

**WHO SPECIFICATIONS AND EVALUATIONS  
FOR PUBLIC HEALTH PESTICIDES**

**PIRIMIPHOS-METHYL**

**O-2-diethylamino-6-methylpyrimidin-4-yl-O,O-  
dimethyl phosphorothioate**



**World Health  
Organization**

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## Disclaimer<sup>1</sup>

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

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

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

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

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

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

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<sup>1</sup> This disclaimer applies to all specifications published by WHO.

## INTRODUCTION

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

From 2002, the development of WHO specifications follows the **New Procedure**, described in the 1st edition of Manual for Development and Use of FAO and WHO Specifications for Pesticides (2002). This **New Procedure** follows a formal and transparent evaluation process. It describes the minimum data package, the procedure and evaluation applied by WHO and the experts of the “FAO/WHO Joint Meeting on Pesticide Specifications” (JMPS).

WHO Specifications now only apply to products for which the technical materials have been evaluated. Consequently, from the year 2002 onwards the publication of WHO specifications under the **New Procedure** has changed. Every specification consists now of two parts, namely the specifications and the evaluation report(s):

**Part One:** The Specification of the technical material and the related formulations of the pesticide in accordance with chapters 4 to 9 of the 1<sup>st</sup> edition of the “FAO/WHO Manual on Pesticide Specifications.”

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

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

**Specifications bear the date (month and year) of publication of the current version. Dates of publication of the earlier versions, if any, are identified in a footnote. Evaluations bear the date (year) of the meeting at which the recommendations were made by the JMPS.**

\* Footnote: The publications are available on the Internet under <http://www.who.int/whopes/quality/en/>.

**PART ONE**  
**SPECIFICATIONS**

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PIRIMIPHOS-METHYL

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## PIRIMIPHOS-METHYL

### INFORMATION

#### ISO common names

pirimiphos-methyl (E-ISO, BSI, ANSI, ESA)

pirimiphos-méthyl ((m) F-ISO)

#### Synonyms

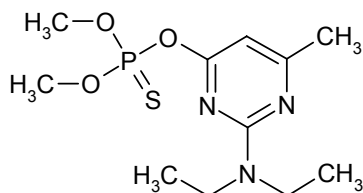
none

#### Chemical names

*IUPAC* O-2-diethylamino-6-methylpyrimidin-4-yl-O,O-dimethyl phosphorothioate

*CA* O-[2-(diethylamino)-6-methyl-4-pyrimidinyl] O,O-dimethyl phosphorothioate

#### Structural formula



#### Empirical formula

$C_{11}H_{20}N_3O_3PS$

#### Relative molecular mass

305.3

#### CAS Registry number

29232-93-7

#### CIPAC number

239

#### Identity tests

UV, IR, NMR and mass spectra. In UV, molar extinction coefficients ( $\epsilon M^{-1} cm^{-1}$ ) in methanol are: 220 nm,  $3.39 \times 10^3$ ; 247 nm,  $2.24 \times 10^4$ ; 301 nm,  $3.69 \times 10^3$ .

# PIRIMIPHOS-METHYL TECHNICAL MATERIAL

WHO Specification 239/TC (April 2006\*)

*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 (239/2004). It should be applicable to relevant products of the company 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, (239/2004) as PART TWO, forms an integral part of this publication.*

## 1 Description

The material shall consist of pirimiphos-methyl together with related manufacturing impurities, and shall be a clear or faintly turbid, mobile, red-brown liquid at temperatures above 18°C, free from visible extraneous matter and added modifying agents, except stabilizers (Note 1).

## 2 Active ingredient

- 2.1 **Identity tests** (239a/TC/M/2, CIPAC Handbook 1C, p.2193, 1985; MT 164, CIPAC Handbook F, p.406, 1995)

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 **Pirimiphos-methyl content** (239a/TC/M/3, CIPAC Handbook 1C p.2193, 1985)

The pirimiphos-methyl content shall be declared (not less than 880 g/kg, Note 2) and, when determined, the average measured content shall not be lower than the declared minimum content.

## 3 Relevant impurities

- 3.1 **O,O-dimethyl phosphorochloridothioate** (DMPCT, R305032, CAS No. 2524-03-0) (Note 3)

Maximum: 5 g/kg.

- 3.2 **O,O,S-trimethyl phosphorodithioate** (MeOOSPS, R305910, CAS No. 2953-29-9) (Note 3)

Maximum: 5 g/kg.

- 3.3 **O,O,S-trimethyl phosphorothioate** (MeOOSPO, R348532, CAS No. 152-20-5) (Note 3)

Maximum: 5 g/kg.

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\* Specifications may be revised and/or additional evaluations may be undertaken. Ensure the use of current versions by checking at: <http://www.who.int/whopes/quality/en/>.

3.4 **O,O,O-trimethyl phosphorothioate** (MeOOOPS, R065249, CAS No. 152-18-1) (Note 3)

Maximum: 5 g/kg

3.5 **O-2-diethylamino-6-methylpyrimidin-4-yl-O,S-dimethyl phosphorothioate** (R037292, *iso*-pirimiphos-methyl, CAS No. 76471-79-9) (Note 3)

Maximum: 5 g/kg.

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

Maximum: 2 g/kg.

#### 4 Physical properties

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

Maximum acidity: 3 g/kg calculated as H<sub>2</sub>SO<sub>4</sub>.

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Note 1 Stabilizers are added to the technical material to prevent degradation in storage. For public health applications, odour suppressants are also added to minimize the formation of volatile sulfur compounds. The identity and concentrations of stabilizers are not part of the WHO specification but, if required, the manufacturer should be contacted for details and the appropriate methods of analysis.

Note 2 The declared value takes into account the addition of stabilizers.

Note 3 The analytical method for determination of these relevant impurities is presented in Appendix 1.

# PIRIMIPHOS-METHYL EMULSIFIABLE CONCENTRATE

WHO Specification 239/EC (April 2006\*)

*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 (239/2004). It should be applicable to relevant products of the company 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, (239/2004) as PART TWO, forms an integral part of this publication.*

## 1 Description

The material shall consist of technical pirimiphos-methyl, complying with the requirements of WHO specification 239/TC (April 2006), dissolved in suitable solvents, together with any other necessary formulants. It shall be in the form of a stable homogeneous liquid, free from visible suspended matter and sediment, to be applied as an emulsion after dilution in water.

