Food and Agriculture Organization
of the United Nations

FAO SPECIFICATIONS AND EVALUATIONS

FOR AGRICULTURAL PESTICIDES

TRIBENURON-METHYL

Methyl 2-[4-methoxy-6-methyl-1,3,5-triaz-in-2-yl(methyl)carbamoyl-sulfamoyl]benzoate

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DISCLAIMER[1]

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

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

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

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[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 1999 onward, the development of FAO specifications follows the **New Procedure**, described first in the 5th edition of the "Manual on the development and use of FAO specifications for plant protection products" and later in the 1st edition of "Manual for Development and Use of FAO and WHO Specifications for Pesticides" (2002) - currently available as 3rd revision of the 1st edition (2016) - , which is available only on the internet through the FAO and WHO web sites.

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

FAO Specifications now only apply to products for which the technical materials have been evaluated. Consequently from the year 1999 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/core-themes/theme/pests/jmps/ps-new/en/) OR IN HARDCOPY FROM THE PLANT PROTECTION INFORMATION OFFICER.

PART ONE

SPECIFICATIONS

TRIBENURON-METHYL

TRIBENURON-METHYL

INFORMATION

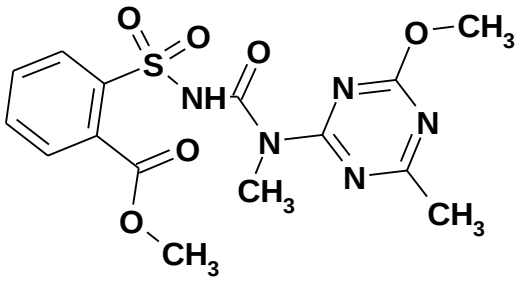
ISO common name
Tribenuron[2] (ISO 1750 published)

Synonyms
Tribenuron-methyl (ANSI, BSI)

Chemical names
IUPAC Methyl 2-[4-methoxy-6-methyl-1,3,5-triazin-2-yl(methyl)carbamoyl-sulfamoyl]benzoate

CA Methyl 2-[[[[(4-methoxy-6-methyl-1,3,5-triazin-2-yl)methylamino]carbonyl]amino]sulfonyl]-benzoate

Structural formula



Molecular formula
$C_{15}H_{17}N_5O_6S$

Relative molecular mass
395.4

CAS Registry number (for tribenuron-methyl)
101200-48-0

CIPAC number (for tribenuron-methyl)
546

Identity tests
HPLC retention time, IR spectrum

[2] The ISO common name refers to the free acid, tribenuron. When this substance is used as an ester or a salt, its identity for example tribenuron-methyl [CAS Registry number 101200-48-0], should be stated.

TRIBENURON-METHYL TECHNICAL MATERIAL

FAO Specification 546 / TC (June 2018*)

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 (546/2002, 546/2010 & 546/2017). It should be applicable to relevant products of these manufacturers but it is not an endorsement of those products, nor a guarantee that they comply with the specifications. The specification may not be appropriate for the TC of other manufacturers. The evaluation reports (546/2002, 546/2010.1, 546/2010.2 & 546/2017) as PART TWO form an integral part of this publication.

1 Description

The material shall consist of tribenuron-methyl together with related manufacturing impurities and shall be an off-white, homogenous, crystalline solid, free from visible extraneous matter and added modifying agents.

2 Active ingredient

2.1 **Identity tests** (546/TC/(M)/2, CIPAC Handbook K, p. 129, 2003)

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 **Tribenuron-methyl content** (546/TC/(M)/3, CIPAC Handbook K, p. 129, 2003)

The tribenuron-methyl 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.

* 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/thematic-sitemap/theme/pests/jmps/ps-new/en

TRIBENURON-METHYL WATER DISPERSIBLE GRANULES

FAO Specification 546 / WG (June 2018*)

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 (546/2002 and 546/2010.2). It should be applicable to relevant products of these manufacturers but it is not an endorsement of those products, nor a guarantee that they comply with the specifications. The specification may not be appropriate for the products of other manufacturers. The evaluation reports (546/2002 and 546/2010.2) as PART TWO form an integral part of this publication.

1 Description

The material shall consist of a homogenous mixture of technical tribenuron- methyl, complying with the requirements of FAO specification 546/TC (June 2018), together with filler(s) and any other necessary formulants. It shall be in granular form, having spherical or cylindrical shapes, to be applied after disintegration and dispersion in water. The product shall be dry, free flowing, and free from visible extraneous matter and hard lumps.

2 Active ingredient

2.1 **Identity tests** (546/WG/(M)/2 , CIPAC Handbook K, p. 132, 2003)

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 **Tribenuron-methyl** (546/WG/(M)/3, CIPAC Handbook K, p. 132, 2003)

The tribenuron-methyl content shall be declared and, when determined, the content obtained shall not differ from that declared by more than the following amount:

Declared content of active ingredient in g/kg	Permitted Tolerance
Above 500	± 25 g/kg

3 Physical properties

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

pH range: 6.0 to 8.5 (Note 1)

3.2 **Wettability** (MT 53.3.1, CIPAC Handbook F, p. 164, 1995)

The formulation shall be completely wetted in 10 sec. without swirling.

* 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/thematic-sitemap/theme/pests/jmps/ps-new/en

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

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

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

Dispersibility: minimum 70% after 1 minute of stirring.

3.5 **Suspensibility** (MT 184, CIPAC Handbook K, p. 142, 2003)

A minimum of 70% of the tribenuron-methyl content found under 2.2 shall be in suspension (Notes 2 and 3) after 30 min. in CIPAC standard water D.

3.6 **Persistent foam** (MT 47.3, CIPAC Handbook O, p. 177, 2017) (Note 3)

Maximum: 60 ml after 1 min.

3.7 **Dustiness** (MT 171.1) (Notes 4 & 5)

Essentially non-dusty

3.8 **Flowability** (MT 172.1, CIPAC Handbook O, p. 187, 2017)

At least 99% 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 46.3)

After storage at 35 ± 2°C for 12 weeks (Note 6), the determined average active content shall not be lower than 95%, relative to the determined average content found under 2.2 before storage (Note 7), 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).

Note 1 The pH of the formulated product must be maintained between 6.0 and 8.5 to ensure product stability.

Note 2 The specification is based upon chemical assay.

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

Note 4 Measurement of dustiness must be carried out on the sample "as received" and, where practicable, the sample should be taken from a newly opened container, because changes in the water content of samples may influence dustiness significantly. The optical submethod of MT 171.1, usually shows good correlation with the gravimetric submethod 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 submethod shall be used.

Note 5 MT 171.1 is the corrected and amended version of MT 171. Prior to its publication in a next Handbook, the method can be downloaded from https://www.cipac.org/index.php/methods-publications/errata

Note 6 Tribenuron-methyl formulations are not completely stable under the standard conditions of 54ºC for 14 days and therefore must be shown to be stable under the conditions specified. Storage under worst-case conditions in practice has shown that the formulations are stable and that the specified conditions provide a meaningful test.

