WHO SPECIFICATIONS AND EVALUATIONS

FOR PUBLIC HEALTH PESTICIDES

d-PHENOTHRIN[1]

3-phenoxybenzyl (1*R*)-*cis, trans*-chrysanthemate

WORLD HEALTH ORGANIZATION
GENEVA

[1] d-Phenothrin is the name given by the manufacturer, in the absence of an ISO common name.

TABLE OF CONTENTS

d-PHENOTHRIN

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

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

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

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

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

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

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

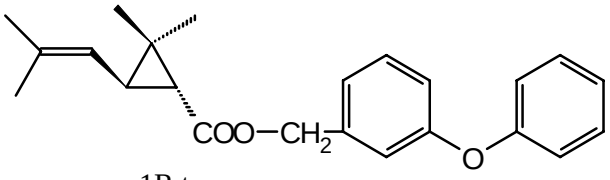
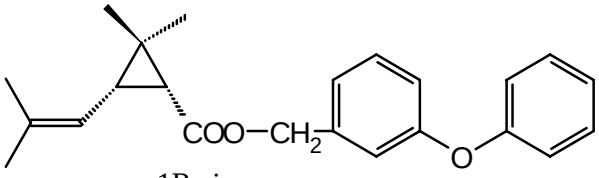
PART ONE

SPECIFICATIONS

---

d-PHENOTHRIN

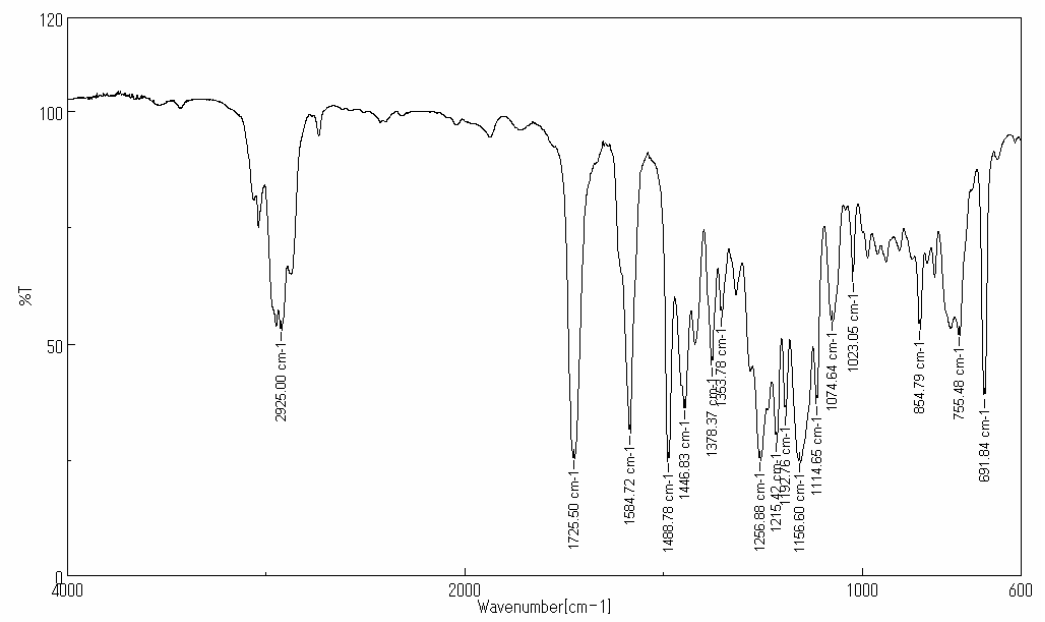
INFORMATION

Common name	No ISO common name for *d*-phenothrin. Footnote 1
Chemical name	**CAS**: (3-phenoxyphenyl)methyl (1*R*)-*cis*-*trans*-2,2-dimethyl-3-(2-methyl-1-propenyl) cyclopropanecarboxylate (proposed CAS name) **IUPAC**: 3-phenoxybenzyl (1*R*)-*cis*, *trans*-chrysanthemate
CAS Registry number	No CAS number available for *d*-phenothrin. Footnote 2
CIPAC number	356
Structural formula	 1R,trans  1R,cis *d*-phenothrin is the 4:1 mixture of the [*1R,trans*] and [*1R,cis*] isomers.
Empirical formula	$C_{23}H_{26}O_3$
Relative molecular mass	350.46
Identity tests	(i) isomer composition (enantiospecific) (ii) GC retention time in the analytical method, capillary GC with FID (not enantiospecific) (iii) IR spectrum (not enantiospecific), Figure 1.

1 Phenothrin is the ISO common name for the racemic mixture of 4 stereoisomers.

2 CAS number for racemic phenothrin: 26002-80-2.

Figure 1. Infra-red spectrum of *d*-phenothrin



d-PHENOTHRIN TECHNICAL MATERIAL

WHO Specification 356/TC (October 2004*)

*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 (*356/2002*). It should be applicable to relevant products of this manufacturer but it is not an endorsement of those products, nor a guarantee that they comply with the specifications. The specification may not be appropriate for the products of other manufacturers. The evaluation report (*356/2002*) as PART TWO forms an integral part of this publication.*

1 Description

The material shall consist essentially of *d*-phenothrin with related manufacturing impurities. It shall be a yellow to yellowish-brown oil, substantially odourless and free from extraneous materials or added modifying agents.

