FAO SPECIFICATIONS AND EVALUATIONS

FOR PLANT PROTECTION PRODUCTS

BETA-CYFLUTHRIN

(1*RS*, 3*RS*; 1*RS*, 3*SR*)-3-(2,2-dichloro-vinyl)-2,2-dimethyl-cyclopropane- carboxylic acid (*RS*)-cyano-(4-fluoro-3-phenoxy-phenyl)-methyl ester

FOOD AND AGRICULTURE ORGANIZATION *of* THE UNITED NATIONS

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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.

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

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

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[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 WHO specifications follows the **New Procedure**, described 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 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. Dates of publication of the earlier versions, if any, are identified in a footnote. Evaluations bear the date (year) of the meeting at which the recommendations were made by the JMPS.

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

PART ONE

SPECIFICATIONS

BETA-CYFLUTHRIN

***BETA*-CYFLUTHRIN**

INFORMATION[2]

Common name

beta-cyfluthrin (ISO 1750 published)

Chemical names

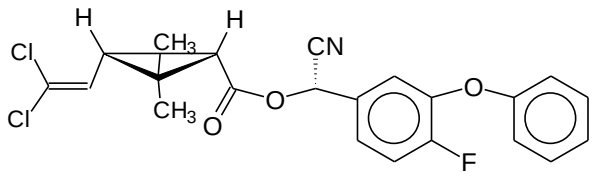
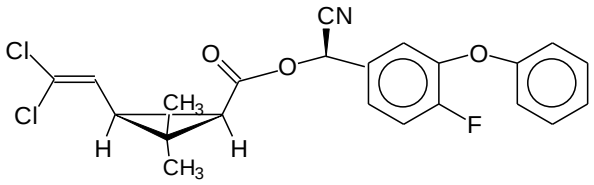
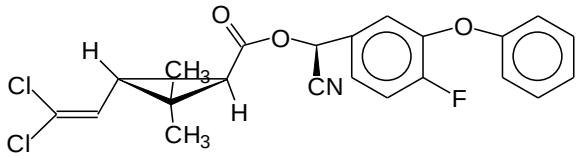
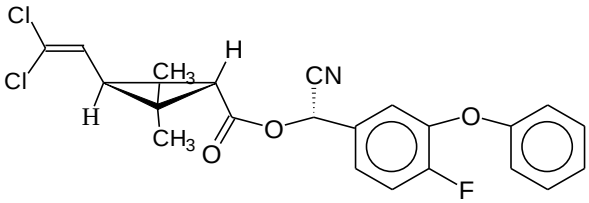
IUPAC a reaction mixture comprising the enantiomeric pair (*R*)-*α*-cyano-4-fluoro-3-phenoxybenzyl (*1S,3S*)-3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropanecarboxylate and (*S*)-α-cyano-4-fluoro-3-phenoxybenzyl (*1R,3R*)-3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropanecarboxylate
in ratio 1:2 with the enantiomeric pair (*R*)-*α*-cyano-4-fluoro-3-phenoxybenzyl (*1S,3R*)-3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropanecarboxylate and (*S*)-*α*-cyano-4-fluoro-3-phenoxybenzyl (*1R,3S*)-3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropanecarboxylate

CA cyclopropanecarboxylic acid, 3-(2,2-dichloroethenyl)-2,2-dimethyl-, (R)-cyano(4-fluoro-3-phenoxyphenyl)methyl ester, (1S,3S)-rel-

CAS Registry number 1820573-27-0

[2] The "Information" Section was updated in September 2017 with regard to the recently assigned CAS name and CAS registry number now specific for *beta*-cyfluthrin.

Structural formulae

	1*R-cis*-α*R*	Diastereomer II
	1*S-cis*-α*S*	
	1*R-trans*-α*R*	Diastereomer IV
	1*R-trans*-α*S*	

Molecular formula

$C_{22}H_{18}Cl_2FNO_3$

Relative molecular mass

434.3

CIPAC code number

482

Identity tests

Retention time in normal phase HPLC, ^{1}H-NMR

BETA-CYFLUTHRIN TECHNICAL MATERIAL

FAO Specification 482 / TC (August 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 (482/1999 & 482/2016). It should be applicable to relevant products of this manufacturer but it is not an endorsement of those products, nor a guarantee that they comply with the specifications. The specification may not be appropriate for the products of other manufacturers. The evaluation reports (482/1999 & 482/2016) as PART TWO form an integral part of this publication.

1 Description

The material shall consist of *beta*-cyfluthrin together with related manufacturing impurities, in the form of a white to yellowish powder, free from visible extraneous matter and added modifying agents.

