WHO SPECIFICATIONS AND EVALUATIONS FOR PUBLIC HEALTH PESTICIDES

PERMETHRIN

(25:75 *cis:trans* isomer ratio, nonracemic)

3-phenoxybenzyl (1*RS*,*3RS*;1*RS*,3*SR*)-3-(2,2 dichlorovinyl)-2,2-dimethyl-cyclopropane carboxylate

World Health Organization

TABLE OF CONTENTS

Disclaimer[1]

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.

---

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

INTRODUCTION

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

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

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

Part One: The Specification of the technical material and the related formulations of the pesticide in accordance with chapters 4 to 9 of the above-mentioned manual.

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

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

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

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

PART ONE

SPECIFICATIONS

PERMETHRIN

PERMETHRIN (25:75 *cis:trans*, nonracemic)

INFORMATION

ISO common name

permethrin (ISO 1750 published), permethrine (F-ISO)

Chemical names

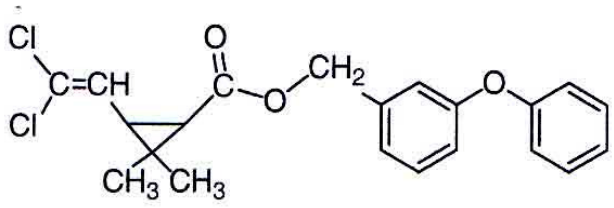
IUPAC: 3-phenoxybenzyl (1*RS*,*3RS*;1*RS*,3*SR*)-3-(2,2-dichlorovinyl)-2,2-dimethylcyclo-propanecarboxylate

CA: (3-phenoxyphenyl)methyl 3-(2,2-dichloroethenyl)-2,2-dimethylcyclopropane-carboxylate

Synonyms

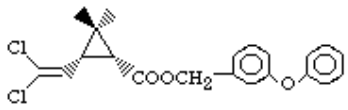
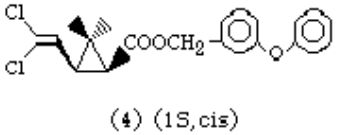
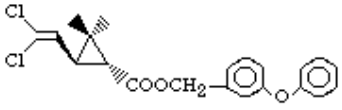
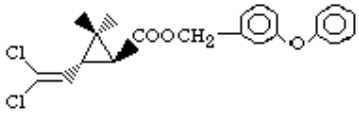
None

Structural formula



Two pairs of diastereomers (each consisting of a nonracemic pair of enantiomers; see below) are present in a ratio of approximately 25:75. In the context of the current specification, the hybrid nomenclature for pyrethroids developed at Rothamsted[2] is used, where the absolute configuration at carbon atom 1 of the cyclopropane moiety is given. The relative position of the C3 substituent (*cis* or *trans*) is then given, followed by the absolute configuration (if necessary, not necessary in the case of permethrin) of the alkyl α-carbon of the esterifying group.

[2] M. Elliott and N.F. Janes, Chem. Soc. Rev. 7, 473 - 505, 1978.

Sl No	Name of isomer	Structure	Proportions
1	1*R*, *cis*	 (2) (1R,cis)	sum ≈ 25%
2	1*S*, *cis*	 (4) (1S,cis)	
3	1*R*, *trans*	 (1) (1R,trans)	sum ≈ 75%
4	1*S*, *trans*	 (3) (1S,trans)	

The ratio of 1*S-cis* to 1*R-cis* and of 1*R-trans* to 1*S-trans* is ≈ 70 to 30.

Molecular formula

$C_{21}H_{20}Cl_2O_3$

Relative molecular mass

391.3

CAS Registry number

52645-53-1

CIPAC number

331

Identity tests

GC retention times, GC mass spectrum, IR spectrum, enantioselective HPLC retention times and enantiomer ratios.

25:75 *cis:trans* (nonracemic) PERMETHRIN TECHNICAL MATERIAL

WHO specification 331/TC (July 2015*)

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 (331/2014). It should be applicable to TC produced by this manufacturer but it is not an endorsement of those products, nor a guarantee that they comply with the specification. The specification may not be appropriate for TC produced by other manufacturers. The evaluation report (331/2014), as PART TWO, forms an integral part of this publication.

1 Description

The material shall consist of permethrin together with related manufacturing impurities, and shall be a light yellow to yellow viscous liquid which may be partially crystallised, free from visible extraneous matter and added modifying agents.

2 Active ingredient

2.1 **Identity tests** (331/TC/M2/2, CIPAC Handbook M, p.155, 2009)

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 **Permethrin content** (331/TC/M2/3, CIPAC Handbook M, p.155, 2009)

The permethrin content shall be declared (not less than 950 g/kg) and, when determined, the average measured content shall not be lower than the declared minimum content.

2.3 **Permethrin diastereomeric ranges** (331/TC/M2/3, CIPAC Handbook M, p.155, 2009)

The [1*RS*,3*RS*] : [1*RS*,3*SR*] (*cis:trans*) permethrin isomer ratio shall be declared and, when determined, the average measured ratio shall be in the range of:

Diastereomer	Range
1*RS-cis*	22.0 to 28.0 %
1*RS-trans*	72.0 to 78.0 %

* 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/

2.4 **Permethrin enantiomeric ranges** (Note 1)

The enantiomer content in the *cis* and *trans* diastereomers, respectively, shall be declared and, when determined, the average measured content shall be in the range of:

Enantiomer	Range g/kg
1*R-cis*	50 to 100
1*S-cis*	150 to 200
1*R-trans*	450 to 550
1*S-trans*	170 to 270

Note1 The peer validated chiral HPLC method (CIPAC/4946) for determination of the permethrin enantiomeric ranges in permethrin TC was presented at the CIPAC Meeting in 2014 in Belgium and accepted as a quantitative stereoselective identity test for permethrin stereoisomers content in permethrin TC. Prior to its publication in the next Handbook, copies of the method can be obtained through the CIPAC website, http://www.cipac.org/prepubme.htm

PART TWO

EVALUATION REPORTS

PERMETHRIN (25:75 *cis:trans*, nonracemic)

PERMETHRIN (25:75 *cis:trans*, nonracemic)

FAO/WHO EVALUATION REPORT 331/2014

Recommendation

The Meeting recommended the following.

(i) The specification for permethrin (25:75 *cis:trans*, nonracemic) TC, proposed by Bayer CropScience, as amended, should be adopted by WHO.

(ii) The WHO specification for *S*-bioallethrin + permethrin + piperonyl butoxide EW (WHO specification 750+331+33/EW (November 2006)) should be revised to refer to the permethrin (25:75 *cis:trans*, nonracemic) TC specification and to the piperonyl butoxide TC specification (September 2011), and updated for published CIPAC methods for *S*-bioallethrin, permethrin and piperonyl butoxide, and persistent foam (MT 47.3).

Appraisal

The Meeting considered data and information submitted by Bayer CropScience (BCS) in 2012 in support of new WHO specifications for a nonracemic permethrin TC with a *cis*/*trans* ratio of 25 to 75. The data submitted by BCS were broadly in accordance with the requirements of the Manual on development and use of FAO and WHO specifications for pesticides (November 2010 - second revision of the First Edition).

