FAO SPECIFICATIONS AND EVALUATIONS

FOR AGRICULTURAL PESTICIDES

PROPOXUR

2-isopropoxyphenyl methylcarbamate

FOOD AND AGRICULTURE ORGANIZATION *of* THE UNITED NATIONS

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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.

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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 FAO specifications follows the **New Procedure**, described in the 1st edition of the "Manual on 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. 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

PROPOXUR

INFORMATION

Common name

Propoxur (E-ISO, F-ISO)

Synonyms

Bay 9010, Baygon, Bayer 39007, Blattanex, Bolfo, BO Q 5812315, OMS 33, PHC (JMAF), Pillargon, UN Carbamate, Tugon, Unden, Undene.

Chemical names

IUPAC: 2-isopropoxyphenyl methylcarbamate

CA: 2-(1-methylethoxy)phenyl methylcarbamate

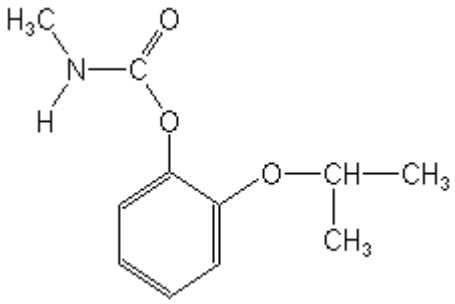
CAS Registry number

114-26-1

CIPAC number

80

Structural formula



Solid propoxur can exist in two crystal forms (modifications I and II) but the technical material usually contains >95% of modification I.

Empirical formula

$C_{11}H_{15}NO_3$

Relative molecular mass

209.25

Identity tests

HPLC retention time, with detection at 280 nm (CIPAC Handbook D, p. 155, 1988); IR and mass spectra; melting point (87.5-90ºC).

PROPOXUR TECHNICAL MATERIAL

FAO Specification 80 / TC (July 2017*)

This specification, which is PART ONE of this publication, is based on an evaluation of data submitted by the manufacturers whose names are listed in the evaluation reports 80/2003 & 80/2016. It should be applicable to TC of these manufacturers but it is not an endorsement of those products, nor a guarantee that they comply with the specification. The specification may not be appropriate for TC produced by other manufacturers. The evaluation reports 80/2003 & 80/2016, as PART TWO, form an integral part of this publication.

1 Description

The material shall consist of propoxur together with related manufacturing impurities, in the form of colourless to pale yellow crystals with a phenolic odour, free from visible extraneous matter and added modifying agents.

2 Active ingredient

2.1 **Identity tests** (80/TC/M2/2, CIPAC Handbook D, p. 155, 1988)

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 **Propoxur content** (80/TC/M2/3, CIPAC Handbook D, p. 155, 1988)

The propoxur content shall be declared (not less than 980 g/kg) and, when determined, the average measured content shall not be lower than the declared minimum content.

3 Relevant impurities

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

Maximum: 2.0 g/kg.

3.2 **Material insoluble in acetone** (MT 27, CIPAC Handbook F, p. 88, 1995)

Maximum: 1.0 g/kg

4 Physical properties

4.1 **Acidity and alkalinity** (MT 31, CIPAC Handbook F, p. 96, 1995)

Maximum acidity: 0.5 g/kg calculated as H_2SO_4.

Maximum: 0.1 g/kg calculated as NaOH.

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

PROPOXUR DUSTABLE POWDER

FAO specification 80 / DP (July 2017*)

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 80/2003. It should be applicable to relevant products of this manufacturer but it is not an endorsement of those products, nor a guarantee that they comply with the specification. The specification may not be appropriate for the products of other manufacturers. The evaluation report 80/2003, as PART TWO, forms an integral part of this publication.

1 Description

The material shall consist of an homogeneous mixture of technical propoxur, complying with the requirements of FAO specification 80/TC (July 2017), together with any other necessary carriers and any other necessary formulants. It shall be in the form of a fine, free-flowing, beige powder, free from visible extraneous matter and hard lumps.

2 Active ingredient

2.1 **Identity tests** (80/TC/M2/2, CIPAC Handbook D, p. 155, 1988)

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 **Propoxur content** (80/DP/M2/3, CIPAC Handbook D, p. 155, 1988)

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

Declared content in g/kg	Tolerance
Up to 25 above 25 up to 100 Note in each range the upper limit is included.	± 15 % of the declared content ± 10 % of the declared content

3 Relevant impurities

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

Maximum: 15 g/kg.

4 Physical properties

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

pH range: 4 to 7 (1% in water).

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

4.2 **Dry sieve test** (MT 59.1, CIPAC Handbook F, p. 177, 1995)

Maximum: 5% retained on a 75 µm test sieve.

Not more than (0.005 x X)% of the mass of the sample used for the test shall be present as propoxur in the residue on the sieve, where X is the propoxur content (g/kg) found under 2.2 (Note 1).

5 Storage stability

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

After storage at 54 ± 2ºC for 14 days, the determined average active ingredient content must not be lower than 97% relative to the determined average content found before storage (Note 2) and the formulation shall continue to comply with the clauses for:

- pH range (4.1);
- dry sieve test (4.2).

Note 1 For example, if the formulation has a determined content of 40 g/kg of propoxur and 20 g of sample is used in the test, then the amount of propoxur in the residue on the sieve should not exceed 0.040 g, i.e.

$$\frac{(0.005 \times 40) \times 20}{100} \text{ g}$$

Note 2 Samples of the formulation taken before and after the storage stability test should be analyzed together after the test in order to reduce the analytical error.

PROPOXUR WETTABLE POWDER

FAO Specification 80 / WP (July 2017*)

This specification, which is PART ONE of this publication, is based on an evaluation of data submitted by the manufacturers whose namse are listed in the evaluation reports 80/2003 & 80/2017. 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 specification. The specification may not be appropriate for the products of other manufacturers. The evaluation reports 80/2003 & 80/2017, as PART TWO, form an integral part of this publication.

1 Description

The material shall consist of an homogeneous mixture of technical propoxur, complying with the requirements of WHO specification 80/TC (August 2016). It shall be in the form of a fine, beige powder free from visible extraneous matter and hard lumps.