## 2 Active ingredient

- 2.1 **Identity tests** (239a/EC/M/2, CIPAC Handbook 1C, p.2197, 1985; MT 164, CIPAC Handbook F, p.406, 1995)

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 **Pirimiphos-methyl content** (239a/EC/M/3, CIPAC Handbook 1C, p.2197, 1985)

The pirimiphos-methyl content shall be declared (g/kg or g/l at  $20 \pm 2^\circ\text{C}$ , Note 1) and, when determined, the average content measured shall not differ from that declared by more than the following tolerances.

Declared content in g/kg or g/l at $20 \pm 2^\circ\text{C}$	Tolerance
above 100 up to 250	$\pm 6\%$ of the declared content
above 250 up to 500	$\pm 5\%$ of the declared content
Note. In each range the upper limit is included	

## 3 Relevant impurities

- 3.1 **O,O-dimethyl phosphorochloridothioate** (DMPCT, R305032, CAS No. 2524-03-0) (Note 2)

Maximum: 0.5% of the pirimiphos-methyl content found under 2.2.

- 3.2 **O,O,S-trimethyl phosphorodithioate** (MeOOSPS, R305910, CAS No. 2953-29-9) (Note 2)

Maximum: 0.5% of the pirimiphos-methyl content found under 2.2.

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\* Specifications may be revised and/or additional evaluations may be undertaken. Ensure the use of current versions by checking at: <http://www.who.int/whopes/quality/en/>.

- 3.3 **O,O,S-trimethyl phosphorothioate** (MeOOSPO, R348532, CAS No. 152-20-5) (Note 2)

Maximum: 0.5% of the pirimiphos-methyl content found under 2.2.

- 3.4 **O,O,O-trimethyl phosphorothioate** (MeOOOPS, R065249, CAS No. 152-18-1) (Note 2)

Maximum: 0.5% of the pirimiphos-methyl content found under 2.2.

- 3.5 **O-2-diethylamino-6-methylpyrimidin-4-yl-O,S-dimethyl phosphorothioate** (R037292, *iso*-pirimiphos-methyl, CAS No. 76471-79-9) (Note 2)

Maximum: 0.5% of the pirimiphos-methyl content found under 2.2.

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

Maximum: 5 g/kg.

#### 4 Physical properties

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

Maximum acidity: 1 g/kg calculated as H<sub>2</sub>SO<sub>4</sub>.

- 4.2 **Emulsion stability and re-emulsification** (MT 36.1.1, CIPAC Handbook F, p.108, 1995) (Note 3)

The formulation, when diluted at 30 ± 2°C with CIPAC Standard Waters A and D, shall comply with the following:

Time after dilution	Limits of stability, MT 36.1
0 h	Initial emulsification complete
0.5 h	'Cream', maximum: 0.1 ml
2 h	'Cream', maximum: 0.1 ml 'Free oil': nil
24 h	Re-emulsification complete
24.5 h	'Cream', maximum: 2 ml 'Free oil', maximum: 2 ml
Note: in applying MT 36.1, tests after 24 h are required only where results at 2 h are in doubt.	

- 4.3 **Persistent foam** (MT 47.2, CIPAC Handbook F, p.152, 1995) (Note 4)

Maximum: 60 ml after 1 min.

#### 5 Storage stability

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

After storage at 0 ± 2°C for 7 days, the volume of solid and/or liquid which separates shall not be more than 0.3 ml.

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

After storage at  $54 \pm 2^\circ\text{C}$  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 5), and the formulation shall continue to comply with the clauses for:

- O-2-diethylamino-6-methylpyrimidin-4-yl-O,S-dimethyl phosphorothioate (*iso*-pirimiphos-methyl) (3.5),
- acidity (4.1),
- emulsion stability and re-emulsification (4.2).

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Note 1 If the buyer requires both g/kg and g/l at  $20^\circ\text{C}$ , then in case of dispute the analytical results shall be calculated as g/kg.

Note 2 The analytical method for determination of these relevant impurities is presented in Appendix 1.

Note 3 This test will normally only be carried out after the heat stability test 5.2.

Note 4 The test should be carried out at the highest application concentration.

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

## PART TWO

### EVALUATION REPORTS

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#### PIRIMIPHOS-METHYL

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WHO SPECIFICATIONS AND EVALUATIONS FOR  
PUBLIC HEALTH PESTICIDES

**PIRIMIPHOS-METHYL**

EVALUATION REPORT 239/2004

**Recommendations**

The Meeting recommended the following.

- (i) Existing FAO specifications for pirimiphos-methyl TC and EC should be withdrawn.
- (ii) Existing WHO specifications for pirimiphos-methyl TC, EC and WP should be withdrawn.
- (iii) The proposed specifications for pirimiphos-methyl TC and EC, as amended, should be adopted by FAO and WHO.

**Appraisal**

The data for pirimiphos-methyl were evaluated for the review of existing WHO specifications for TC, EC and WP (WHO/SIT/30.R1, WHO/SIF/52.R1 and WHO/SIF/53.R1, 1999) and existing FAO specifications for TC and EC (239/a/TC/S and 239/a/EC/S, 1988). Proposed specifications for pirimiphos-methyl TC and EC, and the supporting data were submitted by Syngenta Crop Protection AG, in 2003. The data submitted were in accordance with the requirements of the manual (FAO/WHO, 2002) and supported the draft specifications.

Pirimiphos-methyl is no longer patent protected.

Pirimiphos-methyl is slightly volatile, has low solubility in water and is readily soluble in organic solvents. In aqueous solution, hydrolysis is pH dependent, being fairly rapid at pH 4, very slow at pH 7 and slow at pH 9. Photolysis is very rapid. Pirimiphos-methyl is weakly basic, with pKa of 4.3.

The Meeting was provided with commercially confidential information on the manufacturing process and 5-batch analysis data on all impurities present at or above 1 g/kg. Mass balances were high: 99.6-100.2%. The data were declared to be identical to those submitted to for registration in the EU, the USA and rest of the world. These data, and those for physico-chemical, toxicological and ecotoxicological properties, were confirmed as being identical to those submitted for registration in the UK (although there were certain differences in interpretation, as noted in the hazard summary, above).

