# FAO SPECIFICATIONS AND EVALUATIONS FOR AGRICULTURAL PESTICIDES

## CLODINAFOP-PROPARGYL*

prop-2-ynyl (*R*)-2-[4-(5-chloro-3-fluoro-2-pyridyloxy)phenoxy]propionate


FOOD AND AGRICULTURE ORGANIZATION *of* THE UNITED NATIONS

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* The ISO common name, clodinafop, refers to the free acid. Clodinafop-propargyl refers to the propargyl ester.

**TABLE OF CONTENTS**

## DISCLAIMER[1]

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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 public health 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) and amended with the supplement of this manual (2006), 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 JMPS, rather than the JMPS.]

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

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

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

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

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

* NOTE: PUBLICATIONS ARE AVAILABLE ON THE INTERNET AT (http://www.fao.org/ag/agp/agpp/pesticid/)

OR IN HARDCOPY FROM THE PLANT PROTECTION INFORMATION OFFICER.

**PART ONE**

# SPECIFICATIONS

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CLODINAFOP-PROPARGYL

## CLODINAFOP-PROPARGYL

INFORMATION

*ISO common names*

clodinafop (BSI, E-ISO)
clodinafop-propargyl (modified E-ISO) denotes the propargyl ester

*Synonyms*

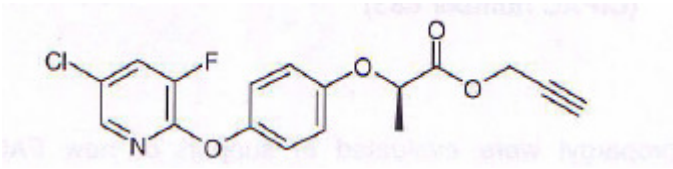
none

*Chemical names*

clodinafop:
*IUPAC* (*R*)-2-[4-(5-chloro-3-fluoro-2-pyridyloxy)phenoxy]propionic acid
*CA* (2*R*)-2-[4-[(5-chloro-3-fluoro-2-pyridinyl)oxy]phenoxy]propanoic acid

clodinafop-propargyl:
*IUPAC* prop-2-ynyl (*R*)-2-[4-(5-chloro-3-fluoro-2-pyridyloxy)phenoxy]propionate
*CA* 2-propynyl (2*R*)-2-[4-[(5-chloro-3-fluoro-2-pyridinyl)oxy]phenoxy]propanoate

*Structural formula* (clodinafop-propargyl)




clodinafop and clodinafop-propargyl are the *R*-enantiomers

*Empirical formula*

clodinafop: $C_{14}H_{11}ClFNO_4$
clodinafop-propargyl: $C_{17}H_{13}ClFNO_4$

*Relative molecular mass*

clodinafop: 311.8
clodinafop-propargyl: 349.8

*CAS Registry number*

clodinafop: 114420-56-3
clodinafop-propargyl: 105512-06-9

*CIPAC number*

clodinafop: 683
clodinafop-propargyl: 683.225

*Identity tests*

HPLC retention times on reversed-phase and enantio-selective columns.

# CLODINAFOP-PROPARGYL TECHNICAL MATERIAL

FAO specification 683.225/TC (May 2008*)

*This specification, which is PART ONE of this publication, is based on an evaluation of data submitted by the manufacturer whose name is listed in the evaluation report (683.225/2006). It should be applicable to TC produced by this manufacturer but it is not an endorsement of it, nor a guarantee that it complies with the specification. The specification may not be appropriate for TC produced by other manufacturers. The evaluation report 683.225/2006, as PART TWO, forms an integral part of this publication.*

## 1 Description

The material shall consist of clodinafop-propargyl together with related manufacturing impurities and shall be a light beige to brown powder, free from visible extraneous matter and added modifying agents.

## 2 Active ingredient

### 2.1 **Identity tests** (683/TC/M/2, CIPAC Handbook, Note 1)

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

### 2.2 **Clodinafop-propargyl content** (683/TC/M/3, CIPAC Handbook, Note 1)

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

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Note 1 Methods for the identification and determination of clodinafop-propargyl content were adopted by CIPAC in 2006 but are not yet published in a Handbook. Prior to publication of the Handbook, copies of the methods may be obtained through the CIPAC website, http://www.cipac.org.

* Specifications may be revised and/or additional evaluations may be undertaken. Ensure the use of current versions by checking at: http://www.fao.org/ag/agp/agpp/pesticid/.

# CLODINAFOP-PROPARGYL WETTABLE POWDER

FAO specification 683.225/WP (May 2008*)

*This specification, which is PART ONE of this publication, is based on an evaluation of data submitted by the manufacturer whose name is listed in the evaluation report (683.225/2006). It should be applicable to relevant products of this manufacturer, and those of any other formulators who use only TC from the evaluated source. The specification is not an endorsement of those products, nor a guarantee that they comply with the specification. The specification may not be appropriate for the products of manufacturers who use TC from other sources. The evaluation report 683.225/2006, as PART TWO, forms an integral part of this publication.*

## 1 Description

The material shall consist of technical clodinafop-propargyl, complying with the requirements of FAO specification 683.225/TC (May 2008), dissolved in suitable solvents, together with filler(s) and any other necessary formulants. It shall be in the form of a fine powder free from visible extraneous matter and hard lumps.

## 2 Active ingredient

### 2.1 **Identity tests** (683/WP/M/2, CIPAC Handbook, Note 1)

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

### 2.2 **Clodinafop-propargyl content** (683/WP/M/3, CIPAC Handbook, Note 1)

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

| Declared content, g/kg | Tolerance |
|---|---|
| above 100 up to 250<br><br>Note: the upper limit is included in the range | ± 6% of the declared content |

## 3 Physical properties

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

The pH of an aqueous dispersion shall be 4.0 to 8.0.

