

# WHO SPECIFICATIONS AND EVALUATIONS FOR PUBLIC HEALTH PESTICIDES

## BENDIOCARB

2,2-dimethyl-1,3-benzodioxol-4-yl methylcarbamate



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## Disclaimer<sup>1</sup>

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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<sup>1</sup> 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/pq-vector-control/prequalified-lists/en/>).

**PART ONE**  
**SPECIFICATIONS**

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# WHO SPECIFICATIONS FOR PUBLIC HEALTH PESTICIDES

## BENDIOCARB

### INFORMATION

*ISO common name*

Bendiocarb (E-ISO, BSI, ANSI, ESA), bendiocarbe ((m) F-ISO)

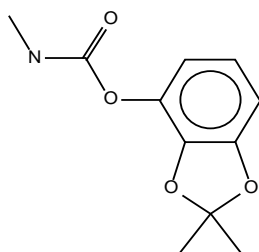
*Synonyms* None

*Chemical names*

*IUPAC:* 2,2-dimethyl-1,3-benzodioxol-4-yl methylcarbamate  
2,3-isopropylidenedioxyphenyl methylcarbamate

*CA:* 2,2-dimethyl-1,3-benzodioxol-4-yl methylcarbamate

*Structural formula*



*Empirical formula*

C<sub>11</sub>H<sub>13</sub>NO<sub>4</sub>

*Relative molecular mass*

223.2

*CAS Registry number*

22781-23-3

*CIPAC number*

232

*Identity tests*

HPLC retention time, <sup>1</sup>H NMR spectrum

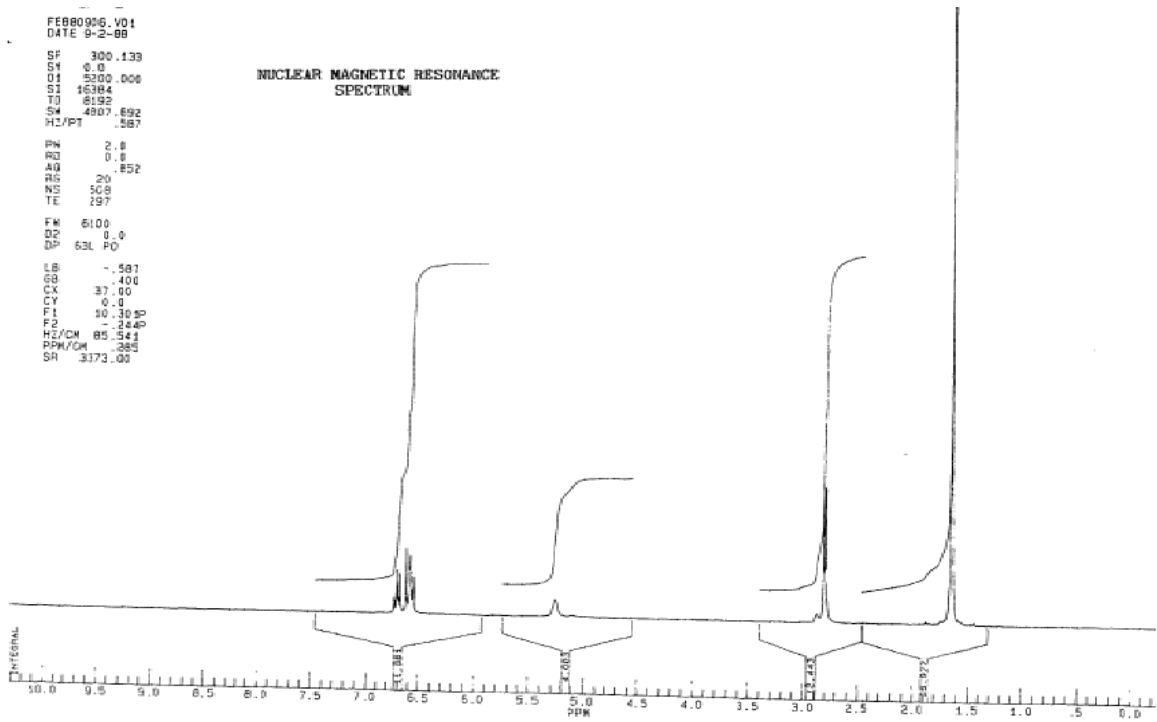
FEB0006.V01  
 DATE 9-2-88  
 SF 300.139  
 Q1 0.0  
 Q2 5200.000  
 SI 16384  
 TO 6132  
 S4 4807.692  
 H1/P1 .587

NUCLEAR MAGNETIC RESONANCE  
 SPECTRUM

PW 2.8  
 RO 0.8  
 AQ 852  
 RG 20  
 NS 508  
 TE 297

FM 6100.0  
 DS 0.0  
 DP 63L PD

LB -.587  
 GB -.400  
 CX 37.00  
 CY 0.0  
 FI 10.30SP  
 FO -.2440  
 HZ/CM 85.541  
 PPM/CM 323  
 SR 3173.08





# WHO SPECIFICATIONS FOR PUBLIC HEALTH PESTICIDES

## BENDIOCARB TECHNICAL MATERIAL

### WHO specification 232/TC (October 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 report (232/2008, 232/2017). 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 (232/2008, 232/2017), as PART TWO, form an integral part of this publication.*

#### 1 Description

The material shall consist of bendiocarb together with related manufacturing impurities and shall be a beige crystalline powder, free from visible extraneous matter and added modifying agents.

#### 2 Active ingredient

##### 2.1 Identity tests (232/TC/(M)/2, CIPAC Handbook D, p.10, 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 Bendiocarb content (232/TC/(M)/3, CIPAC Handbook D, p.11, 1988)

The bendiocarb content shall be declared (not less than 970 g/kg) and, when determined, the average measured content shall not be lower than the declared minimum content.

#### 3 Relevant impurities (Note 1)

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Note1 There are no relevant impurities to be controlled in products of the manufacturers identified in evaluation reports 232/2008 and 232/2017. However, methyl isocyanate and/or toluene can occur as a result of certain manufacturing processes. If methyl isocyanate ( $\geq 1$  g/kg) or toluene ( $\geq 10$  g/kg) would occur in the bendiocarb TC of other manufacturers it may be designated as a relevant impurity and a specification clause may be required to limit its concentration.

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\* Specifications may be revised and/or additional evaluations may be undertaken. Ensure the use of current versions by checking at: <http://www.who.int/pg-vector-control/prequalified-lists/en/>.

# WHO SPECIFICATIONS FOR PUBLIC HEALTH PESTICIDES

## BENDIOCARB WETTABLE POWDER

WHO specification 232/WP (November 2018\*)

*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 (232/2008). It should be applicable to relevant products of this manufacturer, and those of any other formulators who use only TC from the evaluated source. The specification is not an endorsement of those products, nor a guarantee that they comply with the specification. The specification may not be appropriate for the products of other manufacturers who use TC from other sources. The evaluation report (232/2008), as PART TWO, form an integral part of this publication.*

### 1 Description

The material shall consist of a homogeneous mixture of technical bendiocarb, complying with the requirements of WHO specification 232/TC (October 2017), together with filler(s) and any other necessary formulants. It shall be in the form of a fine powder, free from visible extraneous matter and hard lumps.

### 2 Active ingredient

#### 2.1 Identity tests (232/WP/(M)/2, CIPAC Handbook D, p.12, 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 Bendiocarb content (232/WP/(M)/3, CIPAC Handbook D, p.12, 1988)

The bendiocarb content shall be declared (800 g/kg) and, when determined, the average measured content shall not differ from that declared by more than  $\pm 25$  g/kg.

### 3 Relevant impurities (Note 1)

### 4 Physical properties

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

Maximum: 1% retained on a 75  $\mu$ m test sieve.

#### 4.2 Suspensibility (MT 184.1) (Notes 2, 3, 4 & 5)

A minimum of 70% of the bendiocarb content found under 2.2 shall be in suspension after 30 min in CIPAC Standard Water D at  $25 \pm 5^\circ\text{C}$ .

#### 4.3 Persistent foam (MT 47.3, CIPAC Handbook O, p.177, 2017)

Maximum: 50 ml after 1 min.

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\* Specifications may be revised and/or additional evaluations may be undertaken. Ensure the use of current versions by checking at: <http://www.who.int/pg-vector-control/prequalified-lists/en/>.

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

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

### 5 **Storage stability**

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

After storage at  $54 \pm 2^\circ\text{C}$  for 14 days, the determined average active ingredient content must not be lower than 95% relative to the determined mean content found before storage (Note 6) and the formulation shall continue to comply with the clauses for:

- wet sieve test (4.1);
- suspensibility (4.2);
- wettability (4.4).

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Note 1 There are no relevant impurities to be controlled in products of the manufacturer identified in evaluation report 232/2008. However, methyl isocyanate and/or toluene can occur as a result of certain manufacturing processes. If methyl isocyanate ( $\geq 1$  g/kg) or toluene ( $\geq 10$  g/kg) would occur in the formulations of other manufacturers it may be designated as a relevant impurity and a specification clause may be required to limit its concentration.

Note 2 The revision of the CIPAC method MT 184, Suspensibility of formulations forming suspensions on dilution with water (CIPAC/5156) was accepted as provisional CIPAC method in 2018. Prior to its publication in the next Handbook, copies of the method can be obtained through the CIPAC website, <http://www.cipac.org/index.php/methods-publications/pre-published-methods>

Note 3 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 184.1.

Note 4 This test will normally only be carried out after the heat stability test (5.1).

Note 5 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 6 Samples of the formulation taken before and after the storage stability test should be analyzed concurrently after the test in order to reduce the analytical error.

# WHO SPECIFICATIONS FOR PUBLIC HEALTH PESTICIDES

## BENDIOCARB WETTABLE POWDER IN SEALED WATER SOLUBLE BAG

### WHO specification 232/WP-SB (November 2018\*)

*This specification, which is PART ONE of this publication, is based on an evaluation of data submitted by the manufacturer whose name is listed in the evaluation reports (232/2013, 232/2015, 232/2018). It should be applicable to relevant products of this manufacturer, and those of any other formulators who use only TC from the evaluated source. The specification is not an endorsement of those products, nor a guarantee that they comply with the specification. The specification may not be appropriate for the products of other manufacturers who use TC from other sources. The evaluation reports (232/2013, 232/2015, 232/2018), as PART TWO, form an integral part of this publication.*

### 1 Description

The material shall consist of a defined quantity of a homogeneous mixture of technical bendiocarb, complying with the requirements of WHO specification 232/TC (October 2017), together with filler(s) and any other necessary formulants. It shall be in the form of a fine powder, free from visible extraneous matter and hard lumps, contained in a sealed water soluble bag.

