

FAO SPECIFICATIONS AND EVALUATIONS FOR AGRICULTURAL PESTICIDES

DIFLUBENZURON

1-(4-chlorophenyl)-3-(2,6-difluorobenzoyl)urea



FOOD AND AGRICULTURE ORGANIZATION *of* THE UNITED NATIONS

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DISCLAIMER¹

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

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

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

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

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

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.

From 2002, the development of FAO specifications follows the **New Procedure**, described in the Manual on Development and Use of FAO and WHO Specifications for Pesticides, which is available only on the internet through the FAO and WHO web sites.

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

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

Part One: The Specification of the technical material and the related formulations of the pesticide in accordance with chapters 4 to 9 of the “Manual on development and use of FAO and WHO specifications for pesticides”.

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

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

Specifications bear the date (month and year) of publication of the current version. Evaluations bear the date (year) of the meeting at which the recommendations were made by the JMPS.

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

PART ONE
SPECIFICATIONS

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DIFLUBENZURON

INFORMATION

ISO common name

Diflubenzuron (E-ISO, (m) F-ISO, ANSI, ESA)

Chemical names

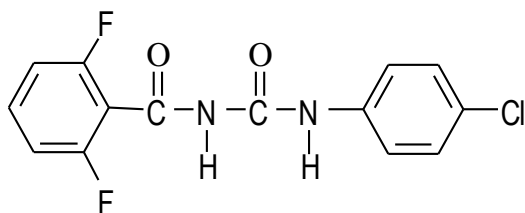
IUPAC 1-(4-chlorophenyl)-3-(2,6-difluorobenzoyl)urea

CA N-[[4-(4-chlorophenyl)amino]carbonyl]-2,6-difluorobenzamide

Synonyms

Dimilin, Micromite, Adept, DU 112307, PH 60-40, TH 6040, ENT-29054, OMS 1804
(Crompton tradenames and/or past development codes).

Structural formula



Molecular formula

$C_{14}H_9ClF_2N_2O_2$

Relative molecular mass

310.7

CAS Registry number

35367-38-5

CIPAC number

339

Identity tests

HPLC retention time; IR spectrum

DIFLUBENZURON TECHNICAL MATERIAL

FAO Specification 339 / TC (September 2017*)

This specification, which is PART ONE of this publication, is based on an evaluation of data submitted by the manufacturers whose names are listed in the evaluation reports (339/2016.1 & 339/2016.2). It should be applicable to TC produced by these manufacturers but it is not an endorsement of those products, nor a guarantee that they comply with the specification. The specification may not be appropriate for TC produced by other manufacturers. The evaluation reports 339/2016.1 & 339/2016.2, as PART TWO, form an integral part of this publication.

1 Description

The material shall consist of diflubenzuron, together with related manufacturing impurities, and shall be an off-white, fine powder, free from visible extraneous matter and added modifying agents.

2 Active ingredient

2.1 Identity tests (339/TC/M/2, CIPAC Handbook N, p. 38, 2012)

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 Diflubenzuron content (339/TC/M/3, CIPAC Handbook N, p. 38, 2012)

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

3 Relevant impurities (Note 1)

Note 1 There are no relevant impurities to be controlled in diflubenzuron products of the manufacturers identified in evaluation reports 339/2016.1 and 339/216.2 However, 4-chloroaniline could occur as a result of certain manufacturing processes. If 4-chloroaniline occurs at ≥ 0.1 g/kg (of diflubenzuron) in the products of other manufacturers, it may be designated as relevant impurity and requires a clause to limit the concentration.

* Specifications may be revised and/or additional evaluations may be undertaken. Ensure the use of current versions by checking at: <http://www.fao.org/agriculture/crops/core-themes/theme/pests/jmps/ps-new/en/>

DIFLUBENZURON TECHNICAL CONCENTRATE

FAO Specification 339 / TK (December 2016*)

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 reports (339/2004, 339/2016.1). 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 specification. The specification may not be appropriate for the products of other manufacturers. The evaluation reports (339/2004, 339/2016.1) as PART TWO form an integral part of this publication.

1 Description

The material shall consist of diflubenzuron, together with related manufacturing impurities, and shall be an off-white, fine powder, free from visible extraneous matter and added modifying agents except for the diluent.

2 Active ingredient

2.1 Identity tests (339/TK/M/2, CIPAC Handbook H, p.142, 1998)

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 Diflubenzuron content (339/TK/M/3, CIPAC Handbook H, p.142, 1998)

The diflubenzuron content shall be declared (900 g/kg) and, when determined, the average measured content shall not differ from that declared by more than ± 25 g/kg.

3 Relevant impurities (Note 1)

4 Physical properties

4.1 Particle size (MT 187, CIPAC Handbook K, p.153, 2003) (Note 2)

Particles smaller than 5 μm : not less than 70% w/w.

Average particle size: not more than 3.75 μm .

Note 1 There are no relevant impurities to be controlled in diflubenzuron products of the manufacturer identified in evaluation report 339/2016.1. However, 4-chloroaniline could occur as a result of certain manufacturing processes. If 4-chloroaniline occurs at ≥ 0.1 g/kg (of diflubenzuron) in the products of other manufacturers, it may be designated as relevant impurity and requires a clause to limit the concentration.

* Specifications may be revised and/or additional evaluations may be undertaken. Ensure the use of current versions by checking at: <http://www.fao.org/agriculture/crops/core-themes/theme/pests/jmps/ps-new/en/>

Note 2 Control of particle size is required to ensure efficacy of the formulated products.

PART TWO

EVALUATION REPORTS

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² Crompton Europe B.V is an entity of Arysta LifeScience.

DIFLUBENZURON

FAO/WHO EVALUATION REPORT 339/2016.2

Recommendations

The Meeting recommended that

- (i) The diflubenzuron TC as proposed by Helm AG should be accepted as equivalent to the diflubenzuron reference.
- (ii) The FAO diflubenzuron TC specification should be extended to encompass the material produced by Helm AG.
- (iii) The WHO diflubenzuron TC specification should be extended to encompass the material produced by Helm AG.

Appraisal

The data for diflubenzuron provided by Helm AG were evaluated in support of an equivalence determination with the existing FAO and WHO specifications for TC.

Diflubenzuron is no longer under patent.

The supporting data were provided in 2011, updated in 2012, 2016 and 2017.

The analytical method for the active ingredient (including identity tests) is derived from a CIPAC method published in Handbook N. Diflubenzuron is determined by reverse phase HPLC on a C₁₈ column using UV detection at 260 nm. The proposer stated that his in-house method offered better resolution of certain impurities from the active substance, and was suitable for the analysis of diflubenzuron TC. A bridging study between the in-house and CIPAC methods was submitted by the proposer. The results of both methods (CIPAC and Helm AG in-house) are in good agreement for all batches.