2 Active ingredient

2.1 **Identity tests** (CIPAC 482/TC/M/2, CIPAC Handbook H, p. 44, 1998)

The active ingredient shall comply with an identity test and, where the identity remains in doubt, it shall comply with at least one additional test.

2.2 ***Beta*-cyfluthrin content** (CIPAC 482/TC/M/3, CIPAC Handbook H, p. 45, 1998)

The *beta*-cyfluthrin content shall be declared (not less than 965 g/kg) and, when determined, the mean measured content shall not be lower than the declared minimum content.

2.3 **Isomer ratio** (CIPAC 482/TC/M/3, CIPAC Handbook H, p. 45, 1998)

Beta-cyfluthrin is a mixture of two diastereoisomers (Note 1) and their ranges shall be:

diastereoisomer II	300 – 400 g/kg
diastereoisomer IV	570 – 670 g/kg

3 Physical properties

3.1 **Acidity** (CIPAC MT 31.1)

Maximum: 2 g/kg calculated as H_2SO_4.

———————————

Note 1 Retention time in HPLC increases from diastereoisomer I to IV.

* 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/

BETA-CYFLUTHRIN EMULSIFIABLE CONCENTRATE

FAO Specification 482 / EC (August 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 (482/1999 & 482/2016). It should be applicable to relevant products of this manufacturer but it is not an endorsement of those products, nor a guarantee that they comply with the specifications. The specification may not be appropriate for the products of other manufacturers. The evaluation report ((482/1999 & 482/2016) as PART TWO form an integral part of this publication.

1 Description

The material shall consist of technical *beta*-cyfluthrin, complying with the requirements of FAO specification 482/TC (August 2016), dissolved in suitable solvents, together with any other necessary formulants. It shall be in the form of a stable homogeneous liquid, free from visible suspended matter and sediment, to be applied as an emulsion after dilution in water.

2 Active ingredient

2.1 **Identity tests** (CIPAC 482/EC/M/2, CIPAC Handbook H, p. 48, 1998)

The active ingredient shall comply with an identity test and, where the identity remains in doubt, it shall comply with at least one additional test.

2.2 ***Beta*-cyfluthrin content** (CIPAC 482/EC/M/3, CIPAC Handbook H, p. 48, 1998)

The *beta*-cyfluthrin content shall be declared (g/kg or g/l at 20 ± 2 °C, Note 1) and, when determined, the content measured shall not differ from that declared by more than the following amounts:

Declared content in g/kg or g/l at 20 °C	Tolerance
up to 25	± 15 % of the declared content
above 25 up to 100	± 10 % of the declared content
Note: In each range the upper limit is included	

* 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/

2.3 Isomer ratio (CIPAC 482/TC/M/3, CIPAC Handbook H, p. 45, 1998)

Beta-cyfluthrin is a mixture of two diastereoisomers (Note 2) and their ranges per 1000 g of beta-cyfluthrin shall be:

diastereoisomer II	300 – 400 g/kg
diastereoisomer IV	570 – 670 g/kg

3 Relevant impurities

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

Maximum: 2.0 g/kg

4 Physical properties

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

pH range: 4.5 to 7.0

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

The formulation, when diluted at 30 ± 2 °C (Note 3) with CIPAC Standard Waters A and D, shall comply with the following:

Time after dilution	Limits of stability, MT 36.3
0 h	initial emulsification complete
0.5 h	“cream”, maximum: 0 ml
2.0 h	“cream”, maximum: 1 ml
	“free oil”, maximum: 0 ml
24 h	re-emulsification complete
24.5 h	“cream”, maximum: 0 ml
	“free oil”, maximum: 0 ml

Note: tests after 24 h are required only where results at 2 h are in doubt.

4.3 **Persistent foam** (CIPAC MT 47.3) (Notes 4 & 5)

Maximum: 10 ml after 1 min.

5 Storage stability

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

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

5.2 **Stability at elevated temperature** (CIPAC MT 46.3, Handbook J, p. 128, 2000)

After storage at 54 ± 2 °C for 14 days, the determined average *beta*-cyfluthrin content must not be lower than 95 % relative to the determined average content found before storage (Note 6) and the formulation shall continue to comply with the clauses for: pH range (4.1) and emulsion stability and re-emulsification (4.2).

Note 1 If the buyer requires both g/kg and g/l at 20 °C, then in case of dispute the analytical results shall be calculated as g/kg.

Note 2 Retention time in HPLC increases from diastereoisomer I to IV.