2 Active ingredient

2.1 **Identity tests** (CIPAC 356/TC/M/2, Notes 1 &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 ***d*-Phenothrin content** (CIPAC 356/TC/M/3, Note 2)

The *d*-phenothrin content shall be declared (not less than 930 g/kg) and, when determined, the average measured content shall not be lower than the declared minimum content.

2.3 **Isomer composition** (CIPAC 356/TC/M/2, HPLC method, Note 2)

The *trans*-isomer content of the *d*-phenothrin shall be declared (not less than 75% and not more than 85%) and, when determined, the average measured trans-isomer content shall not be lower than the declared minimum value nor higher than the declared maximum value.

The *1R*-isomer content of the *d*-phenothrin shall be declared (not less than 95%) and, when determined, the average measured *1R*-isomer content shall not be lower than the declared minimum content.

Note 1 Identity tests may be based upon GC retention time (provided by the CIPAC method 356/TC/M/3) and the IR spectrum but determination of the isomer composition (by the CIPAC 356/TC/M/2 chiral column HPLC method for determination of optical isomer ratios) provides the definitive identity test.

Note 2 Methods for the identification and determination of *d*-phenothrin in TC and AE were adopted by CIPAC in 2004 but are not yet available in a handbook. Prior to publication of the handbook, copies of the methods may be obtained through the CIPAC website, http://www.cipac.org or from the Secretary, Dr László Bura, Central Service for Plant Protection and Soil Conservation, Budaörsi út. 141-145, 1118 Budapest, Hungary.

* 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/.

PART TWO

EVALUATION REPORT(S)

---

d-PHENOTHRIN

WHO SPECIFICATIONS AND EVALUATIONS FOR
PUBLIC HEALTH PESTICIDES

d-PHENOTHRIN

EVALUATION REPORT 356/2002

Explanation

The data for d-phenothrin were evaluated in support of a new WHO specification for the TC. *d*-Phenothrin was evaluated by the WHO/IPCS in 1990 (IPCS, 1990). It was reviewed by the US EPA in 1975 and by the UK Health and Safety Executive prior to 1984. It was evaluated for toxicology by the 1984 and 1988 JMPR (JMPR, 1984; JMPR, 1988).

The draft specification and supporting data were provided by Sumitomo Chemical Company Ltd., Japan, in 2001.

The patent for *d*-phenothrin expired in major markets in 1991.

Uses

d-Phenothrin is a synthetic pyrethroid with high lethal activity against household insect pests. It is used in public health against mosquitoes, houseflies and cockroaches (Okuno *et* al., 1976).

Identity

ISO common name

None (footnote [1])

Chemical name

IUPAC: 3-phenoxybenzyl (1*R*)-*cis, trans*-chrysanthemate
CA: None (footnote [2])

CAS Registry number

None (footnote [3])

CIPAC number

356

1 Phenothrin is the ISO common name for the racemic mixture of 4 stereoisomers; d-phenothrin is the name given by the Sumitomo Chemical Company to the specific ratio of isomers defined by the WHO specification.
2 Proposed CAS name: (3-phenoxyphenyl)methyl (1*R*)-*cis*-*trans*-2,2-dimethyl-3-(2-methyl-1-propenyl) cyclopropanecarboxylate.
3 The CAS number for phenothrin is 26002-80-2.

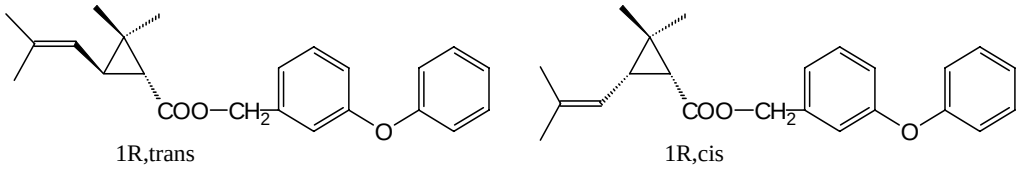
EEC number

None (footnote [1])

Synonyms

Sumithrin, S-2539F, S-2539 Forte

Structural formula



1R,trans 1R,cis

d-phenothrin is the 4:1 mixture of the [*1R,trans*] and [*1R,cis*] isomers.

Molecular formula

$C_{23}H_{26}O_3$

Relative molecular mass

350.46

Identity tests

(i) isomer composition (enantiospecific)

(ii) GC retention time in the analytical method, capillary GC with FID (not enantiospecific).

(iii) IR spectrum (not enantiospecific).

