FAO SPECIFICATIONS AND EVALUATIONS FOR AGRICULTURAL PESTICIDES

PIRIMIPHOS-METHYL

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

FOOD AND AGRICULTURE ORGANIZATION of THE UNITED NATIONS

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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.

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[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 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) - 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 2000 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.

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

PART ONE

SPECIFICATIONS

PIRIMIPHOS-METHYL

PIRIMIPHOS-METHYL

INFORMATION

ISO common names

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

pirimiphos-méthyl ((m) F-ISO)

Synonyms

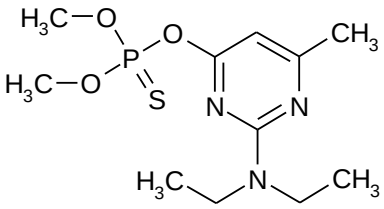
none

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 (ε M^{-1} cm^{-1}) in methanol are: 220 nm, 3.39 x 10^3; 247 nm, 2.24x 10^4; 301 nm, 3.69 x 10^3.

PIRIMIPHOS-METHYL TECHNICAL MATERIAL

FAO Specification 239 / TC (August 2016*)

This specification, which is PART ONE of this publication, is based on an evaluation of data submitted by the manufacturer whose name is listed in the evaluation reports (239/2004 & 239/2016). 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 reports (239/2004 & 239/2016) as PART TWO, form 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** (239/TC/M/2, Note 2)

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** (239/TC/M/3, Note 2)

The pirimiphos-methyl content shall be declared (not less than 880 g/kg, Note 3) 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 4)

Maximum: 5 g/kg.

3.2 ***O,O,S*-trimethyl phosphorodithioate** (MeOOSPS, R305910, CAS No. 2953-29-9) (Note 4)

Maximum: 5 g/kg.

3.3 ***O,O,S*-trimethyl phosphorothioate** (MeOOSPO, R348532, CAS No. 152-20-5) (Note 4)

Maximum: 5 g/kg.

3.4 ***O,O,O*-trimethyl phosphorothioate** (MeOOOPS, R065249, CAS No. 152-18-1) (Note 4)

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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.fao.org/agriculture/crops/core-themes/theme/pests/jmps/ps-new/en/

Maximum: 5 g/kg.

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

Maximum: 2 g/kg.

4 Physical properties

4.1 **Acidity** (MT 191, CIPAC Handbook L, p. 143, 2006)

Maximum acidity: 3 g/kg calculated as H_2SO_4.

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 FAO specification but, if required, the manufacturer should be contacted for details and the appropriate methods of analysis.

Note 2 The capillary GC method for the determination of pirimiphos-methyl in TC, EC and CS formulations (CIPAC/4778) was adopted as a provisional CIPAC method in 2011 and became a full method in 2012. Some modifications to this method were adopted by CIPAC in 2014 (CIPAC/4963/R). Prior to its publication in the next Handbook, copies of the method can be obtained through the CIPAC website, http://cipac.org/index.php/methods-publications/pre-published-methods

Note 3 The declared value takes into account the addition of stabilizers.

Note 4 The peer-validated GC-MS method for the determination of the relevant impurities in pirimiphos-methyl TC, EC and CS formulations (CIPAC/4781) was adopted as provisional CIPAC relevant impurity method in 2011. Some modifications to this method were adopted by CIPAC in 2014 (CIPAC/4963/R). Prior to their publication in the next Handbook, copies of the method can be obtained through the CIPAC website, http://cipac.org/index.php/methods-publications/pre-published-methods

PIRIMIPHOS-METHYL EMULSIFIABLE CONCENTRATE

FAO Specification 239 / EC (August 2016*)

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 & 239/2016). 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 reports (239/2004 & 239/2016) as PART TWO, form an integral part of this publication.

1 Description

The material shall consist of technical pirimiphos-methyl, complying with the requirements of FAO specification 239/TC (August 2016), 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** (239/EC/M/2, Note 1)

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** (239/EC/M/3, Note 1)

The pirimiphos-methyl content shall be declared (g/kg or g/l at 20 ± 2ºC, Note 2) 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 ± 2°C	Tolerance
above 100 up to 250 above 250 up to 500 Note. In each range the upper limit is included	± 6% of the declared content ± 5% of the declared content

3 Relevant impurities

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

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 3)

* 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/core-themes/theme/pests/jmps/ps-new/en/

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

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

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 3)

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

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

Maximum: 5 g/kg.