Note 7 Samples taken before and after this test may be analyzed concurrently to reduce analytical error

PART TWO

EVALUATION REPORTS

TRIBENURON-METHYL

TRIBENURON-METHYL
FAO/WHO EVALUATION REPORT 546/2017

Recommendations

The Meeting recommended the following:

(i) the tribenuron-methyl TC, proposed by Jiangsu Agrochem Laboratory Co., Ltd. should be accepted as equivalent to the tribenuron-methyl reference profile

(ii) The existing FAO specification for tribenuron-methyl TC should be extended to encompass the TC produced by Jiangsu Agrochem Laboratory Co., Ltd.

Appraisal

The Meeting considered data and supporting information provided in 2016 by Jiangsu Agrochem Laboratory Co., Ltd. (Jiangsu Agrochem) for the determination of the equivalence of its tribenuron-methyl TC with the reference profile. The data submitted were broadly in accordance with the requirements of the Manual on development and use of FAO and WHO specifications for Pesticides (3rd revision of the first edition of the Manual, 2016) and demonstrate that the TC under consideration complies with the existing FAO specification for tribenuron-methyl TC. The reference specification and supporting data for tribenuron-methyl were provided by E.I. DuPont de Nemours and Company in 2001 and FAO specifications had been published in 2002.

Tribenuron-methyl belongs to the family of sulfonylurea herbicides. The compound has has not been evaluated by the WHO IPCS or by the FAO/WHO JMPR.

Tribenuron-methyl has been evaluated by the European Commission as part of the EU review of the existing active substances and it was included in Annex I of the Council Directive 91/414/EEC with a minimum purity of 950 g/kg (expressed as tribenuron-methyl). Tribenuron-methyl is widely used to control a range of broad-leafed weeds and it is not under patent.

Jiangsu Agrochem provided the Meeting with commercially confidential information on the manufacturing process for its tribenuron-methyl, five-batch analysis data on all impurities present at or above 1 g/kg and their manufacturing limits in the TC. Mass balances ranged from 1001.57 to 1002.81 g/kg in the 5-batch data. The maximum limits for the impurities were supported by the 5-batch data are statistically justified. The proposer declared the minimum purity of the tribenuron-methyl TC as 980 g/kg which is statistically justified and somewhat higher than the existing FAO TC specification (950g/kg).

The manufacturing process, impurity profile and five batch analyses were compared with the data submitted by DuPont in 2001. The synthesis pathway utilized by Jiangsu Agrochem comprises more steps than that of the reference process. The final step is similar in both manufacturers but the solvent system is different. Based on the updated 5-batch analysis data submitted, the impurity profile of Jiangsu Agrochem Laboratory Co., Ltd. has fewer impurities at or above 1 g/kg than the reference profile and no new impurities were identified except residues of the solvent used in the last reaction step. This residual solvent is considered as a new impurity, however, its presence can be discounted on ground that a maximun of 1.3 g/kg could be tolerated without increasing the hazard of the TC. This is due to a toxicological assessment based on the ADI level (highest acceptable) of the EU, the specification limit of the residual solvent, the US EPA assessment and the JMPS cumulative life-time cancer risk.

The JMPS therefore concluded, that based on these considerations the tribenuron-methyl TC produced by Jiangsu Agrochem can be considered as equivalent to the reference profile by Tier-1.

An *in-vitro* mutagenicity assay on Jiangsu Agrochem's tribenuron-methyl TC has been conducted as Tier-1 data with one of the batches used in the five batch analysis data. The outcome of the study according to OECD guideline 471 allowed the conclusion that the test material did not induce reverse mutation in the *Salmonella typhimurium* strains used in the assay with and without metabolic activation.

The proposer submitted a certificate for pesticide registration which confirmed that Jiangsu Agrochem's tribenuron-methyl TC is registered in Australia (APVMA, 2018) with a declared minimum purity of 980 g/kg which is consistent with the declared minimum purity with the data submitted to FAO.

The company utilized CIPAC method (546/TC), published in CIPAC Handbook K, for the determination of the tribenuron-methyl content in the TC, with some additional validation. The CIPAC method a reversed phase HPLC method with internal standardization using 3-methyl-1,1-diphenylurea (DPMU).

Two different methods were used for the determination of the detected impurities. For one impurity (a residual solvent) a validated GC/ECD method had been used, whereas for the determination of the other specified impurities an external standardization HPLC-UV method had been used. Both methods are adequately validated. The limit of quantification for the residual solvent was set at 0,05% w/w, the lowest recovery level.

The confirmation of the identity of tribenuron-methyl and its associated specified impurities was achieved by ^{1}H-NMR and ^{13}C-NMR, FT Infrared (FT-IR) spectroscopy, liquid-chromatography-mass spectrometry (LC-MS) and UV-spectroscopy.

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

Jiangsu Agrochem also provided a study on *in-vitro* mutagenicity of tribenuron-methyl technical material. The outcome of the study allow the conclusion that its tribenuron-methyl TC does not induce reverse mutations in the strains included in the test.

Furthermore, the Meeting recommended a minor revision of the tribenuron-methyl WG specification with regard to update some MT-methods to more recent, equivalent methods that had been adopted by CIPAC in the last few years. As examples, the revised method for persistent foam (MT 47.3) is now published in Handbook O, and a revised and corrected version of the method to determine the dustiness of granular products (MT 171.1) is now referenced.

SUPPORTING INFORMATION

FOR

EVALUATION REPORT 546/2017

Table 1. Chemical composition and properties of tribenuron-methyl technical material (TC)

Manufacturing process, maximum limits for impurities ≥ 1 g/kg, 5 batch analysis data	Confidential information supplied and held on file by FAO. Mass balances were 100.05 – 100.18 %
Declared minimum tribenuron-methyl content	980 g/kg
Relevant impurities ≥ 1 g/kg and maximum limits for them	None.
Relevant impurities **<** 1 g/kg and maximum limits for them:	None.
Stabilisers or other additives and maximum limits for them:	None.

Parameter	Value and conditions	Purity %	Method reference	Study number
Melting temperature range of the TC and/or TK	145.4~146.4 °C	98.49% w/w	OECD 102	Study 0101
Solubility in organic solvents	40~50g/l in Acetone at 20℃ 160~200g/l in 1.2-dichloroethane at 20℃ 14~20g/l in ethyl acetate at 20℃ 0.0175g/l in n-nexane at 20℃ 2.726g/l in methanol at 20℃ 9.382g/l in xylene at 20℃	98.49% w/w	CIPAC Method 181 (for solubilities >10 g/L) OECD 105 (for solubilities <10 g/L)	Study 0100

METHODS OF ANALYSIS AND TESTING

The method used for the determination of the active ingredient (including identity tests) in the TC is CIPAC 546/TC/(M)/-, published in CIPAC Handbook K. The content of tribenuron-methyl is determined by reversed phase HPLC using UV detection at 254 nm and internal standardisation with 3-methyl-1,1-diphenylurea. The confirmation of the identity of tribenuron-methyl is achieved by comparing UV spectra, mass spectra and ^{1}H-NMR spectra of the sample with a reference standard of tribenuron-methyl.

