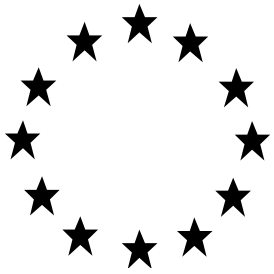
Directive 98/8/EC concerning the placing biocidal products on the market

Inclusion of ***active substances*** in Annex I to Directive 98/8/EC

Assessment Report



Abamectin
Product-type 18
(insecticides, acaricides and products to control other arthropods)

February 2011

The Netherlands

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1 STATEMENT OF SUBJECT MATTER AND PURPOSE

1.1 Procedure followed

This assessment report has been established as a result of the evaluation of abamectin as product-type PT 18 (insecticide), carried out in the context of the work programme for the review of existing active substances provided for in Article 16(2) of Directive 98/8/EC concerning the placing of biocidal products on the market[1], with a view to the possible inclusion of this substance into Annex I or IA to the Directive.

Abamectin (CAS no. 71751-41-2) was notified as an existing active substance in product-type PT18 by Syngenta, hereafter referred to as the applicant.

Commission Regulation 1451/2007 of 4 November 2003[2] lays down the detailed rules for the evaluation of dossiers and for the decision-making process in order to include or not an existing active substance into Annex I or IA to the Directive.

In accordance with the provisions of Article 7(1) of that Regulation, The Netherlands was designated as Rapporteur Member State to carry out the assessment on the basis of the dossier submitted by the applicant. The deadline for submission of a complete dossier for abamectin as an active substance in Product Type PT18 was 30 April 2006, in accordance with Annex V of Regulation (EC) No 1451/2007.

On 27 April 2006, The Netherlands competent authorities received a dossier from the applicant. The Rapporteur Member State accepted the dossier as complete for the purpose of the evaluation on 11 September 2006.

On 12 June 2009, the Rapporteur Member State submitted, in accordance with the provisions of Article 14(4) and (6) of Regulation (EC) No 1451/2007, to the Commission and the applicant a copy of the evaluation report, hereafter referred to as the competent authority report. The Commission made the report available to all Member States by electronic means on 3 July 2009. The competent authority report included a recommendation for the inclusion of abamectin in Annex I to the Directive for PT 18.

In accordance with Article 16 of Regulation (EC) No 1451/2007, the Commission made the competent authority report publicly available by electronic means on 3 July 2009. This report did not include such information that was to be treated as confidential in accordance with Article 19 of Directive 98/8/EC.

In order to review the competent authority report and the comments received on it, consultations of technical experts from all Member States (peer review) were organised by the Commission. Revisions agreed upon were presented at technical and

[1] Directive 98/8/EC of the European Parliament and of the Council of 16 February 1998 concerning the placing biocidal products on the market. OJ L 123, 24.4.98, p.1

[2] Commission Regulation (EC) No 1451/2007 of 4 December 2007 on the second phase of the 10-year work programme referred to in Article 16(2) of Directive 98/8/EC of the European Parliament and of the Council concerning the placing of biocidal products on the market. OJ L 325, 11.12.2007, p. 3

competent authority meetings and the competent authority report was amended accordingly.
On the basis of the final competent authority report, the Commission proposed the inclusion of abamectin in Annex I to Directive 98/8/EC and consulted the Standing Committee on Biocidal Product on [date].

In accordance with Article 11(4) of Regulation (EC) No 2032/2003, the present assessment report contains the conclusions of the Standing Committee on Biocidal Products, as finalised during its meeting held on [date].

1.2 Purpose of the assessment report

This assessment report has been developed and finalised in support of the decision to include abamectin in Annex I to Directive 98/8/EC for product-type PT18. The aim of the assessment report is to facilitate the authorisation in Member States of individual biocidal products in product-type PT18 that contain abamectin. In their evaluation, Member States shall apply the provisions of Directive 98/8/EC, in particular the provisions of Article 5 as well as the common principles laid down in Annex VI.

For the implementation of the common principles of Annex VI, the content and conclusions of this assessment report, which is available at the Commission website[3], shall be taken into account.

However, where conclusions of this assessment report are based on data protected under the provisions of Directive 98/8/EC, such conclusions may not be used to the benefit of another applicant, unless access to these data has been granted.

1.3 Overall conclusion in the context of Directive 98/8/EC

The overall conclusion from the evaluation is that it may be expected that there are products containing abamectin for the product-type PT18, which will fulfil the requirements laid down in Article 5 of Directive 98/8/EC. This conclusion is however subject to:

i. compliance with the particular requirements in the following sections of this assessment report,
ii. the implementation of the provisions of Article 5(1) of Directive 98/8/EC, and
iii. the common principles laid down in Annex VI to Directive 98/8/EC.