The manufacturer proposed that *O,O*-dimethyl phosphorochloridothioate (DMPCT, R305032), *O,O,S*-trimethyl phosphorodithioate (MeOOSPS-triester, R305910), *O,O,S*-trimethyl phosphorothioate (MeOOSPO-triester, R348532) and water should be considered as relevant impurities. The Meeting also considered two other impurities, *O,O,O*-trimethyl phosphorothioate (R065249, CAS No. 152-18-1) and *O*-

2-diethylamino-6-methylpyrimidin-4-yl-O,S-dimethyl phosphorothioate (R037292, “iso-pirimiphos-methyl” CAS No. 76471-79-9), as potentially relevant and (with the exception of water) sought the advice of WHO/PCS on all of the relevant impurity candidates.

The manufacturer provided summaries of two series of acute and sub-acute toxicity data on DMPCT (Table 6). The studies were conducted in 1971, prior to the introduction of standard protocols and GLP but, because the data from the two series correlate well, the manufacturer considered them to provide good evidence of the toxicology of DMPCT.

**Table 1. Acute and sub-acute toxicity of DMPCT from studies conducted in 1971**

Test and duration	Manufacturer and study report No.	
	Stauffer Chemical Co., T-1707 (1971)	ICI IHRL, HO/IH/T/894
	Result (species)	
Acute oral	LD <sub>50</sub> = 1260 mg/kg (rat)	LD <sub>50</sub> = 1300 mg/kg (rat)
Acute dermal	LD <sub>50</sub> = 2150 mg/kg (rabbit)	LD <sub>50</sub> = 330–650 mg/kg (rat)
Acute inhalation (4hr)	LD <sub>50</sub> equivalent to 0.57 mg/l (rat)	-
Skin irritation	Severe (rabbit)	Irritant, (rat)
Eye irritation	Severe to corrosive (rabbit)	Severe (rabbit)
Skin sensitization	-	Sensitizer (Stevens protocol), (Guinea pig)
14-day sub-acute oral	-	3/14 animals died. On day 7 there was a 40% decrease in plasma and RBC cholinesterase. Ulceration in fore-stomachs (rat)
21-day sub-acute inhalation (6 h/day, 5 days a week for 3 weeks)	-	Evidence of cholinesterase inhibition down to 20 ppm; evidence of pulmonary inflammation down to 5 ppm. NOEL = 1 ppm (rat)

DMPCT is irritant to skin and eyes and has properties not shared by the active ingredient, including skin sensitization. The manufacturer confirmed that the batch of pirimiphos-methyl used for some important longer-term toxicological studies (oncogenicity in mouse; rat multi-generation; rabbit developmental study) contained 3.2 g/kg DMPCT. Thus the manufacturer concluded that the toxicological significance of DMPCT as an impurity had been adequately tested in longer term studies.

WHO/PCS secretariat considered the evidence on DMPCT (WHO/PCS 2005). It concluded that DMPCT has acute oral toxicity similar to that of pirimiphos-methyl but that, in contrast to pirimiphos-methyl, it is strongly irritating and may be a skin sensitizer. On this basis, it should therefore be considered a relevant impurity. WHO/PCS secretariat also considered the proposed maximum limit of 5 g/kg for DMPCT. It noted that GHS guidelines (GHS 2003) do not require mixtures to be labelled as skin or eye irritants if they containing less than 10 g/kg of an irritating component. On this basis, the proposed maximum of 5 g/kg would be acceptable as the specification limit for DMPCT in pirimiphos-methyl. However, GHS guidelines indicate two limits for skin sensitizers, 10 g/kg and 1 g/kg, without a clear indication of which should apply in any particular case. The proposed limit of 5 g/kg is thus between the two GHS guideline limits. WHO/PCS secretariat concluded that, the

proposed limit was borderline but acceptable. The Meeting agreed with the WHO/PCS conclusions and noted that the concentration of DMPCT would not increase during storage.

MeOOOPS, MeOOSPO, and MeOOSPS are all more toxic than pirimiphos-methyl ( $LD_{50}$  = 562, 47, 628 and 1400 mg/kg bw, respectively) and therefore WHO/PCS secretariat was of the opinion that these three triester impurities should be considered relevant. The manufacturing specification for each of the triesters was <5 g/kg. At or below this level, they were not expected to contribute significantly to the overall toxicity of the pirimiphos-methyl. The most toxic of them, MeOOSPO, only slightly exceeded the 10% threshold for calculated increase in overall hazard (the criterion usually applied by the JMPS) and WHO/PCS secretariat recommended that the 5/kg limit was appropriate for all three triesters. The Meeting agreed.

The  $LD_{50}$  of *iso*-pirimiphos-methyl was not known but the ratio of the acute toxicity hazards of P=O and P=S analogues of many organophosphorus compounds is in the range 3:1 to 20:1 (Gallo & Lawryk 1991). Considering the TC only, a minimum active ingredient content of 880 g/kg implies a theoretical maximum concentration of *iso*-pirimiphos-methyl of 120 g/kg. If *iso*-pirimiphos-methyl is only 3x as hazardous as pirimiphos methyl (i.e. at the lower end of Gallo & Lawryk's range), the calculated overall hazard of a mixture containing it at 120 g/kg would be about 40% more than that for the active ingredient, which exceeds the 10% threshold used by the JMPS to determine relevance. On this basis, WHO/PCS secretariat considered that the impurity should be designated as relevant and the Meeting agreed.

The original manufacturing specification for *iso*-pirimiphos-methyl was 15 g/kg. If this limit was applied in FAO/WHO specifications, and if *iso*-pirimiphos-methyl is actually 20x as toxic as pirimiphos-methyl (the upper end of Gallo & Lawryk's range), the calculated overall increase in hazard would be 30%, implying that the 15 g/kg limit may be unacceptable. The measured concentration of *iso*-pirimiphos-methyl in pirimiphos-methyl TC was 2.8-3.9 g/kg, in the 5 batches tested. A 5 g/kg limit implies a maximum calculated contribution of 10% to the overall hazard. As this did not exceed the threshold, no additional data were required to support a limit of 5 g/kg and it was recommended as appropriate by WHO/PCS secretariat. The Meeting agreed.

In principle, the concentration of *iso*-pirimiphos-methyl in pirimiphos-methyl could increase during storage, especially at elevated temperature. The manufacturer stated that epoxidized soybean oil is added as a stabilizer to inhibit the isomerization reaction. As it is technically difficult to determine that sufficient stabilizer is present, the Meeting agreed that the clause for storage at elevated temperature, in formulation specifications, should include a requirement for continued compliance with the clause for *iso*-pirimiphos-methyl.

