PROPOXUR

2-isopropoxyphenyl methylcarbamate
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## PART ONE

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Disclaimer

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

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

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

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

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

WHO is not responsible, and does not accept any liability, for the testing of pesticides for compliance with the specifications, nor for any methods recommended and/or used for testing compliance. As a result, WHO does not in any way warrant or represent that any pesticide claimed to comply with a WHO specification actually does so.

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1 This disclaimer applies to all specifications published by WHO.
INTRODUCTION

WHO 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 Manual for Development and Use of FAO and WHO Specifications for Pesticides. This New Procedure follows a formal and transparent evaluation process. It describes the minimum data package, the procedure and evaluation applied by WHO and the experts of the “FAO/WHO Joint Meeting on Pesticide Specifications” (JMPS).

WHO specifications now only apply to products for which the technical materials have been evaluated. Consequently, from the year 2002 onwards the publication of WHO 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 above-mentioned manual.

Part Two: The Evaluation Report(s) of the pesticide, reflecting the evaluation of the data package carried out by WHO and the JMPS. The data are provided by the manufacturer(s) according to the requirements of chapter 3 of the above-mentioned manual 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.

WHO 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. WHO 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.

* Footnote: The publications are available on the Internet under (http://www.who.int/whopes/quality/en/).
PART ONE

SPECIFICATIONS

PROPOXUR

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WHO SPECIFICATIONS FOR PUBLIC HEALTH PESTICIDES

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
C₁₁H₁₅NO₃

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 (87.5-90°C).
WHO SPECIFICATIONS FOR PUBLIC HEALTH PESTICIDES

PROPOXUR TECHNICAL MATERIAL
WHO specification 80/TC (August 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 produced by these manufacturers but it is not an endorsement of those products, nor a guarantee that they comply with the specification. The specification may not be appropriate for TC produced by other manufacturers. The evaluation reports (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.


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 H₂SO₄.

Maximum alkalinity: 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.who.int/whopes/quality/en/.
WHO SPECIFICATIONS FOR PUBLIC HEALTH PESTICIDES

PROPOXUR WETTABLE POWDER

WHO specification 80/WP (August 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 relevant products of these manufacturers, and those of any other formulators who use only TC from the evaluated sources. 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 other manufacturers who use TC from other sources. The evaluation reports (80/2003, 80/2016), 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 (500 g/kg) and, when determined, the average content measured shall not differ from that declared by more than ± 5% of the declared content.

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.

4.2 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.who.int/whopes/quality/en/.
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.

**Note 4** 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.
WHO SPECIFICATIONS FOR PUBLIC HEALTH PESTICIDES

PROPOXUR WETTABLE POWDER IN SEALED WATER SOLUBLE BAG

WHO specification 80/WP-SB (August 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 (80/2016). It should be applicable to relevant products of this manufacturer, and those of any other formulators who use only TC from the evaluated sources. 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 other manufacturers who use TC from other sources. The evaluation report (80/2016), as PART TWO, forms an integral part of this publication.

1 Description

The material shall consist of a defined quantity 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, contained in a sealed water soluble bag.

2 Active ingredient (Note 1)

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 (500 g/kg) and, when determined, the average content measured shall not differ from that declared by more than ± 5% of the declared content.

3 Relevant impurities (Note 1)

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

Maximum: 20 g/kg.

4 Physical properties (Note 1)

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

pH range: 4.5 to 7.5.

4.2 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.who.int/whopes/quality/en/.
4.3 **Suspensibility** (MT 184, CIPAC Handbook K, p.142, 2003) (Notes 2, 3, & 4)

The suspensibility shall be tested on a suspension containing the WP and the bag material in the actual ratio of application, prepared according to the procedure described in Note 4.

A minimum of 60% shall be in suspension after 30 minutes in CIPAC Standard Water D at 30 ± 2°C.

