FAO SPECIFICATIONS AND EVALUATIONS FOR AGRICULTURAL PESTICIDES

PERMETHRIN

(40:60 *cis:trans* isomer ratio)

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

FOOD AND AGRICULTURE ORGANIZATION *of* THE UNITED NATIONS

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DISCLAIMER[1]

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

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

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

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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 1999, the development of FAO specifications has followed the **New Procedure**, described in the 1st edition of "Manual for Development and Use of FAO and WHO Specifications for Pesticides" (2002) and amended with the supplement of this manual (2006), 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 JMPS, 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 plant protection product reflecting the evaluation of the data package carried out by FAO and the JMPS. The data are to be provided by the manufacturer(s) according to the requirements of Appendix A, annex 1 or 2 of the "Manual on the development and use of FAO specifications for plant protection products" 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 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. Dates of publication of the earlier versions, if any, are identified in a footnote. Evaluations bear the date (year) of the meeting at which the recommendations were made by the JMPS.

* NOTE: PUBLICATIONS ARE AVAILABLE ON THE INTERNET AT http://www.fao.org/agriculture/crops/core-themes/theme/pests/pm/jmps/ps/en/)

PART ONE

SPECIFICATIONS

PERMETHRIN

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PERMETHRIN

INFORMATION

ISO common names

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

Chemical name(s)

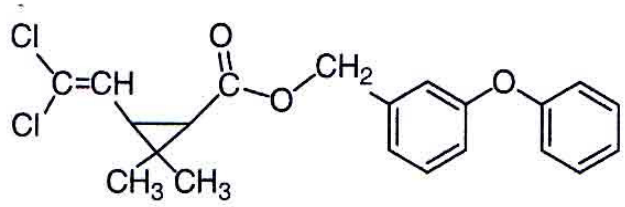
IUPAC: 3-phenoxybenzyl (1*RS*,*3RS*;1*RS*,3*SR*)-3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropanecarboxylate

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

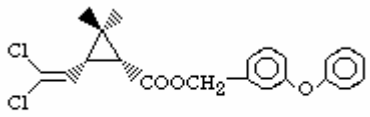
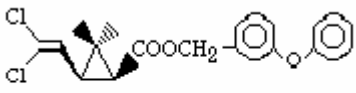
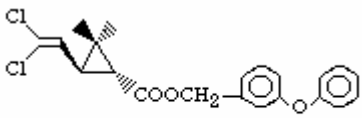
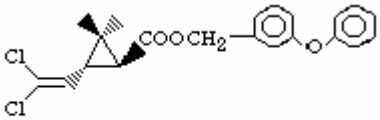
Synonyms

none

Structural formula



Two pairs of diastereoisomers are present in a ratio of approximately 40:60:

 (2) (1R,cis)	sum ≈ 40%
 (4) (1S,cis)	
 (1) (1R,trans)	sum ≈ 60%
 (3) (1S,trans)	