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

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

* Specifications may be revised and/or additional evaluations may be undertaken. Ensure the use of current versions by checking at: http://www.fao.org/ag/agp/agpp/pesticid/.

3.3 **Suspensibility** (MT 184, CIPAC Handbook K, p.142, 2003) (Notes 2 & 3)

A minimum of 60% of the clodinafop-propargyl content found under 2.2 shall be in suspension after 30 min in CIPAC standard water D at 30 ± 2°C (Note 4).

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

Maximum: 60 ml after 1 min.

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

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

## 4 Storage stability

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

After storage at 54 ± 2°C for 14 days, the determined average active ingredient content must not be lower than 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 (3.1),
- wet sieve test (3.2),
- suspensibility (3.3),
- wettability (3.5).

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Note 1 Methods for the identification and determination of clodinafop-propargyl content were adopted by CIPAC in 2006 but are not yet published in a Handbook. Prior to publication of the Handbook, copies of the methods may be obtained through the CIPAC website, http://www.cipac.org.

Note 2 The product should be test at highest and lowest rates of use recommended by the supplier, provided this does not exceed the conditions given in method MT 184.

Note 3 This test will normally only be carried out after the heat stability test, 4.1.

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 determination or solvent extraction determination may be used on a routine basis provided that these methods have been shown to give equal results to those of chemical assay method. In case of dispute, chemical method shall be the "referee method".

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

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

# CLODINAFOP-PROPARGYL EMULSIFIABLE CONCENTRATE

FAO specification 683.225/EC (May 2008*)

*This specification, which is PART ONE of this publication, is based on an evaluation of data submitted by the manufacturer whose name is listed in the evaluation report (683.225/2006). It should be applicable to relevant products of this manufacturer, and those of any other formulators who use only TC from the evaluated source. The specification is not an endorsement of those products, nor a guarantee that they comply with the specification. The specification may not be appropriate for the products of manufacturers who use TC from other sources. The evaluation report 683.225/2006, as PART TWO, forms an integral part of this publication.*

## 1 Description

The material shall consist of technical clodinafop-propargyl, complying with the requirements of FAO specification 683.225/TC (May 2008), dissolved in suitable solvents, together with any other necessary formulants. It shall be in the form of a clear to slightly hazy, 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** (683/EC/M/2, CIPAC Handbook, Note 1)

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

### 2.2 **Clodinafop-propargyl content** (683/EC/M/3, CIPAC Handbook, Note 1)

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

| Declared content, g/kg or g/l at 20 ± 2ºC | Tolerance |
|---|---|
| above 25 up to 100 | ± 10% of the declared content |
| above 100 up to 250 | ± 6% of the declared content |
| Note: the upper limit is included in each range | |

## 3 Physical properties

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

The pH of an aqueous dispersion shall be 4.0 to 8.0.

* Specifications may be revised and/or additional evaluations may be undertaken. Ensure the use of current versions by checking at: http://www.fao.org/ag/agp/agpp/pesticid/.

3.2 **Emulsion stability and re-emulsification** (MT 36.3, CIPAC Handbook K, p.137, 2003) (Note 3)

The formulation, when diluted at 30 ± 2°C with CIPAC standard waters A and D, shall comply with the following:

| Time after dilution | Limits of stability |
|---|---|
| 0 h | Initial emulsification complete |
| 0.5 h | Cream, maximum: 2 ml |
| 2.0 h | "Cream", maximum: 4 ml<br>"Free oil", maximum: trace |
| 24 h | Re-emulsification complete |
| 24.5 h | "Cream", maximum: 2 ml<br>"Free oil" maximum: trace. |
| Note: tests at 24 h are required only where the results at 2 h are in doubt. | |

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

Maximum: 40 ml after 1 min.

## 4 Storage stability

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

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

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

After storage at 54 ± 2°C for 14 days, the determined average active ingredient content must not be lower than 95% relative to the determined average content found before storage (Note 5) and the formulation shall continue to comply with the clauses for:

- pH range (3.1);
- emulsion stability and re-emulsification (3.2).

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Note 1 Methods for the identification and determination of clodinafop-propargyl content were adopted by CIPAC in 2006 but are not yet published in a Handbook. Prior to publication of the Handbook, copies of the methods may be obtained through the CIPAC website, http://www.cipac.org.

Note 2 If the buyer requires both g/kg and g/l at 20°C, then in case of dispute the analytical results shall be calculated as g/kg.

Note 3 This test will normally only be carried out after the heat stability test: 5.2. Emulsion stability should be tested with the formulation at 0.1% concentration.

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

Note 5 Samples of the formulation taken before and after the storage stability test should be analyzed concurrently after the test in order to reduce the analytical error.

**PART TWO**

## EVALUATION REPORTS

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### CLODINAFOP-PROPARGYL

**CLODINAFOP-PROPARGYL**

EVALUATION REPORT 683.225/2006

## Recommendations

The Meeting recommended that the specifications for clodinafop-propargyl TC, EC and WP, proposed by Syngenta Crop Protection AG, should be adopted by FAO.

## Appraisal

The Meeting considered data on clodinafop-propargyl, submitted by Syngenta Crop Protection AG, in support of proposed new FAO specifications for TC, EC and WP.

Clodinafop-propargyl is not under patent in most countries.