Note 3 As outlined in CIPAC MT 36.3, the test concentrations should be based on those in the recommended directions for use supplied with the product. Where several concentrations are recommended, the highest and lowest concentrations within the scope of the method should be used.

Note 4 The mass of sample to be used in the test should correspond to the highest rate of use recommended by the supplier. The test is to be conducted in CIPAC standard water D.

Note 5 MT 47.3 is a revised version of MT 47.2 using a standard measuring cylinder. This new method was accepted as a full CIPAC method in 2013. Prior to publication of the method in a Handbook, copies of the method may be obtained through the CIPAC website, http://www.cipac.org/index.php/methods-publications/pre-published-methods

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

BETA-CYFLUTHRIN SUSPENSION CONCENTRATE

FAO Specification 482 / SC (August 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 (482/1999 & 482/2016). It should be applicable to relevant products of this manufacturer but it is not an endorsement of those products, nor a guarantee that they comply with the specifications. The specification may not be appropriate for the products of other manufacturers. The evaluation report (482/1999 & 482/2016) as PART TWO form an integral part of this publication.

1 Description

The material shall consist of a suspension of fine particles of technical *beta*-cyfluthrin, complying with the requirements of FAO specification 482/TC (August 2016), in an aqueous phase together with suitable formulants. After gentle agitation the material shall be homogeneous (Note 1) and suitable for further dilution in water.

2 Active ingredient

2.1 **Identity tests** (CIPAC 482/SC/M/2, CIPAC Handbook H, p. 49, 1998)

The active ingredient shall comply with an identity test and, where the identity remains in doubt, it shall comply with at least one additional test.

2.2 ***Beta*-cyfluthrin content** (CIPAC 482/SC/M/3, CIPAC Handbook H, p. 49, 1998)

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

Declared content in g/kg or g/l at 20 ± 2 °C	Tolerance
up to 25	± 15% of the declared content
above 25 up to 100	± 10% of the declared content
above 100 up to 250	± 6% of the declared content
Note. In each range the upper limit is included.	

* 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/

2.3 Isomer ratio (CIPAC 482/TC/M/3, CIPAC Handbook H, p. 45, 1998)

Beta-cyfluthrin is a mixture of two diastereoisomers (Note 2) and their ranges per 1000 g of beta-cyfluthrin shall be:

diastereoisomer II	300 – 400 g/kg
diastereoisomer IV	570 – 670 g/kg

3 Physical properties

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

pH range: 4.0 to 5.5 (undiluted)

3.2 **Pourability** (CIPAC MT 148.1, Handbook J, p. 133, 2000)

Maximum residue: 3 %

3.3 **Spontaneity of dispersion** (CIPAC MT 160, Handbook F, p. 391) (Note 4)

A minimum of 90 % of the beta-cyfluthrin content found under 2.2 shall be in suspension after 5 min in CIPAC Standard Water D at 30 ± 2 °C.

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

A minimum of 95 % of the beta-cyfluthrin content found under 2.2 shall be in suspension after 30 min in CIPAC Standard Water D at 30 ± 2 °C.

3.5 **Wet sieve test** (CIPAC MT 185, Handbook K, p. 149, 2003) (Note 5)

Maximum: 0.1 % of the formulation shall be retained on a 75 µm test sieve.

3.6 **Persistent foam** (CIPAC MT 47.3) (Notes 6 &7)

Maximum: 30 ml after 1 min.

4 Storage stability

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

After storage at 0 ± 2 °C for 7 days, the formulation shall continue to comply with suspensibility (3.4) and wet sieve test (3.5).

4.2 **Stability at elevated temperature** (CIPAC MT 46.3, Handbook J, p. 128, 2000)

After storage at 54 ± 2 °C for 14 days, the determined average *beta*-cyfluthrin content must not be lower than 98 % relative to the determined average content found before storage (Note 8) and the formulation shall continue to comply with the clauses for:

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

Note 1 Before sampling to verify the formulation quality, inspect the commercial container carefully. On standing, suspension concentrates usually develop a concentration gradient from the top to the bottom of the container. This may even result in the appearance of a clear liquid on the top and/or of sediment on the bottom. Therefore, before sampling, homogenize the formulation according to the instructions given by the manufacturer or, in the absence of such instructions, by gentle shaking of the commercial container (for example by inverting the closed container several times). Large containers must be opened and stirred adequately. After this procedure, the container should not contain a sticky layer of non-dispersed matter at the bottom. A suitable and simple method of checking for a non-dispersed sticky layer "cake" is by probing with a glass rod or similar device adapted to the size and shape of the container. All the physical and chemical tests must be carried out on a laboratory sample taken after the recommended homogenization procedure.