The stabilizer also inhibits degradation of pirimiphos-methyl to volatile sulfur compounds, responsible for offensive odours. These compounds may also be produced during manufacture and, for this reason, an odour suppressant is normally added to products for use in public health. The identity and concentration of the stabilizers were stated to be not critical and the Meeting agreed that it was not appropriate to include them in the specifications.

The manufacturer stated that water must be regarded as a relevant impurity in order to: minimize degradation of pirimiphos-methyl, especially if the level of stabilizer

drops for any reason during storage; enable production of a satisfactory EC; and minimize the development of offensive odours. The Meeting agreed that water should be considered a relevant impurity in the TC and EC.

The Meeting considered the existing and proposed specifications.

TC. The Meeting welcomed the proposed minimum content of active ingredient (880 g/kg), which was higher than that of the existing FAO and WHO specifications (860 g/kg). With the exception of water, for which the proposed limit was unchanged, no relevant impurities were identified in the existing specification, although the existing WHO specification indicated that stabilizers were added to inhibit the formation of *iso*-pirimiphos-methyl.

EC. The proposed specification was broadly similar to the existing FAO and WHO specifications, though it no longer specified products >500 g/kg and included clauses for the relevant impurities. Proposed limits for emulsion stability were identical to those of the existing FAO specification but better than those of the existing WHO specification (which, in principle, could have permitted the separation of 2 ml oil). The proposed clause for storage stability allowed 5% degradation during the test, whereas the existing specifications required continued compliance with the clause for active ingredient content.

Analytical methods for determination of pirimiphos-methyl in the TC and EC are full CIPAC methods (CIPAC 239a/TC/M/3; 239a/EC/M/3). The analytical method for determination of the five organophosphorus relevant impurities in the TC and EC, which is based on <sup>31</sup>P NMR, has been peer validated. Values for RSD<sub>r</sub> were 1.9-6.0% and those for RSD<sub>R</sub> were 7.1-22%. Given that DMPCT is readily hydrolyzed, and that *iso*-pirimiphos-methyl formation from pirimiphos-methyl is temperature/time dependent, and that sample storage/treatment conditions and times were not identical in the 3 laboratories, the high RSD<sub>R</sub> values (22 and 17%, respectively) for these two impurities may have incorporated differences in their true concentrations. The Meeting accepted that the method for determination of relevant impurities is fit for purpose.

Test methods for determination of physico-chemical properties and water content of the technical active ingredient and formulations were OECD, EPA or CIPAC, as indicated in the specifications.

**SUPPORTING INFORMATION  
FOR  
EVALUATION REPORT 239/2004**

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## Uses

Pirimiphos-methyl is a broad-spectrum organophosphorus insecticide and acaricide, with both contact and fumigant action. In plants, it penetrates leaf tissue and exhibits translaminar action but is of short persistence. When applied to stored agricultural commodities (such as grain and nuts) or to the fabric of buildings, it provides longer-lasting pest control. It is also effective for space treatment and as a mosquito larvicide. Pirimiphos-methyl is used for controlling a wide range of chewing, sucking and boring insects and mites in warehouses, stored grain, animal houses, domestic and industrial premises; various mites on vegetables, ornamentals, bulb flowers, sugar cane, maize, sorghum, rice, citrus and other fruit, olives, vines, alfalfa, cereals; and for controlling certain glasshouse pests (especially whiteflies, thrips, mealybugs, aphids, and mites).

## Identity

*ISO common names:*

pirimiphos-methyl (E-ISO, BSI, ANSI, ESA)

pirimiphos-méthyl ((m) F-ISO)

*Synonyms:*

none

*Chemical name(s):*

IUPAC:

O-2-diethylamino-6-methylpyrimidin-4-yl-O,O-dimethyl phosphorothioate

CA:

O-[2-(diethylamino)-6-methyl-4-pyrimidinyl] O,O-dimethyl phosphorothioate

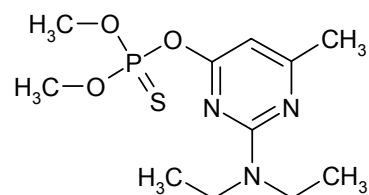
*CAS Registry number:*

29232-93-7

*CIPAC number:*

239

*Structural formula:*



*Molecular formula:*

C<sub>11</sub>H<sub>20</sub>N<sub>3</sub>O<sub>3</sub>PS

*Relative molecular mass:*

305.3

*Identity tests:*

UV, IR, NMR and mass spectra. In UV, molar extinction coefficients ( $\epsilon \text{ M}^{-1} \text{ cm}^{-1}$ ) in methanol are: 220 nm,  $3.39 \times 10^3$ ; 247 nm,  $2.24 \times 10^4$ ; 301 nm,  $3.69 \times 10^3$ .

## Physical and chemical properties

**Table 2. Physical and chemical properties of pure pirimiphos-methyl**

Parameter	Value(s) and conditions	Purity %	Method reference	Reference
Vapour pressure	$2.0 \times 10^{-6}$ kPa at 20°C	99.0%	EEC A4	PP511/0055
Melting point, boiling point and/or temperature of decomposition	Freezing point: 20.8°C (294°K) Boiling point cannot be determined as pirimiphos-methyl decomposes on heating, at approximately 120°C	99.0%	EEC A1	PP511/0055 PP511/0057
Solubility in water	10 mg/l in unbuffered water at 20°C 11mg/l at pH 5 at 20 deg C 10 mg/l at pH 7 at 20 deg C 9.7 mg/l at pH 9	99.0%	CIPAC MT157.1	PP511/0055
Octanol/water partition coefficient	At 20°C, $K_{ow} \log P =$ 4.2 in unbuffered water 3.9 at pH4 4.2 at pH 5 and 7	99.0%	EEC A8	PP511/0055
Hydrolysis characteristics	DT <sub>50</sub> at 25°C: 2, 7, 117 and 75 days at pH 4, 5, 7 and 9, respectively. Two degradation compounds identified: 2-diethylamino-6-methylpyrimidin-4-ol, and O-(2-diethylamino-6-methylpyrimidin-4-yl) O-methylphosphorothioate.	99.0%	EEC C7	PP511/0494
Photolysis characteristics	Estimated DT <sub>50</sub> = 0.46 and 0.47 h at pH 5 and 7, respectively. Test solutions continuously irradiated using a xenon arc lamp, filtered for spectral distribution similar to natural sunlight. Samples were irradiated for up to the equivalent of approximately 4.12 hours Florida summer sunlight, at 25°C. The major degradate, 2-diethylamino-6-methylpyrimidin-4-ol, reached 63% of applied radioactivity at the end of the study. S-2-diethylamino-6-methylpyrimidin-4-yl-O,O-dimethylphosphorothioate was formed up to 14.5% during the study, but degraded rapidly to final levels of 2.8% and 3.3% of applied radioactivity at pH 5 and 7, respectively. An unknown product reach levels of 12.1% and 9.5% of applied radioactivity at pH 5 and 7 but degraded quickly (DT <sub>50</sub> approx. 2 h) and therefore was not characterized.	97.0%	EPA FIFRA Subdiv. N, Guidelines 161-2 and 161-3	PP511/0497
Dissociation characteristics	pKa = 4.30 at 20°C	93.0%	OECD 112	PP511/0055