The Meeting was provided with commercially confidential information on the manufacturing process and five batch analysis data on all impurities present at or above 1 g/kg and their manufacturing limits in the TC. The manufacturing process provided by Helm AG is similar to those supporting the existing FAO and WHO specification for a TC. Mass balances in the 5-batch data ranged from 993 to 1002 g/kg. The percentage of unknowns was no higher than 0.7%. The minimum purity of diflubenzuron in the TC is 960 g/kg and complies with the existing specification. Based on available information and the criteria as defined in the Manual, the Meeting concluded that none of the impurities in the TC had to be considered as relevant.

All the analytical methods used in the 5-batch analysis study were validated for their specificity, linearity of response, accuracy, repeatability and limits of detection and quantification. However, some of required parameters were missing for some of the impurities, such as the recovery data for a certain impurity, and precision data for another

impurity were beyond acceptability criteria as estimated using the Horwitz equation. The proposer explained that the standard for the first impurity was not available, so no recovery data could be obtained. The QC limit of the second impurity was much lower than that of the reference profile, so the poor precision data does not change the status of equivalency.

The Meeting questioned about the levels of residual solvents in the proposer's product, and the proposer stated that the organic solvents were controlled to below 0.1% w/w.

The minimum purity of TC specification registered in Argentina is 950 g/kg. The impurities and their maximum limits in the manufacturing specification were considered to be equivalent to the diflubenzuron impurity profile provided to Argentina authority for registration. The company provided additional data beginning of 2017 with regard to the levels of 4-chloroanilin, demonstrating that in all batches the concentrations of that potentially relevant compound were below 0.1 g/kg.

A closer comparison of the manufacturing specifications of the reference product and the product under evaluation with their associated 5-batch data however revealed some significant differences as follows:

The impurity profile of the second manufacturer showed some new impurities not present in the reference profile at or above 1 g/kg. However these impurities did not give rise to structural alerts other than those present in the active ingredient as judged by the OECD QSAR Toolbox³. The Cramer hazard classification was the same for the impurities and the active ingredient itself (Cramer Class III). Furthermore, in the Tier-2 equivalence determination, the Helm product was not genotoxic *in vitro*, not irritating to the eye or skin nor sensitizing to the skin, nor more hazardous than the reference product in acute toxicity assays. The JMPS therefore concluded that the Helm product is equivalent to the reference product based on Tier-1 and Tier-2 considerations.

The batches used in toxicity and genotoxicity studies were different from those used in 5 batch study. The proposer stated that the batches were from the same commercial manufacturing process as the 5 batches, however the analytical details were not available to establish the links between the hazard and purity/impurity profile data submitted.

The Meeting also recommended, in the WHO WP and DT specifications, to refer to the CIPAC methods MT 47.3 for persistent foam and MT 193 for attrition of tablets respectively, as published in Handbook O.

³ <http://www.oecd.org/chemicalsafety/risk-assessment/oecd-qsar-toolbox.htm>

**SUPPORTING INFORMATION
FOR
EVALUATION REPORT 339/2016.2**

Table 1. Chemical composition of diflubenzuron technical material (TC)

Manufacturing process, maximum limits for impurities ≥ 1 g/kg, 5 batch analysis data	Confidential information supplied and held on file by FAO and WHO. Mass balances were 99.3 – 100.2 % and percentages of unknowns were ≤ 0.7 %.
Declared minimum diflubenzuron 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.

FORMULATIONS AND CO-FORMULATED ACTIVE INGREDIENTS

The proposer did not propose any specifications of formulations.

METHODS OF ANALYSIS AND TESTING

The analytical method for the active ingredient (including identity tests) was based on the CIPAC methods 339/TC/M/2 & 3. Diflubenzuron is determined by reverse phase HPLC on a C₁₈ column using UV detection at 260 nm. Diflubenzuron elutes with a retention time of approximately 34 min.

Test methods for determination of physico-chemical properties of the technical active ingredient were OECD.

CONTAINERS AND PACKAGING

No special requirements for containers and packaging have been identified.

EXPRESSION OF THE CONTENT OF ACTIVE INGREDIENT

The active ingredient diflubenzuron is expressed as g/kg.

ANNEX 1

HAZARD SUMMARY PROVIDED BY THE PROPOSER

Notes.

- (i) The proposer confirmed that the toxicological data included in the summary below were derived from diflubenzuron 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 2. Toxicology profile of diflubenzuron technical material, based on acute toxicity, irritation and sensitization

Species	Test	Purity % Note ⁴	Guideline	Result	Study number
Rat, female	oral	97.5	OECD 423	LD ₅₀ > 5000 mg/kg bw	3790/03
Rat, female and male	dermal	97.5	OECD 402	LD ₅₀ > 2000 mg/kg bw	3791/03
Rat, female and male	inhalation	97.5	OECD 403	LC ₅₀ > 1550 mg/m ³	3792/03
Rabbit, female	skin irritation	97.5	OECD 404	No irritant	3793/03
Rabbit, female	eye irritation	97.5	OECD 405	Mild irritant	3794/03
Guinea Pig, female and male	skin sensitisation	97.5	OECD 406	No sensitizer (Magnusson and Kligman Test)	3795/03

Table B. Mutagenicity profile of diflubenzuron technical material based on *in vitro* tests

Species	Test	Purity % Note ⁴	Guideline	Result	Study number
<i>Salmonella typhimurium</i>	Ames Test – <i>in vitro</i>	98.77	OECD 471	No genotoxic potential	12282- 06AM

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

ANNEX 2 REFERENCES

Study number	Author(s)	year	Study title. Study identification number. Report identification number. GLP [if GLP]. Company conducting the study.
	FAO/WHO	2016	Manual on development and use of FAO and WHO specifications for pesticides. Third Revision of First Edition. FAO Plant Production and Protection Paper 228. www.fao.org/ag/AGP/AGPP/Pesticid/Default.htm and http://whqlibdoc.who.int/publications/2006/9251048576_eng_update2.pdf
3790/03		2004	Acute oral toxicity study (acute toxic class method) with diflubenzuron 97 TC in Wistar rats. Report 3790/03. GLP.
3791/03		2004	Acute dermal toxicity study with diflubenzuron 97 TC in Wistar rats. Report 3791/03. Unpublished.
3792/03		2004	Acute inhalation toxicity study with Diflubenzuron 97 TC in Wistar rats. Report 3792/03. GLP.
3793/03		2004	Acute dermal irritation/corrosion study with Diflubenzuron 97 TC in New Zealand white rabbits. Report 3793/03. GLP.
3794/03		2004	Acute eye irritation/corrosion study with Diflubenzuron 97 TC in New Zealand white rabbits. Report 3794/03. GLP. Unpublished.
3795/03	SM	2004	Skin Sensitisation study (Magnusson and Kligman test) with Diflubenzuron 97 TC in Guinea pigs. Report 3795/03. GLP. Unpublished.
12282-06AM		2007	Bacterial reverse mutation test (Ames Test) for Diflubenzuron 96 Technical Grade Helm. Report 12282-06AM. GLP.
PR04/00		2005	Analytical Profile of Five Batches of Diflubenzuron TC.

DIFLUBENZURON

FAO/WHO EVALUATION REPORT 339/2016.1

Recommendations

The Meeting recommended the following.