Molecular formula

$C_{21}H_{20}Cl_2O_3$

Relative molecular mass

391.3

CAS Registry number

52645-53-1

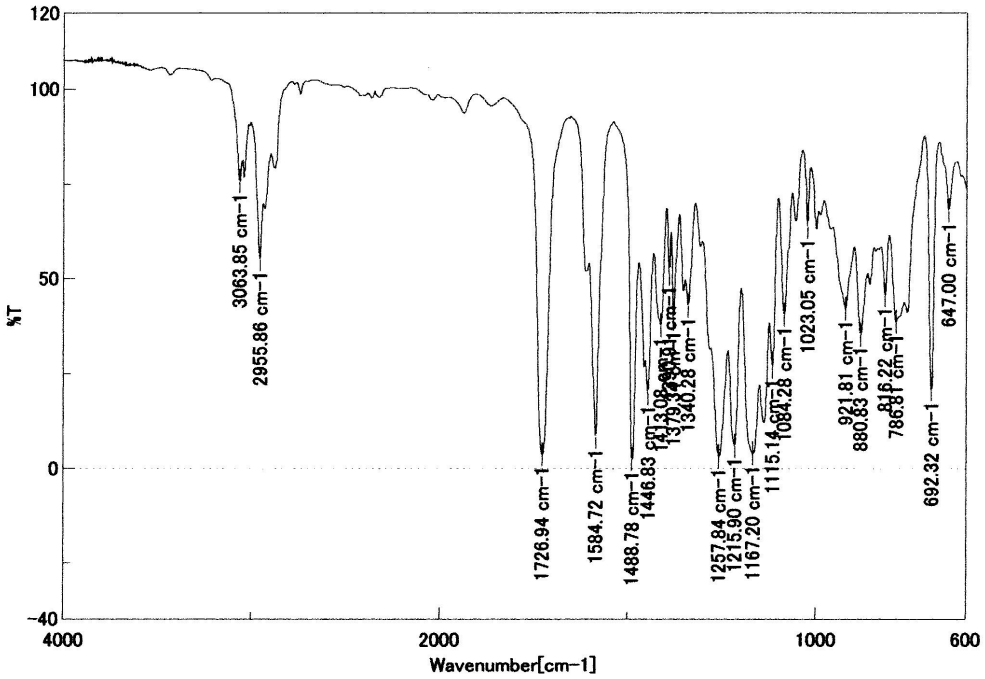
CIPAC number

331

Identity tests

GC retention time, IR spectrum.

Figure 1. IR spectrum of permethrin



40:60 *cis:trans* PERMETHRIN TECHNICAL MATERIAL

FAO Specification 331/TC (March 2009*)

*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 (*331/2008*). It should be applicable to TC produced by this manufacturer but it is not an endorsement of those products, nor a guarantee that they comply with the specifications. The specification may not be appropriate for TC produced by other manufacturers. The evaluation report (*331/2008*), 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 yellow to yellowy-brown viscous liquid, free from visible extraneous matter and added modifying agents.

2 Active ingredient

2.1 **Identity tests** (331/TC/M/2, CIPAC Handbook, 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 **Permethrin content** (331/TC/M/3, CIPAC Handbook, Note 1)

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 isomer ratio** (331/TC/M/3, CIPAC Handbook, Note 1)

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 30:70 to 50:50.

Note 1 Methods for the identification and determination of permethrin content and permethrin isomer ratio in TC and LN were adopted by CIPAC in 2006 but are not yet published in a Handbook. Prior to publication of the Handbook, copies of the methods may be obtained through the CIPAC website, http://www.cipac.org.

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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/pm/jmps/ps/en/.

PART TWO

EVALUATION REPORT

PERMETHRIN

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2008 **FAO/WHO evaluation report** based on submission of data from Sumitomo Chemical Company (incorporating data from Bilag, India) (TC) **7**

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PERMETHRIN

FAO/WHO EVALUATION REPORT 331/2008

Recommendations

The Meeting recommended that:

(i) the specification for 40:60 *cis:trans* permethrin TC, proposed by Sumitomo Chemical Co. Ltd and relating to permethrin TC produced by Bilag Industries Pvt Ltd (India), should be adopted by FAO and WHO;

(ii) the existing (1991) FAO specifications for permethrin TC, WP, DP and EC, and the existing (1999) WHO specifications for permethrin TC and EC, should be withdrawn.

Appraisal

The Meeting considered data and a draft specification (TC only), submitted by Sumitomo Chemical Co. Ltd but including information from Bilag Industries Ltd, for the review of existing (1991) FAO specifications for permethrin TC, WP, DP and EC, and existing (1999) WHO specifications for permethrin TC and EC.

Permethrin is no longer under patent and has been widely manufactured for many years. Technical grade permethrin is composed of 4 stereoisomers, due to the chirality at two carbon atoms in the cyclopropane ring, leading to 2 *cis* and 2 *trans* isomers. The pairs of *cis* and *trans* isomers can be separated using non-chiral techniques but separation of the 2 *cis*, or the 2 *trans*, isomers would require a chiral separation technique and is rarely done routinely.