1 The EEC number for phenothrin is 247-404-5.

Physico-chemical properties of *d*-phenothrin

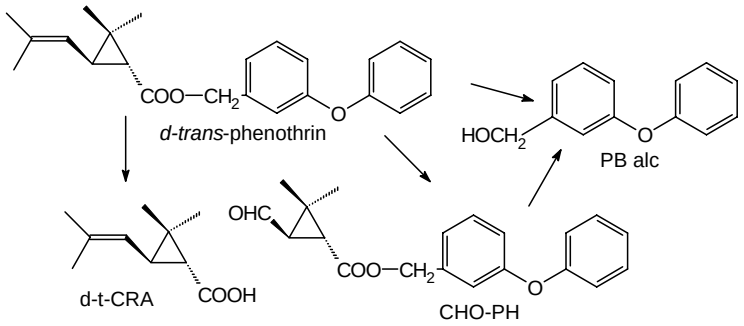
Table 1. Physico-chemical properties of pure *d*-phenothrin

Parameter	Value(s) and conditions	Purity %	Method reference
Vapour pressure:	see vapour pressure for technical material	-	-
Vapour pressure:	0.16 mPa at 20°C	Not stated	IPCS 1990, p17
Melting point and temperature of decomposition:	Melting point: not known (liquid over a wide temperature range) Decomposition temperature: not known	-	-
Solubility in water:	2 mg/l at 25°C see also solubility for technical material	Not stated	IPCS 1990, p17
Octanol / water partition coefficient:	1.03×10^6 at 25°C (log P_{ow} = 6.01)	99.6	OECD 107 (Loken and Pesselman, 1989)
Hydrolysis characteristics of *d-trans*-phenothrin	Half-lives at 25°C (footnote 1) pH 5: (1) approx 60-100 days (2) approx 300 days. pH 7: (1) approx 90-300 days (2) approx 500-620 days pH 9: (1) - (2) 90-120 days	Radiochemical purity: 99.5 and 99.6	EPA Guideline 161-1 (Hatzenbeler and Doran, 2000ab)
Photolysis characteristics[2] of *d-trans*-phenothrin (natural sunlight):	Half-lives at pH 5, 25°C, latitude 37.45°N, California, July-August: 13.8 and 9.1 experiment hours, corresponding to 7.8 and 5.2 sunlight hours	Radiochem purity: 95.5 and 95.6	EPA Guideline 161-2 (Shepler *et al*., 1989ab)
Dissociation characteristics:	Not applicable	-	-

1 **Hydrolysis** rates were measured at 3 µg/l in <1% aqueous acetonitrile in sterile dark conditions for 1 month at pH 5, pH 7 and pH 9. The major hydrolysis products observed were 3-phenoxybenzyl alcohol and 1R-trans-chrysanthemic acid. Also produced was 3-phenoxybenzyl (1*R*,3*R*)-2,2-dimethyl-3-formylcyclopropane carboxylate, an oxidation product rather than an hydrolysis product. The test substance d-trans-phenothrin has very low aqueous solubility and about half of it became deposited on the vessel walls. The hydrolysis half-life was calculated in two ways (1) from disappearance of the test substance from the total system, and (2) from kinetic analysis of typical hydrolysis products.

2 **Photolysis** rates were measured at pH 5 at 3 µg/l in sterile <1% aqueous acetonitrile solution in natural sunlight. Radio-labeled [^{14}C-cyclopropyl] and [^{14}C-benzyl]d-trans-phenothrin were used in the two series of determinations. The methyl-propenyl group was the target for photolytic degradation. The major product of photolysis was 3-phenoxybenzyl(1*R*,3*R*)-2,2-dimethyl-3-formyl cyclopropanecarboxylate. *Cis-trans* isomerization was not significant. d-*Trans*-phenothrin declined quickly in the first few hours at pH 5 and 25ºC in the dark controls.

Hydrolysis routes of *d*-phenothrin



Degradation in aqueous buffers

Photolysis routes of *d*-phenothrin

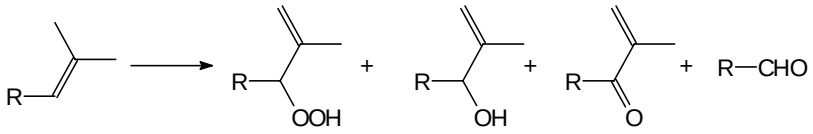


Table 2. Chemical composition and properties of *d*-phenothrin TC

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 98.9-99.5 % and percentages of unknowns were 0.5-1.1%
Declared minimum *d*-phenothrin content:	930 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 or boiling temperature range	Boiling point: >290°C at 760 mm Hg
Vapour pressure (footnote 1) test guideline: 40 CFR 158	94% *d*-phenothrin: 1.9 x 10^{-5} Pa at 21.4°C (observed values: 2.31×10^{-5}, 1.43×10^{-5} Pa at 2 gas flow rates, Semann and Pesselman, 1989).
Solubility in water, test guideline: EPA CG-1500	94% *d*-phenothrin: <9.7 μg/l at 25°C at pH 5.8-6.0 (Saito *et al*., 1989).

Hazard summary

Notes.