The Meeting was provided with commercially confidential data on the manufacturing process, the manufacturing specification and 5-batch analysis data for permethrin 25/75 (nonracemic) and all impurities detected; the limit of detection was 1 g/kg.

The permethrin TC has a nominally *cis*/*trans* ratio of 25/75 similar as that of a permethrin TC whose WHO specification was published in 2010. However, the two diastereomers called *cis* and *trans*, respectively – in general considered as being racemic in themselves – show an excess of the 1*S*-*cis* and 1*R*-*trans* enantiomers respectively, over their respective optical antipodes. The Meeting therefore concluded that the BCS permethrin TC specification cannot be accommodated into the existing 25:75 (racemic) permethrin TC specification and is considered as a new reference profile. The new profile is supported by confidential data on manufacturing and impurity profile, physical-chemical-, analytical-, toxicity and ecotoxicity data package.

The 5-batch analysis study was performed according to GLP guidelines. The CIPAC method 331/TC/M/3 (capillary GC with flame ionization detection and internal standard) was used for determination of total permethrin and *cis*/*trans* ratio. The permethrin manufacturing impurities were determined by GC-FID, except for water that was determined using the CIPAC Karl Fischer method and some residual solvents that were determined by GC-FID. All the analytical methods used in the 5-batch analysis study were fully validated for their specificity, linearity of response, accuracy, repeatability and limits of detection and quantification (for impurities).

The minimum purity of permethrin in the TC is 950 g/kg. Mass balances are acceptable (97.9 to 98.8%), with no unknowns detected. Even though one out of five batches is slightly below the closure of mass balance of 980 to 1020 g/kg, the value was considered acceptable given the more challenging determination of 4 individual permethrin stereoisomers in the technical material.

The adopted CIPAC method for determination of enantiomeric ratio in the *cis* and *trans* diastereomers is based on enantioselective HPLC on a cellulose derivative column in the normal phase mode. This peer validated method adopted by CIPAC allows to fully resolve and quantify all four stereoisomers of permethrin in technical material.

The manufacturing process of the BCS permethrin TC is similar to those evaluated by JMPS (permethrin 40/60 and 25/75). However particular attention has been paid on the chirality aspect and the company has been asked to describe how the desired enantiomeric excesses in the two permethrin diastereomers is produced and controlled. The company explained the manufacturing process yielding the desired enantiomeric excesses in a commonly used intermediate. These excesses are then carried forward to the finished TC material.

Taking these explanations into account, and in agreement with earlier evaluations of other permethrins with different *cis/trans* ratio, the Meeting concluded that none of the impurities ≥ 1 g/kg should be considered as relevant.

The situation is complicated by the fact that the ISO 1750 common name definition for permethrin does neither specify the diastereomeric nor enantiomeric ratio. Therefore, in practice, the common name together with the ratio of *cis* and *trans* diastereomers was used in FAO and WHO specifications in the past. In that way, and in order to unambiguously distinguish the different permethrin TC profiles, the current permethrin was proposed to be designated as “25:75 nonracemic”. The Meeting noted that some pure enantiomers do actually have a common name allocated (e.g. the 1*R-trans* biopermethrin) but this was considered as inappropriate for the permethrin under consideration, as it is an enantio-enriched mixture.

However, the material tested in the toxicity and ecotoxicity tests was not always entirely characterized to fully establish a firm link between the stereoisomer composition and hazard profile. In some tests, the *cis/trans* ratio was determined, in some studies this information was missing and no information on enantiomer ratio was provided.

The company explained that a validated test method to resolve and quantify all four permethrin stereoisomers became available only recently.

The Meeting considered published information on the insecticidal activity, on neurotoxicity in mammals and on the ecotoxicity profile of individual permethrin stereoisomers. The Meeting noted that the *1S*-isomers have low biological activity both in target insects and in mammalians. Therefore, the key determinant of the toxicity/ecotoxicity potential of the nonracemic permethrin is the mammalian toxicity *vs.* insecticidal potency of *1R-trans* permethrin, which is in quantitative excess as compared to the two existing WHO/FAO specifications. There is in addition a minor increase in the ratio of the total *1R*-diastereomers over the *1S*-diastereomers.

The insecticidal potency of permethrin products is dependent on the proportion of the *1R*-diastereomers in the product (Clark and Symington 2012, Soderlund et al 2002). No clear-cut difference seems to exist between the *trans* and *cis* diastereomers. The nonracemic permethrin is no worse than the racemic permethrin.

Only 1*R*-diastereomers of pyrethroids are neurotoxic in mammals. The 1*S*-diastereomers are not neurotoxic even when injected to the central nervous system (Soderlund et al 2002). Also measured as acute toxicity, the 1*R*-diastereomers of permethrin were more toxic in mice than the 1*S*-diastereomers. However, the acute oral toxicity in mice of 1*R-trans* permethrin was 1/30 of that of 1*R-cis* permethrin (Miyamoto 1976). The low toxicity of 1*R-trans* isomer in comparison to the 1*R-cis* is in part due to its rapid hydrolysis, but the comparatively low toxicity of the 1*R-trans* over the 1*R-cis* is also seen after intracerebral administration (Soderlund et al 2002). All four permethrin isomers were inactive in an *in vitro* bacterial mutagenicity assay using *S typhimurium* and *E coli* (Miyamoto 1976).

Trans-permethrins (diastereomers not separated) were rapidly hydrolyzed by isolated rat and human liver and intestinal microsomal preparations and isolated carboxyl esterases from human intestine. *cis*-Permethrin was not hydrolyzed (Crow et al. 2007). The clearance of *trans*-permethrin by human liver microsomes was 45% faster than that by rat microsomes (in contrast to other pyrethroids tested, for which rat microsomes 10-15 times more active). *Cis*-permethrin was not hydrolyzed, but was oxidized by several microsomal cytochromes P450 (Scollon et al. 2009).

In conclusion, 1*R-trans* permethrin thus has clearly lower toxicity to mammals, including humans, than 1*R-cis* permethrin. The nonracemic permethrin apparently is considered to have a lower toxicity potential to humans than the racemic permethrin.

As far as aquatic toxicity is concerned, in killifish, 1*R*-permethrins were more than 100 times more toxic than the 1*S*-diastereomers; there was little difference between the 1*R-trans* and 1*R-cis* diastereomers (Miyamoto 1976).

Because of the slightly higher *R*/*S* ratio of the nonracemic permethrin, this may show a somewhat higher potential of environmental, notably aquatic toxicity. The preferential degradation of the *S-cis*-isomer, further slightly increases the relative aquatic toxicity with time. However, as permethrin products, independent of the isomer composition, are very toxic to the aquatic environment, the slightly more marked toxicity of the nonracemic permethrin over the racemic product does not make much of a difference.

The Meeting therefore concluded, that the TC specification for permethrin 25/75 nonracemic proposed by BCS was chemically non-equivalent to the already adopted 25/75 permethrin TC specification, but its toxicity and ecotoxicity hazard profiles were not worse than those of the already evaluated and published permethrin 40/60 and 25/75.