Differing manufacturing processes lead to different *cis:trans* ratios in technical grade permethrin but, generally in the market, the nominal *cis:trans* ratio is either 25:75 or 40:60. Manufacturing tolerances around these two nominal ratios lead to specification ranges that overlap slightly. The existing FAO (1991) and WHO (1999) specifications for permethrin encompass both nominal ratios. The data submitted for the present review were in support of a proposed FAO/WHO specification for TC, which encompassed only permethrin with a nominal 40:60 *cis:trans* ratio.

Sumitomo provided details of the manufacturing processes and 5-batch analysis data, relating to two sources of 40:60 permethrin, together with manufacturing limits for purity and all impurities ≥1 g/kg. The two sources were Sumitomo (Japan) (SM permethrin) and Bilag (India) (BL permethrin), both in current production but the proposed FAO/WHO specification applies to BL permethrin. Mass balances in the 5-batch analytical data were good in the case of SM permethrin (99.0–99.9%). The Meeting questioned the rather low mass balances (97.8-98.2%, unaccountable fraction ~20 g/kg) in the case of BL permethrin. The manufacturer stated that the unaccountable fraction was believed to represent components, such as water and inorganics, which were undetectable by the GC techniques used. Data used to support registration in the USA showed a similar picture and the Meeting accepted the explanation.

The minimum permethrin content of the TCs were 950 g/kg for both SM and BL permethrin. The data on SM and BL permethrin were stated by Sumitomo to be

identical to those submitted by the company for registration of BL permethrin by Sumitomo in the USA but, for reasons beyond the control of the company, FAO and WHO, this could not be confirmed independently.

The original manufacturers of permethrin no longer produce it and therefore no information was available to the Meeting about the manufacturing limits for impurities applying to the materials used to generate most of the original, very extensive and publicly available database on permethrin hazard characteristics. In the absence of this key information, the original manufacturers' data on hazards could not form the basis of JMPS reference profiles for permethrin.

To address the requirement for reference profiles to support FAO/WHO specifications, Sumitomo provided hazard data generated 20-30 years earlier, using SM permethrin. The proposed FAO/WHO specification was intended to apply to BL permethrin, only, but TC from this source was supported by a limited data package. Therefore, to enable the Meeting to decide whether or not there was sufficient information to support the development of FAO/WHO specifications for 40:60 permethrin, it was necessary: (i) to determine whether or not BL permethrin is equivalent to SM permethrin; and (ii) to define the reference profiles in this case.

Determination of equivalence was not straightforward. The impurity profile originally used as the manufacturing specification for SM permethrin had subsequently been shown by Sumitomo to be incorrect, following the introduction of improved analytical technology. Consequently, the company had recently revised the manufacturing limits for impurities in SM permethrin. However, Sumitomo stated that the manufacturing process had remained unchanged throughout the entire period during which SM permethrin had been produced (a statement was supported by 5-batch analytical data relating to 1998-2005 production) and, on this basis, the Meeting agreed that it was reasonable to assume that the revised manufacturing limits also applied to the TC batches used to generate the hazard data on SM permethrin. Thus the chemical and hazard profiles of SM permethrin were considered by the Meeting to be directly linked.

Although the manufacturing process for BL permethrin differs from that used for SM permethrin, it had been carefully refined to ensure that the manufacturing limits for purity and all impurities were within the (recently revised) manufacturing limits for SM permethrin. Thus, on the basis of their chemical profiles, BL permethrin in current production was considered to be equivalent to SM permethrin. WHO/PCS advised the Meeting that the acute toxicology data on BL permethrin indicate that it is toxicologically equivalent to SM permethrin (Table A). Overall, therefore, the Meeting concluded that BL permethrin is equivalent to SM permethrin.

Given the overall equivalence of BL permethrin and SM permethrin, the Meeting agreed that the purity/impurity profile of BL permethrin and the toxicology profile of SM permethrin (Tables A-D of this evaluation) should be designated as the reference profiles for 40:60 *cis:trans* permethrin.

The *cis:trans* isomer ratio of permethrin can influence certain hazard characteristics. For example, the acute oral LD_{50} of 80:20 *cis:trans* permethrin to rats (220 mg/kg bw) is lower than that of 20:80 *cis:trans* permethrin (6000 mg/kg bw) (JMPR 2002),

although the acute RfD[1] and ADI[2] apply to all ratios of permethrin isomers. However, there is no evidence to suggest that any of the impurities influence the hazard characteristics and the Meeting agreed that none of the impurities in BL permethrin should be designated as relevant.

