Food and Agriculture Organization
of the United Nations

FAO SPECIFICATIONS AND EVALUATIONS

FOR AGRICULTURAL PESTICIDES

METHIOCARB

4-methylthio-3,5-xylyl methylcarbamate

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DISCLAIMER[1]

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

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

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

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

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

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

[1] This disclaimer applies to all specifications published by FAO.

INTRODUCTION

FAO establishes and publishes specifications* for technical material and related formulations of agricultural pesticides, with the objective that these specifications may be used to provide an international point of reference against which products can be judged either for regulatory purposes or in commercial dealings.

From 1999 onward, the development of FAO specifications follows the **New Procedure**, described first in the 5th edition of the "Manual on the development and use of FAO specifications for plant protection products" and later in the 1st edition of "Manual for Development and Use of FAO and WHO Specifications for Pesticides" (2002) - currently available as 3rd revision of the 1st edition (2016) - , which is available only on the internet through the FAO and WHO web sites.

This **New Procedure** follows a formal and transparent evaluation process. It describes the minimum data package, the procedure and evaluation applied by FAO and the Experts of the FAO/WHO Joint Meeting on Pesticide Specifications (JMPS). [Note: prior to 2002, the Experts were of the FAO Panel of Experts on Pesticide Specifications, Registration Requirements, Application Standards and Prior Informed Consent, which now forms part of the JMPM, rather than the JMPS.]

FAO Specifications now only apply to products for which the technical materials have been evaluated. Consequently from the year 1999 onwards the publication of FAO specifications under the **New Procedure** has changed. Every specification consists now of two parts namely the specifications and the evaluation report(s):

Part One: **The Specification** of the technical material and the related formulations of the pesticide in accordance with chapters 4 to 9 of the "Manual on development and use of FAO and WHO specifications for pesticides".

Part Two: The Evaluation Report(s) of the pesticide, reflecting the evaluation of the data package carried out by FAO and the JMPS. The data are provided by the manufacturer(s) according to the requirements of chapter 3 of the "FAO/WHO Manual on Pesticide Specifications" and supported by other information sources. The Evaluation Report includes the name(s) of the manufacturer(s) whose technical material has been evaluated. Evaluation reports on specifications developed subsequently to the original set of specifications are added in a chronological order to this report.

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

Specifications bear the date (month and year) of publication of the current version. Evaluations bear the date (year) of the Meeting at which the recommendations were made by the JMPS.

* NOTE: PUBLICATIONS ARE AVAILABLE ON THE INTERNET AT (http://www.fao.org/agriculture/crops/core-themes/theme/pests/jmps/ps-new/en/) OR IN HARDCOPY FROM THE PLANT PROTECTION INFORMATION OFFICER.

PART ONE

SPECIFICATIONS

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INFORMATION

METHIOCARB

ISO common name: Methiocarb

Chemical names:

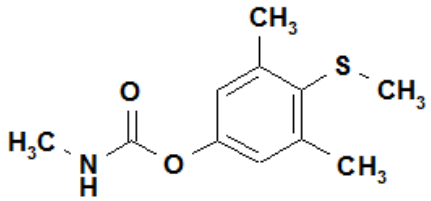
IUPAC: 4-methylthio-3,5-xylyl methylcarbamate

CA: Phenol, 3,5-dimethyl-4-(methylthio)-, methylcarbamate

Synonyms:

Mesurol TC, Mercaptodimethur

Structural formula:



Molecular formula: $C_{11}H_{15}NO_2S$

Relative molecular mass: 225.3

CAS Registry No.: 2032-65-7

CIPAC No.: 165

Identity tests: ^{1}H NMR spectrum

METHIOCARB TECHNICAL MATERIAL

FAO Specification 165 / TC (June 2018*)

This specification, which is PART ONE of this publication, is based on an evaluation of data submitted by the manufacturer whose name is listed in the evaluation report (165/2017). It should be applicable to TC produced by this manufacturer but it is not an endorsement of those products, nor a guarantee that they comply with the specifications. The specification may not be appropriate for the products of other manufacturers. The evaluation report (165/2017) as PART TWO forms an integral part of this publication.

1 Description

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

2 Active ingredient

2.1 Identity tests (165/TC/M/2, CIPAC Handbook D, p.130, 1988)

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

2.2 Methiocarb content (165/TC/M/3, CIPAC Handbook D, p.130, 1988)

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

3 Relevant impurities (Note 1)

4 Physical properties

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

pH range: 5.5 – 8.5

Note 1 There are no relevant impurities to be controlled in products of the manufacturer identified in evaluation report 165/2017. However, methyl isocyanate could potentially occur as a result of certain manufacturing processes. If methyl isocyanate (which has a toxicological cut off limit 0.02%) could occur in the methiocarb TC of other manufacturers, it may be designated as a relevant impurity and a specification clause may be required to limit its concentration.

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

METHIOCARB SUSPENSION CONCENTRATE FOR SEED TREATMENT

FAO Specification 165 / FS (June 2018*)

This specification, which is PART ONE of this publication, is based on an evaluation of data submitted by the manufacturer whose name is listed in the evaluation report (165/2017). It should be applicable to FS produced by this manufacturer but it is not an endorsement of those products, nor a guarantee that they comply with the specifications. The specification may not be appropriate for FS produced by other manufacturers. The evaluation report (165/2017), as PART TWO, forms an integral part of this publication.

1 Description

The material shall consist of a suspension of fine particles of technical methiocarb, complying with the requirements of FAO specification 165/TC (June 2018), in an aqueous phase together with suitable formulants, including colouring matter (Note 1). After gentle stirring or shaking, the material shall be homogeneous (Note 2) and suitable for further dilution with water if necessary.

2 Active ingredient

2.1 **Identity tests** (165/SC/M/2, CIPAC Handbook D, p.133, 1988)

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

2.2 **Methiocarb content** (165/SC/M/3, CIPAC Handbook D, p.133, 1988) (Note 3)

The methiocarb content shall be declared (g/kg or g/l at 20 ± 2ºC, Note 4) and, when determined, the average content measured shall not differ from that declared by more than the appropriate tolerance.

Declared content in g/kg or g/L at 20 ± 2°C	Tolerance
above 250 up to 500	± 5% or of the declared content
above 500 Note: the upper limit is included in the range	± 25 g/kg or g/L of the declared content

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

3.1 **pH range** (MT 75.3, CIPAC Handbook J, p.131, 2000)
pH range: 4.0 to 7.0

3.2 **Pourability** (MT 148.1, CIPAC Handbook J, p.133, 2000)
Maximum "residue": 4 %.

3.3 **Wet sieve test** (MT 185, CIPAC Handbook K, p. 149, 2000) (Note 5)
Maximum: 0.2 % retained on a 75 µm test sieve.

3.4 **Persistent foam** (MT 47.3, CIPAC Handbook O, p. 117, 2017)

If the product is intended to be used after dilution, persistent foam is to be measured at a concentration between 50 and 70% w/v in water. In those conditions, the maximum is 50 mL after 1 min. This clause is not applicable where the product is used without dilution.

3.6 **Adhesion to seeds** (MT 194, CIPAC Handbook N, p. 145, 2011)
The minimum percentage of the methiocarb remaining on the seeds after the test is
Maize: min.: 95%

4 Storage stability

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

After storage at 0 ± 2°C for 7 days, the formulation shall continue to comply with the clause for wet sieve test (3.3).

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

After storage at 54 ± 2°C for 14 days, the determined average active ingredient content must not be lower than 95% relative to the determined average content found before storage (Note 6) and the formulation shall continue to comply with the clauses for:

- pH range (3.1),
- pourability (3.2),
- wet sieve test (3.3),
- adhesion to seeds (3.6)

Note 1 The influence of treatment on germination is of major importance but it is not the subject of a specification clause because no test method is applicable to all types of seeds. To avoid adverse effects, users should apply the formulation strictly according to the recommendations of the manufacturer and should not treat seeds for which effect on germination is not known. Treated seeds should be stored in a suitable container and should be protected from excessive temperature and moisture.
The formulation is expected contain a dye or pigment that permanently colours the seed after treatment (red is recommended). For special purposes however, the dye/pigment can be added at a later stage. In some countries, there may be a legal requirement that a specific colour shall be used. The same colour must not be used for denaturing seeds intended for use as livestock feeding stuffs.