4.4 **Persistent foam** (MT 47.1, CIPAC Handbook O, p.177, 2017) (Notes 4 & 5)

The persistent foam shall be tested on a suspension containing the WP and the bag material in the actual ratio of application, prepared according to the procedure described in Note 4.

Maximum: 10 ml after 1 min.

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

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

4.6 **Dissolution of the bag** (MT 176, CIPAC Handbook F, p.440, 1995) (Note 6)

The dissolution of the bag shall be tested on a sample of the emptied and cleaned bag taken according to the procedure described in Note 6.

Flow time of the suspension: maximum 30 sec.

5 **Storage stability**

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

The package should be enclosed in a watertight sachet, box or any other container at 54 ± 2°C 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 7) and the formulation shall continue to comply with the clauses for:

- pH range (4.1);
- wet sieve test (4.2);
- suspensibility (4.3);
- persistent foam (4.4);
- wettability (4.5);
- dissolution of the bag (4.6)

None of the bags tested should show signs of leakage or rupture during normal handling, before and after storage.

---

**Note 1** Sub-sampling.

Lay the bag on a bench and carefully open one side of the bag with a cutter, taking care not to damage the seals. Transfer the contents of the bag into a suitable flask. This material shall be used to carry out the tests for:

- active ingredient identity (2.1)
- active ingredient content (2.2)
- water content (3.1)
- pH range (4.1)
- wet sieve test (4.2)
The bag is then opened on three sides, completely cleaned from adhering powder by brushing or suction and weighed to the nearest 0.01 g. It shall be used to carry out the dissolution test (4.6). Aliquots of an aqueous solution of the bag material shall be used in the suspensibility (4.3) and persistent foam (4.4) tests.

In the case of delay of the above tests, the bag shall be stored in a watertight container (glass bottle or equivalent) to avoid any change in its properties.

**Note 2** 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 3** Chemical assay is the only fully reliable method to measure the mass of active ingredient still in suspension. However, the 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 4** The procedure for adding the bag material to the solution for the suspensibility and the persistent foam tests should be as follows:

Prepare a stock solution of the bag material (1 mg/ml) by weighing approximately a sample (n mg) of the bag (excluding sealed parts) to the nearest mg. Dissolve this sample by stirring in the standard water used for the tests to give a final volume of n ml. Store the stock solution in a stoppered bottle before use.

Calculate the volume (V ml) of the stock solution of the bag to be added to the test suspension of the wettable powder according to the following equation:

\[
V(\text{ml}) = \frac{X \times 1000B}{W}
\]

Where:
- B (g) = weight of the emptied and cleaned bag
- W (g) = nominal weight of the WP contained in the bag
- X (g) = weight of the WP sample used in the test

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

**Note 6** The sampling of the bag for the dissolution test should be as follows:

Lay the empty cleaned bag in its original configuration (double layer). Delineate and then cut up a test sample including part of the upper seal (5 cm) and symmetrically including the vertical seal (10 cm). If the size of the bag is less than this dimension, use the whole bag.

Carry out the dissolution test immediately to avoid any modification of the sample.

**Note 7** 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

PROPOXUR

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<tr>
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<td>Bayer CropScience (TC, DP, WP, EC)</td>
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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 this 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 respectively. 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 manufacturer, 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 47.1 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.
Physico-chemical properties of propoxur

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

<table>
<thead>
<tr>
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<th>Confidential information supplied and held on file by FAO and WHO. Mass balances were 98.7-99.6 % with no unknowns.</th>
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<tbody>
<tr>
<td>Manufacturing process, maximum limits for impurities ≥ 1 g/kg, 5 batch analysis data</td>
<td>None</td>
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<tr>
<td>Declared minimum propoxur content</td>
<td>980 g/kg</td>
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<tr>
<td>Relevant impurities ≥ 1 g/kg and maximum limits for them</td>
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<tr>
<td>Relevant impurities &lt; 1 g/kg and maximum limits for them</td>
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<tr>
<td>Stabilisers or other additives and maximum limits for them</td>
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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