2 Active ingredient

2.1 **Identity tests** (80/TC/M2/2, CIPAC Handbook D, p.155, 1988)

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 **Propoxur content** (80/WP/M2/3, CIPAC Handbook D, p.155, 1988)

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

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

3 Relevant impurities

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

Maximum: 20 g/kg.

4 Physical properties

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

pH range: 4.5 to 7.5.

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

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

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

4.3 **Suspensibility** (MT 184, CIPAC Handbook K, p.142, 2003) (Note 1)

A minimum of 60% of the propoxur content found under 2.2 shall be in suspension after 30 min in CIPAC Standard Water D at 30 ± 2ºC (Note 2).

4.4 **Persistent foam** (MT 47.1, CIPAC Handbook O, p.177, 2017) (Note 3)

Maximum: 10 ml after 1 min.

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

The formulation shall be completely wetted in 2 min without swirling.

5 Storage stability

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

After storage at 54 ± 2ºC for 14 days, the determined average active ingredient content must not be lower than 97% relative to the determined average content found before storage (Note 4) and the formulation shall continue to comply with the clauses for:

- pH range (4.1);
- wet sieve test (4.2);
- suspensibility (4.3);
- wettability (4.5).

Note 1 The formulation should be tested at the highest and lowest rates of use recommended by the supplier, provided this does not exceed the conditions given in method MT 184.

Note 2 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 chemical assay. In case of dispute, chemical assay shall be the "referee method".

Note 3 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 4 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.

PROPOXUR EMULSIFIABLE CONCENTRATE

FAO Specification 80 / EC (July 2017*)

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 80/2003. It should be applicable to relevant products of this manufacturer but it is not an endorsement of those products, nor a guarantee that they comply with the specification. The specification may not be appropriate for the products of other manufacturers. The evaluation report 80/2003, as PART TWO, forms an integral part of this publication.

1 Description

The material shall consist of technical Propoxur, complying with the requirements of FAO specification 80/TC (July 2017), dissolved in suitable solvents, together with any other necessary formulants. It shall be in the form of a stable, clear homogeneous, slightly yellow 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** (80/TC/M2/2, CIPAC Handbook D, p. 155, 1988)

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 **Propoxur content** (80/EC/M2/3, CIPAC Handbook D, p. 155, 1988)

The propoxur content shall be declared (g/kg or g/l at 20 ± 2ºC, Note 1) and, when determined, the average content measured shall not differ from that declared by more than the following tolerance.

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

3 Relevant impurities

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

Maximum: 10 g/kg.

4 Physical properties

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

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

pH range: 3.0 to 4.2 (at 1% in water)

4.2 **Emulsion stability and re-emulsification** (MT 36.3, CIPAC Handbook K, p. 137, 2003) (Note 2)

The formulation, when diluted at 30 ± 2ºC 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: 1 ml
2.0 h	"Cream", maximum: 2 ml "Free oil", maximum: 0 ml
24 h	Re-emulsification complete
24.5 h	"Cream", maximum: 1 ml "Free oil", maximum: 0 ml
Note: in applying MT 36.1, tests after 24 h are required only where results at 2 h are in doubt	

5 Storage stability

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

After storage at 0 ± 1ºC for 7 days, the volume of solid and/or liquid which separates shall not be more than 0.3 ml.

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

After storage at 54 ± 2ºC for 14 days, the determined average active ingredient content must not be lower than 97% relative to the determined average content found before storage (Note 3) and the formulation shall continue to comply with the clauses for:

- pH range (4.1);
- 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 This test will normally only be carried out after the heat stability test, clause 5.2.

Note 3 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

PROPOXUR

PROPOXUR

FAO/WHO EVALUATION REPORT 80/2016

Recommendations

The Meeting recommended the following.

(i) The propoxur TC as proposed by Tagros Chemicals India Limited should be accepted as equivalent to the propoxur reference profile.

(ii) The existing FAO specifications for propoxur TC and WP should be extended to encompass the corresponding products of Tagros Chemicals India Limited.

(iii) The existing WHO specifications for propoxur TC and WP should be extended to encompass the corresponding products of Tagros Chemicals India Limited.

(iv) The specification for propoxur WP-SB, proposed by Tagros Chemicals India Limited, as amended, should be adopted by WHO.

Appraisal

The Meeting considered information, specifications and data submitted by Tagros Chemicals India Limited (India) in support of extension of the existing FAO and WHO specifications for propoxur TC and WP and in support of a new WHO specification for propoxur WP-SB. The data submitted by Tagros were broadly in accordance with the requirements of the Manual on development and use of FAO and WHO specifications for pesticides (November 2010 - second revision of the First Edition).

Propoxur TC

Tagros provided the Meeting with confidential information on the manufacturing process, 5-batch analysis data and manufacturing quality control limits for propoxur and all detectable impurities.

Tagros stated that their propoxur TC has been submitted for registration in Indonesia. The confidential information (manufacturing process, purity and impurity profile) submitted to FAO/WHO was confirmed by the Indonesian registration authorities as being identical to that submitted for registration in Indonesia, and was evaluated and considered acceptable by the Indonesian registration authorities.

The manufacturing process of propoxur TC from Tagros differs from the reference process (Bayer CropScience), mainly for one of the starting materials used in the synthesis and for the solvent used in the crystallization step, but the principle remains the same.

The purity / impurity profile was supported by a GLP 5-batch analysis study. The batches of propoxur TC were manufactured from September 2013 to January 2014.

Propoxur content was determined by reverse phase HPLC-DAD after dissolution in acetonitrile and internal standard calibration. The method was fully validated on its specificity (with additional confirmation by LC-MS), linearity of response, accuracy and precision. This method is similar to the CIPAC method 80/TC/M2/3 published in Handbook D, except that ethyl benzoate was used as internal standard instead of butyrophenone, the weight of propoxur in the calibration and samples solutions was decreased in order to avoid further dilution, and the chromatographic conditions were slightly adapted. The

manufacturer explained that the CIPAC method for propoxur was developed in the 1980's and since that time major advances in HPLC column technology have taken place. In the 5-batch analysis study, a number of potential internal standards were evaluated and of those, ethyl benzoate was found to be completely resolved from all of the known impurities of propoxur. The Meeting agreed that both methods are equivalent.