The analytical methods for determination of the active ingredient (including tests for identity and isomer ratio) involve capillary GC-FID and internal standardization with triphenylphosphate. The methods were adopted by CIPAC in 2006, for analysis of permethrin TC and LN. Permethrin impurities were determined by the manufacturers, using capillary GC-FID.

Permethrin is a viscous liquid at room temperature; it does not dissociate in water and has extremely low water solubility and volatility. It is stable to hydrolysis at pH 4–7 but is slowly hydrolysed at pH 9. Permethrin only decomposes at extremely high temperature and, although photochemical degradation was observed in laboratory studies, this was stated by Sumitomo to be of negligible significance in the field.

The Meeting considered the proposed FAO/WHO specification for 40:60 *cis:trans* permethrin TC, noting that the existing (1991) FAO and (1999) WHO specifications applied to permethrin of both 25:75 and 40:60 ratios.

The Meeting welcomed the increase in minimum active ingredient content from 900 g/kg to 950 g/kg. The Meeting also welcomed a clarification and narrowing of the tolerance for permethrin isomer ratio[3].

The existing FAO (1991) and WHO (1999) specifications for permethrin TC included clauses for control of water, acetone-insolubles and acidity but the permethrin TC is not used by the proposer to prepare EC formulations and permethrin is stable under acidic conditions. None of these characteristics was therefore considered to be an appropriate quality criterion for the purposes of the FAO/WHO specification.

The proposer declared that the 40:60 *cis:trans* permethrin manufactured by Bilag and sold by Sumitomo complies with the proposed FAO/WHO specification for TC.

The Meeting noted that the existing (1991) FAO specifications for permethrin DP, WP and EC, and the existing (1999) WHO specification for permethrin EC, were not supported by the manufacturer.

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[1] The acute RfD for permethrin was set on the basis of acute neurotoxicity of 40:60 *cis:trans* permethrin, not on the acute oral LD_{50} (JMPR 2002).

[2] The ADI for permethrin was originally set on the basis of data derived from 40:60 *cis:trans* permethrin but later confirmed as appropriate for 25:75 *cis:trans* permethrin (JMPR 1987).

[3] The 1991 FAO specification provided a tolerance of ±10% for the 40:60 ratio and the 1999 WHO specification provided a tolerance of ±10% for all ratios. Both were ambiguous because, with respect to a nominal 40:60 ratio, the tolerance might be interpreted as encompassing a range of 36-44:64-56, or 34-46:66-54, or 30-50:70-50.

SUPPORTING INFORMATION

FOR

EVALUATION REPORT 331/2008

Uses

Permethrin is a non-systemic pyrethroid insecticide, with contact and stomach action and some repellent effects. It has many applications in agriculture, animal health and public health.

Identity

ISO common names[1]

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

Chemical names[1]

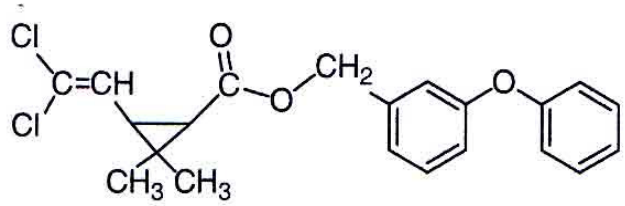
IUPAC: 3-phenoxybenzyl (1*RS*,*3RS*;1*RS*,3*SR*)-3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropanecarboxylate

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

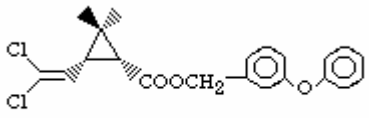
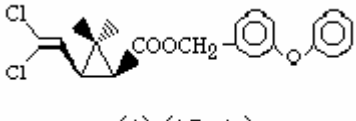
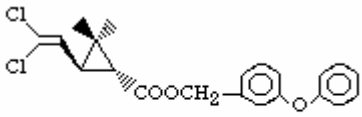
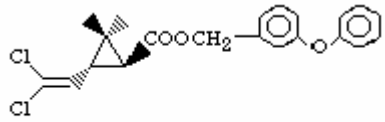
Synonyms

none

Structural formula



Two pairs of diastereoisomers are present in a ratio of approximately 40:60:

 (2) (1R,cis)	sum ≈ 40%
 (4) (1S,cis)	
 (1) (1R,trans)	sum ≈ 60%
 (3) (1S,trans)	

[1] Note: the ISO common names and the IUPAC and CA names do not define the isomer ratio.