### 2 Active ingredient

#### 2.1 Identity tests (232/WP/(M)/2, CIPAC Handbook D, p.12, 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 Bendiocarb content (232/WP/(M)/3, CIPAC Handbook D, p.12, 1988)

The bendiocarb content shall be declared (400 or 800 g/kg) and, when determined, the average measured content shall not differ from that declared by more than the following tolerances:

Declared content in g/kg	Tolerance
above 250 up to 500	± 5% of the declared content
above 500	± 25 g/kg
<u>Note</u> in each range the upper limit is included	

### 3 Relevant impurities (Note 1)

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\* Specifications may be revised and/or additional evaluations may be undertaken. Ensure the use of current versions by checking at: <http://www.who.int/pg-vector-control/prequalified-lists/en/>.

#### 4 **Physical properties** (Note 2)

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

Maximum: 1% retained on a 75 µm test sieve.

##### 4.2 **Suspensibility** (MT 184.1) (Notes 2, 3, 4, 5, 6 & 7)

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 7.

A minimum of 70% shall be in suspension after 30 minutes in CIPAC Standard Water D at 25 ± 5°C.

##### 4.3 **Persistent foam** (MT 47.3, MT 47.3, CIPAC Handbook O, p.177, 2017) (Notes 2 & 7)

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 7.

Maximum: 50 ml after 12 min.

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

The formulation shall be completely wetted in 4 min without swirling.

##### 4.5 **Dissolution of the bag** (MT 176, CIPAC Handbook F, p. 440, 1995) (Notes 2 & 8)

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 7.

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°C for 14 days. The determined average active ingredient content must not be lower than 95% relative to the determined average content found before storage (Note 9) and the formulation shall continue to comply with the clauses for:

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

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

Note 1 There are no relevant impurities to be controlled in products of the manufacturer identified in evaluation reports 232/2008, 232/2013 and 232/2015. However, methyl isocyanate and/or toluene can occur as a result of certain manufacturing processes. If methyl isocyanate ( $\geq 1$  g/kg) or toluene ( $\geq 10$  g/kg) would occur in the formulations of other manufacturers it may be designated as a relevant impurity and a specification clause may be required to limit its concentration.

Note 2 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)
- wet sieve test (4.1)
- suspensibility (4.2)
- persistent foam (4.3)
- wettability (4.4)
- dissolution of the bag (4.5)

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 (4.5). Aliquots of an aqueous solution of the bag material shall be used in the suspensibility (4.2) and persistent foam (4.3) 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 3 The revision of the CIPAC method MT 184, Suspensibility of formulations forming suspensions on dilution with water (CIPAC/5156) was accepted as provisional CIPAC method in 2018. Prior to its publication in the next Handbook, copies of the method can be obtained through the CIPAC website, <http://www.cipac.org/index.php/methods-publications/pre-published-methods>

Note 4 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 184.1.

Note 5 This test will normally only be carried out after the heat stability test (5.1).

Note 6 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 7 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 ( $\underline{n}$  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  $\underline{n}$  ml. Store the stock solution in a stoppered bottle before use.

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

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

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 8 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 9 Samples of the formulation taken before and after the storage stability test should be analyzed concurrently after the test in order to reduce the analytical error.

**PART TWO**  
**EVALUATION REPORTS**

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**BENDIOCARB**

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## BENDIOCARB

### FAO/WHO EVALUATION REPORT 232/2018

#### Recommendations

The Meeting recommended that the existing WHO specification for bendiocarb wettable powder in sealed water soluble bag (WP-SB) should be extended to encompass the corresponding product of Saerfu (Henan) Agrochemical Co., Ltd.

#### Appraisal

The Meeting considered data and information submitted by Saerfu (Henan) Agrochemical Co., Ltd. to support the extension of the existing WHO specification 232/WP-SB (October 2017) for bendiocarb wettable powder in sealed water soluble bag (WP-SB).

Saerfu (Henan) Agrochemical Co., Ltd. provided data on physical-chemical properties of their bendiocarb 80% WP-SB formulation in water soluble bag including persistent foam, wettability, suspensibility, wet sieve test, dissolution rate of water soluble bags and stability after storage at  $54 \pm 2^\circ\text{C}$  for 14 days. Saerfu indicated that the specification is representative of the quality of their bendiocarb WP-SB and confirmed this statement by providing historical quality control data (five different batches). The data submitted by Saerfu were broadly in accordance with the requirements of the Manual on development and use of FAO and WHO specifications for pesticides (2016 - third revision of the first edition) and complied with the existing specification for bendiocarb WP-SB.

Saerfu (Henan) Agrochemical Co., Ltd. tested their WP-SB for all physical-chemical properties using the most recent CIPAC methods. Saerfu used the official CIPAC method (232/WP/(M)/3), published in Handbook D, for the determination of the bendiocarb content in the WP-SB formulation (before and after storage). This method is by reversed phase HPLC using UV detection at 254 nm and internal standardization with propiophenone.

The stability of the WP-SB in the accelerated storage test MT 46.3 was demonstrated to be acceptable, and no significant deterioration was observed in terms of active ingredient content, suspensibility, residues after sieving, persistent foam, wettability and dissolution rate of water soluble bags.

The Meeting also recommended, in the WP and WP-SB specifications, to refer to the revised CIPAC method MT 184.1 for suspensibility. This method was accepted as provisional CIPAC method in 2018 and is available through the CIPAC pre-published methods scheme.

## ANNEX 2: REFERENCES

Study number	Author(s)	Year	Study title. Study identification number. Report identification number. GLP [if GLP]. Company conducting the study
PQ-SN-16-040	Justin Wang	2017	Physical-Chemical Analysis of Bendiocarb 80% WP-SB. Bendiocarb WP-SB: Bendiocarb wettable powder in sealed water soluble bag. Study PQ-SN-16-040. Amendment 1 to Final Report PQ-SN-16-040. GLP. Pilarcise Laboratory Co., Ltd. Unpublished.
	ICAMA	2018	Certificate for Pesticide registration (Ministry of Agriculture, People's Republic of China).
		2018	Bendiocarb 80WP-SB Test report, Saerfu (Henan) Agrochemical Co., Ltd, non GLP.

## BENDIOCARB

### FAO/WHO EVALUATION REPORT 232/2017

#### Recommendations

The Meeting recommended the following.

- (i) The bendiocarb TC as proposed by Saerfu (Henan) Agrochemical Co., Ltd. should be accepted as equivalent to the bendiocarb reference profile.
- (ii) The WHO specification for bendiocarb TC should be extended to encompass the material produced by Saerfu (Henan) Agrochemical Co., Ltd.

#### Appraisal

The Meeting considered data and supporting information submitted in October 2015 by Saerfu (Henan) Agrochemical Co., Ltd. in support of extension of the existing WHO specification for bendiocarb TC. The data submitted 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) and supported the draft specification. The current reference specification with supporting data for bendiocarb was provided by Bayer CropScience in 2006, in support of the review of the previously existing WHO specification and was published in 2008.

Bendiocarb is a white crystalline solid, which is not under patent. It has been evaluated by JMPR, with the most recent JMPR evaluation in 1984. JMPR established an acceptable daily intake (ADI) of 0-0.004 mg/kg bw based on long term studies in rats.

Bendiocarb has been classified according to CLP (Classification, Labelling and Packaging Regulation (EC) No 1272/2008 based on the United Nations' Globally Harmonised System (GHS)) in the following hazard classes and categories (CLP00/ATP10): Acute Tox. 2 (H300, fatal if swallowed), Acute Tox. 3 (H311, toxic in contact with skin), Acute Tox. 3. (H331, toxic if inhaled), Aquatic Acute 1 (H400, very toxic to aquatic life) and Aquatic Chronic 1 (H410, very toxic to aquatic life with long lasting effect).

The Meeting was provided with commercially confidential information on the manufacturing process and five batch analysis data on all impurities present and their manufacturing limits in the TC. Mass balances ranged from 984.0 g/kg to 1011.7 g/kg in the 5-batch data. The proposer declared the minimum purity of the bendiocarb TC as 980 g/kg which is not statistically justified due to a particular batch leading to a high standard deviation between batches (mean value minus 3 times the standard deviation = 962 g/kg). Nevertheless the purity of the TC in all batches was higher than 980 g/kg and therefore higher than the existing WHO specification (not less than 970 g/kg). The percentage of unknowns ranged between 7.3 to 16.0 g/kg and it was considered acceptable by the Meeting.

The proposer submitted a 'Certificate for Pesticide Registration' which confirmed that the Saerfu's bendiocarb TC is registered in China with a declared minimum purity of 980 g/kg which is consistent with the declared minimum purity in the data submitted to WHO.

The manufacturing process, impurity profile and five batch analysis data were compared with the data submitted by Bayer CropScience in 2006. Saerfu (Henan) Agrochemical Co., Ltd. and Bayer CropScience synthesis pathways include two reaction steps. Synthesis pathways from both proposers are very similar. There are differences only in the solvent being used in the first reaction step. The impurity profile of Saerfu (Henan) Agrochemical Co., Ltd. is different as it has fewer impurities than the reference profile of Bayer CropScience. From the impurities analysed in the 5 batch analysis data of Saerfu (Henan), one impurity was specified, while three others were found below their LOQ. Methyl isocyanate and toluene were among the impurities found below the LOQ. The LOQ determined by Saerfu for methyl isocyanate and toluene are 0.07% w/w and 0.08% w/w respectively.