(i) The proposer provided written confirmation that the toxicological and ecotoxicological data included in the summary below were derived from *d*-phenothrin 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.

1 Vapour pressure was measured by a gas-saturation method. Dry nitrogen gas streams were passed through gas-saturation tubes at 21.4°C and then through traps in dry ice/ethanol for approx 4 days at flow rates of 4.4 and 3.3 ml/min. The contents of the traps were measured by HPLC.

The JMPR (JMPR 1984) compared impurity profiles and toxicology of phenothrin and *d*-phenothrin. The level of *d*-phenothrin is higher and the levels of impurities are generally lower in the modern (2000-2001) 5-batch analysis than in the batches recorded in 1984. The JMPR concluded that: "Data presented indicate the similarity in metabolism and toxicity of phenothrin and *d*-phenothrin, thus indicating that data for phenothrin can be used to support the toxicological data base for *d*-phenothrin".

In the following tables, S-2539F and S-2539 Forte are synonymous with *d*-phenothrin.

Table 3. Toxicology profile of *d*-phenothrin technical material, based on acute toxicity, irritation and sensitization.

Species	Test	Duration and conditions	Result	Purity	Reference
Rats, male and female	Oral	Japan-MAFF	LD_{50} = (male) >5000, (female) >5000 mg/kg bw	93.8% S-2539F	Suzuki *et al*., 1987
Rats, male and female	Dermal	EPA Guideline 81-2	LD_{50} = (male) >5000, (female) >5000 mg/kg bw	94.0%	Misaki *et al*., 1996
Rats, male and female	Inhalation	4 hours EPA Guideline 81-3	LC_{50} = (male) >2100, (female) >2100 mg/m^3	93.8%	Hoffman *et al*., 1995
Rabbits, male and female	Skin irritation	EPA Guideline 81-5	Not irritant	94.2%	Nakanishi *et al*., 1988a
Rabbits, male and female	Eye irritation	EPA Guideline 81-4	Minimal irritant	94.2%	Nakanishi *et al*., 1988a
Guinea pigs	Skin sensitisation	Maximization method, EPA Guideline 81-6	Not sensitizing	94.2%	Nakanishi *et al*., 1988b

Table 4. Toxicology profile of *d*-phenothrin technical material based on repeated administration (sub-acute to chronic)

Species	Test	Duration and conditions	Result	Purity	Reference
Rats, male and female	Inhalation	3 months, EPA Guideline 82-4	NOEL = 0.104 mg/L	94.2%	Kenny *et al*., 1989
Rats, male and female	feeding, toxicity	6 months, no-guideline	NOEL = 1000 ppm in diet equivalent to: male: 55.4 mg/kg/day, female: 63.6 mg/kg/day	92.9% S-2539 Forte	Miyamoto *et al*., 1981
Mice, male and female	feeding, toxicity	5 weeks, no-guideline	NOEL (both sexes) = 10000 ppm	92.6%	Amyes *et al*., 1983
Dogs, male and female	feeding, toxicity	6 months, no-guideline	NOEL (both sexes) = 300ppm	95.5% S-2539F	Pence *et al*., 1981 IPCS 1990, p39
Dogs, male and female	feeding, toxicity	1 year, EPA Guideline 83-1	NOEL (both sexes) = 300ppm	92.7%	Cox *et al.*, 1987 IPCS 1990, p39

Species	Test	Duration and conditions	Result	Purity	Reference
Rats, male and female	feeding, carcinogenicity	2 years, EPA Guideline 83-2	NOEL = 1000 ppm in diet, equivalent to: male: 47 mg/kg/day, female: 56 mg/kg/day. Carcinogenicity: negative	92.6%	Martin *et al*., 1987 IPCS 1990, p38 JMPR 1988, p56
Mice, male and female	feeding, carcinogenicity	2 years, EPA Guideline 83-2	NOEL (male) = 300 ppm in diet, equivalent to 40 mg/kg/day. NOEL (female) =1000 ppm in diet, equivalent to 164 mg/kg/day, Carcinogenicity: negative	92.9%	Amyes *et al.*, 1987 IPCS 1990, p39 JMPR 1988, p54
Rats, male and female	feeding, 2 generation reproduction	EPA Guideline 83-4	NOEL:= 1000 ppm	92.9%	Tesh *et al*., 1986
Rats, male and female	feeding, teratogenicity and embryotoxicity	EPA Guideline 83-3	NOEL = 300 ppm	92.6%	Tesh *et al*., 1983
Rabbits, male and female	feeding, teratogenicity and embryotoxicity	EPA Guideline 83-3	NOEL for embryo toxicity, fetotoxicity and teratogenicity = 300 mg/kg/day	94.1%	Nemec, 1989

Table 5. Mutagenicity profile of *d*-phenothrin technical material based on *in vitro* and *in vivo* tests

Species	Test	Conditions	Result	Purity	Ref.
Salmonella typhimurium, Escherichia coli	Gene mutation (Ames)	No guideline	Negative	93.5%	Kishida and Suzuki, 1981 IPCS 1990, p40
Human cells (Hela 53)	Unscheduled DNA synthesis	No guideline	Negative	92.6%	Forster *et al*., 1984 IPCS 1990, p40 JMPR 1988, p57
Chinese hamster ovary cells	*in vitro* Chromosomal aberration test	EPA Guideline 84-2	Negative	94.2%	Murli and Spicer, 1989

Table 6. Ecotoxicology profile of *d*-phenothrin technical material.