<table>
<thead>
<tr>
<th>Species</th>
<th>Test</th>
<th>Purity %</th>
<th>Guideline, duration, doses and conditions</th>
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<tbody>
<tr>
<td><em>Salmonella typhimurium</em> (TA1537, TA1535, TA102, TA100 and TA98)</td>
<td>Reverse Mutation Assay (Ames test), <em>in vitro</em></td>
<td>98.20%</td>
<td>OECD No. 471 Dosage: 128, 320, 800, 2000 and 5000 µg/plate Solvent: DMSO</td>
<td>Negative</td>
<td>14_14_058</td>
</tr>
</tbody>
</table>
### ANNEX 2: REFERENCES

<table>
<thead>
<tr>
<th>Study number</th>
<th>Author(s)</th>
<th>Year</th>
<th>Study title. Study identification number. Report identification number. GLP [if GLP]. Company conducting the study</th>
</tr>
</thead>
<tbody>
<tr>
<td>5083</td>
<td>Nageswara T.</td>
<td>2015</td>
<td>Determination of Foam Persistence of Propoxur 50% WP-SB. Study No. 5083. RCC Laboratories India Private Limited, India. GLP, Unpublished.</td>
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<tr>
<td>5084</td>
<td>Nageswara T.</td>
<td>2015</td>
<td>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.</td>
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<tr>
<td>DNA3080</td>
<td>Norris David</td>
<td>2015</td>
<td>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.</td>
</tr>
</tbody>
</table>
WHO SPECIFICATIONS AND EVALUATIONS FOR
PUBLIC HEALTH PESTICIDES

PROPOXUR

FAO/WHO EVALUATION REPORT 80/2003

Explanation


Propoxur is no longer under patent.


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 name:

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:

![Structural formula image]

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 (87.5-90°C).

Physico-chemical properties of propoxur

Table 1. Physico-chemical properties of pure propoxur

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value(s) and conditions</th>
<th>Purity %</th>
<th>Method reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vapour pressure:</td>
<td>1.29 mPa at 20°C</td>
<td>99.9</td>
<td>OECD 104</td>
</tr>
<tr>
<td></td>
<td>2.78 mPa at 25°C</td>
<td></td>
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</tr>
<tr>
<td></td>
<td>(extrapolated)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Melting point and temperature of decomposition:</td>
<td>Melting point:</td>
<td>99.9</td>
<td>OECD 102/113</td>
</tr>
<tr>
<td></td>
<td>Crystal modification I: 87.5°C</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Crystal modification II: 90.0°C</td>
<td></td>
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</tr>
<tr>
<td></td>
<td>Stable under ambient conditions, no decomposition occurs below 150°C</td>
<td></td>
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<tr>
<td></td>
<td>Decomposition starts at about 220°C and the consequent multi-stage process evolves about 300 kJ/kg.</td>
<td></td>
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</tr>
<tr>
<td>Solubility in water:</td>
<td>1.75 g/l at 20°C</td>
<td>99.8</td>
<td>US-EPA Guidelines</td>
</tr>
<tr>
<td>Octanol/water partition coefficient:</td>
<td>$\log P_{OW} = 1.56$ at 20°C</td>
<td>99.8</td>
<td>US-EPA Guidelines</td>
</tr>
<tr>
<td>Hydrolysis characteristics:</td>
<td>Half-life at 22°C</td>
<td></td>
<td>OECD 111</td>
</tr>
<tr>
<td></td>
<td>&gt;1 year at pH 4</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>93.2 days at pH 7</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>30.1 hours at pH 9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dissociation characteristics:</td>
<td>Propoxur has no distinct acidic or basic properties in aqueous solution.</td>
<td>99.9</td>
<td>OECD 112</td>
</tr>
<tr>
<td>Parameter</td>
<td>Value(s) and conditions</td>
<td>Purity %</td>
<td>Method reference</td>
</tr>
<tr>
<td>---------------------------</td>
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</tr>
<tr>
<td>Density</td>
<td>1.17 g/cm³ at 20°C</td>
<td>99.9</td>
<td>OECD reference</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th></th>
<th>Confidential information supplied and held on file by WHO. Mass balances were 99.9 to 100.1% with no unidentified impurities.</th>
</tr>
</thead>
</table>
| Manufacturing process, maximum limits for impurities ≥ 1 g/kg, 5 batch analysis data. | 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 90°C  
Density | 1.17 g/cm³ at 20°C  
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.