The methods for determination of impurities are based on reversed phase high performance liquid chromatography, using UV detection at 230 nm and external standardisation and GC-ECD (for a residual solvent).

PHYSICAL PROPERTIES

Test methods for determination of physical-chemical properties of the technical active ingredient were OECD and CIPAC as appropriate. The physical properties and the methods for testing them comply with the requirements of the FAO/WHO Manual (2016 edition).

CONTAINERS AND PACKAGING

No special requirements for containers and packaging have been identified

EXPRESSION OF THE ACTIVE INGREDIENT

The the content of the active ingredient tribenuron-methyl is expressed as tribenuron-methyl.

ANNEX 1

HAZARD SUMMARY PROVIDED BY THE PROPOSER

(i) The proposer confirmed that the mutagenicity data included in the summary below were derived from tribenuron-methyl 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. Mutagenicity profile of the technical material based on an *in vitro* test

Species	Test	Purity % Note[3]	Guideline, duration, doses and conditions	Result	Study number
Salmonella typhimurium	Mutagenicity	98.5%	OECD 471; *S. typhimurium* ;TA 98, TA 100, TA 1535, TA 1537 and TA 102, 3.16-10.0-31.6-100-316-1000-2500-5000µg/plate/ tube(with and without S9 mix)	non-mutagenic	161192

[3] 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.
0078		2015	Five Batches Analysis of Tribenuron-methyl Technical; Jiangsu Agrochem Laboratory; Lab study No. 0078; GLP: Yes
0100		2016	Solubility of Tribenuron-methyl Technical in organic solvents. Report study 0100. GLP: yes. Jiangsu Agrochem Laboratory, China. Unpublished.
0101		2016	Melting Point of of Tribenuron-methyl Technical. Report study 0101. GLP: yes. Jiangsu Agrochem Laboratory, China. Unpublished.
161192		2016	Reverse Mutation Assay using Bacteria (*Salmonella typhimurium*) with Tribenuron-methyl. Report study 161192. GLP: yes
	APVMA, Australia	2018	Confirmation of registration of tribenuron-methyl produced by Jiangsu Agrochem Ltd. China, dated 13 April 2018

TRIBENURON-METHYL

FAO/WHO EVALUATION REPORT 546/2010.2

Recommendation

The Meeting recommended that

(i) the tribenuron-methyl TC as proposed by Cheminova A/S be accepted as equivalent to the tribenuron-methyl reference profile

(ii) the existing FAO specification for tribenuron-methyl TC and WG should be extended to encompass the products of Cheminova.

Appraisal

The meeting considered data on tribenuron-methyl, submitted by Cheminova A/S in 2009, in support of extension of existing FAO specifications for tribenuron-methyl TC and WG (2002).

Tribenuron-methyl is not under patent. Tribenuron-methyl has not been evaluated by the FAO/WHO JMPR. and WHO/IPCS. It was evaluated by the European Commission and was included into Annex I, according to Directive 91/414, on March 1, 2006. Tribenuron-methyl is also registered in the United States of America, Canada, Australia and other countries.

The Meeting was provided with commercially confidential information on the manufacturing process and manufacturing specification for purity and impurities, supported by 5 batch analysis data for one manufacturing plant. Mass balances were >990g/kg and no unidentified impurities greater than 1 g/kg were reported. A statement has been provided confirming that the confidential data on the manufacturing process and declaration of composition submitted to the FAO were the same as those submitted to the US National regulatory authority. The data provided supported a minimum tribenuron-methyl content of 950g/kg.

Initial evaluation of the manufacturing information and batch analysis data revealed:

i) For one impurity, the limit in the Cheminova specification was greater than 3 g/kg and 50% of the content in the reference profile.
ii) There was an impurity present in the Cheminova specification that was not present in the reference profile.
The new impurity in the Cheminova tribenuron-methyl technical material is structurally very similar to an impurity found in both the Cheminova and reference profiles, differing by the substitution of a methyl group with an OH group. It was therefore considered unlikely to be differently toxic or more toxic than the impurity already present.

To further support this, a mutagenicity test conducted using a technical batch of tribenuron-methyl was considered. The batch tested was one of the batches analysed in the 5 batch study provided, therefore the tested batch is considered to be representative of production material. The study concluded that the test material did not induce mutation under the conditions of the study. The Meeting concluded that the new impurity was considered not relevant and that the increase in the level of the

other impurity was not significant in that sense that it was highly unlikely that it significantly contributed to an increase in hazard in the Cheminova material.

The meeting concluded that Tier-1 information was sufficient to decide on equivalence of Cheminova technical tribenuron-methyl with the reference profile.

The analytical method for the TC is by HPLC with UV detection as described in the CIPAC Method 546/TC/ published in Handbook K. It is a reversed phase method based on an internal standard, 3-methyl-1,1-diphenylurea (DPMU) and UV detection.

The proposer confirmed that the appearance of their technical material would comply with the description of the tribenuron-methyl TC as provided in the current FAO specification.

The proposer also confirmed that the physical properties, the methods for testing them and the limits proposed for the Cheminova WG formulations, comply with the requirements described in the existing FAO specification for tribenuron-methyl WG formulation (FAO Specification 546/WG (2002), with an editorial revision 2011).

Some minor inconsistencies in the CIPAC coding system were noted. The ISO common name - tribenuron- refers to the free acid, with a statement that possible salts or esters have to be identified. The CIPAC code 546 however refers to the tribenuron-methyl ester instead of the free acid combined with the extension for the methyl ester. In order to avoid confusion, the not entirely correct numbering was maintained to identify the specification and for reference to CIPAC methods for this compound.

SUPPORTING INFORMATION

FOR

EVALUATION REPORT 546/2010

Table 1. Chemical composition and properties of tribenuron-methyl technical materials (TC)

Manufacturing process, maximum limits for impurities ≥ 1 g/kg, 5 batch analysis data	Confidential information supplied and held on file by FAO. Mass balances were 99.35 – 100.30 % and percentages of unknowns were 0.0 – 0.65 %.
Declared minimum [a.i.] content	950 g/kg
Relevant impurities ≥ 1 g/kg and maximum limits for them	None
Relevant impurities **<** 1 g/kg and maximum limits for them:	None
Stabilisers or other additives and maximum limits for them:	None

Parameter	Value and conditions	Purity %	Method reference	Study number
Melting temperature range of the TC and/or TK	138 - 140 °C. Decomposition occurs (endothermic reaction).	98.0	OECD 102	1
Solubility in organic solvents	40-50 g/l Acetone at 20 °C 57-67 g/l Acetonitrile at 20 °C 200-250 g/l 1,2-Dichloroethan at 20 °C 29-33 g/l Ethyl acetate at 20 °C 0.020 in n-Hexane at 20 °C 2.271 g/l Methanol at 20 °C 8.122 g/l Xylene at 20 °C	98.0	CIPAC Method 181 (for solubilities >10 g/L) EEC Method A.6 (for solubilities <10 g/L)	2

USES

Tribenuron-methyl is a selective herbicide that inhibits the biosynthesis of branched amino acids in sensitive plants by competitively binding to the enzyme system which catalyzes the formation of these amino acids, the acetolactate synthase (ALS). It is used in cereals for the control of broadleaved weeds.