Species	Test	Duration and conditions	Result	Purity	Ref.
Honey bees	Acute contact toxicity	EPA Guideline 141-1	LD_{50} (48 hr) = 0.005 µg/bee	94.2%	Hoxter *et al*., 1989
Bobwhite quail	Acute dietary toxicity	EPA Guideline 71-2	LC_{50} >5620 ppm	94.2%	Grimes *et al*., 1988
Bobwhite quail	Acute dietary toxicity	8 days	LD_{50} >5000 ppm	not reported	IPCS 1990, p33
Mallard duck	Acute dietary toxicity	8 days	LD_{50} >5620 ppm	not reported	IPCS 1990, p33

Species	Test	Duration and conditions	Result	Purity	Ref.
Bluegill	Acute flow-through toxicity	EPA Guideline 72-1	LC_{50} (96 hr) = 16 µg/L	94.2%	Bowman *et al*., 1988a
Rainbow trout	Acute flow-through toxicity	EPA Guideline 72-1	LC_{50} (96 hr) = 2.7 µg/L	Not reported	Bowman *et al*., 1988b
Rainbow trout	Early life stage toxicity	EPA Guideline 72-4	NOEC = 1.1 µg/L	Not reported	Sousa, 1998
Daphnia	Acute flow-through toxicity	EPA Guideline 72-2 48 hours	EC_{50} (48 hr) = 4.3 µg/L	Not reported	Graves and Swigert, 1994
Daphnia	Life cycle toxicity study	EPA Guideline 72-4	NOEC = 0.47 µg/L	Not reported	Putt, 1998

d-Phenothrin was evaluated by the WHO/IPCS in 1990, with the following conclusions (IPCS, 1990, p13-14).

General population. The exposure of the general population to *d*-phenothrin is expected to be very low and is not likely to present a hazard when it is used as recommended.

Occupational exposure. With reasonable work practices, hygiene measures and safety precautions, *d*-phenothrin is unlikely to be an occupational hazard.

Environment. The rapid breakdown of *d*-phenothrin in sunlight and its use principally on stored grain imply that environmental exposure should be very low. Environmental effects of the compound are, therefore, extremely unlikely.

The WHO hazard classification of technical *d*-phenothrin is: “unlikely to present an acute hazard in normal use“ (WHO, 1988).

The ADI for *d*-phenothrin is 0.07 mg/kg bw (JMPR 1988).

Formulations

The main formulation types available are AE (oil-based and water-based aerosols). These formulations are registered and sold in many countries throughout the world.

In oil-based aerosol products, the concentration of *d*-phenothrin generally ranges from 0.5 to 2 g/kg. The aerosol is composed largely of a solvent, such as deodorized kerosene, and a propellent, such as liquefied petroleum gas. The normal ratio of solvent to propellent is 60/40. The inner pressure of dispensers ranges from 3.5 to 4.5 kg/cm^2.

In water-based aerosol products, the concentration of *d*-phenothrin generally ranges from 0.5 to 2 g/kg. The aerosol is composed largely of a solvent for the active ingredient, an emulsifier, de-ionized water and the propellent. The ratio of solvent, water and propellent is usually 10/50/40. The inner pressure of dispensers ranges from 3.5 to 4.5 kg/cm^2.

Methods of analysis and testing

The analytical method for the active ingredient (including identity tests) is under development, through CIPAC. The *d*-phenothrin content is determined by capillary GC with FID. The method was submitted to JMPS in 2002 (Furuta, 2002).

Analytical methods for isomer composition are available (Fujita, 2002). The optical

isomer ratios are determined by HPLC using a chiral stationary phase, while the geometric isomer ratio is determined by GLC on a non-chiral stationary phase. The method has been validated by Sumitomo Chemical Company Ltd. The isomer composition serves as an identity test for *d*-phenothrin.

Another identity test relies on matching the IR spectrum of the test sample with the IR spectrum for *d*-phenothrin.

Test methods for physical-chemical properties of the technical active ingredient were OECD and EPA, while those for the formulations were the WHO guideline specifications for household insecticide products.

Containers and packaging

No special requirements for containers and packaging have been identified.

Expression of the active ingredient

The active ingredient is expressed as *d*-phenothrin.

Appraisal

The data submitted were in accordance with the requirements of the FAO Manual (5th edition) and supported the draft specifications.

The technical material, *d*-phenothrin is the 4:1 mixture of the [*1R*,*trans*] and [*1R*,*cis*] isomers of phenothrin.

The CIPAC number for *d*-phenothrin is 356. A CAS name and a number are available for phenothrin, but not for *d*-phenothrin.