<table>
<thead>
<tr>
<th>Species</th>
<th>Test</th>
<th>Duration and conditions</th>
<th>Purity</th>
<th>Result</th>
<th>Reference</th>
</tr>
</thead>
</table>
| 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 | LD₅₀ = 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 | LD₅₀ = Males: 196 mg/kg bw  
<p>| Rat, male, female         | dermal | 24 h, in Lutrol, applied to intact dorsal skin, observation period 14 days | 99.6%   | LD₅₀ &gt;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 | LC₅₀ = 654 mg/m³ | Pauluhn 1993 |</p>
<table>
<thead>
<tr>
<th>Species</th>
<th>Test</th>
<th>Duration and conditions</th>
<th>Purity</th>
<th>Result</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rat, male, female</td>
<td>inhalation</td>
<td>4 h, 5 animals per sex, con. 28.7, 110.1, 330.4, 497.5 mg/m³</td>
<td>99.6%</td>
<td>LC₅₀ &gt;0.5 mg/l</td>
<td>JMPR 1989, USEPA 1997, Pauluhn 1988</td>
</tr>
<tr>
<td>Rabbit</td>
<td>skin irritation</td>
<td>500 mg, 4 hours, 6 animals</td>
<td>not stated</td>
<td>No manifestations of irritation</td>
<td>USEPA 1997 Sheets &amp; Fuss 1991</td>
</tr>
<tr>
<td>Rabbit, New Zealand White</td>
<td>skin irritation</td>
<td>Dose not recorded 24 or 72 hours</td>
<td>99.2%</td>
<td>No manifestations of irritation</td>
<td>JMPR 1989 Thyssen 1978</td>
</tr>
<tr>
<td>Rabbit, New Zealand White</td>
<td>eye irritation</td>
<td>0.1 g, 9 animals, examinations 1, 24, 48, 72 and 96 h</td>
<td>99.6%</td>
<td>No manifestations of irritation Severe miosis, which disappeared within 24 hours, no signs of irritation up to 96 hours post-application</td>
<td>JMPR 1989 Yamane 1986b</td>
</tr>
<tr>
<td>Rabbit, New Zealand White</td>
<td>Eye irritation</td>
<td>65 mg, 6 males, 48 h</td>
<td>99.8%</td>
<td>Instillation resulted in minor eye irritation (redness and discharge) which cleared within 48 h</td>
<td>USEPA 1997 Sheets, 1990a</td>
</tr>
<tr>
<td>Guinea-pig</td>
<td>skin sensitization</td>
<td>Magnusson and Kligman test, 30 animals</td>
<td>98.8%</td>
<td>No evidence of skin-sensitizing potential</td>
<td>JMPR 1989 Heimann 1982a</td>
</tr>
<tr>
<td>Wistar rat, male, female</td>
<td>acute neurotoxicity</td>
<td>14 days, groups of 12 male and female rats, doses of 0, 2, 10, 25mg/kg</td>
<td>99.4%</td>
<td>NOEL could not be determined, LOEL = 2mg/kg, based on brain CHE inhibition in both sexes 45 min after dosing</td>
<td>USEPA 1997 Dreist &amp; Popp 1994</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Species</th>
<th>Test</th>
<th>Duration and conditions</th>
<th>Purity</th>
<th>Result</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rat, Wistar male, female</td>
<td>oral, gavage</td>
<td>5 days, 5 animals per sex and, doses 0, 15, 30 mg/kg bw/day of propoxur of two different purities</td>
<td>98.6% Technical and 99.2% recrystallized</td>
<td>Dose-related convulsions and apathy the only adverse effects, no difference between the two purities.</td>
<td>JMPR 1989 Heimann 1983</td>
</tr>
<tr>
<td>Wistar rat, female</td>
<td>Oral, feeding, toxicity</td>
<td>14 weeks, 100 rats, doses of 0, 8000 ppm via the feed</td>
<td>99.9%</td>
<td>NOAEL &gt;8000 ppm</td>
<td>JMPR 1989 Hahnemann &amp; Rühl-Fehlert 1988d</td>
</tr>
<tr>
<td>Species</td>
<td>Test</td>
<td>Duration and conditions</td>
<td>Purity</td>
<td>Result</td>
<td>Reference</td>
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</tr>
<tr>
<td>Wistar rat, female</td>
<td>Oral, feeding, toxicity</td>