Note 2 Unless homogenization is carried out carefully, it is possible for the sample to become aerated. This can lead to errors in the determination of the mass per millilitre and in calculation of the active ingredient content (in g/l) if methods other than MT 3.3 are used. If the buyer requires both g/kg and g/l at 20 °C, then in case of dispute the analytical results shall be calculated as g/kg.

Note 3 Retention time in HPLC increases from diastereoisomer I to IV.

Note 4 Chemical assay is the only fully reliable method to measure the mass of active ingredient still in suspension. However, simpler methods such as gravimetric and solvent extraction determination may be used on a routine basis provided that these methods have been shown to give equal results to those of the chemical assay method. In case of dispute, the chemical method shall be the referee method.

Note 5 This test detects coarse particles (e.g. caused by crystal growth) or agglomerates (crust formation) or extraneous materials which could cause blockage of spray nozzles or filters in the spray tank.

Note 6 The mass of sample to be used in the test should be specified at the application rate of use recommended by the supplier.

Note 7 MT 47.3 is a revised version of MT 47.2 using a standard measuring cylinder. This new method was accepted as a full CIPAC method in 2013. Prior to publication of the method in a Handbook, copies of the method may be obtained through the CIPAC website, http://www.cipac.org/index.php/methods-publications/pre-published-methods.

Note 8 Samples of the formulation taken before and after the storage stability test may be analyzed concurrently after the test in order to reduce the analytical error.

PART TWO

EVALUATION REPORTS

BETA-CYFLUTHRIN

BETA-CYFLUTHRIN

FAO/WHO EVALUATION REPORT 482/2016

Recommendations

The Meeting recommended that:

i) the revised specification for beta-cyfluthrin TC, proposed by Bayer CropScience, as amended, should be adopted by FAO.

ii) the specifications for the beta-cyfluthrin EC and SC formulations should be editorially updated

Appraisal

A draft specification and a confidential data package in support of the revision of the TC specification was received in 2015.

The FAO specification for *beta*-cyfluthrin dates back to 1999 and belonged to the first compounds that were evaluated under the "New procedure". The compound is a pyrethroid insecticide where the ISO common name refers to a mixture of two diastereomers out of possible four for cyfluthrin.

In the meantime, it became apparent that the TC specification for *beta*-cyfluthrin was not in line with the ISO common name definition for that compound and some newer data on composition of the TC had become available. Whereas cyfluthrin consists of 8 stereoisomers that can be grouped into 4 diastereomers (called I to IV according to increasing retention time in liquid chromatography) *beta*-cyfluthrin essentially consists of diastereomers II and IV that are racemic in themselves. Diastereomer II has two enantiomers with 1*R*-*cis*-α*S* and 1*S*-*cis*-α*R* configuration, and IV has two enantiomers with 1*R*-*trans*-α*S* and 1-*S*-*trans*-α*R* configuration, respectively, using the Rothamsted nomenclature (Elliott, 1974). These two diastereomers show higher insecticidal activity than diastereomers I and III.

A confidential data package on synthesis and composition of 5 typical batches was received (BCS, 2015). The mass balances were in the range of 985 to 998 g/kg and no impurities unrelated to cyfluthrin were detected. The minimum purity of beta-cyfluthrin is 965 g/kg and the range of the contents of diastereomers II and IV are 300 - 400 g/kg and 570 to 670 g/kg, respectively. The method used to identify, separate and quantify the cyfluthrin diastereomers is similar as the CIPAC method, but considered acceptable under these circumstances, as a kind of internal standardization is used when comparing peak areas of the cyfluthrin isomers and the method was fully validated.

The CIPAC Method 482/TC/M/2.1 published in Handbook H is based on normal phase HPLC with UV detection and allows separation and quantification of four cyfluthrin diastereomers in TC, EC and SC formulations.

Comparing the published specification for *beta*-cyfluthrin with the new data, the chemical purity for *beta*-cyfluthrin (expressed as sum of diastereomer II and IV) remains unchanged with 965 g/kg, and no relevant impurities were proposed and identified. The relative amounts of II and IV remain unchanged as well (300 to 400 g/kg and 570 to 670 g/kg) but

diastereomers I and III not being part of the ISO common name definition are no longer mentioned and are considered as non-relevant impurities.

The EC and SC specifications were updated with regard to the insertion of a clause for stereoisomers content and for the physical-chemical test methods e.g. emulsion stability (MT 36.1.1 replaced by MT 36.3), determination of water (MT 30 replaced by MT 30.5) and persistent foam (MT 47.2 replaced by MT 47.3).