The propoxur manufacturing impurities and residual solvents were determined by reverse phase HPLC-DAD and GC-FID, except water which was determined using the CIPAC method MT 30.5. Acetone insolubles and free acidity were also determined according to the CIPAC methods MT 27 and MT 31 respectivelly. All the analytical methods used for impurities were fully validated on their specificity (with additional confirmation by LC-MS for propoxur related impurities), linearity of response, accuracy, precision and limits of detection (LOD) and quantification (LOQ).

The minimum purity of propoxur in the TC is 980 g/kg and complies with the existing FAO/WHO specification. No relevant impurities were declared. Mass balances for the 5 batches are high (98.7 - 99.6%), with no unknown detected, and similar to those of the reference profile of Bayer CropScience (99.9 - 100.1%). The 5-batch analysis study report indicates that no other significant impurity (each at or above 1 g/kg) was found in any of the 5 batches and that there is no indication that the assays employed missed any significant process related impurity. The water content, material insoluble in acetone and acidity measured in the 5 batches fully comply with the FAO/WHO specifications for propoxur TC.

The manufacturer was questioned about the possible presence of a chlorinated solvent in the final TC. The manufacturer provided a GLP 5-batch study showing that this chlorinated solvent measured by a GC-MS validated method was not detected in any of the 5 batches above the LOQ level of 0.05 g/kg, which is well below 10% of the GHS level of 1 g/kg.

Mutagenicity data were provided on *Salmonella typhimurium* (reverse mutation Ames test) following the OECD guideline 471. The study was performed in compliance with GLP, and the results led to the conclusion that the propoxur TC from Tagros is considered as non-mutagenic.

No studies on physico-chemical properties of pure propoxur nor on the toxicology and ecotoxicology profiles were provided by Tagros.

On basis of Tier-1 data provided by Tagros (manufacturing process, purity / impurity profile, 5-batch analysis data, mutagenicity profile), the Meeting concluded that the propoxur TC from Tagros should be considered as equivalent to the reference profile supporting the existing FAO and WHO specifications (FAO/WHO evaluation report 80/2003).

Propoxur WP and WP-SB

Tagros provided the Meeting with specifications for propoxur WP and WP-SB. The specification for the WP was similar to the existing FAO/WHO specifications for propoxur WP. The new WP-SB specification was supported by GLP studies performed on one single batch as well as quality control data on several batches of propoxur WP-SB.

Propoxur WP is recommended by WHOPES for indoor residual spraying against malaria vectors at a dosage of 1-2 g a.i./m² for an effective action duration of 3-6 weeks (WHO 2006).

Tagros submitted GLP reports on appearance, propoxur content, water content, pH of a 10% aqueous suspension, wet sieve test, suspensibility, persistent foam, wettability, dissolution of the water soluble bag and accelerated storage stability at 54°C for 14 days. The analytical method used for propoxur content was the CIPAC method 80/WP/M2/3 published in CIPAC Handbook D and was fully validated on its specificity, linearity of response, accuracy and precision. The methods used for the physico-chemical tests were all CIPAC methods. Nevertheless, pH was performed in CIPAC water D instead of in distilled or de-ionized water, but it was considered acceptable by the Meeting. The manufacturer of the reference specification (Bayer CropScience) was questioned about the pH clause at 10% in water while the CIPAC method MT 75.3 recommends to perform the test at 1%. Bayer CropSCience agreed to revise the pH range from 4.5 to 7.5% at 1% in water.

The suspensibility test was initially performed on the WP in presence of the soluble bag at a 1.25% a.i. concentration which is the maximum rate of use recommended by the supplier. As the suspensibility index can vary depending on the concentration of use of the product, the FAO/WHO specification guideline for WP and WP-SB recommends to perform the suspensibility test at the highest and lowest rates of use recommended by the supplier. At the request of the Meeting, the manufacturer provided additional suspensibility data at the minimum (1% a.i.) and maximum (1.25% a.i.) recommended concentrations with and without the soluble bag, and before and after accelerated storage.

The persistent foam test was performed on the WP with and without the soluble bag. Despite different concentrations were used in the test (4% a.i. for the WP and 1% a.i. for the WP-SB), these concentrations are higher or quite close to the highest rate of use of 1.25% a.i. recommended by the manufactrurer, and it was considered acceptable by the Meeting.

Tagros initially specified a tolerance of 95% in the WP-SB specification for the active ingredient content remaining after accelerated storage at 54°C for 14 days while the tolerance is 97% in the existing FAO/WHO specification for propoxur WP. The results from the GLP study on propoxur WP-SB showed that the active ingredient after accelerated storage is well higher than 97% relative to the content before storage and that the product still complies with the clauses for pH range, wet sieve test, suspensibility, persistent foam, wettability and dissolution of the soluble bag. The manufacturer finally agreed to comply with the 97% tolerance for the active ingredient after accelerated storage.

The results from the GLP studies and the quality control data on the propoxur WP and WP-SB from Tagros showed that their WP fully comply with the existing FAO/WHO specification for the neat WP formulation and that their WP-SB fully comply with the proposed specification for the WP-SB.

The Meeting agreed also :

- to update in the specification for propoxur WP the CIPAC methods for wet sieve test (MT 185 instead of MT 59.3), suspensibility (MT 184 instead of MT 15.1 or MT 177) and persistent foam (MT 47.3 instead of MT 47.2);
- and to update in the specification for propoxur EC the CIPAC method for emulsion stability (MT 36.3 instead of MT 36.1.1)

to be in line with the current CIPAC methods.

SUPPORTING INFORMATION
FOR
EVALUATION REPORT 80/2016

Physico-chemical properties of propoxur

Table 1. Chemical composition and properties of propoxur technical material (TC)

Manufacturing process, maximum limits for impurities ≥ 1 g/kg, 5 batch analysis data	Confidential information supplied and held on file by FAO and WHO. Mass balances were 98.7-99.6 % with no unknowns.
Declared minimum propoxur 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

Methods of analysis and testing

Propoxur is determined by HPLC using internal standardization with ethyl benzoate and UV detection at 280 nm. This method is similar to the CIPAC method except that ethyl benzoate is used as internal standard instead of butyrophenone. Propoxur is identified by HPLC retention time and by IR and mass spectra.