FORMULATIONS AND CO-FORMULATED ACTIVE INGREDIENTS

The main formulation type available is WG (agricultural formulations).

Tribenuron-methyl may be formulated alone or co-formulated with other sulfonylureas, such as thifensulfuron-methyl.

Cheminova's tribenuron-methyl WG formulations are registered and sold in Ukraine and the United States of America.

METHODS OF ANALYSIS AND TESTING

The analytical method for the active ingredient (including identity tests) is CIPAC Method 546/WG/M/-. Tribenuron-methyl is determined by HPLC using a reverse phase gradient system and ultra-violet (UV) detection at 254 nm.

The method(s) for determination of impurities are based on HPLC using a reverse phase gradient system and ultra-violet (UV) detection. Quantification is by external calibration.

Test methods for determination of physico-chemical properties of the technical active ingredient were OECD, 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 WG formulations, comply with the requirements described in the existing FAO specification for tribenuron-methyl WG formulation (FAO Specification 546/WG (2002)).

CONTAINERS AND PACKAGING

No special requirements for containers and packaging have been identified

EXPRESSION OF THE ACTIVE INGREDIENT

The active ingredient is expressed as tribenuron-methyl.

ANNEX 1

HAZARD SUMMARY PROVIDED BY THE PROPOSER

Note: Cheminova A/S provided written confirmation that the toxicological data included in the following summary were derived from tribenuron-methyl having impurity profiles similar to those referred to in Table 1, above

Table 2. Mutagenicity profile of the tribenuron-methyl technical material based on an in vitro test

Species	Test	Purity % Note[4]	Guideline, duration, doses and conditions	Result	Study number
Salmonella typhimurium *Escherichia coli*	*In vitro* test. Reverse mutation in four strains of *Salmonella typhimurium* and one strain of *Escherichia coli.*	97.38	OECD 471, Method B13/14 (EC), OPPTS 870.5100 Technical tribenuron-methyl was tested in concentrations ranging from 15 to 5000 µg/plate in the absence and presence of S-9 in the four strains of *Salmonella typhimurium* and one strain of *Escherichia coli*. The plates were incubated at 37 °C for 48 hrs.	The sensitivity of the assay was validated. Technical tribenuron-methyl did not increase the frequency of revertant colonies in the four strains of *Salmonella typhimurium* and the one strain of *Escherichia coli* when tested in concentrations up to the lower limit of toxicity. Therefore, technical tribenuron-methyl was considered to be non-mutagenic under the conditions of this test.	3

ACUTE TO CHRONIC TOXICITY

No information was available on acute to subacute to chronic toxicity of the tribenuron-methyl technical material produced by Cheminova.

MUTAGENICITY

No information was available on the mutagenicity profile of the tribenuron-methyl technical material produced by Cheminova beside the mutagenicity test provided in Table 2.

ECOTOXICITY

No information was available on ecotoxicity of the tribenuron-methyl technical material produced by Cheminova

ANNEX 2

References

Study number	Author(s)	year	Study title. Study identification number. Report identification number. GLP [if GLP]. Company conducting the study.
1	Woolley AJ and O'Connor BJ	2009	Tribenuron-methyl Technical: Determination of Melting Point/Melting Range. CHA Doc. No.: 165 TBM. 0545/0734. GLP. Harlan Laboratories Ltd., United Kingdom. Unpublished.
2	Dardemann J	2009	Determination of the Solubility of Tribenuron-Methyl in different organic Solvents. CHA Doc. No.: 167 TBM. CHE0309-PC-053. GLP. Stähler International GmbH & Co., Germany. Unpublished.
3		2009a	Tribenuron-methyl Technical (Batch No. 070708): Reverse Mutation Assay "Ames Test" using Salmonella Typhimurium and Escherichia Coli. CHA Doc. No.: 164 TBM. 0545/0738. GLP. Unpublished.

TRIBENURON-METHYL

FAO/WHO EVALUATION REPORT 546/2010.1

Recommendation

The Meeting recommended that

(i) the tribenuron-methyl TC as proposed by Helm AG be accepted as equivalent to the tribenuron-methyl reference profile

(ii) the existing FAO specification for tribenuron-methyl TC, should be extended to encompass the product of Helm AG.

Appraisal

The data for tribenuron-methyl were evaluated in support of the extension of the existing FAO specification 546/TC (2002).

Tribenuron-methyl is not under patent. Tribenuron-methyl has not been evaluated by the FAO/WHO JMPR or the WHO IPCS. It was evaluated/ reviewed by the European Commission with Sweden as the rapporteur member state in the year 2005 and will be under evaluation/review by the US EPA in 2011.

The reference specification and the supporting data were provided by E.I. du Pont de Nemours and Company, U.S.A., in 2001.

Data on tribenuron-methyl, submitted by Helm AG in 2009, in support of extension of existing FAO specifications for tribenuron-methyl TC were considered by the JMPS.

The meeting were provided with commercially confidential information on the manufacturing process and manufacturing specification for purity and impurities, supported by 5 batch analysis data for one manufacturing plant. Mass balances were >990g/kg and no unidentified impurities greater than 1 g/kg were reported. A statement has been provided confirming that the confidential data on the manufacturing process and declaration of composition submitted to the FAO were the same as those submitted to the Italian national regulatory authority. The data provided supported a minimum tribenuron-methyl content of 950 g/kg. It was noted that a mutagenicity (bacteria, in vitro) test had not been submitted as required, however this provided on request.

There are no relevant impurities proposed and identified.

The analytical method for the TC is by HPLC with UV detection as described in the CIPAC Method 546/TC/ published in Handbook K. It is a reversed phase method based on an internal standard, 3-methyl-1,1-diphenylurea (DPMU) and UV detection.

The data submitted was sufficient to come to a conclusion on equivalence of Helm AG technical tribenuron-methyl with the reference profile. The meeting concluded that Helm AG tribenuron-methyl TC was equivalent to the tribenuron-methyl reference TC based on Tier 1 evaluation as detailed in the FAO and WHO specification manual (2010 edition). The Tier1 is mainly based on chemical evidence (impurity profile, manufacturing specifications etc.) and includes only a mutagenicity study to detect the presence of exceptionally hazardous - mutagenic - impurities,

which could go undetected by chemical analysis. For that reason, the hazard data package is reduced to an *in vitro* mutagenicity study with *S. typhimurium*. As with the reference material, the Ames-test was negative. This reduced data package is reflected in the Annex 1 Hazard summary containing just the Ames test.