**Table 3. Chemical composition and properties of technical pirimiphos-methyl (TC)**

Manufacturing process, maximum limits for impurities $\geq 1$ g/kg, 5 batch analysis data	Confidential information supplied and held on file by WHO and FAO. Mass balances were 99.6 – 100.2% and no unidentified impurities were reported.
Declared minimum pirimiphos-methyl content	880 g/kg
Relevant impurities $\geq 1$ g/kg and maximum limits for them	O,O-dimethylphosphorochloridothioate (DMPCT, R305032, CAS RN 2524-03-0), 5 g/kg O,O,S-trimethylphosphorodithioate (R305910, CAS RN 2953-29-9), 5 g/kg O,O,S-trimethylphosphorothioate (R348532, CAS RN 152-20-5), 5 g/kg O,O,O-trimethylphosphorothioate (R065249, CAS RN 152-18-1), 5 g/kg O-2-diethylamino-6-methylpyrimidin-4-yl-O,S-dimethylphosphorothioate (R037292, "iso-pirimiphos-methyl" CAS No. 76471-79-9), 5 g/kg Water, 2 g/kg.
Relevant impurities $< 1$ g/kg and maximum limits for them:	None.
Stabilisers or other additives and maximum limits for them:	Epoxidized soybean oil is added as stabilizer – maximum limit 44g/kg. Odour suppressants are also added for public health applications.
Melting temperature range	16-22°C (freezing point range)

### Background information on toxicology/ecotoxicology

The toxicology of pirimiphos-methyl was evaluated by the FAO/WHO JMPR in 1974, 1976 and 1992, the 1992 JMPR establishing an acceptable daily intake (ADI) of 0.00-0.03 mg/kg bodyweight (JMPR, 1992b). The only biochemical effect consistently noted in acute, short-term and long-term, or chronic toxicity tests was inhibition of cholinesterase. The JMPR concluded that pirimiphos-methyl is not genotoxic. Residues of pirimiphos-methyl were considered by the JMPR in 1974, 1976, 1977, 1979, 1983, 1985, 1994 and 2003. In assessing short-term intake of residues, the 2003 JMPR noted that an acute reference dose (acute RfD) may be required for pirimiphos-methyl but had not been established (JMPR, 1992a).

The European Commission is currently reviewing pirimiphos-methyl under the EU Directive 91/414.

A review of pirimiphos-methyl conducted as part of the UK routine review programme and considered by the Advisory Committee on Pesticides in 1997 produced the following conclusions (PSD 2003). The ADI is 0-0.005 mg/kg bw/day and pirimiphos-methyl is of relatively low acute toxicity by oral, dermal and inhalation routes and, though a weak irritant to skin and eyes, it is not classifiable as an irritant or a skin sensitizer under EU criteria. Pirimiphos-methyl should be regarded as: not carcinogenic to rat or mouse; not teratogenic to rat or rabbit; not a reprotoxin and has no effect on reproduction in rats; not considered to be non-genotoxic; and there was no evidence of delayed neurotoxicity. Pirimiphos methyl should be categorized under EC criteria as R50 (very toxic to aquatic organisms) and, as it is not readily

biodegradable it should also be categorised as R53 (may cause long-term adverse effects in the aquatic environment).

The WHO classification of pirimiphos-methyl is class III, slightly hazardous (WHO 2002)

### **Formulations**

The main formulation types available are emulsifiable concentrates (EC) and these are registered and sold in many countries throughout the world for both for agricultural and public health uses.

### **Methods of analysis and testing**

The analytical method for the active ingredient (including identity tests) is a full CIPAC method (CIPAC 1C). Pirimiphos-methyl is determined by GC with FID and internal standardization with n-octadecane.

The method for determination of the relevant impurities (except water) is based on <sup>31</sup>P NMR and was peer-validated in three laboratories (Syngenta 2005).

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

### **Physical properties**

The physical properties, the methods for testing them and the limits proposed for the EC formulations, comply with the requirements of the Manual (FAO/WHO, 2002).

### **Containers and packaging**

No special requirements for containers and packaging have been identified.

### **Expression of the active ingredient**

The active ingredient is expressed as pirimiphos-methyl.

## **ANNEX 1**

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

Note: The proposer provided written confirmation that the toxicological and ecotoxicological data included in the following summary were derived from pirimiphos-methyl having impurity profiles similar to those referred to in Table 3, above.

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

Species	Test	Purity %	Duration and conditions or guideline adopted	Result	Reference
Rat, male and female	Oral	91.7	OECD 401	LD <sub>50</sub> = 1414 mg/kg bw	PP511/0132
Rat, male and female	Inhalation	90.6	OECD 403	LC <sub>50</sub> >5.04 mg/m <sup>3</sup> [ $>4.7$ mg/l*]	PP511/0129
Rat, male and female	Dermal	91.7	OECD 402	LD <sub>50</sub> >2000 mg/kg bw	PP511/0133
Rabbit, male and female	Skin irritancy	91.7	OECD 404	Slight irritant [slight but not classifiable*]	PP511/0134
Rabbit, male and female	Eye irritancy	91.7	OECD 405	Mild irritant [mild but not classifiable*]	PP511/0135
Guinea pig	Skin sensitization	91.7	OECD 406	Mild sensitizer [mild but not classifiable*]	PP511/0136

\* Conclusions of the UK Pesticide Safety Directorate (PSD 2003).