Molecular formula

$C_{21}H_{20}Cl_2O_3$

Relative molecular mass

391.3

CAS Registry number[1]

52645-53-1

CIPAC number[1]

331

Identity tests

GC retention time, IR spectrum.

Physico-chemical properties of permethrin

Table 1. Physico-chemical properties of pure 40:60 cis:trans permethrin or the resolved diastereoisomers

Parameter	Value(s) and conditions	Purity %	Method	Reference
Vapour pressure	6.9 x 10^{-6} Pa at 25°C	99.6	OECD 104	0483/0059
Melting point	Melting point: <20°C	99.6	OECD 102	0483/0059
Temperature of decomposition	252°C	99.6	OECD 102	0483/0059
Solubility in water at 20°C	11.1 µg/l at 20 ± 0.5°C at pH 7.0-9.3	100% (*trans* isomer)	OECD 105	JP-0023
Octanol/water partition coefficient	log P_{OW} >6.5 at 40°C	99.6	OECD 117	0483/0059
Hydrolysis characteristics, half-life at 25ºC	Sterile aqueous buffer solutions at pH 4, 7, and 9 in the dark, testing *cis* and *trans* isomers separately (both cyclopropyl 1-^{14}C labelled). pH 4 and 7, both isomers stable. half-life at pH 9: *cis* = 42.3 d *trans* = 37.7 d.	Radiochemical purity, both isomers >98%	Japan-MAFF guideline No.12-Nosan No.8147, Part 2-6-1 (similar to OECD)	JM-0014
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-^{14}C labelled). Irradiation equivalent to natural sunlight (Tokyo, 35°N, April-June) for 30 days. Half-life: c*is* = 23.1 d (buffer), 14.6 d (SHW) *trans* = 36.8 d (buffer), 25.5 d (SHW)	Radiochemical purity, both isomers >98%98%	Japan-MAFF guideline No.12-Nosan No.8147, Part 2-6-2 (similar to OECD)	JM-0016

[1] Note: the CAS Registry No. and CIPAC number do not define the isomer ratio.

Table 2. Chemical composition and properties of technical (BL) 40:60 *cis:trans* permethrin (TC)

Manufacturing process, maximum limits for impurities ≥ 1 g/kg, 5 batch analysis data	Confidential information supplied and held on file by FAO and WHO. Mass balances were 97.8-98.2%, no unidentified impurities were reported.
Declared minimum 40:60 *cis:trans* 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
Melting temperature of the TC	<20°C

Pure permethrin *cis*-isomer forms colourless crystals at room temperature but a mixture of *cis* and *trans* isomers normally occurs as a liquid, with its appearance depending on the ratio of isomers. Pure permethrin (40:60) is a colourless, viscous liquid, whereas the TC is a yellow to yellow-brown viscous liquid.

Hazard summary

SM permethrin was evaluated by the Japanese Ministry of Health and Welfare in 1977[1]. Data on SM and BL permethrin, submitted by Valent BioSciences Corporation (a subsidiary company of Sumitomo Chemical Co., Ltd. in the USA), were evaluated by US-EPA and led to registration of BL permethrin in the USA in 2005[2].

Permethrin has been evaluated for toxicology 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

The formulation type available for public health applications is LN, in which the permethrin is not co-formulated with other pesticides. The LN formulations are registered and sold in Colombia, Dominican republic, Honduras, Indonesia, Kenya, Malaysia, Myanmar, Peru, Philippines, Singapore, Sri Lanka, Thailand, Tanzania and Trinidad.