#### Methyl isocyanate

Methyl isocyanate has been classified according to CLP, from toxicological point of view, in the following hazard classes and categories (CLP00/ATP01): Acute Tox. 3 (H301, toxic if swallowed), Acute Tox. 3 (H311, toxic in contact with skin), Skin Irrit. 2 (H315, causes skin irritation), Eye Dam. 1 (H318, causes serious eye damage), Skin Sens. 1 (H317, may cause allergic skin reaction), Acute Tox. 2 (H330, fatal if inhaled), STOT SE 3 (H335, may cause respiratory irritation) and Resp. Sens. 1 (H334, may cause allergy or asthma symptoms or breathing difficulties if inhaled). Furthermore, methyl isocyanate is referred as an impurity of potential concern in the Appendix III of the "Guidance Document on the assessment of the equivalence of technical materials of substances regulated under Regulation (EC) 1107/2009 (SANCO/10597/2003-rev. 10.1 of 13 July 2012)". In the proposer's technical material, methyl isocyanate was not detectable at levels higher than the method's LOQ (LOQ = 0.7 g/kg) in all presented data. The Meeting considered that the LOQ for this impurity was unusually high considering the properties of the impurity. However it was agreed that this impurity is only relevant at values  $\geq 1$  g/kg according to the reference specification and therefore the LOQ of 0.7 g/kg is acceptable. The Meeting therefore agreed that it was not necessary to designate methyl isocyanate as a relevant impurity in the proposer's TC. Although a specification clause is not necessary in that case, the Meeting agreed that the cautionary note should remain in the specification, alerting users on the possibility that this impurity may occur at levels higher than 1 g/kg in the bendiocarb TC of other manufacturers with a consequence of a required control.

The method used for the determination of methyl isocyanate is a GC-FID method with internal standardization. The analysis was performed with a DB-Wax capillary column (30 m x 0.53 mm i.d. x 1  $\mu$ m) and was fully validated with respect to linearity, specificity, accuracy, precision, limits of detection and quantification.

#### Toluene

Toluene has been classified according to CLP, from toxicological point of view, in the following hazard classes and categories (CLP00): Skin irritant 2 (H315, causes skin irritation), Asp. Tox. 1 (H304, may be fatal if swallowed and enters airways) and STOT RE 2 (H373, may cause damage to organs through prolonged or repeated

exposure). According to the reference specification of bendiocarb this impurity is only relevant at values  $\geq 10$  g/kg. However, in the proposer's bendiocarb TC, toluene was not detectable at levels higher than the method's LOQ (LOQ = 0.8 g/kg) in all presented data and this value is well below 10 g/kg. The Meeting agreed that it was not necessary to designate toluene as a relevant impurity in the proposer's TC. Although a specification clause is not necessary in that case, the Meeting agreed that the cautionary note should remain in the specification, alerting users on the possibility that this impurity may occur at levels higher than 10 g/kg in bendiocarb TC of other manufacturers with a consequence of a required control.

The method used for the determination of toluene is a reversed phase HPLC method with detection at 210 nm. The method was fully validated with respect to linearity, specificity, accuracy, precision, LOQ and LOD.

A validated reversed phase HPLC method with UV detection at 210 nm and internal standardization for the determination of the third impurity found below LOQ was provided to the Meeting. The technical material was screened by the above HPLC/UV method, however by using bendiocarb as reference item, and it was demonstrated that no further impurities with a content of more than 0.1 % area of the active substance could be observed.

The analytical method used for determination of the active ingredient is a full CIPAC method (232/TC/(M)/3 published in CIPAC Handbook D validated for the analysis of bendiocarb TC). Bendiocarb is determined by reversed phase HPLC, using UV detection at 254 nm and internal standardization with propiophenone. The identity of bendiocarb was verified by UV-spectroscopy and HPLC retention time.

Originally, since the proposer did not provide the mutagenicity data (OECD 471) and the melting point for its own technical material, the Meeting could not conclude on the equivalence with the reference profile. For that reason the manufacturer was requested to conduct the appropriate studies under GLP. The proposer submitted the requested GLP studies.

Regarding the mutagenicity test, the results of the GLP study allowed the conclusion that the test material did not induce mutation in *Salmonella typhimurium* strains TA 98, TA 100, TA 1535, TA 1537 and TA 102 used in the assay.

The melting point of the test material was determined under GLP with the OECD testing guidelines 102. The melting point of the proposer technical material was 127.7°C. The difference in comparison with the reference TC (129°C) is due to the difference in purity of the test material (98.2% versus 98.5% in the reference material).

The data submitted allowed the Meeting to conclude on equivalence of the Saerfu (Henan) Agrochemical Co., Ltd. technical bendiocarb with the reference profile based on Tier-1 evaluation.

The Meeting also recommended, in the WP and WP-SB specifications, to refer to the CIPAC method MT 47.3 for persistent foam as published in Handbook O.

**SUPPORTING INFORMATION  
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## Uses

Bendiocarb is an insecticide; it is effective against a wide range of nuisance and disease vector insects. It is used in horticulture against mosquitoes, flies, wasps, ants, fleas, cockroaches, silverfish, ticks and other pests in homes, industrial plants, and food storage sites

## Physico-chemical properties of bendiocarb

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

Manufacturing process, maximum limits for impurities $\geq 1$ g/kg, 5 batch analysis data		Confidential information supplied and held on file by FAO and WHO. Mass balances were 98.4 - 101.2% and no unidentified impurities were reported.		
Declared minimum bendiocarb content		980 g/kg		
Relevant impurities $\geq 1$ g/kg and maximum limits for them		None		
Relevant impurities $< 1$ g/kg and maximum limits for them		None		
Stabilisers or other additives and maximum limits for them		None		
Parameter	Value and conditions	Purity %	Method reference	Study number
Melting temperature range of the TC	127.7°C	98.2	OECD 102	43624

## Formulations and co-formulated active ingredients

The main formulation types available are WP and WP-SB. Bendiocarb is not usually co-formulated with other pesticides.

## Methods of analysis and testing

The analytical method for the active ingredient (including identity tests) is a full CIPAC method. Bendiocarb is determined by HPLC using UV detection at 254 nm and internal standardization with propiophenone (CIPAC Handbook D).

The method(s) for determination of impurities are based on HPLC-UV and GC-FID. The identity of the impurities was verified by comparison of the retention time in the technical material to those of a certified reference item.

Test method used for the determination of the melting point of the technical material was OECD 102.

## Containers and packaging

No special requirements for containers and packaging have been identified.

**Expression of the active ingredient**

The active ingredient is expressed as bendiocarb.



## **ANNEX 1**

### **HAZARD SUMMARY PROVIDED BY THE PROPOSER**

Notes.

- (i) The proposer confirmed that the toxicological data included in the summary below were derived from bendiocarb 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 A. Mutagenicity profile of bendiocarb technical material based on *in vitro* tests**

Species	Test	Purity %	Guideline, duration, doses and conditions	Result	Study number
<i>Salmonella typhimurium</i> strains: TA 98, TA100, TA1535, TA1537 and TA102	Reverse Mutation Assay using Bacteria ( <i>Salmonella typhimurium</i> ) with bendiocarb	98.2	OECD 471, OPPTS 870.5100, GLP. Duration: from July 11, 2016 to August 9, 2016. Dose (µg/plate): 31.6, 100, 316, 1000, 2500 and 5000. Conditions: in two independent experiments several concentrations of the test item were used. Each assay was conducted with and without metabolic activation. The concentrations, including the controls, were tested in triplicate.	Non-mutagenic	165087

## ANNEX 2: REFERENCES

Study number	Author(s)	Year	Study title. Study identification number. Report identification number. GLP [if GLP]. Company conducting the study
	ECCHA	2017	Classification, Labelling and Packaging (CLP) Regulation (EC) No 1272/2008. Classification of substances and mixtures. <a href="https://echa.europa.eu/regulations/clp/classification">https://echa.europa.eu/regulations/clp/classification</a>
D95934	von Wantoch Rekowski	2015	Quantification of the Active Substance and Water in Five Batches of Bendiocarb Technical. Study D95934. Report D95934. GLP. Harlan Laboratories Ltd.
E00412	von Wantoch Rekowski	2015	Quantification of the Impurities in Five Batches of Bendiocarb Technical. Study E00412. Report E00412. GLP. Harlan Laboratories Ltd.
43624	Catherine Wo	2016	Bendiocarb 98% TC: Physical and Chemical Characteristics: Melting Point. GLP. Product Safety Labs.
165087	Gudrun Schreib	2106	Reverse Mutation Assay using Bacteria (Salmonella typhimurium) with Bendiocarb. Study 165087. Report 165087. Eurofins BioPharma Product Testing Munich GmbH.

## BENDIOCARB

### FAO/WHO EVALUATION REPORT 232/2015

#### Recommendations

The Meeting recommended that:

- (i) The specification for bendiocarb 400 g/kg WP-SB, proposed by Bayer CropScience, as amended, should be adopted by WHO.
- (ii) The specification for the product containing 400 g/kg should be merged with that for 800 g/kg bendiocarb.

#### Appraisal

A draft specification for bendiocarb 400 g/kg WP-SB, provided by Bayer CropScience, was received in 2015 and considered by the JMPS for development of a new WHO specification. A data package on physical-chemical properties of the formulation in the water soluble bag was also received (Mo5227, 2015) and supported the clauses and the proposed limits.

Bendiocarb has been developed as mosquito adulticide for indoor residual spraying (IRS) by the company and the specification is therefore limited to WHO. The product was successfully evaluated by WHOPES and has a recommendation for IRS. The product is intended to complement the existing WHO specification for bendiocarb WP-SB containing 800 g/kg active ingredient. As content and physical-chemical properties do slightly differ, the published WHO specification for 800 g/kg with its limits had to be somewhat extended to accommodate the product with 400 g/kg (with respect to the limits for persistent foam and wettability).

The proposed specification for bendiocarb WP-SB was broadly in agreement with the guidelines given in the Manual (FAO/WHO 2010).

#### Formulation type, description, active ingredient content and analytical method

Bendiocarb is formulated as a wettable powder packed in a water soluble bag. Up to now, a bendiocarb WP-SB with 800 g/kg was available (WHO, June 2014). The product is intended to complement the existing WHO specification for bendiocarb WP-SB containing 800 g/kg active ingredient. As content and physical-chemical properties do slightly differ, the content clause with its tolerance was amended.

#### Description clause

The formulation is intended for IRS with a target dose of 0.1 to 0.4 g bendiocarb per m<sup>2</sup>. A certain defined amount of bendiocarb WP with a declared content of 400 g/kg is packed in a water soluble sachet so that dosing in a standard compression sprayer is facilitated without direct contact of the operator with the powder.

### Physical-chemical properties

In certain tests to be carried out to assess the physical-chemical parameters of the WB-SB, the neat formulation is used (e.g. in the wet sieve test and wettability). Whereas bendiocarb as WP formulation is fairly stable at 54°C for two weeks, the water soluble polymer material used for the bag may deteriorate and have an impact on the limits of certain clauses like dissolution of the bag and wettability. The test results of samples before and after storage at 54°C for two weeks showed that the majority of physical-chemical parameters were not adversely affected after storage at 54°C. The most significant effect was on the wettability that increased to around 200 seconds. The Meeting also noted that both the fresh and aged product showed the development of a significant amount of foam (typically 80 to 100 mL after 1 min, at concentrations of 2.5 and 5 % w/v, respectively).