4 Physical properties

4.1 **Acidity** (MT 191, CIPAC Handbook L, p. 143, 2006)

Maximum acidity: 1 g/kg calculated as H_2SO_4.

4.2 **Emulsion stability and re-emulsification** (MT 36.3, CIPAC Handbook K, p.137, 2003) (Notes 4 & 5)

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 36.3
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 36.3, tests after 24 h are required only where results at 2 h are in doubt.	

4.3 **Persistent foam** (MT 47.3) (Notes 6 & 7)

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 ± 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 8), and the formulation shall continue to comply with the clauses for:

- acidity (4.1),
- emulsion stability and re-emulsification (4.2).

Note 1 The capillary GC method for the determination of pirimiphos-methyl in TC, EC and CS formulations (CIPAC/4778) was adopted as a provisional CIPAC method in 2011 and became a full method in 2012. Some modifications to this method were adopted by CIPAC in 2014 (CIPAC/4963/R). Prior to its publication in the next Handbook, copies of the method can be obtained through the CIPAC website, http://cipac.org/index.php/methods-publications/pre-published-methods

Note 2 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 3 The peer-validated GC-MS method for the determination of the relevant impurities in pirimiphos-methyl TC, EC and CS formulations (CIPAC/4781) was adopted as provisional CIPAC relevant impurity methods in 2011. Some improvements to this method were adopted by CIPAC in 2014 (CIPAC/4963/R). Prior to their publication in the next Handbook, copies of the method can be obtained through the CIPAC website, http://cipac.org/index.php/methods-publications/pre-published-methods

Note 4 This test will normally only be carried out after the heat stability test 5.2.

Note 5 As outlined in CIPAC MT 36.3, the test concentrations should be based on those in the recommended directions for use supplied with the product. Where several concentrations are recommended, the highest and lowest concentrations within the scope of the method should be used.

Note 6 The CIPAC method MT 47.2 published in Handbook F for determination of persistent foam created when formulations are added to water before use was updated to MT 47.3. This new method was accepted as a full CIPAC method in 2013. Prior to its publication in the next Handbook, copies of the method can be obtained through the CIPAC website, http://cipac.org/index.php/methods-publications/pre-published-methods

Note 7 The mass of sample to be used in the test should correspond to the highest rate of use recommended by the supplier. The test is to be conducted in CIPAC standard water D.

Note 8 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

PIRIMIPHOS-METHYL

PIRIMIPHOS-METHYL

FAO/WHO EVALUATION REPORT 239/2016

Recommendations

The Meeting recommended that:

(i) The impurity *iso*-pirimiphos-methyl in pirimiphos-methyl TC, EC and CS should no longer be considered as relevant.

(ii) The published WHO specifications for pirimiphos-methyl TC, EC and CS should be revised to reflect the non-relevance of the impurity *iso*-pirimiphos-methyl.

(iii) The published FAO specifications for pirimiphos-methyl TC and EC should be revised to reflect the non-relevance of the impurity *iso*-pirimiphos-methyl and editorially revised and brought in line with the WHO specifications for TC and EC.

Appraisal

The data for pirimiphos-methyl TC, EC and CS were evaluated by JMPS in 2004 and 2014. Several impurities were identified as relevant - *O,O*-dimethyl phosphorochloridothioate (DMPCT), *O,O,S*-trimethyl phosphorodithioate (MeOOSPS), *O,O,S*-trimethyl phosphorothioate (MeOOSPO), *O,O,O*-trimethyl phosphorothioate (MeOOOPS), *O*-2-diethylamino-6-methylpyrimidin-4-yl-*O,S*-dimethyl phosphorothioate, *iso*-pirimiphos-methyl (R37292), and water, with limits of 5 g/kg each in the TC, and 2 g/kg for water.