The methods for determination of impurities were based on HPLC.

Containers and packaging

Propoxur should be packed in polyethylene or polyamide using additional outer packaging.

ANNEX 1

HAZARD SUMMARY PROVIDED BY THE PROPOSER

Note:

Tagros Chemicals India Limited provided written confirmation that the toxicological data included in the following summary were derived from propoxur having impurity profiles similar to those referred to in Table 1, above.

All data has been generated only with the Tagros technical grade active ingredient.

Table A. Mutagenicity profile of propoxur technical material based on *in vitro* tests

Species	Test	Purity %	Guideline, duration, doses and conditions	Result	Study number
Salmonella typhimurium (TA1537, TA1535, TA102, TA100 and TA98)	Reverse Mutation Assay (Ames test), *in vitro*	98.20%	OECD No. 471 Dosage: 128, 320, 800, 2000 and 5000 µg/plate Solvent: DMSO	Negative	14_14_058

ANNEX 2: REFERENCES

Study number	Author(s)	Year	Study title. Study identification number. Report identification number. GLP [if GLP]. Company conducting the study
EPP00146	W Bruce Craig	2014	5-Batch Analysis of Propoxur TGAI in Accordance with Regulation (EC) No. 1107/2009, Referencing SANCO 3030/99 rev. 4. Study No. AN140129A. Report No. EPP00146. EPP Limited, UK. GLP, Unpublished.
14_14_058	Kapil Nikam	2014	Bacterial Reverse Mutation Test of Propoxur Technical in Salmonella typhimurium Tester Strains. Study No. 14_14_058. Sa-FORD, India. GLP, Unpublished.
5083	Nageswara T.	2015	Determination of Foam Persistence of Propoxur 50% WP-SB. Study No. 5083. RCC Laboratories India Private Limited, India. GLP, Unpublished.
5084	Nageswara T.	2015	Determination of Accelerated Storage Stability and Relevant Physico-chemical properties (Foam Persistence) of Propoxur 50% WP-SB. Study No. 5084. RCC Laboratories India Private Limited, India. GLP, Unpublished.
G9778	Ravikanth Gogineni	2014	Method validation and active ingredient analysis of propoxur 50% WP-SB. Study No. G9778. Advinius Therapeutics Limited, India. GLP, Unpublished.
G9779	Shanthaveerappa K. S.	2014	Determination of color, odor and physical state of propoxur 50% WP-SB. Study No. G9779. Advinius Therapeutics Limited, India. GLP, Unpublished.
G9780	Shanthaveerappa K. S.	2014	Determination of moisture content of propoxur 50% WP-SB. Study No. G9780. Advinius Therapeutics Limited, India. GLP, Unpublished.
G9781	Shanthaveerappa K. S.	2014	Determination of pH of 10% (w/v) aqueous suspension of propoxur 50% WP-SB. Study No. G9781. Advinius Therapeutics Limited, India. GLP, Unpublished.
G9782	Shanthaveerappa K. S.	2014	Wet sieve test for propoxur 50% WP-SB. Study No. G9782. Advinius Therapeutics Limited, India. GLP, Unpublished.
G9783	Shanthaveerappa K. S.	2014	Determination of suspensibility of propoxur 50% WP-SB. Study No. G9783. Advinius Therapeutics Limited, India. GLP, Unpublished.
G9784	Shanthaveerappa K. S.	2014	Determination of persistent foam of propoxur 50% WP-SB. Study No. G9784. Advinius Therapeutics Limited, India. GLP, Unpublished.
G9785	Shanthaveerappa K. S.	2014	Determination of wettability of propoxur 50% WP-SB. Study No. G9785. Advinius Therapeutics Limited, India. GLP, Unpublished.
G9786	Shanthaveerappa K. S.	2014	Determination of dissolution rate of water soluble bags of propoxur 50% WP-SB. Study No. G9786. Advinius Therapeutics Limited, India. GLP, Unpublished.
G9787	Shanthaveerappa K. S.	2014	Accelerated storage stability test of propoxur 50% WP-SB. Study No. G9787. Advinius Therapeutics Limited, India. GLP, Unpublished.
DNA3080	Norris David	2015	Analysis of 5 batches of Propoxur Technical to determine the content of a specified solvent, with associated validation, in Compliance with Good Laboratory Practice. Study Number DNA3080. David Norris Laboratories Ltd. GLP, Unpublished.
	WHO	2006	Pesticides and their application for the control of vectors and pests of public health importance (sixth edition). Document WHO/CDS/NTDWHOPES/GCDPP/2006.1. WHO, 2006. Available at http://whqlibdoc.who.int/hq/2006/WHO_CDS_NTD_WHOPES_GCDPP_2006.1_eng.pdf?ua=1

PROPOXUR

FAO/WHO EVALUATION REPORT 80/2003

Explanation

The data for propoxur were evaluated for review of existing FAO and WHO specifications for propoxur. Existing FAO full specifications for TC, DP, WP and EC (80/TC/S/F, 1991; 80/DP/S/F, 1992; 80/WP/S/F, 1991; 80/EC/S/F, 1991) were published as AGP: CP/332 in 1995. Existing WHO full specifications for TC and WP (WHO/SIT/18.R4 and WHO/SIF/30.R4, respectively) were published in 1999.

Propoxur is no longer under patent.

Propoxur was evaluated by the FAO/WHO JMPR in 1973, 1977, 1981, 1983 1989 and 1996. Propoxur has also been submitted to the EU as notification for the Biocidal Products Directive (Directive 98/8/EC) under notification no. N353.

The draft specification and the supporting data were provided by Bayer Crop Science AG, Germany, in 2002.

Uses

Propoxur is an *N*-methylcarbamate insecticide and acaricide. It is non-systemic is a contact and stomach poison, which does not accumulate. The mode of action is interference with nervous transmission across the synaptic gap through inhibition of acetylcholinesterase.

Propoxur is used both for agricultural and public health purposes, being applied by spraying or as a dust. It is used against insect pests such as chewing and sucking insects, ants, cockroaches, crickets, flies and mosquitoes. Agricultural crop applications include sugar cane, cocoa, grapes and other fruit, maize, rice, vegetables, cotton, lucerne, forestry and ornamentals.