- (i) The new specification for diflubenzuron TC, proposed by Arysta LifeScience, and as amended, should be adopted by FAO and WHO.
- (ii) The existing FAO and WHO specifications for diflubenzuron TK should be revised taking the newly submitted data into account.
- (iii) The WHO specifications for diflubenzuron formulated products (WP, GR, DT) should be editorially revised to refer to the latest physical-chemical test methods.

Appraisal

The first specifications for diflubenzuron TK under the "New procedure" have been published by WHO and FAO in 2005. The data were proposed by Crompton Europe B.V. in 2003. In the meantime diflubenzuron has been reviewed by EU in 2010 based on data submitted by Chemtura, a successor company of Crompton (DG SANCO, 2010) and clear differences in minimum purity and other parameters between the published TK specifications and those of the EU review became apparent. The Meeting therefore requested the successor of Chemtura, Arysta LifeScience (Arysta), to submit an updated data package for this compound based on Section 2.7 of the FAO/WHO Pesticide Specification Manual (Review of specifications). Subsequently a new data package with confidential and non-confidential data was provided by Arysta.

A comparison of the manufacturing processes shows that they have remained essentially the same. The difference is that a TC is isolated that later may be converted to a TK with the addition of some inert material.

The TC has the aspect of an off-white fine powder. The declared minimum content of the active ingredient is 950 g/kg. Mass balances in the new 8-batch analysis data were high (> 98%) and no unidentified impurities were detected. The purity and impurity profiles were equivalent to those submitted in 2004, and the reference profile is renewed based on new batch analysis results and QC data.

A limit of 0.03 g/kg for impurity 4-chloroaniline was specified after the EU evaluation. However, in the context of FAO/WHO pesticide specification evaluation, the impurity at this level was not considered relevant. However a note was added to specify that if 4-chloroaniline occurs at ≥ 0.1 g/kg (of diflubenzuron) in the products of other manufacturers, it may be designated as relevant impurity and requires a clause to limit its concentration.

The methods for the identification and determination of diflubenzuron in the TC are the CIPAC methods.

The clause of diflubenzuron content in the TK specification was revised to 900 g/kg with a tolerance of ± 25 g/kg to reflect the requirement of the FAO/WHO Pesticide Specification Manual.

The TK is used to formulate some solid formulations like the WP, GR and DT. These specifications, therefore, refer to the TK material rather than the TC.

The Meeting also recommended to update the CIPAC physical-chemical methods for WP and GR formulations where necessary (e.g. wet sieve test: MT 185 instead of MT 59.3, persistent foam: MT 47.3 instead of MT 47.2, nominal size range: MT 170 instead of MT 58, dustiness: MT 171.1 instead of MT 171) and to refer to the renamed “attrition of tablets” MT 193 method for DT formulation.

ANNEX 1: REFERENCES

Study number	Author(s)	Year	Study title. Study identification number. Report identification number. GLP [if GLP]. Company conducting the study
FR-12508	Riggs, A.S	2007	Preliminary Analysis of Diflubenzuron Technical. Study Number GRL-12508, report number FR-12508. Test facility: Chemtura Canada Co. Cie Guelph Technology Centre. Ontario. Canada.
SANCO/83 1/08 - final1	DG SANCO	2010	Review report for the active substance diflubenzuron.

DIFLUBENZURON

FAO/WHO EVALUATION REPORT 339/2004

Explanation

The data for diflubenzuron were evaluated in support of review of existing WHO specifications, WHO/SIT/25.R1 for diflubenzuron technical concentrate (TK) and WHO/SIF/47.R1 for diflubenzuron wettable powder (WP), as developed by WHOPES following the old procedure and revised on 10 December 1999. New specifications were proposed for diflubenzuron granules (GR) and tablets for direct application (DT) in public health and for suspension concentrates (SC) for use in agriculture.

Diflubenzuron is not under patent.

Diflubenzuron was evaluated by the FAO/WHO JMPR and WHO/IPCS in 1981, 1984, 1988 and 2002. The US EPA published a Re-registration Eligibility Decision for diflubenzuron in August 1997. Diflubenzuron is currently under review by the European Commission under Directive 91/414/EC. Crompton Europe B.V. has notified diflubenzuron as an existing biocidal active ingredient under the Biocidal Products Directive 98/8/EC.

The draft specification and the supporting data were provided by Crompton Europe B.V. in October 2003 and February 2004.

Uses

Diflubenzuron is an insect growth regulator, used in agriculture, horticulture and forestry against larvae of Lepidoptera, Coleoptera, Diptera, Hymenoptera and in public health against larvae of mosquitoes and other noxious insects.

Identity

ISO common name

Diflubenzuron (E-ISO, (m) F-ISO, ANSI, ESA)

Chemical names

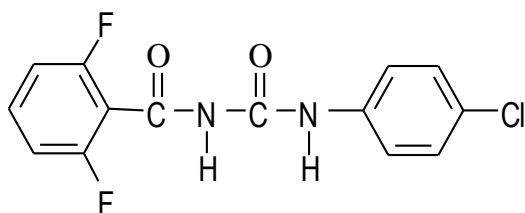
IUPAC: 1-(4-chlorophenyl)-3-(2,6-difluorobenzoyl)urea

CAS: *N*-[[[(4-chlorophenyl)amino]carbonyl]-2,6-difluorobenzamide

Synonyms

Dimilin, Micromite, Adept, Du-Dim, Device, DU 112307, PH 60-40, TH 6040, ENT-29054, OMS 1804 (Crompton trade names and/or past development codes).

Structural formula



Molecular formula



Relative molecular mass

310.7

CAS Registry number

35367-38-5

CIPAC number

339

Identity tests

HPLC retention time; IR spectrum.

Physical and chemical properties

Table 1. Physicochemical properties of pure diflubenzuron

Characteristic	Value	Purity, %	Method	Reference
Vapour pressure	$\leq 1.2 \times 10^{-7}$ Pa at 25°C	>99.5	OECD guideline 104	DI 7081
Melting point, boiling point and/or temperature of decomposition	Melting point: 228°C Boiling point: Not required, because diflubenzuron is neither a liquid, nor a low melting substance Decomposition temperature: no decomposition at melting point	99.9	OECD guideline 102	DI 9321 DI 11496 DI 9321
Solubility in water	0.08 mg/l at 25°C at pH 7 0.10 mg/l at pH 4 0.32 mg/l at pH 10	>99.5	EEC guideline A6	DI 7233 DI 9167
Octanol/water partition coefficient	Log P_{ow} = 3.89 at 22°C at pH 3	99.9	EEC guideline A8	DI 7016
Hydrolysis characteristics	Half-life > 180 days at 25°C at pH 5 and 7 Half-life = 32.5 days at 25°C at pH 9	97.1	EPA guideline CG5000	DI 6799
Photolysis characteristics	The estimated half-life of diflubenzuron in natural sunlight at latitude 40° N is 80 days at 25°C (from 40 days continuous irradiation with a 450 W Xenon arc lamp)	97.1	EPA guideline CG6000	DI 6799 DI 6689
Dissociation characteristics	Does not dissociate	99.9	OECD guideline 112	DI 11387

Table 2. Chemical composition and properties of diflubenzuron technical concentrate (TK)

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 99.0-100.3%.
Declared minimum diflubenzuron content:	875 g/kg
Relevant impurities ≥ 1 g/kg and maximum limits for them:	None *
Relevant impurities < 1 g/kg and maximum limits for them:	None
Stabilizers or other additives and maximum limits for them:	None
Melting or boiling temperature range	228°C, no decomposition at melting point.
Particle size	Particles smaller than 5 μm : not less than 70% w/w. Average particle size: not more than 3.75 μm .