References appraisal

Authors(s)	year	Document/Journal
BCS	2015	Confidential Data On Beta-Cyfluthrin
M. Elliott, N. F. Janes & D. A. Pulman,	1974	J. Chem. Soc., Perkin Trans. I, 1974, p. 2470 (first footnote)

BETA-CYFLUTHRIN

EVALUATION REPORT 482/1999

Explanation

An evaluation of proposed new specifications for an active ingredient protected under patent in the USA until 16.06.2006 (No. 4 782 174, 1988).

Beta-cyfluthrin is currently under review by the European Commission, according to Regulation 3600/92/EEC. It has not been evaluated by the FAO/WHO JMPR.

The draft specifications and the supporting data were provided by Bayer AG in 1999.

Uses

Beta-cyfluthrin is an insecticide, acting as a contact and stomach poison. It combines a rapid knock-down effect with long lasting efficacy. It is not systemic in plants. It is used in agriculture, horticulture (field and protected crops) and viticulture. It is also used against migratory locusts and grasshoppers and in public health and hygiene.

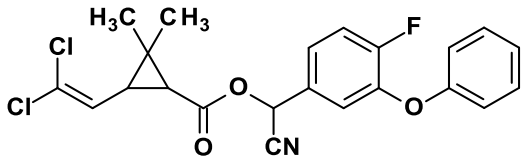
Identity

ISO common name
beta-cyfluthrin (accepted)

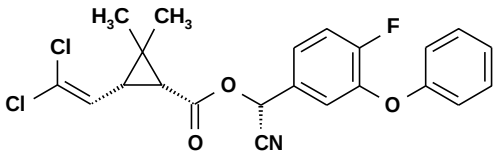
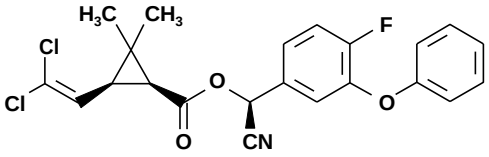
Synonyms
none

Chemical names IUPAC
3-(2,2-dichloro-vinyl)-2,2-dimethyl-cyclopropane-carboxylic acid cyano-(4-fluoro-3-phenoxy-phenyl)-methyl ester (unstated stereochemistry)
CA
Cyclopropanecarboxylic acid, 3-(2,2-dichloroethenyl)-2,2-dimethyl-, cyano (4-fluoro-3-phenoxyphenyl) methyl ester (unstated stereochemistry)

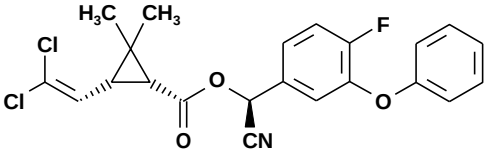
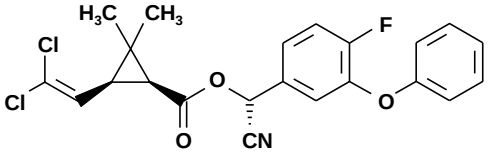
Structural formula



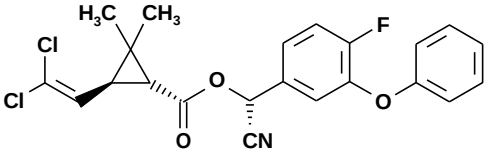
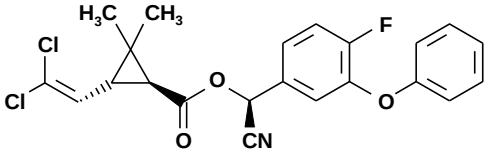
Beta-cyfluthrin is a mixture, predominantly of two diastereoisomers, II and IV. The diastereoisomers I and III are present in low proportion (< 5 %).

I:  + 

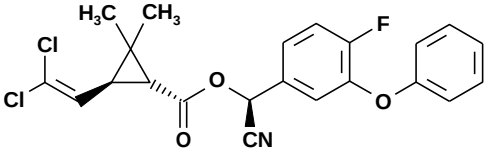
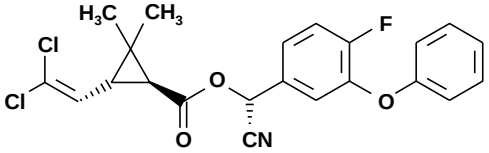
1R, 3R, αR (= 1,3-cis) 1S, 3S, αS (= 1,3-cis)

II:  + 

1R, 3R, αS (= 1,3-cis) 1S, 3S, αR (= 1,3-cis)

III:  + 

1R, 3S, αR (= 1,3-trans) 1S, 3R, αS (= 1,3-trans)