<td>104 weeks, 610 animals, doses from 0, 50, 250, 1000, 3000, 5000, 8000 ppm (0 to 348.46 mg/kg bw/day)</td>
<td>99.6-99.9%</td>
<td>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</td>
<td>JMPR 1989 Hahnemann &amp; Rühl-Fehlert 1988d</td>
</tr>
<tr>
<td>Mouse</td>
<td>Oral, feeding, toxicity</td>
<td>53 weeks, 50 female NMRI mice, diets containing 0, 3000, 8000 ppm</td>
<td>99.6-99.9%</td>
<td>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.</td>
<td>JMPR 1989 Hahnemann &amp; Rühl-Fehlert 1988c</td>
</tr>
<tr>
<td>Hamster</td>
<td>Oral, feeding, toxicity</td>
<td>53 weeks, 50 female Syrian golden hamsters, diets containing 0, 3000, 8000 ppm.</td>
<td>99.6-99.9%</td>
<td>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.</td>
<td>JMPR 1989 Hahnemann &amp; Rühl-Fehlert 1988a</td>
</tr>
<tr>
<td>Species</td>
<td>Test</td>
<td>Duration and conditions</td>
<td>Purity</td>
<td>Result</td>
<td>Reference</td>
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<td>-----------------------------------------------</td>
</tr>
<tr>
<td>Dog</td>
<td>Oral, feeding,</td>
<td>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</td>
<td>99.4%</td>
<td>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.</td>
<td>JMPR 1989, USEPA 1997, Hoffmann &amp; Gröning, 1984</td>
</tr>
<tr>
<td>Rhesus monkey</td>
<td>(intubation),</td>
<td>13 weeks, 6 rhesus monkeys (m/f), doses of 40 mg/kg bw/day</td>
<td>99.6%</td>
<td>Cholinergic symptoms observed but no adverse effect on urinary bladder epithelium.</td>
<td>JMPR 1989, USEPA 1997, Hoffmann &amp; Rühl, 1985</td>
</tr>
<tr>
<td>Mouse, male, female</td>
<td>Oral, feeding,</td>
<td>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</td>
<td>99.6%</td>
<td>NOAEL = Males: 2000 ppm Females: 6000 ppm. No indications of oncogenic effects in any treatment group.</td>
<td>JMPR 1989, Bomhard &amp; Löser 1981, Patterson 1980</td>
</tr>
<tr>
<td>Chinchilla rabbit,</td>
<td>Dermal</td>
<td>5 male and 5 female rabbits, 14 applications, exposure period 24 hours, doses of 0 and 500 mg/kg bw/day</td>
<td>Not stated</td>
<td>Clinical, clinical chemical and haematological examinations did not detect any indications of damage or local irritant effects.</td>
<td>Kimmerle &amp; Solmecke 1971</td>
</tr>
<tr>
<td>New Zealand white</td>
<td>Dermal</td>
<td>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</td>
<td>100%</td>
<td>NOAEL = 1000 mg/kg bw</td>
<td>USEPA 1997, Diesing &amp; Flucke 1989</td>
</tr>
<tr>
<td>Species</td>
<td>Test</td>
<td>Duration and conditions</td>
<td>Purity</td>
<td>Result</td>
<td>Reference</td>
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</tr>
<tr>
<td>Wistar rat, male, female</td>
<td>inhalation</td>
<td>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/m³</td>
<td>98.9%</td>
<td>Only effect observed was depression of cholinesterase activity in plasma, erythrocytes and brain, at 31.7 mg/m³ only.</td>
<td>JMPR 1989, Kimmerle &amp; Iyatomi 1976</td>
</tr>
<tr>
<td>Wistar rat, male, female</td>
<td>feeding, 2 generation reproduction</td>
<td>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)</td>
<td>99.8%</td>
<td>NOAEL = Parent: 30 ppm Reproduction: 80 ppm</td>
<td>USEPA 1997, Suter 1990, Dotti 1992</td>
</tr>
<tr>
<td>Wistar rats, female</td>
<td>feeding, teratogenicity and embryotoxicity</td>
<td>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/Cremoph or EL</td>
<td>99.4%</td>
<td>NOAEL = 3 mg/kg bw/day for maternal toxicity No evidence of embryotoxicity or teratogenicity even at the highest dose tested (27 mg/kg bw).</td>