Note 2 Before sampling to verify the formulation quality, inspect the commercial container carefully. On standing, suspension concentrates usually develop a concentration gradient from the top to the bottom of the container. This may even result in the appearance of a clear liquid on the top and/or sediment on the bottom. Therefore, before sampling, homogenize the formulation according to the instructions given by the manufacturer or, in the absence of such instructions, gently shake the commercial container (for example by inverting the closed container several times, large containers must be opened and stirred adequately). After this procedure, the container should not contain a sticky layer of non-dispersed matter at the bottom. A suitable and simple method of checking for a non-dispersed sticky layer ("cake") is by probing with a glass rod or similar device adapted to the size and shape of the container. All the physical and chemical tests must be carried out on a sample taken after the recommended homogenization procedure.

Note 3 The method of analysis for methiocarb in the FS formulation is CIPAC analytical method 165/SC/M/-. The FS formulation being a suspension concentrate for seed treatment, it shares the physical chemical characteristics of an SC formulation. The sample preparation of the FS prior to the analysis is the same as for a SC. The CIPAC analytical method 165/SC/M/- is therefore considered applicable for the FS formulation as well.

Note 4 Unless homogenization is carried out carefully, it is possible for the sample to become aerated. This can lead to errors in the determination of the mass per millilitre, and in calculation of the active ingredient content (in g/l) if methods other than OECD 109 or MT 3.3 are used. If the buyer requires both g/kg and g/l at 20°C, then in case of dispute the analytical results shall be calculated as g/kg.

Note 5 This test should detect coarse particles (e.g. caused by crystal growth) or extraneous materials which could cause blockage of spray nozzles or filters of the application equipment.

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

PART TWO

EVALUATION REPORTS

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METHIOCARB

FAO/WHO EVALUATION REPORT 165/2017

Recommendations

The Meeting recommended:

(i) The specifications for methiocarb TC and FS, proposed by Bayer CropScience and as amended, should be adopted by FAO

(ii) The FAO specifications for methiocarb TC, TK, WP, GR and FS developed under the "Old procedure" and published 1991 should be withdrawn

Appraisal

The Meeting considered data and supporting information submitted in April 2016 by Bayer Crop Science (BCS) for the conversion of the FAO "Old procedure" specifications for methiocarb TC and FS into the corresponding "New procedure" specifications. The company explained that the specifications for methiocarb TK, WP and GR were no longer supported.

The data submitted were broadly in accordance with the requirements of the Manual on development and use of FAO and WHO specifications for Pesticides (2016 - 3rd revision of the 1st edition) and supported the draft specifications.

Methiocarb is a carbamate insecticide, that also has acaricidal, molluscicidal activity, is a bird repellent and acts as acetylcholinesterase inhibitor.

The main formulation type available is the FS (flowable concentrate for seed treatment). Methiocarb is not co-formulated with other pesticides.This formulation is registered and sold in many countries globally but mainly in EU.

Methiocarb was evaluated by the FAO/WHO JMPR in 1981, 1983, 1984, 1985, and 1987, and by the 1998 Meeting within the CCPR periodic review programme. Methiocarb is currently (2017) under review in Europe, and was included in Annex I of the Commission Directive 91/414/EEC effective from 1 October 2007 (Commission Directive 2007/5/EC dated 7 February 2007).

The confidential data presented to the FAO are identical to those submitted for registration in Europe, within the renewal of approval process of active pesticide substances.

The Meeting was provided with commercially confidential information on the manufacturing process and five batch analysis data on all impurities present at or above 1 g/kg, as well as any relevant impurities below 1 g/kg, and their manufacturing limits in the TC. Mass balances ranged from 100.3% to 100.7% in the 5-batch data. The maximum limits for the impurities were supported by the 5-batch data and they are statistically justified. The company declared the minimum purity of the methiocarb TC as 980 g/kg which is statistically justified (mean

value - 3 standard deviation = 989.95 g/kg) and it is higher than the FAO specifications from 1991 (minimum declared: 970.0 g/kg).

The methiocarb content was determined by a reversed phase HPLC method with gradient elution and UV detection. The method was adequately validated following the guideline SANCO 3030/99 rev. 4. The CIPAC method for methiocarb in CIPAC Handbook D is based on reversed phase HPLC on a ODS column with internal standardization and is suitable for the determination of methiocarb in TC, WP, DS, SC and DP. BCS provided a bridging study demonstrating that both the in-house and the CIPAC method give equivalent results for the determination of methiocarb content in the technical material.

The methods for determination of impurities occurring at or higher than 1 g/kg are based on an external standard HPLC method with DAD detection. The content of residual water was determined using the CIPAC-method MT 30.5, Karl-Fischer method using pyridine-free reagents.

As methiocarb does not contain any relevant impurities no methods are required for their determination.

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

The Meeting noted that the method of analysis for methiocarb in the FS formulation was CIPAC analytical method 165/SC/M/-. The company stated that an FS formulation is a suspension concentrate for seed treatment, and as a consequence it shares all the physical chemical characteristics of an SC formulation. The difference is in the intended application target. It is noted that the sample treatment of the FS prior to the analysis remain the same. Therefore it can be concluded that the established CIPAC analytical method 165/SC/M/- is also applicable for the FS formulation.

With respect to the FS specification, the meeting recommended that the clause for suspensibility should be removed, because the product is only slightly diluted, and therefore the use concentration exceeds the upper limit of MT 184 being around 10 %.

Based on the manufacturing pathway, the Meeting considered the potential for low concentrations of methyl isocyanate (MIC) to remain in the technical material; however, the company provided data on levels of methyl isocyanate that demonstrated assays of less than 0.02%, with no peak detected in chromatograms. The Meeting therefore agreed that methyl isocyanate (MIC) will not be listed as a relevant impurity, but will be included in a foot note (toxicological cut off limit 0.02%) in the TC specification, as it is used as part of the method of manufacture.

An *in vitro* mutagenicity study (Ames test, OECD 471) for methiocarb TC has been provided. The test results allowed the conclusion that methiocarb TC does not induce reverse mutations in the strains tested.

SUPPORTING INFORMATION
FOR
EVALUATION REPORT 165/2017

USES

Methiocarb is an insecticide, acaricide, molluscicide and bird repellent of the carbamate family and an acetylcholinesterase inhibitor. It is used in maize, corn, several vegetables and fruits and ornamental plants mainly against *Oscinella frit*, *Frankliniella occidentalis*, *Thrips tabaci* and as a bird repellent.

The main formulation type available is the FS (flowable concentrate for seed treatment). Methiocarb is not co-formulated with other pesticides.This formulation is registered and sold in numerous countries globally but mainly in EU.