The Meeting concluded that, considering the chemical evidence for an own specification and the hazard data presented, the new specification for permethrin 25/75 nonracemic was deemed acceptable. The Meeting therefore recommended that the specification should be adopted by WHO.

The permethrin under consideration has been approved in 2014[3] as biocide in EU with Ireland as Rapporteur Member State. A letter of access was received for the national authority in Ireland for comparing the confidential data. The Irish Department of Agriculture, Food and the Marine as national authority for pesticides and biocides confirmed that permethrin 25:75 nonracemic from Bayer was evaluated

[3] EU Com 1090/2014 from 16 October 2014.

as a biocide (EC, 2014) and that the confidential data package submitted in Ireland is the same as submitted to the JMPS.

There is one specification for a formulated product – the WHO specification for an EW comprising *S*-bioallethrin, permethrin 25:75 and piperonyl butoxide (November 2006). This specification needs revision with respect to the following points:

- Permethrin 25:75 nonracemic is used to formulate the product and the information section and the reference in the EW specification should refer to the published specification for permethrin 25:75 nonracemic.
- Piperonyl butoxide from an approved source (Endura, WHO specification 33/TC, September 2011) should be referenced.
- The analytical methods for determination of *S*-bioallethrin, permethrin 25:75 nonracemic and piperonyl butoxide in EW formulations were adopted in the last years by CIPAC and published in recent Handbooks. These references need to be updated.
- Some CIPAC MT methods, e.g. for persistent foam, MT 47.2 were revised and replaced by a newer method, in that case by MT 47.3. The latest developments in CIPAC MT methods should be included.

SUPPORTING INFORMATION

FOR

EVALUATION REPORT 331/2014

Explanation

The data for permethrin were evaluated in support of a new WHO specification for permethrin 25:75 *cis:trans* (nonracemic) TC.

Permethrin is not under patent.

Permethrin was evaluated by the FAO/WHO JMPR and WHO/IPCS initially in 1979 and subsequently on a number of occasions, over many years (e.g. in 1987, 1999, 2002). It was evaluated / reviewed by the US EPA in 2006, 2007 and 2009 and is currently under evaluation/review by the European Commission.

The draft specification and the supporting data were provided by Bayer S.A.S., Environmental Science in 2012.

Uses

Permethrin is a non-systemic pyrethroid insecticide, with contact and stomach action and some repellent effects. It is mainly used in public and animal health.

Identity of the active ingredient

ISO common name

permethrin (E-ISO), permethrine (F-ISO)

Chemical name(s)

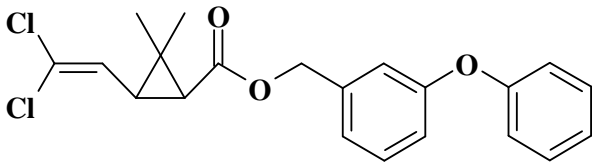
IUPAC: 3-phenoxybenzyl (1*RS*,3*RS*;1*RS*,3*SR*)-3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropanecarboxylate

CA: (3-phenoxyphenyl)methyl 3-(2,2-dichloroethenyl)-2,2-dimethylcyclopropanecarboxylate

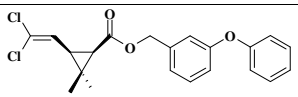
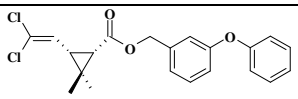
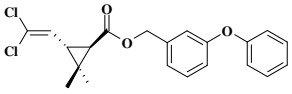
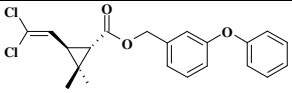
Synonyms

none

Structural formula



Two pairs of diastereoisomers are present in a ratio of approximately 25:75 (each diastereoisomers consisting of a pair of enantiomers in a ratio of 70:30%).

Isomer nomenclature	*Chemical structure*	*Enantiomer content [g/kg]*	*Diastereomer proportion*
1R, cis		*50-100*	*25*
1S, cis		*150-200*	
1R, trans		*450-550*	*75*
1S, trans		*170-270*	

Molecular formula

$C_{21}H_{20}Cl_2O_3$

Relative molecular mass

391.3

CAS Registry number

52645-53-1

CIPAC number

331

Identity tests for permethrin 25:75 nonracemic

Retention times in nonchiral capillary GC (permethrin and cis/trans ratio), enantioselective normal phase HPLC (enantiomeric ratios)

Physico-chemical properties of permethrin

Table 1. Physico-chemical properties of pure permethrin

Parameter	Value(s) and conditions	Purity %	Method reference (and technique if the reference gives more than one)	Study number
Vapour pressure	cis: 2.88 µPa at 25°C trans: 0.92 µPa at 25°C	cis: 99.7 trans: 99.6	Gas saturation, GLP	P-2242
Melting point	cis: 55.2°C trans: 43.9°C TC 25-75: 28°C	cis: 99.3 trans: 99.0 TC: 96.5 (25:75)	OECD Test Guidelines 102, EPA Product Properties Test Guidelines OPPTS 830.7200	M-412132-01-1 M-412135-01-1 M-413049-01-1
Temperature of decomposition	cis: the active substance starts to decompose at 265°C with exothermal effect within the range of 265 - 400°C with an energy of 362 to 447 J/g. trans: the active substance starts to decompose at 240°C with exothermal effect within the range of 240 - 390°C with an energy of 359 to 371 J/g. TC 25-75: the technical active substance starts to decompose at 255°C with exothermal effect within the range of 255 - 335 °C with an energy of 217 to 220 J/g	cis: 99.3 trans: 99.0 TC: 96.5 (25:75)	OECD Test Guidelines 113	M-412132-01-1 M-412135-01-1 M-413049-01-1
Solubility in water	< 4.95 µg/l at 20°C	≥ 99.0 (25:75)	EC official guideline method L383A A6	1430/016
Octanol/water partition coefficient	cis: log P_{OW} = 6.6 at 25°C (pH 5.7) trans: log P_{OW} = 6.4 at 25°C (pH 5.7)	cis: 99.3 trans: 99.0	OECD Guideline 117 European Commission Council Regulation (EC) No 440/2008, Annex, Part A, method A.8. EPA Product Properties Test Guideline OPPTS 830.7570	M-412144-01-1 M-412156-01-1
Hydrolysis characteristics, Half-life at 25°C	Sterile aqueous buffer solutions at pH 4, 7, and 9 in the dark, testing *cis* and *trans* isomers separately (both cyclopropyl 1-14C labelled). pH 4 and 7, both isomers stable. half-life at pH 9: cis = 42.3 d trans = 37.7 d	Radio-chemical purity, both isomers >98	Japan-MAFF guideline No.12-Nosan No.8147, Part 2-6-1 (similar to OECD)	JM-0014