Hydrolysis and photolysis properties were provided for *d-trans*-phenothrin, which may be extrapolated to *d*-phenothrin because *d-trans*-phenothrin comprises 80% of *d*-phenothrin.

The vapour pressure of 94% technical *d*-phenothrin is 1.9×10^{-5} Pa at 21.4°C (full experimental details provided), which differs somewhat from a value of 1.6×10^{-4} Pa at 20°C (no experimental details) reported for pure *d*-phenothrin.

It has very low water solubility, reported as <9.7 µg/l at 25°C for 94% technical *d*-phenothrin (full experimental details provided). A reported value of 2 mg/l for pure material (no details) appears to be too high. The octanol-water partition coefficient (log P_{OW} = 6.01 at 25°C) makes *d*-phenothrin a fat-soluble compound.

Accurate measurement of hydrolysis rates for *d-trans*-phenothrin was difficult because the chosen concentration, 3 µg/l, was approximately at the limit of solubility. After a short time, 40-50% of the test material was no longer in solution but was deposited on the container walls and perhaps was less available for hydrolysis. Hydrolysis rates were estimated in two ways: (1) the rate of disappearance of total *d-trans*-phenothrin from the solution and container rinsings; and (2) the rate of appearance of typical hydrolysis products. Competing and sequential processes (hydrolysis, container wall adsorption-desorption, oxidation) mean that the data do not readily match a first-order or pseudo-first-order reaction. Estimated half-lives for hydrolysis should be treated as approximations.

The half-life for disappearance of *d-trans*-phenothrin during sunlight photolysis

(latitude 37.45°N, California, July-August) was 13.8 and 9.1 experiment hours or 7.8 and 5.2 sunlight hours. *Cis-trans* isomerization was not significant. Substantial losses of *d-trans*-phenothrin (30% and 90%) occurred in the dark controls over the total 240 hours of the experiment.

The Meeting was provided with commercially confidential information on the manufacturing process and batch analysis data on all impurities present at or above 1 g/kg. Analyses of 5 batches of *d*-phenothrin produced in 2000 and 2001 accounted for 98.9 to 99.5% of the material, including 0.2-0.3% of impurities identified only as "other related compounds."

These data were declared by the NRA (National Registration Authority for Agricultural and Veterinary Chemicals) to be very similar to those submitted to the authorities for registration in Australia (Sethi, 2002).

The NRA letter stated: "The method of manufacture of *d*-phenothrin has been slightly modified. However, the modification is unlikely to change the composition of the active constituent. There are some variations to the composition of the active submitted to the FAO [sic, meaning WHO] and the NRA at the time of evaluation."

The manufacturing limits for two impurities differed between the WHO and NRA specifications, those for the WHO specifications being lower. The actual values in the 5-batch analysis for both of these impurities were at or below 1 g/kg. The technical material in the present submission and the material evaluated by the NRA may be accepted as substantially equivalent.

None of the impurities was identified as a relevant impurity.

Toxicology studies on *d*-phenothrin generally showed low mammalian toxicity. The IPCS evaluation in 1990 concluded that under recommended conditions of use, the exposure of the general population to *d*-phenothrin is expected to be very low and is not likely to present a hazard. Also, with the usual precautions, *d*-phenothrin is unlikely to be an occupational hazard. The WHO hazard classification of *d*-phenothrin is: "unlikely to present an acute hazard in normal use." The ADI for *d*-phenothrin is 0.07 mg/kg bw.

The attention of the Meeting was drawn to the recent restriction on household uses of synthetic pyrethroids in The Netherlands, because of reports of neuronal effects following the exposure of neonatal mice (Schreuder 2002).

d-Phenothrin is of low toxicity to birds but toxic to fish and very toxic to honey-bees. The IPCS evaluation in 1990 concluded that, because of its rapid breakdown in sunlight and its principal use at that time (use on stored grain), the environmental effects were extremely unlikely.

The IPCS evaluation of 1990 was relevant to the uses at that time. It is reasonable to conclude that *d*-phenothrin is hazardous to fish and honey-bees, while the risk will depend on their exposure.

The analytical method for active ingredient (capillary GC with FID) is proposed for CIPAC evaluation*. This method also serves as an identity test. An IR spectrum is available as an additional identity test.

An analytical method for isomer composition is available. The optical isomer ratios

* August 2004 footnote. The methods for identification and determination of *d*-phenothrin were adopted by CIPAC in June 2004, with provisional status.

are determined by HPLC using a chiral stationary phase, while the geometric isomer ratio is determined by GLC on a non-chiral stationary phase. It has been company validated. The method for isomer composition is recommended as the primary identity test.

No special requirements for containers and packages have been identified.

Draft specifications for *d*-phenothrin TC are proposed. The specifications require the determination of *d*-phenothrin content in the TC*. Also required are measurements of *trans*-isomer and *1R*-isomer contents in the active ingredient, to distinguish *d*-phenothrin from phenothrin*.