Identity

ISO common name:

propoxur (E-ISO, F-ISO 1750)

Chemical names:

IUPAC: 2-isopropoxyphenyl methylcarbamate
CA: 2-(1-methylethoxy)phenyl methylcarbamate

CAS No:

114-26-1

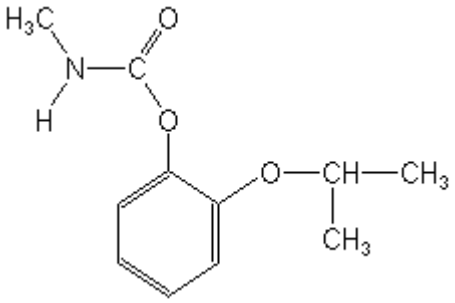
CIPAC No:

80

Synonyms:

Bay 9010, Baygon, Bayer 39007, Blattanex, Bolfo, BO Q 5812315, OMS 33, PHC (JMAF), Pillargon, UN Carbamate, Tugon, Unden, Undene

Structural formula:



Solid propoxur can exist in two crystal forms (modifications I and II) but the technical material usually contains >95% of modification I.

Molecular formula:

$C_{11}H_{15}NO_3$

Relative molecular mass:

209.25

Identity tests:

HPLC retention time, with detection at 280 nm (CIPAC Handbook D, p. 155, 1988); IR and mass spectra; melting point (87.5-90ºC).

Physico-chemical properties of propoxur

Table 1. Physico-chemical properties of pure propoxur

Parameter	Value(s) and conditions	Purity %	Method reference
Vapour pressure:	1.29 mPa at 20ºC 2.78 mPa at 25ºC (extrapolated)	99.9	OECD 104
Melting point and temperature of decomposition:	Melting point: Crystal modification I: 87.5ºC Crystal modification II: 90.0ºC Stable under ambient conditions, no decomposition occurs below 150ºC Decomposition starts at about 220ºC and the consequent multi-stage process evolves about 300 kJ/kg.	99.9	OECD 102/113
Solubility in water:	1.75 g/l at 20ºC	99.8	US-EPA Guidelines
Octanol/water partition coefficient:	log P_{OW} = 1.56 at 20ºC	99.8	US-EPA Guidelines
Hydrolysis characteristics:	Half-life at 22ºC >1 year at pH 4 93.2 days at pH 7 30.1 hours at pH 9	Not reported	OECD 111
Dissociation characteristics:	Propoxur has no distinct acidic or basic properties in aqueous solution.	99.9	OECD 112
Density	1.17 g/cm³ at 20ºC	99.9	OECD 109

Table 2. Chemical composition and properties of propoxur technical materials (TC)

Manufacturing process, maximum limits for impurities ≥ 1 g/kg, 5 batch analysis data.	Confidential information supplied and held on file by WHO. Mass balances were 99.9 to 100.1% with no unidentified impurities.
Declared minimum propoxur content:	980 g/kg
Crystal modification ratio of propoxur (discernible by IR)	Modification I: > 950 g/kg Modification II: < 50 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	87.5 to 90ºC
Density	1.17 g/cm³ at 20ºC
Bulk density	0.52 kg/l

Hazard summary

Notes

(i) The Proposer confirmed that the toxicological and ecotoxicological data included in the summary below were derived from propoxur having impurity profiles similar to those referred to in the table above.

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

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

Species	Test	Duration and conditions	Purity	Result	Reference
Rat, Wistar, male, female	oral	60 animals, 14 days observation period, in polyethylene glycol 400, doses from 0 to 127.9 mg/kg bw	not stated	LD_{50} = Males: 89.7 mg/kg bw Females: 78.5 mg/kg bw	Sturdivant & Halliburton 1998
Rat, Wistar, male, female	oral	40 animals, in Lutrol, doses from 10 to 500 mg/kg bw	not stated	LD_{50} = Males: 196 mg/kg bw Females: 126 mg/kg bw	JMPR 1989, USEPA 1997, Flucke 1980
Rat, male, female	dermal	24 h, in Lutrol, applied to intact dorsal skin, observation period 14 days	99.6%	LD_{50} >5000 mg/kg bw	JMPR 1989, USEPA 1997, Flucke 1980
Rat, male, female	inhalation	4 h, 40 animals, conc. in air from 0 to 912 mg/m³	not stated	LC_{50} = 654 mg/m³	Pauluhn 1993
Rat, male, female	inhalation	4 h, 5 animals per sex, con. 28.7, 110.1, 330.4, 497.5 mg/m³	99.6%	LC_{50} >0.5 mg/l	JMPR 1989, USEPA 1997, Pauluhn 1988
Rabbit	skin irritation	500 mg, 4 hours, 6 animals	not stated	No manifestations of irritation	USEPA 1997 Sheets & Fuss 1991

Species	Test	Duration and conditions	Purity	Result	Reference
Rabbit, New Zealand White	skin irritation	Dose not recorded 24 or 72 hours	99.2%	No manifestations of irritation	JMPR 1989 Thyssen 1978
Rabbit, New Zealand White	eye irritation	0.1 g, 9 animals, examinations 1, 24, 48, 72 and 96 h	99.6%	No manifestations of irritation Severe miosis, which disappeared within 24 hours, no signs of irritation up to 96 hours post-application	JMPR 1989 Yamane 1986b
Rabbit, New Zealand White	Eye irritation	65 mg, 6 males, 48 h	99.8%	Instillation resulted in minor eye irritation (redness and discharge) which cleared within 48 h	USEPA 1997 Sheets, 1990a
Guinea-pig	skin sensitization	Magnusson and Kligman test, 30 animals	98.8%	No evidence of skin-sensitizing potential	JMPR 1989 Heimann 1982a
Wistar rat, male, female	acute neurotoxicity	14 days, groups of 12 male and female rats, doses of 0, 2, 10, 25mg/kg	99.4%	NOEL could not be determined, LOEL = 2mg/kg, based on brain CHE inhibition in both sexes 45 min after dosing	USEPA 1997 Dreist & Popp 1994

