 1.8 x 10^{-3} g/l E_gC_{50} 30 x 10^{-3} g/l NOEC(growth) 1.8 x 10^{-3} g/l
Earthworm	acute toxicity	14-day, OECD 207	LC_{50} >1000.0 mg/kg dry soil NOEC 309.0 mg/kg dry soil
Apis mellifera (honey bee)	acute oral toxicity	48 hours, Working document No.13 of the UK Pesticide Safety Precautions scheme	LD_{50} >100 µg/bee NOEC 100 µg/bee
Apis mellifera (honey bee)	acute contact toxicity	24 hours, US EPA 141-1, 1989, EPPO 170, 1992	LD_{50} >20 µg/bee (highest dose tested)
Apis mellifera (honey bee)	acute contact toxicity	48 hours, US EPA 141-1, 1989, EPPO 170, 1992	LD_{50} >100 µg/bee NOEC 100 µg/bee
Coturnix coturnix japonica Japanese quail	acute toxicity	not applicable, US EPA	NOEL(male) 7895 mg/kg bw NOEL (female) 6637 mg/kg bw
Anas platyrhynchos Mallard duck	acute toxicity	not applicable, US EPA	NOEL (male) 4092 mg/kg bw NOEL (female) 4850 mg/kg bw
Colinus virginianus Bobwhite quail	short-term toxicity	5-days, US EPA 71-2, 1982, OECD 205	NOEC 5200 mg/kg diet
Colinus virginianus Bobwhite quail	sub-chronic toxicity and reproduction	22 weeks (10 weeks prior to the start of egg production and during 12 weeks of egg production) to assess the effects of dietary administration of technical procymidone on reproduction in bobwhite quail, US EPA 71-4, 1982, OECD 206	NOEC 1000 mg/kg diet

Summary of the ecotoxicological data

Ecotoxic effects are dependent on the application of the formulation. Procymidone has a low oral toxicity to birds as demonstrated in testing with quail and mallard ducks. Procymidone is moderately toxic to *Daphnia magna* (water flea) and *Oncorhyncus mykiss* (rainbow trout), of low toxicity to *Lepomis macrochirus* (bluegill sunfish) and *Oryzius lapipes* (killifish).

The log Pow of procymidone is 3.30. However, the bioconcentration study in fish showed that the BCF is rather low (*ca.* 110 to 130). Thus, no bioconcentration in birds

and mammals is expected. Based on the endpoints, procymidone has a low acute toxicity to birds and mammals.

The acute toxicity to earthworms is low. The results of the acute oral and contact tests on bees also indicate a low toxicity of procymidone. There is a low to moderate toxicity to algae .

Hazard evaluations

Procymidone was evaluated by the FAO/WHO JMPR in (JMPR 1981, 1989, 1990, 1993 and 1998). The ADI was set at 0 to 0.1 mg/kg bw. Codex MRLs have been established for cherry, common bean, cucumber, gherkin, grape, lettuce head, onion bulb, pepper, raspberry, strawberry, sunflower seeds, sunflower seed oil and tomato.

The WHO/PCS hazard classification of procymidone is: “a technical product unlikely to present acute hazard in normal use” (Table 5).

Formulations and co-formulated active ingredients

The main formulation types available are WP, SC and WG. Procymidone is not co-formulated with other pesticides.

The WP formulation is registered and sold in Belgium, France, Italy, Luxembourg, The Netherlands, Portugal, Spain, Albania, Bulgaria, Czech, Hungary, Macedonia, Romania, Slovakia, Belarus, Kirgystan, Latvia, Moldova, Russia, Ukraine, Algeria, Jordan, Kenya, Lebanon, Morocco, Saudi Arabia, Syria, Turkey, Zimbabwe, Australia, China, Indonesia, Japan, New Zealand, South Korea, Taiwan, Thailand, Argentina, Brazil, Chile, Colombia, Peru, Uruguay and Venezuela.

The SC formulation is registered and sold in France, Italy, The Netherlands, Bulgaria, Croatia, Poland, Romania, Yugoslavia, South Africa, Australia and New Zealand.

The WG formulation is registered and sold in Austria, Greece, Italy, Switzerland and Egypt.

Methods of analysis and testing

The analytical method for the active ingredient (including identity tests) is CIPAC 383/TC, WP, WG, SC/(M). The procymidone is determined by capillary GC with FID and internal standardisation with dibutyl sebacate.

The methods for determination of impurities are based on temperature programmed GC with FID, and UV spectroscopy, according to the impurity.

Test methods for determination of physico-chemical properties of the technical active ingredient were OECD and EC, 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 TC, WP, WG and SC formulations, comply with the requirements of the FAO Manual (5^{th} edition). the products.

Containers and packaging

No special requirements for containers and packaging have been identified.

Expression of the active ingredient

The active ingredient is expressed as procymidone.

Appraisal

Procymidone had not previously been the subject of FAO specifications. It is a solid compound with a melting range of 163- 164.5^{0}C. The octanol-water partition coefficient suggests that moderate bioconcentration could occur but the bioconcentration factor is low. The vapour pressure is 2.30 x 10^{-5} Pa at 25 ^{0}C. In water, procymidone is very slowly degraded at pH 2 but rapidly degraded at pH 9.0.

The purity of the TC quoted by the JMPR (JMPR 1989) was 96.3 % in most studies but 95% in a minority of studies. The Proposer declared a minimum content of 985 g/kg procymidone in the TC.

The Proposer confirmed that the toxicological and ecotoxicological data used in the studies for the toxicological and ecotoxicological data were derived from TC having impurity profiles similar to those for which the 5-batch analysis data were presented.

The purity of the TC used to establish the physico-chemical data was at least 99% procymidone.

Confidential information on the manufacturing process and the identity of the impurities present at =1 g/kg was provided. Limits of the impurities were supported by the 5 batch analysis data. Mass balances were high, from 989 to 998 g/kg.

Analytical methods for the TC, WP, WG and SC were adopted as full CIPAC methods in 2001. The content of active substance is determined by a capillary GC method and the identity is proved by infra-red spectroscopy. The test methods for physical properties are full CIPAC methods.

Data provided to FAO for development of the specifications were similar to the equivalent data provided for registration in The Netherlands and the European Union.

The JMPR concluded that procymidone had a low acute toxicity in the species examined and that there was no evidence of genotoxicity. At high doses of procymidone fed to rats, testicular tumours were formed in the long-term study but this was explained by effects of procymidone on the endrocine system and was not a reflection of genotoxic carcinogenicity.

The JMPR allocated an ADI of 0 to 0.1 mg/kg body weight for procymidone, based on sub-chronic effects in rats, mice and dogs and on chronic effects in mice and rats.

The purity of the technical material used in these studies was somewhat lower than that of commercial products, being 963 g/kg whereas the specification is for a minimum of 985 g/kg.

MRLs were established by JMPR 1998 for a number of crops.

Specifications were submitted for three formulation types: WP, WG and SC and they conform with the requirements of the 5th edition of the FAO Manual (FAO 1999).

Recommendations

The meeting recommended that the specifications for procymidone TC, WP, WG and SC, presented by Sumitomo, should be adopted as FAO specifications.

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