The ISO common name, clodinafop, applies to the free acid, whereas esters or salts of the acid may be identified by addition of the appropriate extension to the name. The clodinafop molecule has one centre of asymmetry and the ISO common name applies only to the *R*-enantiomer, not the *S*-enantiomer. The modified ISO common name, clodinafop-propargyl (denoting the propargyl ester), therefore applies only to the *R*-enantiomer.

Clodinafop-propargyl is a solid at room temperature, having low volatility and low water solubility but it is very soluble in certain organic solvents, such as acetone and toluene. It hydrolyzes only slowly in water under acidic conditions but is rapidly hydrolyzed under alkaline conditions. Photolysis occurs rapidly, producing a plethora of products but not including clodinafop (free acid). Clodinafop-propargyl, as the intact ester, has no acidic or basic characteristics.

Confidential information on the manufacturing process and 5 batch analysis data for all impurities present at or above 1 g/kg were provided to the Meeting, together with the manufacturing specification for the TC. The minimum active ingredient content in clodinafop-propargyl TC was not less than 960 g/kg. These data were confirmed as being similar to those submitted for registration in The Netherlands and for assessment in the EU.

The Meeting agreed with the manufacturer that none of the impurities should be designated as relevant, for specification purposes.

Draft specifications were submitted broadly in accordance with the requirements of the Manual (FAO/WHO, 2006) but the Meeting addressed the following minor issues.

WP and EC, pH range. The Meeting questioned the proposed upper limit (pH 8), given the rapidity of hydrolysis of clodinafop-propargyl at pH 9, and, if hydrolysis does not actually occur in practice, whether the pH range is an appropriate quality criterion. The manufacturer stated that racemization and/or hydrolysis can occur in products outside the proposed pH range (4.0-8.0), with hydrolysis being the main issue as there is always a small amount of water present in these formulations. Within the proposed range, the active ingredient was stated to be stable. Although hydrolysis or racemization may be detected in the storage stability test, the manufacturer explained that pH range provides a simple and rapid indication of product stability and the Meeting accepted this justification.

WP and EC, persistent foam. The Meeting asked whether proposed limit of 60 ml for the WP could be lower, as it was the maximum normally accepted. The manufacturer explained that the proposed limit represented the optimum compromise between adequate suspensibility and the production of foam. The Meeting accepted the proposed limit. In contrast, and on the basis of data provided by the manufacturer, the Meeting questioned whether the proposed limit of 40 ml for EC would be too low. The Meeting accepted the manufacturer's assurance that the EC complies with the limit .

Analytical methods for the identification and determination of clodinafop-propargyl in TC, WP and EC were adopted by CIPAC, with provisional status, in 2006. Determination and primary identification is by (achiral) reversed-phase HPLC method (in which *R*- and *S*-enantiomers are not separated), with detection by UV-absorption at 305 nm and external standardization. Confirmation of identity in the TC and formulations is by enantio-selective HPLC, with detection by UV-absorption at 230 nm and measurement of the peak area ratio of *R*- and *S*-enantiomers present. The clodinafop-propargyl content measured by reversed-phase HPLC is adjusted by the ratio found by enantio-selective HPLC, because the *S*-enantiomer is not part of the active ingredient.

# SUPPORTING INFORMATION
# FOR
# EVALUATION REPORT 683.225/2006

## Uses

Clodinafop-propargyl is a systemic herbicide, used in agriculture for the post-emergence control of annual grass weeds in cereals.

## Identity of the active ingredient

*ISO common names*

clodinafop (BSI, E-ISO)
clodinafop-propargyl (modified E-ISO) denotes the propargyl ester

*Synonyms*

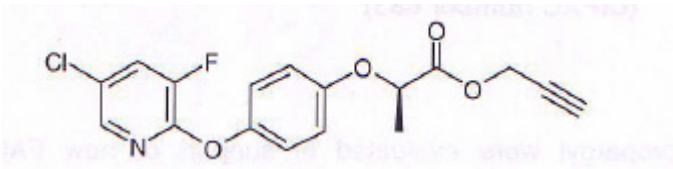
none

*Chemical names*

clodinafop:
*IUPAC* (*R*)-2-[4-(5-chloro-3-fluoro-2-pyridyloxy)phenoxy]propionic acid
*CA* (2*R*)-2-[4-[(5-chloro-3-fluoro-2-pyridinyl)oxy]phenoxy]propanoic acid

clodinafop-propargyl:
*IUPAC* prop-2-ynyl (*R*)-2-[4-(5-chloro-3-fluoro-2-pyridyloxy)phenoxy]propionate
*CA* 2-propynyl (2*R*)-2-[4-[(5-chloro-3-fluoro-2-pyridinyl)oxy]phenoxy]propanoate

*Structural formula* (clodinafop-propargyl)




clodinafop and clodinafop-propargyl are the *R*-enantiomers

*Empirical formula*

clodinafop: $C_{14}H_{11}ClFNO_4$
clodinafop-propargyl: $C_{17}H_{13}ClFNO_4$

*Relative molecular mass*

clodinafop: 311.8
clodinafop-propargyl: 349.8

*CAS Registry number*

clodinafop: 114420-56-3
clodinafop-propargyl: 105512-06-9

*CIPAC number*

clodinafop: 683
clodinafop-propargyl: 683.225

*Identity tests*

HPLC retention times on reversed-phase and enantio-selective columns.

