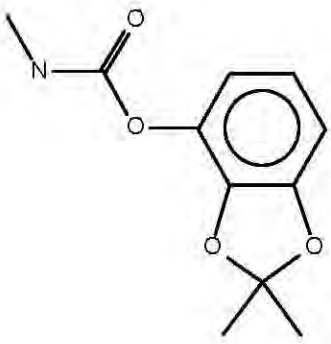
Section A1 – Applicant

1.1 Applicant	Name: Bayer Environmental Science SAS Business Unit of Bayer CropScience Address: 16 rue Jean-Marie Leclair 69266 Lyon France Contact person (1): [redacted] Telephone: Fax number: E-mail address: Contact person (2): [redacted] Telephone: Fax number: E-mail address:	
1.2 Manufacturer of active substance (if different)	Name: Bayer Environmental Science SAS, Business Unit of Bayer CropScience Address: 16 rue Jean-Marie Leclair 69266 Lyon France Contact person: [redacted] Telephone: Fax number: E-mail address: Manufacturing site: Name: [redacted] Address:	
1.3 Manufacturer of product(s) (if different)	Name: Bayer Environmental Science SAS Business Unit of Bayer CropScience Address: 16 rue Jean-Marie Leclair 69266 Lyon France Contact person: [redacted] Telephone: Fax number: E-mail address: Manufacturing site: Name: [redacted] Address:	

Section A2 – Identity of Active Substance

Subsection (Annex Point)						Official use only
2.1	Common name (IIA2.1)	Bendiocarb				
2.2	Chemical name (IIA2.2)	2,2-dimethyl-1,3-benzodioxol-4-yl methylcarbamate				
2.3	Manufacturer's development code number(s) (IIA2.3)	AB052020; NC 6897				X
2.4	CAS No and EC numbers (IIA2.4)					
2.4.1	CAS-No	22781-23-3				
	Isomer 1	Not applicable as the material does not include isomers				
	Isomer n	Not applicable as the material does not include isomers				
2.4.2	EC-No	245-216-8				
	Isomer 1	Not applicable as the material does not include isomers				
	Isomer n	Not applicable as the material does not include isomers				
2.4.3	Other	CIPAC 232				
2.5	Molecular and structural formula, molecular mass (IIA2.5)					
2.5.1	Molecular formula	$C_{11}H_{13}NO_4$				
2.5.2	Structural formula					
2.5.3	Molecular mass	223.23				
2.6	Method of manufacture of the active substance (IIA2.1)	See confidential Appendix I to this document				
2.7	Specification of the purity of the active substance, as appropriate (IIA2.7)	g/kg	g/l	% w/w	% v/v	
		970		97		

2.8	**Identity of impurities and additives, as appropriate (IIA2.8)**	See Confidential Appendix I to this document	
2.8.1	**Isomeric composition**	Not applicable as the material does not include isomers	
2.9	**The origin of the natural active substance or the precursor(s) of the active substance (IIA2.9)**	Not applicable as the material is synthetic in nature	

	EVALUATION BY COMPETENT AUTHORITIES
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	01/2007
Materials and methods	The specification data was provided from a 5 typical batch analysis of AE B052020 (Bendiocarb).
Conclusion	Adopt applicant's version with the following amendment. 2.3 Manufacturer's development code should be AEB052020.
Reliability	1
Acceptability	Acceptable
Remarks	The UK CA has reviewed and accepted the data submitted for a 5 typical batch analysis of AE B052020 (Bendiocarb).
	COMMENTS FROM …
Date	
Results and discussion	
Conclusion	
Reliability	
Acceptability	
Remarks	

Section A2.10 Annex Point IIA2.10	Identity of Active Substance A2.10 Exposure Data in Conformity with Annex VIIA to Council Directive 92/32/EEC (OJ No L, 05.06.1992, p. 1) Amending Council Directive 67/548/EEC

2.10 Exposure data in conformity with Annex VIIA to Council Directive 92/32 EEC (OJ No L 154, 5.6.1992, p.1) amending Council Directive 67/548/EEC

Subsection			Official use only
2.10.1	**Human exposure towards active substance**		
2.10.1.1	**Production**		
	i) Description of process	**Active substance:** Technical bendiocarb is produced [redacted] Therefore description of the exposure situation during the production process is not necessary. **Formulation (Ficam W):** Ficam W is manufactured at an industrial production plant [redacted] by trained professionals using [redacted] process described in DocIIIB Confidential Appendix. The production line is operated by 35 staff who works in a double or triple shift pattern of 8 hours. Five days a year are assigned to Ficam W production. Big bags of Ficam W produced [redacted] are re-packaged in 500 g packs and 15 g water soluble sachets at [redacted]. 12-15 trained professionals are assigned to Ficam W re-packaging for 15-30 days a year.	
	ii) Workplace description	**Active substance:** Technical bendiocarb is produced [redacted] Therefore description of the workplace is not necessary. **Formulation (Ficam W):** Bendiocarb technical is formulated into Ficam W at [redacted] The site covers 17 hectares and employs 85 people. This site is Seveso II classified (high threshold –seuil haut) and ISO 9002 certified. The working code for operators is followed, and the ICPE legislation (Installation Classified for the Protection of the Environment) is adhered to. [redacted] has also been audited by BayerCropScience (BCS) Industrial Operations (IOP) and was shown to be working according to BCS production guidelines.	

The production lines are not dedicated to any single product, such that after each campaign the production lines are cleaned down and the waste water incinerated. Wipe tests and/or concentrations dust and active substance in air are conducted monthly. The production line is a closed system, whilst loading and packaging are carried out in a ventilated semi-open area by operators wearing personal protective equipment (PPE). Air flow is 5000 – 10000 m^3/hr.

During the production of Ficam W, charging ingredients, filling and packaging, the following personal safety measures are required: self breathing hood, protective gloves and chemical resistant suit.

[redacted] where Ficam W is re-packed is Seveso II classified (low threshold – seuil bas) and the site adheres to ICPE legislation (Installation Classified for the Protection of the Environment). The repackaging of Ficam W operates in a closed automated, whilst opening/closing of big bags and positioning of the empty packs are carried out in a ventilated semi-open area by operators wearing personal protective equipment: self breathing hood, protective gloves and chemical resistant suit.

Occupational medical surveillance (see Point 6.12.1/04, Document M-266376-01-1) has been performed biannually on a routine basis since 2000 [redacted]. About 30 workers are exposed to bendiocarb technical, during the production of Ficam W. The surveillance did not reveal any unwanted effects in the workers, apart from skin effects (itches). The examinations included the following laboratory parameters, medical and technical examinations:

Laboratory examinations	Differential blood count Cholinesterase rate Creatinine Urine status Hepatic enzyme etc.
Medical examinations	Full physical examination with orientating neurological status (reflexes, sensitivity coordination) Skin status.
Technical examinations	Audiometry Vision testing Lung function Ergometry etc.

During the last production period (2000 – 2005), there was only one case of intoxication with bendiocarb technical. The worker felt unwell for a few hours. His cholinesterase rate had decreased, but was normal again after a few days.

Medical surveillance is also carried out at [redacted] where Ficam W is re-packed based on similar procedures.

iii) Inhalation exposure	**Active substance:** Technical bendiocarb is produced [redacted] Therefore assessment of inhalation exposure is not necessary. **Formulation (Ficam W):** Due to i) the effective personal protective measures (self breathing hood) ii) the ventilation in the semi-open area (loading and packaging), iii) and the otherwise closed system inhalation exposure is not expected for the people involved in the production/re-packaging of Ficam W. Following biannual medical surveillance, during the last production period (2000 – 2005), there was only one case of intoxication with bendiocarb technical. The worker felt unwell for a few hours. His cholinesterase rate had decreased, but was normal again after a few days.	
iv) Dermal exposure	**Active substance:** Technical bendiocarb is produced [redacted] Therefore assessment of dermal exposure is not necessary. **Formulation (Ficam W):** Due to the effective personal protective measures worn during the above mentioned tasks (self breathing hood, protective gloves and chemical resistant suit) dermal exposure is not expected for the people involved in the production/re-packaging of Ficam W. Following biannual medical surveillance, during the last production period (2000 – 2005), the surveillance did not reveal any unwanted effects in the workers, apart from skin effects (itches).	
2.10.1.2 Intended use(s)		
1.Professional Uses		
i) Description of process	See Document II-B of the dossier	
ii) Workplace description	See Document II-B of the dossier	
iii) Inhalation exposure	See Document II-B of the dossier	
iv) Dermal exposure	See Document II-B of the dossier	
2. Non-professional Uses including the general public	The product is for professional use only. Secondary exposure as a consequence of professional use of the product is discussed in Document II-B of the dossier	
i) via inhalational contact	Non-professional use is not considered	
ii) via skin contact	Non-professional use is not considered	

iii) via drinking water	Non-professional use is not considered	
iv) via food	Non-professional use is not considered	
v) indirect via environment	Non-professional use is not considered	
2.10.2 Environmental exposure towards active substance		
2.10.2.1 Production		
i) Releases into water	**Active substance:** Technical bendiocarb is produced [redacted] Therefore assessment of release into water is not necessary. **Formulation (Ficam W):** No release, the waste water is incinerated, along with all other effluent from the production/re-packaging process (solid and liquid). ICPE legislation (Installation Classified for the Protection of the Environment) is adhered to.	
ii) Releases into air	**Active substance:** Technical bendiocarb is produced [redacted] Therefore assessment of release into air is not necessary. **Formulation (Ficam W):** Outlet air from the production plant is filtered by a double filter system. The first filter is cleaned *in situ*, and subsequently incinerated. The second barrier filter is replaced every two/three years, again disposed of *via* incineration. Emissions into the air from the plant are controlled via twice yearly checks on dust emissions form each chimney. Current permissible discharge levels exist at 5 mg/m^3 total dust and 2 mg/ m^3 toxic dust, although controls show a maximum discharge level of 0.2 mg/m^3 of dust. ICPE legislation (Installation Classified for the Protection of the Environment) is adhered to.	
iii) Waste disposal	**Active substance:** Technical bendiocarb is produced [redacted] Therefore assessment of waste disposal is not necessary. **Formulation (Ficam W):** All waste (solid, liquid and waste water from cleaning) from production/re-packaging plants is eliminated in incineration facilities. ICPE legislation (Installation Classified for the Protection of the Environment) is adhered to.	

2.10.2.2 Intended use(s)		
Affected compartment(s):		
Water	See Document II-B of the dossier	
Sediment	See Document II-B of the dossier	
Air	See Document II-B of the dossier	
Soil	See Document II-B of the dossier	
Predicted concentrations in the affected compartment(s):		
Water	See Document II-B of the dossier	
Sediment	See Document II-B of the dossier	
Air	See Document II-B of the dossier	
Soil	See Document II-B of the dossier	

EVALUATION BY COMPETENT AUTHORITIES	
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	26/06/07
Comments	The Applicant's version is acceptable.
Remarks	
	COMMENTS FROM …
Date	
Results and discussion	
Conclusion	
Reliability	
Acceptability	
Remarks	

Section A3 – Physical and Chemical Properties

Subsection (Reference)	Method	Purity/ Specification Batch	Results	Remarks/ Justification	GLP (Y/N)	Reliability	Reference	Official use only
3.1 Melting point, boiling point, relative density (IIA3.1)								
3.1.1 Melting point								
Melting pt. 1	OECD 102 (Differential Scanning Calorimetry and Capillary Tube in a Metal Block)	98.5% 860402 (pure)	*Result:* 129°C *Pressure: atmospheric*		Y	1	Smeykal (2005a) Doc C047471 3.1.1/01	x
3.1.2 Boiling point								
Boiling pt. 1	OECD 103 (Differential Scanning Calorimetry and Capillary Tube in a Metal Block)	98.5% 860402 (pure)	Decomposed under boiling at 264°C at atmospheric pressure		Y	1	Smeykal (2005a) Doc C047471 3.1.2/01	x
3.1.3 Bulk density/relative density								
Relative density	Pycnometer 84/449/EEC A3	99.0% R000174	1.29 at 20°C		Y	1	Bright (1988a) Doc A90081 3.1.3/01	x

Subsection (Reference)	Method	Purity/ Specification Batch	Results	Remarks/ Justification	GLP (Y/N)	Reliability	Reference	Official use only
3.2 Vapour pressure (IIA3.2)								
Vapour pressure	Gas saturation method	99.8% R000087	4.6 x 10^{-5} hPa at 25°C (4.6 x 10^{-3} Pa) (3.5 x 10^{-5} mm Hg)	Clapeyron-Clausius analysis from 30–60°C temperature range	Y	1	Lowes and Bright (1988) Doc A90090 3.2/01	x
3.2.1 Henry's Law Constant (Pt. I-A3.2)	Clausius-Clapeyron equation	n.a.	K= 1.54 x 10^{-3} Pa m^3 mol^{-1}		n.a.	1	Bascou (2005) Doc M-256629-01-1 3.2.1/01	
3.3 Appearance (IIA3.3)								
3.3.1 Physical state	Directive 94.37/EC Annex I; 2.4	98.5% 860402 (pure) B920701 (technical)	Technical: crystalline powder Pure: powder		Y	1	Eyrich (2005) Doc M-258785-01-1 3.3.1/01	x
3.3.2 Colour	Directive 94.37/EC Annex I; 2.4	As above	Technical: beige Pure: light beige		Y	1	Eyrich (2005) Doc M-258785-01-1 3.3.2/01	x
3.3.3 Odour	Directive 94.37/EC Annex I; 2.4	As above	Technical: None Pure: None		Y	1	Eyrich (2005) Doc M-258785-01-1 3.3.3/01	x

Subsection (Reference)	Method	Purity/ Specification Batch	Results	Remarks/ Justification	GLP (Y/N)	Reliability	Reference	Official use only
3.4 Absorption spectra (IIA3.4)								
UV/VIS		99.0% R000174	Max.: 204, 236, 280 nm	See Doc A90101 for spectra	Y	1	Johnson (1988) Doc A90101 3.4/01	x
IR	KCl disc	99.0% R000174		See Doc A90101 for spectra	Y	1	Johnson (1988) Doc A90101 3.4/02	x
NMR	Proton	99.0% R000174		See Doc A90101 for spectra	Y	1	Johnson (1988) Doc A90101 3.4/03	x
MS	GC-MS	99.0% R000174	m/z: 223, 166, 151, 126, 79, 58	See Doc A90101 for spectra	Y	1	Johnson (1988) Doc A90101 3.4/04	x
3.5 Solubility in water (IIA3.5)								
Water solubility 1	84/449/EEC A6 OECD Guideline 105	99.3% R001062	Temperature: 20 °C 0.31 g/l at pH 3 – pH 5 0.28 g/l at pH 7 0.03 g/l at pH 9 – pH 11 with significant hydrolysis	A significant temperature difference was found (>3% per degree C)	Y	1	Stalker and Ward (1992) Doc A90138 3.5/01	x

Subsection (Reference)	Method	Purity/ Specification Batch	Results	Remarks/ Justification	GLP (Y/N)	Reliability	Reference	Official use only
3.6 Dissociation constant (-)	EPA OPPTS 830.6310 UV spectrophotometric method	99.0% R000174	The dissociation constant was not accessible as bendiocarb hydrolyses rapidly in alkaline solution. For the parent phenol of bendiocarb (NC 7312), pKa = 8.8 at 20 °C		Y	1	Bright (1988b) Doc A90087 3.6/01	x
3.7 Solubility in organic solvents, including the effect of temperature on solubility (IIIA3.1)								
Solubility in organic solvents 1	Analytical method (low solubilities) Solubility Range by Direct Addition (higher solubilities)	99.3% R001062	Temperature: 20°C Solubility g/litre solvent Acetone 150 – 200 Dichloromethane 200 – 300 Ethyl acetate 60 – 75 n-Hexane 0.225 Methanol 75 – 100 p-Xylene 11.7		Y	1	Bright and Stalker (1992) Doc A90134 3.7/01	x
Solubility in organic solvents 2	Analytical method (low solubilities) Solubility Range by Direct Addition (higher solubilities)	99.0% R000174	Temperature: 25°C Solubility g/litre solvent Acetone 200 – 300 Dichloromethane 300 – 600 Dimethylsulphoxide 200 – 300 Ethanol 30 – 50 Xylene 16		Y	1	Bright and Scott (1988) Doc A90083 3.7/02	x