Parameter	Value(s) and conditions	Purity %	Method reference (and technique if the reference gives more than one)	Study number
Photolysis characteristics	Xenon lamp with filter (blocking IR & radiation <290 nm), in sterile buffer solution (pH 4) or synthetic humic water (SHW), with dark control, testing *cis* and *trans* isomers separately (both cyclopropyl 1-14C labelled). Irradiation equivalent to natural sunlight (Tokyo, 35°N, April-June) for 30 days. Half-life: cis = 23.1 d (buffer), 14.6 d (SHW) trans = 36.8 d (buffer), 25.5 d (SHW)	Radio-chemical purity, both isomers >98	Japan-MAFF guideline No.12-Nosan No.8147, Part 2-6-2 (similar to OECD)	JM-0016
Dissociation characteristics	Molecule is not expected to dissociate	-	-	-

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

Manufacturing process, maximum limits for impurities ≥ 1 g/kg, 5 batch analysis data	Confidential information supplied and held on file by WHO. Mass balances were 97.9 to 98.8% and percentages of unknowns were 0.54 – 0.58 %.
Declared minimum permethrin content	950 g/kg
Relevant impurities ≥ 1 g/kg and maximum limits for them	None
Relevant impurities < 1 g/kg and maximum limits for them	None
Stabilisers or other additives and maximum limits for them	None

Parameter	Value and conditions	Purity %	Method reference	Study number
Melting temperature range of the TC	22 - 48°C	96.5 (25:75)	OECD Test Guidelines 102, EPA Product Properties Test Guidelines OPPTS 830.7200	M-413049-01-1
Solubility in organic solvents	20°C Hexane >250g/L Toluene >250g/L Dichloromethane >250g/L Methanol >250g/L Acetone >250g/L Ethyl acetate >250g/L 30°C Hexane >250g/L Toluene >250g/L	97.3 (25:75)	CIPAC method MT 181	M-296952-01-1

Hazard summary

In 2004 permethrin 25:75 has been submitted to the RMS (IE) by Bayer Environmental Science/Sumitomo Chemicals consortium for the purpose of consideration for inclusion in Annex 1 of the Biocidal Products Directive 98/8/EC. In 2008 Tagros Chemicals India Ltd. as second notifier submitted data on permethrin for the purpose of annex 1 inclusion. Both sets of data have been evaluated and approved by the European Commission in October 2014.

Permethrin was evaluated by the FAO/WHO JMPR on a number of occasions, over many years. The ADI of 0-0.05 mg/kg bw, previously set by the JMPR, was extended from 40:60 permethrin to include 25:75 permethrin (JMPR 1987) and an acute RfD of 1.5 mg/kg bw was subsequently allocated (JMPR 2002). The WHO hazard classification of permethrin is Class II, moderately hazardous (WHO 2002).

Formulations and co-formulated active ingredients

The main formulation types available are DP, WP, EC and EW for public health.

Permethrin 25:75 may be co-formulated with bioallethrin, esdepallethrine or tetramethrin. A synergist (piperonyl butoxide) may be added.

These formulations are registered and sold in many countries throughout the world.

Methods of analysis and testing

The analytical method for the active ingredient (including identity tests and isomer ratio) is a CIPAC method (CIPAC Handbook M, p. 155 for TC, EW and LN). Permethrin is determined by capillary GC with FID and internal standard with triphenylphosphate. The older packed column GC method published in Handbook C p. 2173 1985 is applicable for TC, DP, WG and WP.

The method for determination of the ratio of the steroisomers is a normal-phase HPLC method using a cellulose derivative and is capable to baseline resolve and quantify all four stereoisomers of permethrin.

The methods for determination of impurities are based on external standard GC-FID method.

Test methods for determination of physico-chemical properties of the active ingredient were OECD, EC, JMAFF, EPA and CIPAC, as indicated in the specification and supporting documentation.

Physical properties

The physical properties, the methods for testing them and the limits proposed for the EW formulation, comply with the requirements of the FAO/WHO Manual (2010 edition).

Containers and packaging

No special requirements for containers and packaging have been identified.

Expression of the active ingredient

The active ingredient is expressed as permethrin in g/kg or g/L, as the sum of *cis* and *trans* isomers, present in a nominal ratio of 25:75, with a permitted range from 22% to 28% and 72% to 78%.

ANNEX 1

HAZARD SUMMARY PROVIDED BY THE PROPOSER

Notes:

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

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

(i) Data included in the summary below relate to a *cis*:*trans* range of 25:75 to 40:60 isomeric ratio of permethrin. In 1999 JMPR included in the ADI of 0-0.05 mg/kg bw permethrin products with a *cis:trans* ratio from 40:60 to 25:75. Hence in regard to toxicology JMPR assume similarity for the different forms of permethrin within this range of *cis:trans* isomeric ratio. Therefore it is reasonable to conclude that also the ecotoxicity profile for this range of isomeric ratios of permethrin is similar.

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

Species	Test	Purity % Note[4]	Guideline, duration, doses and conditions	Result	Study number **Error! Bookmark not defined.**
Rat, Wistar 5 ♂+ 5 ♀ per dose level	Oral	Purity and ratio not stated	Dosage/condition: 400, 450, 500, 560, 630 mg/kg permethrin administered in corn oil by gavage as single dose Duration: 14 days post-exposure observation Guideline: pre-guideline, pre-GLP	LD_{50} = 480 mg/kg	2739-75
Rat, Long Evans 5 ♂+ 5 ♀ per dose level	Oral	95.5 (25:75)	Dosage: 590, 885, 1328, 1992, 2990 mg/kg permethrin administered in corn oil by gavage as single dose Duration: 14 days post-exposure observation Guideline: pre-guideline, pre-GLP	LD_{50} = 1623 mg/kg	2186-74
Rabbit, New Zealand White Unspecified sex 5 abraded, 5 non-abraded	Dermal	Purity and ratio not stated	Dosage: 2000 mg/kg permethrin Duration: 14 days post-exposure observation Guideline: 16 CFR 1500.40, pre-GLP	LD_{50} > 2000 mg/kg	2908-75
Rat, Wistar albino 5 ♂+ 5 ♀	Inhalation	Purity and ratio not stated	Dosage: 23.5 mg/L permethrin Duration: 4 hours exposure, 14 days post-exposure observation Guideline: pre-guideline, pre-GLP	LC_{50} > 23.5 mg/L	2911-75
Rabbit New Zealand White Unspecified sex 6 animals with abraded and intact skin	Skin irritation	Purity and ratio not stated	Dosage: 0.5 mL of 1 g/mL permethrin aqueous slurry administered per test site Duration : 24 hours exposure, 72 hours post-exposure examination Guideline: 16 CFR 1500.41, pre-GLP	Primary Dermal Irritation Index = 0.25 Permethrin was not found to be a skin irritant and does not warrant classification.	2909-75

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

Rabbit New Zealand White Unspecified sex 9 animals	Eye irritation	Purity and ratio not stated	Dosage: 0.1 mL of permethrin test material applied Duration: 7 days post-exposure observation Guideline: 16 CFR 1500.42, pre-GLP	Low irritation potential Permethrin was not found to be an eye irritant and does not warrant classification.	2910-75
Guinea pig Dunkin/Hartley ♀ 20 test animals	Skin sensitization	Purity not stated (25:75)	Dosage: as supplied + 50% v/v in corn oil Guideline: EPA FIFRA 81-6 (GPMT) GLP	Negative (0/20)	91626D/ WLC 159/SS