Recommendations

The meeting recommended that the draft specification for *d*-phenothrin TC proposed by Sumitomo Chemical Company Ltd, with amendments, should be adopted by WHO/FAO, subject to acceptable validation and adoption of the analytical methods by CIPAC*.

References

Amyes SJ, Martin PA, Ashby R, Lee P, Brown PM, Fowler JSL and Finn JP, 1987	Sumithrin: Oncogenicity and toxicity study in mice. Life Science Research Limited, Sumitomo report # ET-0109. Unpublished.
Amyes SJ, Macrae SM, Whitney JC, 1983	Sumithrin: five week range-finding toxicity study in mice final report. Life Science Research Limited, Sumitomo report # ET-0086. Unpublished.
Bowman JH, Lucash KJ, Schuster LL, Swigert IP, Franklin BB, Mullen L, Exendine T, Brush CM and Chambers KM, 1988a	Acute flow-through toxicity of Sumithrin to bluegill sunfish (LEPOMIS MACROCHIRUS). Analytical Bio-Chemistry Laboratories, Inc. Sumitomo report # EW-0005. Unpublished.
Bowman JH, Lucash KJ, Schuster LL, Swigert IP, Stimatze AP, Franklin BB, Mullen L, Exendine T, Brush CM and Chambers KM, 1988b	Acute flow-through toxicity of Sumithrin to rainbow trout (SALMO GAIRDNERI). Analytical Bio-Chemistry Laboratories, Inc. Sumitomo report # EW-0004. Unpublished.
Cox RH, Sutherland JD, Voelker RW, Alsaker RD, Vargas KJ, Lewis SA and Hagen WH, 1987	Chronic toxicity study in dogs with Sumithrin technical grade. Hazleton Laboratories, Sumitomo report # ET-0108. Unpublished.
Forster R, Tippins RS, Venezia VD and Nunziata A, 1984	Unscheduled DNA synthesis in human cells, cell line: Hela S3, test substance : Sumithrin. Life Science Research Limited, Sumitomo report # ET-0095. Unpublished.
Fujita T, 2002	Analytical methods of isomers composition in *d*-phenothrin. Sumitomo Chemical Co. Unpublished.
Furuta R, 2002	*d*-Phenothrin (no 356)). Small scale collaborative study and analytical method. CIPAC/4272/R and CIPAC/4271/m.

* August 2004 footnote. The methods for identification and determination of *d*-phenothrin were adopted by CIPAC in June 2004, with provisional status.

Graves WC and Swigert JP, 1994	A 96-hour flow-through acute toxicity test with the cladoceran (Daphnia magna). Wildlife International Ltd., Sumitomo report # EW-0018. Unpublished.
Grimes J, Jaber M, Graves WC and Swigert JP, 1988	Sumithrin: a dietary LC50 study with the bobwhite. Wildlife International Ltd, Sumitomo report # EW-0003. Unpublished.
Hatzenbeler C and Doran TJ, 2000a	A hydrolysis study of [benzyl-^{14}C]-*d-trans*-phenothrin in water. Ricerca, Inc., Sumitomo report # EM-0037. Unpublished.
Hatzenbeler C and Doran TJ, 2000b	A hydrolysis study of [cyclopropyl-1-^{14}C]-*d-trans*-phenothrin in water. Ricerca, Inc., Sumitomo report # EM-0038. Unpublished.
Hoffman GM, Richter WR, Auletta CS, Madarasz AJ, Newton PE, Streeton RL, Reese PO, Kusznir TS, Waggoner TB, Bowden DJ, Pillsbury BD, Vogt JH and Jonassen H, 1995	An acute (4-hour) inhalation toxicity study of Sumithrin in the rat via whole-body exposure. Huntingdon Research Centre ltd., Sumitomo report # ET-0172. Unpublished.
Hoxter KA, Thompson MM and Jabar M, 1989	An acute contact study with the honey bee. Wildlife International Ltd., Sumitomo report # EW-0009. Unpublished.
IPCS, 1990	*d*-phenothrin. *Environmental Health Criteria 96,* WHO, Geneva.
JMPR, 1984	Pesticide residues in food – 1984. Evaluations. *FAO Plant Production and Protection Paper* 67.
JMPR, 1988	Pesticide residues in food – 1988. Part II – Toxicology. *FAO Plant Production and Protection Paper* 93/2
Kenny TJ, Coombs DW, Hardy CJ, Clark GC, Crook D and Gopinath C, 1989	Sumithrin T.G. 90-day Inhalation toxicity study in the rat. Huntingdon Research Centre lTd., Sumitomo report # ET-0122. Unpublished.
Kishida F and Suzuki H, 1981	Gene mutation test of Sumithrin in bacterial system, Sumitomo Chemical Co., Ltd, Sumitomo report # ET-0068. Unpublished.
Loken RG and Pesselman RL, 1989	Octanol/water partition coefficient determination of Sumithrin. Hazleton Laboratories, Sumitomo report # EP-0060. Unpublished.
Martin PA, Amyes SJ, Ashby R, Lee P, Brown PM, Fowler JSL and Finn JP, 1987	Sumithrin: combined toxicity and oncogenicity study in rats. Life Science Research Limited, Sumitomo report # ET-0102. Unpublished.
Misaki Y, Yoshitake A and Seki T, 1996	Acute dermal toxicity study of Sumithrin in rats. Sumitomo Chemical Co., Ltd., Sumitomo report # ET-0174. Unpublished.
Miyamoto J, Murakami M, Hiromori T, Ito S and Hosokawa S, 1981	Six month oral toxicity study of S-2539 Forte in rats. Sumitomo Chemical Co., Ltd, Sumitomo report # ET-0059. Unpublished.
Murli H and Spicer CS, 1989	Sumithrin T.G. in an in vitro cytogenetic assay measuring chromosomal aberration frequencies in Chinese hamster ovary (CHO) cells, Hazleton Laboratories, Sumitomo report # ET-0115. Unpublished.