Subsection (Reference)	Method	Purity/ Specification Batch	Results	Remarks/ Justification	GLP (Y/N)	Reliability	Reference	Official use only
3.8 Stability in organic solvents used in b.p. and identity of relevant breakdown products (IIIA3.2)	n.a.	n.a.	n.a.	The a.s. as manufactured is a solid and does not contain organic solvents	n.a.	n.a.	-	
3.9 Partition coefficient n-octanol/water (IIA3.6)								
log Pow 1	84/449/EEC A8 OECD Guideline 107	99.0% R000174	Pow = 52 log_{10} Pow = 1.7 at 25°C (pH 6.9)		Y	1	Bright (1988c) Doc A90075 3.9/01	x
3.10 Thermal stability, identity of relevant breakdown products (IIA3.7)	OECD 113 (Differential Scanning Calorimetry)	98.5% 860402 (pure)	Melts at 110 – 145°C Further endothermic reaction at 160 – 205°C Exothermic reaction at 240 – 400°C with an energy value of 525 J/g and 720 J/g respectively		Y	1	Smeykal (2005a) Doc C047471 3.10/01	x
3.11 Flammability, including auto-flammability and identity of combustion products (IIA3.8)	Directive 67/548/EEC Annex V A10 (flammability) A16 (auto-flammability)	98.5% B920701 (technical)	Not flammable Not autoflammable		Y	1	Smeykal (2005b) Doc M-259054-01-1 3.11/01 Smeykal (2005c) Doc M-259063-01-1 3.11/02	x

Subsection (Reference)	Method	Purity/ Specification Batch	Results	Remarks/ Justification	GLP (Y/N)	Reliability	Reference	Official use only
3.12 Flash-point (IIA3.9)	n.a.	n.a.	n.a.	Test not needed as the substance is a solid	n.a.	n.a.	-	
3.13 Surface tension (IIA3.10)								
Surface tension	92/69/EEC A5 OECD Guideline 115	98.9% B920702	σ = 63.29 mN/m at 20 °C		Y	1	Mühlberger and Lemke (2004) Doc C040312 3.13/01	x
3.14 Viscosity	n.a.	n.a.	n.a.	Test not needed as the substance is a solid	n.a.	n.a.	-	
3.15 Explosive properties (IIA3.11)	Directive 67/548/EEC Annex V A14	98.5% B920701 (technical)	Not explosive		Y	1	Smeykal (2005d) Doc M-259059-01-1 3.15/01	x
3.16 Oxidizing properties (IIA3.12)	Directive 67/548/EEC Annex V A17	98.5% B920701 (technical)	Not oxidizing		Y	1	Smeykal (2005e) Doc M-259066-01-1 3.16/01	x
3.17 Reactivity towards container material (IIA3.13)	EPA OPPTS 830.6313	≥ 97% Technical	The substance did not have any effect on metal or polythene containers during manufacture or in storage stability tests		Y	1	Johnson (1989) Doc A90110 3.17/01	

EVALUATION BY COMPETENT AUTHORITIES	
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	01/2007
Materials and methods	The applicant's version is acceptable with the following additions: 3.1.1 - 3.2, 3.3 – 3.7 and 3.9 – 3.17: 860402, R000174, R000087, B920701, B920702, R001062 are batch numbers of the bendiocarb samples used for testing. 3.1.3 Bulk/Relative density Method The method used is equivalent to 92/69/EEC, A3 3.2 Vapour Pressure Method The method used is equivalent to 92/69/EEC, A4 Result 1.9×10^{-3} Pa at 20 °C 3.3.1 Physical state Result The physical state was determined at ambient room temperature (23 – 26 °C) rather than at 20 °C as stated in the Technical Guidance Document. The UK CA considers this to be acceptable. 3.3.2 Colour Result The colour was determined at ambient room temperature (23 – 26 °C) rather than at 20 °C as stated in the Technical Guidance Document. The UK CA considers this to be acceptable. 3.3.3 Odour Result The odour was determined at ambient room temperature (23 – 26 °C) rather than at 20 °C as stated in the Technical Guidance Document. The UK CA considers this to be acceptable.

3.5 Water solubility

Method

The method used is equivalent to 92/69/EEC A6

Result

The solubility at 13 °C and pH 3 to 5 was 0.26 g/l

The solubility at 13 °C and neutral pH was 0.24 g/l

The solubility at 30 °C and pH 3 to 5 was 0.44 g/l

The solubility at 30 °C and neutral pH was 0.38 g/l

3.6 Dissociation Constant

Results

It is not necessary to report the pKa of the parent phenol of Bendiocarb.

3.9 Partition coefficient n-octanol/water

Method

The method used is equivalent to 92/69/EEC A8

Remarks/Justification – effects of pH

As shown in the water solubility report there is no effect of pH on the water solubility of the active substance, in the pH range where bendiocarb is stable (pH: 3-7). At pH > 9 (not relevant for the environment), bendiocarb is unstable (rapidly hydrolyzed) therefore, the value of the water solubility is not reliable. To demonstrate that there is no effect of pH on log P_{ow} of bendiocarb at environmental pHs, a modelisation has been conducted with the ACD log D® software version 9. This software permits the calculation of the curve: log P_{ow} = f (pH). The result obtained from the ACD lab software is log P_{ow} = 1.86 ± 0.38. By comparison, the measured value of 1.7 found in the study is within the uncertainty range of the calculated value. This shows that the ACD log D® software version 9 is reliable.

pH	4	5	6	7	8	9	10
Log D	1.86	1.86	1.86	1.86	1.86	1.86	1.86

The modelling clearly demonstrates that there is no effect of pH on log P_{ow} of bendiocarb at environmental pHs.

Remarks/Justification – effects of temperature

As shown in the water solubility report, there is a significant temperature dependence on the solubility of bendiocarb in water (>3% per °C).

Temperature	20 °C	30 °C	Increase %	Increase % per °C
Solubility in	0.28 g/l	0.38 g/l	36	3.6

water pH 7				
Solubility in water pH 3 - 5	0.31 g/l	0.44 g/l	42	4.2

It can be estimated that there is roughly a 4 % increase in water solubility per °C for bendiocarb.

Based on the two study reports on solubility of bendiocarb in organic solvents, it appears that there is a temperature dependence on the solubility of bendiocarb in organic solvents (> 3 % per °C).

The temperature dependence on the solubility of bendiocarb in water and in organic solvents follows the same direction (increased solubility at higher temperatures) and is of same order of magnitude. In addition, the value of log P_{ow} at a particular temperature is within the range of uncertainty given by the software of ACD Lab version 9 for bendiocarb at 20 °C: log P_{ow} = 1.86 ± 0.38. Therefore, it can be concluded that there is no significant effect of temperature on log P_{ow} for bendiocarb.

3.10 Thermal Stability

Method

Method used is equivalent to 92/69/EEC A1

Remarks/ Justification

The second endothermic reaction is a first indication of the boiling process (increase of pressure) in the closed cup. In the open cup this endothermic reaction is not visible.

The substance is considered to be stable at room temperature if no decomposition or chemical transformation is found below 150 °C.

3.11 Flammability including auto-flammability and identity of combustion products - flammability

Method

Method used is equivalent to 92/69/EEC A10

3.11 Flammability including auto-flammability and identity of combustion products – autoflammability

Method

Method used is equivalent to 92/69/EEC A16

3.12 Flash-point

Remarks/ Justification

This test is not applicable as the active substance is not a liquid and does not contain any solvents which could ignite.

	3.15 Explosive properties Method Method used is equivalent to 92/69/EEC A14 3.16 Oxidizing properties Method Method used is equivalent to 92/69/EEC A17
Conclusion	Adopt applicant's version with the above additions.
Reliability	2
Acceptability	Acceptable
Remarks	All data and endpoints presented in the study summary have been checked against the original study and are correct.

	COMMENTS FROM …
Date	
Results and discussion	
Conclusion	
Reliability	
Acceptability	
Remarks	

Section A4 – Analytical Methods for Detection and Identification

4.1 Determination of active substance

			Official use only
		1. REFERENCE	
1.1	**Reference**	a) Cichy, M. (2004) Analytical Method: Determination of Bendiocarb (AE B052020) In Technical Grade and Pure Active Ingredient by HPLC – AE B052020 Bendiocarb Bayer CropScience GmbH Document C042572 4.1/01 15 April 2004 Unpublished b) Cichy, M. and Ridder, I. (2004) Validation of HPLC-method AM001304FP1: Bendiocarb (AE B052020) In Technical Grade and Pure Active Ingredient/HPLC external Standard Bayer CropScience GmbH Document C043613 4.1/02 18 August 2004 Unpublished	
1.2	**Data protection**	Yes	
1.2.1	Data owner	Bayer CropScience AG	
1.2.2	Companies with letter of access	n.a.	
1.2.3	Criteria for data protection	Data submitted to the MS after 13 May 2000 on existing a.s. for the purpose of its entry into Annex I.	
		2. GUIDELINES AND QUALITY ASSURANCE	
2.1	**Guideline study**	a) EU 91/414/EEC Annex II 4.1 US EPA OPPTS 830.1700 b) EU Directive 91/414/EEC Annex II and Annex III, amended by Directive 96/46/EC Annex I 4.1 US EPA Product Properties Guideline OPPTS 830.1800	
2.2	**GLP**	No. Not required for analytical methods	
2.3	**Deviations**	No	
		3. MATERIALS AND METHODS	
3.1	**Preliminary treatment**		
3.1.1	Enrichment	n.a. – analysis of technical and pure active substance (TGAI)	
3.1.2	Cleanup	n.a. – analysis of technical and pure active substance (TGAI)	
3.2	**Detection**		
3.2.1	Separation method	HPLC (HP 1100 series) on a reversed stationary phase (Prodigy ODS 2, 250 x 4.6 mm, particle size: 5µm). Mobile phase 225 ml methanol, 225 ml acetonitrile, 550 ml water. Flow rate 1.5 ml/min, 30 °C.	

3.2.2	Detector	UV absorption, 254 nm	
3.2.3	Standard(s)	Bendiocarb reference standard; external	
3.2.4	Interfering substance(s)	No interferences from reagent blanks or minor compounds in impurity standards and technical material.	
3.3	**Linearity**		
3.3.1	Calibration range	500 – 2000 mg/kg	
3.3.2	Number of measurements	5 concentrations, double measurements	
3.3.3	Linearity	r^2 >0.999	
3.4	**Specificity: interfering substances**	The specificity of the method was demonstrated by the absence of interference from reference substances of impurities and by fortification of a technical sample with [redacted] during the determination of accuracy. Chromatograms of blank, reference substances and sample were free of interfering compounds.	
3.5	**Recovery rates at different levels**	99.9% The evaluation of accuracy was obtained by 5 synthetic samples containing known amounts of a.i. and of the impurities. Technical material was spiked with impurity reference substance [redacted] at fortification levels of about 2% w/w (20g/kg).	
3.5.1	Relative standard deviation	0.3%	
3.6	**Limit of determination**	Not relevant for determination of TGAI	
3.7	**Precision**		
3.7.1	Repeatability	Procedure conducted 5 times, double measurement; RSD 0.4%	
3.7.2	Independent laboratory validation	No. This is a method for determining the active substance in technical material.	
		4. APPLICANT'S SUMMARY AND CONCLUSION	
4.1	**Materials and methods**	Bendiocarb was analysed in technical and pure a.i. by HPLC on a reversed stationary phase with UV detection. The method was validated using a batch of technical bendiocarb (batch B920701, 98.5% purity). The mean recovery rate and relative standard deviation were 99.9% and 0.3%, respectively.	
4.2	**Conclusion**		
4.2.1	Reliability	1	
4.2.2	Deficiencies	No	

	EVALUATION BY COMPETENT AUTHORITIES
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	01/2007
Materials and methods	Adopt applicant's version.
Conclusion	Adopt applicant's version.
Reliability	1
Acceptability	Acceptable
Remarks	No claim for GLP compliance has been made for this study, however the principles of GLP have been followed. That said, as validation can be considered an intrinsic part of method development, the UK CA believes GLP compliance inappropriate. This method was appropriately validated, and in accordance with the relevant requirements of section 4.1 of TNsG on DRs. All data and endpoints presented in the study summary have been checked against the original study and are correct. The Technical Guidance document does not specify which way to determine the LOD/LOQ. The SANCO guidance is just that, its guidance and other methods maybe used. Therefore, the LOD/LOQ were determined according to a SOP which looks at signal/noise ratio. This approach has been used in another regulatory forum e.g. PPPD so we think it is scientifically justified. Therefore, the UK does not consider it is justified to ask for this again.
	COMMENTS FROM …
Date	
Results and discussion	
Conclusion	
Reliability	
Acceptability	
Remarks	

4.2 Analytical methods: soil, air, water, animal and human body fluids and tissues

4.2.1 Soil

		1. REFERENCE	Official use only
1.1	**Reference**	Brumhard, B. (2005) Analytical Method 00941 for the Determination of Residues of Bendiocarb (AE B052020) in Soil by HPLC-MS/MS Bayer CropScience AG Document M-252272-01-1 4.2.1/01 13 June 2005 Unpublished	
1.2	**Data protection**	Yes	
1.2.1	Data owner	Bayer CropScience AG	
1.2.2	Companies with letter of access	n.a.	
1.2.3	Criteria for data protection	Data submitted to the MS after 13 May 2000 on existing a.s. for the purpose of its entry into Annex I.	
		2. GUIDELINES AND QUALITY ASSURANCE	
2.1	**Guideline study**	EC Guidance Document on residue analytical methods, SANCO/825/00 Rev.8 of March 17, 2004. BBA Guideline: Residue analytical methods for post-registration control purposes of July 21, 1998. Commission Directive 96/46/EC amending Council Directive 91/414/EEC of 16 July 1996.	
2.2	**GLP**	Yes	
2.3	**Deviations**	No	
		3. MATERIALS AND METHODS	
3.1	**Preliminary treatment**		
3.1.1	Enrichment	Soil samples of 20 g are extracted in a microwave extractor with 40 ml of a mixture of water and acetonitrile.	
3.1.2	Cleanup	After extraction, a subsample is centrifuged to remove fine particles of soil.	
3.2	**Detection**		
3.2.1	Separation method	See 3.1.1 and 3.1.2.	
3.2.2	Detector	HPCL using MS/MS detection.	
3.2.3	Standard(s)	Bendiocarb	
3.2.4	Interfering substance(s)	None	
3.3	**Linearity**		
3.3.1	Calibration range	1.25 – 100 µg/l	
3.3.2	Number of measurements	6 concentrations, double measurements	

3.3.3	Linearity	For all mass transitions the mass spectrometric detector showed linear response in the range of about 1.25 µg/l to 100 µg/l for bendiocarb with correlation coefficients ranging from 0.9997 to 0.9998.	
3.4	**Specificity: interfering substances**	None	
3.5	**Recovery rates at different levels**	20 recovery experiments were conducted by injecting each sample twice into the HPLC instrument. The mean recovery rates for bendiocarb (m/z 167) determined at a fortification level of 5 µg/kg and 50 µg/kg were 83% (relative standard deviation (RSD) = 12.0%) and 86% (RSD 5.5%) respectively. The overall mean recovery rate and relative standard deviation for bendiocarb (m/z 167) were 84% and 9.2%, respectively. The mean recovery rates for bendiocarb (m/z 109) were 82% (relative standard deviation (RSD) = 13.3%) and 86% (RSD 5.4%) respectively. The overall mean recovery rate and relative standard deviation for bendiocarb (m/z 109) were 84% and 10.0%, respectively.	
3.5.1	Relative standard deviation	Overall mean RSD = 9.2% for bendiocarb (m/z 167) and overall mean RSD = 10.0% for bendiocarb (m/z 109)	
3.6	**Limit of determination**	The limit of quantitation of the method is 5 µg/kg for bendiocarb in soil. The limit of detection of the method is 1.5 µg/kg.	
3.7	**Precision**		
3.7.1	Repeatability	20 samples were analysed (double measurements); overall mean RSD = 9.2% for bendiocarb (m/z 167) and overall mean RSD = 10.0% for bendiocarb (m/z 109)	
3.7.2	Independent laboratory validation	No	