The proposer confirmed that the appearance of their technical material would comply with the description of the tribenuron-methyl TC as provided in the current FAO specification. The meeting noted that the proposer was seeking equivalence to the existing TC specification only, but not for the specification for the WG formulation. The reason for this is the fact that Helm sells its TC to formulators, but does not formulate its tribenuron-methyl into end-use products.

Some minor inconsistencies in the CIPAC coding system were noted. The ISO common name - tribenuron- refers to the free acid, with a statement that possible salts or esters have to be identified. The CIPAC code 546 however refers to the tribenuron-methyl ester instead of the free acid combined with the extension for the methyl ester. In order to avoid confusion, the not entirely correct numbering was maintained to identify the specification and for reference to CIPAC methods for this compound.

SUPPORTING INFORMATION

FOR

EVALUATION REPORT 546/2010

Table 1. Chemical composition and properties of tribenuron-methyl technical materials (TC)

Manufacturing process, maximum limits for impurities ≥ 1 g/kg, 5 batch analysis data	Confidential information supplied and held on file by FAO. Mass balances were 99.8 – 101.9% and percentages of unknowns (individually present < 0.1% w/w) were 0.26 – 0.29%.
Declared minimum [a.i.] content	950 g/kg
Relevant impurities ≥ 1 g/kg and maximum limits for them	None.
Relevant impurities < 1 g/kg and maximum limits for them:	None.
Stabilisers or other additives and maximum limits for them:	None.

Parameter	Value and conditions	Purity %	Method reference	Study number
Melting temperature of the TC	148.8°C	98.1% w/w	OECD 102/ EEC A1	Ref 1
Solubility in organic solvents	Not available	-	-	-

USES

Tribenuron-methyl is a selective herbicide that inhibits the biosynthesis of branched amino acids in sensitive plants by competitively binding to the enzyme system which catalyzes the formation of these amino acids, the acetolactate synthase (ALS). It is used in cereals for the control of broadleaved weeds.

FORMULATIONS

Helm AG manufactures TC only and sells it to formulators.

METHODS OF ANALYSIS AND TESTING

The analytical method for the active ingredient (including identity tests) is CIPAC Method 546/TC/(M)/3 (Ref. 3). Tribenuron-methyl is determined by reversed phase HPLC with UV detection. The methods for determination of impurities are based on reverse phase chromatography with UV detection and internal standardisation.

Test methods for determination of physico-chemical properties of the technical active ingredient were based on guidelines from OECD, EPA OPPTS and EEC.

CONTAINERS AND PACKAGING

No special requirements for containers and packaging have been identified.

EXPRESSION OF THE ACTIVE INGREDIENT

The active ingredient is expressed as tribenuron-methyl.

ANNEX 1

HAZARD SUMMARY PROVIDED BY THE PROPOSER

Note: Helm AG provided written confirmation that the toxicological data included in the following summary were derived from tribenuron-methyl having impurity profiles similar to those referred to in Table 1, above

Table 2. Mutagenicity profile of the technical material based on an in vitro test

Species	Test	Purity % Note[5]	Guideline, duration, doses and conditions	Result	Study number
Salmonella typhimurium	Ames Test, *in vitro*	97.2	OECD 471; EC 440/2008 B.13/14; OPPTS 870/5100 strains: TA 98, TA 100, TA 1535, TA 1537 and TA 102; 3.16,10, 31.6, 100, 316, 1000, 2500 and 5000 µg/plate (with and without metabolic activation)	Negative	Ref. 2

ACUTE TO CHRONIC TOXICITY

No information was available on acute to subacute to chronic toxicity of the tribenuron-methyl technical material produced by Helm AG.

MUTAGENICITY

No information was available on the mutagenicity profile of the tribenuron-methyl technical material produced by Helm AG beside the mutagenicity test provided in Table 2.

ECOTOXICITY

No information was available on ecotoxicity of the tribenuron-methyl technical material produced by Helm AG.

ANNEX 2

References

Ref number	Author(s)	year	Study title. Study identification number. Report identification number. GLP [if GLP]. Company conducting the study.
1	Wo, Catherine	2009	Tribenuron-methyl Physical and Chemical characteristics: Colour, physical state, odour, oxidation/reduction, pH, UV/visible absorption, Melting point and Bulk density; Eurofins Product Safety Laboratories; Lab study no 27813; GLP: Yes
2	Nakinust, D	2010	Reverse Mutation Assay using Bacteria *(Salmonella typhimurium)* With Tribenuron-methyl TC;BSL BioService Scientific Laboratories GmbH; Lab study no 102673; GLP: Yes

TRIBENURON-METHYL

EVALUATION REPORT 546/2002

Explanation

The data for tribenuron-methyl were evaluated in support of new FAO specifications for the technical material (546/TC) and water dispersible granules (546/WG).

Tribenuron methyl is under patent in Austria, Belgium, Denmark, Finland, France, Germany, Greece, Hungary, Ireland, Italy, Luxembourg, Netherlands, Norway, Portugal, Sweden, Switzerland and the United Kingdom, until May 2006.

Tribenuron-methyl has not been evaluated by the FAO/WHO JMPR or WHO/IPCS. It is currently under review by the European Commission for registration in the European Union, with Sweden as the rapporteur member state.

The draft specification and supporting data were provided by E.I. du Pont de Nemours and Company, U.S.A., in 2001.

Uses

Tribenuron-methyl is a selective herbicide that inhibits the biosynthesis of branched amino acids in sensitive plants by competitively binding to the enzyme system which catalyzes the formation of these amino acids, the acetolactate synthase (ALS). It is used in cereals for the control of broadleaved weeds.

Identity

ISO common name

Tribenuron (ISO 1750 published[6])

Chemical name(s)

IUPAC

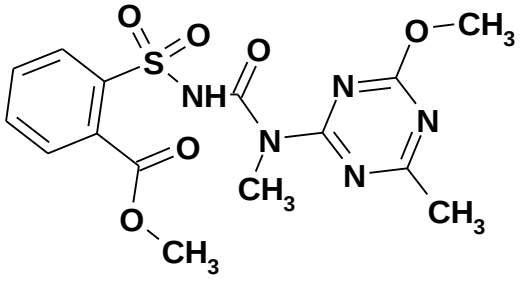
Methyl 2-[4-methoxy-6-methyl-1,3,5-triazin-2-yl(methyl)carbamoyl-sulfamoyl]benzoate

CA

Methyl 2-[[[[(4-methoxy-6-methyl-1,3,5-triazin-2-yl)methylamino]carbonyl]amino]sulfonyl]-benzoate

[6] The ISO common name refers to the free acid, see footnote on p. 3

Structural Formula



Molecular formula

$C_{15}H_{17}N_5O_6S$

Relative molecular mass

395.4

CAS Registry number

101200-48-0

CIPAC number

546

Identity tests

HPLC retention time and IR spectrum.