## Physico-chemical properties of clodinafop-propargyl

### Table 1. Physico-chemical properties of pure clodinafop-propargyl

| Parameter | Value(s) and conditions | Purity % | Method | Reference [company report No.; year of completion] |
|---|---|---|---|---|
| Vapour pressure | 3.19 x $10^{-6}$ Pa at 25ºC (extrapolated) | 99.5% | EEC A.4 | CGA184927 /0232; 1992 |
| Melting point | 59.5°C | 99.5% | EEC A.1 | CGA184927 /0478; 1994 |
| Boiling point | 100.6°C at 0.082 Pa | 99.9% | EEC A.2 | CGA184927 /4628; 1997 |
| Temperature of decomposition | starts at about 285°C | 99.5% | EEC A.2<br>OECD 113 | CGA184927 /4628; 1997<br>CGA184927 /4709; 2000 |
| Solubility in water | 4.0 mg/l at 25°C | 99.5% | OECD 105 | CGA184927 /0230; 1991 |
| Octanol/water partition coefficient | log $P_{OW}$ = 3.90 at 25°C | 99.5% | OECD 117 | CGA184927 /0231; 1991 |
| Hydrolysis characteristics, half-life at 25ºC | 17.9 days at pH 4<br>26.8 days at pH 5<br>4.8 days at pH 7<br>0.07 days (1.68 hours) at pH 9 | >99% | OECD 111 | CGA184927 /4851; 2001 |
| Photolysis characteristics | In bi-distilled water at 25°C and irradiated with a mercury arc lamp, with and without acetone as a sensitizer, photolysis half-lives were:<br>non-sensitized, 3.2 hours<br>sensitized, 0.7 hours<br>These values correspond to estimated half-lives of 8.5 days and 6.0 days at latitude 40°N in spring/summer and 12.5days and 7.0 days at latitude 50°N in spring/summer.<br>The photodecomposition led to a multitude of products, which were more polar than clodinafop-propargyl and which could not be identified. Clodinafop (free acid) was not found. No significant degradation occurred in the dark control. The average material balance was 99.6%. | >98% radio-purity | In-house adaptation of EPA and OECD guidelines | CGA184927 /0017; 1990 |
| Dissociation characteristics | Protonation/deprotonation of clodinafop-propargyl is not expected to occur in the range pH 2 to 12 (liberation of the free acid by hydrolysis occurs rapidly under alkaline conditions) | - | By estimation | CGA184927 /0234; 1991 |

### Table 2. Chemical composition and properties of technical clodinafop-propargyl (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 98.7-99.5%, with no unknowns detected. |

| | |
|---|---|
| Declared minimum clodinafop-propargyl content | 960 g/kg |
| Relevant impurities ≥ 1 g/kg and maximum limits for them | None. |
| Relevant impurities < 1 g/kg and maximum limits for them | None |
| Stabilizers or other additives and maximum limits for them | None |
| Melting temperature of the TC | 48.2-57.1 °C |

## Hazard summary

Clodinafop-propargyl has not been evaluated by the FAO/WHO JMPR, nor by IPCS.

An EU review of clodinafop-propargyl (according to EU directive 91/414) was completed recently (EU 2005). According to European Commission Directive 2001/59/EC (28$^{th}$ adaptation of Council Directive 67/548/EEC), it was classified as harmful with respect to acute toxicity.

The US EPA published tolerances for clodinafop-propargyl in 2000 (USEPA 2000).

Clodinafop-propargyl has not yet (December 2006) been assigned a WHO hazard classification by the WHO Programme on Chemical Safety.

## Formulations

The main formulation types available are EC and WP. EC formulations are registered and sold in many countries throughout the world. WP formulations are currently registered and sold in Asia and Egypt. Clodinafop-propargyl is always co-formulated with a safener.

## Methods of analysis and testing

The analytical method for identification and determination of clodinafop-propargyl content is based on a non-chiral separation using reversed-phase HPLC with external standardization and UV detection at 305 nm. For identification of clodinafop-propargyl as the *R*-isomer, a quantitative chiral method is used, involving enantio-selective HPLC with external standardization and UV detection at 230 nm. The methods for analysis of TC, WP and EC were adopted by CIPAC with provisional status in 2006.

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

## Physical properties

The physical properties, the methods for testing them and the limits proposed for the EC and WP formulations, comply with the requirements of the manual (FAO/WHO 2006).

## Containers and packaging

No special requirements for containers and packaging have been identified.

## Expression of the active ingredient

The active ingredient is expressed as clodinafop-propargyl.

# ANNEX 1

## HAZARD SUMMARY PROVIDED BY THE PROPOSER

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

## Table A. Toxicology profile of clodinafop-propargyl technical material, based on acute toxicity, irritation and sensitization

| Species | Test | Purity | Duration and conditions or guideline adopted | Result | Reference |
|---|---|---|---|---|---|
| Rat (m,f) | Acute oral | 93.7% | OECD 401. 14 d observation period; dose levels 500, 2000 or 5000 mg/kg bw. | $LD_{50}$ = 1829 mg/kg bw (males 1392 mg/kg, females 2271 mg/kg) | CGA184927/ 0045; 1987 |
| Mouse | Acute oral | 94.2% | OECD 401. 14 d observation period; highest dose 2000 mg/kg bw | $LD_{50}$ >2000 mg/kg bw | CGA184927/ 0169; 1991 |
| Rat | Acute dermal | 93.7% | OECD 402. 14 d observation period; highest dose 2000 mg/kg bw | $LD_{50}$ >2000 mg/kg bw | CGA184927/ 0034; 1987 |
| Rat | Acute inhalation | 93.7% | OECD 403. 4 h exposure, 14 d observation period; nominal concentration 2340 mg/$m^3$ | $LC_{50}$ >2325 mg/$m^3$ | CGA184927/ 0035; 1987 |
| Rabbit | Skin irritation | 93.7% | OECD 404. 1-72 h; dose 0.5 g/ml | Non-irritating | CGA184927/ 0036; 1987 |
| Rabbit | Eye irritation | 93.7% | OECD 405. 1-72 h; 48 mg/eye | Non-irritating | CGA184927/ 0037; 1987 |
| Guinea pig | Skin sensitization (optimization test) | 93.7% | OECD 406. 48 h; dose 0.1% or 5% | Sensitizer | CGA184927/ 0039; 1987 |

According to the manufacturer, clodinafop-propargyl is classifiable as Class III (slightly hazardous) by the WHO hazard classification system.