IV:  + 

1R, 3S, αS (= 1,3-trans) 1S, 3R, αR (= 1,3-trans)

Molecular formula

$C_{22}H_{18}Cl_2FNO_3$

Relative molecular mass

434.3

CAS Registry numbers

68359-37-5 (unstated stereochemistry)
86560-92-1 (diastereoisomer I)
86560-93-2 (diastereoisomer II)
86560-94-3 (diastereoisomer III)
86560-95-4 (diastereoisomer IV)

CIPAC number

482

Identity tests

CIPAC Method Handbook H (1998), Beta-Cyfluthrin 482/TC/M/2, pp 44-45. HPLC retention time and chromatographic pattern; thin-layer chromatography*; IR (KBr)*; ^{1}H-NMR (200 MHz, CD_2Cl_2).

* Note: beta-cyfluthrin and cyfluthrin cannot be distinguished by these tests.

Physico-chemical properties of the pure active ingredient

Vapour pressure	Diastereoisomer II (purity 97.4 %): 1.4 x 10^{-8} Pa at 20 °C (by extrapolation). Diastereoisomer IV (purity 98.9 %): 8.5 x 10^{-8} Pa at 20 °C (by extrapolation). Method: OECD 104 / EC A4. The vapour pressure of beta-cyfluthrin is very low.
Melting point	Diastereoisomer II (purity 99.2 %): 80.71 °C. Diastereoisomer IV (purity 99.8 %): 106.19 °C. Method: EC A1.
Solubility in water	Diastereoisomer II (purity 97.5%): 2.1 µg/l at 20 °C. Diastereoisomer IV (purity 95.9%): 1.2 µg/l at 20 °C. The pH was not declared. Method: OECD 105/EC A6. Beta-cyfluthrin is of very low solubility in water.
Octanol/water partition coefficient	Diastereoisomer II (purity 97.5%): log P_{OW} = 6.18 at 22 °C.Diastereoisomer IV (purity 95.9%): log P_{OW} = 6.18 at 22 °C. The pH was not declared. Method: OECD 107 / EC A8. Beta-cyfluthrin is lipophilic with a tendency for bioaccumulation.
Hydrolysis characteristics	The material used was a mixture of 4 diastereoisomeric pairs (purity 99.0 %). Under all conditions tested diastereoisomers II and IV isomerized partially to diastereoisomers I and III, respectively, before degradation by hydrolysis became significant. Isomerization rates were not determined. Therefore, it was only possible to determine half-lives for the degradation of the sums of diastereoisomers I and II and diastereoisomers III and IV. 20 °C / 25 °C pH 4 diastereoisomers I + II: > 1 yr / > 1 yr diastereoisomers III + IV: > 1 yr / > 1 yr pH 7 diastereoisomers I + II: 270 d / 120 d diastereoisomers III + IV: 160 d / 75 d pH 9 diastereoisomers I + II: 42 h / 21 h diastereoisomers III + IV: 33 h / 17 h Method: OECD 111 / C7. Beta-cyfluthrin is very stable to hydrolysis at pH 4, stable at pH 7 but readily hydrolysed at pH 9.

Chemical composition and properties of the technical material (TC and TK)

Confidential information on the manufacturing process and the impurity profile (5 batch analysis data and maximum content of all impurities present at or above 1 g/kg) was presented by the Proposer and is held on file by FAO.

Declared minimum content

minimum 965 g/kg (total of isomers I - IV).

Ratio of diastereoisomers, as a proportion of the sum

diastereoisomer I, maximum 2.0 %

diastereoisomer II, 30.0 – 40.0 %

diastereoisomer III, maximum 3.0 %

diastereoisomer IV, 57.0 – 67.0 %.

Relevant impurities and maximum limits for them

none of the impurities reported in the analytical profile of batches was considered relevant.

Hazard summary

The evaluation is based partly on beta-cyfluthrin and partly on cyfluthrin. In general both substances have the same toxicological profile. Depending on different administration vehicles, beta-cyfluthrin has approximately 2 to 5 times higher acute toxicity than cyfluthrin.

Toxicological profile of the technical material based on acute oral, dermal and inhalation toxicity; skin and eye irritation, skin sensitization

Acute oral toxicity

Rat, male (fasted)	LD_{50}	11 mg/kg body weight (water/Cremophor EL)
Rat, male (fasted)	LD_{50}	380 mg/kg body weight (PEG 400)
Rat, female (fasted)	LD_{50}	651 mg/kg body weight (PEG 400)
Mouse, male (fasted)	LD_{50}	91 mg/kg body weight
Mouse, female (fasted)	LD_{50}	165 mg/kg body weight
Dog, male (fasted)	LD_{50}	> 5000 mg/kg body weight
Dog, female (fasted)	LD_{50}	> 5000 mg/kg body weight

Acute oral toxicity depends on the nature of the vehicle employed.