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

Species	Test	Duration and conditions	Purity	Result	Reference
Rat, Wistar male, female	oral, gavage	5 days, 5 animals per sex and , doses 0, 15, 30 mg/kg bw/day of propoxur of two different purities	98.6% technical and 99.2% recrystallized	Dose-related convulsions and apathy the only adverse effects, no difference between the two purities.	JMPR 1989 Heimann 1983
Wistar rat, female	Oral, feeding, toxicity	14 weeks, 100 rats, doses of 0, 8000 ppm via the feed	99.9%	NOAEL >8000 ppm	JMPR 1989 Hahnemann & Rühl-Fehlert 1988d
Wistar rat, female	Oral, feeding, toxicity	104 weeks, 610 animals, doses from 0, 50, 250, 1000, 3000, 5000, 8000 ppm (0 to 348.46 mg/kg bw/day)	99.6-99.9%	NOAEL = 250 ppm (14.47 mg/kg bw/day) Growth retardation, ChE inhibition, urinary bladder alterations. Hyperplastic and neoplastic changes to bladder were diet-dependent and hyperplastic changes were reduced by administration of ammonium chloride	JMPR 1989 Hahnemann & Rühl-Fehlert 1988d

Species	Test	Duration and conditions	Purity	Result	Reference
Mouse	Oral, feeding, toxicity	53 weeks, 50 female NMRI mice, diets containing 0, 3000, 8000 ppm	99.6-99.9%	Growth slightly decreased at 8000 ppm. Increased liver weight and fatty degeneration at 3000 and 8000 ppm. Relative lung weight increased at 8000 ppm only. No adverse effect on urinary bladder epithelium.	JMPR 1989 Hahnemann & Rühl-Fehlert 1988c
Hamster	Oral, feeding, toxicity	53 weeks, 50 female Syrian golden hamsters, diets containing 0, 3000, 8000 ppm.	99.6-99.9%	At both dose levels mortality incidence slightly increased, general state of animals impaired, growth retarded. Relative weights of kidneys and adrenals increased at 8000 ppm only. No adverse effect on urinary bladder epithelium.	JMPR 1989 Hahnemann & Rühl-Fehlert 1988a
Dog	Oral, feeding, toxicity	52 weeks, 12 Beagle dogs (m/f), 0, 200, 600 ppm. Additional groups weeks 1-40, 1800 ppm; weeks 41-44, 3600 ppm; weeks 45-52, 5400 ppm	99.4%	Cholinergic symptoms observed at highest dose level, after elevation of dose to 5400 ppm and 1/6 animals died. The following were also increased in this group: thrombocyte, leucocyte and reticulocyte counts, incidence of Heinz bodies, ALAT and SAP, liver weight and thyroid weight; thymus weight decreased. At highest dose and at 600 ppm, growth was retarded and plasma cholesterol and liver *N*-demethylase increased. NOAEL = 200 ppm.	JMPR 1989 USEPA 1997 Hoffmann & Gröning, 1984
Rhesus monkey	Oral, feeding, (intubation), toxicity	13 weeks, 6 rhesus monkeys (m/f), doses of 40 mg/kg bw/day	99.6%	Cholinergic symptoms observed but no adverse effect on urinary bladder epithelium.	JMPR 1989 USEPA 1997 Hoffmann & Rühl, 1985

Species	Test	Duration and conditions	Purity	Result	Reference
Mouse, male, female	Oral, feeding, carcinogenicity	SPF mice, strain CF1/W74, 2 years, groups of 50 male and 50 female rats, doses of 0, 700, 2000 or 6000 ppm in feed	99.6%	NOAEL = Males: 2000 ppm Females: 6000 ppm. No indications of oncogenic effects in any treatment group.	JMPR 1989 Bomhard & Löser 1981, Patterson 1980
Chinchilla rabbit, male, female	Dermal	5 male and 5 female rabbits, 14 applications, exposure period 24 hours, doses of 0 and 500 mg/kg bw/day	Not stated	Clinical, clinical chemical and haematological examinations did not detect any indications of damage or local irritant effects.	Kimmerle & Solmecke 1971
New Zealand white rabbit, male, female	Dermal	10 male, 10 female rabbits, 13 weeks, exposure period 6 hours/day, 5 days/week, doses of 0, 50, 250 and 1000 mg/kg bw/day in Cremophor	100%	NOAEL = 1000 mg/kg bw	USEPA 1997 Diesing & Flucke 1989
Wistar rat, male, female	inhalation	12 weeks, (6 h per day, 5 days a week), groups of 10 male and 10 female rats, concentrations of 0, 5.7, 18.7 or 31.7 mg/m^3	98.9%	Only effect observed was depression of cholinesterase activity in plasma, erythrocytes and brain, at 31.7 mg/m^3 only.	JMPR 1989, Kimmerle & Iyatomi 1976
Wistar rat, male, female	feeding, 2 generation reproduction	groups of 25 male and 25 female rats, duration 330 days, pre-mating exposure 70 days both groups, 0, 30 and 80 ppm in feed for entire period (preparation, mating, gestation and rearing)	99.8%	NOAEL = Parent: 30 ppm Reproduction: 80 ppm	USEPA 1997, Suter 1990, Dotti 1992

Species	Test	Duration and conditions	Purity	Result	Reference
Wistar rats, female	feeding, teratogenicity and embryotoxicity	25 mated females per group, exposure period from day 6 through 15 of gestation, in daily oral doses of 0, 3, 9 and 27 mg/kg bw, formulated in water/Cremophor EL	99.4%	NOAEL = 3 mg/kg bw/day for maternal toxicity No evidence of embyotoxicity or teratogenicity even at the highest dose tested (27 mg/kg bw).	JMPR 1989 USEPA 1997 Becker *et al*. 1989b
Rabbit, female, Chinchilla strain	feeding, teratogenicity and embryotoxicity	4 groups, 16 females per group, from 6th to 18th day of gestation, in daily oral doses of 0, 3, 10 and 30 mg/kg bw, formulation agent water/Cremophor EL	99.4%	NOAEL = 10 mg/kg bw/day for maternal toxicity and Embryotoxicity. Increased post-implantation losses at 30 mg/kg bw/day. Not teratogenic	JMPR 1989 USEPA 1997 Becker *et al*. 1989a
Wistar rat, male, female	sub-chronic neurotoxicity	13 weeks, groups of 12 male and 12 female rats, doses of 0, 500, 2000 and 8000 ppm equivalent to 0, 39, 163 and 703 mg/kg bw/day for females and 0, 33, 132 and 543 mg/kg bw/day males	99.5%	NOEL (functional observation battery and motor and locomotor activity changes) = males: 543 mg/kg bw Females: 163 mg/kg bw	USEPA 1997, Dreist & Popp 1994
White leghorn hens	sub-chronic delayed neurotoxicity	8 hens, 30 days, doses of 0, 300, 1500, 3000 and 4500 ppm	Not stated	No evidence of delayed neurotoxicity during feeding or 4 weeks post-treatment.	Kimmerle 1966a Hobik 1967
B6C3F1 mice	Oncogenicity	2 groups of 50 males and 50 females in 0, 500, 2000, 8000 ppm, 2 years	99.6%	NOEL = 500 ppm, LOEL = 2000 ppm	USEPA 1997 Bomhard 1992