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

| Species | Test | Purity | Duration and conditions or guideline adopted | Result | Reference |
|---|---|---|---|---|---|
| Rat, Tif:RAIf, Sprague-Dawley | Short term toxicity | 93.7% | 3 month dietary; OECD 408, dose levels: 0, 2, 15, 120, 1000 ppm | NOAEL = 0.92 mg/kg bw/d (15 ppm)<br>LOAEL = 8.24 mg/kg bw/d (120 ppm) | CGA184927/ 0041; 1989 |
| Dog, beagle | Short term toxicity | 93.7% | 3 month dietary; FIFRA 82-1; dose levels: 0, 1, 10, 50, 200 ppm | NOAEL = 7.26 mg/kg bw/d (200 ppm)<br>LOAEL = 17 mg/kg bw/d (500 ppm) | CGA184927/ 0042; 1989 |
| Dog, beagle | Short term toxicity | 93.7% | 1 year dietary; FIFRA 83-1, OECD 452; dose levels: 0, 10, 100, 500 ppm | NOAEL = 3.3 mg/kg bw/d (100 ppm)<br>LOAEL = 15.2 mg/kg bw/d (500 ppm) | CGA184927/ 0158; 1990 |

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

| Species | Test | Purity | Duration and conditions or guideline adopted | Result | Reference |
|---|---|---|---|---|---|
| Mouse, Tif:MAGf | Carcinogenicity | 93.7% | 18 months dietary; FIFRA 83-2, OECD 451; dose levels: 0, 1, 10, 100, 250 ppm | No carcinogenic effects relevant for humans; target organ: liver<br>NOAEL = 1.1 mg/kg bw/d (10 pm)<br>LOAEL = 11 mg/kg bw/d (100 ppm) | CGA184927/ 0202; 1992 |
| Rat, Tif:RAIf | Chronic toxicity and carcinogenicity | 93.7% | 2 year dietary, FIFRA 83-2, OECD 453, 1984; dose levels: 0, 1, 10, 300, 750 ppm | Not carcinogenic; target organ: liver<br>NOAEL = 0.32 mg/kg bw/d (10 ppm)<br>LOAEL = 10.2 mg/kg bw/d (300 ppm) | CGA184927/ 0225; 1992 |
| Rat, Crl:CD(DD)BR | Reproductive toxicity | 93.7% | 2 generation, dietary; OECD 416, FIFRA 83-4; dose levels: 0, 5, 50, 500, 1000 ppm | No effects on reproductive parameters<br>NOAEL = 4.6 mg/kg bw/d (50 ppm)<br>LOAEL = 44 mg/kg bw/d (500 ppm)<br>NOAEL for reproductive effects >89 mg/kg bw/d (>1000 ppm) | CGA184927/ 0156; 1991 |
| Rat, Ico:OFA SD | Developmental toxicity | 93.7% | Gavage feeding; OECD 414, FIFRA 83-3; dose levels: 0, 5, 40, 160 mg/kg bw/day | Not teratogenic<br>NOAEL (maternal and developmental toxicity) = 40 mg/kg bw/d<br>LOAEL = 160 mg/kg bw/d | CGA184927/ 0053; 1989 |
| Rabbit, HyCr | Developmental toxicity | 93.7% | Gavage feeding; OECD 414, FIFRA 83-3; dose levels: 0, 5, 25, 125, 175 mg/kg bw/day | Not teratogenic<br>NOAEL (maternal toxicity) = 25mg/kg bw/d<br>NOAEL (developmental toxicity) >125 mg/kg bw/d<br>LOAEL (maternal toxicity) = 125 mg/kg bw/day | CGA184927/ 0054; 1990 |

**Table C. Mutagenicity profile of clodinafop-propargyl technical material, based on *in vitro* and *in vivo* tests**

| Species | Test | Purity | Conditions and dose levels | Results | Reference |
|---|---|---|---|---|---|
| Salmonella/E.coli | Bacterial gene mutation, *in vitro* | 93.7% | OECD 471;<br>0 to 5000 µg/plate, ±S9 activation | Negative | CGA1849 27/0046; 1987 |
| Chinese hamster, V79 cells | Gene mutation *in vitro* | 93.7% | OECD 476;<br>-S9 activation: 0 to 500 µg/ml<br>+S9 activation: 0 to 50 µg/ml | Negative | CGA1849 27/0049; 1988 |
| Human lymphocytes | Cytogenetic test *in vitro* | 93.7% | OECD 473;<br>-S9 activation: 0 to 850 µg/ml<br>+S9 activation: 0 to 88 µg/ml | Negative | CGA1849 27/0050; 1988 |