Table 1. Physico-chemical properties of pure tribenuron-methyl

Parameter	Value(s) and conditions	Purity %	Method reference
Vapour pressure	5.2×10^{-8} Pa at 25 °C (extrapolated)	99.3% a.i.	EPA 63-9 (Reference 1)
Melting point, boiling point and/or temperature of decomposition	Melting point: 142 +/- 1.1°C Boiling point: not applicable Decomposition temperature: Decomposes in the range 145°C to 185°C	97.76% a.i.	EEC A.1. OECD 102 (capillary method) EPA 830.7200
Solubility in water	0.0489 g/l at 20 °C at pH 5 2.04 g/l at 20 °C at pH 7 18.3 g/l at 20 °C at pH 9	99.3% a.i.	EPA 63-8 CIPAC 157 Shake flask method
Partition coefficient n-octanol/water	log P_{OW} = 2.6 at 25 °C at pH 5 log P_{OW} = 0.78 at 25 °C at pH 7 log P_{OW} = 0.30 at 25 °C at pH 9	97.76% a.i.	EEC A.8. EPA 830.7570 OECD 107 HPLC method
Hydrolysis characteristics	Half-life <1 day at 25°C at pH 5 <15.8 days at 25°C at pH 7 stable at 25°C at pH 9	97% radiochemical purity for each of two different labels	EPA 161-1 and EPA 161-2 (References 2 and 3, respectively)
Photolysis characteristics	Tribenuron-methyl was photolytically stable at pH 5, 7, and 9 at 25 °C	97% radiochemical purity for each of two different labels	EPA 161-2 (Reference 3)
Dissociation characteristics	pKa = 4.7	99.3% a.i.	OECD 112 EPA 63-11 Spectrophotometric method

Table 2. Chemical composition and properties of tribenuron-methyl technical material

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 989.0 to 997.5 g/kg.
Declared minimum [a.i.] content	950 g/kg
Relevant impurities ≥ 1 g/kg and maximum limits for them	None.
Relevant impurities < 1 g/kg and maximum limits for them:	None.
Stabilisers or other additives and maximum limits for them:	None.
Melting or boiling temperature range	Melting range 141 to 143°C, decomposition occurs from 145 to 185°C.

ANNEX 1

HAZARD SUMMARY PROVIDED BY THE PROPOSER

Note: DuPont provided written confirmation that the toxicological data included in the following summary were derived from tribenuron-methyl having impurity profiles similar to those referred to in Table 2, above

Table 3. Toxicology profile of the tribenuron-methyl technical material, based on acute toxicity, irritation and sensitization

Species	Test	Duration and conditions or guideline adopted	Result
Male and Female Rat (Crl:CD®(SD)IGS BR)	Oral	USEPA 870.1100 (1998), OECD 401 (1987), 59 NohSan No. 4200 (1985), EEC Method B.1. (1992) Tribenuron-methyl technical (97.8% a.i.)	LD_{50} = >5000 mg/kg bw No mortalities were observed. No clinical signs were observed in males. No clinical signs were observed in females after test day 10.
Male and Female Rat (Crl:CD®(SD)IGS BR)	Dermal	USEPA 870.1200 (1998), OECD 402 (1987), 59 NohSan No. 4200 (1985), EEC Method B.3. (1992) Tribenuron-methyl technical (97.8% a.i.)	LD_{50} = >5000 mg/kg bw No mortalities were observed. No clinical signs were observed after test day 2.
Male and Female Rat (Crl:CD®(SD)IGS BR)	Inhalation	USEPA 870.1300 (1996), 59 NohSan No. 4200 (1985), OECD 403 (1981) Tribenuron-methyl technical (97.7% a.i.)	LC_{50} = 6.0 mg/L No mortalities were observed. No clinical signs were observed after test day 6.
Male Rabbit (New Zealand White)	Skin irritation	OECD 404 (1992), 92/69 Annex V – EEC Method B4 (1992), 59 NohSan No. 4200 (1985), USEPA 81-5 (1984). Tribenuron-methyl technical (95.8% a.i.)	Dermal non-irritant (according to Directive 67/548/EEC)
Female Rabbit (New Zealand White)	Eye irritation	USEPA 81-4 (1982) Tribenuron-methyl technical (96.6% a.i.)	Ocular non-irritant (according to EU Directive 67/548/EEC)
Female Guinea Pig (Dunkin-Hartley albino)	Skin sensitization (Maximisation)	EEC Method B.6. (1984) Tribenuron-methyl technical (purity not stated)	Sensitizing (according to Directive 67/548/EEC)
Male and Female Guinea Pig (Dunkin-Hartley albino)	Skin sensitization (Buehler)	US EPA 81-6 Tribenuron-methyl technical (96.6% a.i.)	Non-sensitizing (10% response upon rechallenge)
Male Guinea Pig (Hartley albino)	Skin sensitization (Modified Draize)	Not listed; method pre-dates current guidelines, but is comparable to OECD/EEC guidelines Tribenuron-methyl technical (94% a.i.)	Non-sensitizing

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

Species	Test	Duration and conditions or guideline adopted	Result
Male and Female Rat (Crl:CD®(SD)BR)	Oral 90 day feeding study	FIFRA 82-1 Tribenuron-methyl technical (99% a.i.)	NOAEL = 100 ppm (7 and 8 mg/kg/day respectively for males and females)
Male and Female Mouse (Crl:CD®-1(ICR)BR)	Oral 90 day feeding study	USEPA 82-1 (1982) Tribenuron-methyl technical (98% a.i.)	NOAEL = 500 ppm (70 and 90 mg/kg/day respectively for males and females)
Male and Female Dog (Beagle)	Oral 1 year feeding study	USEPA 83-1 (1982) Tribenuron-methyl technical (95.8% a.i.)	NOAEL = 250 ppm (8.16 and 8.18 mg/kg/day respectively for males and females)
Male and Female Rat (Crl:CD®BR)	Oral 2 year chronic toxicity and carcinogenicity study	US EPA 83-5 Tribenuron-methyl technical (96.8% a.i.)	NOAEL = 25 ppm (0.95 and 1.2 mg/kg/day respectively for males and females)
Male and Female Mouse (Crl:CD®-1(ICR)BR)	Oral 18 month carcinogenicity feeding study	US EPA 83-2 (1985) Tribenuron-methyl technical (94.2% a.i.)	NOAEL = 200 ppm (25 and 35 mg/kg/day respectively for males and females) Not a carcinogen.
Male and Female Rat (Crl:CD®(SD)BR)	Two-generation reproduction study	US EPA 83-4 (1982) Tribenuron-methyl technical (94.2% a.i.)	NOAEL = 25 ppm (1.9 - 2.28 and 2.15 - 2.64 mg/kg/day respectively for males and females)
Female Rat (Crl:COBS®CD®(SD)BR)	Developmental toxicity study	US EPA (1982) Tribenuron-methyl technical (94.2% a.i.)	NOAEL = 20 mg/kg for both maternal and fetal effects