Table B. Toxicology profile of the permethrin technical material based on repeated administration (subacute to chronic)

Species	Test	Purity % Note[5]	Guideline, duration, doses and conditions	Result	Study number
Rat, Wistar 18 ♂ and 18 ♀ per dose level (20 (♂+♀) per treatment group +16 (♂+♀) recovery group)	Oral (diet)	Purity not stated (25:75)	Dosage: 0, 200, 600, 2000, 4000 ppm permethrin ≡ 17.0, 49.9, 179.6, 357.4 mg/kg bw/day ♂ or 18.5, 56.2, 176.5 and 356.7 mg/kg bw/day ♀ Duration: 90 days treatment (+36 days recovery) Guideline: pre-guideline, pre-GLP	NOAEL = 2000 ppm ≡ 175 mg/kg bw/day LOEL = 4000 ppm ≡ 355 mg/kg bw/day	HEFG 76-1
Dog, Beagle 4 ♂ and 4 ♀ per dose level	Oral (capsule)	94.5 (25:75)	Dosage: 0, 10, 50, 250 mg/kg bw/day Duration: 180 days Guideline: pre-guideline, pre-GLP	NOAEL = 10 mg/kg bw/day based on increased liver weight LOEL = 50 mg/kg bw/day	HEFG 78-14
Dog, Beagle 6 ♂ and 6 ♀ per dose level	Oral (capsule)	92.5 (32.3:60.2)	Dosage: 0, 5, 100, 1000 mg/kg bw/day Duration: one year Guideline:pre-guideline, pre-GLP	NOAEL = 5 mg/kg bw/day LOEL = 100 mg/kg bw/day	CTL/P/647
Rat, Charles River CD 5 ♂ and 5 ♀	Inhalation, repeated toxicity	94.7 (25.2:69.5)	Dosage: 0, 5, 50 and 500 mg/m^3 administered via aerosol Duration: 15 x 6 hour exposure periods over a 21 day period: 2 consecutive days week 1, 5 consecutive days week 2, 5 consecutive days week 3, 3 consecutive days week 4 Guideline: pre-guideline, pre-GLP	NOAEL = 6.1 mg/m^3 LOEL = 42.2 mg/m	WLC 34/80323
Rat, Wistar 60 ♂ and 60♀ per dose level (main study) 15 ♂ and 15♀ per dose level (satellite study of blood and urine)	Carcinogenicity, chronic oral (diet)	Purity not stated (25:75)	Dosage: 0, 10, 50, 250 mg/kg bw/day Duration: 103 weeks Guideline: pre-guideline, pre-GLP	NOAEL = 10 mg/kg bw/day LOEL= 50 mg/kg bw/day	80/WRL003 /283

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

Rat, Wistar 12 ♂ and 12 ♀ per dose level at interim sacrifice 24 ♂ and 24 ♀ per dose level at terminal sacrifice	Carcinogenicity, chronic oral (diet)	≥93.9 (40:60)	Dosage: 0, 25, 50, 125 mg/kg bw/day Duration: 104 weeks Guideline: pre-guideline, GLP	NOAEL = 50 mg/kg bw/day LOEL= 125 mg/kg bw/day	M-179674-01-1
Mouse, Swiss 10 ♂ and 10 ♀ per dose level at interim sacrifice 25 ♂ and 25 ♀ per dose level at terminal sacrifice	Carcinogenicity, chronic oral (diet)	≥93.9 (40:60)	Dosage: 0, 38, 150, 380 mg/kg bw/day Duration: 98 weeks Guideline: pre-guideline, GLP	NOAEL = 150 mg/kg bw/day LOEL = 380 mg/kg bw/day	M-179674-01-1
Rat, Wistar 20 ♂ and 20 ♀ per dose level and generation	Multigeneration reproduction, oral (diet) (limit test)	93.3 (26.3:73.7)	Dosage: 0, 5, 30, 180 mg/kg bw/day Duration: Exposure before mating: P generation 84 days; F1 and F2 generations, 63 days. Exposure in general: P generation, 27 weeks; F1 and F2 generations, 26 weeks. Guideline: pre-guideline, GLP	No critical effect NOAEL = 180 mg/kg bw/day (parental, F1, F2, ♂, ♀) LOEL > 180 mg/kg bw/day (parental, F1, F2, ♂, ♀)	BPAT 79/3
Rat, Wistar 22 or 23 ♀ per group	Teratogenicity, oral (gavage) (limit test)	Purity not stated (25:75)	Dosage: 200 mg/kg bw administered in corn oil Duration: Exposure at days 6-16 post-mating; 4 days post-exposure observation Guideline: pre-guideline, pre-GLP	No maternal, teratogenic or embryo-toxic effects. NOAEL = 200 mg/kg (maternal tox, teratogenicity, embryotoxicity) LOEL > 200 mg/kg (maternal tox, teratogenicity, embryotoxicity)	BPAT 74/10

Rabbit, New Zealand White 18-24 ♀ per dose level	Teratogenicity, oral (gavage) (full test)	94.8 (25:75)	Dosage: 0, 100, 200, 400 mg/kg bw administered in corn oil Duration: Exposure at days 6-18 post-mating; 11 days post-exposure observation Guideline: pre-guideline, pre-GLP	No maternal, embryo-toxic or terato-genic effects. NOAEL = 400 mg/kg (maternal tox, teratogenicity, embryotoxicity) LOEL > 400 mg/kg (maternal tox, teratogenicity, embryotoxicity)	HEFG-80-4
Mouse, NMRI 40 ♂ and 40♀ per dose leve	Neurotoxicity, inhalation	96.8 (Ratio not stated)	Dosage: 0, 2.5, 25, 250 mg/m^3 Duration: 6.3 h for 7 consecutive days; 10 days post-exposure observation Guideline: pre-guideline, GLP	NOAEL = 2.5 mg/m^3 LOEL = 25 mg/m^3 (based on receptor changes at age 4 months in females)	M-197449-01-1