However, in practice, the apparent ageing of the product that occurs under the rather harsh conditions of the accelerated storage at 54°C for two weeks in original packaging is not expected to have such an impact on the two physical-chemical parameters when stored under moderate conditions for longer time. The company explained, that under practical conditions the product rapidly mixes with water in the pressurized sprayer for IRS and the foam that is formed is decaying readily. For these reasons, the use of the product will not lead to a higher risk for the spray personnel and environment.

The Meeting accepted these explanations. As the new persistent foam method, MT 47.3, allows for two observation times - 1 and 12 min - the longer time and a limit of 50 mL was chosen. A significant increase in foam volume was observed with higher concentrations (5 %). Apparently - and not surprising - the dissolved bag material seems to contribute to the occurrence of foam in the persistent foam test.

### Storage stability

The clauses and limits in the physical-chemical subsection were broadly in agreement with the requirement of the Manual. In addition to standard clauses for a WP-SB formulation, the persistent foam after storage was included, in agreement with the latest amendments of the Manual. After accelerated storage at 54°C for 2 weeks, the products still complies with the clauses for wet sieve test, dissolution of the bag, suspensibility, wettability and persistent foam.

## ANNEX 1: REFERENCES

Study number	Author(s)	Year	Study title. Study identification number. Report identification number. GLP [if GLP]. Company conducting the study
Mo5227	Brux A.	2015	Determination of physico-chemical properties and storage stability of bendiocarb BND WP-SB 40. GLP. BioGenius, Germany.

## BENDIOCARB

### FAO/WHO EVALUATION REPORT 232/2013

#### Recommendations

The Meeting recommended that the specification for bendiocarb wettable powder in sealed water soluble bag (WP-SB), proposed by Bayer CropScience, as amended, should be adopted by WHO.

#### Appraisal

A draft specification for bendiocarb WP-SB, provided by Bayer CropScience, was received in 2013 and considered by the JMPS for development of a new WHO specification. A data package on physical-chemical properties of the formulation in the water soluble bag was also received (Brux A. 2013) and supported the clauses and the proposed limits. Bendiocarb has been developed as mosquito adulticide for indoor residual spraying (IRS) by the company and the specification therefore is limited to WHO. The product was successfully evaluated by WHOPES and has a recommendation for IRS.

The proposed specification for bendiocarb WP-SB was broadly in agreement with the guidelines given in the Manual (FAO/WHO 2010).

#### Formulation type, description, content of active ingredient and analytical method

Bendiocarb is formulated as a wettable powder packed in a water soluble bag. Up to now, a neat bendiocarb WP specification (WHO, December 2008) was available. Therefore, the clauses dealing with the formulation itself are expected to remain the same, but some clauses – especially those referring to the description and to the physical-chemical properties where the soluble bag as a part of the formulation is tested with the WP – do change. This reflects the advantages of the soluble bag that helps to minimize operator exposure. The Meeting concluded that bendiocarb WP and bendiocarb WP-SB should be standalone specifications.

#### Description clause

The formulation is intended for IRS with a target dose of 0.1 to 0.4 g bendiocarb per m<sup>2</sup>. A certain defined amount of bendiocarb WP with a declared content of 800 g/kg is packed in a water soluble sachet so that dosing in a certain amount of water is facilitated without direct contact of the operator with the powder.

#### Physical-chemical properties

The clauses and limits in the physical-chemical subsection were essentially in agreement with the requirement of the Manual. In certain tests to be carried out to assess the physical-chemical parameters of the WB-SB, the neat formulation is used (e.g. in wet sieve test and wettability). Suspensibility and persistent foam tests have to be carried out on the neat formulation with the bag material in the actual ratio of application.

### Storage stability

The Meeting questioned some parameters and limits, e.g. the temperature used in the accelerated storage test. Whereas bendiocarb as WP formulation is fairly stable at 54°C for two weeks, the water soluble polymer material used for the bag may deteriorate, and have an impact on the limits of certain clauses like dissolution of the bag and wet sieve test. The company responded that both bag material and formulation are stable under these conditions and that the limits proposed are well supported by the studies submitted.

In addition to standard clauses for a WP-SB formulation, the persistent foam after storage was included, in agreement with the latest amendments of the Manual. After accelerated storage at 54°C for 2 weeks, the product still complies with the clauses for wet sieve test, suspensibility, persistent foam, wettability and dissolution of the bag.

The Meeting agreed also to update in the specification for bendiocarb WP the CIPAC method for persistent foam (MT 47.3 instead of MT 47.2) to be in line with the current CIPAC method.



## ANNEX 1: REFERENCES

Study number	Author(s)	Year	Study title. Study identification number. Report identification number. GLP [if GLP]. Company conducting the study
Mo4640	Biogenius	2013	Determination of physico-chemical properties and storage stability of bendiocarb WP-SB 80. GLP. BioGenius, Germany.
	FAO/WHO	2010	Manual on development and use of FAO and WHO specifications for pesticides. Second revision of the 1 <sup>st</sup> edition. FAO, Rome and WHO, Geneva, November 2010 (internet publications).
	WHO	2002	Report of the Sixth WHOPES Working Group Meeting, WHO/HQ, Geneva, 6-7 November 2002. WHO, Geneva, document WHO/CDS/WHOPES/2002.6

## BENDIOCARB

### FAO/WHO EVALUATION REPORT 232/2008

#### Recommendations

The Meeting recommended that:

- (i) the specifications for bendiocarb TC and WP, proposed by Bayer CropScience and as amended, should be adopted by WHO; and
- (ii) the existing WHO specifications for bendiocarb TC, WP, DP and UL should be withdrawn.

#### Appraisal

The Meeting considered data and draft specifications (TC and WP only) for bendiocarb, submitted by Bayer CropScience in support of a review of existing WHO specifications for bendiocarb (TC, WP, DP, UL, all published in 1999). Existing specifications for bendiocarb DP and UL were not supported by the proposer.

Bendiocarb is not under patent.

Bendiocarb is a crystalline solid of low solubility in highly polar solvents (including water), and in solvents of low polarity, but is very soluble in various organic solvents of intermediate polarity. Bendiocarb is rapidly hydrolysed under moderately alkaline conditions but only slowly hydrolysed under moderately acidic conditions. Although it is subject to photolysis, degradation by this route does not occur very readily. It has no measurable acidic or basic properties.

The Meeting was provided with commercially confidential information on the manufacturing process and 5-batch analysis data on purity and all impurities  $\geq 1$  g/kg. These data were confirmed as identical to those submitted to the Health and Safety Executive (HSE) for registration in the U.K. Mass balances in the batch analytical data were good (98.7-99.7%) and the bendiocarb was of high purity (982-991 g/kg).

The Meeting and proposer considered in detail whether or not methyl isocyanate and toluene should be designated relevant impurities, for the purposes of WHO specifications, on the basis of their hazard characteristics.

The Meeting noted that the hazards associated with both impurities differ from those of bendiocarb but that their hazards have been well-characterized in the scientific literature. The Meeting also noted that both impurities are very volatile, in contrast with the low volatility of bendiocarb. In consequence, the patterns and routes of user and environmental exposure to the active ingredient and the two impurities were considered likely to be very different. Thus the simple "concentration and relative toxicity" approach, used by JMPS to determine the relevance of impurities having characteristics similar to those of the active ingredient, was not entirely appropriate in this case.

Methyl isocyanate. WHO/PCS advised the Meeting that methyl isocyanate is an eye and skin irritant and perhaps a respiratory sensitizer. However, in the proposer's bendiocarb TC, it was not detectable at or above 1 g/kg, the manufacturing limit

below which all impurities (other than those associated with exceptional hazards) are considered to become non-relevant. The Meeting therefore agreed that it was not necessary to designate methyl isocyanate as a relevant impurity in the proposer's TC, nor in WP prepared using TC from that source. The extent to which this volatile impurity would be likely to persist in (crystalline) bendiocarb TC or WP was unknown but the Meeting agreed that, although a specification clause is unnecessary in this case, a cautionary note should be appended to the specifications, alerting users to the possibility that the impurity may occur at  $\geq 1$  g/kg (and thus require control) in the bendiocarb products of other manufacturers.

Toluene. The large body of information available on the hazards involved in exposures to toluene would have been ignored by the default approach of JMPS to the determination of the relevance of impurities which have a hazard profile different from that of the active ingredient (i.e., the application of the GHS labelling limits for mixtures). Therefore, WHO/PCS proposed that a more refined approach should be adopted.

WHO/PCS advised that the assessment of toluene toxicity and classification by the European Union (EU 2003) is based on its toxicity arising from inhalation exposure, making it pertinent to the JMPS assessment of toluene in bendiocarb. The key end points that determine whether or not toluene should be designated as a relevant impurity in FAO/WHO specifications are related to its reproductive toxicity.

WHO/PCS advised that, with respect to reproductive toxicity, there are no data to indicate that toluene affects fertility or that it is teratogenic. However, it has been associated with developmental neurotoxicity in experimental animals and spontaneous abortions in humans. As there is uncertainty in the interpretation of these studies, the European union has classified toluene in reproductive toxicity category 3, corresponding to the GHS category 2. In addition, case reports have been published of "fetal alcohol syndrome" among toluene sniffers, with no information on exposure, although high levels almost certainly would have been involved. No information is available to show whether bendiocarb could produce similar effects but, to determine whether or not toluene levels should be controlled in bendiocarb, it was therefore conservatively assumed that the effects would be produced only by the toluene.

In the most informative study (Hass *et al.* 1999), adverse neuro-developmental effects were observed in rats exposed to air containing 4500 mg toluene/m<sup>3</sup> for 6 h/d from pregnancy day 7 to post-natal day 18<sup>1</sup>. These effects have not been studied at lower concentrations, so a no-observed-adverse-effect-concentration (NOAEC) is not available and the test level was considered to be the lowest-observed-adverse-effect-concentration (LOAEC).

Two studies in humans have indicated a possible increase of spontaneous abortions among women exposed to toluene, either alone (Ng *et al.* 1992) or in combination with other solvents (Taskinen *et al.* 1994). In the study involving exposure only to toluene, in which limited quantitative exposure data were available, an elevated incidence of spontaneous abortions was observed among

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<sup>1</sup> The effects were not observed in animals exposed only during the pre-natal period.

women exposed to an average concentration of 330 mg toluene/m<sup>3</sup> air in the workplace.