* Water is a relevant impurity in GR (20 g/kg) and DT (40 g/kg), because these formulations contain effervescent systems.

Hazard summary

Notes.

(i) The proposers provided written confirmation that the toxicological and ecotoxicological data included in the summary below were derived from diflubenzuron having impurity profiles similar to those referred to in the table above.

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

(iii) The acute toxicity data relate to studies with diflubenzuron TC and/or with diflubenzuron VC-90, a TK containing 90% diflubenzuron, which has the same toxicological profile as the active ingredient itself.

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

Species	Test	Duration and conditions	Result	Reference
Rat (male and female)	Oral	OECD guideline 401, purity 90%	LD ₅₀ >5000 mg/kg bw	DI 4959
Rat; mouse (male and female)	Oral (gavage)	Guideline not stated, purity 99.6%	LD ₅₀ >4640 mg/kg bw	DI 2207
Mouse (male and female)	Oral (gavage)	Guideline not stated, purity 99.6%	LD ₅₀ >4640 mg/kg bw	DI 2203
Rat (male and female)	Dermal	OECD guideline 402, purity 90%	LD ₅₀ >2000 mg/kg bw	DI 4958
Rat	Dermal	24 hours. PSD, UK (1971) purity 99.6%	LD ₅₀ >10000 mg/kg bw	DI 2227
Rat (male and female)	Inhalation	OECD guideline 403 purity 90%	LC ₅₀ >2490 mg/m ³	DI 5710
Rat	Inhalation	Guideline not stated, purity 99.6%	LC ₅₀ >2900 mg/m ³	DI 3513
Rabbit (male and female)	Skin irritation	OECD guideline 404, purity 90%	Non-irritant	DI 4961
Rabbit (male and female)	Eye irritation	OECD guideline 405, purity 90%	Slightly irritating (Note 1)	DI 4960
Guinea pig	Skin sensitization	OECD guideline 406, purity 95.6%	Non-sensitizer	DI 8423

Note 1: Although a slight reaction was observed during the eye irritation tests, the findings did not trigger classification of diflubenzuron as an eye irritant.

Table 4. Toxicology profile of technical diflubenzuron based on repeated administration (sub-acute to chronic)

Species	Test	Duration and conditions	Result	Reference
Mouse	Oral 6-week	No guideline specified, Dose range tested: 0; 16 & 50 ppm; purity 99.6%	NOAEL = 2.0 mg/kg bw/day (16 ppm)	DI 3523
Mouse	Oral 90-day	No guideline specified, Dose range tested: 0; 16; 50; 400; 2,000; 10,000 & 50,000 ppm; purity 97.2%	NOAEL = 7.1 mg/kg bw/day (50 ppm)	DI 2212 DI 3522
Mouse	Oral 14-week	No guideline specified, Dose range tested: 0; 80; 400; 2000; 10,000 & 50,000 ppm; purity 97.2%	NOAEL = 10.4 mg/kg bw/day (80 ppm)	DI 4155
Rat	Oral 28-day	No guideline specified, dose range tested: 0; 800; 4,000; 20,000 & 100,000 ppm; purity 98.5%.	LOEL = 84 mg/kg bw/day (800 ppm)	DI 4161
Rat	Oral 90-day	No guideline specified, dose range tested: 0; 3.125; 12.5; 50 & 200 ppm; purity 96.0%.	NOAEL = 21.6 mg/kg bw/day (200 ppm)	DI 2376 DI 3528
Rat	Oral 90-day	No guideline specified, Dose range tested: 0; 160; 400; 2,000; 10,000 & 50,000 ppm; purity 96.0%	NOAEL = 12.6 mg/kg bw/day (160 ppm)	DI 2168 DI 4279
Rat	Oral 9-week	No guideline specified; Dose range tested: 0; 10,000 & 100,000 ppm; purity 98.5%	LOEL = 1000 mg/kg bw/day (10.000 ppm)	DI 3517
Dog	Oral 90-day	No guideline specified, Dose range tested: 0; 10; 20; 40 & 160 ppm; purity 99.6%	NOAEL = 0.84 mg/kg bw/day (20 ppm)	DI 2375
Dog	Oral 90-day	No guideline specified, Dose range tested: 0; 2; 4; 50 & 250 mg/kg bw/day; purity 97.6%	NOAEL = 4 mg/kg b.w./day	DI 987
Dog	Oral 1-year	No guideline specified, Dose range tested: 0; 2; 10; 50 & 500 mg/kg b.w./day; purity 97.6%	NOAEL = 2 mg/kg b.w./day	DI 4852
Rat	Inhalation 28-day (1 hr/day)	No guideline specified, Dose range tested: 0; 0.5/0.12; 5.0/0.87 & 50/1.85 mg/L (nominal/actual); purity: 99.6%	NOAEL = 0.12 mg/L (actual)	DI 2359