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

Species	Test	Purity % Note[6]	Guideline, duration, doses and conditions	Result	Study number Error! Bookmark not defined.
Salmonella typhimurium strains: TA 1535, TA 1537, TA 98, TA 100, TA 1538	Salmonella /Mammalian Microsome Plate Incorporation and Pre-Incubation Assays (*in vitro*)	Batch 8E8026 = 94.1-96.3 Batch 8I8012 =95.91-97.3 (25:75)	Dosage: 0, 0.5, 2.6, 13.0, 25.0, 50.0 µL/plate ± S9 Guideline: pre-guideline, pre-GLP	+S9: negative -S9: negative	015-560-150A-1 and 015-560-150A-2
Human lymphocyte cultures and CHO cells	Mammalian chromosome aberrations test (*in vitro*)	99.5 (Ratio not stated)	Dosage: Human lymphocytes: 0, 50, 75, 100, 150, 200 µg/mL -S9, 0, 50, 75, 100, 150 µg/mL +S9 CHO cells: 0, 20, 50, 100 µg/mL ±S9 Guideline: UKEMS Recommended Procedures, Non-GLP	+S9: negative -S9: positive	
Mouse lymphoma cells L5178Y/TK$^{+/-}$	Mammalian cell gene mutation test (*in vitro*)	Purity not stated (25:75)	Dosage: -S9 Experiment 1: 0, 31, 47, 62, 94, 125 µg/mL Experiment 2: 0, 45 µg/mL Experiment 3: 0, 30, 40, 50 µg/mL +S9 Experiment 1: 0, 16, 31, 47, 62, 94 µg/mL Experiment 2: 0, 20, 30, 40, 50 µg/mL Guideline: pre-guideline, pre-GLP	+S9: negative -S9: negative	TTEP / 77 / 0001
Mouse, Swiss albino 5 ♂ and 5 ♀ per dose level	Mammalian erythrocyte micro-nucleus test (*in vivo*)	94 (Ratio not stated)	Dosage: 0, 107, 215, 430 mg/kg bw, single oral dose administered in peanut oil by gavage Duration: 24 hours post exposure Guideline: OECD 474 EC B. 12 US EPA PAG 84-2 GLP	negative	M-197307-01-1

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

Mouse, Swiss albino 5 ♂ and 5 ♀ per dose level	Chromosomal aberration assay (*in vivo*)	94 (Ratio not stated)	Dosage: 0, 107, 215, 430 mg/kg bw, single oral dose administered in peanut oil by gavage Duration: 24 hours post exposure Guideline: OECD 475 EC B. 11 US EPA PAG 84-2 GLP	negative	M-196736-01-1
Mouse, CD 1 10♂ + 180♀ per group	Rodent dominant lethal test (*in vivo*)	Purity not stated (25:75)	Dosage: 452 mg/kg bw oral dose x 5 (24 h intervals) administered in corn oil by gavage Guideline: pre-guideline, pre-GLP	negative	HEFG 75-10

Table D. Ecotoxicology profile of the permethrin technical material

Species	Test	Purity % Note[7]	Guideline, duration, doses and conditions	Result	Study number
Daphnia magna (water flea)	Acute toxicity	94.5 (25:75)	Design: static Dosage: Mean measured at 0 hours : 0.00039, 0.00053, 0.0008, 0.00157, 0.00245, 0.00416, 0.00874, 0.0154, 0.0322, 0.0623 mg permethrin/L Duration: 48h Guideline: none	EC_{50} = 0.00127 mg/l (based on mean measured concentration)	HEFG 78-10
Daphnia magna (water flea)	Chronic toxicity	94.8 (Ratio not stated)	Design: Flow-through system Dosage: nominal conc. 0, 40, 80, 160, 320, 640 ng/L Duration: 21 d Guideline: ASTM Standard guide for *Daphnia magna* lifecycle, GLP	$EC_{50\ mort}$ = >0.00034 mg/L	BL5443/B
Oncorhynchus mykiss (Rainbow trout)	Acute toxicity	94.5 (25:75)	Design: flow through Dosage: nominal conc. 0.001 – 0.056 mg/L Duration: 96h Guideline: Pre-guideline, pre-GLP	LC_{50} = 0.0051 mg/L (based on mean measured concentration)	HEFG 78-11
Fathead minnows and snails	Chronic toxicity	92 (Ratio not stated)	Design: flow system Dosage: measured conc. 0.11 – 1.40 µg/L Duration: 28 d Guideline: none	NOEC = 0.0006 mg/L (Mortality)	M-172283-01-1
Sheepshead minnows	Chronic toxicity	93 (Ratio not stated)	Design: Intermittent flow system Dosage: Mean measured conc. 1.6 – 42 µg/L Duration: 28 d Guideline: none	NOEC = 0.01 mg/L (Fry survival)	M-286977-01-1
Pseudokirchneriella subcapitata (green algae)	Growth inhibition	97.3 (26.7:73.3)	Design: static Dosage: nominal conc. 0.0286 – 3.0 mg/L Duration: 72 h Guideline: OECD 201	E_rC_{50} = > 1.13 mg/L E_rC_{10} = 0.0023mg/L NOE_rC < 0.0131 mg/L	M-298015-01-2

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

Eisenia foetida (Earthworm)	Mortality	94 (Ratio not stated)	Design: contact Dosage: Initial conc. 0, 100, 200, 400, 800, 1600 mg/kg Duration: 14 d Guideline: OECD 207	LC_{50} = 126 mg/kg dry soil (converted to artificial soil)	M-196729-01-1
Apis mellifera (honey bee)	Mortality/ oral and contact / sublethal effects	93.1 (No information about ratio)	Design: oral: sucrose solution contact: acetone solution Dosage: Oral: 0.0005 – 0.025 µg/bee Contact: 0.005 – 0.2 µg/bee Duration: 48h Guideline: UK Pesticides Safety Precautions Scheme Working Document D3: Laboratory testing for toxicity to honey bees	24 h $LD_{50\ oral}$ = 0.169 µg/bee 48 h $LD_{50\ oral}$ = 0.163 µg/bee 24 h $LD_{50\ contact}$ = 0.0262 µg/bee 48 h $LD_{50\ contact}$ = 0.0235 µg/bee	RJ1344B
Bobwhite quail	Mortality/ growth	95.7 (Ratio not stated)	Design: short-term Dietary Dosage: 464 – 10000 ppm Duration: 8 days Guideline: none	LC_{50}> 10 000 ppm	HEFG-79-C89
Northern Bobwhite	Reproduction	95.2 (No information about ratio)	Design: Long-term Dietary Dosage: 0 – 500 ppm Duration: 20 w Guideline: none	NOEC = 500 ppm	104-166: A90-3330
Mallard duck	Mortality/ growth	95.7 (Ratio not stated)	Design: Acute Oral/Gavage Dosage: 215 – 4640 mg/kg Duration: 8 days Guideline: none	LD_{50}> 4640 mg/kg bw	HEFG-79-C90

ANNEX 2: REFERENCES

References for appraisal

Author(s)	Year	Journal
Dr. Finbar Brown, Regulatory and Enforcement Unit (Biocides), Pesticide Control Division, Department of Agriculture, Food and the Marine, Ireland	2015	e-mail communication on 16 June 2015 confirming the similarity of confidential data submitted by Bayer to JMPS and Regulatory and Enforcement Unit (Biocides).
Burt, P., Elliott, M., Farnham, A. et al.	1974	Pestic Sci 5:791-799.
Clark, J. M., Symington, S. B.	2012	Top Curr Chem 314:49-72.
Crow, J. A., Borazjani, A., Potter, P. M. et al.	2007	Toxicol Appl Pharmacol 221:1-12.
Elliott, M., Farnham, A., Janes, N. F. et al.	1975	Pestic Sci 6:537-542.
EC (European Commission)	2014	Commission Implementing Regulation (EU) No 1090/2014.
Burt, P., Elliott, M., Farnham, A. et al.	1974	Pestic Sci 5:791-799.
Clark, J. M., Symington, S. B.	2012	Top Curr Chem 314:49-72.
Crow, J. A., Borazjani, A., Potter, P. M. et al.	2007	Toxicol Appl Pharmacol 221:1-12.
Liu, W., Gan, J., Lee, S. et al.	2005a	Environ Toxicol Chem 24:1861-1866.
Liu, W., Gan, J., Schlenk, D. et al.	2005b	Proc Natl Acad Sci U S A 102:701-706.
Liu, W., Gan, J. J., Qin, S.	2005c	Chirality 17 Suppl:S127-133.
Miyamoto, J.	1976	Environ Health Perspect 14:15-28.
Scollon, E. J., Starr, J. M., Godin, S. J. et al.	2009	Drug Metab Dispos 37:221-228.
Soderlund, D. M., Clark,. M., Sheets, L. P. et al.	2002	Toxicology 171:3-59.