Acute dermal toxicity

The dermal toxicity of beta-cyfluthrin is very low (rat LD_{50} > 5000 mg/kg body weight).

Acute inhalation toxicity

Rat (aerosol: a.i. in ethanol/PEG 400)	LC_{50} (4 h):	81 – 100 mg/m³
Rat (dust)	LC_{50} (4 h):	532 – 967 mg/m³

Skin irritation

New Zealand White rabbits tolerated the application of beta-cyfluthrin without exhibiting any manifestation of irritation.

Eye irritation

The treatment produced slight irritation of the conjunctivae of New Zealand White rabbits. However, the changes were reversible within 2 days of application.

Skin sensitisation

No evidence of a skin sensitising potential has been found in the maximisation test on guinea pigs according to the Magnusson and Kligman protocol.

Toxicological profile of the technical material based on repeated administration (from subacute to chronic) and studies such as reproductive an development toxicity, genotoxicity, carcinogenicity, etc.

Sub-acute/sub-chronic toxicity

Groups of rats were treated orally by gavage with beta-cyfluthrin at doses of 0, 0.25, 1, 4 or 16 mg/kg body weight/day for 4 weeks. Treatment up to 1 mg/kg body weight/day was tolerated without adverse signs.

Rats were exposed to beta-cyfluthrin aerosols for 4 weeks (6 h per day, 5 days per week). Concentrations up to 0.2 mg/m³ air were tolerated without adverse effects.

Groups of rats and dogs received beta-cyfluthrin in their feed for 13 weeks. Concentrations up to 125 mg/kg respectively 60 mg/kg feed were tolerated by male and female rats respectively male and female dogs without effects.

Chronic toxicity

Long-term feeding studies were conducted with cyfluthrin on rats, mice and dogs. The following concentrations were tolerated without effects:

Rat (24 months)	50 mg/kg feed (ppm)*
Mouse (23 months)	200 mg/kg feed (ppm)*
Dog (12 months)	160 mg/kg feed (ppm)*

* applied to the diastereoisomers ratio in cyfluthrin.

Carcinogenicity

In a.m. chronic feeding studies with rats and mice, no evidence of oncogenic potential of cyfluthrin was found. Cyfluthrin studies are regarded as representative for beta-cyfluthrin.

Reproduction

Groups of 10 male and 20 female rats received cyfluthrin via the feed throughout an entire experimental period (3 successive generations, 2 matings each). Concentrations up to 50 mg/kg feed had no effect on the fertility and did not induce malformations in the young.

Developmental toxicity

Groups of inseminated rats and rabbits were treated with cyfluthrin in daily oral doses. No primary embryotoxic or teratogenic effects were observed.

Genotoxicity

The mutagenic potential of beta-cyfluthrin was studied in various in-vitro and in-vivo test systems. None of the test systems used revealed any evidence of mutagenic and/or genotoxic potential of beta-cyfluthrin.

Neurotoxicity

In sub-chronic studies with cyfluthrin on rats and chickens no signs of delayed neurotoxicity were observed on either the clinical or the histological level.

Ecotoxicological profile

Acute toxicity to fish

In laboratory flow-through studies the following results (LC_{50}, 96 h) were obtained:

Golden orfe (*Leuciscus idus melanotus,* 20 – 22 °C):	331 ng/l
Rainbow trout (*Oncorhynchus mykiss*, 12 – 13 °C):	89 ng/l

Acute toxicity to Daphnia

The acute toxicity of beta-cyfluthrin technical to water fleas was determined under flow-through conditions. The 48-hour EC_{50} value for *Daphnia magna* exposed to beta-cyfluthrin at 20 °C was approximately 0.3 µg a.i./l.

Effects on algal growth

The effects of beta-cyfluthrin technical on the growth of the green alga, *Scenedesmus subspicatus*, were determined in a 96-hour laboratory study under static test conditions using test concentrations of 1 and 10 µg a.i./l nominal concentration at 23 °C. Because of the low water solubility of this compound it was impossible to test higher concentrations. The EC_{50} for the growth rate was determined to be > 10 µg a.i./l. The no-observed-effect-concentration was >10 µg a.i./l. No toxic signs were observed at 10 µg a.i./l, the highest concentration tested.