Nakanishi T, Yamada H, Kato T and Kohda A, 1988a	Primary eye and skin irritation tests with Sumithrin in rabbits. Sumitomo Chemical Co., Ltd., Sumitomo report # ET-0112. Unpublished.
Nakanishi T, Yamada H, Kogiso S, Yoshitake A, Kato T and Kohda A, 1988b	Skin sensitization test with Sumithrin in guinea pigs. Sumitomo Chemical Co., Ltd., Sumitomo report # ET-0113. Unpublished.
Nemec MD, 1989	A teratology study in rabbits with Sumithrin, WIL Research Laboratories, Inc., Sumitomo report # ET-0121. Unpublished.
Okuno Y, Yamaguchi T and Fujita Y, 1976	Insecticidal activity of a new synthetic pyrethroidal compound, 3-phenoxybenzyl (+)-*cis,trans*-chrysanthemate (*d*-phenothrin). *Botyu-Kagaku* 41, 42-55
Pence DH, Hagen WH, Alsaker RD, Hastings TF, Dawkins BG, Tacey RL and Marshall PM, 1981	Subchronic toxicity study of S-2539F in dogs. Final report (26 weeks). Hazleton Laboratories, Sumitomo report # ET-0066. Unpublished.
Putt AE, 1998	Sumithrin-the chronic toxicity to daphnia magna under flow-through conditions, Springborn Laboratories, Inc., Sumitomo report # EW-0022. Unpublished.
Saito S, Yamada H, Matsuda T and Tanoue A, 1989	Water solubility of Sumithrin TGAI, Sumitomo Chemical Co., Ltd., Sumitomo report # EP-90-0043. Unpublished.
Schreuder R, 2002	Personal communication to the JMPS, relating to two unpublished documents: (i) minutes of the European Commission's Special Meeting of the Working Group "Pesticides - Evaluation", held 19 June 2002, to discuss questions related to developmental neurotoxicity (incorporating comments of the Swedish delegation, 20 June, 2002). (ii) "Synthetic pyrethroids/28-08-02", letter from the Netherlands government to the European Commission, 2002.
Semann TM and Pesselman RL, 1989	Vapor pressure determination of Sumithrin, Hazleton Laboratories, Sumitomo report # EP-91-0059. Unpublished.
Sethi P, 2002	WHO specifications for d-allethrin and *d*-phenothrin, letter 30 May 2002, National Registration Authority, Australia
Shepler K, Ruzo LO and McGovern PA, 1989a	Aqueous solution photolysis of [^{14}C-cyclopropyl]-*d-trans*-phenothrin in natural sunlight, Pharmacology and Toxicology Research Laboratory, Sumitomo report # EM-0020. Unpublished.
Shepler K, Ruzo LO and McGovern PA, 1989b	Aqueous solution photolysis of [^{14}C-benzyl]-*d-trans*-phenothrinin natural sunlight, Pharmacology and Toxicology Research Laboratory, Sumitomo report # EM-0021. Unpublished.
Sousa JV, 1998	Sumithrin - early life-stage toxicity test with rainbow trout (Oncorhynchus mykiss), Sprinbborn Laboratories, Inc.,Sumitomo report # EW-0024. Unpublished.
Suzuki T, Kato T, Misaki Y and Okuno Y, 1987	Acute oral toxicity of S-2539F in rats, Sumitomo Chemical Co., Ltd., Sumitomo report # ET-0104. Unpublished.
Tesh JM, Willoughby CR, Lambert EP, Wilby OK and Tesh SA, 1983	Sumithrin: Effects of oral administration upon pregnancy in the rat 2 main study, Life Science Research Limited, Sumitomo report # ET-0085. Unpublished.

Tesh JM, Willoughby CR and Fowler JSL, 1986	Sumithrin: effects upon reproductive performance of rats treated continuously throughout two successive generations, Life Science Research Limited, Sumitomo report # ET-0101. Unpublished.
WHO, 1988	The WHO recommended classification of pesticides by hazard and guideline to classification 1988-1989, WHO, World Health Organization (WHO/VBC/88.953)