References for non-confidential data (sorted by study number)

Bayer CropScience document No. or Report No. or other reference	Author(s)	Year	Study title. Study identification number. Report identification number. GLP [if GLP]. Company conducting the study.
M-172283-01-1	Spehar, R.L., Tanner, D.K., Nordling, B.R.	1983	Toxicity of the synthetic pyrethroids, permethrin and AC222,705 and their accumulation in early life stages of fathead minnows and snails; Aquatic toxicology; 3; 171-182; US EPA laboratory, Published.
M-179674-01-1	Ishmael J. & Litchfield M.H.	1988	Chronic Toxicity and Carcinogenic Evaluation of permethrin in Rats and Mice; Imperial Chemical Industries PLC, UK; Fundam. Appl. Toxicol. 11, 308-322, Published.
M-196729-01-1	Kumar, A.	1997	Permethrin Technical Acute toxicity in Earthworm. Report No. 1054/JRF/ECO/97, Jai Research Foundation, India; Bayer CropScience, GLP, Unpublished.
M-196736-01-1	Prabakaran P.	1997	Chromosomal Aberration Study of Permethrin Technical in Mice; Report No. 1269/JRF/TOX/97, Jai Research Foundation, India; Bayer CropScience, 14.10.1997, GLP, Unpublished.
M-197307-01-1	Prabakaran P.	1997	Micronucleus Test of Permethrin Technical in Mice; Report No. 1270/JRF/TOX/97, Jai Research Foundation, India; Bayer CropScience, 27.09.1997, GLP, Unpublished.
M-197449-01-1	Ivens I, Pauluhn J & Schmuck G.	1997	Motor activity measurements in male and female mice postnatally exposed to Permethrin by inhalation; Report No. C008387, Bayer AG, Germany; 03.07.1997, GLP, Unpublished.
M-286977-01-1	Hansen D.J., Goodman L.R, Moore J.C., Higdon P.K.	1983	Effect of the synthetic pyrethroids AC222,705, permethrin and Fenvalerate on Sheepshead minnows in early life stages toxicity test ; Environmental Toxicology and Chemistry; 2; pp 251-258; US EPA laboratory, non GLP, Published.
M-293274-01-1	Guebert C.	2007	Spectral Data (1H-NMR, 13C-NMR, MS) of the isomers cis-permethrin (BCS-AA10041) and trans-permethrin (BCS-AA10042)of permethrin (AE F032639), study identification AF07/101, Bayer CropScience AG, Germany, non GLP, Unpublished.
M-296952-01-1	Foster, B.	2008	Biocidal testing for solvent solubility; CEMAS report n°CEMS-3768, for Bayer SAS, Environmental Science, GLP, Unpublished.
M-297179-01-1	Walker and O'Connor	2007	Cis-permethrin and trans-permethrin : infrared spectra, SPL project number 2491/0001, Safepharm Laboratories Limited, UK, for Bayer SAS, Environmental Science, GLP, Unpublished.
M-298015-01-2	Dorgerloh, M.	2008	Pseudokirchneriella subcapitata growth inhibition test with permethrin (techn.); Study No. E323 3265-4, Bayer CropScience AG, Germany, GLP, Unpublished.
M-412132-01-1	Smeykal, H.	2011	Permethrin, cis-isomer (BCS-AA10041), pure substance: Melting point, boiling point, thermal stability. Report N° 20110258.01, Siemens AG, Germany, for Bayer CropScience, GLP, Unpublished.
M-412135-01-1	Smeykal, H.	2011	Permethrin, trans-isomer (BCS-AA10042), pure substance: Melting point, boiling point, thermal stability. Report N° 20110258.02, Siemens AG, Germany, for Bayer CropScience, GLP, Unpublished.

M-412144-01-1	Bogdoll, B. and Eyrich, U.	2011	Permethrin, cis-isomer (BCS-AA10041): Partition coefficient 1-octanol / water (HPLC method). Study N˚ PA11/074, Bayer CropScience AG, Germany, GLP, Unpublished.
M-412156-01-1	Bogdoll, B. and Eyrich, U.	2011	Permethrin, trans-isomer (BCS-AA10042): Partition coefficient 1-octanol / water (HPLC method). Study N˚ PA11/076, Bayer CropScience AG, Germany, GLP, Unpublished.
M-413049-01-1	Smeykal, H.	2011	Permethrin, 25/75 TC, technical substance (AE F032639): Melting boiling point, thermal stability. Report N˚ 20110276.01, Siemens AG, Germany, for Bayer CropScience, GLP, Unpublished.
80/WRL003/283	McSheehy TW & Finn J.P.	1980	21Z: Potential Toxicity and Oncogenicity in Dietary Administration to Rats for a Period of 104 Weeks; Life Science Research, Elm Farm Laboratories, UK; Sumitomo Chemical, 10.1980, Unpublished.
015-560-150A-1 and 015-560-150A-2	Haworth S.R.	1979	Salmonella/Mammalian-Microsome Plate Incorporation and Pre-Incubation Mutagenesis Assays of Burroughs Wellcome Compound Permethrin Tech BW 0021Z73 #8E8026 and 8I8012; EG&G Mason Research Institute, USA; Sumitomo Chemical, 16.10.1979, Unpublished.
104-166: A90-3330	Beavers, J.; Foster, J.; Lynn, S.	1992	Permethrin: A one-generation study with the Northern Bobwhite (Colinus virginianus); Wildlife Intl.; Sumitomo Chemical, GLP, Unpublished.
1430/016	White, D.F et al.	2004	Permethrin: Determination of general Physico-Chemical properties; Safepharm Laboratories; Sumitomo Chemical, GLP, Unpublished.
2186-74	Marowitz LA & Strauss WF	1974	Acute Oral Toxicity in Rats Compound No. FMC 33297; Bio/dynamics Inc., USA; Sumitomo Chemical, 15.10.1974, non GLP, Unpublished.
2739-75	Braun WG & Killeen JC	1975	Acute Oral Toxicity in Rats; Compound No.: FMC 33297, LOT #C6725-57; Bio/dynamics Inc., USA; Sumitomo Chemical, 06.08.1975, non GLP, Unpublished.
2908-75	Braun WG & Killeen JC	1975	Acute Dermal Toxicity in Rabbits Compound No. FMC 33297; Bio/dynamics Inc., USA; Sumitomo Chemical, 07.11.1975, non GLP, Unpublished.
2909-75	Braun, WG & Killeen, JC	1975	Rabbit Primary Dermal Irritation Compound No. FMC 33297; Bio/dynamics Inc., USA; Sumitomo Chemical, 31.10.1975, non GLP, Unpublished.
2910-75	Braun, WG & Killeen, JC	1975	Rabbit Eye Irritation Compound No. FMC 33297; Bio/dynamics Inc., USA; Sumitomo Chemical, 31.10.1975, non GLP, Unpublished.
2911-75	Braun WG & Killeen JC	1976	Acute Inhalation Compound No. FMC 33297; Bio/dynamics Inc., USA; Sumitomo Chemical,11.02.1976, non GLP, Unpublished.
91626D/WLC 159/SS	Parcell, BI	1991	Skin Sensitisation in the Guinea-Pig of a Permethrin 25/75 cis/trans Isomer Ratio; Huntingdon Research Centre Ltd., England; Sumitomo Chemical, 13.12.1991, GLP, Unpublished.
BL5443/B	Kent, S.; Williams, N.; Gillings, E.; Morris D.S.	1995	Permethrin: Chronic toxicity to Daphnia magna; Zeneca Brixham Environmental Lab; Sumitomo Chemical, GLP, Unpublished.
BPAT 74/10	James DA	1976	Foetal Toxicity Study of 21Z73 (NRDC 143) in the Rat; Wellcome Research Laboratories, England; Sumitomo Chemical, 03.1976, non GLP, Unpublished.