<td>JMPR 1989, USEPA 1997 Becker et al. 1989b</td>
</tr>
<tr>
<td>Rabbit, female, Chinchilla strain</td>
<td>feeding, teratogenicity and embryotoxicity</td>
<td>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/Cremoph or EL</td>
<td>99.4%</td>
<td>NOAEL = 10 mg/kg bw/day for maternal toxicity and Embryotoxicity. Increased post-implantation losses at 30 mg/kg bw/day. Not teratogenic</td>
<td>JMPR 1989, USEPA 1997 Becker et al. 1989a</td>
</tr>
<tr>
<td>Species</td>
<td>Test</td>
<td>Duration and conditions</td>
<td>Purity</td>
<td>Result</td>
<td>Reference</td>
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<td>-----------------------------------------------</td>
</tr>
<tr>
<td>Wistar rat, male, female</td>
<td>sub-chronic neurotoxicity</td>
<td>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</td>
<td>99.5%</td>
<td>NOEL (functional observation battery and motor and locomotor activity changes) = males: 543 mg/kg bw Females: 163 mg/kg bw</td>
<td>USEPA 1997, Dreist &amp; Popp 1994</td>
</tr>
<tr>
<td>White leghorn hens</td>
<td>sub-chronic delayed neurotoxicity</td>
<td>8 hens, 30 days, doses of 0, 300, 1500, 3000 and 4500 ppm</td>
<td>Not stated</td>
<td>No evidence of delayed neurotoxicity during feeding or 4 weeks post-treatment.</td>
<td>Kimmerle 1966a, Hobik 1967</td>
</tr>
<tr>
<td>B6C3F1 mice</td>
<td>Oncogenicity</td>
<td>2 groups of 50 males and 50 females in 0, 500, 2000, 8000 ppm, 2 years</td>
<td>99.6%</td>
<td>NOEL = 500 ppm, LOEL = 2000 ppm</td>
<td>USEPA 1997, Bomhard 1992</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Species</th>
<th>Test</th>
<th>Conditions</th>
<th>Purity</th>
<th>Result</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Salmonella typhimurium</em> (TA 100, TA 98, TA1535, TA 1537, TA 1538)</td>
<td>Ames test, <em>in vitro</em></td>
<td>Concentrations: 50 nmol/plate</td>
<td>95%</td>
<td>Negative</td>
<td>JMPR 1989, Blevins <em>et al.</em> 1977b</td>
</tr>
<tr>
<td><em>Salmonella typhimurium</em> (TA 100, TA 98, TA1535, TA 1537, TA 1538)</td>
<td>Ames test, <em>in vitro</em></td>
<td>Concentrations: 0.1-1000 µg/plate, solvent DMSO</td>
<td>98%</td>
<td>Negative</td>
<td>JMPR 1989, Inukai &amp; Iyatomi 1978</td>
</tr>
<tr>
<td><em>Saccharomyces cerevisiae</em> (D4)</td>
<td>Mitotic gene conversion test, <em>in vitro</em></td>
<td>Concentrations: 2 ml of suspension (containing 1000 ppm a.i.) at 5 x 10 cells; solvent DMSO</td>
<td>99.8%</td>
<td>Negative</td>
<td>JMPR 1989, Siebert &amp; Lemperle 1974, Siebert &amp; Eisenbrand 1974</td>
</tr>
<tr>
<td>Male mice</td>
<td>Dominant lethal test, <em>in vivo</em></td>
<td>Concentrations: 10 mg/kg bw; p.o.</td>
<td>99.2%</td>
<td>Negative</td>
<td>JMPR 1989, Herbold 1980a</td>
</tr>
<tr>
<td>Species</td>
<td>Test</td>
<td>Conditions</td>
<td>Purity</td>
<td>Result</td>
<td>Reference</td>
</tr>
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<td>---------------------------------------------</td>
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<td>----------------------------------------------------------------------------</td>
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<td>----------------------</td>
</tr>
<tr>
<td>Male and female NMRI-mice bone marrow cells</td>
<td>Micronucleus test, <em>in vivo</em></td>
<td>2 x 5 mg/kg bw; 2 x 10 mg/kg bw; p.o.</td>
<td>99.2%</td>
<td>Negative</td>
<td>JMPR 1989, Herbold 1980b</td>
</tr>
</tbody>
</table>