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

Species	Study type	Purity %	Result	Reference
Rat	90-day toxicity	93.1	NOAEL: 8 ppm (2.8-3.6 mg/kg/day). Based on reduction in plasma, erythrocyte and brain cholinesterase activity.	PP511/0141
Dog	90-day toxicity	99.0	NOAEL: 0.5 mg/kg/day. Based on reduction in plasma and erythrocyte (but not brain) cholinesterase activity.	PP511/0146
Rat	2-year toxicity and carcinogenicity	86.8%	Not carcinogenic NOAEL = 10 ppm (0.4 mg/kg bw/d), based on depression of brain cholinesterase activity (>10%) at 50 and 300 ppm. [NOAEL for carcinogenicity = 50 ppm (2.1 mg/kg bw/d) based on equivocal increased incidence of rare pancreatic and brain tumours at 300 ppm (12.6 mg/kg bw/d)*. Manufacturer proposed carcinogenicity NOAEL = 10 ppm, considering the tumours to be unrelated to treatment.]	PP511/0559
Mouse	78 week carcinogenicity	89.8%	Not carcinogenic NOAEL: 50 ppm, based on reduction in plasma, erythrocyte and brain cholinesterase activity. [NOAEL for carcinogenicity is >300ppm (>57 mg/kg bw/day), the highest dose tested. Significant inhibition of brain and erythrocyte cholinesterase activity was seen at the lowest dose level of 50 ppm(9 mg/kg bw/day), therefore an overall NOAEL cannot be determined*.]	PP511/0149
Rat	2-generation reproduction	86.7%	Not a reprotoxin NOAEL >160 ppm	PP511/0155

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

Species	Study type	Purity %	Result	Reference
Rat	Teratogenicity, maternal and developmental toxicity	88.5%	Not teratogenic Fetotoxicity NOAEL: 15 mg/kg/day	PP511/0645
Rabbit	Teratogenicity, maternal and developmental toxicity	86.7%	Not teratogenic No effects on developmental parameters NOAEL: 48 mg/kg/day. [Alterations in the pelvis seen at 48 mg/kg bw/d are uncommon and considered to be an indication of fetotoxicity, not teratogenicity. NOAELs for teratogenicity and fetotoxicity are thus 48 mg/kg bw/d and 24 mg/kg bw/d respectively*.]	PP511/0153

\* Conclusions of the UK Pesticide Safety Directorate (PSD 2003).

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

Species	Study Type	Purity %	Results	Reference
<i>S. typhimurium</i>	Ames reverse mutation	88.9	negative	PP511/0671
Mouse lymphoma cells	L5178Y mammalian cell gene mutation	90.7	negative	PP511/0158
Hyman lymphocytes	<i>In vitro</i> clastogenicity	90.7	negative	PP511/0159
Chinese hamster lung fibroblasts	Sister chromatid exchange	90.7	equivocal	PP511/0160
Hamster kidney fibroblasts	Mammalian cell transformation	Not stated	negative	PP511/0663
Rat hepatocytes	<i>In vivo</i> UDS	93.5	negative	PP511/0161
Mouse	Dominant lethal	Not reported	negative	PP511/0156

Pirimiphos-methyl was observed to induce small increases in sister chromatid exchange in Chinese hamster fibroblasts but such minor increases were not thought to be of any toxicological significance. Evidence from *the in vitro* studies therefore suggests that pirimiphos-methyl is not genotoxic. Data from *in vivo* studies were unequivocally negative, in that pirimiphos-methyl did not induce DNA repair in the rat liver nor elicit a dominant lethal response in mice.

**Table D. Ecotoxicology profile of pirimiphos-methyl technical material**

Species	Test	Duration and conditions	Results	Reference
<i>Daphnia magna</i> (water flea)	Immobilization	48 h, EEC method C2, purity not recorded	EC <sub>50</sub> = 0.21 µg/l	PP511/0528
<i>Oncorhynchus mykiss</i> (rainbow trout)	Mortality	96 h, EEC method C1, purity not recorded	LC <sub>50</sub> = 0.2 mg/l	PP511/0520
<i>Selenastrum capricornutum</i> (green alga)	Growth	96 h based on OECD 201, purity 91%	EC <sub>50</sub> >1000 µg/l	PP511/0533

**Table D. Ecotoxicology profile of pirimiphos-methyl technical material**

Species	Test	Duration and conditions	Results	Reference
Bobwhite quail	Acute oral	GLP, single dose 14 day oral, purity 89.8%	LD <sub>50</sub> = 40 mg/kg bw	PP511/0516
Bobwhite quail	Dietary	GLP, 5-day treatment, 3-day observation, purity 89.3%	LC <sub>50</sub> = 304 mg/kg diet.	PP511/0515
Hen	Reproduction	28 days, pre-GLP, purity not recorded	NOAEL = 40 mg/kg diet.	PP511/0517