BPAT 79/3	James DA	1979	A Multigeneration Reproduction Study of 21Z73 (Permethrin) in the Rat; Wellcome Research Laboratories, England; Sumitomo Chemical, 26.01.1979, GLP, Unpublished.
CTL/P/647	Kalinowski, AE, Banham, PB, Chart, IS, Cook, SK, Gore, CW, Moreland, SF & Woolen, BH	1982	Permethrin: One Year Oral Dosing Study in Dogs; Imperial Chemical Industries PLC, UK; AMVAC (Syngenta), 24.02.1982, non GLP, Unpublished.
HEFG 75-10	Chesher BC, Malone JC & Parker MJ	1975	21Z73, Dominant Lethal Study in Male Mice; Wellcome Research Laboratories, England; Sumitomo Chemical, 27.11.1975, non GLP, Unpublished.
HEFG 76-1	Williams LM, Thomson PM, Clampitt RB & Malone JC	1976	21Z73, Rat Oral 90 Day Study; Wellcome Research Laboratories, England; Sumitomo Chemical, 25.02.1976, non GLP, Unpublished.
HEFG 78-10	Thompson R.S. and Williams T.D.	1978	Determination of the acute toxicity of compound 21Z (WRL) to daphnia magna using acetonr as the solvent. Wellcome Research Laboratories, England; Sumitomo Chemical, non GLP, Unpublished.
HEFG 78-11	Maddock, B.G	1978	Determination of the Acute Toxicity of Compound 21z (WRL) to Rainbow Trout (Salmo gairdneri) Using Dimethyl Sulphoxide as the Solvent. The Wellcome Foundation Ltd.; Sumitomo Chemical, non GLP, Unpublished.
HEFG 78-14	Reynolds J, Piercy DWT, Clampitt RB, James JA, Thompson PM, Farebrother DA & Dayan AD	1978	Permethrin Oral Administration to Dogs for 6 Months; Wellcome Research Laboratories, England; Sumitomo Chemical, 01.12.1978, non GLP, Unpublished.
HEFG-79-C89	Fink, R.	1975	Eight-day dietary LC50 in Bobwhite Quail with FMC33297. Wildlife Research Division Report 104-113, Sumitomo Chemical, non GLP, Unpublished.
HEFG-79-C90	Fink, R	1975	Acute oral LD50 in Mallard Duck with FMC33297. Wildlife Research Division Report 104-115; Sumitomo Chemical, non GLP, Unpublished.
HEFG-80-4	Tesh JM, Ross FW, Budgen EK & Tesh SA	1979	21Z: Effects of Oral Administration Upon Pregnancy in the Rabbit; 79/WRL005/459, The Wellcome Foundation Ltd, 02.10.1979, Sumitomo Chemical, non GLP, Unpublished.
JM-0014		2005	Hydrolysis of [14C]Permethrin at pH 4, 7, and 9. Sumitomo Chemical, Unpublished
JM-0016		2005	Aqueous Photolysis of [14C]Permethrin in pH 4 Buffer and Synthetic Humic Water Buffered at pH 7 by Artificial Light. Sumitomo Chemical, Unpublished.
P-2242	Alvarez	1989	Permethrin: Physical Properties; FMC Corportation; Sumitomo Chemical, GLP, Unpublished.
RJ1344B	Gough, H.J, Jackson, D, Lewis, G.B	1993	Permethrin: Acute Contact and Oral toxicity to Honey Bees (Apis mellifera) of technical material; Jealott's Hill Research Station; Sumitomo Chemical, 18 Jan 1993; GLP, Unpublished.

TTEP / 77 / 0001	Clive D	1977	Mutagenicity of BW 21Z73 in L5178Y/TK+/- Mouse Lymphoma Cells with and without Metabolic Activation; Burroughs Wellcome Co., USA; Sumitomo Chemical, 05.01.1977, non GLP, Unpublished.
WLC 34/80323	Alexander DJ, Clark GC, Jackson GC, Gregson RL, Offer JM & Prentice DE	1980	Permethrin Technical Inhalation Study in Rats 15 x 6 Hour Exposures Over a 3 Week Period; Huntingdon Research Centre, England; Sumitomo Chemical, 11.11.1980, GLP, Unpublished.
	Barrueco C, Herrera A, Caballo C & de la Peña E	1994	Induction of Structural Chromosome Aberrations in Human Lymphocyte Cultures and CHO Cells by permethrin; Centro Nacional de Sanidad Ambiental, Instituto de Salud Carlos III1, Seguridad Química, Ministerio de Sanidad y Consumo2, Centro de Ciencias Medioambientales, Consejo Superior de Investigaciones Científicas3, Madrid, Spain; Teratogenesis, Carcinogenesis, and Mutagenesis 14:31-38; 1994, non GLP, Published.
	CIPAC		CIPAC Method 331 TC/m/-, CIPAC/4503/m PERMETHRIN, CIPAC Handbook M, p. 155 for TC and EW and Handbook C p. 2173 1985 for DP & WP, Published.
	FAO/WHO	2006	Manual on development and use of FAO and WHO specifications for pesticides. February 2006 Revision of First Edition. FAO Plant Production and Protection Paper. Revised. http://www.fao.org/ag/AGP/AGPP/Pesticid/Default.htm and http://whqlibdoc.who.int/publications/2006/9251048576_eng_update2.pdf