Table 6. Ecotoxicology profile of propoxur technical material

<table>
<thead>
<tr>
<th>Species</th>
<th>Test</th>
<th>Duration and conditions</th>
<th>Purity</th>
<th>Result</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Daphnia magna</em> (water flea)</td>
<td>Acute toxicity</td>
<td>48 h</td>
<td>98.8%</td>
<td></td>
<td>USEPA 1997, Lamb 1981</td>
</tr>
<tr>
<td><em>Lepomis macrochirus</em> (bluegill sunfish)</td>
<td>Short-term toxicity, flow-through</td>
<td>96h, concentrations from 2.2 to 10 ppm, temperature 22 °C</td>
<td>98.8%</td>
<td></td>
<td>USEPA 1997, Lamb 1981</td>
</tr>
<tr>
<td>Rainbow trout</td>
<td>Short-term toxicity, flow-through</td>
<td>96h, 5 concentrations: 2.2 to 10 ppm, temperature 22 °C</td>
<td>98.8%</td>
<td></td>
<td>USEPA 1997, Lamb 1981</td>
</tr>
<tr>
<td><em>Scenedesmus subspicatus</em> (green algae)</td>
<td>Effect on growth, static water</td>
<td>Directive 92/69/EEC</td>
<td>99.6%</td>
<td>IC&lt;sub&gt;50&lt;/sub&gt; = 22 mg/l NOEC = 3.1 mg/l</td>
<td>Caspers 2001</td>
</tr>
<tr>
<td>Bobwhite quail</td>
<td>sub-acute toxicity</td>
<td>5 days, 10 birds per dietary level, doses of 500, 1000, 2000, 4000 and 8000 ppm</td>
<td>98.8%</td>
<td>LC&lt;sub&gt;50&lt;/sub&gt; = 2828 ppm NOEL = 1000 ppm</td>
<td>USEPA 1997, Lamb 1981</td>
</tr>
</tbody>
</table>

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<sub>d</sub> 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<sub>50</sub>s are <10 mg/kg); highly toxic to birds on a sub-acute dietary basis (LC<sub>50</sub> in the range of 51-500 ppm); moderately toxic to freshwater fish (some LC<sub>50</sub>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<sub>50</sub> <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 $\geq 1$ 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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