The default uncertainty factor used by the JMPR to derive acute reference doses (ARfD) and acceptable daily intakes (ADIs) from no-observable-adverse-effect-levels (NOAELs) is 100 (10 for inter-species extrapolation, 10 for inter-individual variation). When the NOAEL is not available to the JMPR, the use of the lowest-observed-adverse-effect-level (LOAEL) is usually compensated by incorporating an additional uncertainty factor of 3-10 (IPCS 1994, 1999; JMPR 2002; Solecki *et al.* 2005). WHO/PCS proposed that, for the hazard characterization of toluene in bendiocarb, the tolerable inhaled concentration (TIC), conceptually similar to the ARfD and ADI<sup>1</sup>, should be used. The TIC represents a range<sup>2</sup> of concentrations of a chemical in air that may be inhaled without health consequences over a day (TIC for acute effects) or over long periods of time (TIC for chronic effects). Calculated TIC maximum values, equivalent to JMPR ARfD maximum values (developmental effects being considered acute effects), for an 8-h daily airborne exposure of humans<sup>3</sup> to toluene would be:

$$(6/8 \times 4500) / (10 \times 10 \times [3 \text{ to } 10]) = 3.4 \text{ to } 11 \text{ mg/m}^3,$$

derived from data on adverse neuro-developmental effects in the study of reproductive toxicity in rats; and

$$(330 / (10 \times [3 \text{ to } 10])) = 3.3 \text{ to } 11 \text{ mg/m}^3,$$

derived from data on spontaneous abortions in the human study.

The estimated maximum values for the TIC thus converge toward a geometric mean of 6 mg/m<sup>3</sup>.

In most circumstances when solid bendiocarb TC or WP is exposed to air, any volatilized toluene impurity would be diluted by the environmental air. However, if bendiocarb becomes airborne as a dust<sup>4</sup> the toluene impurity concentration in air is maximized, as is the potential inhalation exposure to toluene. In such conditions, the toluene concentration in bendiocarb, the concentration of bendiocarb in air, and the toluene concentration in the air are related by the formula:

$$a = b \times c / 1000$$

where: a = toluene-in-air (mg/m<sup>3</sup>);  
b = bendiocarb-in-air (mg/m<sup>3</sup>);  
c = toluene-in- bendiocarb (g/kg).

So, for example, a toluene-in-air concentration of 6 mg/m<sup>3</sup> (the estimated TIC maximum) would be reached at a toluene-in-bendiocarb concentration of 11 g/kg and a corresponding a bendiocarb-in-air concentration of 550 mg/m<sup>3</sup>. The corresponding bendiocarb-in-air concentration equals the 4-h inhalation toxicity LC<sub>50</sub> (rat) for bendiocarb. Therefore, at a toluene-in-bendiocarb concentration of 11 g/kg, the risk associated with the acute inhalation hazard of the bendiocarb active ingredient greatly overshadows the risk associated with the reproductive

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<sup>1</sup> "Dose" being considered to be the amount inhaled at the TIC concentration over a working day.

<sup>2</sup> The minimum of the range being zero.

<sup>3</sup> The rats were exposed for 6 h/d.

<sup>4</sup> For example, during pouring or other transfer operations.

hazards of the toluene impurity and thus the contribution of toluene impurity to the overall hazard of the bendiocarb product is negligible. WHO/PCS therefore concluded that, at concentrations less than 10 g/kg of bendiocarb, toluene is a non-relevant impurity.

WHO/PCS also advised that the minimum toluene concentration for ignition in air is about 1% v/v and thus, as an impurity in bendiocarb, the toluene would present no fire/explosion risk at or about the proposed cut-off value of 10 g/kg.

The manufacturing limit for toluene in the proposer's bendiocarb was well below 10 g/kg and the Meeting agreed that it was not necessary to designate it as a relevant impurity in the proposer's TC, nor in WP prepared using TC from that source.

As in the case of methyl isocyanate, the extent to which (volatile) toluene would be likely to persist in (crystalline) bendiocarb TC or WP was unknown but, again, the Meeting agreed that, although a specification clause is unnecessary in this case, a cautionary note should be appended to the specifications, alerting users to the possibility that the impurity may occur at  $\geq 10$  g/kg (and require control) in the products of other manufacturers.

The Meeting agreed that none of the other impurities should be designated as relevant.

The analytical method for determination of the active ingredient (including identity tests) is a full CIPAC method, validated for analysis of TC and WP. Bendiocarb is determined by reversed-phase HPLC, using UV detection at 254 nm and internal standardization with propiophenone.

Test methods for determination of physico-chemical properties of the technical active ingredient were OECD, EPA or EC, while those for the WP formulation were CIPAC, as indicated in the specification. The Meeting questioned the melting point quoted for TC, as it was the same as that for the pure active ingredient. The proposer stated the similarity is a reflection of the generally very high purity of the TC in current production.

Noting that the existing WHO specifications for bendiocarb DP and UL were not supported by the proposer, the Meeting considered the following issues arising from the proposed specifications for TC and WP, which were otherwise in accordance with the requirements of the manual (FAO/WHO 2006).

TC. The Meeting welcomed the proposed increase in purity of bendiocarb (940 g/kg in the existing WHO specification) to 970 g/kg.

The existing clause for water content had been deleted. Although bendiocarb is subject to rapid hydrolysis under alkaline conditions, this does not occur in the crystalline solid TC and water is not considered to be a quality criterion for a TC used in the preparation of WP formulations.

WP. The Meeting noted that the existing WHO specification encompassed bendiocarb contents in the ranges 250-500 and  $>500$  g/kg but was informed that only the 800 g/kg WP had been evaluated for efficacy by WHOPES. The Meeting therefore agreed that the new specification should be restricted to 800 g/kg products.

The Meeting questioned whether the existing specification limits for certain physical properties remained appropriate for the new specification, as they represented values at or about the limit of acceptability. After checking current product performance, the proposer revised the specification limits for wet sieve test (from 2% to 1% of the formulation retained on a 75 µm sieve); suspensibility (from 50% to 70% in suspension after 30 min in hard water); persistent foam (from 60 ml to 50 ml); and wettability (from 2 min to 1 min for complete wetting without swirling). These improvements were welcomed by the Meeting.

The Meeting questioned the need for a proposed clause to limit the pH range, as this was not included in the existing specification. Although bendiocarb is unstable in alkaline solution, the manufacturer agreed that significant degradation is unlikely in the storage and use of the WP and the proposed clause was withdrawn.

**SUPPORTING INFORMATION  
FOR  
EVALUATION REPORT 232/2008**

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## Uses

Bendiocarb is a cholinesterase-inhibitor *N*-methyl carbamate insecticide. It is mainly used in public health, industrial and storage applications, having low odour and no corrosive or staining properties.

## Identity

### *ISO common names*

Bendiocarb (E-ISO, BSI, ANSI, ESA), bendiocarbe ((m) F-ISO)

*Synonyms* None

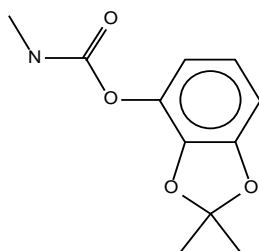
### *Chemical names*

*IUPAC:* 2,2-dimethyl-1,3-benzodioxol-4-yl methylcarbamate

2,3-isopropylidenedioxyphenyl methylcarbamate

*CA:* 2,2-dimethyl-1,3-benzodioxol-4-yl methylcarbamate

### *Structural formula*



### *Empirical formula*

C<sub>11</sub>H<sub>13</sub>NO<sub>4</sub>

### *Relative molecular mass*

223.2

### *CAS Registry number*

22781-23-3

### *CIPAC number*

232

### *Identity tests*

HPLC retention time, <sup>1</sup>H NMR spectrum.



## Physico-chemical properties of bendiocarb

**Table 1. Physico-chemical properties of pure bendiocarb**

Parameter	Value(s) and conditions	Purity %	Method	Reference
Vapour pressure	4.6 x 10 <sup>-3</sup> Pa at 25°C (extrapolated)	99.8	gas saturation	M-166699-01-1
Melting point	129°C	98.5	OECD 102	M-248943-01-1
Boiling point	decomposed with boiling at about 264°C	98.5	OECD 103	M-248943-01-1
Temperature of decomposition	≥240°C	98.5	OECD 103	M-248943-01-1
Solubility in water at 20°C	0.31 g/l at pH 3-5 0.28 g/l at pH 7 0.03 g/l at pH 9-11 with significant hydrolysis	99.3	84/449/EEC A6	M-166763-01-1
Octanol/water partition coefficient	K <sub>ow</sub> log P = 1.7 at 25°C at pH 6.9	99.0	84/449/EEC A8	M-166668-01-1
Hydrolysis characteristics, half-life at 25°C	46.5 d at pH 5 48.1 h at pH 7 43.8 min at pH 9	99.0	OECD 111	M-166890-01-1
Photolysis characteristics	Half-life = 37.3 d (corrected for dark reaction); 187 d (extrapolated to natural sunlight 40° north, midday, summer); 1070-20000 days (using the quantum yield) *	99.0	US EPA NTIS PB83-153973 (1982)	M-166721-01-1 M-166722-01-1
Dissociation characteristics	Not measurable due to rapid hydrolysis in alkaline solution. Not protonated under acidic conditions. The "parent phenol" of bendiocarb (NC7312) has pK <sub>a</sub> = 8.8 at 20°C	99.0	US EPA OPPTS 830.6310, UV spectrophotometric method	M-166694-01-1

**Table 2. Chemical composition and properties of technical bendiocarb (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 98.7-99.7% and no unidentified impurities were reported.
Declared minimum bendiocarb content	970 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 temperature of the TC	129°C

\* Data from a laboratory study at pH 5 (to minimize hydrolysis) under artificial light conditions (light source: Hg-arc TQ 150, light intensity corresponding to about 2.5x natural sunlight at 290-320 nm, being the region in which bendiocarb absorbs sunlight).

## **Hazard summary**

Bendiocarb was evaluated by the FAO/WHO JMPR in 1982 and 1984. In 1984, the JMPR set an ADI for bendiocarb of 0-0.004 mg/kg bw.

The WHO hazard classification of bendiocarb is: moderately hazardous, class II (WHO 2002).