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

Species	Test	Conditions	Result
Salmonella typhimurium	*In vitro* bacterial gene mutation assay	Absence and presence of an exogenous S9 metabolic activation system US EPA 84-2 (1982) Tribenuron-methyl technical (94%)	Negative for mutagenic activity
Human Lymphocytes	*In vitro* mammalian cytogenetics test using human peripheral blood lymphocytes (HPBL)	Absence and presence of an exogenous S9 metabolic activation system USEPA 870.5375 (1996), USEPA 84-2 (1982), EEC 92/69 method B.10 (1992) Tribenuron-methyl technical (97.8%)	Negative for the induction of structural chromosome aberrations
Chinese hamster ovary (CHO) cells	*In vitro* mammalian cell gene mutation assay	Absence and presence of an exogenous S9 metabolic activation system USEPA 870.5300 (1996), USEPA 84-2 (1982), EEC 87/302 part B (1987) Tribenuron-methyl technical (97.8%)	Negative for CHO/HGRPT gene mutations
Rat Primary Hepatocytes	*In vitro* unscheduled DNA synthesis (UDS)	U.S. EPA Pesticide Assessment Guidelines, Subdivision F, 83-1 Tribenuron-methyl technical (96.8%)	Negative for UDS
Male and Female Rat (Cr1:CD®(SD)BR)	*In vivo* bone marrow metaphase analysis for chromosome aberrations	EEC Method B.11. (1984) Tribenuron-methyl technical (96.8%)	Negative for the induction of structural chromosome aberrations in bone marrow cells and is considered nonclastogenic
Male and Female Mouse (Crl:CD®-1(ICR)BR)	*In vivo* bone marrow micronucleus assay	EEC Method B.11. (1984) Tribenuron-methyl technical (96.8%)	Negative for induction of micronuclei in bone marrow cells

Table 6. Ecotoxicology profile of the technical material

Species	Test	Duration and conditions	Result
Daphnia magna (Water flea)	Acute 48-hour static toxicity	U.S. EPA Pesticide Assessment Guideline; FIFRA 72-2 (a); OECD Guideline for Testing Chemicals, No. 202 (adopted April 1984); EEC 92/69 Annex V, Method C.2 (1992) Tribenuron-methyl technical (98.9% a.i.)	LC_{50} and EC_{50} = >894.0 mg/l NOEC = 894.0 mg/l
Daphnia magna (Water flea)	21-day semi-static chronic toxicity	U.S. EPA Pesticide Assessment Guideline; Subdivision E, 72-4; OECD Guideline for Testing Chemicals, No. 202 (1984) Tribenuron-methyl technical (95.8% a.i.)	Survival: LOEC = 940.0 mg/l NOEC = 480.0 mg/l Immobilisation: EC_{50} = > 940.0 mg/l Reproduction: EC_{50} = 900.0 mg/l LOEC = 480.0 mg/l NOEC = 250.0 mg/l Growth: LOEC = 250.0 mg/l NOEC = 120.0 mg/l
Selenastrum capricornutum (Green alga)	120-hour effect on growth and growth rate	OECD Guideline for Testing Chemicals, No. 201 (adopted April 1984); EU Commission Directive 92/69/EEC, Method C3; U.S. EPA; Non-Target Aquatic Plant Studies, Pesticide Assessment Guidelines, Subdivisions J, 122-2, 123-2 (1987) Tribenuron-methyl technical (97.4% a.i.)	**Cell Density:** EC_{50} = 0.0221 mg a.s./l NOEC = 0.004 mg a.s./l **Area under growth curve:** EC_{50} = 0.0208 mg a.s./l NOEC = 0.004 mg ai/l **Growth rate:** EC_{50} = 0.1119 mg a.s./l NOEC = 0.004 mg a.s./l
Anabaena flos-aquae (Blue-green alga)	120-hour effect on growth and growth rate	U.S. Environmental Protection Agency (USEPA), Non-Target Aquatic Plant Studies, Pesticides Assessment Guidelines, Subdivision J, 122-2, 123-2 (1982) Tribenuron-methyl technical (97.4% a.i.)	**Cell Density:** EC_{50} = 4.2 mg a.s./l NOEC = 1.25 mg a.s./l **Area under growth curve:** EC_{50} = 2.6 mg a.s./l NOEC = <0.63 mg a.s./l **Growth rate:** EC_{50} = 13.1 mg a.s./l NOEC = 1.25 mg a.s./l

Table 6. Ecotoxicology profile of the technical material, continued

Species	Test	Duration and conditions	Result
Lemna gibba G3	14-day influence on growth and reproduction	U.S. EPA-FIFRA, 40 CFR, Part 158.540, Pesticide Assessment Guidelines, Sub-division J, 123-2 Tribenuron-methyl technical (92.56% a.i.)	**Frond number:** EC_{50} = 0.00425 mg a.s./l NOEC = 0.00102 mg a.s./l **Frond biomass:** EC_{50} = 0.00559 mg a.s./l NOEC = 0.00102 mg a.s./l
Eisenia fetida (Savigny) (Earthworm)	14-day soil exposure acute toxicity	OECD No. 207 (1984); ISO 11268-1 (1993) Tribenuron-methyl technical (97.76% a.i.)	LC_{50} = 1000 mg/kg dry soil
Apis mellifera (Honey bee)	48-hour acute oral and contact toxicity	EPPO 170 Tribenuron-methyl technical (98.44% a.i.)	**Contact:** LD_{50} and NOEL = >98.4 µg a.s./bee **Oral:** LD_{50} and NOEL = > 9.1 µg a.s./bee
Colinus virginianus (Bobwhite quail)	Acute oral toxicity	US EPA (1982) Tribenuron-methyl technical (96.8% a.i.)	LD_{50}= >2250 mg ai/kg bw NOEL = <292 mg ai/kg bw
Colinus virginianus (Bobwhite quail chicks)	5-day acute dietary study	US EPA 71-2 (1982) Tribenuron-methyl technical (96.8% a.i.)	LC_{50}= >5620 ppm NOEL = 1780 ppm
Anas platyrhynchos (Mallard ducklings)	5-day acute dietary study	US EPA 71-2 (1982) Tribenuron-methyl technical (96.8% a.i.)	LC_{50}= >5620 ppm NOEL = 1780 ppm
Colinus virginianus (Bobwhite quail)	23-week sub-chronic toxicity and reproduction	US EPA 71-4 (1988), OECD 206 (1984) Tribenuron-methyl technical (95.8% a.i.)	NOEC = 180 mg a.s./kg diet (Based on a slight reduction in offspring survival)