Effects on aquatic ecosystems

In studies with beta-cyfluthrin in natural and artificial ponds a pronounced but transient depression of populations of crustaceans was observed. Due to the rapid disappearance of the compound from the water phase (low water solubility and extremely high adsorption to organic material), recovery of the crustacean population is also rapid. No adverse effects on flora and other fauna of the ecosystem, fish included, were observed.

Effects on earthworms

The acute toxicity of beta-cyfluthrin to earthworms was determined to be LC_{50} > 1000 mg/kg dry weight soil, *i.e.* beta-cyfluthrin can be regarded as non toxic to earthworms.

Effects on bees

The acute toxicity of beta-cyfluthrin to bees was determined to be LD_{50} < 0.025 µg/bee, *i.e.* beta-cyfluthrin must be regarded as toxic to bees.

Effects on birds

Beta-cyfluthrin is practically non-toxic to birds, as indicated by an acute TEL (threshold effect level) of > 2000 mg a.i./kg b.w. for bobwhite quail. The TEL for bobwhite quail of cyfluthrin is in the same range. The short term TEC (threshold effect concentration) for cyfluthrin was determined to be 2200 mg a.i./kg diet for bobwhite quail and 3200 mg a.i. /kg diet for mallard duck.

WHO (IPCS) evaluation

IPCS has not evaluated beta-cyfluthrin.

WHO IPCS hazard classification

moderately hazardous, class II.

FAO/WHO JMPR evaluation

FAO/WHO JMPR has not evaluated beta-cyfluthrin.

Formulations

Main formulation types available in the market

EC, SC.

Main countries where the formulations are registered and sold

Both formulation types are registered and sold in many countries all over the world.

Methods of analysis and testing

Chemical analysis method for active ingredient (identity tests included)

CIPAC Method, Handbook H (1998), Beta-cyfluthrin 482/TC/M/-, pp 43-51. Beta-cyfluthrin is determined by normal phase HPLC, using UV detection at 235 nm with external standardisation.

Physical testing methods

Test methods used to determine the physico-chemical properties of the active ingredient were OECD and EU, while those used for the formulations were CIPAC, corresponding to those indicated in the specifications.

Physical properties

The physical properties, the methods for testing them and the limits proposed for the EC and the SC formulations, comply with the recommendations of the FAO Manual, 5th edition.

Containers and packaging

No special requirements were identified for containers and packaging:

Expression of the active ingredient

The active ingredient is expressed as beta-cyfluthrin in g/kg or g/l for liquid formulations at 20±2°C.

Appraisal

The data submitted are in accordance with the requirements of the FAO Manual, 5th edition, and support the specifications.

Beta-cyfluthrin is an isomeric mixture consisting predominantly of 2 diastereoisomeric pairs (II + IV) of enantiomers. Melting points of enantiomer pairs II and IV are 80.71°C and 106.19°C respectively. Beta-cyfluthrin is very slightly volatile and very slightly soluble in water. It is hydrolytically very stable at pH 4, stable at pH 7 but readily hydrolysed at pH 9. It is a lipophilic compound with a tendency for bioaccumulation.

It is formulated as emulsifiable concentrates (EC) and suspension concentrates (SC).

The Meeting was provided with commercially confidential information on the manufacturing process and batch analysis data on impurities present at or above 1 g/kg, which were declared to be identical to those submitted for registration in Germany.

The acute oral toxicity of beta-cyfluthrin is rather high, the dermal toxicity very low, while the acute inhalation toxicity is higher as an aerosol than in the form of a dust.

There is no evidence of genotoxic potential, delayed neurotoxicity, carcinogenic potential or effects on reproduction.

Based on toxicity data and exposure estimates, the risks to birds and mammals are considered low. Acute and chronic toxicity studies show that the technical material and formulations of beta-cyfluthrin are highly toxic to fish and aquatic invertebrates and moderately toxic to algae. It is classified as presenting a high risk to honey bees and other arthropod species. Its effects on earthworms and other soil macro- or micro-organisms are considered to be small.

Recommendations

The Meeting recommended that the specifications for TC, EC, SC proposed by Bayer should be adopted as FAO specifications.

References

Food and Agriculture Organization of the United Nations (1999), Manual on Development and Use of FAO Specifications for Plant Protection Products, 5th edition, FAO Plant production and protection paper 149, FAO, Rome.

W. Dobrat and A. Martijn, Eds. (1998), CIPAC Handbook H, Collaborative International Pesticides Analytical Council, Harpenden, UK.

W. Dobrat and A. Martijn, Eds. (1995), CIPAC Handbook F, Collaborative International Pesticides Analytical Council, Harpenden, UK.