In the absence of specific toxicological data on *iso*-pirimiphos-methyl (R37292) at time of evaluation, the conclusion on the relevance of that impurity was based on an analogy: R37292 was considered to be a relevant impurity by comparing the acute toxicity of thiono- (P=S; pirimiphos-methyl-like) and oxono- (P=O; R37292-like) analogues of other organophosphates, which indicated a ratio of acute toxicity hazard in the range of 3:1 to 20:1 (Gallo and Lawryk (1991)). The higher acute toxicity of P=O analogues reported by Gallo and Lawryk is consistent with the fact that conversion of the P=S moiety to P=O is a key step in formation of the active cholinesterase inhibiting moiety in vivo. The maximum limit of 5 g/kg was considered an appropriate level for R37292 by the WHO/PCS secretariat as this would have no impact on the overall toxicity of pirimiphos-methyl, even if the impurity was twenty times more toxic than parent pirimiphos-methyl (the very upper end of Gallo and Lawryk's range).

However, Syngenta submitted in May 2016 some specific studies that had been generated in the 1970's by a predecessor company (ICI) using a limited amount of *iso*-pirimiphos-methyl (Laboratory Report, 1970, R37292). The study was conducted in 1970, prior to the introduction of standard protocols and GLP, nevertheless the report contains sufficient information to provide new evidence of the toxicology of *iso*-pirimiphos-methyl.

In an acute oral range finding test, female rats received a single oral dose of *iso*-pirimiphos-methyl in the dosing vehicle propylene glycol at a constant concentration of 50 mg/ml. The dose volume was adjusted to achieve doses of 100, 400, 1600 or 2000 mg/kg bodyweight and the animals were observed for 14 days.

There were no treatment related mortalities. Females administered 1600 mg/kg or 2000 mg/kg R37292 showed clinical signs of toxicity (incontinence and subdued behaviour) for the first 24hours post dose, the signs of incontinence persisted for up to 3 days post dose for the single female given 2000 mg/kg. At all other dose levels and time points there were no signs of clinical toxicity.

The data indicates that *iso*-pirimiphos-methyl is not 20 times more toxic than pirimiphos-methyl, since single doses up to 2000 mg/kg were well tolerated in rats, indicating it is of lower acute toxicity than pirimiphos-methyl which has an LD50 of 1414 mg/kg. The data thereby infers R37292 has indeed a lower activity as a cholinesterase inhibitor than pirimiphos-methyl.

The Meeting therefore concluded that the assumption on a higher toxicity of *iso*-pirimiphos-methyl in comparison to pirimiphos-methyl is no longer valid and that the impurity *iso*-pirimiphos-methyl should no longer be considered as relevant. The WHO specifications for TC, EC and CS should be revised accordingly and the FAO specifications for TC and EC should be brought in line with those of WHO.

The Meeting also recommended:

- to withdraw the reference to the analytical method for the determination of relevant impurities in pirimiphos-methyl TC and EC by ^{31}P NMR (Syngenta analytical method SD-876/2).
- to refer in the specifications for TC and EC to the new analytical methods adopted by CIPAC for pirimiphos-methyl and relevant impurities identity and content.
- to update the CIPAC physical-chemical methods where necessary (e.g. acidity: MT 191 instead of MT 31, emulsion stability: MT 36.3 instead of 36.1.1, persistent foam: MT 47.3 instead of MT 47.2).

ANNEX 1: REFERENCES

Study number	Author(s)	Year	Study title. Study identification number. Report identification number. GLP [if GLP]. Company conducting the study
	Gallo M.A and Lawryk, N.J.1991	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.
K-CA 5.8.2 / 08, Laboratory Report, 1970	ICI	1970	Range finding test. Laboratory Report No.AR2923 issue date 11 February 1970. Unpublished. (Syngenta File No. R37292_10000)

PIRIMIPHOS-METHYL

FAO/WHO 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_{50} = 1260 mg/kg (rat)	LD_{50} = 1300 mg/kg (rat)
Acute dermal	LD_{50} = 2150 mg/kg (rabbit)	LD_{50} = 330–650 mg/kg (rat)
Acute inhalation (4hr)	LD_{50} 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

permitted the separation of 2 ml cream and/or oil at 2h). 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 5 organophosphorus relevant impurities in the TC and EC, which is based on ^{31}P NMR, has been peer validated. Values for RSD_r were 1.9-6.0% and those for RSD_R 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_R 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