		4. APPLICANT'S SUMMARY AND CONCLUSION	
4.1	**Materials and methods**	The present method validation was performed for the determination of the active ingredient bendiocarb (AE B052020) in soil. Soil samples of 20 g are extracted in a microwave extractor with 40 ml of a mixture of water and acetonitrile. After extraction, a subsample is centrifuged to remove fine particles of soil. Identification and quantitation of the active substance is done by high performance liquid chromatography using MS/MS detection in the Multiple Reaction Monitoring mode (two mass transitions used). The first MRM transition of bendiocarb is the product ion with the mass 167 (Bendiocarb m/z 167) and the second MRM transition is the product ion with the mass 109 (Bendiocarb m/z 109). For all mass transitions the mass spectrometric detector showed linear response in the range of about 1.25 µg/l to 100 µg/l for bendiocarb with correlation coefficients ranging from 0.9997 to 0.9998. The mean recovery rates for bendiocarb (m/z 167) determined at a fortification level of 5 µg/kg and 50 µg/kg were 83% (relative standard deviation (RSD) = 12.0%) and 86% (RSD 5.5%) respectively. The overall mean recovery rate and relative standard deviation for bendiocarb (m/z 167) were 84% and 9.2%, respectively. The mean recovery rates for bendiocarb (m/z 109) were 82% (relative standard deviation (RSD) = 13.3%) and 86% (RSD 5.4%) respectively. The overall mean recovery rate and relative standard deviation for bendiocarb (m/z 109) were 84% and 10.0%, respectively. The blank values in all control samples were below 1.5 µg/kg (<$^1/_3$ x LOQ), demonstrating that no background level of bendiocarb was present in the test systems. The limit of quantitation of the method is 5 µg/kg for bendiocarb in soil. The limit of detection of the method is 1.5 µg/kg.	
4.2	**Conclusion**		
4.2.1	Reliability	1	
4.2.2	Deficiencies	No	

	EVALUATION BY COMPETENT AUTHORITIES
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	01/2007
Materials and methods	Adopt applicant's version.
Conclusion	Adopt applicant's version.
Reliability	1
Acceptability	Acceptable
Remarks	This method was appropriately validated, and in accordance with the relevant requirements of section 4.2 of TNsG on DRs. All data and endpoints presented in the study summary have been checked against the original study and are correct.
	COMMENTS FROM …
Date	
Results and discussion	
Conclusion	
Reliability	
Acceptability	
Remarks	

4.2.2 Air

			Official use only
		1. REFERENCE	
1.1	**Reference**	Class, T. (2005) Bendiocarb: Analytical Method for the Determination of Bendiocarb in Air PTRL Europe, Germany Document C048621 4.2.2/01 25 May 2005 Unpublished	
1.2	**Data protection**		
1.2.1	Data owner	Bayer CropScience AG	
1.2.2	Companies with letter of access	n.a.	
1.2.3	Criteria for data protection	Data submitted after 13 May 2000 on existing a.s. for the purpose of entry into Annex I	
		2. GUIDELINES AND QUALITY ASSURANCE	
2.1	**Guideline study**	EU Directive 91/414/EEC Annex II (Part A, Section 4.2), as amended by Commission Directive 96/46/EC EC Guidance Document on Residue Analytical Methods, SANCO/825/00 rev. 7 17/03/04	
2.2	**GLP**	Yes	
2.3	**Deviations**	No	
		3. MATERIALS AND METHODS	
3.1	**Preliminary treatment**		
3.1.1	Extraction	Air is drawn through XAD adsorption tubes at about 1L/min. for 6 hours (total air sampling ~0.4m^3). The adsorption material is then extracted with acetonitrile	
3.1.2	Cleanup	None	
3.2	**Detection**		
3.2.1	Separation method	Bendiocarb is determined by liquid chromatography using a Phenomenex Aqua C_{18} column with a gradient mobile phase comprising ratios of 0.1% formic acid and 4mM ammonium formate in water and 0.1% formic acid and 4mM ammonium formate in methanol.	
3.2.2	Detector	Applied Biosystems MDS Sciex API 3000 triple quadrapole LC-MS/MS (with TurboIonspray ESI and Heated Nebulizer APCI source)	
3.2.3	Standard(s)	Bendiocarb was used as an external standard using LC/MS software.	
3.2.4	Interfering substance(s)	No interference was found (<0.015 µg/m^3) (LC/MS/MS is highly specific).	
3.3	**Linearity**		
3.3.1	Calibration range	0.25 to 50 or 100 ng/mL	

3.3.2	Number of measurements	8
3.3.3	Linearity	Linear, $r^2 = 0.999$
3.4	**Specificity: interfering substances**	No interference – monitoring two parent-daughter ion transitions is highly selective
3.5	**Recovery rates at different levels**	Fortified at 0.05 µg to 0.50 µg (m/z = 167) recovery 106%, Range 100 – 110%* 0.05 µg to 0.50 µg (m/z = 109) recovery 105%, Range 101 – 109%* Fortified at 0.05 µg to 0.50 µg (m/z = 167) recovery 106%, Range 96 – 112%** 0.05 µg to 0.50 µg (m/z = 109) recovery 105%, Range 97 – 109%** *Ambient air; **Warm, humid air
3.5.1	Relative standard deviation	Fortified at 0.05 µg to 0.50 µg (m/z = 167) recovery 106%, RSD 4% (n=10)* 0.05 µg to 0.50 µg (m/z = 109) recovery 105%, RSD 2% (n=10)* Fortified at 0.05 µg to 0.50 µg (m/z = 167) recovery 106%, RSD 5% (n=10)** 0.05 µg to 0.50 µg (m/z = 109) recovery 105%, RSD 4% (n=10)** *Ambient air; **Warm, humid air
3.6	**Limit of determination**	Limit of detection ≤ 0.015 µg/m^3 Limit of quantitation 0.12 µg/m^3
3.7	**Precision**	
3.7.1	Repeatability	Five samples, duplicate injections of each (from recovery data) Fortified at 0.05 µg (m/z = 167) RSD 1%; (m/z = 109) RSD 2% (n=5)* 0.50 µg (m/z = 167) RSD 2%; (m/z = 109) RSD 3% (n=5)* Fortified at 0.05 µg (m/z = 167) RSD 4%; (m/z = 109) RSD 3% (n=5)** 0.50 µg (m/z = 167) RSD 6%; (m/z = 109) RSD 4% (n=5)** *Ambient air; **Warm, humid air
3.7.2	Independent laboratory validation	No

	4. APPLICANT'S SUMMARY AND CONCLUSION	
4.1	**Materials and methods**	The air sample (~0.4 m^3) is collected by drawing air through an adsorption tube containing two portions of XAD porous polymer (A = 100 mg, B = 50 mg) separated by a glass wool plug, each end of the tube is also closed with glass wool plugs. Air is drawn through the tube by a membrane pump at a rate of about 1 L/min. for 6 hours to give a total sample of ~0.4 m^3; the air flow is determined several times during sampling using a soap bubble meter. The total sampling time, air temperature and relative humidity of the air are recorded. For extraction, the adsorption portion A (the first portion in the tube), together with the first and second (middle) glass wool plugs are transferred to a centrifuge vial. Adsorption portion B, together with the third (end) glass wool plug are similarly transferred to a second centrifuge vial, if breakthrough is to be determined. The empty glass tube is then rinsed with acetonitrile (~3 mL) and the rinse solution is added to the vial containing absorption portion A. The vial is then briefly sonicated before transferring the extract, without removing the particles, into a graduated centrifuge vial. The extraction procedure is repeated twice using ~3 mL of acetonitrile. The extracts are combined and made up to a volume of 10mL. For breakthrough determination an extract of absorption portion B is prepared as above. For analysis, 0.50 mL of the extract is pipetted into an autosampler vial, 0.50 mL of water is added and bendiocarb is assayed by LC/MS/MS. The samples are analysed on an Agilent 1100 Series HPLC system using a reverse phase Phenomenex Aqua C_{18} column (length 50mm, i.d. 2.0mm, particle size 5 micron) with a Phenomenex C_{18} guard column (length 4mm, i.d.2.0mm, particle size 5 micron). A gradient solvent system is used comprising ratios of 0.1% formic acid and 4mM ammonium formate in water and 0.1% formic acid in 4mM ammonium formate in methanol. The MS/MS is an Applied Biosystems MDS Sciex API 3000 triple quadrapole MS/MS with TurboIonspray ESI and heated Nebulizer APCI source. Under the conditions used the retention time of bendiocarb is about 6.2 minutes. Quantification of bendiocarb is carried out with an external standard method using two parent daughter ion transitions (m/z 224 to m/z 167 and m/z 109). The analytical method for bendiocarb in air has been validated over the range of 0.12 µg/m^3 to 1.2 µg/m^3 with acceptable recovery rates (overall mean recovery rates: 105-106%) and reproducibility (RSD ≤ 6%). Breakthrough to the back portion of the absorption tubes is < 5%. The method is highly specific as it uses two parent – daughter ion transitions, and does not, therefore, require further confirmation of detected residues.
4.2	**Conclusion**	
4.2.1	Reliability	1
4.2.2	Deficiencies	No

	EVALUATION BY COMPETENT AUTHORITIES
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	01/2007
Materials and methods	Adopt applicant's version.
Conclusion	Adopt applicant's version.
Reliability	1
Acceptability	Acceptable
Remarks	This method was appropriately validated, and in accordance with the relevant requirements of section 4.2 of TNsG on DRs. All data and endpoints presented in the study summary have been checked against the original study and are correct.
	COMMENTS FROM …
Date	
Results and discussion	
Conclusion	
Reliability	
Acceptability	
Remarks	

4.2.3 Water

			Official use only
		1. REFERENCE	
1.1	**Reference**	Bright, J.H.M. (1989) Analytical method for the Determination of Bendiocarb in Drinking Water by High Performance Liquid Chromatography Schering Agrochemicals Ltd. Document A90322 4.2.3/01 3 May 1989 Unpublished	
1.2	**Data protection**	Yes	
1.2.1	Data owner	Bayer CropScience AG	
1.2.2	Companies with letter of access	n.a.	
1.2.3	Criteria for data protection	Data submitted to the MS after 13 May 2000 on existing a.s. for the purpose of its entry into Annex I.	
		2. GUIDELINES AND QUALITY ASSURANCE	
2.1	**Guideline study**	Company in-house method	
2.2	**GLP**	No. Not required for analytical methods	
2.3	**Deviations**	n.a.	
		3. MATERIALS AND METHODS	
3.1	**Preliminary treatment**		
3.1.1	Enrichment	Partition of bendiocarb into dichloromethane (DCM).	
3.1.2	Cleanup	Concentration of DCM extract.	
3.2	**Detection**		
3.2.1	Separation method	High performance liquid chromatography (HPLC) – Varian 5000. Spherisorb 5 ODS column, 15 cm, i.d. 4.6 mm	
3.2.2	Detector	UV detection – Kratos Spectroflow 747 at 208 nm	
3.2.3	Standard(s)	2-Naphthol (marker)	
3.2.4	Interfering substance(s)	Occasional small co-extraction peaks could be removed by using alternative HPLC conditions.	
3.3	**Linearity**		
3.3.1	Calibration range	0.05 to 1.5 µg/ml bendiocarb in standard solution	
3.3.2	Number of measurements	10 concentrations, number of measurement not specified	
3.3.3	Linearity	Linear over the tested range of 0.05 to 1.5 µg/ml bendiocarb in standard solutions (1 to 30 ng injected).	
3.4	**Specificity: interfering substances**	Occasional small co-extraction peaks could be removed by using alternative HPLC conditions.	

3.5	**Recovery rates at different levels**	A mean recovery efficiency (20 tests) of 100.3% was obtained for bendiocarb (fortified in the range 0.1 to 1.0 ppb). The recovery rates ranged from 81 to 111%.	
3.5.1	Relative standard deviation	8.7%	
3.6	**Limit of determination**	A level of 0.1 µg/l (0.1 ppb) bendiocarb in drinking water is the lowest concentration at which residues have been accurately quantified in terms of recovery efficiency. Limit of detection estimated as 0.2 ng bendiocarb injected into the HPLC.	
3.7	**Precision**		
3.7.1	Repeatability	A mean recovery efficiency (20 tests) of 100.3% was obtained for bendiocarb (fortified in the range 0.1 to 1.0 ppb). The relative standard deviation for these recoveries was 8.7%.	
3.7.2	Independent laboratory validation	No	
		4. APPLICANT'S SUMMARY AND CONCLUSION	
4.1	**Materials and methods**	This report describes the analytical method developed for the determination of bendiocarb in drinking water. Water samples are partitioned with dichloromethane. The dichloromethane extract is then concentrated and a marker solution added. The final determination of bendiocarb is by HPLC using UV detection.	
4.2	**Conclusion**	Validity criteria can be considered as fulfilled. A mean recovery efficiency (20 tests) of 100.3% was obtained for bendiocarb (fortified in the range 0.1 to 1.0 ppb) with a Relative Standard Deviation of 8.7%. A level of 0.1 µg/l (0.1 ppb) bendiocarb in drinking water is the lowest concentration at which residues have been accurately quantified in terms of recovery efficiency. Limit of detection estimated as 0.2 ng bendiocarb injected into the HPLC.	
4.2.1	Reliability	1	
4.2.2	Deficiencies	No	

	EVALUATION BY COMPETENT AUTHORITIES
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	01/2007
Materials and methods	Adopt applicant's version.
Conclusion	Adopt applicant's version.
Reliability	1
Acceptability	Acceptable
Remarks	No claim for GLP compliance has been made for this study, however the principles of GLP have been followed. That said, as validation can be considered an intrinsic part of method development, the UK CA believes GLP compliance inappropriate. This method was appropriately validated, and in accordance with the relevant requirements of section 4.2 of TNsG on DRs. All data and endpoints presented in the study summary have been checked against the original study and are correct.
	COMMENTS FROM …
Date	
Results and discussion	
Conclusion	
Reliability	
Acceptability	
Remarks	

			Official use only
		1. REFERENCE	
1.1	**Reference**	Krebber, R. (2005) Analytical Method 00942 for the Determination of Bendiocarb (AE B052020) and its Metabolite NC 7312 in Drinking and Surface Water by HPLC-MS/MS Bayer CropScience AG, Germany Document M-254110-01-1 4.2.3/02 7 July 2005 Unpublished	
1.2	**Data protection**		
1.2.1	Data owner	Bayer CropScience AG	
1.2.2	Companies with letter of access	n.a.	
1.2.3	Criteria for data protection	Data submitted to the MS after 13 May 2000 on existing a.s. for the purpose of its entry into Annex I	
		2. GUIDELINES AND QUALITY ASSURANCE	
2.1	**Guideline study**	Commission Directive 96/46/EC amending Council Directive 91/414/EC of 16 July, 1996 Guidance Document on Residue Analytical Methods, SANCO/825/00 rev. 7 of March 17, 2004 BBA Guideline: Residue Analytical Methods for Post-Registration Control Purposes of July 21, 1998	
2.2	**GLP**	Yes	
2.3	**Deviations**	No	
		3. MATERIALS AND METHODS	
3.1	**Preliminary treatment**		
3.1.1	Extraction	Water samples are analysed after adjusting to pH 3 with formic acid by direct injection into an HPLC-MS/MS instrument.	
3.1.2	Cleanup	None	
3.2	**Detection**		
3.2.1	Separation method	Bendiocarb is determined by liquid chromatography using a Phenomenex Aqua C_{18} column with a gradient mobile phase comprising ratios of water/acetonitrile/acetic acid (900/100/0.1 v/v/v) and acetonitrile/acetic acid (1000/0.1 v/v) The metabolite, NC 7312, is determined by liquid chromatography using a Hypersil Keystone Betamax Acid column with a gradient mobile phase comprising ratios of water/ammonia solution 25% NH_3 (1000/0.1 v/v) and acetonitrile.	
3.2.2	Detector	Applied Biosystems Ionics EP10+ MS/MS with turbo-ionspray interface mass selective detector upgrade API 365. The parameters for the mass spectrometer were set to give optimal results for daughter ions m/z 167 (quantitation) and 108 (confirmatory ion) for bendiocarb and m/z 125 for NC 7312 (quantitation)	