Within the EU, according to the 19th adaptation to technical progress of Council Directive 67/548/EEC, bendiocarb is classified as: “toxic by inhalation and if swallowed (T, R23/25)”; “harmful in contact with skin (Xn, R21)”; and “very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment (N, R50/53)”.

In May 2005, as part of a review of anticholinesterase compounds, the UK Health & Safety Executive classified bendiocarb as: “toxic by inhalation and if swallowed (T, R23/25)” and “harmful in contact with skin (Xn, R21)”.

## **Formulations**

The main formulation type available for public health is a wettable powder (WP), which is registered and/or sold in many countries throughout the world.

Bendiocarb is not usually co-formulated with other pesticides.

## **Methods of analysis and testing**

The analytical method for the active ingredient (including identity tests) is a full CIPAC method, in which bendiocarb is determined by reversed-phase HPLC, using UV detection at 254 nm and internal standardization with propiophenone (CIPAC Handbook D). It was validated for analysis of the TC and WP formulation.

Test methods for determination of physico-chemical properties of the technical active ingredient were OECD, EPA or EC, while those for the formulation were EC or CIPAC, as indicated in the specifications.

## **Physical properties**

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

## **Containers and packaging**

No special requirements for containers and packaging have been identified.

## **Expression of the active ingredient**

The active ingredient is expressed as bendiocarb.

## **ANNEX 1**

### **HAZARD SUMMARY PROVIDED BY THE PROPOSER**

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

**Table A. Toxicology profile of bendiocarb technical material, based on acute toxicity, irritation and sensitization**

Species	Test	Purity %	Duration and conditions or guideline adopted	Result	Reference
Rat, Sprague Dawley (m)*	Oral	91-98.9	Single dose by gavage, in 0.5% w/v aqueous gum tragacanth, to groups of 6 m. Observed 7 d.	LD <sub>50</sub> = 71.9-155.9 mg/kg bw (m)	M-167182-01-1
Rat, Sprague Dawley (m,f)*	Oral	98.8	Single dose by gavage, in corn oil, to 4 groups of 6 m and 6 f. Observed 14 d.	LD <sub>50</sub> = 25 mg/kg bw (m) 27.3 mg/kg bw (f)	M-167235-01-1
Rat, Wistar (m,f)*	Oral	"pure"	Single dose by gavage, in glycerol formal, to 6 groups of 2-10 m and 8 groups of 2-6 f. Observed 24 h.	LD <sub>50</sub> = 45-48 mg/kg bw (m) 34-40 mg/kg bw (f)	M-167655-01-1
Rat, strain not specified (m)*	Oral	not known	Single dose by gavage, in glycerol formal, to 10 groups of 4 m. Observation period not specified.	LD <sub>50</sub> = 40-64 mg/kg bw (m)	M-167657-01-1
Mouse, CFW (f)*	Oral	"pure"	Single dose by gavage, in glycerol formal, to 3 groups of 2-4 f. Observed 24 h.	LD <sub>50</sub> = 45 mg/kg bw (f)	M-167655-01-1
Mouse, CD-1 (m,f)*	Oral	91.8	Single dose by gavage, in 0.5% w/v aqueous gum tragacanth, to 9 groups of 6 m and 6 f. Observed 14 d.	LD <sub>50</sub> = 28.3 mg/kg bw (m) 28.2 mg/kg bw (f)	M-167195-01-1
Guinea pig, strain not specified (f)*	Oral	"pure"	Single dose by gavage, in glycerol formal, to 2 groups of 2 f. Observed 24 h.	LD <sub>50</sub> = 35mg/kg bw (f)	M-167655-01-1
Hamster, Syrian (f)*	Oral	not known	Single dose by gavage, in water, to 5 groups of 4 f. Observed 7 d.	LD <sub>50</sub> = 141 mg/kg bw (f)	M-167102-01-1
Rabbit, strain not specified (m,f)*	Oral	"pure"	Single dose by gavage, in glycerol formal, to 3 groups of 2 m and 2 groups of 2 f. Observed 24 h.	LD <sub>50</sub> = 35 mg/kg bw (f) 40 mg/kg bw (m)	M-167655-01-1

\* Studies performed prior to introduction of testing guidelines and GLP regulations but conducted according to good scientific practice.

**Table A. Toxicology profile of bendiocarb technical material, based on acute toxicity, irritation and sensitization**

Species	Test	Purity %	Duration and conditions or guideline adopted	Result	Reference
Rat, Wistar (m,f)*	Dermal	not known	In glycerol, applied to skin of 4 m and 4 f, 400, 800 mg/kg bw, held in contact by occlusive patch 24 h. Observed 7 d.	LD <sub>50</sub> = 566 mg/kg bw (m,f)	M-167065-01-1
Rat, Wistar (f)*	Dermal	"pure"	In glycerol formal, applied to skin of 2 m and 2 f, 400, 800 mg/kg bw, held in contact by occlusive patch 24 h. Observed 7 d.	LD <sub>50</sub> = 800 mg/kg bw (f)	M-167655-01-1
Rat, Sprague Dawley (m,f)	Inhalation	97.9	OECD 403, US EPA guideline 81-3 (GLP). Groups of 5 m and 5 f exposed whole body, 4 h, to 248, 377, 512, 701 mg/m <sup>3</sup> bendiocarb by dust generator at 25 l/min. Observed 14 d.	LC <sub>50</sub> = 550 mg/m <sup>3</sup> (0.55 mg/l of air) (m,f)	M-167335-01-1
Rabbit, New Zealand White (m,f)**	Skin irritation	not known	US EPA guideline 40 CFR 162	Not a skin irritant	M-167702-01-1
Rabbit, New Zealand White (m,f)**	Eye irritation	99.2	US EPA guideline 40 CFR 162.	Not an eye irritant	M-167153-01-1
Guinea pig, Dunkin/Hartley albino (f)	Skin sensitization	97.5	OECD guideline 406 (Buehler test - GLP).	Not a sensitizer	M-167357-01-1

\* Studies performed prior to introduction of testing guidelines and GLP regulations but conducted according to good scientific practice.

\*\* Study conducted prior to introduction of GLP regulations.

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

Species	Test	Purity %	Duration and conditions or guideline adopted	Result	Reference
Rat, Sprague Dawley (m,f)*	Oral (dietary), sub-chronic	92.7-98	Administered to groups of 10 m and 10 f in diet for 13 weeks at 0, 2, 10, 50, 250 ppm (equivalent to 0, 0.13, 0.65, 3.45, 17.3 mg/kg bw/d).	NOAEL = 0.65 mg/kg bw/d based on inhibition of whole blood cholinesterase activity (up to 20%) at 3.45 mg/kg bw/d dose. LOAEL = 3.45 mg/kg bw/d	M-167672-01-1
Dog, beagle (m,f)*	Oral (dietary), sub-chronic	96-97	Administered to groups of 4 m and 4 f in diet for 16 weeks at 0, 20, 100, 500-1000 ppm (1000 ppm for the last 4 weeks of the study) (equivalent to 0, 0.2, 1.0, 6.25 mg/kg bw/d).	NOAEL = 1.0 mg/kg bw/d based on inhibition of whole blood (43-46%) and brain (28-42%) cholinesterase activity at 6.25 mg/kg bw/d. LOAEL = 6.25 mg/kg bw/d	M-167076-01-1
Rat, Sprague Dawley (m,f)	Inhalation, sub-chronic	97.2-97.6	US EPA guideline 82.4 (GLP). Groups of 10 m and 10 f exposed snout-only 6 h/d to particulate aerosol at 0, 0.18, 1.97, 19.3 mg/m <sup>3</sup> of bendiocarb. Exposure 5 d/week for 13 weeks.	NOAEL = 0.9 mg/m <sup>3</sup> = 0.24 mg/kg bw/d based on slight inhibition of whole blood cholinesterase activity at week 6 at 2 mg/m <sup>3</sup> . LOAEL = 2 mg/m <sup>3</sup> = 0.54 mg/kg bw/d	M-266196-01-1
Rat, Wistar (m)*	Dermal, repeated dose toxicity	80% WP	Doses 50, 100, 200, 400 or 800 mg bendiocarb/kg bw/d, aqueous suspension, to skin of 5 groups of 6 m under occlusive dressing for 6 h/d, 5 d/week for 3 weeks.	NOAEL = 50 mg/kg bw/d based on dose-related decrease in whole blood cholinesterase activity from 100 to 800 mg/kg bw/d. LOAEL = 100 mg/kg bw/d	M-167061-01-1
Rabbit, New Zealand White (m,f)	Dermal, repeated dose toxicity	31% WP**	US EPA guideline 82.2 and Japan 59 NohSan No. 4200 (1985) (GLP). Administered daily to intact skin of 5 m and 5 f at 1.67, 5, 15 mg bendiocarb/kg bw/d for 21 consecutive days.	NOAEL = 5 mg/kg bw/d based on reduction in erythrocyte and plasma cholinesterase levels at 15 mg/kg bw/d. LOAEL = 15 mg/kg bw/d	M-167323-01-1

\* Studies performed prior to introduction of testing guidelines and GLP regulations but conducted according to good scientific practice and in-house quality assurance standards.

\*\* Ficam Plus wettable powder formulation, nominally containing 31% bendiocarb, 3.0% natural pyrethrins and 7% piperonyl butoxide.