Identity of the active ingredient

ISO common name:

Methiocarb

Chemical name(s):

IUPAC:

4-methylthio-3,5-xylyl methylcarbamate

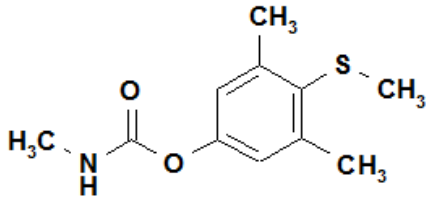
CA:

Phenol, 3,5-dimethyl-4-(methylthio)-, methylcarbamate

Synonym(s):

Methiocarb TC, Mesurol TC, Mercaptodimethur

Structural formula:



Molecular formula: $C_{11}H_{15}NO_2S$

Relative molecular mass: 225.3

CAS Registry No.: 2032-65-7

CIPAC No.: 165

Identity tests: ^{1}H NMR spectrum

Table 1 Physical-chemical properties of pure methiocarb

Parameter	Value(s) and Conditions	Purity (%)	Method Reference (and technique if the reference gives more than one)	Study number
Vapour pressure	1.5×10^{-5} Pa at 20 °C (extrapolated) 3.6×10^{-5} Pa at 25 °C (extrapolated)	99.5	OECD 104 ≅ EC A.4 Very slightly volatile	M-003906-01-1
Melting point	118 - 119 °C	99.5	EC A.1 (melt microscope)	M-055091-01-1
Temperature of decomposition	DTA indicated melting occurred between 120 and 150°C with measurable exothermic decomposition. TGA indicated melting below 150°C. Weight loss (evaporation, sublimation) commenced at 130°C. Methiocarb may be considered stable at room temperature.	99.1	OECD 113	M-003926-01-2
Solubility in water	27 mg/L at 20 °C 18 mg/L at 20 °C pH dependence not investigated due to the active substance not dissociating and degrading at pH 9	99.5 99.5	OECD 105 ≅ EC A.6 (column method)	M-003916-01-1 M-055091-01-1
Octanol/water partition coefficient	at 20 °C unbuffered: Pow 1200, log Pow 3.08 pH 4: Pow 1300, log Pow 3.11 pH 7: Pow 1500, log Pow 3.18 pH 9: degradation	99.5	OECD 107 ≅ EC A.8 (shaking method) Log P_{ow} result indicates the potential for methiocarb to be fat soluble	M-003922-01-1

Hydrolysis characteristics	at 25 °C pH 5: $t_{1/2}$ = 321 days pH 7: $t_{1/2}$ = 24 days pH 9: $t_{1/2}$ = 0.2 days	98.0	EPA, subdivision N § 161-1 (OECD 111) One of the major hydrolysis products was methiocarb-phenol with small quantities of methiocarb-sulfoxide and methiocarb-sulfoxide-phenol being detected	M-013292-02-1
Photolysis characteristics	in water at pH 5.0: DT_{50} : 128 days (photolysis only, 88 days incl. hydrolysis, dark controls 238 days)	99.4	EPA, subdivision N § 161-2	M-013358-01-1
Dissociation characteristics	Methiocarb shows neither basic nor acidic properties in aqueous systems. It is not possible to specify a pKa value for Methiocarb in water. No dissociation.	99.5	OECD 112	M-003914-01-2
Solubility in organic solvents	(g/L at 20 °C): n-heptane 0.57 dichloromethane >250 2-propanol 42 xylene 20 1-octanol 31 acetone 144 acetonitrile 67 ethylacetate 87 polyethyeneglycol 72 dimethylsulfoxide >250	99.5	CIPAC MT 157, part 2	M-055091-01-1

Table 2 Chemical composition and properties of methiocarb technical material (TC)

Manufacturing process, maximum limits for impurities ≥ 1 g/kg, 5 batch analysis data	Confidential information supplied and held on file by FAO. Mass balances were 100.3 – 100.7 % and no unidentified impurities were reported.			
Declared minimum methiocarb content	980 g/kg			
Relevant impurities ≥ 1 g/kg and maximum limits for them	None			
Relevant impurities < 1 g/kg and maximum limits for them:	None			
Stabilisers or other additives and maximum limits for them:	None			
Parameter	Value and conditions	Purity (%)	Method Reference	Study number
Melting temperature range of the TC and/or TK	see Table 1 (not applicable for TK)	-	-	-
Solubility in organic solvents	see Table 1	-	-	-

FORMULATIONS AND CO-FORMULATED ACTIVE INGREDIENTS

The main formulation type available is the FS (flowable concentrate for seed treatment).
Methiocarb is not co-formulated with other pesticides.
This formulation is registered and sold in numerous countries globally but mainly in EU.

METHODS OF ANALYSIS AND TESTING

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

CONTAINERS AND PACKAGING

No special requirements for containers and packaging have been identified.

EXPRESSION OF THE ACTIVE INGREDIENT

The content of the active ingredient methiocarb is expressed as methiocarb.

ANNEX 1

HAZARD SUMMARY PROVIDED BY THE PROPOSER

Notes

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

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

Table 3 Toxicology profile of methiocarb TC, based on acute toxicity, irritation and sensitization

Species	Test	Purity % Note[2]	Guideline, duration, doses and conditions	Result	Study number
Rat (Sprague-Dawley), male and female	oral	98.0%	At the time of study conduct no guideline was in place , but in general accordance with OECD Guideline 401 (1981)	LD_{50} = 33 – 47 mg/kg bw	M-026415-01-1
Rat (Wistar), male and female	oral	99.0%	At the time of study conduct no guideline was in place	Not determined	M-009378-01-1
Rabbit (NZW), male and female	dermal to abraded skin	99.0%	At the time of study conduct no guideline was in place	LD_{50} > 2000 mg/kg bw	M-015282-01-1
Rat (Wistar), male and female	dermal	98.1%	At the time of study conduct no guideline was in place , but in general accordance with OECD Guideline 402 (1981)	LD_{50} = > 5000 mg/kg bw	M-010260-01-1
Rat (Sprague-Dawley), male and female	inhalation	97.5% - 99.3%	US-EPA-FIFRA Sec. 158.135, Guideline 81-3; in general accordance with OECD 403 (1981)	LC_{50} = 585 mg/m^3 (males) LC_{50} = 433 mg/m^3 (females)	M-009885-01-1
Rabbit (NZW), not stated	skin irritation	99.0%	abraded & non-abraded skin, 24 h exposure At the time of study conduct no guideline was in place	Not irritating	M-015323-01-1
Rabbit (NZW), not stated	eye irritation	99.0%	At the time of study conduct no guideline was in place, but in general accordance with OECD Guideline 405 (1987)	Not irritating	M-015323-01-1
Guinea pig (DHPW), male	skin sensitisation (Maximisation test)	97.8%	Not stated, but substantially compliant with OECD Guideline 406 (1992)	Not sensitizing	M-008929-01-1
Guinea pig (Dunkin Hartley), male	skin sensitisation (Buehler test)	97.5% - 99.3%	EPA Health Effects Test Guidelines (Federal Register, Vol. 50 No. 188); OECD guidelines (1981) in general accordance with 406 (1981)	Not sensitizing	M-010126-01-1

[2] Note: Purity is the content of pure active ingredient in the technical material, expressed as a percentage.

Species	Test	Purity % Note[2]	Guideline, duration, doses and conditions	Result	Study number
BALB/c 3T3 cells	In vitro phototoxicity	98.2%	OECD 432; Commission Regulation (EC) No. 440/2008, B 41; Committee for Proprietary Medicinal Products (CPMP) Note for Guidance on Photosafety testing, EMEA, CPMP/SWP/398/01	Not phototoxic	M-536022-01-1

Table 4 Toxicology profile of methiocarb technical material based on repeated administration (subacute to chronic)

Species	Test	Purity % Note[3]	Guideline, duration, doses and conditions	Result	Study number
Short-term toxicity					
Rat (Wistar), male and female	4-week oral, gavage	99.0%	At the time of study conduct no guideline was in place 0-1-3-10-mg/kg bw/day Examinations for plasma, RBC and brain AChE activity	Both sexes: NO(A)EL = 3 mg/kg bw/d LO(A)EL = 10 mg/kg bw/d Main findings observed at LO(A)EL: ↓ of plasma, erythrocyte and brain AChE activity; cholinergic symptoms, No accumulation of AChE inhibition	M-009378-01-1
Rat (Sprague-Dawley), female	4-week oral, gavage	97.0%	At the time of study conduct no guideline was in place 0-0-5-2 mg/kg bw/day (5d/week) Examinations for plasma and RBC AChE activity	NO(A)EL = 0.5 mg/kg bw/d LO(A)EL = 2 mg/kg bw/d Main findings observed at LO(A)EL: Tremors (during the first days only), ↓ (> 25%) of plasma and erythrocyte AChE activity (during the first week only)	M-009348-01-1

[3] Note: Purity is the content of pure active ingredient in the technical material, expressed as a percentage.