Species	Test	Duration and conditions	Result	Reference
Rabbit	Inhalation 21-day (1 hr/day)	No guideline specified, Dose range tested: 0; 0.5/0.15; 5.0/0.75; 25/1.79 mg/L (nominal/actual); purity 99.6%	NOAEL = 0.15 mg/L (actual)	DI 2360
Rat	Inhalation 28-day (6 hr/day)	OECD Guideline 412; Dose range tested: 0; 10/12; 30/34 & 100/109 mg/m ³ (nominal/actual); purity 96.5%	NOAEL = 34 mg/m ³ (actual)	DI 11497
Rabbit	Percutaneous 21-day	No guideline specified, Dose range tested: 0; 69.6; 150 & 322.5 mg/kg/day; purity 99.6%	NOAEL = 150 mg/kg/day	DI 2216
Rabbit	Percutaneous 21-day	No guideline specified, Dose range tested: 0; 113 & 345 mg/kg/day; purity 99.6%	Not established	DI 2217
Rat	Percutaneous 21-day	Guideline US EPA FIFRA vol 43, no 163, Dose range tested: 0; 20; 500 & 1,000 mg/kg/day; purity 96.7%	NOAEL = 20 mg/kg/day	DI 9429
Rat	104 weeks dietary carcinogenicity	No guideline specified; Dose range tested: 0; 10; 20; 40; and 160 ppm; purity 99.6%	NOAEL = 1.43 mg/kg bw (males) and 1.73 mg/kg bw (females) (40 ppm) Not carcinogenic	DI 4037
Rat	104 weeks dietary carcinogenicity	Guideline US EPA FIFRA vol. 43 no. 163; Dose range tested: 0; 156; 625; 2,500 and 10,000 ppm; purity 97.6%	LOAEL = 7.8 mg/kg bw/day (156 ppm) Not carcinogenic	DI 8147
Mouse	80 weeks dietary carcinogenicity	No guideline specified; Dose range tested: 0; 4; 8; 16 and 50 ppm; purity: 99.6%	> 7.4 mg/kg bw/day (> 50 ppm) Not carcinogenic	DI 3525
Mouse	91 weeks dietary carcinogenicity	No guideline specified; Dose range tested: 0; 16; 80; 400; 2,000 and 10,000 ppm; purity 97.6%.	NOAEL = 2.4 mg/kg bw/day (16 ppm) Not carcinogenic	DI 8146
Rat	3-generation parental and reproduction toxicity	No guideline specified; Dose range tested: 0, 10, 20, 40 and 160 ppm; purity 99.6%	NOAEL = 8 mg/kg bw/day (160 ppm)	DI 3516
Rat	1-generation reproduction toxicity	No guideline specified; Dose range tested: 0, 1000 and 100000 ppm; purity 98.5%	NOAEL = 50 mg/kg bw/day (1000 ppm)	DI 3462
Rat	2-generation reproduction toxicity	OECD guideline 416; Dose range tested: 0, 500, 5000 and 50000 ppm; purity 97.1%	NOAEL for reproductive function = 2500 mg/kg bw/day (50000 ppm)	DI 9182

Species	Test	Duration and conditions	Result	Reference
Rat	Teratogenicity (gavage)	No guideline specified; Dose range tested: 0, 1,2 and 4 mg/kg bw during days 6-15 of gestation; purity 98.5%	Pregnancy rates were unaffected	DI 2349
Rat	Teratogenicity (gavage)	US EPA guideline 83-3 subdivision F; Dose range tested: 0 and 1000 mg/kg bw during days 6-15 of gestation; purity 98.5%	No maternal or embryotoxicity at 1000 mg/kg bw/day	DI 6552
Rabbit	Teratogenicity (gavage)	No guideline specified; Dose range tested: 0, 1,2 and 4 mg/kg bw during days 6-19 of gestation; purity 98.5%	Pregnancy rates were unaffected	DI 2350
Rabbit	Teratogenicity (gavage)	US EPA guideline 83-3 subdivision F; Dose range tested: 0 and 1000 mg/kg bw during days 7-19 of pregnancy; purity 98.5%	NOAEL for maternal and embryotoxicity = 1000 mg/kg bw/day	DI 6553

- a Highest dose tested.
b Lowest dose tested.

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

Species	Test	Conditions	Result	Reference
<i>Salmonella typhimurium</i>	<i>In vitro</i> genotoxicity test	OECD guideline 471, purity 96.9%	Negative	DI 7988
<i>Saccharomyces cerevisiae</i>	<i>In vitro</i> genotoxicity test	OECD guideline 471, purity 98.5%	Negative	DI 2261
BALB/3T3 cells	<i>In vitro</i> genotoxicity test	OECD guideline 471, purity 98.5%	Negative	DI 2263
CHO cells	<i>In vitro</i> genotoxicity test	OECD guideline 473, purity 97.6%	Negative	DI 5707
Rat hepatocytes	<i>In vivo</i> genotoxicity test	OECD guideline 482, purity 96.9%	Negative	DI 7987
WI-38	<i>In vivo</i> genotoxicity test	OECD guideline 486, purity 98.5%	Negative	DI 2264
Mouse germ cells	Dominant lethal study in mice. <i>In vivo</i> genotoxicity test	Guideline not stated, purity not stated	Negative	DI 2348

Table 6. Ecotoxicology profile of diflubenzuron technical concentrate

Species	Test	Duration and conditions	Result	Reference
<i>Daphnia magna</i>	Acute toxicity	48 hr, 20°C, Guideline ASTM E729-80, purity 97.6%	EC ₅₀ = 2.6-7.1 µg/l NOEC 0.45 µg/l	DI 6773
<i>Daphnia magna</i>	Acute toxicity	48 hr, 20°C OECD Guideline 202, purity 79.4% (WG, Note 1)	EC ₅₀ = 3.2 µg WG-80/l NOEC = 0.38 µg WG-80/l	DI 9180
Zebra fish (<i>Brachydanio rerio</i>)	Acute toxicity	96 hr, 22°C OECD Guideline 203, purity 95.6%	LC ₅₀ >0.2 mg/l	DI 8925
Minnow (<i>Cyprinodon variegates</i>)	Acute toxicity	96 hr, 22°C Guideline US EPA 40 CFR 158.145 72-3, purity 100% (Note 1)	LC ₅₀ >130 µg/l	DI 6152
Zebra fish (<i>Brachydanio rerio</i>)	Acute toxicity	96 hr, 22°C OECD Guideline 203, purity 79.4% (WG, Note 1)	LC ₅₀ >106 mg a.i./l	DI 8929
Minnow (<i>Cyprinodon variegates</i>)	Acute toxicity	96 hr, 22°C Guideline US EPA FIFRA Subdivision E 72-3 and OECD 203, purity 95.6%	LC ₅₀ >130 µg a.i./l	DI 8668
Rainbow trout (<i>Oncorhynchus mykiss</i>)	Acute toxicity	96 hr, 15°C Guideline OECD 203, purity 95.6% but WG 80 formulation used purity 79.4% (Note 1)	LC ₅₀ >65 mg/l	DI 8926
Rainbow trout (<i>Oncorhynchus mykiss</i>)	Acute toxicity	96 hr, 15°C Guideline OECD 203, purity 79.4% (Note 1)	LC ₅₀ >106 mg a.i./l	DI 8927
<i>Selenastrum capricornutum</i> (green alga)	Growth rate test	5 days, 22°C Guideline US EPA FIFRA Subdivision J, Series 123-2, purity 95.6% but WG formulation used (Note 1)	EC ₅₀ >80 mg a.i./l NOEC = 80 mg a.i./l	DI 8667
<i>Selenastrum capricornutum</i> (green alga)	Acute toxicity	OECD guideline 201, purity 79.4%	EC ₅₀ >80 mg a.i./l NOEC = 80 mg a.i./l	DI 9104
Earthworm (<i>Eisenia fetida</i>)	Acute toxicity	14 days exposure, 22°C according to OECD guideline 207, purity 95.6%	LC ₅₀ >780 mg/kg dry soil	DI 8580
<i>Apis mellifera</i> (honey bee)	Acute oral toxicity and field test	Various laboratory, semi-field and field tests under varying conditions. BBA Guideline, purity 79.4% (Note 1).	LD ₅₀ >100 µg/bee (adults) Dimilin can be applied in the field without affecting honeybee colonies	DI 7234 DI 9386

Species	Test	Duration and conditions	Result	Reference
Bobwhite quail	Acute oral toxicity	Diflubenzuron administered as a single oral exposure by gavage, birds observed for 14 days. No guideline specified, purity 99.4%	LD ₅₀ >5000 mg/kg bw	DI 3598
Mallard duck	Acute oral toxicity	Diflubenzuron administered as a single oral exposure by gavage, birds observed for 14 days. No guideline specified, purity 99.4%	LC ₅₀ >5000 mg/kg bw	DI 3597
Mallard duck	8-day dietary exposure	Birds housed in thermostatically controlled brooders. No guideline specified, purity 100%	LC ₅₀ >4640 ppm diet (Note 2)	DI 3603
Bobwhite quail	8-day exposure	Birds housed in thermostatically controlled brooders. No guideline specified, purity 100%	LC ₅₀ >4640 ppm diet (Note 2)	DI 3604

Note 1: Due to the low solubility of diflubenzuron in water (0.08 mg/l), the acute toxicity was established using Dimilin WG-80 to suspend the active ingredient in water during the test.