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

Species	Test	Purity %	Duration and conditions or guideline adopted	Result	Reference
Dog, beagle (m,f)*	Oral, chronic	98.1-99	Groups of 8 m and 8 f dosed in diet for 104 weeks at 0, 20, 100, 500 ppm (equivalent to 0, 0.65, 3.12, 16.24 mg/kg bw/d).	NOAEL = 0.65 mg/kg bw/d based on inhibition of brain cholinesterase activity (20%) at 3.12 mg/kg bw/d. LOAEL = 3.12 mg/kg bw/d	M-167690-01-1
Rat, Sprague Dawley (m,f)**	Oral, long-term dietary & carcinogenicity	96.5	OECD guideline 453. 50 m and 50 f weanlings (100 animals/sex in control) from F <sub>1</sub> litters of fertility study given 0, 10, 20, 200 ppm in diet for 104 weeks (equivalent to approx. 0, 0.4, 0.8, 8 (m) and 0, 0.5, 1, 10 (f) mg/kg bw/d)	NOAEL = 0.8/1 mg/kg bw/d (m/f) based on whole blood and brain cholinesterase inhibition at 8/10 mg/kg bw/d. No evidence of carcinogenicity. LOAEL = 8/10 mg/kg bw/d (m/f)	M-265313-01-1, M-265496-01-1
Mouse, CD-1 (m,f)**	Oral, long-term dietary & carcinogenicity	92.7	OECD guideline 453. 50 m and 50 f (100 animals/sex in control group) administered 0, 50, 250, 1250 ppm in diet for 104 weeks (equivalent to approx. 0, 8.06, 42.4, 211 (m) and 0, 10.7, 56.8, 286 (f) mg/kg bw/d).	NOAEL = 211/286 mg/kg bw/d (m/f). No evidence of carcinogenicity.	M-167163-01-1
Rat, Sprague Dawley (m,f)**	Oral (dietary), 3-generation	97.0-99.3	OECD 2-generation reproduction toxicity study guideline. Groups of 30 m and 30 f (F <sub>0</sub> ) fed continuously at 0, 10, 50, 250 ppm in diet (equivalent to approx. 0, 1, 4, 18 mg/kg bw/d) for 90 d prior to pairing, and during mating (max. 21 d), gestation and lactation of 2 litters, F <sub>1A</sub> and F <sub>1B</sub> . Repeated for 2 litters of 2d (F <sub>2</sub> ) and 3d (F <sub>3</sub> ) generations.	Parental and offspring toxicity NOAEL = 18 mg/kg bw/d (250 ppm)  No effect upon fertility, no significant parental toxicity.	M-167165-01-1

\* Studies performed prior to introduction of testing guidelines and GLP regulations but conducted according to good scientific practice and in-house quality assurance standards.

\*\* Study conducted prior to introduction of GLP regulations.

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

Species	Test	Purity %	Duration and conditions or guideline adopted	Result	Reference
Rat, Sprague Dawley (f)	Teratogenicity	97.2	US EPA guideline 83.3 (GLP). Groups of 25-30 pregnant f dosed by oral gavage 0, 0.4, 2, 10 mg/kg bw/d in 1% methylcellulose on 6-15 d gestation (sacrifice 20 d gestation).	NOAEL developmental and maternal toxicity = 2 mg/kg bw/d  No teratogenic effect.	M-167345-01-1
Rabbit, New Zealand White (f)**	Teratogenicity	97.7-98.5	OECD guideline. Groups of 27-29 pregnant (artificially inseminated) f dosed by oral gavage 0, 1, 2.5, 5 mg/kg/d in 0.5% w/v aqueous gum tragacanth on d 6-28 of gestation (sacrifice on 29 d gestation).	NOAEL developmental toxicity = 2.5 mg/kg bw/d based on increased incidence of foetuses with incomplete ossification of cranial bones at highest dose. NOAEL maternal toxicity <1 mg/kg bw/d based on whole blood cholinesterase inhibition in dams at 1 mg/kg bw/d. No teratogenic effect.	M-167160-01-1
Hen, domestic (f)**	Acute delayed neurotoxicity	not known	US EPA guideline 162, 81-8. 4 groups of 10 hens dosed at 20% concentration in corn oil (doses 0, 189, 378, 757 mg/kg), birds protected by atropine intramuscular injection at 1% concentration in sterile water at 10 mg/kg bw. Observed 21 days.	No signs of delayed neurotoxicity at levels up to and including 757 mg/kg.	M-167141-01-1

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\*\* Study conducted prior to introduction of GLP regulations.



**Table C. Mutagenicity profile of bendiocarb technical material based on *in vitro* and *in vivo* tests**

Species	Test	Purity %	Conditions and doses	Result	Reference
<i>S. typhimurium</i> (TA98, 100, 1535, 1537, 1538)	Ames test, <i>in vitro</i>	100	GLP study, ± S9 metabolic activation. 15, 50, 150, 500, 1500 µg/plate.	Negative	M-167333-01-1
<i>S. typhimurium</i> (TA98, 100, 1535, 1537, 1538) and <i>E. coli</i> (WP2)**	Ames test, <i>in vitro</i>	98.8	Japanese guideline for Ames test. ± S9 metabolic activation. 5, 10, 50, 100, 500, 1000, 5000 µg/plate.	Negative	M-167201-01-1
<i>S. cerevisiae</i> (D7)*	Conversion and mitotic recombination, <i>in vitro</i>	98.5	500, 1000, 2000, 4000, 6000 µg/plate ± S9 and 375, 750, 1500, 3000, 6000 µg/plate +S9.	Negative	M-167217-01-1
Human lymphocytes	Chromosome aberration, <i>in vitro</i>	97.6	US EPA guideline 84-2; OECD guideline 473 (GLP). 17, 85, 170 µg/ml - S9 and 14.3, 71.5, 143 µg/ml -S9 and 30, 150, 225, 300 µg/ml +S9.	Positive (+S9) Negative (-S9)	M-167334-01-1
Human epithelioid (HeLa) cells	Unscheduled DNA synthesis, <i>in vitro</i>	96.4	US EPA guideline 84-2; EPA TSCA 560/6-83-001; OECD guideline 482 (GLP). ± S9 metabolic activation. 1.25 to 2560 µg/ml.	Negative	M-167336-01-1
Mouse lymphoma L5178Y cells*	Gene mutation, <i>in vitro</i>	98.5	± S9 metabolic activation. 0.2 to 25 µg/ml.	Negative	M-167209-01-1
Rat, Sprague Dawley (m,f) bone marrow	Clastogenicity (metaphase analysis), <i>in vivo</i>	96.4	US EPA guideline 84-2; EPA TSCA 560/6-83-001; OECD guideline 475 (GLP). Single dose of 1% w/v in methylcellulose by oral gavage to groups of 5 m and 5 f at 2.6, 13, 26 mg/kg bw. 5 m and 5 f each group sacrificed 6, 24, 48 h after dosing	Negative	M-167338-01-1
Mouse, Charles River CD-1 (m) bone marrow *	Clastogenicity (micronucleus), <i>in vivo</i>	97.9	2 intra-peritoneal injection in propylene glycol 24 h apart to groups of 5 m at 0.625, 1.25, 2.5 mg/kg bw. Femoral bone marrow cells harvested 6 h after 2 <sup>nd</sup> dose	Negative	M-167214-01-1

\*\* Study conducted prior to introduction of GLP regulations.

\* Studies performed prior to introduction of testing guidelines and GLP regulations but conducted according to good scientific practice and in-house quality assurance standards.

**Table C. Mutagenicity profile of bendiocarb technical material based on *in vitro* and *in vivo* tests**

Species	Test	Purity %	Conditions and doses	Result	Reference
Rat, Sprague Dawley (m,f)*	Dominant lethal mutations, <i>in vivo</i>	99	Administered in diet to groups of 20 m at 10, 50 or 250 ppm for 13 weeks. Treated m mated with untreated, mature virgin f for 7 d. Pregnant and non-pregnant f sacrificed 14 d post-mating and examined for numbers of <i>corpora lutea</i> , implantation sites, live and dead fetuses and early and late resorptions. Males subjected to gross pathological examination, those with abnormal gonads also examined histopathologically.	Negative	M-167098-01-1

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\* Studies performed prior to introduction of testing guidelines and GLP regulations but conducted according to good scientific practice and in-house quality assurance standards.

**Table D. Ecotoxicology profile of bendiocarb technical material**

Species	Test	Purity %	Duration and conditions	Results	Reference
<i>Daphnia magna</i> (water flea)	Acute toxicity	97.62	OECD guideline 202, EEC C2 and US EPA guideline 72.2 (GLP). 48-h flow-through. 0.015, 0.029, 0.050, 0.11, 0.16 mg/l.	EC <sub>50</sub> (48 h) = 0.0377 mg/l	M-259123-01-1
<i>Cyprinodon variegatus</i> (sheephead minnow)	Acute toxicity	98.0	US EPA guideline 72.3 (GLP). 96-h flow-through. 2.6, 1.9, 1.0, 0.64, 0.45 mg/l.	LC <sub>50</sub> (96 h) = 0.86 mg/l	M-167340-01-1
<i>Pseudokirchneriella subcapitata</i> (green alga)	Acute/chronic toxicity	97.62	OECD guideline 201 (GLP). 72-h, flasks. 0.015, 0.035, 0.087, 0.17, 0.54 mg/l.	ErC <sub>50</sub> (0-48 h) = 0.408 mg/l NOEC (0-48h, growth rate) = 0.087 mg/l	M-259108-01-1
<i>Eisenia foetida andrei</i> (earthworm)	Acute toxicity	97.62	OECD guideline 207 (GLP). 14-d. 0.1, 0.18, 0.32, 0.56, 1.0, 3.2, 10, 100, 178, 316, 562, 1000 mg/kg dry soil.	LC <sub>50</sub> (14 d) = 188 mg/kg dry soil	M-253937-03-1
<i>Colinus virginianus</i> (bobwhite quail)	Acute toxicity	97.5	EPA guideline 71-1 (GLP). Doses 20, 33, 54, 90, 148 mg/kg bw.	LD <sub>50</sub> = 26 mg/kg bw	M-167304-01-1
<i>Anas platyrhynchos</i> (mallard duck)	Acute toxicity	97.5	EPA guideline 71-1 (GLP). Doses levels of 2, 4, 8, 16, 32 mg/kg bw.	LD <sub>50</sub> = 8.7 mg/kg bw	M-167302-01-1
<i>Colinus virginianus</i> (bobwhite quail)**	Short-term toxicity	not known	US EPA guideline 162 70-4. Groups of 10 birds exposed 5 d to diet containing 10.0, 21.5, 46.4, 100.0, 215.0, 464.0, 1000.0, 2150.0, 2750.0, 3500.0, 4500.0 ppm. Observed 3 days.	LC <sub>50</sub> = 1770 ppm	M-167138-01-1

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\*\* Study conducted prior to introduction of GLP regulations.