## Table C. Mutagenicity profile of clodinafop-propargyl technical material, based on *in vitro* and *in vivo* tests

| Species | Test | Purity | Conditions and dose levels | Results | Reference |
|---|---|---|---|---|---|
| Chinese hamster cells | Cytogenetic test *in vitro* | 93.7% | OECD 473;<br>-S9 activation: 0 to 100 µg/ml<br>+S9 activation: 0 to 50 µg/ml | -S9 negative<br>+S9 positive at highest dose | CGA1849 27/4720; 2000 |
| Rat hepatocytes | DNA repair *in vitro* | 94.2% | OECD 482;<br>0 to 70 µg/ml | Negative | CGA1849 27/0047; 1987 |
| Mouse bone marrow cells | Micronucleus test *in vivo* | 93.7% | OECD 474;<br>0, 1667, 5000 mg/kg bw | Negative | CGA1849 27/0048; 1987 |
| Rat hepatocytes | DNA repair *in vivo/in vitro* | 93.7% | OECD 486;<br>0, 1000, 2000 mg/kg bw | Negative | CGA1849 27/4678; 1999 |

A positive response in the chromosome aberration test in Chinese hamster cells *in vitro* occurred only at the highest concentration (with metabolic activation), which was cytotoxic. The effect was considered to be secondary to the cytotoxicity and not of relevance when assessing the overall mutagenic potential of clodinafop-propargyl. An *in vivo* DNA repair study on rat hepatocytes showed no mutagenic potential of clodinafop-propargyl. Thus it was concluded that clodinafop-propargyl is not genotoxic.

## Table D. Ecotoxicology profile of clodinafop-propargyl technical material

| Species | Test | Purity | Duration and conditions | Results | Reference |
|---|---|---|---|---|---|
| Anas platyrhynchos (mallard duck) | Acute oral | 93.7% | Observation 14 d; EPA guidelines, E, 1982; doses: 500, 1000, 2000 mg a.s./kg bw | $LC_{50}$ >2000 mg/kg feed<br>NOEL >2000 mg/kg feed | CGA1849 27/0008; 1990 |
| Colinus virginianus (bobwhite quail) | Acute oral | 93.7% | Observation 14 d; EPA guidelines, E, 1982; doses: 500, 1000, 2000 mg a.s./kg bw | $LC_{50}$ >1455 mg/kg feed<br>NOEL 521 mg/kg feed | CGA1849 27/0009; 1990 |
| Anas platyrhynchos (mallard duck) | Short-term | 93.7% | Treatment 5 d, observation 3 d; EPA guidelines, E, 1982; doses: 163, 325, 650, 1300, 2600, 5200 mg/kg feed | $LC_{50}$ >5200 mg/kg feed<br>NOEC = 325 mg/kg feed | CGA1849 27/0007; 1989 |
| Colinus virginianus (bobwhite quail) | Short-term | 93.7% | Treatment 5 d, observation 3 d; EPA guidelines, E, 1982; doses: 163, 325, 650, 1300, 2600, 5200 mg/kg feed | $LC_{50}$ >5200 mg/kg feed<br>NOEC = 1300 mg/kg feed | CGA1849 27/0061; 1990 |
| *Anas platyrhynchos* (mallard duck) | Sub-chronic | 94.2% | Treatment 24 weeks; age 20 weeks; EPA guidelines, E, 1982; doses 0, 80, 200, 500 mg a.s./kg feed | LLC (lowest lethal concentration) >500 mg/kg feed; NOEC > 500 mg/kg feed | CGA1849 27/0380; 1993 |
| *Colinus virginianus* (bobwhite quail) | Sub-chronic | 94.2% | Treatment 22 weeks; age: 52 weeks; EPA guidelines, E, 1982; doses 0, 50, 200, 500 mg a.s./kg feed | LLC (lowest lethal concentration) >500 mg/kg feed; NOEC > 500 mg/kg feed | CGA1849 27/0379; 1993 |