Species	Test	Duration and conditions	Result
Anas platyrhynchos (Mallard duck)	21-week Subchronic toxicity and reproduction	US EPA 71-4 (1982), OECD 206 (1984) Tribenuron-methyl technical (95.8% a.i.)	NOEC = 180 mg a.s./kg diet (Based on egg production and hatchling body weight)
Oncorhynchus mykiss (Rainbow trout)	Acute 96 hour static toxicity	OECD Method 203; EEC 92/69 Annex V Method C.1 (1992) Tribenuron-methyl technical (98.9% a.i.)	LC_{50}= 738 mg/l
Lepomis macrochirus (Bluegill sunfish)	Acute 96-hour static toxicity	U.S. EPA Pesticide Assessment Guidelines; Subdivision E, 72-1 Tribenuron-methyl technical (96.8% a.i.)	LC_{50}= >1000 mg/l
Salmo gairdneri *(Rainbow trout)*	Flow through 21-day toxicity on juveniles	OECD Guideline for Testing Chemicals, No. 204 (adopted 4 April 1984) Tribenuron-methyl technical (95.8% a.i.)	LC50 and EC50 = >560.0 mg/l

Hazard Summary

Tribenuron-methyl has not been evaluated by the WHO IPCS or by the FAO/WHO JMPR.

Tribenuron-methyl has not been classified according to IPCS hazard.

European Union classifications are N R 50/53 ECB, very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment. The classification is driven by the algal toxicity endpoint according to Annexes I, II, III, IV to Commision Directive 93/21/EEC of 27 April 1993.

Formulations

The main formulation type available is of water dispersible granules (WG). This type of formulation is registered and sold in many countries throughout the world.

Methods of analysis and testing

The analytical method for the active ingredient (including identity tests) was adopted with provisional status by CIPAC in 2002. The tribenuron-methyl is determined by reversed-phase HPLC, using UV detection at 254 nm and internal standardisation with 3-methyl-1,1-diphenylurea. The method for determination of impurities was based on reversed-phase HPLC, using UV detection at 230 nm and external standardisation.

Test methods for determination of physico-chemical properties of the technical active ingredient were OECD, CIPAC, EPA and EEC, 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 WG formulations, comply with the requirements of the FAO Manual (5th edition).

Containers and packaging

No extraordinary container or packaging requirements are necessary.

Expression of the active ingredient

The active ingredient is expressed as tribenuron-methyl.

Appraisal

Tribenuron-methyl is a post emergence sulfonyl urea herbicide, acting through foliar uptake with little or no soil activity. It is used for the control of a wide range of broad-leaved weeds in cereal crops including wheat, barley, oats and rye. It affects sensitive plants by inhibition of the plant enzyme acetolactate synthase. It is applied once or twice per growing season at a maximum seasonal rate of 30g ai/ha.

Pure tribenuron-methyl is an off-white powdered solid with a slight pungent odour, that melts at 142°C and decomposes after melting in the range of 145°C to 185°C.

A major route of dissipation in the environment is aqueous hydrolysis. Hydrolysis half-lives for tribenuron-methyl were less than one day at pH 5 and 15.8 days at pH 7 but it is reported to be stable at pH 9. The proton attached to the nitrogen-atom in the sulfonylurea moiety shows acidic properties, so that the pKa of tribenuron-methyl with a value of 4.7 is comparable to the acidity of a carboxylic acid. As a consequence, the aqueous solubility is pH dependent, with solubility increasing as pH increases (with formation of the salt). The aqueous solubility at 20°C is 0.0489, 2.04 and 18.3 g/l at pH 5, 7, and 9 respectively It is interesting to note, that the hydrolysis rate increases with lowering the pH. No significant photolysis of tribenuron-methyl occurs over the pH range 5 to 9 at 25°C. The *n*-octanol:water partition coefficient (log Pow) is 2.6, 0.78, and 0.30 at 25°C at pH 5, 7 and 9 respectively.

Volatilisation is not expected to contribute significantly to the dissipation of tribenuron-methyl in the environment, as indicated by the low vapour pressure of 5.2×10^{-8} Pa at 25°C.

Confidential information on the method of manufacture, the technical specification and data from the analysis of production batches was presented to the meeting. The proposer stated that the confidential data presented were identical to those submitted for registration in the European Union, with Sweden as the rapporteur. In addition, the data were confirmed as being the same as those provided for registration in Greece. Mass balances were 98.9 to 99.75% and the minimum purity of the technical material was 950 g/kg. All production batches showed minimum purities well above this value. The meeting did not consider any of the impurities of tribenuron-methyl to be relevant.

The analytical method for the active ingredient (including identity tests) was adopted with provisional status by CIPAC in 2002. The tribenuron-methyl is determined by

reversed-phase HPLC, using UV detection at 254 nm and internal standardisation with 3-methyl-1,1-diphenylurea. The method for determination of impurities was based on reversed-phase HPLC, using UV detection at 230 nm and external standardisation.

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

The meeting considered the use of a modified Draize test to be questionable for determination of skin sensitization, as it was originally intended for skin irritation. The proposer provided data from Buehler and Maximization tests, the latter showing a weak response which, in the EU evaluation of tribenuron-methyl, was not considered positive or indicative of a likely human sensitizer. The meeting acknowledged that the risks had been assessed as acceptable in the many countries in which tribenuron-methyl has been registered.

The data provided for the technical material supports the specification for the TC as proposed.

In considering the specification for the water dispersible granules (WG) formulation, the meeting accepted the proposer's statement that it is essential to manufacture the product so that the pH of an aqueous dispersion is within the range 6.0 to 8.5, to ensure that product stability is maintained. With respect to the test for stability at elevated temperature, the proposer explained that, at 54ºC for 14 days, more than 5% of the tribenuron-methyl is degraded. The proposer presented data showing that if the test is carried out at 35ºC for 12 weeks, the degradation does not exceed 4%. The proposer stated that the product is stable in hot climates and provided evidence from a 2-year shelf-life study, showing that storage under practical high temperature conditions does not lead to significant degradation of the active ingredient.

Recommendations

The meeting recommended that the specifications for tribenuron-methyl TC and WG should be adopted as new FAO specifications.

ANNEX 2

References

1 U.S. Environmental Protection Agency, Pesticide Assessment Guidelines, Subdivision N, Product Chemistry, Series 63-9, National Technical Information Service Document No. PB 83-153890, October 1982.

2 U.S. Environmental Protection Agency, Pesticide Assessment Guidelines, Subdivision N, Chemistry, Environmental Fate, Series 161-1, National Technical Information Service Document No. PB 83-153973, October 1982.

3 U.S. Environmental Protection Agency, Pesticide Assessment Guidelines, Subdivision N, Chemistry, Environmental Fate, Series 161-2, National Technical Information Service Document No. PB 83-153973, October 1982.