**Table D. Ecotoxicology profile of bendiocarb technical material**

Species	Test	Purity %	Duration and conditions	Results	Reference
<i>Anas platyrhynchos</i> (mallard duck)**	Short term toxicity	not known	US EPA guideline 162 70-4. Groups of 10 birds exposed 5 d to diet containing 50, 100, 200, 400, 800, 1600, 2400, 3200, 4000 ppm. Observed 3 days.	LC <sub>50</sub> = 477 ppm	M-167665-01-1

## ANNEX 2. REFERENCES

Bayer CropScience document number or other reference	Year and title of report or publication details
CIPAC Handbook D	Collaborative International Pesticides Analytical Council, 1988. Handbook D, pp.10-12, Harpenden, U.K.
EU 2003	European Union Risk Assessment Report. Toluene, CAS No: 108-88-3, EINECS No: 203-625-9. European Communities, 2003. Available at: <a href="http://ecb.jrc.ec.europa.eu/esis/">http://ecb.jrc.ec.europa.eu/esis/</a> .
FAO/WHO 2006	Manual on the development and use of FAO and WHO specifications for pesticides, March 2006 revision of the first edition. Available only on the internet at <a href="http://www.fao.org/ag/agp/agpp/pesticid/">http://www.fao.org/ag/agp/agpp/pesticid/</a> or <a href="http://www.who.int/whopes/quality/">http://www.who.int/whopes/quality/</a>
GHS 2007	Globally Harmonized System of Classification and Labelling of Chemicals of the United Nations Economic Commission for Europe (UNECE), 2 <sup>nd</sup> revised edition. Accessible under the Transport of Dangerous Goods heading at <a href="http://www.unece.org/trans/">http://www.unece.org/trans/</a> .
Hass <i>et al.</i> 1999	Hass U, Lund SP, Hougaard KS, Simonsen L, 1999. Developmental neurotoxicity after toluene inhalation exposure in rats. <i>Neurotoxicol. Teratol.</i> , <b>21</b> (4), 349-57.
IPCS 1994	Environmental Health Criteria 170. Assessing human health risks of chemicals: derivation of guidance values for health-based exposure limits. Available at: <a href="http://www.who.int">http://www.who.int</a> .
IPCS 1999	IPCS 1999. Environmental Health Criteria 210. Principles for the assessment of risks to human health from exposure to chemicals. Available at: <a href="http://www.who.int/ipcs/publications/ehc/ehc_numerical/en/index.html">http://www.who.int/ipcs/publications/ehc/ehc_numerical/en/index.html</a> .
JMPR 2002	FAO/WHO Joint Meeting on Pesticide Residues (JMPR), 2002. Pesticide residues in food – 2002. Report of the Joint Meeting of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Core Assessment Group on Pesticide Residues Rome, Italy. 16- 25 September, 2002. Available at: <a href="http://www.fao.org/ag/AGP/AGPP/Pesticid/JMPR/Download/2002_rep/2002JMPRReport2.pdf">http://www.fao.org/ag/AGP/AGPP/Pesticid/JMPR/Download/2002_rep/2002JMPRReport2.pdf</a>
M-164244-01-1	1995. Bendiocarb: Rat 13-Week Inhalation Toxicity Study (Snout-Only Exposure) and Range Finding Studies.
M-166668-01-1	1988. Bendiocarb: Determination of the Partition Coefficient Between n-Octanol and Water at 25°C.
M-166694-01-1	1988. 63-10 Dissociation Constant – Bendiocarb (R000174).
M-166699-01-1	1988. Determination of the Vapour Pressure of Bendiocarb.
M-166721-01-1	1988. The Photolysis of Bendiocarb (Schering Code No. ZK 52 020) in Aqueous Solution.
M-166722-01-1	1992. The Photolysis of Bendiocarb (Schering Code No. ZK 52 020) in Aqueous Solution (supplement to APC 46/88 = A90107).
M-166763-01-1	1992. Bendiocarb (R001062): Solubility in Water.
M-166890-01-1	1988. The Hydrolysis of Bendiocarb at Acid, Neutral and Alkaline pH.
M-167061-01-1	1972. Toxicology of NC 6897: 15-Dose Cumulative Dermal Study with Ficam 80 in Male Rats.
M-167065-01-1	1972. The Toxicology of NC 6897: Acute Dermal Toxicity of Technical Bendiocarb.
M-167076-01-1	1974. 16 Week Sub-Acute Toxicity Study in Dogs (NC 6897 Technical).
M-167098-01-1	1977. Test for the Induction of Dominant Lethal Mutations in Male Rats by Technical CR 4799/1 NC 6897.
M-167102-01-1	1977. The Acute Oral Toxicity to the Hamster of Technical Bendiocarb.
M-167138-01-1	1978. The subacute dietary LC50 of NC 6897 technical, CR 4799/4 to the bobwhite quail.
M-167141-01-1	1978. Examination of NC 6897 for Neurotoxicity in the Domestic Hen.
M-167145-01-1	1981. NC 6897 Toxicity and Tumorigenicity to Rats in Long-Term Dietary Administration (Final Report – Reproductive Phase and Main Phase) Main Phase = 104 weeks.

Bayer CropScience document number or other reference	Year and title of report or publication details
M-167153-01-1	1979-1981. Technical Bendiocarb Ex-Muskegon Primary Eye Irritancy in rabbits.
M-167160-01-1	1981. Technical NC 6897: Effects of Oral Administration upon Pregnancy in the Rabbit (5) Definitive Study.
M-167163-01-1	1981. A Chronic Toxicity and Carcinogenicity Study in Mice with Technical NC 6897 (Final Report).
M-167165-01-1	1981. Technical NC 6897 (CR 4799/1): Effects of Dietary Administration upon Reproductive Performance and Teratogenic Response of Rats Treated Continuously through Three Successive Generations.
M-167182-01-1	1980. A Comparison of the Acute Oral Toxicities of Bendiocarb CR 4971/2, CR 799/9 and CR 4500/20, to the Male Rat.
M-167195-01-1	1981. The Acute Oral Toxicity of Unformulated Bendiocarb (NC 6897, CR 4799/10) to the Male and Female Mouse.
M-167201-01-1	1981. The Microbial Mutagenicity Study of Bendiocarb (KNT).
M-167209-01-1	1982. The Assessment of Mutagenic Potential with NC 6897 in the Mouse Lymphoma Mutation Assay.
M-167214-01-1	1982. A Micronucleus Study in Mice using Technical NC 6897, CR 4971/2.
M-167217-01-1	1982. Technical Bendiocarb: Induction of the Conversion and Mitotic Recombination in Yeast.
M-167235-01-1	1983. The Acute Oral Toxicity of Technical Bendiocarb in the rat: Comparison with Dichlorvos and Propoxur.
M-167302-01-1	1984. The acute oral toxicity (LD50) of technical bendiocarb and technical FBC 34570 to the mallard duck.
M-167304-01-1	1984. The acute oral toxicity (LD50) of technical bendiocarb and technical FBC 34570 to the bobwhite quail.
M-167323-01-1	1986. Ficam Plus WP Formulation: Twenty-one Day Dermal Toxicity Study in Rabbits.
M-167333-01-1	1987. Technical Bendiocarb: Ames Bacterial Mutagenicity Test.
M-167334-01-1	1988. Technical Bendiocarb: Metaphase Chromosome Analysis of Human Lymphocytes Cultivated <i>in vitro</i> .
M-167335-01-1	1988. Technical Bendiocarb: Acute (4-Hour Exposure) Inhalation Toxicity Study in Rats.
M-167336-01-1	1988. Technical Bendiocarb: Unscheduled DNA Synthesis in Cultured Mammalian cells.
M-167338-01-1	1989. Technical Bendiocarb: Analysis of Metaphase Chromosomes from Rat Bone Marrow.
M-167340-01-1	1989. Acute Toxicity of Bendiocarb Technical to Sheepshead Minnow ( <i>Cyprinodon variegatus</i> ) under Flow-Through Conditions.
M-167345-01-1	1991. Technical Bendiocarb: Rat Oral Developmental Toxicity (Teratogenicity) Study.
M-167357-01-1	1992. Technical Bendiocarb Guinea Pig Skin Sensitisation Study (Buehler Test).
M-167655-01-1	1971. The Toxicology of NC 6897: Acute Toxicity of Pure NC 6897.
M-167657-01-1	1970. The Toxicology of NC 6897: Acute Toxicity To The Rat of Technical Grade NC 6897.
M-167665-01-1	1978. Subacute dietary toxicity (LC50) of NC 6897 technical CR 4799/6 to the mallard duck.
M-167672-01-1	1979. NC 6897 Technical (CR 4799/3) toxicity to Rats when Administered in the Diet for 13 Weeks (Final Report).
M-167690-01-1	1980. NC 6897 Toxicity Study in Beagle Dogs. Final Report: Dietary Intake for 104 Weeks. (Test Compound Technical NC 6897 CR 4799/3).
M-167702-01-1	1978. Technical Bendiocarb Primary Skin Irritancy Study on Rabbits.
M-248943-01-1	2005. Bendiocarb; Substance pure AE B052020 00 1B99 0005 – Melting point; Boiling point; Thermal stability.
M-253937-03-1	2007. 2d amendment to study report: Bendiocarb (tech): Acute Toxicity to Earthworms ( <i>Eisenia fetida</i> ) tested in Artificial Soil.

Bayer CropScience document number or other reference	Year and title of report or publication details
M-259108-01-1	2005. Bendiocarb technical: Alga, Growth Inhibition Test with <i>Pseudokirchneriella subcapitata</i> (syn. <i>Selenastrum capricornutum</i> ).
M-259123-01-1	2005. Bendiocarb technical: Acute immobilisation test with daphnids ( <i>Daphnia magna</i> ) under flow-through conditions.
M-265313-01-1	2005. Historical Control Incidence of Survival in Sprague Dawley CD Rats at [laboratory] (1982-1987).
M-265496-01-1	2005. Historical Control Incidence of Lenticular Opacities in Sprague Dawley CD Rats at [laboratory] (1982-1987).
M-266196-01-1	2006. Regulatory Toxicology – Position Paper: Benchmark Dose Analysis of Whole Blood Acetylcholinesterase Activity of the Rat 90-day Inhalation Toxicity Study of Bendiocarb.
Ng <i>et al.</i> 1992	Ng TP, Foo SC, Yoong T, 1992. Risk of spontaneous abortion in workers exposed to toluene. <i>British J. Ind. Med.</i> , <b>49</b> , 804-808.
Solecki <i>et al.</i> 2005	Solecki R, Davies L, Dellarco V, Dewhurst I, van Raaij M, Tritscher A, 2005. Guidance on setting of acute reference dose (ARfD) for pesticides. <i>Food and Chemical Toxicology</i> <b>43</b> , 1569–1593.
Taskinen <i>et al.</i> 1994	Taskinen H, Kyyrönen P, Hemminki K, Hoikkala M, Lajunen K, Lindbohm M-L, 1994. Laboratory work and pregnancy outcome. <i>J. Occup. Med.</i> <b>36</b> , 311-319.
WHO 2002	The WHO recommended classification of pesticides by hazard and guidelines to classification, 2000-2002. World Health Organization, Geneva, 2002.