3.2.3	Standard(s)	Bendiocarb and NC 7312 were used to prepare standard calibration curves
3.2.4	Interfering substance(s)	No interference is found (LC/MS/MS is highly specific)
3.3	**Linearity**	
3.3.1	Calibration range	Bendiocarb and NC 7312: 0.04 µg/L to 10.0 µg/L
3.3.2	Number of measurements	Bendiocarb and NC 7312: 7 measurements in duplicate
3.3.3	Linearity	Linear; Bendiocarb: correlation coefficient 0.9997 NC 7312: correlation coefficient 0.9998
3.4	**Specificity: interfering substances**	No interfering substances are found
3.5	**Recovery rates at different levels**	Validation was performed with surface water. A validation for drinking water was not necessary because the LOQ for surface water is below the drinking water limit of 0.1 µg/L. Bendiocarb 0.05 µg/L Mean recovery rate 92% (m/z 167) 0.50 µg/L Mean recovery rate 98% Bendiocarb 0.05 µg/L Mean recovery rate 99% (m/z 108) 0.50 µg/L Mean recovery rate 100% NC 7312 0.05 µg/L Mean recovery rate 99% (m/z 125) 0.50 µg/L Mean recovery rate 105%
3.5.1	Relative standard deviation	Bendiocarb 0.05 µ/L: Range 88 – 103%, RSD 4.4% (n=10) (m/z 167) 0.50 µ/L: Range 93 – 113%, RSD 5.7% (n=10) Bendiocarb 0.05 µ/L: Range 89 – 110%, RSD 6.1% (n=10) (m/z 108) 0.50 µ/L: Range 95 – 116%, RSD 6.3% (n=10) NC 7312 0.05 µg/L: Range 95 – 100%, RSD 1.7% (n=10) (m/z 125) 0.50 µg/L: Range 103 – 107%, RSD 1.2% (n=10) Note: Because of the direct measurement of fortified samples without separate extraction and clean-up steps it is not possible to determine recovery rates and, therefore, the validation samples (see 3.7.1 below) were evaluated like recovery rates.
3.6	**Limit of determination**	Limit of detection Bendiocarb and NC 7312 : 0.017 µg/L Limit of quantitation Bendiocarb and NC 7312 : 0.05 µg/L
3.7	**Precision**	
3.7.1	Repeatability	Bendiocarb (m/z 167): 0.05 µg/L Mean peak area 2709 units, RSD 4.4% (n=10) 0.50 µg/L Mean peak area 28734 units, RSD 5.7% (n=10) Bendiocarb (m/z 108): 0.05 µg/L Mean peak area 1568 units, RSD 6.0% (n=10) 0.50 µg/L Mean peak area 16972 units, RSD 6.3% (n=10) NC 7312 (m/z 125): 0.05 µg/L Mean peak area 16688 units, RSD 1.7% (n=10) 0.50 µg/L Mean peak area 171158 units, RSD 1.2% (n=10)
3.7.2	Independent laboratory validation	No

		4. APPLICANT'S SUMMARY AND CONCLUSION	
4.1	**Materials and methods**	Surface water samples were adjusted to pH 3 with formic acid before aliquots (20 µL) were taken for injection into the HPLC instrument. HPLC was carried out using an Agilent 1100 system fitted with an HTC PAL system autosampler coupled to an Applied Biosystems Ionics EP10+ MS/MS with turbo-ionspray interface mass selective detector upgrade API 365. The parameters for the mass spectrometer were set to give optimal results for daughter ions m/z 167 (quantitation) and 108 (confirmatory ion) for bendiocarb and m/z 125 for NC 7312 (quantitation). Bendiocarb was chromatographed on a Phenomenex Aqua C_{18} column (length 150mm, i.d. 2mm, particle size 5 microns) fitted with a pre-column – Phenomenex Aqua 10 micron C_{18} – using a gradient mobile phase comprising ratios of water/acetonitrile/acetic acid (900/100/0.1 v/v/v) and acetonitrile/acetic acid (1000/0.1 v/v). The metabolite, NC 7312, was chromatographed on a Hypersil Keystone Betamax Acid column (length 250mm, i.d. 3mm, particle size 5 microns) using a gradient mobile phase comprising ratios of water/ammonia solution 25% NH_3 (1000/0.1 v/v) and acetonitrile. The measured concentration of each analyte was calculated by comparison of the responses to standard calibration curves.	
4.2	**Conclusion**	The method for the determination of bendiocarb and its metabolite, NC 7312, has been validated with surface water over the range 0.05 to 0.5 µg/L with acceptable recovery rates (mean recovery rates: 92-100% for bendiocarb and 99-105% for NC 7312) and reproducibility (≤ 6.3% for bendiocarb and ≤ 1.7% for NC 7312). The method is highly specific for both bendiocarb and NC 7312 as it uses parent-daughter ion transitions and does not, therefore, require further confirmation of detected residues. A validation for drinking water was not necessary because the LOQ for surface water is below the drinking water limit of 0.1 µg/L.	
4.2.1	Reliability	1	
4.2.2	Deficiencies	No	

	EVALUATION BY COMPETENT AUTHORITIES
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	01/2007
Materials and methods	Adopt applicant's version
Conclusion	Adopt applicant's version
Reliability	1
Acceptability	Acceptable
Remarks	This method was appropriately validated, and in accordance with the relevant requirements of section 4.2 of TNsG on DRs. All data and endpoints presented in the study summary have been checked against the original study and are correct.
	COMMENTS FROM …
Date	
Results and discussion	
Conclusion	
Reliability	
Acceptability	
Remarks	

4.2.4 Animal and human body fluids and tissues

		1. REFERENCE	Official use only
1.1	**Reference**	Frenzel, T. *et al* (1998) Rapid GC Multimethod for Verification and Determination of Toxic Pesticides in Whole Blood by Means of Capillary GC-MS AgrEvo GmbH, Germany Document A67646 4.2.4/01 9 July 1998 Unpublished Frenzel, T. *et al* (2000) Rapid Multimethod for Verification and Determination of Toxic Pesticides in Whole Blood by Means of Capillary GC-MS *Journal of Analytical Toxicology*, Volume 24, Number 5, 365 – 371 Document C011634 4.2.4/02 July/August 2000 Published Brennecke, R. (1998) Independent Laboratory Validation of Method EM F-05/98-0 "Rapid Multimethod for Verification and Determination of Toxic Pesticides in Whole Blood by Means of Capillary GC-MS" Bayer AG, Crop Protection, Germany Document C002476 4.2.4/03 21 December 1998 Unpublished	
1.2	**Data protection**	Yes	
1.2.1	Data owner	Bayer CropScience GmbH	
1.2.2	Companies with letter of access	n.a.	
1.2.3	Criteria for data protection	Data submitted to the MS after 13 May 2000 on existing a.s. for the purpose of its entry into Annex I	
		2. GUIDELINES AND QUALITY ASSURANCE	
2.1	**Guideline study**	Internal method (EU Commission Directive 96/46/EC section 4.2.5).	
2.2	**GLP**	No. Not required for analytical methods	
2.3	**Deviations**	n.a.	
		3. MATERIALS AND METHODS	
3.1	**Preliminary treatment**		
3.1.1	Enrichment	Whole blood is haemolysed by ultrasonic vibration and then deproteinised by addition of acetone.	

3.1.2	Cleanup	After centrifugation, the supernatant is cleaned up on a disposable Kieselguhr column. The remaining precipitate from the blood is successively mixed with eluent I (ethyl acetate/dichloromethane 2:1) and then eluent II (n-hexane). After centrifugation each corresponding supernatant is poured on the Kieselguhr column. The combined eluates from the column are evaporated under a nitrogen flow to a remainder 200 µl and the internal standard is added.	
3.2	**Detection**		
3.2.1	Separation method	Blood levels are determined by gas chromatography-mass spectrometry. Capillary GC (HP 5890) with an MSD (HP 5970) and autosampler (HP 7673 A) equipped with programmed temperature vaporization (PTV, e.g., Gerstel) and an HP 5-MS 30-m x 0.25-mm i.d. fused-silica capillary column coated with 0.25 µm 95% dimethyl-5% phenyl-silicone. The carrier gas was helium (99.996%), and the column inlet pressure was 85 kPa. The temperature program was as follows: 45°C (2.66 min) to 170°C at 40°C/min, to 220°C at 4°C/min, and to 280°C at 20°C/min (15.72 min). PTV occurred as follows: splitless mode at 40°C to 280°C at 6°C/s (2 min), then open split valve until end of chromatography. The injection volume was 1 µL. The coupling to MS was a closed interface at 285°C	
3.2.2	Detector	Mass spectrometer (HP 5970) *Full scan mode.* Ions with *m/z* 50 to *mlz* 400 were monitored. The windows for ion-extraction were as follows: deltamethrin/ tralomethrin, t_R - 4.50 min to t_R + 0.50 min; βcyfluthrin, t_R - 4.50 min to t_R + 1.00 min; all other active substances, t_R - 0.50 min to t_R + 0.50 min. The mass fragments (m/z) for bendiocarb are 151; 166; 223 – the preferred one being 151. *Single ion monitoring (SIM) mode.* Sampling time/mass was 100 ms; for bromophos-methyl it was 300 ms. The windows for ion-extraction were as follows: t_R - 4.50 min to t_R + 0.50 min for deltamethrin and tralomethrin and t_R - 0.50 min to t_R + 0.50 min for all other active substances with t_R being the retention time of the respective active substance.	
3.2.3	Standard(s)	Bromophos methyl – internal standard	
3.2.4	Interfering substance(s)	No interfering substances	
3.3	**Linearity**		
3.3.1	Calibration range	50 – 4000 ng/ml	
3.3.2	Number of measurements	5 concentrations with 3 repetitions	
3.3.3	Linearity	$r^2 = 0.998$	
3.4	**Specificity: interfering substances**	No interfering substances	
3.5	**Recovery rates at different levels**	5 samples at 6 fortification levels (50 – 2000 ng/ml) – overall mean recovery rate: 94% (mean recovery rate of each level: 89 - 108%)	

3.5.1	Relative standard deviation	Overall RSD: 7.4%	
3.6	**Limit of determination**	LOD: 25 ng/ml LOQ: 50 ng/ml	
3.7	**Precision**		
3.7.1	Repeatability	The method has an excellent precision, with a relative standard deviation of 6%.	
3.7.2	Independent laboratory validation	5 samples at 3 fortification levels (50, 100 & 500 ng/ml) – mean recovery rates vary between 83 and 98% depending on the MS detection mode (full scan or SIM) and the corresponding RSD vary between 1.8 and 7.2%.	
		4. APPLICANT'S SUMMARY AND CONCLUSION	
4.1	**Materials and methods**	A rapid and single multimethod was developed to determine substances of different pesticide classes in whole blood in the event of acute human intoxications, as required by EU Commission Directive 96/46. The method was validated by an in-house and an independent laboratory validation. Whole blood is haemolysed and then deproteinised. After extraction of the supernatant, blood levels are determined by gas chromatography-mass spectrometry. The method, which can be performed within 120 min, covers 15 active substances (8 organophosphate pesticides, 2 carbamates, 3 pyrethroids, 1 azole, and 1 organochlorine pesticide) classified as toxic or very toxic. These compounds can be identified down to concentrations between 100 and 1000 ng/mL by comparison of their mass spectra to those in a commercial pesticide mass spectra library. Using the standard addition method, they can be quantitated down to concentrations between 30 and 200 ng/mL. These limits of quantitation are considered to be sufficient in comparison to respective LD_{50} values. For bendiocarb, mean recovery rates between 89 and 108% were obtained over a range of 50 to 2000 ng/ml (RSD between 2 and 10%). The method has been validated by an independent laboratory with acceptable mean recovery rates between 83 and 98% (RSD between 1.8 and 7.2%). The LOQ is 50 ng/ml.	
4.2	**Conclusion**		
4.2.1	Reliability	1	
4.2.2	Deficiencies	No	

	EVALUATION BY COMPETENT AUTHORITIES
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	01/2007
Materials and methods	Adopt applicant's version.
Conclusion	Adopt applicant's version.
Reliability	1
Acceptability	Acceptable
Remarks	This method was appropriately validated, and in accordance with the relevant requirements of section 4.2 of TNsG on DRs. All data and endpoints presented in the study summary have been checked against the original study and are correct.
	COMMENTS FROM …
Date	
Results and discussion	
Conclusion	
Reliability	
Acceptability	
Remarks	

4.3 Analytical methods for residues in/on food or feedstuffs

	JUSTIFICATION FOR NON-SUBMISSION OF DATA	Official use only
Other existing data [ ]	**Technically not feasible [ ] Scientifically unjustified [ ]**	
Limited exposure [✓]	**Other justification [ ]**	
Detailed justification:	The product is not to be used to treat food-handling surfaces nor is it intended to treat when uncovered food is present. Labelling restrictions include the following: DO NOT APPLY TO SURFACES on which food or feed is stored, prepared or eaten. COVER FOOD, FOOD PREPARING EQUIPMENT AND EATING UTENSILS before application. As the product is only for use by trained pest control operators, these precautions are normally taken in the course of treatment. Therefore, an analytical method should not be required.	
Undertaking of intended data submission [ ]		

EVALUATION BY COMPETENT AUTHORITIES	
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	01/2007
Materials and methods	The UK CA agrees with the justification.
Conclusion	The UK CA agrees with the justification.
Reliability	0
Acceptability	Acceptable
Remarks	The justification presented has been reviewed.
	COMMENTS FROM …
Date	
Results and discussion	
Conclusion	
Reliability	
Acceptability	
Remarks	

Section A5 – Effectiveness Against Target Organisms and Intended Uses

Subsection (Annex Point)			Official use only
5.1	**Function (IIA5.1)**	Insecticide	
5.2	**Organism(s) to be controlled and products, organisms or objects to be protected (IIA5.2)**		
5.2.1	Organism(s) to be controlled (IIA5.2)	Bendiocarb's spectrum of activity is extremely broad, and embraces numerous tested species of public health and stored-product insect pests including cockroaches, ants, fleas, flies, bed bugs, carpet pests, wasps, wild bees, stored product pests, silverfish and other bristle tails, ground beetles, earwigs, crickets, booklice and woodlice. Bendiocarb also has activity against arachnid pests (see Section A5.3 and B5 for details). All these pests are found throughout Europe, hence the active substance bendiocarb could be used throughout the EU community.	
5.2.2	Products, organisms or objects to be protected (IIA5.2)	Protects homes and public buildings as well as rubbish sites. Protect rooms including carpets, wallpaper, furniture, bedframes, mattresses, books etc.	
5.3	**Effects on target organisms, and likely concentration at which the active substance will be used (IIA5.3)**		
5.3.1	Effects on target organisms (IIA5.3)	Control: Bendiocarb acts on harmful organisms by contact and ingestion resulting in death. Bendiocarb expresses a knock-down effect (see Section 5.3 Summary Table of Experimental data, namely, evidence of a knock-down effect is presented in Summary Table).	X
5.3.2	Likely concentrations at which the A.S. will be used (IIA5.3)	0.12 g product/m^2 (0.096 g a.s./m^2). The dose rate is independent of where the product is applied within the EU.	
5.4	**Mode of action (including time delay) (IIA5.4)**		

5.4.1	Mode of action	Bendiocarb is a carbamate which acts on harmful organisms by contact and ingestion resulting in death. It has residual activity as well as expressing a knock-down effect. Like other carbamates, it reversibly inhibits acetylcholinesterase, an enzyme required for normal transmission of nerve impulses. Bendiocarb binds to the active site of this enzyme leading to an accumulation of acetylcholine, required for the transmission of nerve impulses in the body, at nerve muscle sites (The Pesticide Manual, 13th edition, 2003).	X
5.4.2	Time delay	Knock-down (see Sections A5.3 and B5.10).	X
5.5	**Field of use envisaged (IIA5.5)**		
	MG03: Pest control	PT18 – Insecticides, Acaricides and Products to Control Other Arthropods	
	Further specification	Indoor and outdoor use	
5.6	**User (IIA5.6)**		
	Industrial	Formulation into the biocidal product	
	Professional	Yes Operators may be exposed when mixing, loading and applying Bendiocarb products for spray applications. The following tasks are undertaken: • Dilution of product in water, • Application of product in compression sprayer (e.g. knapsack.) • Maintenance and cleaning of spraying equipment. Impermeable coveralls, gloves and full face mask are recommended as a general precaution.	
5.7	**Information on the occurrence or possible occurrence of the development of resistance and appropriate management strategies (IIA5.7)**		

5.7.1	Development of resistance	Bendiocarb is a carbamate insecticide. Some resistance to carbamates has been found to varying degrees, depending on the pest species and location (Anon. 1987). Laboratory tests on resistance strains from the field in Europe and worldwide have shown varying resistant factors for a range of insects: *Blatella germanica* (Barson & McCheyne, 1978, Barson & Renn, 1983; Chapman *et al.*, 1993; Rust *et al.*, 1993), *Musca domestica*, (Harris *et al.*, 1982) and *Anopheles atroparvus* (Hemingway & Davidson, 1983). Cross-resistance of pest species to the group of carbamates is to be anticipated due to a common mode of action, and instances of cross-resistance (or multiple resistance) between organophosphate and carbamate insecticides have been reported (Hemingway & Davidson, 1983)	
5.7.2	Management strategies	Because resistance is well known to be a potential problem, strategies to avoid resistance are normal practice. For example, the use of alternating sequences, mixtures and avoidance of frequent repeated use are standard.	
		General advice is provided by IRAC (Anon. 1987). The principles of strategies for managing the development of resistance are similar for bendiocarb as they are for other organo-carbamates. These are: • where possible, application treatments should be recommended to be combined with non-chemical measures • products should always be used in accordance with label recommendations • applications should always be made against the most susceptible stages in the pest life cycle • where an extended period of control is required, treatments should be alternated with products with different modes of action • levels of effectiveness should be monitored, and instances of reduced effectiveness should be investigated for possible evidence of resistance, noting that sanitary conditions and proximity of untreated refugia can contribute to the risk of re-infestation. • in cases where label rates, correctly applied, fail to give the expected level of control and resistance is demonstrated, use of any product containing the same class of chemistry should cease.	X
5.8	**Likely tonnage to be placed on the market per year (IIA5.8)**	Likely tonnage is indicated in the Confidential Document	

EVALUATION BY COMPETENT AUTHORITIES	
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	22.2.07
Materials and methods	N/A
Conclusion	N/A
Reliability	N/A
Acceptability	Applicant's version is considered acceptable.
Remarks	**5.3.1.** The Applicant has indicated that 'Bendiocarb expresses a knock-down effect -see Section A5'. Section A5 is the whole 'Effectiveness Against Target Organisms and Intended Uses' section, and not a particular sub-section of this section. One of the studies cited as key by the Applicant – Lee, *et al*, 1996 – has not been included in the summary table in Section 5.3. The UK CA does not consider this to be a significant omission. **5.3.1, 5.4.1 & 5.4.2**. Although the Applicant indicates that bendiocarb expresses a knock-down effect, this is not a specific claim made for the associated biocidal product Ficam W. The Applicant claims that the product is for the 'control' of the range of target pests. **5.7.2**. Of the advice outlined in the bullet points, the last three are advice that should be present on the label for the associated biocidal product Ficam W. This is also the case with all other bendiocarb products, which should be labelled properly to cover the potential problem of resistance.