Species	Test	Purity % Note[3]	Guideline, duration, doses and conditions	Result	Study number
Dog (Beagle), male and female	29-day, oral, capsule	97.0%	At the time of study conduct no guideline was in place 0-0.05-0.5 mg/kg bw/day (capsule) Examinations for plasma and RBC AChE activity	Both sexes: NO(A)EL = 0.05 mg/kg bw/d LO(A)EL = 0.5 mg/kg bw/d Main findings observed at LO(A)EL: Cholinergic signs, slight ↓ of erythrocyte AChE activity (2 h post application)	M-009577-01-1
Rat (Sprague-Dawley), male and female	16-week, oral, diet	N/A	At the time of study conduct no guideline was in place 0-5-10-50 ppm	Both sexes: NO(A)EL = 1 mg/kg bw/d (10 ppm) LO(A)EL = 50 ppm Main findings observed at LO(A)EL: ↓ of AChE activity in submaxillary glands with significant ↓ of plasma AChE activity (both sexes)	M-016133-01-1
Rat, male and female	13-week + 4 weeks recovery, oral, diet	98.9% – 99.4%	OECD 408 (1998); JMAFF 59 NohSan No.4200; Directive 83/571/EEC, Annex I; US-EPA OPPTS 870.3100 (1998) 0-100-300-900 ppm 0-7.34-22.72-67.59 mg/kg bw/day (males) 0-10.0-30.71-90.74 mg/kg bw/day (females)	Male: NO(A)EL = 7.34 mg/kg bw/d LO(A)EL = 22.72 mg/kg bw/d Female: NO(A)EL = 10 mg/kg bw/d LO(A)EL = 30.71 mg/kg bw/d Main findings observed at LO(A)EL: stat. sign. ↓ glucose (m), ↓ urine volume, ↑ absolute adrenal weights (f) due to lower bw	M-088469-01-1

Species	Test	Purity % Note[3]	Guideline, duration, doses and conditions	Result	Study number
Dog (Beagle), male and female	3-months, oral, diet	98.9% – 99.4%	US-EPA-FIFRA Guideline 82-1; US-EPA-TSCA 40 CFR Section 798.2650; US-EPA OPPTS 870.3150; OECD 409; JMAFF 59 NohSan No. 4200; US-FDA Toxicological Principles for the Safety Assessment of Direct Food Additives and Color Additives Used in Food, Appendix II Guidelines For Toxicological Testing 0-10-50-250 ppm 0-0.3-1.32-6.46 mg/kg bw/day (males) 0-0.25-1.33-6-5.91 mg/kg bw/day (females)	NO(A)EL = 50 ppm LO(A)EL = 250 ppm Male: NO(A)EL = 1.32 mg/kg bw/d LO(A)EL = 6.46 mg/kg bw/d Female: NO(A)EL = 1.33 mg/kg bw/d LO(A)EL = 5.90 mg/kg bw/d Main findings observed at LO(A)EL: Vomiting, trend of ↓ food consumption, marked ↓ bw gain, non-significant ↑ N-DEM (m), stat. sign. ↓ erythrocyte AChE activity	M-030181-01-1
Dog (Beagle), male and female	2-year, oral, diet	98.4% - 99.4%	At the time of study conduct no guideline was in place, but in general accordance with OECD 452 (1981) 0-15 (5)**-60-240 ppm 0-0-2-2.2-8.6 mg/kg bw/day ** The lowest test dose was reduced from 15 to 5 ppm after 15 days due to the depression of plasma AChE activity at 15 ppm	Both sexes: NO(A)EL = 2.2 mg/kg bw/d (60 ppm) LO(A)EL = 8.6 mg/kg bw/d (240 ppm) Main findings observed at LO(A)EL: Cholinergic effects, vomiting, ↓ food consumption associated with ↓ plasma AChE activity	M-010201-01-1
Rabbit (NZW), male and female	21-day, dermal	97.5% - 99.3%	US-EPA FIFRA 40 CFR, Part 158.340, 82-2 In accordance with OECD 410 (1981) 0-60-150-375 mg/kg bw/day (6h/day)	Both sexes: NO(A)EL = 150 mg/kg bw/d LO(A)EL = 375 mg/kg bw/d Main findings observed at LO(A)EL: stat. sign. ↓ plasma AChE activity (m), ↓ food consumption No effects on erythrocyte and brain AChE activity	M-009558-01-1

Species	Test	Purity % Note[3]	Guideline, duration, doses and conditions	Result	Study number
Rabbit (NZW), male and female	21-day, dermal	97.5% - 99.3%	US-EPA FIFRA 40 CFR, Part 158.340, 82-2 In accordance with OECD 410 (1981) 0-500 mg/kg bw/day (6h/day)	Both sexes: NO(A)EL < 500 mg/kg bw/d LO(A)EL = 500 mg/kg bw/d Main findings observed at LO(A)EL: ↓ Food consumption, ↓ bw (f), stat. sign. ↓ plasma AChE activity (not biol. relevant) No effects on erythrocyte and brain AChE activity	M-009552-01-1
Rat (Wistar), male and female	3-week, inhalation	97.9%	Not stated, but substantially compliant with OECD Guideline 412 (1981) 0-solvent control – 6-23-96 mg/m^3 15 x 6 h/day	Males: NO(A)EL = 6 mg/m^3 bw/d LO(A)EL = 23 mg/m^3 bw/d Females: NO(A)EL = 23 mg/m^3 bw/d LO(A)EL = 96 mg/m^3 bw/d Main findings observed at LO(A)EL: stat. sign. ↓ plasma AChE activity (m), moderate ↓ plasma AChE activity (f), moderate ↓ brain AChE activity (m)	M-009879-01-1

Species	Test	Purity % Note[3]	Guideline, duration, doses and conditions	Result	Study number
Long-term toxicity and Carcinogenicity					
Rat (Wistar), male and female	2-year, oral, diet	98.6% - 99.2%	Not stated, but substantially compliant with OECD Guideline 453 (1981) and also in general accordance with OECD 453 (2009) 0-67-200-600 ppm 0-3.27/4.98-9.3/13.9-29/42 mg/kg bw/day (m/f)	NO(A)EL = 200 ppm LO(A)EL = 600 ppm Male: NO(A)EL = 9.3 mg/kg bw/d LO(A)EL = 29 mg/kg bw/d Female: NO(A)EL = 13.9 mg/kg bw/d LO(A)EL = 42 mg/kg bw/d Main findings observed at LO(A)EL: Slight stat. sign. ↓ bw, (–6.2%/–7.6% (m/f)) No carcinogenicity was observed (in line with conclusions from JMPR 1998).	M-009809-02-1
Mouse (NMRI), male and female	2-year, oral, diet	98.1% - 98.8%	Not stated, but substantially compliant with OECD Guideline 453 (1981) and also in general accordance with OECD 453 (2009) 0-67-200-600 ppm 0-14.67/19.8-42.8/57-131.9/173.3 mg/kg bw/day (m/f)	NO(A)EL = 67 ppm LO(A)EL = 200 ppm Male: NO(A)EL = 14.7 mg/kg bw/d LO(A)EL = 57 mg/kg bw/d Female: NO(A)EL = 19.8 mg/kg bw/d LO(A)EL = 42.8 mg/kg bw/d Main findings observed at LO(A)EL: ↑ ALT indicating liver toxicity Slight stat. sign. ↓ of plasma AChE (only after 1 month) No carcinogenicity was observed (in line with conclusions from JMPR 1998).	M-008825-02-1