## Table D. Ecotoxicology profile of clodinafop-propargyl technical material

| Species | Test | Purity | Duration and conditions | Results | Reference |
|---|---|---|---|---|---|
| *Oncorhynchus mykiss* (rainbow trout) | Short-term | 94.7% | 96h flow-through; OECD 203, doses 0.15, 0.24, 0.40, 0.67 and 1.1 mg/l | $LC_{50}$ = 0.31-0.39 mg a.s./l<br>NOEC = 0.14-0.22 mg a.s./l | CGA184927/0062; 1989<br>CGA184927/0681; 1998 |
| *Lepomis macrochirus* (bluegill sunfish) | Short-term | 93.7% | 96h flow-through; OECD 203, doses 0.32, 0.58, 1.0, 1.8, 3.2 mg/l | $LC_{50}$ = 0.21 mg a.s./l<br>NOEC < 0.12 mg a.s./l | CGA184927/0162; 1989 |
| *Cyprinus carpio* (carp) | Short-term | 93.7% | 96h flow-through; OECD 203; doses 0.18, 0.32, 0.58, 1.0, 1.8 mg/l | $LC_{50}$ = 0.43 mg a.s./l<br>NOEC = 0.12 mg a.s./l | CGA184927/0010; 1989 |
| *Ictalurus punctatus* (catfish) | Short-term | 93.7% | 96h flow-through; OECD 203; doses 0.58, 1.0, 1.8, 3.2, 5.8 mg/l | $LC_{50}$ = 0.46 mg a.s./l<br>NOEC = 0.23 mg a.s./l | CGA184927/0011; 1989 |
| *Oncorhynchus mykiss* (rainbow trout) | Chronic toxicity (juvenile fish) | 93.7% | 21 days, flow-through ; OECD 204; doses 0.58, 1.0, 1.8, 3.2, 5.8 mg/l | LLC (lowest lethal concentration) 0.28 mg a.s./ l; NOEC = 0.15 mg a.s./ l | CGA184927/0077; 1990 |
| *Oncorhynchus mykiss* (rainbow trout) | Chronic toxicity | 94.2% | 21 d, flow-through; OECD 204; doses 0.005, 0.016, 0.05, 0.16, 0.5 mg/l | LLC (lowest lethal concentration) 0.40 mg a.s./ l; NOEC= 0.1 mg a.s./ l | CGA184927/0586; 1996 |
| *Daphnia magna* (water flea) | Acute | 93.7% | Static, 48 h exposure; EPA guideline 1982; doses 10, 18, 32, 58, 100 mg/l | $EC_{50}$ = > 60 mg a.s./l<br>NOEC > 60 mg a.s./l | CGA184927/0012; 1988 |
| *Daphnia magna* (water flea) | Acute | 94.7% | Flow-through, 48 h exposure; EPA guideline 1982; doses 10, 18, 32, 58, 100 mg/l | $EC_{50}$ = >2 mg a.s./l<br>NOEC > 2 mg a.s./l | CGA184927/0682; 1998 |
| *Daphnia magna* (water flea) | Chronic | 93.7% | Static, 48 h exposure; EPA guideline 1982; doses 10, 18, 32, 58, 100 mg/l | $EC_{50}$ = > 60 mg a.s./l<br>NOEC > 60 mg a.s./l | CGA184927/0585; 1996 |
| *Scenedesmus subspicatus* (green alga) | Growth inhibition | 93.7% | 3 d; OECD 201; doses 10, 18, 32, 58, 100 mg/l | $EC_{50}$ >62mg a.s./l<br>NOEC >62 mg a.s./l | CGA184927/0013; 1988 |
| *Scenedesmus subspicatus* (green alga) | Growth inhibition | 94.2% | 3 d; OECD 201; doses 4.8, 8, 13, 22, 36, 60, 100 mg/l | $EC_{50}$ >6.5mg a.s./l<br>NOEC = 0.47 mg a.s./l | CGA184927/0584; 1996 |
| *Selanastrum capricornutum* (green alga) | Growth inhibition | 94.2% | 5 d; EPA guideline 123-2; doses 0.26, 0.50, 1.0, 2.0, 4.0 mg/l | $EC_{50}$ >3.9 mg a.s./l<br>NOEC = 1.7 mg a.s./l | CGA184927/0680; 1998 |
| *Anabaena flos-aquae* (blue-green alga) | Growth inhibition | 94.7% | 5 d; EPA 123-2; doses 0.26, 0.50, 1.0, 2.0, 4.0 mg/l | $EC_{50}$ >3.6 mg a.s./l<br>NOEC >3.6 mg a.s./l | CGA184927/0679; 1998 |
| *Microcystis aeruginosa* (blue-green alga) | Growth inhibition | 94.2% | 5 d; ASTM Guideline E 1218-90; doses 13, 22, 36, 60, 100 mg/l | $EC_{50}$ >78.1 mg a.s./l<br>NOEC >78.1 mg a.s./l | CGA184927/0278; 1993 |

## Table D. Ecotoxicology profile of clodinafop-propargyl technical material

| Species | Test | Purity | Duration and conditions | Results | Reference |
|---|---|---|---|---|---|
| *Navicula pelliculosa* (blue-green alga) | Growth inhibition | 94.2% | 4 d; ASTM Guideline E 1218-90; doses 13, 22, 36, 60, 100 mg/l | $EC_{50}$ = 12.55 mg a.s./l<br>NOEC = 1.1 mg a.s./l | CGA184927/0280; 1993 |
| *Lemna gibba* (duckweed) | Growth inhibition | 94.2% | 14 d; similar to EPA FIFRA guidelines 122-2 and 123-2; nominal dose 4.0 mg/l | $EC_{50}$ = 2.4 mg a.s./l<br>NOEC (reproduction) >2.4 mg a.s./l | CGA184927/0343; 1993 |
| *Glyceria maxima* | Growth inhibition | 24% EC | 14 d exposure,14 d recovery; formulation equivalent to doses of 0.024, 0.072, 0.24, 0.72, 2.4 mg a.s./l. No standard test guideline available | $EC_{50}$ = 0.15 mg a.s./l<br>NOEC >0.018 mg a.s./l | CGA184927/4753; 2000 |
| *Chironomus riparius* (midge) | Emergence rate | 93.6% | 28 d; OECD test with Chironomidae, 1997; doses 0.5, 1, 2, 4, 8, 16 mg/l nominal | $EC_{50}$ >16 mg a.s./l<br>NOEC >16 mg a.s./l | CGA184927/0684; 1998 |
| *Chironomus riparius* (midge) | larval develop-ment rate | 93.6% | 28 d; OECD test with Chironomidae, 1997; doses 0.5, 1, 2, 4, 8, 16 mg/l nominal | $EC_{50}$ >16 mg a.s./l<br>NOEC >16 mg a.s./l | CGA184927/0684; 1998 |
| *Apis mellifera (honey bee)* | Oral, mortality / behaviour | 93.7% | 48 h; EPA FIFRA 71-2; limit test at 100 µg/bee | $LD_{50}$ >100 µg a.s./bee<br>NOEC >100 µg a.s./bee | CGA184927/0015; 1987 |
| *Apis mellifera (honey bee)* | Contact, mortality / behaviour | 93.7% | 48 h; EPA FIFRA 71-2; limit test at 100 µg/bee | $LD_{50}$ >100 µg a.s/bee<br>NOEC >100 µg a.s/bee | CGA184927/0015; 1987 |
| *Eisenia foetida foetida (earthworm)* | Acute toxicity, mortality / behaviour | 93.7% | 14 d; OECD 207; doses 62.5, 125, 250, 500, 1000 mg a.s./kg soil | $LC_{50}$ = 210 mg/kg soil<br>NOEL = 62.5 mg a.s./kg soil | CGA184927/0014; 1988 |