Section 5.3 **Summary Table of Experimental Data on The Effectiveness of The Active Substance Against Target Organisms At Different Fields Of Use Envisaged, Where Applicable**

<table>
<tr><th>Function</th><th>Field of use envisaged</th><th>Test substance</th><th>Test organism(s)</th><th>Test method</th><th>Test conditions</th><th>Test results: effects, mode of action, resistance</th><th>Reference*)</th></tr>
<tr>
<td>Insecticide</td>
<td>PT18</td>
<td>Bendiocarb</td>
<td>Lasius niger</td>
<td>Glass plates were treated with known deposits of Bendiocarb applied in acetone solution. When the plates were dry, glass rings, coated with fluon were placed on the plates and infested with approximately 20 worker ants.

Counts were made to obtain rate of knockdown and a mortality count was made at 24 hours.</td>
<td>During the exposure period the ants were fed with honey solution.

A.I dose, 0.001 & 0.1 g/m^2</td>
<td>Rate of Knockdown (selected data)
Bendiocarb (NC 6897)
<table>
<tr><th rowspan="2">g/m^2</th><th colspan="5">% knockdown after continuous exposure (mins)</th></tr>
<tr><th>1</th><th>2</th><th>4</th><th>8</th><th>15</th></tr>
<tr><td>0.1</td><td>0</td><td>5</td><td>100</td><td></td><td></td></tr>
<tr><td>0.001</td><td>0</td><td>0</td><td>0</td><td>25</td><td>100</td></tr>
</table>
KD_{50} (0.1g/m^2) = 3 mins
KD_{50} (0.001g/m^2) = 10 mins
<table>
<tr><th colspan="5">Percent mortality bendiocarb at 24hrs (g/m^2) (n = 3)</th></tr>
<tr><td>0.1</td><td>0.001</td><td>0.0003</td><td>0.0001</td><td>0.00003</td></tr>
<tr><td>100</td><td>100</td><td>100</td><td>17</td><td>0</td></tr>
<tr><td>100</td><td>29</td><td>0</td><td>0</td><td>0</td></tr>
<tr><td>100</td><td>100</td><td>0</td><td>0</td><td>0</td></tr>
</table>
</td>
<td>Lemon, R.W (1970), A90675/ M-167393-01-1
5.3/01</td>
</tr>
</table>

<table>
<tr><th>Function</th><th>Field of use envisaged</th><th>Test substance</th><th>Test organism(s)</th><th>Test method</th><th>Test conditions</th><th>Test results: effects, mode of action, resistance</th><th>Reference*)</th></tr>
<tr>
<td>Insecticide</td>
<td>PT18</td>
<td>Bendiocarb</td>
<td>Tineola bisselliella,

Anthrenus flavipes
Attagenus megatoma.
(2 carpet beetles)</td>
<td>For the larval tests, discs of pure woolen cloth approx. 8 cm. diameter were treated with solutions of Bendiocarb in acetone and after drying were placed in 9 cm. petri dishes. Each was infested with 20 larvae of the test insect which were counted after 7 days exposure. Two replicates of each treatment were included. For the adult carpet beetle test, glass plates were treated with Bendiocarb in acetone and the beetles were confined on the deposit in brass rings for 24 hours after which time the mortality was determined.</td>
<td>AI dose:
Larval tests: 10, 30, 100, 300 & 1000 ppm.

Adult test: 3, 11, 32, 108 & 323 mg m^{-2}.</td>
<td>Larval Tests: Tineola bisselliella,
<table>
<tr><th>ppm</th><th>% mortality</th><th>LD_{50}</th></tr>
<tr><td>1000</td><td>100</td><td rowspan="5">65 ppm</td></tr>
<tr><td>300</td><td>100</td></tr>
<tr><td>100</td><td>100</td></tr>
<tr><td>30</td><td>0</td></tr>
<tr><td>10</td><td>0</td></tr>
</table>
Larval Tests: Anthrenus flavipes
<table>
<tr><th>ppm</th><th>% mortality</th><th>LD_{50}</th></tr>
<tr><td>300</td><td>100</td><td rowspan="4">25 ppm</td></tr>
<tr><td>100</td><td>100</td></tr>
<tr><td>30</td><td>67</td></tr>
<tr><td>10</td><td>0</td></tr>
</table>
Larval Tests: Attagenus megatoma
<table>
<tr><th>ppm</th><th>% mortality</th><th>LD_{50}</th></tr>
<tr><td>1000</td><td>100</td><td rowspan="4">100 ppm</td></tr>
<tr><td>300</td><td>73</td></tr>
<tr><td>100</td><td>53</td></tr>
<tr><td>30</td><td>0</td></tr>
</table>
Adult test: Attagenus megatoma
<table>
<tr><th colspan="2">% knockdown and mortality at rate indicated (mg m^{-2}) mortality</th><th>LC_{50}</th></tr>
<tr><td>323</td><td>100</td><td rowspan="5">4.4 mg m^{-2}</td></tr>
<tr><td>108</td><td>100</td></tr>
<tr><td>32</td><td>100</td></tr>
<tr><td>11</td><td>100</td></tr>
<tr><td>3</td><td>30</td></tr>
</table>
</td>
<td>Lemon, R.W (1970), A90690/ M-167498-01-1
5.3/02</td>
</tr>
</table>

<table>
<tr><th>Function</th><th>Field of use envisaged</th><th>Test substance</th><th>Test organism(s)</th><th>Test method</th><th>Test conditions</th><th>Test results: effects, mode of action, resistance</th><th>Reference*)</th></tr>
<tr><td>Insecticide</td><td>PT18</td><td>Bendiocarb</td><td>Periplaneta americana</td><td>2 µl acetone Bendiocarb solution applied to ventral side of thorax between mid coxae. 10 adult cockroaches per treatment.

Mortality assessed over a four day period</td><td>AI dose:
10, 3, 1, 0.3 & 0.1 (µg/insect)</td><td>
<table>
<tr><th>days</th><th colspan="5">% knockdown and dead (µg/insect)</th></tr>
<tr><td></td><td>10</td><td>3</td><td>1</td><td>0.3</td><td>0.1</td></tr>
<tr><td>1</td><td>90</td><td>60</td><td>40</td><td>10</td><td>0</td></tr>
<tr><td>2</td><td>100</td><td>80</td><td>50</td><td>10</td><td>0</td></tr>
<tr><td>3</td><td>100</td><td>80</td><td>50</td><td>20</td><td>0</td></tr>
<tr><td>4</td><td>100</td><td>80</td><td>50</td><td>20</td><td>10</td></tr>
</table>
The results indicate a LD_{50} of approximately 1 µg/insect.
</td><td>Lemon, R.W (1971), A90652 / M-167370-01-1 5.3/03</td></tr>
<tr><td>Insecticide</td><td>PT18</td><td>Bendiocarb</td><td>Monomorium pharaonis

Acheta domesticus</td><td>Pharaoh's ant culture was obtained from the Pest Infestation Laboratory, the house crickets were collected from Chesterford Park. Glass plates were treated with known deposits of Bendiocarb applied in acetone. The insects were confined to the plates in glass rings. Mortality measurements were made after 24 hours continuous exposure.</td><td>A.I doses, 0.0001, 0.0003, 0.001, 0.01 and 0.03 g/m²</td><td>Monomorium pharaonis
<table>
<tr><th colspan="5">Percent mortality bendiocarb at 24hrs (g/m²)</th></tr>
<tr><td>0.03</td><td>0.01</td><td>0.001</td><td>0.0003</td><td>0.0001</td></tr>
<tr><td>100</td><td>100</td><td>100</td><td>100</td><td>35</td></tr>
</table>
<table>
<tr><th colspan="4">Time to complete knockdown bendiocarb at (g/m²) (ms)</th></tr>
<tr><td>0.03</td><td>0.01</td><td>0.003</td><td>0.001</td></tr>
<tr><td>5 ms</td><td>7 ms</td><td>1ms</td><td>9 ms</td></tr>
</table>
Acheta domesticus
<table>
<tr><th colspan="5">Percent mortality bendiocarb at 24hrs (g/m²) (n = 3)</th></tr>
<tr><td>0.03</td><td>0.01</td><td>0.003</td><td>0.0001</td><td>0.0003</td></tr>
<tr><td>100</td><td>91</td><td>89</td><td>60</td><td>0</td></tr>
</table>
</td><td>Lemon, R.W (1971), A90676/ M-167394-01-1
5.3/04</td></tr>
</table>

<table>
<tr><th>Function</th><th>Field of use envisaged</th><th>Test substance</th><th>Test organism(s)</th><th>Test method</th><th>Test conditions</th><th>Test results: effects, mode of action, resistance</th><th>Reference*)</th></tr>
<tr><td>Insecticide</td><td>PT18</td><td>Bendiocarb</td><td>Lepisma saccharina</td><td>Bendiocarb pure material was applied to glass plates in acetone solution to obtain deposits of 100 and 30 mg/m. Propoxur, technical material was included for comparison. Silverfish were exposed to the fresh deposits for 24 hours.</td><td>A.I dose 100 g/m^2</td><td><table><tr><th colspan="3">Percent mortality bendiocarb at 24hrs (g/m^2)</th></tr><tr><td></td><td>100</td><td>30</td></tr><tr><td>Bendiocarb</td><td>100</td><td>100</td></tr><tr><td>Propoxur</td><td>100</td><td>100</td></tr></table></td><td>Lemon, R.W (1972), A90681/ M-167399-01-1 5.3/05</td></tr>
<tr><td>Insecticide</td><td>PT18</td><td>Bendiocarb</td><td>Ctenocephalides felis Xenopsylla cheopis</td><td>Bendiocarb, was tested against adult C. felis (sex not reported). Following application to filter papers, mortality was assessed after 24 h, and an LC_{50} calculated.

In the same study, bendiocarb, were tested against adult Xenopsylla cheopis (Oriental rat flea). Bendiocarb was applied to filter papers at an application rate of 50 mg bendiocarb m^2. Bioassays, consisting of the addition of 10 X. cheopis (sex not reported), were conducted 1, 2 and 4 w post-treatment, and thereafter at 4 w intervals up to 24 w. Mortality was assessed 24 h after each bioassay was initiated, and percentage mortality was determined.</td><td>A.I dose 50 g/m^2</td><td>C. felis:
The LC_{50} for bendiocarb was determined to be 50 mg bendiocarb l^{-1}

<i>Xenopsylla cheopis:</i>
Bendiocarb provided 100 % mortality up to week 16, falling to 95 % at week 20, and 80 % at week 24

Residual activity of bendiocarb and malathion against adult <i>Xenopsylla cheopis</i> 50 mg a.s./m^2<table><tr><th colspan="3">% mortality</th></tr><tr><th>weeks</th><th>bendiocarb</th><th>malathion</th></tr><tr><td>8</td><td>100</td><td>100</td></tr><tr><td>12</td><td>100</td><td>80</td></tr><tr><td>16</td><td>100</td><td>90</td></tr><tr><td>20</td><td>95</td><td>85</td></tr><tr><td>24</td><td>80</td><td>45</td></tr></table></td><td>Goose, J. 1977 A90853, M-167569-01-1 5.3/06</td></tr>
</table>

<table>
<tr><th>Function</th><th>Field of use envisaged</th><th>Test substance</th><th>Test organism(s)</th><th>Test method</th><th>Test conditions</th><th>Test results: effects, mode of action, resistance</th><th>Reference*)</th></tr>
<tr><td>Insecticide</td><td>PT18</td><td>Bendiocarb</td><td>Musca domestica</td><td>The ability of a range of insecticides, including bendiocarb, to control two resistant strains (A & B) and a susceptible strain (C) of Musca domestica (house fly), was assessed under laboratory conditions. Insecticidal solutions were prepared in 19:1 acetone:olive oil and applied directly to M. domestica using a Potter's tower. The insecticides were made up at concentrations of 0 (solvent group), 1 x 10^{-3}, 3.3 x 10^{-3}, 1 x 10^{-2}, 3.3 x 10^{-2}, 0.1, 0.33 and 1 % solution (w/v). Two groups of 10 M. domestica (1:1 male:female) were tested at each dose level. Mortality counts were made 18 h after treatment. Each screening test was repeated and the results of the 2 tests were averaged and corrected for natural mortality using Abbott's formula.</td><td>Treated flies were placed in containers covered with a Petri dish and held in a chamber at 27 ± 1°C and 65 % r.h., and continuous light.