Reproductive toxicity					
Rat (FB 30), male and female	multi generation, diet	Not available	At the time of study conduct no guideline was in place 0-30-100-300 ppm	Both sexes: NO(A)EL = 15 mg/kg bw/d (300 ppm) LO(A)EL > 15 mg/kg bw/d (>300 ppm) Main findings observed at LO(A)EL: No significant maternal, fetal or reproductive toxicity at the highest dose tested	M-010170-01-1
Rat (Wistar), male and female	1- generation, diet, dose rangefinder	98.9% – 99.4%	US-EPA OPPTS 870.3800; OECD 416 (Draft); OECD 415 0-100-300-900 ppm 0-6.1/8.1-18.5/22.4-52.4/76.5 mg/kg bw/day	NO(A)EL = 100 ppm LO(A)EL = 300 ppm Male: NO(A)EL = 6.1 mg/kg bw/d LO(A)EL = 18.5 mg/kg bw/d Female: NO(A)EL = 8.1 mg/kg bw/d LO(A)EL = 22.4 mg/kg bw/d Main findings observed at LO(A)EL: Maternal: retarded body weight gain, ↓ plasma AChE in week 4 Offspring: retarded body weight (up to -21%) and body weight gain reproduction: no effects	M-035507-01-1

Rat (Wistar), male and female	2-generation, diet	98.9% – 99.4%	US-EPA OPPTS 870.3800; OECD 416; JMAFF (1985) 0-50-150-500 ppm F0: 0-4.3/5.5-12.5/15.4-41/52.1 mg/kg bw/day (m/f) F1: 0-4.2/6-13.5/18.6-43.5/61.3 mg/kg bw/day (m/f)	NO(A)EL = 50 ppm LO(A)EL = 150 ppm Male: NO(A)EL = 4.3 mg/kg bw/d LO(A)EL = 12.5 mg/kg bw/d Female: NO(A)EL = 5.5 mg/kg bw/d LO(A)EL = 18.6 mg/kg bw/d Main findings observed at LO(A)EL: Maternal: ↓ body weights during lactation (F1) offspring: ↓ litter size (F1) reproduction: ↓ lactation index (F2&F2b)#	M-036790-01-1

Rat (Wistar), male and female	2-generation, diet	98.6% - 99.4 %	US-EPA OPPTS 870.3800; OECD 416; JMAFF (1985) 0-50-150-500 ppm F0: 0-4.6/6.9-14.8/21.3-55.1/83.9 mg/kg bw/day (m/f) F1: 0-7.6/5.6-22.3/16.3-89/69 mg/kg bw/day (m/f)	Dam: NO(A)EL = 4.6 mg/kg bw/d (50 ppm) LO(A)EL = 21.3 mg/kg bw/d (150 ppm) Fetal: NO(A)EL = 14.8/21.3 mg/kg bw/d (150 ppm) LO(A)EL = 55.10/83.9 mg/kg bw/d (500 ppm) Main findings observed at LO(A)EL: Maternal: ↓ RBC AChE offspring: ↓ body weight (F1&F2), clinical signs, ↓ lactation index (F1) ↓ plasma & RBC AChE slightly delayed vaginal opening and balano-preputial separation in F2 due to lower pup weights ↑ incidence of pups with poor condition (food pasted mouth/nose and empty stomach or intestine)	M-064945-01-1
Rat (Wistar), dam and fetal	special subchronic, diet	98.9% – 99.4%	Not conducted according to a special Guideline. 0-50-150-500 ppm	Fetal: NO(A)EL = 50 ppm LO(A)EL = 150 ppm Main findings observed at LO(A)EL: Offspring: ↓ plasma AChE in both sexes	M-088195-01-1

Rat (FB 30), females	Developmental, oral, gavage	98.2% - 99.4%	At the time of study conduct no guideline was in place 0-1-3-10 mg/kg bw/day (GD 6-15)	Dam: NO(A)EL = 3 mg/kg bw/d LO(A)EL = 10 mg/kg bw/d Fetal: NO(A)EL = 10 mg/kg bw/d LO(A)EL > 10 mg/kg bw/d Main findings observed at LO(A)EL: Maternal: significant ↓ body weight No teratogenicity was observed (in line with conclusions from JMPR 1998).	M-009391-02-1
Rat (Wistar), female	Developmental, oral, gavage	98.9% – 99.4%	OPPTS 870.3700; OECD 414; Health Canada PMRA DACO 4.5.2; JMAFF 12-Nousan No. 8147; Guideline 87/302/EEC 0-0.5-1.5-5.0 mg/kg bw/day (GD 6-19)	Dam: NO(A)EL = 0.5 mg/kg bw/d LO(A)EL = 1.5 mg/kg bw/d Fetal: NO(A)EL = 5 mg/kg bw/d LO(A)EL > 5 mg/kg bw/d Main findings observed at LO(A)EL: Maternal: cholinergic signs and muscle fasciculation No teratogenicity was observed (in line with conclusions from JMPR 1998).	M-038693-01-1

Rabbit (NZW), femalesl	Developmental, oral, gavage	98.1% - 98.8%	At the time of study conduct no guideline was in place 0-1-3-10 mg/kg bw/day (GD 6-18)	Dam: NO(A)EL = 3 mg/kg bw/d LO(A)EL = 10 mg/kg bw/d Fetal: NO(A)EL = 10 mg/kg bw/d LO(A)EL > 10 mg/kg bw/d Main findings observed at LO(A)EL: Maternal: clinical signs (increased respiratory rate, loss of coordination, muscular tremors), marked transient ↓ body weight No teratogenicity was observed (in line with conclusions from JMPR 1998).	M-010210-01-1
Rabbit (Chinchilla), females	Developmental, dermal	99.6%	US-EPA Series 83-3; OECD 414 0-250-500-750 mg/kg bw/day 6h/day (GD 6-18)	Dam: NO(A)EL = 50 mg/kg bw/d LO(A)EL = 250 mg/kg bw/d Fetal: NO(A)EL = 50 mg/kg bw/d LO(A)EL > 250 mg/kg bw/d Main findings observed at LO(A)EL: Maternal: ↓ food consumption, ↓ body weight gain Offspring: ↓ birth weight no teratogenicity	M-009985-03-1

The lactation indices were generally lower in F2/F2b pups in all groups including control in comparison to F1 and HCD.

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

Test system	Test	Purity % Note[4]	Guideline, duration, doses and conditions	Result	Study number
S. typhimurium TA98, TA100, TA1535, TA1537	*in vitro* mutagenicity test (Ames test)	98.5%	At the time of study conduct no guideline was in place +/–S9 mix Up to 2500 µg/plate	negative	M-009542-01-1
S. typhimurium TA98, TA100, TA1535, TA1537	*in vitro* mutagenicity test (Ames test)	97.6% - 98.4%	Not stated, but substantially compliant with OECD Guideline 471 (1983) +/–S9 mix Up to 12.500 µg/plate	negative	M-010145-01-1
S. typhimurium TA98, TA100, TA1535, TA1537, TA102	*in vitro* mutagenicity test (Ames test)	98.2%	OECD 471; Commission Regulation (EC) No. 440/2008, B13/14; US-EPA 712-C-98-247, OPPTS 870.5100 +/–S9 mix Up to 5000 µg/plate	negative	M-524333-01-1
Chinese hamster ovary (CHO) cells	*in vitro* mammalian cell gene mutation test (HGPRT)	98.2% - 99.4%	Not stated, but substantially compliant with OECD Guideline 476 (1984) Up to 30 µg/mL (with S9) Up to 60 µg/mL (without S9)	negative	M-008916-01-1
E. coli	*in vitro* Pol A-Test	98.6%	Not according to a specific guidleine +/–S9 mix Up to 10.000 µg/plate	negative	M-010151-01-1
Primary rat hepatocytes	*in vitro* Unscheduled DNA synthesis (UDS) assay	97.5% - 99.3%	US-EPA Guideline 84-4; in accordance with OECD 482 (1986) Up to 60 µg/mL (without S9)	negative	M-009902-01-1

[4] Note: Purity is the content of pure active ingredient in the technical material, expressed as a percentage.