# ANNEX 2. REFERENCES

| Syngenta document number or other reference | Year and title of report or publication details |
|---|---|
| CGA184927/0232 | 1992 - Vapour pressure |
| CGA184927/0478 | 1994 - Melting point |
| CGA184927/4628 | 1997 - Boiling point |
| CGA184927/4628 | 1997 - Temperature of decomposition |
| CGA184927/4709 | 2000 |
| CGA184927/0230 | 1991 - Solubility in water |
| CGA184927/0231 | 1991 - Octanol/water partition coefficient |
| CGA184927/4851 | 2001 - Hydrolysis characteristics |
| CGA184927/0017 | 1990 - Photolysis characteristics |
| CGA184927/0234 | 1991 - Dissociation characteristics |
| CGA184927/0045 | 1987 - Acute oral tox rat |
| CGA184927/0169 | 1991 - Acute oral tox mouse |
| CGA184927/0034 | 1987 - Acute dermal tox |
| CGA184927/0035 | 1987 - Acute inhalation |
| CGA184927/0036 | 1987 - Skin irritation |
| CGA184927/0037 | 1987 - Eye irritation |
| CGA184927/0039 | 1987 - Skin sensitization |
| CGA184927/0041 | 1989 - Short term toxicity rat |
| CGA184927/0042 | 1989 - Short term toxicity dog 3 month |
| CGA184927/0158 | 1990 - Short term toxicity 1 year |
| CGA184927/0202 | 1992 - Mouse carcinogenicity |
| CGA184927/0225 | 1992 - Rat chronic toxicity and carcinogenicity |
| CGA184927/0156 | 1991 - Rat reproductive toxicity |
| CGA184927/0053 | 1989 - Rat developmental toxicity |
| CGA184927/0054 | 1990 - Rabbit developmental toxicity |
| CGA184927/0046 | 1987 - Bacterial gene mutation |
| CGA184927/0049 | 1988 - CHO gene mutation |
| CGA184927/0050 | 1988 - Human lymphocytes cytogenetic test |
| CGA184927/4720 | 2000 - CHO cytogenetic test |
| CGA184927/0047 | 1987 - Rat hepatocytes DNA repair in vitro |
| CGA184927/0048 | 1987 - Mouse micronucleus test |
| CGA184927/4678 | 1999 - Rat hepatocytes DNA repair *in vivo/in vitro* |
| CGA184927/0008 | 1990 - Acute oral mallard |
| CGA184927/0009 | 1990 - Acute oral bobwhite quail |
| CGA184927/0007 | 1989 - Short-term tox mallard |
| CGA184927/0061 | 1990 - Short-term tox bobwhite quail |
| CGA184927/0380 | 1993 - Sub-chronic tox mallard |
| CGA184927/0379 | 1993 - Sub-chronic tox bobwhite quail |
| CGA184927/0062 | 1989 - Short-term tox rainbow trout |
| CGA184927/0681 | 1998 |
| CGA184927/0162 | 1989 - Short-term tox bluegill sunfish |
| CGA184927/0010 | 1989 - Short-term tox carp |
| CGA184927/0011 | 1989 - Short-term tox catfish |
| CGA184927/0077 | 1990 - Chronic toxicity rainbow trout juvenile |
| CGA184927/0586 | 1996 - Chronic toxicity rainbow trout |
| CGA184927/0012 | 1988 - Acute tox Daphnia static |

| Syngenta document number or other reference | Year and title of report or publication details |
|---|---|
| CGA184927/0682 | 1998 - Acute tox Daphnia flow-through |
| CGA184927/0585 | 1996 - Chronic toxicity Daphnia |
| CGA184927/0013 | 1988 - *Scenedesmus* growth inhibition 93.7% purity |
| CGA184927/0584 | 1996 - *Scenedesmus* growth inhibition 94.2% purity |
| CGA184927/0680 | 1998 - *Selanastrum* growth inhibition |
| CGA184927/0679 | 1998 - *Anabaena* growth inhibition |
| CGA184927/0278 | 1993 - *Microcystis* growth inhibition |
| CGA184927/0280 | 1993 - *Navicula* growth inhibition |
| CGA184927/0343 | 1993 - *Lemna* growth inhibition |
| CGA184927/4753 | 2000 - *Glyceria* growth inhibition |
| CGA184927/0684 | 1998 - *Chironomus* emergence rate |
| CGA184927/0684 | 1998 - *Chironomus* larval development rate |
| CGA184927/0015 | 1987 - Acute oral tox honey bee |
| CGA184927/0015 | 1987 - Acute contact tox honey bee |
| CGA184927/0014 | 1987 - Acute tox earthworm |
| EPA 2000 | 2000 - Clodinafop-propargyl; pesticide tolerances (EPA-738-F-95-015). *Federal Register*, **65**, No.121, pp.38765-39774, 2000. |
| EU 2005 | 2005 - “Conclusion regarding the peer review of the pesticide risk assessment of the active substance Clodinafop”. 10 August, 2005. http://www.efsa.eu.int/science/praper/conclusions/1111_en.html. |
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