A.I doses: 0.001, 0.0033, 0.01, 0.03, 0.1, 0.33 and 1 % w.v</td><td>An LD_{50} of 1.7 x 10^{-2} % w/v bendiocarb solution was recorded for strain C (susceptible strain).
<table>
<tr><th colspan="4">Percent mortality (n=2)</th></tr>
<tr><th colspan="2">Strains</th><th>A</th><th>B</th><th>C</th></tr>
<tr><td rowspan="7">Bendi-ocarb (w/v)</td><td>1</td><td>100</td><td>80</td><td>N/T</td></tr>
<tr><td>0.33</td><td>95</td><td>70</td><td>N/T</td></tr>
<tr><td>0.1</td><td>85</td><td>36</td><td>100</td></tr>
<tr><td>0.03</td><td>35</td><td>11</td><td>100</td></tr>
<tr><td>0.01</td><td>0</td><td>5</td><td>45</td></tr>
<tr><td>0.0033</td><td>0</td><td>0</td><td>3</td></tr>
<tr><td>0.001</td><td>0</td><td>6</td><td>0</td></tr>
</table>
N/T = Not tested.</td><td>Harris et al., 1982, M-264660-01-1
5.3/07</td></tr>
</table>

<table>
<tr><th>Function</th><th>Field of use envisaged</th><th>Test substance</th><th>Test organism(s)</th><th>Test method</th><th>Test conditions</th><th>Test results: effects, mode of action, resistance</th><th>Reference*)</th></tr>
<tr><td>Insecticide</td><td>PT18</td><td>Bendiocarb</td><td>Anopheles atroparvus</td><td>The ability of bendiocarb, to control 5 strains of varying insecticide susceptibility was assessed. An insecticide susceptible strain (strain 1), a multiple resistant strain (strain 2), a fenitrothion resistant strain (strain 3), a propoxur resistant strain (strain 4), a malathion resistant strain (strain 5), and a fenthion resistant strain (strain 6). Adult An. atroparvus were treated by the tarsal contact method using the standard WHO test kits. Filter papers were treated with bendiocarb at a rate of 0.36 mg m^{-2}. Olive oil, silicon oil and risella oil were added to acetone as controls. The insects were exposed to the insecticidal concentrations for 1 h.</td><td>A.I dose:
0.36 mg m^{-2}</td><td>Percentage mortality (and number of mosquitoes tested in parenthesis) of 6 strains of An. atroparvus after exposure to 0.36 mg bendiocarb m^{-2} for 1 h
<table>
<tr><th>Strain</th><th>Treatment: bendiocarb</th></tr>
<tr><td>1</td><td>100 (12)</td></tr>
<tr><td>2</td><td>46 (99)</td></tr>
<tr><td>3</td><td>12 (41)</td></tr>
<tr><td>4</td><td>0 (62)</td></tr>
<tr><td>5</td><td>8 (37)</td></tr>
<tr><td>6</td><td>0 (39)</td></tr>
</table>
Controls no effect.</td><td>Hemingway and Davidson, (1983)
M-264671-01-1
5.3/08</td></tr>
</table>

Function	Field of use envisaged	Test substance	Test organism(s)	Test method	Test conditions	Test results: effects, mode of action, resistance	Reference*)
Insecticide	PT18	Bendiocarb	*Blattella germanica*	Topical application of 1µl of test compound in acetone at a predetermined dose of insecticide was applied to the first segment of the abdominal stemites. In each experiment, 10 – 30 insects (depending on availability) were tested at each dose level. All experiments were done in the morning and replicated three to seven times. Cockroaches aged 3 – 14 days were used. Mortality was scored at 24 hours post-treatment. The criterion for death was as follows: cockroaches lying on their back were touched on their abdomen with a forcep; those that were unable to back themselves to normal posture in two minutes were considered dead.	Upon treatment, the cockroaches were kept in clean polyethylene petri dishes (diam = 9 cm; height =1.5 cm) with ten individuals per container, each provided with a piece of mouse pellet and a wet cotton bung. The dose levels used were not reported.	All LD_{50}, values were converted from µg/insect to µg/g insect to avoid the possible effect of weight differences on toxicity. Test for statistical significance between LD_{50} values was the failure of their 95% fiducial limits to overlap. The test results showed LD_{50} of 13 µg bendiocarb per insect and 51 µg bendiocarb per insect for males and females, respectively.	Rust M. *et al* (1993) M-264666-01-1 5.3/09

<table>
<tr><th>Function</th><th>Field of use envisaged</th><th>Test substance</th><th>Test organism(s)</th><th>Test method</th><th>Test conditions</th><th>Test results: effects, mode of action, resistance</th><th>Reference*)</th></tr>
<tr><td>Insecticide</td><td>PT18</td><td>Bendiocarb</td><td>Blattella germanica</td><td>The activity of technical grade (97.3 %) bendiocarb was assessed on 2 – 3 week-old adult males of a susceptible laboratory strain, an American strain collected from a housing estate of unknown treatment history, and 3 UK field strains obtained from unnamed locations in London.
Two sets of tests were conducted. In the first series the insecticide was tested using a tarsal contact method based on the standard WHO method (1970). In the second series a topical application method was used in which 5 different concentrations of bendiocarb in pentan-3-one were tested (concentrations not reported). Each concentration was replicated 3 times on 15 adult male cockroaches. Knockdown counts were made daily for 7 d. Pentan-3-one was applied to 3 replicates of 15 insects as controls. The control results were not reported.</td><td>Reared: 27°C, 45 RH using a 10:14 h light:dark regime, on an appropriate diet.

A.I dose 240 mg bendiocarb m^{-2}</td><td>KT and LD values for bendiocarb against laboratory susceptible and field strains of B. germanica

<table>
<tr><th rowspan="2">Strain</th><th colspan="2">Tarsal contact*</th></tr>
<tr><th>KT_{50}(min)</th><th>KT_{95}(min)</th></tr>
<tr><td>Susceptible</td><td>22</td><td>31</td></tr>
<tr><td>UK_1</td><td>165</td><td>2754</td></tr>
<tr><td>UK_2</td><td>N/T</td><td>N/T</td></tr>
<tr><td>UK_3</td><td>N/T</td><td>N/T</td></tr>
<tr><td>America</td><td>41</td><td>130</td></tr>
</table>
* Application rate = 240 mg bendiocarb m^{-2}, N/T = Not tested

<table>
<tr><th rowspan="2">Strain</th><th colspan="2">Topical application</th></tr>
<tr><th>LD_{50} µg/insect</th><th>LD_{95} µg/insect</th></tr>
<tr><td>Susceptible</td><td>0.3</td><td>0.4</td></tr>
<tr><td>UK_1</td><td>0.6</td><td>2</td></tr>
<tr><td>UK_2</td><td>0.7</td><td>2</td></tr>
<tr><td>UK_3</td><td>2</td><td>7</td></tr>
<tr><td>America</td><td>0.4</td><td>3</td></tr>
</table></td><td>Chapman, P.A., et al (1993)

265401-01-1 5.0/01</td></tr>
</table>

Function	Field of use envisaged	Test substance	Test organism(s)	Test method	Test conditions	Test results: effects, mode of action, resistance	Reference*)
Insecticide	PT18	Ficam W Bendiocarb 80% w/w	*Blattella germanica*	Two field strains (B and D) of *Blattella germanica* were collected from survivors of Bendiocarb 80% treatments in England and bred in the laboratory. They were compared with a laboratory susceptible strain (S) in a tarsal contact method for resistance to bendiocarb, fenitrothion and dieldrin. Adult female cockroaches have been confined on glass plates treated with a range of concentrations of the insecticides between 1.7 and 220 mg/m² as residual deposits. After exposure for time periods of 5 min, 60 min or 24 h the insects were placed in Petri dishes and knockdown (KD) was assessed in 30 min intervals for the first 6 h. KD and mortality were assessed in 24 h intervals over 7 days.	Experiments conducted at 27°C, 45% r.h., 12h photoperiod at 22 lux	The resistance factors for Bendiocarb were at the LC_{50} level 5.6 and 6.2 for the field strains D and B and 1.7 and 2.0 at the LC 95 level. Knockdown resistance was detected with resistance factors of 10.6 and 8.1 at the KD_{50} level. At shorter exposure times of 5 and 60 min 2 - 20% of the field strains survived 55 or 110 mg m^{-2} where no survivors were observed for the susceptible strain.	Barson, G. & McCheyne, N.G M-264646-01-1 5.7.1/01

Function	Field of use envisaged	Test substance	Test organism(s)	Test method	Test conditions	Test results: effects, mode of action, resistance	Reference*)
Insecticide	PT18	Ficam W Bendiocarb 80% w/w	*Blattella germanica*	In addition to the scusceptible strain SS and the bendiocarb restistant strain D a strain H has been bred from survivors of a number of treatments with malathion and a treatment history with DDT, γ-HCH, malathion, fenitrothion and pyrethrins. Resistance of these strains was tested with a tarsal contact method using Bendiocarb 80% WP and 9 other insecticides. Glass plates (31 x 31 cm) were treated with 5 ml aliquots of insecticides in aqueous dilution to obtain a range of 6 concentrations of dry deposit. 5 replicates of 10 adult female cockroaches were confined for the exposition period of 24h on the surface of these glassplates and then removed to untreated covered cristallising dishes. Knockdown (KD) was assessed in 30 min intervals for the first 6 h. KD and mortality were assessed in 24 h intervals for up to 7 days. Selection for resistance was carried out by exposure of final-instar nymphs to Bendiocarb in two stages at increasing concentrations (110 and 220 mg/m²) and subsequent breeding of the survivors yielding the strains D_{SL1} and D_{SL2}. For Malathion selection was carried out on strain H by breeding survivors of an exposure to 125 mg/m².	Experiments conducted at 27°C, 45% r.h., 12h photoperiod at 22 lux. During the experimental stage no feed or water was given to the cock-roaches	Resistance in terms of mortality was demonstrated for bendiocarb, dioxacarb and dieldrin in both strains and for malathion in strain H. The resistance factor for bendiocarb was 10.6 for the KD_{50} and 5.6 for the LC_{50} but only 1.7 for the LC_{95}. These resistance factors were incraesed in the selected strain D_{SL1} by a factor of 4 for the LC_{50} and x3 for the KD_{50}. Little or no cross resistance to propoxur, but evidence of cross resistance to dioxacarb on LC_{50} and KD_{50} levels, but not at the 95 % level.	Barson, G. & Renn, N., M-264650-01-1 5.7.1/02

*) References efficacy 5.3

Author	Year	Title, Origin, Report No, Date
Chapman, P.A., Learmount, J., Pinniger, D.B., Wildey, K.B (Editor) and Robinson, W.H (Editor)	1993	Insecticide resistance in *Blattella germanica* (L.) in the United Kingdom. Proceedings of the 1st International Conference on Insect Pests in the Urban Environment, 125-133. M-265401-01-1
Goose, J	1977	The Use of Bendiocarb to Control Fleas Schering Agrochemicals Ltd, UK *Proceeding of the International Conference on Fleas*, 21 – 25 June 1977, pp 315-320 21 June 1977 Published. cument A90853, M-167569-01-1
Harris, C.R., Turnbull, S.A., Whistlecraft, J.W. and Surgeoner, G.A	1982	Multiple resistance shown by field strains of house fly, *Musca domestica* (Diptera: Muscidae), to organochlorine, organophosphorus, carbamate and pyrethroid insecticides. The Canadian Entomologist, May, pp 447-454. M-264660-01-1
Hemingway, J. and Davidson, G	1983	Resistance to organophosphate and carbamate insecticides in *Anopheles atroparvus*. Parassitologia **25**, pp 1-8. M-264671-01-1
Rust, M., Reierson, D.A. and Zeichneri, B.C.	1993	Relationship between insecticide resistance and performance in choice tests of field collected German cockroaches (Dictyoptera: Blattellidae). J. Econ. Entomol., 86(4), 1124-1130. M-264666-01-1
Lee, C.Y., Yap, H.H. and Chong, N.L.,	1996	Insecticide toxicity on the adult German cockroach Blattella germanica (L.). Malays. J. Sci., Ser. A, 17(A),1-9. M-263749-01-1
Lemon, R.W	1970	The activity of NC 6897 against the common garden ant Acanthomyops niger (syn. Lasius niger), Unpublished, A90675/ M-167393-01-1
Lemon, R.W	1970	The activity of NC 6897 and Baygon against the cloth moth and two species of the carpet beetle, Unpublished A90690/ M-167498-01-1
Lemon, R.W	1971	NC 6897 Topical Application Test Against the American Cockroach (*Periplaneta americana*) , Unpublished, A90652 / M-167370-01-1
Lemon, R.W	1971	The activity of NC 6897 against Pharoah's ant, Monomorium pharaonis and the house cricket Acheta domesticus, Unpublished, A90676/ M-167394-01-1
Lemon, R.W	1972	The activity of NC 6897 against silverfish (Lepisma saccharina) Unpublished, A90681/ M-167399-01-1
Barson, G. and McCheyne, N.G	1978	Resistance of the German cockroach *Blattella germanica* to bendiocarb. Ann. Appl. Biol., **90**(2), 147-154. M-264646-01-1
Barson, G. and Renn, N.,	1983	Laboratory assessment of resistance to commercial insecticide formulations in two strains of the German cockroach *Blattella germanica* (L.) (Dictyoptera: Blattellidae). Bull. Entomol. Res., **73**(3), 491-499. M-264650-01-1

Section A6 – Toxicological and Metabolic Studies

Certain toxicological studies (including long term and developmental studies) have been conducted using bendiocarb technical produced in the late 1970s or early 1980s. Bayer Environmental Science has reviewed the manufacturing processes, the purity of the starting materials used and the specifications of the active substances produced with these processes and has concluded that the technical material used in the older studies is of the same quality as the technical material produced currently (see Confidential Appendix I). Therefore, all testing presented herein has been conducted with active substances representative of the current technical material.

6.1 Acute toxicity

6.1.1 Acute oral

		1. REFERENCE	Official use only
1.1	**Reference**	[redacted] (1980) A Comparison of the Acute Oral Toxicities of Various Batches of Bendiocarb CR 4971/2, CR 4799/9, CR 4799/4 and CR 4500/20, to the Male Rat [redacted] Document A90464 6.1.1/01 May 1980 Unpublished	
1.2	**Data protection**	Yes	
1.2.1	Data owner	Bayer CropScience AG	
1.2.2	Companies with letter of access	n.a.	
1.2.3	Criteria for data protection	Data submitted to the MS after 13 May 2000 on existing a.s. for the purpose of its entry into Annex I.	
		2. GUIDELINES AND QUALITY ASSURANCE	
2.1	**Guideline study**	No, but the study was conducted in line with good scientific practice.	
2.2	**GLP**	No, the study was conducted prior to the introduction of GLP as a standard requirement.	
2.3	**Deviations**	n.a.	
		3. MATERIALS AND METHODS	
3.1	**Test material**	Bendiocarb	
3.1.1	Lot/Batch number	CR 4971/2, CR 4799/9, CR 4799/4 and CR 4500/20,	
3.1.2	Specification	As given in Section 2	
3.1.2.1	Description	White powder	
3.1.2.2	Purity	CR 4971/2: 98.9% CR 4799/9: 97.0% CR 4799/4: 91% CR 4500/20: 97.8%	
3.1.2.3	Stability	Not specified but bendiocarb is not known to decompose at room temperature	
3.2	**Test Animals**		

3.2.1	Species	Rat
3.2.2	Strain	Sprague-Dawley
3.2.3	Source	Charles River (UK) Ltd, Margate, Kent
3.2.4	Sex	Male
3.2.5	Age/weight at study initiation	Young adult, 191 – 232 g
3.2.6	Number of animals per group	6
3.2.7	Control animals	Yes
3.3	**Administration/ Exposure**	Oral
3.3.1	Postexposure period	7 days
3.3.2	Type	Gavage
3.3.3	Concentration	To establish oral LD_{50} values for the 4 batches of bendiocarb by contemporal administration and observation, it was necessary to perform two studies and also to add or delete dose levels to and from those originally in the protocols. Additionally, in the first test using CR 4971/2, CR4799/9 and CR 4799/4 low doses were included in an effort to establish a median effective dose (i.e. a dose to cause any clinical effect in 50% of the animals, the ED_{50}). Gavage mg/kg bw CR 4971/2 0.75, 1.5, 3.0, 6.0, 12, 24, 48, 67.8, 96, 135.7, 192 CR 4799/9 1.5, 3.0, 6.0, 12, 24, 48, 67.8, 96, 135.7, 192, 271.5 CR 4799/4 0.75, 1.5, 3.0, 6.0, 12, 24, 48, 67.8, 96, 135.7, 192 CR 4500/20 96, 135.7, 192, 271.5, 384
3.3.4	Vehicle	0.5% w/v aqueous gum tragacanth
3.3.5	Concentration in vehicle	Test 1: 20 mg a.i./ml suspension Test 2: 80 mg a.i./ml suspension
3.3.6	Total volume applied	Volume calculated from dose rate (see 3.3.3) and concentration in vehicle (see 3.3.5)
3.3.7	Controls	Vehicle
3.4	**Examinations**	Clinical observations, necropsy and macroscopic examination
3.5	**Method of determination of LD_{50}**	Weil
3.6	**Further remarks**	-

		4. RESULTS AND DISCUSSION	
4.1	**Clinical signs**	No mortality was seen up to 12 mg/kg, except for a single death at 3.0 mg/kg, in one experiment. Although the Authors did not state whether this death was due to bendiocarb or not, it was unlikely that this was treatment-related. There were 1/18, 0/18, 8/30, 9/42, 24/42, 34/36, 12/12 and 6/6 deaths from 24 up to 384 mg/kg respectively. The clinical signs observed from 1.5 mg/kg were typical of those arising from exposure to a carbamate cholinesterase inhibitor; fibrillation was followed by urinary incontinence and salivation in most animals at doses of about 12 mg/kg and above. Lacrimation and chromodacryorrhoae were also seen in a few animals. Coarse muscular jerking, cyanosis, exophthalmus and piloerection were seen in severely affected animals at the higher end of the dose range, primarily occurring before death.	
4.2	**Pathology**	No gross pathological changes considered to be of toxicological significance were seen at post-mortem.	
4.3	**Other**	Significantly reduced body weight gain (of between 25 and 64% in comparison to mean body weight gain in controls), was seen from 48 mg/kg to 135.7 mg/kg.	
4.4	**LD_{50}**	71.9 – 155.9 mg/kg (see 5.2)	
		5. APPLICANT'S SUMMARY AND CONCLUSION	
5.1	**Materials and methods**	The acute oral toxicity of 4 batches of bendiocarb (purity range 91 – 98.9%) was compared using LD_{50} tests in Sprague-Dawley rats (males only; 6/group). Dosing was by single gavage and animals received 0.75, 1.5, 3.0, 6.0, 12, 24, 48, 67.8, 96, 135.7, 192, 271.5 or 384 mg/kg, as suspension in 0.5% aqueous gum tragacanth. A different range of doses was used for each batch of bendiocarb investigated. In all the experiments, the rats were observed for 7 d after dosing (not the standard 14 d), with a gross pathological examination carried out on all interim deaths and after sacrifice of survivors on day 8.	
5.2	**Results and discussion**	No mortality was seen up to 12 mg/kg, except for a single death at 3.0 mg/kg, in one experiment. Although the Authors did not state whether this death was due to bendiocarb or not, it was unlikely that this was treatment-related. There were 1/18, 0/18, 8/30, 9/42, 24/42, 34/36, 12/12 and 6/6 deaths from 24 up to 384 mg/kg respectively. The clinical signs observed from 1.5 mg/kg were typical of those arising from exposure to a carbamate cholinesterase inhibitor; fibrillation was followed by urinary incontinence and salivation in most animals at doses of about 12 mg/kg and above. Lacrimation and chromodacryorrhoae were also seen in a few animals. Coarse muscular jerking, cyanosis, exophthalmus and piloerection were seen in severely affected animals at the higher end of the dose range, primarily occurring before death. Significantly reduced body weight gain (of between 25 and 64% in comparison to mean body weight gain in controls), was seen from 48 mg/kg to 135.7 mg/kg. No gross pathological changes considered to be of toxicological significance were seen at post-mortem.	