Note 2: Highest dose tested.

Diflubenzuron was evaluated by IPCS in 1994 (IPCS 1994) and by the FAO/WHO JMPR for toxicology in 2001 (JMPR 2001) and for residues in 2002 under the periodic review programme of the Codex Committee on Pesticide Residues (JMPR 2002). The 2002 JMPR concluded that the long-term intake of residues of diflubenzuron in food resulting from its uses that have been considered by JMPR is unlikely to present a public health concern. The WHO panel of the 2001 JMPR 2001 that an acute RfD is unnecessary and therefore the 2002 JMPR concluded that the short-term intake of diflubenzuron residues is unlikely to present a public health concern. The 2001 JMPR re-confirmed the previously established ADI of 0-0.02 mg/kg bw.

The WHO hazard classification of diflubenzuron is: unlikely to present acute hazard in normal use (WHO 2002).

Formulations

The main formulation types available are WP (25%), SC (48%, 24%, 22%, 15%), WG (80%), GR (4%), OF (45% and 6%, the latter a ready-to-use formulation) for both agricultural and public hygiene use. Effervescent GR (2%) and DT (2%) formulations are under development and testing for use in public hygiene and submissions have been made for registration of this use.

These formulations are registered and sold in many countries throughout the world. Europe: Austria, Belarus, Belgium, Bulgaria, Cyprus, Czech Republic, Denmark, Estonia,

Finland, France, Germany, Greece, Hungary, Ireland, Italy, Lithuania, Macedonia, Moldova, Netherlands, Norway, Poland, Portugal, Romania, Russia, Slovakia, Spain, Sweden, Switzerland, U.K. Uzbekistan, Yugoslavia. Middle East: Egypt, Iran, Israel, Jordan, Saudi Arabia, Syria, Turkey, United Arab Emirates. Africa: Algeria, Burkina Faso, Cape Verde, Chad, Gambia, Guinea Bissau, Kenya, Madagascar, Mali, Mauritania, Morocco, Niger, Senegal, South Africa, Zimbabwe. Australasia and Asia: Australia, P. R. China, India, Indonesia, Japan, Kazakhstan, Korea South, Kyrgyzstan, Malaysia, Nepal, New Zealand, Pakistan, Taiwan, Thailand. Americas: Argentina, Bolivia, Brazil, Chile, Colombia, Ecuador, Guatemala, Mexico, Paraguay, Peru, USA, Uruguay.

Methods of analysis and testing

The analytical method for determination of the active ingredient (including identity tests) in the TK and WP is a full CIPAC method (CIPAC H). Diflubenzuron is determined by reversed-phase HPLC, using a C-18 column and acetonitrile/water mobile phase, with UV detection at 254 nm and linuron as the internal standard. The method has not been validated for GR, WG, OF, SC or DT formulations⁵.

The methods for determination of impurities were based on HPLC-UV, using external standardization.

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

Containers and packaging

No special requirements for containers and packaging have been identified.

Expression of active ingredient

The active ingredient is expressed as diflubenzuron, in g/kg in solid formulations, and in g/kg or g/l at 20 ± 2°C in liquid formulations.

Appraisal

The Meeting considered data on diflubenzuron, submitted by Crompton Europe B.V. for the review of existing WHO specifications for the TK and WP. New specifications were considered for diflubenzuron granules (GR) and tablets for direct application (DT) in public health and for suspension concentrates (SC) for use in agriculture. The data submitted were in accordance with the requirements of the manual (FAO/WHO 2002).

Diflubenzuron is a benzoylurea insect growth regulator, used in agriculture, horticulture, forestry and public health applications. It is not under patent.

Diflubenzuron has low solubility in water and is stable in aqueous solution, although its half-life is significantly shorter at higher pH, and it is reasonably stable to photolysis.

The Meeting was provided with confidential information on the manufacturing process and manufacturing specifications for purity and impurities, which were supported by 5-batch analysis data, and a comparison of these data with those submitted for registration in the USA and EU. Mass balances in the 5-batch analyses were high (99.3-100.3%) and no

⁵ Extension of the analytical method to GR, DT and SC was validated and adopted by CIPAC in 2005.

unidentified impurities were detected. A statement was provided by the Australian Pesticides and Veterinary Medicines Authority, confirming that the confidential data on the manufacturing process and declaration of composition (specification limits for the active and impurities) for diflubenzuron provided to the APVMA by Crompton were identical to those provided to the FAO/WHO.

The Meeting agreed that none of the impurities should be regarded as relevant.

Diflubenzuron toxicity was assessed using the relatively pure TC, the TK (VC-90, 90% diflubenzuron), or, for wildlife studies in water, an 80% WG. Diflubenzuron is generally of low acute toxicity and, although a slight reaction was observed in eye irritation tests, this did not warrant its classification as an eye irritant according to EU Directive 67/548/EEC. Diflubenzuron was not observed to cause any carcinogenic, mutagenic, teratogenic or neurotoxic effects. Diflubenzuron is generally of low toxicity to other wildlife, other than insects, with *Daphnia magna* being the most sensitive species reported.

Diflubenzuron was last reviewed by IPCS in 1994 and by the FAO/WHO JMPR in 2001 and 2002. The WHO hazard classification is: unlikely to present acute hazard in normal use.

A full CIPAC analytical method is available for determination and identification of diflubenzuron in the TK and WP. It has not been validated according to CIPAC guidelines for the analysis of GR, DT or SC formulations but it was validated and compared with another method by the manufacturer in a GLP study, in accordance with U.K. PSD guidelines⁶. The two methods are compared in the following table.

	CIPAC Method 339/TK/M/-	GC Laboratories Ltd Method M569
Column	250 x 4.6 mm Zorbax TM _{BP} -C ₈ Spherisorb ODS 5 µm	250 x 4.6 mm 4 µm Synergi Polar-RP
Mobile phase	Acetonitrile-water-dioxane (450+450+100 v/v)	Dioxane-water (55+45 v/v)
Flow rate	1.3 ml/min	1.0 ml/min
Column temperature	Ambient	30°C
Detector wavelength	254 nm	254 nm
Injection volume	20 µl	5 µl
Internal standard	Linuron	Diphenyl phthalate
Retention times	Diflubenzuron about 7 min Linuron about 4 min	Diflubenzuron 8.9 min Diphenyl phthalate 12.5 min
Sample solute	Dioxane	Dimethylformamide

Test methods for the determination of physical properties of the TK and formulations are full CIPAC methods.