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

Species	Test	Conditions	Purity	Result	Reference
Salmonella typhimurium (TA 100, TA 98, TA1535, TA 1537, TA 1538)	Ames test, *in vitro*	Concentrations: 50 nmol/plate	95%	Negative	JMPR 1989, Blevins *et al*. 1977b
Salmonella typhimurium (TA 100, TA 98, TA1535, TA 1537, TA 1538)	Ames test, *in vitro*	Concentrations: 0.1-1000µg/plate, solvent DMSO	98%	Negative	JMPR 1989, Inukai & Iyatomi 1978
Escherichia coli (WP2 hcr. B/r try WP2)	Reverse mutation test, *in vitro*	Concentrations: 20 µl/disk	Not stated	Negative	JMPR 1989 Shirasu *et al*. 1976
Saccharomyces cerevisiae (D4)	Mitotic gene conversion test, *in vitro*	Concentrations: 2 ml of suspension (containing 1000 ppm a.i.) at 5 x 10 cells; solvent DMSO	99.8%	Negative	JMPR 1989, Siebert & Lemperle 1974, Siebert & Eisenbrand 1974
Male mice	Dominant lethal test, *in vivo*	Concentrations: 10 mg/kg bw; p.o.	99.2%	Negative	JMPR 1989 Herbold 1980a
Male and female NMRI-mice bone marrow cells	Micronucleus test, *in vivo*	2 x 5 mg/kg bw; 2 x 10 mg/kg bw; p.o.	99.2%	Negative	JMPR 1989 Herbold 1980b

Table 6. Ecotoxicology profile of propoxur technical material

Species	Test	Duration and conditions	Purity	Result	Reference
Daphnia magna (water flea)	Acute toxicity	48 h	98.8%	EC_{50} = 0.011 ppm	USEPA 1997 Lamb 1981
Lepomis macrochirus (bluegill sunfish)	Short-term toxicity, flow-through	96h, concentrations from 2.2 to 10 ppm, temperature 22°C	98.8%	LC_{50} = 6.2 mg/l	USEPA 1997 Lamb 1981
Rainbow trout	Short-term toxicity, flow-through	96h, 5 concentrations: 2.2 to 10 ppm, temperature 22°C	98.8%	LC_{50} = 3.7 mg/l	USEPA 1997 Lamb 1981
Scenedesmus subspicatus (green algae)	Effect on growth, static water	72 h, Directive 92/69/EEC	99.6%	IC_{50} = 22 mg/l NOEC = 3.1 mg/l	Caspers 2001
Bobwhite quail	sub-acute toxicity	5 days, 10 birds per dietary level, doses of 500, 1000, 2000, 4000 and 8000 ppm	98.8%	LC_{50} = 2828 ppm NOEL = 1000 ppm	USEPA 1997 Lamb 1981

Propoxur was evaluated by WHOPES in 1976 and re-evaluated in 1999.

Propoxur was evaluated by the FAO/WHO JMPR in 1973, 1977, 1981, 1983, 1989, 1991 and 1996. with the toxicological reviews conducted in 1973 and 1989. The JMPR (JMPR 1989) concluded that propoxur showed moderate acute toxicity in the animal species examined. After reviewing all available data from *in vitro* and *in vivo* short-term tests, the JMPR concluded that there was no evidence of genotoxicity. The JMPR recommended an ADI of 0.02 mg/kg bw/day for propoxur.

The US EPA also evaluated propoxur (USEPA 1997) and concluded that it is likely to be moderately persistent under aerobic or anaerobic soil conditions (a metabolic half-life of several months), mobile (K_d values less than 1) and may potentially leach to groundwater. It is hydrolytically stable at acid or neutral pH (3-7) but degrades rapidly in alkaline conditions. Propoxur was categorized as very highly toxic to birds on an acute basis (some LD_{50}s are <10 mg/kg); highly toxic to birds on a sub-acute dietary basis (LC_{50} in the range of 51-500 ppm); moderately toxic to freshwater fish (some LC_{50}s in the range >1-10 ppm); highly toxic to bees (<11 µg/bee) on an acute contact basis; and very highly toxic to freshwater invertebrates (daphnid EC_{50} <1 ppm).

The WHO hazard classification of propoxur is: “moderately hazardous, class II“ (WHO 2000) and the USEPA classification of acute toxicity is also class II (USEPA 1997).

Formulations

The main formulation types available are WP, DP and EC, which are registered and sold in more than 45 countries throughout the world.

Methods of analysis and testing

The analytical method for the active ingredient (which also provides an identity test) is CIPAC 80/TC/M/2/3. Propoxur is determined by HPLC, using internal standardization with butyrophenone and UV detection at 280 nm. Propoxur may be identified by HPLC retention time and by IR and mass spectra.

The methods for determination of impurities were based on HPLC.

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

Physical properties

The properties and limits proposed for the specifications for TC, WP and EC comply with the requirements of the WHO/FAO Manual (FAO/WHO 2002).

Containers and packaging

Propoxur should be packed in polyethylene or polyamide using additional outer packaging.

Expression of the active ingredient

The active ingredient is expressed as propoxur.

Appraisal

The Meeting considered data, provided by Bayer Crop Science AG, for the review of existing full FAO (TC, DP, WP, EC) and WHO (TC, WP) specifications for propoxur. Propoxur is no longer under patent, it is presently registered in more than 45 countries and

has been used in agriculture and public health applications for many years. It is, however, not approved for use in agriculture in the USA and the proposer reported that registration of propoxur for crop applications in Europe would not be supported.