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

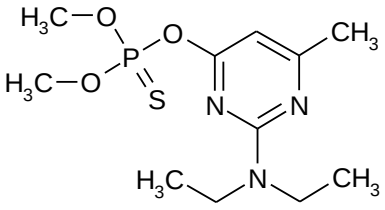
CAS Registry number:

29232-93-7

CIPAC number:

239

Structural formula:



Molecular formula:

$C_{11}H_{20}N_3O_3PS$

Relative molecular mass:

305.3

Identity tests:

UV, IR, NMR and mass spectra. In UV, molar extinction coefficients (ε M^{-1} cm^{-1}) in methanol are: 220 nm, 3.39 x 10^3; 247 nm, 2.24x 10^4; 301 nm, 3.69 x 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 x 10^{-6} kPa at 20ºC	99.0%	EEC A4	PP511/0055
Melting point, boiling point and/or temperature of decomposition	Freezing point: 20.8ºC (294ºK) Boiling point cannot be determined as pirimiphos-methyl decomposes on heating, at approximately 120ºC	99.0%	EEC A1	PP511/0055 PP511/0057
Solubility in water	10 mg/l in unbuffered water at 20ºC 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 20ºC, 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_{50} at 25ºC: 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_{50} = 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 25ºC. 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_{50} 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 20ºC	93.0%	OECD 112	PP511/0055

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

Manufacturing process, maximum limits for impurities ≥ 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 ≥ 1 g/kg and maximum limits for them	*O,O*-dimethyl phosphorochloridothioate (DMPCT, R305032, CAS RN 2524-03-0), 5 g/kg *O,O,S*-trimethyl phosphorodithioate (R305910, CAS RN 2593-29-9), 5 g/kg *O,O,S*-trimethyl phosphorothioate (R348532, CAS RN 152-20-5), 5 g/kg *O,O,O*-trimethyl phosphorothioate (R065249, CAS RN 152-18-1), 5 g/kg *O*-2-diethylamino-6-methylpyrimidin-4-yl-*O,S*-dimethyl phosphorothioate (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 44 g/kg. Odour suppressants are also added for public health applications.
Melting temperature range	16-22ºC (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 ^{31}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_{50} = 1414 mg/kg bw	PP511/0132
Rat, male and female	Inhalation	90.6	OECD 403	LC_{50} >5.04 mg/m^3 [>4.7 mg/l*]	PP511/0129
Rat, male and female	Dermal	91.7	OECD 402	LD_{50} >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
S. typhimurium	Ames reverse mutation	88.9	negative	PP511/0671
Mouse lymphoma cells	L5178Y mammalian cell gene mutation	90.7	negative	PP511/0158
Hyman lymphocytes	*In vitro* 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	*In vivo* 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 5. Ecotoxicology profile of pirimiphos-methyl technical material

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

Table 5. 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_{50} = 40 mg/kg bw	PP511/0516
Bobwhite quail	Dietary	GLP, 5-day treatment, 3-day observation, purity 89.3%	LC_{50} = 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, http://www.unece.org/trans/danger/publi/ghs/ghs_rev00/english
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 (http://www.inchem.org/documents/jmpr/jmpmono/v074pr32.htm)
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 (http://www.inchem.org/documents/jmpr/jmpmono/v092pr16.htm)
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 Unschedulled DNA Synthesis Assay.
PP511/0494	1996, Pirimiphos-methyl: Aqueous Hydrolysis in pH4, 5, 7 and 9 solutions at 25ºC.
PP511/0497	1999, Pirimiphos-methyl: Aqueous Photolysis at pH5 and 7 at 25ºC.
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.

Syngenta document No. or other reference	Year and title or publication details
PP511/0520	1973. Pirimiphos-Methyl: Acute Toxicity to Rainbow Trout (Salmo gairdneri) and to Common Carp (Cyprinus carpio).
PP511/0528	1976. Pirimiphos-methyl: Acute toxicity to common carp (Cyprinus carpio) in a 96-hour flow-through test.
PP511/0533	1989. Pirimiphos-methyl: Determination of Toxicity to the Green Alga (Selenastrum capricornutum).
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: http://www.who.int/whopes/quality/en/Malathion_july04.pdf
WHO/PCS 2005	Relevant impurities of pirimiphos-methyl, Chemical safety information, WHO/PCS, AAi/ATr/JTe/TMe, 12 January 2005.