Test system	Test	Purity % Note[4]	Guideline, duration, doses and conditions	Result	Study number
Chinese hamster ovary (CHO) cells	*in vitro* Mammalian chromosome aberration test	98.2% - 99.4%	Not stated, but substantially compliant with OECD Guideline 473 (1983) Up to 50.8 µg/mL (+S9) up to 197 µg/mL (–S9)	Positive (at high concentrations)	M-010190-01-1
Chinese hamster ovary (CHO) cells	*in vitro* Sister chromatid exchange (SCE)	97.0%	Not stated, but in general accordance with OECD Guideline 479 (1986) Up to 40 µg/mL	negative	M-010134-01-1
NMRI mouse bone marrow cells	*in vivo* micronucleus test (bone marrow)	98.5%	At the time of study conduct no guideline was in place. But in general accordance with OECD 474 (1983) 0-5-10-20 mg/kg bw	negative	M-009544-01-1 (M-536382-01-1 suppl. Historical Control data)
NMRI mouse	*in vivo* dominant lethal test	98.5%	At the time of study conduct no guideline was in place. 6 mg/kg bw (oral gavage, single application)	negative	M-009533-01-1

Table 6 Ecotoxicology profile of methiocarb technical material

Species	Test	Purity % Note[5]	Guideline, duration, doses and conditions	Result	Study number
Fish					
Rainbow trout *Oncorhynchus mykiss*	Acute, semi-static	98.6% – 99.4%	OECD No. 203 Directive 92/69/EEC, C.1	LC_{50}: 1.1 mg a.s./L (nominal)	M-021375-01-1
Bluegill sunfish *(Lepomis macrochirus)*	Acute, flow through	98.6% – 99.4%	OECD No. 203 Directive 92/69/EEC, C.1	LC_{50}: 0.65 mg a.s./L (nominal)	M-021382-01-1
Rainbow trout *Oncorhynchus mykiss*	ELS, static	97.0%	Not stated, but substantially compliant with OECD Guideline 210 (1992)	NOEC: 0.05 mg a.s./L (nominal) NOEC based on clinical signs of intoxication; all other NOEC and LOEC-values, based on weight, time to swim-up, hatching and survival were ≥ 0.100 mg/L.	M-012845-01-1
Bluegill Sunfish (*Lepomis macrochirus*)	BCF, flow through	>99%	Not stated, but substantially compliant with OECD Guideline 305 (1996)	BCF: 60 - 90	M-012920-01-1
Invertebrates					
Daphnia magna	Acute, semi-static	98.6% – 99.4%	OECD No. 202, Part I Directive 92/69/EEC, C.2	EC_{50}: 0.0077 mg a.s./L (mean measured)	M-034439-01-1
Daphnia magna	Chronic, flow through	98.7%	U.S. EPA-FIFRA, 40 CFR, Section 158.145 Guideline 72-4	NOEC: 0.0001 mg a.s./L (mean measured)	M-012825-01-1
Green Algae					
Desmodesmus subspicatus	acute	98.6% – 99.4%	OECD No. 201 Directive 92/69/EEC, C.3	EbC_{50}: 0.82 mg a.s./L (mean measured) ErC_{50}: 2.2 mg a.s./L (mean measured)	M-024134-01-1
Nematocera					

[5] Note: Purity is the content of pure active ingredient in the technical material, expressed as a percentage.

Chironomus riparius	Acute, static	98.2%	OECD Guideline No. 235 (Guideline for Testing of Chemicals, "Chironomus sp., Acute Immobilisation Test, adopted July 28, 2011)	EC_{50}: 0.103 mg a.s./L (mean measured)	M-493345-01-1
Chironomus riparius	Chronic, static	98.2% - 99.5%	OECD Guideline 219: "Sediment-Water Chironomid Toxicity Test Using Spiked Water" (adopted 13 April 2004)	NOEC (emergence): 0.160 mg a.s./L (nominal)	M-268292-01-1
Arthropods					
Folsomia candida	reproduction	FS 500 496 g/L	ISO 11267 ISO Soil Quality - Inhibition of reproduction of Collembola (Folsomia Candida) by soil pollutants, 1999	NOEC: 37.5 mg a.s./kg dry weight soil	M-062852-01-1
Hypoaspis aculeifer	reproduction	FS 500 503.2 g/L	OECD 226: Guidelines for the testing of chemicals - Predatory Mite (Hypoaspis (Geolaelaps) aculeifer) reproduction test in artificial soil, adopted October 03, 2008	NOEC: 20.12 mg a.s./kg dry weight soil	M-469819-01-1
Apis mellifera (honey bee)	acute and conctact	99.8%	EPPO Guideline No. 170	LD50 – oral: .0.47 µg a.s./bee LD50 – contact: 0.23 µg a.s./bee	M-013166-01-1
Apis mellifera (honey bee)	acute and conctact	99.4% - 99.7%	OECD 213 and 214 (1998)	LD50 – oral: .0.08 µg a.s./bee LD50 – contact: 0.43 µg a.s./bee	M-308072-01-1
Bumble bee	contact	98.2%	No specific guidelines are available. The test design is based on OEPP/EPPO 170 (4) (2010) and OECD Guideline 214 (1998), and on the review article of VAN DER STEEN (2001)	LD50 – contact: 19.3 µg a.s./ bumble bee	M-479538-01-1
Honey bee brood	*in vitro,* acute	98.2%	GLP compliant study based on the OECD TG 237 (2013)	NOED: 0.064 µg a.s./larva LD50: 0.547 µg a.s./larva	M-514260-01-1
Earthworms					

Eisenia fetida	acute	98.6% – 99.4%	OECD-Guideline No. 207 "OECD-Guideline for Testing Chemicals," "Earthworm, Acute Toxicity Tests", April 4, 1984	The LC50 (14d): 1322 mg/kg dry weight substrate NOEC: 32 mg/kg dry weight substrate LOEC: 1 mg/kg dry weight substrate	M-023185-01-1
Eisenia fetida	reproduction	FS 500 503.2 g/L	OECD, Guideline for the testing of chemicals No. 222, Earthworm, Reproduction Test (adopted April 13, 2004) ISO-Guideline 11268-2, Soil quality - Effects of pollutants on earthworm (Eisenia fetida) - Part 2: Determination of effects on reproduction, International Organization for Standardization, 1998	NOEC: ≥ 0.447 mg a.s./kg dry weight soil	M-465336-01-1
Birds					
Japanese quail *(Coturnix coturnix)*	acute, oral	98.6%	Not applicable	LD_{50}: 5 mg a.s./kg bw	M-012876-01-2
Bobwhite quail *Colinus virginianus*	21-day, oral, diet	99.1%	Commission Directive 96/46/EC of 16 July 1996 amending Council Directive 91/414/EEC	NOEC: 213 mg a.s./kg diet NOED: 17.8 mg a.s./kg bw/d	M-039501-01-1
Bobwhite quail *Colinus virginianus*	Reproduction, 25-weeks, diet	97.0%	Not stated, but substantially compliant with OCSPP 850.2300	NOEC: ≥ 50 mg a.s./kg diet NOED: ≥ 4.95 mg a.s./kg bw/d	M-012904-01-1
Mallard duck *(Anus platyrhynchos)*	Reproduction, 19-weeks, diet	97.0%	Not stated, but substantially compliant with OECD Guideline OCSPP 850.2300	NOEC: 50 mg a.s./kg diet NOED: 4.51 mg a.s./kg bw/d	M-012909-01-1

The WHO hazard classification of Methiocarb is: highly hazardous, class 1B, and the GHS classification for oral exposure, Category 2, fatal if swallowed.
Classification of the mixture in accordance with Regulation (EC) No 1272/2008 on classification, labelling and packaging of substances and mixtures, as amended:

Acute toxicity:	Category 2; H300 Fatal if swallowed.
	Category 2; H330 Fatal if inhaled
Acute aquatic toxicity:	Category 1; H400 Very toxic to aquatic life.
Chronic aquatic toxicity:	Category 1; H410 Very toxic to aquatic life with long lasting effects.