The proposed specifications were in accordance with the guidelines given in the manual (FAO/WHO 2002), with the following exceptions.

TK. The Meeting considered whether the specification related to a TC or TK but the manufacturer explained that the TK is a minimally diluted TC, intended for the manufacture of formulations. The nominal content of diflubenzuron in the TK was confirmed to be 900 g/kg, with a tolerance of ±25 g/kg, giving a minimum of 875 g/kg. Additional clauses were proposed for wet sieving, bulk density and particle size

⁶ U.K. Pesticides Safety Directorate. Guidelines for the Validation of Analytical Methods for Pesticides (PRD 2400), Commission Directive 96/46/EC and SANCO/3030/99 rev 4 'Guidance for generating and reporting methods of analysis in support of pre- and post-registration data requirements for Annex III (part A, Section 5) of Directive 91/414'.

distribution. The manufacturer explained that control of particle size is important for good efficacy of the formulations prepared from the TK and the Meeting agreed that a clause for particle size should be included in the specification.

WP. The Meeting questioned the limit of 2 minutes for wettability. The manufacturer explained that this reflected the low affinity of diflubenzuron for water and the Meeting accepted the limit. The manufacturer specified a maximum retention of 1% in the wet sieve test, based on the use of a 44 µm test sieve. The Meeting agreed that the clause should be based on the usual 75 µm test sieve, the manufacturer stated that a limit of 1% would be required and this was accepted by the Meeting.

GR. The Meeting and manufacturer agreed that the term “bulk density” should be replaced by “pour density” and that a clause for pH range was unnecessary. The Meeting agreed that water should be specified as a relevant impurity and that a high limit is required for acidity, after the manufacturer explained that the granules contain an effervescent system, for disintegration of the granules after application to water for insect control. The granules are not intended for dispersion in water prior to application to water in the field and the Meeting agreed that it was not necessary to include a clause for granule disintegration.

DT. The Meeting and manufacturer agreed that a clause for pH range was unnecessary. The Meeting agreed that water should be specified as a relevant impurity and that a high limit is required for acidity, after the manufacturer explained that the tablets contain an effervescent system. The manufacturer explained that the majority of the acid present is not consumed in the effervescent reaction (which aids dispersion of the active ingredient) but, following application of the tablets to water for insect control, also aids dispersal of the active ingredient by simple dissolution. The tablets are not intended for dispersal in water prior to application in the field. Diflubenzuron is a slow-acting insecticide and effects on larvae are generally seen after 24-48 hours. The manufacturer stated that, at water temperatures where mosquito larvae can survive, the tablets fully disintegrate within 10-30 minutes. The Meeting accepted that the high content of water-soluble acid should be sufficient to ensure dispersion, even in the absence of the effervescence reaction, and that therefore it was not necessary to include a clause for tablet disintegration.

SC. The Meeting and manufacturer agreed that a clause for acidity/alkalinity or pH is not required, because diflubenzuron has a very low solubility in water and does not dissociate. The manufacturer proposed a specification for wet sieve testing, based on a maximum retention of 0.1% of the formulation on a 150 µm test sieve. The Meeting agreed that the usual 75 µm test sieve should be specified. The manufacturer stated that tests indicated that maximum residue retention on a 75 µm sieve is less than 1% and the Meeting accepted this as an appropriate limit.

Recommendations

The Meeting recommended that:

- (i) existing WHO specifications for diflubenzuron TK and WP should be withdrawn;
- (ii) the proposed specification for diflubenzuron TK, as amended, should be adopted by FAO and WHO;

- (iii) the proposed specification for diflubenzuron SC, as amended, should be adopted by FAO, subject to CIPAC adoption of the analytical method extension to SC⁷;
- (iv) the proposed specification for diflubenzuron WP, as amended, should be adopted by WHO;
- (v) the proposed specifications for diflubenzuron GR and DT should be adopted by WHO, subject to CIPAC adoption of the analytical method extensions to these formulations⁷ and successful WHOPES testing/evaluation of the GR and DT for public health use⁸.

⁷ Extension of the analytical method to GR, DT and SC was validated and adopted by CIPAC in 2005.

⁸ WHOPES evaluation was successfully completed in 2005 (WHOPES 2005).

References

Crompton document No.	Year and title or published reference
CIPAC H	Diflubenzuron, <i>in</i> W. Dobrat and A Martijn, Eds., CIPAC Handbook H, pp. 141-146. Collaborative International Pesticides Analytical Council, Harpenden, U.K., 1998.
DI 11387	1999. Determination of the dissociation constant of diflubenzuron.
DI 11496	1999. The boiling point of diflubenzuron technical.
DI 11497	1999. A 4-week inhalation toxicity study of Dimilin technical in rats.
DI 2168	1980. Subchronic dietary toxicity study in rats-diflubenzuron.
DI 2203	1977. Acute oral toxicity study with DU 112307 Technical in mice.
DI 2207	1973. Acute toxicity studies with DU 112307 in mice and rats.
DI 2212	1980. Ninety-day subchronic toxicity study in mice - diflubenzuron technical.
DI 2216	1975. Effect of repeated applications of DU 112307 to the skin of rabbits for three weeks.
DI 2217	1975. Effect of repeated applications of DU 112307 to the skin of rabbits for three weeks.
DI 2227	1976. Acute toxicity in rats of DU 112307 Technical after dermal application.
DI 2261	1977. Mutagenic evaluation of diflubenzuron technical batch FL 44/605201.
DI 2263	1977. Evaluation of diflubenzuron in vitro malignant transformation in BALB/3t3 Cells.
DI 2264	1977. Evaluation of diflubenzuron unscheduled DNA synthesis in Wi-38 cells.
DI 2348	1974. Mutagenic study with TH 6040 In albino mice.
DI 2349	1975. Effect of DU 112307 on Pregnancy of the Rat.
DI 2350	1975, Effect Of DU 112307 on Pregnancy of the New Zealand white rabbit.
DI 2359	1975. Subacute inhalation toxicity to the rat of DU 112307 insecticide powder (technical) (evaluation of methaemoglobinaemia).
DI 2360	1975. Acute inhalation toxicity to the rabbit of DU 112307 technical grade powder.
DI 2375	1974. DU 112307 toxicity in repeated dietary administration to beagle dogs (repeated administration for 13 weeks).
DI 2376	1973. Dietary administration of DU 112307 to male and female rats for three months. 1973. Appendix III to Report No.56645/13a/1973 individual data: dietary administration of DU 112307 to male and female rats for 3 months.
DI 3462	1978. Effect of dietary administration of DU 112307 on reproductive function of one generation in the rat.
DI 3513	1973. Acute inhalation toxicity to the rat of DU 112307 technical grade powder.
DI 3516	1975. Effect of DU 112307 on reproductive function of multiple generations in the rat.
DI 3517	1979. Effects of DU 112307 in dietary administration to rats for 9 weeks.
DI 3522	1980 Histopathologic evaluation of mice administered diflubenzuron in the diet.
DI 3523	1974. DU 112307 preliminary assessment of the toxicity to male mice in dietary administration for 6 weeks.
DI 3525	1975. Tumorigenicity study of DU 112307 to mice. Dietary administration for 80 weeks.
DI 3528	1977. Addendum report to the chronic studies with DU 112307 a. dietary adm. to rats for 104 weeks b. dietary adm. to mice for 80 weeks.
DI 3597	1976. Study: acute oral toxicity in mallard ducks. Compound: TH6040 99.4% pure (air milled).
DI 3598	1976. Study: acute oral toxicity in bobwhite quail. Compound: TH 6040 99.4% pure (air milled).
DI 3603	1973. Eight-day dietary LC50-Mallard ducks Technical TH-6040 Final report.
DI 3604	1973. Eight-day dietary LC50-Bobwhite Quail Technical TH-6040 Final report.
DI 4037	1976. Effects of DU 112307 in dietary administration to rats for 104 weeks.
DI 4155	1981. The effects of dietary administration of diflubenzuron to male and female HC/CFLP mice for 14 weeks.