## ANNEX 2. REFERENCES

Syngenta document No. or other reference	Year and title or publication details
CIPAC 1C	Collaborative International Pesticides Analytical Council (CIPAC). Handbook 1C, p.2192, 1985, Harpenden, U.K.
FAO/WHO, 2002	Manual on development and use of FAO and WHO specifications for pesticides. First edition. FAO Plant Production and Protection Paper 173. Food and Agriculture Organization of the United Nations, Rome, 2002
Gallo & Lawryk 1991	Gallo M.A. & Lawryk N.J., 1991. Organic phosphorus pesticides. In: Handbook of pesticide toxicology, volume 2, Classes of pesticides. Hayes W.J. Jr & Laws E.R. Jr, eds. Academic Press, Inc., San Diego. pp. 917-957.
GHS 2003	Globally Harmonized System of Classification and Labelling of Chemicals, United Nations, New York and Geneva, 2003, <a href="http://www.unece.org/trans/danger/publi/ghs/ghs_rev00/english">http://www.unece.org/trans/danger/publi/ghs/ghs_rev00/english</a>
JMPR, 1992a	FAO/WHO Joint Meeting on Pesticide Residues. Pesticide residues in food – 1992 evaluations. Part I – Residues. FAO Plant Production and Protection Paper 116, 1993 ( <a href="http://www.inchem.org/documents/jmpr/jmpmono/v074pr32.htm">http://www.inchem.org/documents/jmpr/jmpmono/v074pr32.htm</a> )
JMPR, 1992b	FAO/WHO Joint Meeting on Pesticide Residues. Pesticide residues in food – 1992 evaluations. Part II – Toxicology. World Health Organization, WHO/PCS/93.34 ( <a href="http://www.inchem.org/documents/jmpr/jmpmono/v092pr16.htm">http://www.inchem.org/documents/jmpr/jmpmono/v092pr16.htm</a> )
PP511/0055	1997, Pirimiphos-methyl: Physical and Chemical Properties of Pure Material.
PP511/0057	1998, Pirimiphos-methyl: Physical and Chemical Properties of Technical Material.
PP511/0129	1990. Pirimiphos-methyl: 4hr Acute Inhalation Toxicity Study in the Rat.
PP511/0132	1999. Pirimiphos-methyl: Acute Oral Toxicity Study in Rats.
PP511/0133	1999. Pirimiphos-methyl: Acute Dermal Toxicity Study in Rats.
PP511/0134	1999. Pirimiphos-methyl: Skin Irritation Study in Rabbits.
PP511/0135	1999. Pirimiphos-methyl: Eye Irritation Study in Rabbits.
PP511/0136	1999. Pirimiphos-methyl: Skin Sensitisation Study in Guinea Pigs.
PP511/0141	1970. Pirimiphos-methyl: 90-Day Oral Toxicity in Rats.
PP511/0146	1973. Pirimiphos-methyl: Oral Toxicity Study in Beagle Dogs (Repeated Daily Dosage for 2 Years).
PP511/0149	1996. Pirimiphos-methyl: 78 Week Carcinogenicity in Mice With Administration By Diet.
PP511/0153	1994. Pirimiphos-methyl: Developmental Toxicity Study in Rabbits.
PP511/0155	1995. Pirimiphos-methyl: Two Generation Reproduction Study in Rats.
PP511/0156	1975. Dominant Lethal Study in Mice of Pirimiphos-methyl.
PP511/0158	1986. Pirimiphos-methyl: Assessment of Mutagenic Potential Using L5178Y Mouse Lymphoma Cells.
PP511/0159	1986. Pirimiphos-methyl: A Cytogenetic Study in Human Lymphocytes In Vitro.
PP511/0160	1986. Pirimiphos-methyl: An In Vitro Sister Chromatid Exchange Study in Chinese Hamster Lung Fibroblasts.
PP511/0161	1998. Pirimiphos-methyl: In Vivo Rat Liver Unscheduled DNA Synthesis Assay.
PP511/0494	1996, Pirimiphos-methyl: Aqueous Hydrolysis in pH4, 5, 7 and 9 solutions at 25°C.
PP511/0497	1999, Pirimiphos-methyl: Aqueous Photolysis at pH5 and 7 at 25°C.
PP511/0515	1990. Pirimiphos-Methyl Technical: Dietary Toxicity (LC50) to the Bobwhite Quail.
PP511/0516	1994. Pirimiphos-Methyl: An Acute Oral Toxicity Study with the Northern Bobwhite.
PP511/0517	1975. Egg Production and Hatchability Following Inclusion of Pirimiphos-Methyl at Various Levels in the Diet of the Laying Hen.
PP511/0520	1973. Pirimiphos-Methyl: Acute Toxicity to Rainbow Trout ( <i>Salmo gairdneri</i> ) and to Common Carp ( <i>Cyprinus carpio</i> ).

Syngenta document No. or other reference	Year and title or publication details
PP511/0528	1976. Pirimiphos-methyl: Acute toxicity to common carp ( <i>Cyprinus carpio</i> ) in a 96-hour flow-through test.
PP511/0533	1989. Pirimiphos-methyl: Determination of Toxicity to the Green Alga ( <i>Selenastrum capricornutum</i> ).
PP511/0559	1974. Pirimiphos-methyl: 2yr Feeding Study in the Rat.
PP511/0645	1985. Pirimiphos-methyl: Teratogenicity Study in the Rat.
PP511/0663	1983. An Examination of Pirimiphos-methyl Using the Mammalian Cell Transformation Test.
PP511/0671	1984. Pirimiphos-methyl: An Evaluation in the Salmonella Mutagenicity Assay.
PSD 2003	FAO/WHO specification for pirimiphos-methyl. Letter of 22.12.2003. Approvals Committee Branch, Pesticides Safety Directorate, UK.
Syngenta 2005	2005. Pirimiphos-methyl: peer review of analytical method SD-876/2 for the determination of five impurities in pirimiphos-methyl technical material and EC formulations.
WHO 2003	WHO specifications and evaluations of public health pesticides. Malathion. Available at: <a href="http://www.who.int/whopes/quality/en/Malathion_july04.pdf">http://www.who.int/whopes/quality/en/Malathion_july04.pdf</a>
WHO/PCS 2005	Relevant impurities of pirimiphos-methyl, Chemical safety information, WHO/PCS, AAi/ATr/JTe/TMe, 12 January 2005.

## Appendix 1

### **Analytical method for the determination of relevant impurities in pirimiphos-methyl TK and EC** (Syngenta analytical method SD-876/2)

#### **Outline of method**

The sample of pirimiphos-methyl technical material or EC formulation is dissolved in deuterated chloroform and the impurities determined as percentage w/w, relative to the pirimiphos-methyl content, by quantitative  $^{31}\text{P}$  NMR.

#### **Reagents**

*d*-chloroform ( $\text{CDCl}_3$ ). Solutions used in this method are stable at room temperature for at least 22 hours.

#### **Apparatus**

NMR equipped with  $^{31}\text{P}$  probe, Varian Inova 400, or equivalent, with 5mm HFCP liquid probe.

Electronic integrator or data system.

#### **Method**

##### NMR operating conditions (typical)

*Pulse programme:* standard one X-pulse experiment with inverse gated decoupling; relaxation delay -  $90^\circ$ -X-pulse - acquisition (with proton decoupling).

*Observed nucleus:*  $^{31}\text{P}$ .

*Relaxation delay:* >50s.

*Pulse width:*  $90^\circ$ .

*Decoupler nucleus:*  $^1\text{H}$ .

*Decoupler mode:* inverse gated.

*Decoupler modulation mode:* broadband WALTZ decoupling.