		The LD_{50} values established were: Test CR LD_{50} mg/kg 95% confidence limits mg/kg 1 4971/2 107.6 70.3 – 164.8 2 4971/2 120.8 100.2 – 145.6 1 4799/9 110.1 88.9 – 136.5 2 4799/9 155.9 126.0 – 193.2 1 4799/4 71.9 58.5 – 88.5 2 4799/4 135.5 112.5 – 163.3 2 4500/20 152.3 126.5 – 183.7 The variation in response of the male Sprague-Dawley rat to the toxic effects of the same batch of bendiocarb between tests one and two shows that, within the range of values encountered (71.9 – 155.9 mg/kg for the four batches from the two tests), there is no meaningful difference between the acute oral LD_{50} values of the four batches of bendiocarb tested. The LD_{50} of bendiocarb is considered to be 71.9 mg/kg.	
5.3	**Conclusion**		
5.3.1	Reliability	2	
5.3.2	Deficiencies	No	

Table A6.1.1-1 Table for Acute Toxicity

Dose [mg/kg]	Test	Batch No. (CR)	Number of dead/number of investigated	Time of death (range)	Observations
0.75	1	4971/2	0/6	-	
0.75	1	4799/4	0/6	-	
1.5	1	4971/2	0/6	-	
1.5	1	4799/9	0/6	-	
1.5	1	4799/4	0/6	-	
3.0	1	4971/2	1/6	5 min	
3.0	1	4799/9	0/6	-	
3.0	1	4799/4	0/6	-	
6.0	1	4971/2	0/6	-	
6.0	1	4799/9	0/6	-	
6.0	1	4799/4	0/6	-	
12	1	4971/2	0/6	-	
12	1	4799/9	0/6	-	
12	1	4799/4	0/6	-	
24	1	4971/2	1/6	3 min	
24	1	4799/9	0/6	-	
24	1	4799/4	0/6	-	
48	1	4971/2	0/6	-	
48	1	4799/9	0/6	-	
48	1	4799/4	0/6	-	
67.8	1	4971/2	3/6	5 - 21 min	
67.8	2	4971/2	0/6	-	
67.8	1	4799/9	1/6	12 min	
67.8	1	4799/4	4/6	10 - 11 min	
67.8	2	4799/4	0/6	-	
96	1	4971/2	1/6	47 min	
96	2	4971/2	1/6	19.5 h	
96	1	4799/9	1/6	1.5 d	
96	2	4799/9	1/6	1.5 d	
96	1	4799/4	4/6	8 - 10 min	
96	2	4799/4	1/6	17 min	
96	2	4500/20	0/6	-	

Dose [mg/kg]	Test	Batch No. (CR)	Number of dead/number of investigated	Time of death (range)	Observations
135.7	1	4971/2	4/6	12 min - 1.5 d	
135.7	2	4971/2	4/6	10 - 21 min	
135.7	1	4799/9	5/6	12 min - 20.5 h	
135.7	2	4799/9	1/6	20.5 h	
135.7	1	4799/4	6/6	18 - 81 min	
135.7	2	4799/4	2/6	72 min – 22 ¾ h	
135.7	2	4500/20	2/6	20.5 h - 1.5 d	
192	1	4971/2	6/6	11 min - 3.75 h	
192	2	4971/2	6/6	7 min - 21.75 h	
192	1	4799/9	6/6	13 min - 4.5 h	
192	2	4799/9	6/6	15 min - 21.5 h	
192	2	4799/4	6/6	12 min	
192	2	4500/20	5/6	21 h	
271.5	2	4799/9	6/6	23 min - 17.5 h	
271.5	2	4500/20	6/6	17.25 h - 3 d	
384	2	4500/20	6/6	50 min - 17 h	
0	1	Control	0/6	-	
0	2	Control	0/6	-	
LD_{50} value	71.9 – 155.9 mg/kg (see 5.2)				

	EVALUATION BY COMPETENT AUTHORITIES
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	30th August 2006
Materials and methods	As described by the applicant
Conclusion	As described by the applicant
Reliability	2
Acceptability	Acceptable
Remarks	This study comprises two experiments with four batches of bendiocarb, with the purity ranging from 91% to 98.9%. In accordance with the provisions laid down in Council Directive 67/548/EEC, bendiocarb should be regarded as 'Toxic if swallowed' and labelled with R25 (LD50 > 25 ≤ 200mg/kg).
	COMMENTS FROM …
Date	
Results and discussion	
Conclusion	
Reliability	
Acceptability	
Remarks	

			Official use only
		1. REFERENCE	
1.1	**Reference**	[redacted] (1983) The Acute Oral Toxicity of Technical Bendiocarb in the rat: Comparison with Dichlorvos and Propoxur [redacted] Document A90517 6.1.1/02 July 1983 Unpublished	
1.2	**Data protection**	Yes	
1.2.1	Data owner	Bayer CropScience AG	
1.2.2	Companies with letter of access	n.a.	
1.2.3	Criteria for data protection	Data submitted to the MS after 13 May 2000 on existing a.s. for the purpose of its entry into Annex I	
		2. GUIDELINES AND QUALITY ASSURANCE	
2.1	**Guideline study**	No, but the study was conducted in line with good scientific practice.	
2.2	**GLP**	No, the study was conducted prior to the introduction of GLP as a standard requirement.	
2.3	**Deviations**	n.a.	
		3. MATERIALS AND METHODS	
3.1	**Test material**	Bendiocarb	
3.1.1	Lot/Batch number	CR 4971/2	
3.1.2	Specification	As given in Section 2	
3.1.2.1	Description	Not specified but bendiocarb is known as a white/beige powder	
3.1.2.2	Purity	98.8%	
3.1.2.3	Stability	Test material was stable in the vehicle between preparation and treatment	
3.2	**Test Animals**		
3.2.1	Species	Rat	
3.2.2	Strain	Sprague-Dawley	
3.2.3	Source	Charles River (UK) Ltd, Margate, Kent	
3.2.4	Sex	Male and female	
3.2.5	Age/weight at study initiation	Males: 6-week old, 224-281 g Females: 7-week old, 174-208 g	
3.2.6	Number of animals per group	6	
3.2.7	Control animals	Yes	
3.3	**Administration/ Exposure**	Oral	
3.3.1	Postexposure period	14 days	

3.3.2	Type	Gavage	
3.3.3	Concentration	17.0, 25.0, 35.3 and 50.0 mg technical bendiocarb/kg bw	
3.3.4	Vehicle	Corn oil	
3.3.5	Concentration in vehicle	50 mg/ml	
3.3.6	Total volume applied	Male: 0.08, 0.12, 0.18 and 0.24 ml/rat for 17.0, 25.0, 35.3 and 50.0 mg bendiocarb/kg bw, respectively Female: 0.07, 0.10, 0.14 and 0.20 ml/rat for 17.0, 25.0, 35.3 and 50.0 mg bendiocarb/kg bw, respectively	
3.3.7	Controls	Vehicle	
3.4	**Examinations**	Clinical observations, necropsy and macroscopic examination	
3.5	**Method of determination of LD_{50}**	Weil	
3.6	**Further remarks**	-	
		4. RESULTS AND DISCUSSION	
4.1	**Clinical signs**	The clinical symptoms included salivation, muscular fibrillations, body tremors, facial soiling, urinary incontinence followed by soiling of the urinogenital region, gasping, exophthlamus, lacrimation, chromodacryorrhea, reduced activity and other associated effects.	
4.2	**Pathology**	Apparent congestion of the lungs was seen in early deaths. No macroscopic post mortem abnormalities were noted at necropsy of survivors.	
4.3	**Other**	Body weight gains between Day 1 and Day 8 were significantly decreased in males which received 17.7 mg bendiocarb/kg bw. In females body weight gains over this period were similar to the controls. Between Day 8 and Day 15 body weight gains were increased in females given 25.0 mg bendiocarb/kg bw when compared with controls.	
4.4	**LD_{50}**	Male: 25.0 mg/kg Female: 27.3 mg/kg (see 5.2)	
		5. APPLICANT'S SUMMARY AND CONCLUSION	
5.1	**Materials and methods**	The acute oral toxicity of technical bendiocarb in the rat has been compared with two similar carbamate cholinesterase inhibitors of known toxicity, dichlorvos and propoxur. Groups comprising six males and six females were dosed with 17.0, 25.0, 35.3 and 50.0 mg technical bendiocarb/kg bw, 50.0, 70.7, 100.0 and 141.0 mg dichlorvos/kg bw, and 35.3, 50.0, 70.7, 100.0 and 141.0 mg propoxur/kg bw. Six male and six female control rats were dosed with the vehicle, corn oil. Animals were observed for 14 days after treatment.	

5.2	**Results and discussion**	Bendiocarb, dichlorvos and propoxur produced similar symptoms both in type and time course except that salivation and urinary incontinence were less severe in animals dosed with dichlorvos and propoxur. Symptoms included muscular fibrillations and body tremors, salivation, facial soiling, urinary incontinence followed by soiling of the urinogenital region, gasping, exophthalmus, lacrimation, chromodacryorrhoea, reduced activity and other associated effects. LD_{50} values (with 95% confidence limits) were: Bendiocarb: male 25.0 (17.9 - 35.1) mg/kg bw female 27.3 (20.0 - 37.2) mg/kg bw Dichlorvos: male 70.7 (52.4 - 94.4) mg/kg bw female 75.8 (60.0 - 95.7) mg/kg bw Propoxur: male 56.0 (35.3 - 89.0) mg/kg bw female 89.0 (56.1 - 141.5) mg/kg bw Body weight gains between Day 1 and Day 8 were significantly decreased in males which received 17.7 mg bendiocarb/kg bw and those which received 35.3 mg propoxur/kg bw when compared with control. In females body weight gains over this period were similar to the controls. Between Day 8 and Day 15 body weight gains were increased compared with controls in males dosed with 35.3 mg propoxur/kg bw and in females given 25.0 mg bendiocarb/kg body weight. Findings noted at post mortem of early deaths caused by bendiocarb, dichlorvos or propoxur were soiling round the nose and mouth resulting from salivation, and soiling round the eyes. Salivary soiling of the chest and forelimbs, and soiling of the urinogenital region was noted with greatest frequency in animals dosed with bendiocarb. Apparent congestion of the lungs was seen in early deaths from each treatment. No macroscopic post mortem abnormalities noted at necropsy of survivors. The acute oral toxicity of technical bendiocarb in the study using corn oil as vehicle was slightly greater than found in previous acute oral toxicity studies which employed gum tragacanth as the vehicle.	
5.3	**Conclusion**		
5.3.1	Reliability	2	
5.3.2	Deficiencies	No	

Table A6.1.1-2 Table for Acute Toxicity

Dose [mg/kg]	Number of dead/ number of investigated	Time of death (range)	Observations
Male rat			
0	0/6	-	
17.7	1/6	7m	
25.0	3/6	7m-10m	
35.3	5/6	11m-67m	
50.0	5/6	7m-18m	
Female rat			
0	0/6	-	
17.7	1/6	15m	
25.0	2/6	13m-19m	
35.3	5/6	7m-19m	
50.0	5/6	4m-17m	
LD_{50} value:	male female	25.0 (17.9 - 35.1) mg/kg bw 27.3 (20.0 - 37.2) mg/kg bw	

EVALUATION BY COMPETENT AUTHORITIES	
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	31st August 2006
Materials and methods	As described by the applicant
Conclusion	As described by the applicant
Reliability	2
Acceptability	Acceptable
Remarks	In accordance with the provisions laid down in Council Directive 67/548/EEC, bendiocarb should be regarded as 'Toxic if swallowed' and labelled with R25 (LD50 > 25 ≤ 200mg/kg).
	COMMENTS FROM …
Date	
Results and discussion	
Conclusion	
Reliability	
Acceptability	
Remarks	

			Official use only
		1. REFERENCE	
1.1	**Reference**	[redacted] (1971a) The Toxicology of NC 6897: Acute Toxicity of Pure NC 6897 [redacted] Document A90940 6.1.1/03 January 1971 Unpublished	
1.2	**Data protection**	Yes	
1.2.1	Data owner	Bayer CropScience AG	
1.2.2	Companies with letter of access	n.a.	
1.2.3	Criteria for data protection	Data submitted to the MS after 13 May 2000 on existing a.s. for the purpose of its entry into Annex I	
		2. GUIDELINES AND QUALITY ASSURANCE	
2.1	**Guideline study**	No, but the study was conducted in line with good scientific practice.	
2.2	**GLP**	No, the study was conducted prior to the introduction of GLP as a standard requirement.	
2.3	**Deviations**	n.a.	
		3. MATERIALS AND METHODS	
3.1	**Test material**	Bendiocarb	
3.1.1	Lot/Batch number	Batches 15, 24 & 33	
3.1.2	Specification	As given in Section 2	
3.1.2.1	Description	Not specified but bendiocarb is known as a white/beige powder	
3.1.2.2	Purity	Specified as 'pure' without any additional information.	
3.1.2.3	Stability	Not specified, but bendiocarb is not known to decompose at room temperature.	
3.2	**Test Animals**		
3.2.1	Species	Rat, mouse, guinea pig and rabbit	
3.2.2	Strain	Wistar (rat), CFW (mouse) Not specified for guinea pig and rabbit	
3.2.3	Source	Not specified	
3.2.4	Sex	Rat: male and female Mouse: female Guinea pig: female Rabbit: male and female	
3.2.5	Age/weight at study initiation	Rat: males 115-358 g; females 140-350 g Mouse: females 14-19 g Guinea pig: females 262-646 g Rabbit: males 1426-2696 g; females 1940-2354 g	
3.2.6	Number of animals per group	Rat: 2-10 Mouse: 2-4 Guinea pig & rabbit: 2	

3.2.7	Control animals	No	
3.3	**Administration/ Exposure**	Oral	
3.3.1	Postexposure period	24 hours	
3.3.2	Type	Gavage	
3.3.3	Concentration	Rat: females 10, 20, 40, 80, 160 mg/kg bw Rat: males 20, 25, 40, 50, 80, 100 mg/kg bw Mouse: females 16, 32, 64 mg/kg bw Guinea pig: females 25, 50 mg/kg bw Rabbit: females 20, 40 mg/kg bw Rabbit; males 20, 40, 80 mg/kg bw	
3.3.4	Vehicle	Glycerol formal	
3.3.5	Concentration in vehicle	Rat: 4-8% Mouse, guinea pig: 8% Rabbit: 8-20%	
3.3.6	Total volume applied	Volume calculated from dose rate and concentration in vehicle.	
3.3.7	Controls	No	
3.4	**Examinations**	Clinical observations	
3.5	**Method of determination of LD_{50}**	Not specified	
3.6	**Further remarks**	-	
		4. RESULTS AND DISCUSSION	
4.1	**Clinical signs**	Toxic effects were typical of a direct inhibitor of cholinesterase, developing within a few minutes in all species after dosing. Deaths mainly occurred after 5 min – 2 hours and survivors started to recover after ½ - 2 h. Recovery was visually complete well within 24 h.	
4.2	**Pathology**	-	
4.3	**Other**	-	
4.4	**LD_{50}**	Rat: 34-40 mg/kg bw (F) and 45-48 mg/kg bw (M) Mouse: 45 mg/kg bw (F) Guinea pig: 35 mg/kg bw (F) Rabbit: 35 mg/kg bw (F) and 40 mg/kg bw (M)	
		5. APPLICANT'S SUMMARY AND CONCLUSION	
5.1	**Materials and methods**	Wistar rats (M & F; 2-10 animals/sex/group), CFW mice (F; 2-4 animals/group), guinea pigs (F; 2 animals/group) and rabbits (M & F; 2 animals/group) were dosed by single oral gavage with 'pure' bendiocarb dissolved in glycerol formal (4-20%). Male rats received 20-100 mg/kg and females 10-160 mg/kg respectively. Female mice received 16-64 mg/kg, female guinea pigs received 25, 50 mg/kg, male rabbits received 20-80 mg/kg and female rabbits received 20, 40 mg/kg. The duration of the observation period was not specified.	