Methods of analysis and testing

The analytical method for the active ingredient (including identity tests and isomer ratio) is carried out by capillary GC with FID and internal standardization with

[1] Permethrin/Eksmin, registration number 52AP-409, 5 March 1977.
[2] PramexB technical insecticide, registration number 73049-418, 14 September 2005.

triphenylphosphate. The method was adopted as a full CIPAC method in 2007[1], for the analysis of TC and LN.

Permethrin impurities were determined by capillary GC with FID detection.

Test methods for determination of physico-chemical properties of the technical active ingredient were OECD and US-EPA.

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, specifically defined as a mixture of *cis*- and *trans*-isomers present in a nominal [1*RS*,3*RS*]:[1*RS*,3*SR*] (*cis*:*trans*) ratio of 40:60, with a permitted range for the average measured ratio of 30:70 to 50:50.

[1] Methods for the identification and determination of permethrin content and permethrin isomer ratio in TC and LN were adopted by CIPAC in 2006 but are not yet published in a Handbook. Prior to publication of the Handbook, copies of the methods may be obtained through the CIPAC website, http://www.cipac.org.

ANNEX 1

HAZARD SUMMARY PROVIDED BY THE PROPOSER

Note: Sumitomo Chemical Co. Ltd. (Japan) provided written confirmation that the toxicological and ecotoxicological data included in the following summary were derived from permethrin having impurity profiles similar to those referred to in Table 2, above.

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

Species	Test and permethin used	Purity % & *cis:trans* ratio	Duration and conditions or guideline adopted	Result	Reference
Rat, Sprague-Dawley (f)	Acute oral SM & BL permethrin in the same study	SM: 96.3, 40:60 BL: 96.9, 40:60	Observation: 14 d, dose: 2000 mg/kg bw, OECD guideline 423	No mortality, no clinical signs observed. LD_{50} >2000 mg/kg bw for both SM and BL permethrin	QJT-0001
Mouse, dd strain (m)	Acute oral SM permethrin only	92.4, 46:54	Observation: 14 d, no guideline[1]	LD_{50} >650 mg/kg bw (m)	JT-0009
Rat, Sprague-Dawley, (m)	Acute oral SM permethrin only	92.4, 46:54	Observation: 14 d, guideline not stated	LD_{50} >430 mg/kg bw (m)	JT-0009
Rat, Sprague-Dawley (m,f)	Acute dermal SM & BL permethrin in the same study	SM 96.3, 40:60 BL 96.9, 40:60	Observation: 14 d dose: 2,000 mg/kg bw OECD guideline 402	No mortality, no clinical signs observed. LD_{50} >2000 mg/kg bw for both SM and BL permethrin	QJT-0002
Mouse, dd strain (m,f)	Acute dermal SM permethrin only	92.4, 46:54	Observation: 14 d, no guideline[1]	LD_{50} >2500 mg/kg bw	JT-0009
Rat, Sprague-Dawley, (m,f)	Acute dermal SM permethrin only	92.4, 46:54	Observation: 14 d, no guideline[1]	LD_{50} >2500 mg/kg bw	JT-0009
Rat, Sprague-Dawley (m,f)	Acute inhalation SM & BL permethrin in the same study	SM 96.3, 40:60 BL 96.9, 40:60	Exposure 4 h, observation 14 d, dose 5000 mg/m^3	BL permethrin: initial tremor, no mortality observed, LC_{50} >5000 mg/m^3 SM permethrin: initial tremor, 2 f died, LC_{50} >5000 mg/m^3	QJT-0003
Mouse, dd strain (m,f)	Acute inhalation SM permethrin only	92.4, 45:55	Exposure period 3 h, observation 28 d, no guideline[1]	LC_{50} >685 mg/m^3	JT-0015
Rat, Sprague-Dawley (m,f)	Acute inhalation SM permethrin only	92.4, 45:55	Exposure period 3 h, observation 28 d, no guideline[1]	LC_{50} >685 mg/m^3	JT-0015
Rabbit, Japanese White (f)	Skin irritation BL permethrin only	96.9, 40:60	OECD guideline 404	Non-irritant	QJT-0005

[1] Study conducted prior to the introduction of guidelines but techniques and conditions equivalent to current international guidelines.