Based on the table of tox data shown above Category 2 H300 (Fatal if swallowed) and H330 (Fatal if inhaled) are appropriate under 1272/2008 as proposed by the company. It is noted however that the current classification under 1272/2008 is Acute tox category 3 H301 (toxic if swallowed). Given that the company have proposed a hazard classification of Category 2; H300 (Fatal if swallowed) and Category 2; H330 (Fatal if inhaled), and this is supported by the data, it is appropriate to support this classification for this FAO Specification.

Labelling in accordance with Regulation (EC) No 1272/2008 on classification, labelling and packaging of substances and mixtures, as amended.
Hazard label for supply/use required.
Hazardous components which must be listed on the label:
• Methiocarb

Signal word: Danger
Hazard statements

H300 + H330	Fatal if swallowed or inhaled.
H410	Very toxic to aquatic life with long lasting effects.

Precautionary statements

P273	Avoid release to the environment.
P284	Wear respiratory protection.
P304 + P340	IF INHALED: Remove person to fresh air and keep comfortable for breathing.
P310	Immediately call a POISON CENTER/doctor/physician.
P501	Dispose of contents/container in accordance with local regulation.

ANNEX 2
REFERENCES

References (sorted by study number)

Study number	Authors	year	Study title, Company conducting the study, Study identification number/Report identification number. GLP/GEP
M-003906-01-1		1988	Vapour pressure curve of methiocarb Bayer AG, Leverkusen, Germany Bayer CropScience, Report No.: PC744, GLP/GEP: no, unpublished
M-003916-01-1		1989	Water solubility of methiocarb Bayer AG, Wuppertal, Germany Bayer CropScience, Report No.: PC746, GLP/GEP: no, unpublished
M-003922-01-1		1995	Partition coefficient of methiocarb in octanol - water as a function of pH Bayer AG, Leverkusen, Germany Bayer CropScience, Report No.: PC1117, GLP/GEP: yes, unpublished
M-003926-01-2		1986	Thermal stability of the agrochemical active ingredient methiocarb (Mercaptodimethur) Bayer AG, Leverkusen, Germany Bayer CropScience, Report No.: PC749, GLP/GEP: no, unpublished
M-008825-02-1		1983	H 321 (Mercaptodimethur, the active ingredient of Mesurol) - Chronic toxicity study on mice (2-year feeding experiment) Bayer CropScience, Report No.: 11908, GLP/GEP: no, unpublished
M-008916-01-1		1989	H 321 (c.n. Methiocarb) - Mutagenicity study for the detection of induced forward mutations in the CHO-HGPRT assay in vitro Bayer CropScience, Report No.: 18280, GLP/GEP: no, unpublished

M-008929-01-1		1984	H321 (c.n. mercaptodimethur) - Study for skin-sensitising effect on guinea pigs Bayer CropScience, Report No.: 13125, GLP/GEP: yes, unpublished
M-009348-01-1		1981	Cholinesterase no-effect level of Mesurol and Mesurol sulfoxide in female rats Bayer CropScience, Report No.: BC199, GLP/GEP: yes, unpublished
M-009378-01-1		1973	Mercaptodimethur - Effect of acute and subacute oral doses on Acetylcholinesterase-activity in plasma, erythrocytes and brain of rats Bayer CropScience, Report No.: 4284, GLP/GEP: no, unpublished
M-009391-02-1		1971	Mesurol active ingredient (BAY 37344) - Study for embryotoxic effects in rats in oral administration Bayer CropScience, Report No.: 3133, GLP/GEP: no, unpublished
M-009533-01-1		1979	H 321 - Dominant lethal study on male mouse to test for mutagenic effects Bayer CropScience, Report No.: 8395, GLP/GEP: no, unpublished
M-009542-01-1		1978	H 321 (active ingredient of Mesurol) - Salmonella/microsome test for determination of point mutations Bayer CropScience, Report No.: 7978, GLP/GEP: no, unpublished
M-009544-01-1		1979	H 321 (active ingredient of Mesurol) - Micronucleus test for mutagenic effect on mice Bayer CropScience, Report No.: 8426, GLP/GEP: no, unpublished
M-009552-01-1		1989	A 21-day dermal toxicity study of Mesurol technical in albino rabbits Bayer CropScience, Report No.: BC1160, GLP/GEP: yes, unpublished
M-009558-01-1		1988	A 21-day dermal toxicity study of Mesurol technical in albino rabbits Bayer CropScience, Report No.: BC1084, GLP/GEP: yes, unpublished

M-009577-01-1		1981	Cholinesterase evaluation study of Methiocarb technical and Methiocarb sulfoxide in dogs Bayer CropScience, Report No.: BC202, GLP/GEP: yes, unpublished
M-009809-02-1		1981	H 321 (Mercaptodimethur, the active ingredient of Mesurol) - Chronic toxicity on rats (2-year feeding experiment) Bayer CropScience, Report No.: 10039, GLP/GEP: no, unpublished
M-009879-01-1		1983	H 321 (Mesurol active ingredient) - Subacute inhalation study with rats Bayer CropScience, Report No.: 12120, GLP/GEP: no, unpublished
M-009885-01-1		1987	Acute four-hour inhalation toxicity study with Mesurol technical in rats Bayer CropScience, Report No.: BC870, GLP/GEP: yes, unpublished
M-009902-01-1		1988	Unscheduled DNA synthesis in rat primary hepatocytes - Mesurol Bayer CropScience, Report No.: BC1007, GLP/GEP: yes, unpublished
M-009985-03-1		1992	Embryotoxicity (including teratogenicity) with H 321 (c. n. Methiocarb) in the rabbit (dermal application) Bayer CropScience, Report No.: R5627, GLP/GEP: yes, unpublished
M-010126-01-1		1988	EPA/OECD dermal sensizitation test of Mesurol technical in guinea pigs Bayer CropScience, Report No.: BC1015, GLP/GEP: yes, unpublished
M-010134-01-1		1986	Mesurol technical - Sister chromatid exchange assay in chinese hamster ovary (CHO) cells Bayer CropScience, Report No.: BC790, GLP/GEP: yes, unpublished
M-010145-01-1		1986	H 321 (c.n.Mercaptodimethur) - Salmonella/microsome test for point mutagenic effects Bayer CropScience, Report No.: 14205, GLP/GEP: yes, unpublished
M-010151-01-1		1983	H 321, Mercaptodimethur (the active ingredient of Mesurol) - Study of DNA damage using the E.coli Pol A- test Bayer CropScience, Report No.: 11928, GLP/GEP: yes, unpublished

M-010170-01-1		1970	BAY 37344 - Generation studies on rats Bayer CropScience, Report No.: 2208, GLP/GEP: no, unpublished
M-010190-01-1		1990	Mutagenicity test on H 321 in an in vitro cytogenetic assay measuring chromosomal aberration frequencies in chinese hamster ovary (CHO) cells with a confirmatory assay Bayer CropScience, Report No.: R4980, GLP/GEP: yes, unpublished
M-010201-01-1		1980	H 321 (Mesurol active ingredient - mercaptodimethur) - Chronic toxicity study on dogs (two-year feeding experiment) Bayer CropScience, Report No.: 9626, GLP/GEP: no, unpublished
M-010210-01-1		1981	H 321 - Effects of oral administration upon pregnancy in the rabbit - 2. main study Bayer CropScience, Report No.: R2173, GLP/GEP: yes, unpublished
M-010260-01-1		1977	H 321 - Determination of acute toxicity (LD50) Bayer CropScience, Report No.: MO-99-010732, GLP/GEP: no, unpublished
M-012825-01-1		1988	Chronic toxicity of 14C-Mesurol to *Daphnia magna* under flow-through test conditions Bayer CropScience, Report No.: 96731, GLP/GEP: yes, unpublished
M-012845-01-1		1985	Toxicity of methiocarb (Mesurol) technical to early life stages of rainbow trout Bayer CropScience, Report No.: 682, GLP/GEP: yes, unpublished
M-012876-01-2		1983	Bird toxicity, oral / Japanese quail (*Coturnix coturnix japonica*) with H 321 Bayer CropScience, Report No.: VW-77, GLP/GEP: no, unpublished
M-012904-01-1		1982	Methiocarb reproduction study with bobwhite quail Bayer CropScience, Report No.: 329, GLP/GEP: no, unpublished
M-012909-01-1		1982	Methiocarb reproduction study with mallard duck Bayer CropScience, Report No.: 325, GLP/GEP: no, unpublished