Propoxur has been registered for many years in numerous countries world-wide. Information including that related to toxicology and ecotoxicology on propoxur is available from publications/websites of the US EPA, JMPR, WHO and EXTOXNET (http://extoxnet.orst.edu/pips/propoxur.htm). The Proposer stated that the data provided for this evaluation were similar to those provided to the JMPR for evaluation but was unable to state categorically that they were similar to those submitted to the US EPA (USEPA 1997).

Propoxur is an *N*-methyl carbamate insecticide which is fairly soluble in water, very soluble in polar organic solvents but only slightly soluble in non-polar organic solvents. It is hydrolyzed very slowly at pH 4, slowly at pH 7 but rather rapidly at pH 9.

Propoxur is of moderate mammalian toxicity, it is rapidly metabolized and does not accumulate in tissues. It is not sensitizing or irritant to skin and is not irritant to the eye, although transient severe miosis occurred following application to the eye. There is no evidence that propoxur is carcinogenic, teratogenic or embryotoxic (post-implantation loss occurred only at doses above the level at which maternal toxicity occurred). In a 5-day study on rats, comparing the toxicity of technical (purity 98.6%) and recrystallized (purity 99.2%) propoxur, no difference in toxicity was found. The JMPR has recommended an ADI of 0.02 mg/kg bw/day for propoxur.

As may be expected for such a carbamate insecticide, propoxur is highly toxic to honeybees, aquatic invertebrates and birds, though its toxicity varies according to the species. It is moderately to slightly toxic to fish. The reported 96-hour LC50 values are 3.7 mg/L in rainbow trout, and 6.6 mg/L in bluegill sunfish. Propoxur is highly toxic to freshwater invertebrates and very highly or highly toxic to birds, its toxicity varying according to species. Propoxur is rather persistent and mobile in soils, having characteristics which could produce leaching to groundwater.

The Meeting was provided with confidential information on the current manufacturing process, together with data from 5-batch analyses and the manufacturing specifications for all impurities ≥1 g/kg. Mass balances were high (99.9-100.1%) and no unidentified impurities were present. The current (2000-on) manufacturing process produces a higher purity TC than previously and no new impurities are found (Riegner 2005). The data were stated by the manufacturer to be identical to those submitted for registration in Mexico, Australia, the Philippines, Thailand, Venezuela and Malaysia. The data were confirmed as being essentially similar to those submitted to Australia (Sethi 2005).

The proposed specification for propoxur TC was in accordance with the requirements of the manual (FAO/WHO 2002), with the exception of the three clauses considered below. Meeting noted the proposed higher minimum purity of 980 g/kg (1991 FAO specification minimum 970 g/kg, 1999 WHO specification minimum 950 g/kg).

(i) The manufacturer initially proposed a clause to control the crystal form ratio of propoxur TC, on the basis that crystal modification II has an adverse effect on the suspensibility of water dispersible formulations (Grohs 2004a). The two forms can apparently be distinguished by IR or x-ray diffraction methods but it was subsequently stated that the problem occurs only in WPs formulated with high concentrations (above 50%) of propoxur, which are no longer marketed (Grohs 2004b). The clause is not required for the low concentration and liquid formulations currently marketed and therefore the proposal was withdrawn.

(ii) A proposed clause for melting point of the TC, with a range of 87.5-90ºC (instead of 86-91.5ºC in the existing FAO and WHO specifications) was not in accordance with current guidelines in the manual (FAO/WHO 2002). The Meeting agreed that it should not be included but that it could be used as a supporting identity test.

(iii) The manufacturer explained (Grohs 2004a) that a proposed clause to limit acidity in the TC was necessary because, although propoxur is stable to hydrolysis in acid conditions, the TC is used to formulate water-based aerosols and the presence of excessive acid could initiate rapid rusting of the aerosol canister.

The proposed specifications for DP, WP and EC were broadly in accordance with the requirements of the manual (FAO/WHO 2002) but the following points were discussed and agreed with the manufacturer.

(i) The Meeting noted that the proposed minimum active ingredient content after the test of storage at elevated temperature was 95% (relative to the determined average content found before storage) compared to 97% in the existing FAO specification but the manufacturer subsequently confirmed that the limits should be 97% (Grohs 2004a).

(ii) The manufacturer initially specified the use of 63 µm sieve in the dry sieve test for the DP but agreed that the clause should be restricted to the standard 75 µm sieve (Grohs 2004a).

(iii) The manufacturer initially specified the use of a 40 µm sieve in the wet sieve test for the WP but agreed that the clause should be restricted to the standard 75 µm sieve (Grohs 2004a).

(iv) The Meeting questioned the long (2 min) wettability time specified for the WP. The manufacturer stated that propoxur is non-polar and therefore difficult to wet, that the 2 min limit is given in existing FAO and WHO specifications, and that the wettability had not given rise to practical problems in the field after many years of use (Grohs 2004a). Although it was noted that propoxur is not of exceptionally low polarity (it is slightly soluble in water), the Meeting agreed to accept the 2 min limit.

(v) The Meeting questioned the relatively high limit for water (10 g/kg) in the EC. The manufacturer stated that the EC is not turbid at <10 g/kg (Grohs 2004a) but that the water content must be kept below 10 g/kg in order to meet cold stability requirements. At temperatures below -5°C, ice crystals function as crystallization points and reduce the solubility of propoxur in the EC, causing sedimentation (Grohs 2004a). The Meeting noted that, although the proposed specification for propoxur WP (at the 500 g/kg level) is the same for both agricultural and public health applications, users should adhere to the label recommendations and not use the products interchangeably.

The analytical and physical test methods to be used in support of the proposed specifications are all CIPAC methods.

Recommendations

The Meeting recommended that:

(i) the existing FAO specifications for propoxur TC, DP, WP and EC and the existing WHO specifications for propoxur TC and WP should be withdrawn;

(ii) the proposed specifications (amended as described in the appraisal, above) for propoxur TC and WP should be adopted by FAO and WHO;

(iii) the proposed specifications (amended as described in the appraisal, above) for propoxur DP and EC should be adopted by FAO.

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