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

Species	Test and permethin used	Purity % & *cis:trans* ratio	Duration and conditions or guideline adopted	Result	Reference
Rabbit, Japanese White (m)	Skin irritation SM permethrin only	91.8, 40:60	No guideline[1]	Non-irritant	JT-0046
Rabbit, Japanese White (f)	Eye irritation BL permethrin only	96.9, 40:60	OECD guideline 405	Non-irritant	QJT-0004
Rabbit, Japanese White (m)	Eye irritation SM permethrin only	91.8, 40:60	No guideline[1]	Non-irritant	JT-0046
Guinea pig, Hartley (f)	Skin sensitization BL permethrin only	96.9, 40:60	OECD guideline 406	Non-sensitizer	QJT-0006
Guinea pig, Hartley (m)	Skin sensitization SM permethrin only	94.6, 40:60	No guideline[1]	Non-sensitizer	JT-0011

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

Species	Test	Purity % & *cis:trans* ratio	Duration and conditions or guideline adopted	Result	Reference
Rat, Sprague-Dawley (m,f)	Feeding toxicity	93.3, 40:60	No guideline[1], duration 180 d, doses: 375, 750, 1500, 3000 ppm	NOEL = 1500 ppm, equivalent to 92.9 mg/kg bw/d (m) 110 mg/kg bw/d (f)	JT-0013
Rat, Sprague-Dawley (m,f)	Inhalation toxicity	92.4, 40:60	No guideline[1], duration 28 d consecutive, 3 h/d, doses: 20, 50, 100 mg/m^3	NOAEL = 50 mg/m^3 (m,f)	JT-0015
Rat, Sprague-Dawley (m,f)	Feeding, teratogenicity, embryotoxicity	92.4, 40:60	No guideline[1], oral exposure during days 9-14 of gestation. Doses: 10, 20, 50 mg/kg bw/d.	The dams treated with 50 mg/kg bw/d showed slight toxic symptoms, (ataxia, tremor, hyper-sensitivity)	JT-0102
Rabbit, Japanese White (m,f)	Feeding, teratogenicity, embryotoxicity	92.5, 40:60	No guideline[1], oral gavage, 4 doses during days 6-18 inclusive of pregnancy, doses: 600, 1200, 1800 mg/kg bw/d	Embryotoxic at the two higher levels of treatment, toxic to dams at 1800 mg/kg bw/day but not teratogenic at any level	JT-0082

[1] Study conducted prior to the introduction of guidelines but techniques and conditions equivalent to current international guidelines.

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

Species	Test	Purity % & *cis:trans* ratio	Conditions and doses	Result	Reference
Salmonella typhimurium (TA100, TA98, TA1535, TA1537, TA1538), Escherichia coli (WP-2 hcr^-)	Gene mutation, Ames test (*in vitro*)	93.3, 40:60	10, 50, 100, 500, 1000, 5000 µg/plate, ±S9, in-house method equivalent to OECD guideline 471	Negative	JT-0024
Mouse, ICR (m) *Salmonella typhimurium* (G46)	Host-mediated assay, gene mutation (*in vivo* & *in vitro*)	93.3, 40:60	50, 200 mg/kg bw, administered orally twice, in-house method	Negative	JT-0024
Bacillus subtilis M45 rec^- and H17 strains	Recombinant DNA, damage and repair (*in vitro*)	93.3, 40:60	20, 100, 200, 500, 1000, 2000 µg/disc, in-house method	Negative	JT-0024

Table D. Ecotoxicology profile of SM permethrin technical material

Species	Test	Purity % & *cis:trans* ratio	Duration and conditions	Results	Reference
Pseudokirchneriella subcapitata (freshwater green alga)	Effect on growth	94.4, 40:60	OECD 201	EC_{50} (72hr) = 540 µg/l NOEC (72hr) = 0.21 µg/l	JW-0041
Colinus virginianus (northern bobwhite)	Acute oral toxicity	94.4, 40:60	EPA OPPTS 850.2100	LD_{50} >2000 mg/kg	JW-0040

ANNEX 2. REFERENCES

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QJT-0006	2006. A skin sensitization study of Permethrin in guinea pigs.
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