*Transmitter Offset:* 48ppm.

*Number of points in FID:* 256k total points (real + imaginary).

*Number of scans:* 64.

*Spectral width:* 150ppm.

*Temperature:* ambient.

##### Data acquisition and integration

Conduct the NMR experiment in accordance with the instrument manufacturer's recommendations and local practice. Typical data processing would be 1Hz Lorentzian line broadening and zero filling to at least 512k total points. Careful phasing and baseline correction are essential. It is important to ensure each sample is correctly shimmed during data acquisition (e.g. by examination of the pirimiphos-methyl line shape), to ensure reliable curve-fitting. Re-analyze the sample if necessary.

Integral regions should be set using peak deconvolution. If necessary, they may be set manually but peak deconvolution provided best accuracy in the validation study. Normalize the integral of pirimiphos-methyl to a value of 100. Plot the spectrum and integral list.

#### Preparation of sample solutions

Prepare two test solutions (A and B) from each sample to be tested, as follows.

Technical material (TC). Shake the TC thoroughly to ensure homogeneity. Transfer approximately 125 mg to a 4 ml sample bottle. Add 0.75 ml CDCl<sub>3</sub> and mix well on a mixer. Transfer approximately 0.7 ml solution to a 5mm NMR-tube.

EC formulation. Shake the EC thoroughly to ensure homogeneity. Transfer a volume of EC, corresponding to approximately 125mg pirimiphos-methyl, to a 4ml sample bottle. Add 0.5 ml CDCl<sub>3</sub> and mix well on a mixer. Transfer approximately 0.7ml of the solution to a 5mm NMR-tube.

#### Assignment

Reference the spectra according to local practice, or set the pirimiphos-methyl signal to 64 ppm, whichever is more convenient.

Table of shifts relative to 85% H<sub>3</sub>PO<sub>4</sub>

compound	chemical shift, ppm
pirimiphos-methyl	64
O,O,S-trimethylphosphorothioate (MeOOSPO)	32
O,O-dimethylphosphorochloridothioate (DMPCT)	72.8
O,O,O-trimethylphosphorothioate (MeOOOPS)	73.2
O-2-diethylamino-6-methylpyrimidin-4-yl-O,S-dimethylphosphorothioate ( <i>iso</i> -pirimiphos-methyl)	93
O,O,S-trimethylphosphorodithioate (MeOOSPS)	100

#### Calculation

Using the integral obtained from the impurity and pirimiphos-methyl, the % w/w of impurity, relative to pirimiphos-methyl, should be calculated using the appropriate equation below.

If the pirimiphos-methyl NMR integral was set to 100:

$$\text{impurity \% w/w (relative to pirimiphos-methyl)} = \text{impurity NMR integral} \times \text{impurity m.w. ratio}^*$$

If the pirimiphos-methyl NMR integral was not set to 100:

$$\text{impurity \% w/w (relative to pirimiphos-methyl)} = \frac{\text{impurity NMR integral} \times \text{impurity m.w. ratio}^* \times 100}{\text{pirimiphos-methyl NMR integral}}$$

\* m.w. ratio – ratio of molecular weight relative to pirimiphos-methyl, as indicated in the table below.

compound	m.w. ratio
pirimiphos-methyl	1.00
O,O,S-trimethylphosphorothioate (MeOOSPO)	0.51
O,O-dimethylphosphorochloridothioate (DMPCT)	0.53
O,O,O-trimethylphosphorothioate (MeOOOPS)	0.51
O-2-diethylamino-6-methylpyrimidin-4-yl-O,S-dimethylphosphorothioate ( <i>iso</i> -pirimiphos-methyl)	1.00
O,O,S-trimethylphosphorodithioate (MeOOSPS)	0.56

To calculate the impurity concentration in TC as g/kg:

$$\text{impurity, g/kg} = \frac{\text{impurity \% w/w (relative)} \times \text{pirimiphos-methyl content of TC (g/kg)}}{100}$$

### Typical spectra

Figure 1. Full spectral range

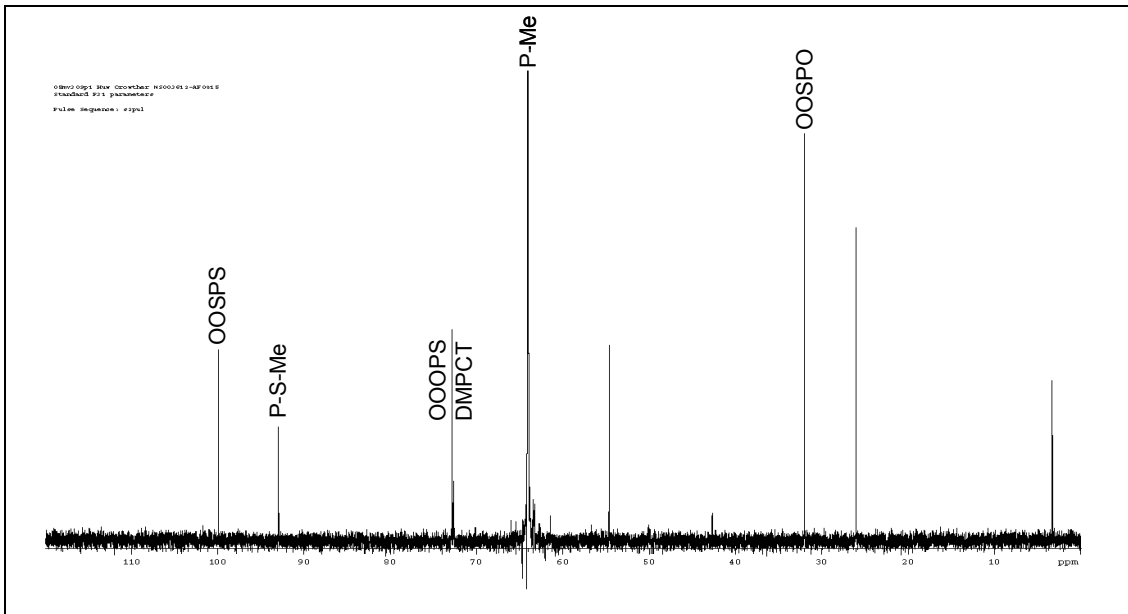


Figure 2. Expanded around 73ppm, showing resolution of MeOOOPS from DMPCT