M-012920-01-1		1974	Accumulation and persistence of residues in bluegill fish exposed to Mesurol-^{14}C Bayer CropScience, Report No.: 40096, GLP/GEP: no, unpublished
M-013166-01-1		1995	Testing toxicity to honeybee - *Apis mellifera* L. (laboratory) according to EPPO Guideline No. 170 - Methiocarb (techn.) Bayer CropScience, Report No.: 95 10 48 059, GLP/GEP: yes, unpublished
M-013292-02-1		1981	Mesurol hydrolysis in sterile buffers Bayer CropScience, Report No.: MR69272, GLP/GEP: no, unpublished
M-013358-01-1		1988	Photochemical degradation of [14C] mesurol in aqueous solutions Bayer CropScience, Report No.: M1053, GLP/GEP: no, unpublished
M-015282-01-1		1972	The dermal toxicity of Mesurol technical and Mesurol 75% wettable powder to rabbits Bayer CropScience, Report No.: 34477, GLP/GEP: no, unpublished
M-015323-01-1		1970	The skin and eye irritating properties of BAY 37344 technical to rabbits Bayer CropScience, Report No.: 28304, GLP/GEP: no, unpublished
M-016133-01-1		1962	Subacute (16-weeks) oral toxicity of Bayer 37344 to male and female rats Bayer CropScience, Report No.: 9456, GLP/GEP: no, unpublished
M-021375-01-1		2000	Acute toxicity of methiocarb to rainbow trout (Oncorhynchus mykiss) in a 96-hour semi-static test Bayer CropScience, Report No.: 729347, GLP/GEP: yes, unpublished
M-021382-01-1		2000	Acute toxicity of methiocarb to bluegill (*Lepomis macrochirus*) in a 96 hour flow-through test Bayer CropScience, Report No.: 729360, GLP/GEP: yes, unpublished
M-023185-01-1		2000	Acute toxicity of methiocarb (tech.) to earthworms (*Eisenia fetida*) Bayer CropScience, Report No.: MPE/RG 342/00, GLP/GEP: yes, unpublished

M-024134-01-1		2000	Toxicity of methiocarb to *Scenedesmus subspicatus* in a 72-hour algal growth inhibition test Bayer CropScience, Report No.: 729325, GLP/GEP: yes, unpublished
M-026415-01-1		1979	Acute oral toxicity of Mesurol technical and metabolites to rats Bayer CropScience, Report No.: MOB32, GLP/GEP: no, unpublished
M-030181-01-1		2000	Technical grade Mesurol - A subchronic toxicity feeding study in the beagle dog Bayer CropScience, Report No.: BC9387, GLP/GEP: yes, unpublished
M-034439-01-1		2000	Acute toxicity of methiocarb to *Daphnia magna* in a 48-hour semi-static immobilization test Bayer CropScience, Report No.: 740002, GLP/GEP: yes, unpublished
M-035507-01-1		2002	H 321 - One-generation study in Wistar rats - Pilot study for a two-generation study Bayer CropScience, Report No.: 31755, GLP/GEP: yes, unpublished
M-036790-01-1		2002	H 321 - Two-generation study in Wistar rats Bayer AG, Wuppertal, Germany Bayer CropScience, Report No.: 31760, GLP/GEP: yes, unpublished
M-038693-01-1		2002	Technical grade Methiocarb (Mesurol) - A prenatal developmental toxicity study in the Wistar rat Bayer CropScience, Report No.: 110923, GLP/GEP: yes, unpublished
M-039501-01-1		2002	Technical Mesurol: A subacute dietary test with bobwhite quails Bayer CropScience, Report No.: 110982, GLP/GEP: no, unpublished
M-055091-01-1		2001	Melting point, boiling point, density, surface tension and solubility in representative organic solvents of Methiocarb Bayer CropScience, Report No.: 1400320972, GLP/GEP: yes, unpublished
M-062852-01-1		2002	Methiocarb FS 500: Effects on reproduction of the collembola *Folsomia candida* in artificial soil Bayer CropScience, Report No.: 13151016, GLP/GEP: yes, unpublished

M-064945-01-1		2002	H 321 - Two-generation study in Wistar rats (supplementary study to the two-generation study T4069306) Bayer CropScience, Report No.: AT00047, GLP/GEP: yes, unpublished
M-088195-01-1		2003	H 321 - Special subchronic study in Wistar rats (A feeding study where F1 rats received H 321 during their pre- and postnatal development and the up to post-weaning week twelve) Bayer CropScience, Report No.: AT00341, GLP/GEP: yes, unpublished
M-088469-01-1		2001	H 321 - Study for subchronic oral toxicity in rats (feeding study over 13 weeks and 4 weeks recovery period) Bayer CropScience, Report No.: 31598, GLP/GEP: yes, unpublished
M-268292-01-1		2006	*Chironomus riparius* 28-day chronic toxicity test with Methiocarb (tech.) in a water-sediment system using spiked water Bayer CropScience, GLP/GEP: yes, unpublished
M-308072-01-1		2008	Effects of methiocarb technical (acute contact and oral) on honey bees (*Apis mellifera* L.) in the laboratory Bayer CropScience, Report No.: 44011035, GLP/GEP: yes, unpublished
M-360693-03-1	FAO/ WHO	2010	Manual on development and use of FAO and WHO specifications for pesticides - second revision of the first edition FAO/WHO, Joint Meeting on Pesticides Specifications (JMPS), Rome, GLP/GEP: n.a., published
M-465336-01-1		2013	Methiocarb FS 500 G: Effects on reproduction and growth of earthworms *Eisenia fetida* in artificial soil Bayer CropScience, Report No.: 82592022, GLP/GEP: yes, unpublished
M-469819-01-1		2013	Methiocarb FS 500 G: Effects on reproduction of the predatory mite *Hypoaspis aculeifer* in artificial soil Bayer CropScience, Report No.: 82591089, GLP/GEP: yes, unpublished
M-479538-01-1		2014	Methiocarb (tech.): Acute contact toxicity to the bumble bee, *Bombus terrestris* L. under laboratory conditions Bayer CropScience, Report No.: S13-05155, GLP/GEP: yes, unpublished

M-493345-01-1		2014	Acute toxicity of methiocarb (tech.) to larvae of *Chironomus riparius* in a 48 h static laboratory test system Bayer CropScience, Report No.: EBMEN038, GLP/GEP: yes, unpublished
M-514260-01-1		2015	Honey bee (*Apis mellifera* L.) larval toxicity test on methiocarb, technical, single exposure Bayer CropScience, Report No.: 87511032, GLP/GEP: yes, unpublished
M-524333-01-1		2015	Methiocarb, technical: *Salmonella typhimurium* reverse mutation assay Bayer CropScience, Report No.: 1690601, GLP/GEP: yes, unpublished
M-536022-01-1		2015	Methiocarb, technical: Cytotoxicity assay in vitro with BALB/c 3T3 cells: Neutral red (NR) test during simultaneous irradiation with artificial sunlight Bayer CropScience, Report No.: 1690602, GLP/GEP: yes, unpublished
M-536382-01-1		2015	Historical control data for the *in vivo* micronucleus test Bayer CropScience, GLP/GEP: no, unpublished