Crompton document No.	Year and title or published reference
DI 4161	1977. Preliminary assessment of the effect of DU 112307 on the rat.
DI 4279	1980. Histopathologic evaluation of rats administered diflubenzuron in the diet.
DI 4852	1985. Diflubenzuron. 52 week oral toxicity study in dogs. (volume 1 and 2).
DI 4958	1984. Acute dermal toxicity study with diflubenzuron VC-90 in rats.
DI 4959	1984. Acute oral toxicity study with diflubenzuron VC-90 in rats.
DI 4960	1984. Primary irritation of diflubenzuron VC-90 to the rabbit eye.
DI 4961	1984. Primary irritation of diflubenzuron VC-90 to the rabbit skin.
DI 5707	1986. Mutagenicity evaluation of diflubenzuron technical in an in vitro cytogenetic assay measuring chromosome aberration frequencies in chinese hamster ovary cells.
DI 5710	1986. Diflubenzuron VC 90 acute inhalation toxicity study in rats (limit test).
DI 6152	1987. Acute toxicity of diflubenzuron technical to sheepshead minnow (<i>Cyprinodon variegatus</i>).
DI 6552	1987. Diflubenzuron Oral (Gavage) Rat Teratology Limit Study.
DI 6553	1987. Diflubenzuron oral (gavage) rabbit teratology limit study.
DI 6689	1993. Photodegradation of [¹⁴ C]-diflubenzuron in water: an estimation of the quantum yield.
DI 6773	1988. The acute toxicity of diflubenzuron to <i>Daphnia magna</i> .
DI 6799	1988. Hydrolysis of ¹⁴ C-labelled diflubenzuron in buffer solutions at pH 5, pH 7 and pH 9.
DI 7016	1988. Determination by HPLC of the log P value of diflubenzuron and its primary metabolites.
DI 7081	1988. The vapour pressure of diflubenzuron.
DI 7233	1989. Solubility of diflubenzuron in water at 298 K.
DI 7234	Kuijpers, L.A.M. 1993. The impact of Dimilin on honey-bees: a review.
DI 7987	1990. Evaluation of DNA repair inducing ability of diflubenzuron in a primary culture of rat hepatocytes (with independent repeat).
DI 7988	1990. Study to examine the possible mutagenic activity of diflubenzuron in the Ames Salmonella/microsome assay.
DI 8146	1984. The effect of diflubenzuron given by oral administration with the feed on toxicity and tumour development in male and female HC/CFLP mice.
DI 8147	1984. Oncogenicity study in rats, diflubenzuron.
DI 8423	1992. Sensitization study with diflubenzuron technical in guinea pigs.
DI 8580	1992. The acute toxicity of diflubenzuron to the earthworm <i>Eisenia fetida</i> .
DI 8667	1993. Diflubenzuron: a 5-day toxicity test with the freshwater alga (<i>Selenastrum capricornutum</i>).
DI 8668	1993. Diflubenzuron: A 96-hour flow-through acute toxicity test with the sheepshead minnow (<i>Cyprinodon variegatus</i>).
DI 8925	1994. The acute toxicity of diflubenzuron to zebra fish (<i>Brachydanio rerio</i>).
DI 8926	1994. The acute toxicity of diflubenzuron to rainbow trout (<i>Oncorhynchus mykiss</i>).
DI 8927	1994. The acute toxicity of Dimilin WG-80 to rainbow trout (<i>Oncorhynchus mykiss</i>).
DI 8929	1994. The acute toxicity of Dimilin WG-80 to zebra fish (<i>Brachydanio rerio</i>).
DI 9104	1994. The acute toxicity of Dimilin WG-80 to the alga <i>Selenastrum capricornutum</i> .
DI 9167	1995. Solubility of diflubenzuron at pH 4, 7 and 10.
DI 9180	1995. The acute toxicity of Dimilin WG-80 to <i>Daphnia magna</i> compared to diflubenzuron.
DI 9182	1995. Diflubenzuron technical – the effect on reproductive function of two generations in the rat. 1995. Diflubenzuron technical – the effect on reproductive function on two generations in the rat: addendum 1 – individual pups body weights
DI 9321	1995. Determination of the UV-vis spectra and melting point of diflubenzuron.
DI 9386	1995. Assessment of side effects of Dimilin WG-80 on the honey bee (<i>Apis mellifera</i> L.) in the field by application during bee flight.

Crompton document No.	Year and title or published reference
DI 9429	1996. 21-day dermal toxicity study in rats.
DI 987	1983, Oral (capsule) 6-weeks dose-range-finding study with diflubenzuron in male and female beagle dogs.
FAO/WHO 2002	Manual on development and use of FAO and WHO specifications for pesticides, 1st edition. FAO plant production and protection paper 173. FAO, Rome, 2002.
IPCS 1994	WHO/IPCS Environmental Health Criteria 184. Diflubenzuron. World Health Organization, Geneva, 1996 (publication date).
JMPR 2001	Diflubenzuron. Pesticide residues in food 2001; Evaluations, part II – toxicological, pp. 980-992. WHO/PCS/02.1. WHO, Geneva, 2002.
JMPR 2002	Diflubenzuron. Pesticide residues in food 2002; Evaluations, part I – residues, volume 1, pp. 359-578. FAO plant production and protection paper 175/1, FAO, Rome, 2003.
WHO 2002	The WHO recommended classification of pesticides by hazard and guidelines to hazard classification 2000-2002. WHO, Geneva, 2002.
WHOPES 2005	Report of the ninth WHOPES Working Group Meeting, WHO/HQ, Geneva, 5-9 December 2005. Geneva, World Health Organization (document WHO/CDS/NTD/WHOPES/2006.2).