5.2	**Results and discussion**	Toxic effects were typical of a direct inhibitor of cholinesterase, developing within a few minutes in all species after dosing. Deaths mainly occurred after 5 min - 2 hours and survivors started to recover after ½ - 2 h. Recovery was visually complete well within 24 h. LD_{50} values for the different species are summarized below: - rat: 34-40 mg/kg bw (F) and 45-48 mg/kg bw (M) - mouse: 45 mg/kg bw (F) - guinea pig: 35 mg/kg bw (F) - rabbit: 35 mg/kg bw (F) and 40 mg/kg bw (M) The acute oral toxicity of 'pure' bendiocarb to the four species varies between 34 and 48 mg/kg bw.	
5.3	**Conclusion**		
5.3.1	Reliability	2	
5.3.2	Deficiencies	No	

Table A6.1.1-3 Table for Acute Toxicity

Dose [mg/kg]	Conc. %	Batch No.	Number of dead/number of investigated	Time of death (range)	Observations
Female rat					
10	8	15	0/2	-	
20	8	15	0/4	-	
20	4	33	0/6	-	
40	8	15	3/4	12 min	
40	4	33	3/6	13-20 min	
80	8	15	2/2	13-18 min	
80	4	33	6/6	10 min-0.5h	
160	8	15	2/2	7-9 min	
Male rat					
20	8	24	0/4	-	
25	5-8	15	0/6	-	
40	8	24	1/4	16 min	
50	5-8	15	6/10	18 min	
80	8	24	4/4	14 min-2.5d	
100	5-8	15	2/2	9-13 min	
Female mouse					
16	8	15	0/2	-	
32	8	15	1/4	13 min	
64	8	15	3/4	7-11 min	

Dose [mg/kg]	Conc. %	Batch No.	Number of dead/number of investigated	Time of death (range)	Observations
Female guinea pig					
25	8	15	0/2	-	
50	8	15	2/2	16-28 min	
Male rabbit					
20	8	15	0/2	-	
40	8	15	1/2	37 min	
80	8	15	2/2	19-39 min	
Female rabbit					
20	20	33	0/2	-	
40	20	33	2/2	1.5-2h	
LD_{50} value	Rat 34-40 mg/kg bw (F) and 45-48 mg/kg bw (M) Mouse 45 mg/kg bw (F) Guinea pig 35 mg/kg bw (F) Rabbit 35 mg/kg bw (F) and 40 mg/kg bw (M)				

EVALUATION BY COMPETENT AUTHORITIES	
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	31st August 2006
Materials and methods	As described by the applicant
Conclusion	As described by the applicant
Reliability	2
Acceptability	Acceptable
Remarks	The UK CA notes that the purity of bendiocarb is not specified but is technical grade, which is considered by the applicant to be equivalent to the technical grade chemical produced currently. In accordance with the provisions laid down in Council Directive 67/548/EEC, bendiocarb should be regarded as 'Toxic if swallowed' and labelled with R25 (LD50 > 25 ≤ 200mg/kg).
	COMMENTS FROM …
Date	
Results and discussion	
Conclusion	
Reliability	
Acceptability	
Remarks	

			Official use only
		1. REFERENCE	
1.1	**Reference**	[redacted] (1970) The Toxicology of NC 6897: Acute Toxicity To The Rat of Technical Grade NC 6897 [redacted] Document A90942 6.1.1/04 February 1970 Unpublished	
1.2	**Data protection**	Yes	
1.2.1	Data owner	Bayer CropScience AG	
1.2.2	Companies with letter of access	n.a.	
1.2.3	Criteria for data protection	Data submitted to the MS after 13 May 2000 on existing a.s. for the purpose of its entry into Annex I	
		2. GUIDELINES AND QUALITY ASSURANCE	
2.1	**Guideline study**	No, but the study was conducted in line with good scientific practice.	
2.2	**GLP**	No, the study was conducted prior to the introduction of GLP as a standard requirement.	
2.3	**Deviations**	n.a.	
		3. MATERIALS AND METHODS	
3.1	**Test material**	Bendiocarb	
3.1.1	Lot/Batch number	Batches of technical material 27, 28, 29 & 30	
3.1.2	Specification	As given in Section 2	
3.1.2.1	Description	Not specified but bendiocarb is known as a white/beige powder	
3.1.2.2	Purity	Not specified	
3.1.2.3	Stability	Not specified, but bendiocarb is not known to decompose at room temperature	
3.2	**Test Animals**		
3.2.1	Species	Rat	
3.2.2	Strain	Not specified	
3.2.3	Source	Not specified	
3.2.4	Sex	Male	
3.2.5	Age/weight at study initiation	191-300 g	
3.2.6	Number of animals per group	4	
3.2.7	Control animals	No	
3.3	**Administration/ Exposure**	Oral	
3.3.1	Postexposure period	Not specified	

3.3.2	Type	Gavage	
3.3.3	Concentration	16, 20, 32, 40, 64, 80 or 128 mg/kg bw	
3.3.4	Vehicle	Glycerol formal	
3.3.5	Concentration in vehicle	8%	
3.3.6	Total volume applied	Volume calculated from dose rate and concentration in vehicle	
3.3.7	Controls	No	
3.4	**Examinations**	Clinical observations	
3.5	**Method of determination of LD_{50}**	Not specified	
3.6	**Further remarks**	-	
		4. RESULTS AND DISCUSSION	
4.1	**Clinical signs**	Toxic effects were typical of a direct inhibitor of cholinesterase, developing within a few minutes of dosing. Deaths mainly occurred after 5 min – 2 hours and survivors started to recover after ½ - 2 h. Recovery was visually complete well within 24 h. Mortality occurred at 32 mg/kg and above.	
4.2	**Pathology**	-	
4.3	**Other**	-	
4.4	**LD_{50}**	40 - 64 mg/kg bw	
		5. APPLICANT'S SUMMARY AND CONCLUSION	
5.1	**Materials and methods**	Technical grade bendiocarb was dosed to male rats (4/dose group) via single oral gavage in glycerol at doses of 16, 20, 32, 40, 64, 80 or 128 mg/kg. Animals were observed for an unspecified number of days.	
5.2	**Results and discussion**	Toxic effects were typical of a direct inhibitor of cholinesterase, developing within a few minutes of dosing. Deaths mainly occurred after 5 min - 2 hours and survivors started to recover after ½ - 2 h. Recovery was visually complete well within 24 h. Mortality occurred at 32 mg/kg and above. LD_{50} = 40 - 64 mg/kg bw	
5.3	**Conclusion**		
5.3.1	Reliability	2	
5.3.2	Deficiencies	No	

Table A6.1.1-4 Table for Acute Toxicity

Dose [mg/kg]	Conc. %	Batch No.	Number of dead/number of investigated	Time of death (range)	Observations
Male rat					
16	8	27	0/4	-	
16	8	28	0/4	-	
20	8	29	0/4	-	
20	8	30	0/4	-	
32	8	27	0/4	-	
32	8	28	1/4	15 min	
40	8	29	2/4	15 min	
40	8	30	1/4	13 min	
80	8	29	4/4	10 – 19 min	
128	8	27	4/4	5 – 12 min	
LD_{50} value	40 – 64 mg/kg				

EVALUATION BY COMPETENT AUTHORITIES	
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	31st August 2006
Materials and methods	As described by the applicant
Conclusion	As described by the applicant
Reliability	2
Acceptability	Acceptable
Remarks	The UK CA notes that the purity of bendiocarb is not specified but is technical grade, which is considered by the applicant to be equivalent to the technical grade chemical produced currently. In accordance with the provisions laid down in Council Directive 67/548/EEC, bendiocarb should be regarded as 'Toxic if swallowed' and labelled with R25 (LD50 > 25 ≤ 200mg/kg).
	COMMENTS FROM …
Date	
Results and discussion	
Conclusion	
Reliability	
Acceptability	
Remarks	

			Official use only
		1. REFERENCE	
1.1	**Reference**	[redacted] (1981) The Acute Oral Toxicity of Unformulated Bendiocarb (NC 6897, CR 4799/10) to the Male and Female Mouse [redacted] Document A90477 6.1.1/05 January 1981 Unpublished	
1.2	**Data protection**	Yes	
1.2.1	Data owner	Bayer CropScience AG	
1.2.2	Companies with letter of access	n.a.	
1.2.3	Criteria for data protection	Data submitted to the MS after 13 May 2000 on existing a.s. for the purpose of its entry into Annex I	
		2. GUIDELINES AND QUALITY ASSURANCE	
2.1	**Guideline study**	No, but the study was conducted in line with good scientific practice.	
2.2	**GLP**	No, the study was conducted prior to the introduction of GLP as a standard requirement.	
2.3	**Deviations**	n.a.	
		3. MATERIALS AND METHODS	
3.1	**Test material**	Bendiocarb	
3.1.1	Lot/Batch number	CR 4799/10	
3.1.2	Specification	As given in Section 2	
3.1.2.1	Description	Not specified but bendiocarb is known as a white/beige powder	
3.1.2.2	Purity	91.8%	
3.1.2.3	Stability	The active substance was found to be stable in the test suspension	
3.2	**Test Animals**		
3.2.1	Species	Mouse	
3.2.2	Strain	CD-1	
3.2.3	Source	Charles River U.K., Ltd., Margate, Kent.	
3.2.4	Sex	Male and female	
3.2.5	Age/weight at study initiation	Males: 5 weeks old; 32 – 36 g Females: 4 weeks old; 28 - 30 g	
3.2.6	Number of animals per group	6/sex/dose	
3.2.7	Control animals	Yes	
3.3	**Administration/ Exposure**	Oral	
3.3.1	Postexposure period	14 days	
3.3.2	Type	Gavage	

3.3.3	Concentration	0, 7.1, 10.0, 14.1, 20.0, 28.3, 40.0, 56.6, 80.0 or 113.1 mg/kg bw	
3.3.4	Vehicle	0.5% w/v aqueous gum tragacanth	
3.3.5	Concentration in vehicle	15 mg a.s./ml suspension in 0.5% w/v aqueous gum tragacanth	
3.3.6	Total volume applied	Dose level (mg a.s./kg bw) / Mean individual dose volume (ml/rat): Males / Females 0: 0.240 / 0.212 7.1: 0.0155 / 0.0137 10.0: 0.0233 / 0.0192 14.1: 0.031 / 0.027 20.0: 0.044 / 0.040 28.3: 0.062 / 0.054 40.0: 0.090 / 0.077 56.6: 0.134 / 0.109 80.0: 0.171 / 0.155 113.1: 0.258 / 0.218	
3.3.7	Controls	Vehicle only at 7.5 ml/kg	
3.4	**Examinations**	Clinical observations, necropsy and gross post-mortem examination	
3.5	**Method of determination of LD_{50}**	Weil	
3.6	**Further remarks**	-	
		4. RESULTS AND DISCUSSION	
4.1	**Clinical signs**	In males 3 deaths occurred at 28.3 mg/kg (out of 6 animals), with no surviving animals at 40, 56.6, 80 and 113.1 mg/kg. In females, 1 out of 6 animals died at 20 mg/kg, 2 out of 6 died at 28.3 mg/kg, with only 1 surviving animal at the doses between 40 and 113.1 mg/kg. Observed clinical signs of toxicity seen at 10 mg/kg and above in both sexes, were typical of those expected for a rapidly reversible cholinesterase inhibitor, and included fibrillation and reduced activity. Straub tail and salivation were seen in a few animals, and urinary incontinence was seen at the top dose level only (10/12 animals at 113.1 mg/kg). In all animals exhibiting clinical signs of toxicity, fibrillation was noted first, starting 1-18 min after dosing, with recovery in survivors occurring between 5 min and 2.5 h post dosing.	
4.2	**Pathology**	There were no treatment-related gross pathological findings	
4.3	**Other**	There were no significant variations from control in the bodyweight gains.	
4.4	**LD_{50}**	Male: 28.3 mg/kg bw Female: 28.2 mg/kg bw	
		5. APPLICANT'S SUMMARY AND CONCLUSION	
5.1	**Materials and methods**	CD-1 mice (6 animals/sexe/dose) were dosed by oral gavage with unformulated bendiocarb (purity 91.8%) at doses of 0, 7.1, 10.0, 14.1, 20.0, 28.3, 40.0, 56.6, 80.0 or 113.1 mg/kg in 0.5% aqueous gum tragacanth. Animals were observed for 14 days after dosing for mortality and clinical signs of toxicity, after which they were killed and subjected, to a gross post-mortem examination.	

5.2	**Results and discussion**	In males 3 deaths occurred at 28.3 mg/kg (out of 6 animals), with no surviving animals at 40, 56.6, 80 and 113.1 mg/kg. In females, 1 out of 6 animals died at 20 mg/kg, 2 out of 6 died at 28.3 mg/kg, with only 1 surviving animal at the doses between 40 and 113.1 mg/kg. Observed clinical signs of toxicity seen at 10 mg/kg and above in both sexes, were typical of those expected for a rapidly reversible cholinesterase inhibitor, and included fibrillation and reduced activity. Straub tail and salivation were seen in a few animals, and urinary incontinence was seen at the top dose level only (10/12 animals at 113.1 mg/kg). In all animals exhibiting clinical signs of toxicity, fibrillation was noted first, starting 1-18 min after dosing, with recovery in survivors occurring between 5 min and 2.5 h post dosing. There were no significant variations from control in the bodyweight gains and no treatment-related gross pathological findings. The oral LD_{50} value for male and female mouse was established at approximately 28 mg/kg	
5.3	**Conclusion**		
5.3.1	Reliability	2	
5.3.2	Deficiencies	No	

Table A6.1.1-5 Table for Acute Toxicity

Dose [mg/kg]	Number of dead/ number of investigated	Time of death (range)	Observations
Male mouse			
0	1*/6	3 days	
7.1	0/6	-	
10.0	0/6	-	
14.1	0/6	-	
20.0	0/6	-	
28.3	3/6	7 – 8 min	
40.0	6/6	3 – 11 min	
56.6	6/6	3 – 5 min	
80.0	6/6	3 – 11 min	
113.1	6/6	2 – 4 min	
Female mouse			
0	0/6	-	
7.1	0/6	-	
10.0	0/6	-	
14.1	0/6	-	
20.0	1/6	7 min	
28.3	2/6	4 – 7 min	
40.0	6/6	2 – 8 min	
56.6	5/6	1 – 6 min	
80.0	6/6	3 – 8 min	
113.1	6/6	1 – 6 min	
LD_{50} value:	male 28.3 (24.2-33.0) mg/kg bw female 28.2 (23.4-34.0) mg/kg bw		

* killed following excessive damage to hind legs from fighting