Furthermore, these conclusions were reached within the framework of the uses that were proposed and supported by the applicant (see Appendix II). Extension of the use pattern beyond those described will require an evaluation at product authorisation level in order to establish whether the proposed extensions of use will satisfy the requirements of Article 5(1) and of the common principles laid down in Annex VI to Directive 98/8/EC.

[3] http://ec.europa.eu/comm/environment/biocides/index.htm

2 OVERALL SUMMARY AND CONCLUSIONS

2.1 Presentation of the Active Substance

2.1.1 Identity, Physico-Chemical Properties & Methods of Analysis

2.1.1.1 Identity of the active substance

ISO-name:	Abamectin (ISO) is a mixture of avermectin B_{1a} (min 80%) and avermectin B_{1b} (max 20%)	
CAS-No.:	Abamectin	71751-41-2
	Avermectin B_{1a}	65195-55-3
	Avermectin B_{1b}	65195-56-4
EINECS No.:	Abamectin	none
	Avermectin B_{1a}	265-610-3
	Avermectin B_{1b}	265-611-9
CIPAC No.:	Abamectin	495
	Avermectin B_{1a}	none
	Avermectin B_{1b}	none
ELINCS No.:	none	

2.1.1.2 Purity of the active substance

Min. 900 g/kg abamectin (sum of avermectin B1a and avermectin B1b)
Min. 830 g/kg avermectin B1a
Max. 80 g/kg avermectin B1b.
The purity as given by the ISO common name is avermectin B1a : avermectin B1b = >80% : <20%
The natural fermentation process for the production of abamectin technical material produces several impurities in the technical material, which are structurally similar to avermectin B1a and avermectin B1b. Because of their low concentration level and their expected similar (eco)toxicity to avermectin B1a and avermectin B1b, these impurities are considered not (eco)toxicologically relevant in the technical material.

2.1.1.3 Physico-chemical properties of the active substance

Abamectin is a white powder, with a water solubility of 1.21 mg/L. Solubility in organic solvents ranges from 0.11 g/L in hexane to 470 g/L in dichloromethane. Abamectin does not dissociate at pH 1 - 12. The log K_{ow} is 4.4 at pH 7.2, the vapour pressure is < 3.7×10^{-6} Pa. The melting point ranges between 161.8 °C – 169.4 °C and abamectin starts to decompose at 162 °C. Degradation products are likely to be oxides of carbon and water. The relative density is 1.18 at 22 °C. Abamectin is considered surface active, the surface tension is 52.4 Nm/m. Abamectin is considered not highly flammable, does not self-ignite, and has no explosive or oxidising properties.

2.1.1.4 Analysis of the active substance as manufactured

MethodsAW-211/2 (HPLC-UV) and method SA-25/1 (HPLC-UV) are considered valid for the determination of abamectin in the technical material.
Methods AK-211/1 (HPLC-UV, GC-FID, Karl Fisher) and SB-25/1 (HPLC-UV, GC-FID, Karl Fisher) are considered valid for the determination of significant impurities (> 1 g/kg) in the technical material.

2.1.1.5 Residue analysis in soil, water and air

A valid method is available for the determination of residues of avermectin B1a, avermectin B1b, [8,9-Z]-avermectin B1a, 8a-oxo-avermectin B1a, 8a-hydroxy-avermectin B1a, 4,8a-dihydroxy-avermectin B1a, and 4-hydroxy-8a-oxo-avermectin B1a in soil. For water, a valid method is available for avermectin B1a, avermectin B1b, [8,9-Z]-avermectin B1a, 4"-oxo-avermectin B1a, and 3"-demethyl-avermectin B1a. A valid method is also present for determination of avermectin B1a and avermectin B1b in air, but confirmatory techniques are not available. However the analytical method for water is specific and can therefore be used for confirmatory purposes.

2.1.1.6 Residue analysis in animal and human body fluids and tissues

As abamectin is classified as very toxic a validated method for human body fluids and tissues is required. Relevant residues for monitoring human body fluids and tissues are avermectin B1a, 8,9-Z isomer of avermectin B1a and avermectin B1b.

HPLC-MS-MS method REM 198.02 is considered valid for the determination of avermectin B1a, 8,9-Z isomer of avermectin B1a and avermectin B1b in meat and whole blood in the range 0.002-0.02 mg/kg.

2.1.1.7 Residue analysis food and feed of plant origin

The active ingredient is used as biocide for control of ants and cockroaches in- and outdoors. The biocidal product will not be used on any food or feed of plant origin and therefore analytical methods for the analysis of abamectin residues in food or feed of plant origin are not required.

2.1.1.8 Residue analysis in food and feed of animal origin

The active ingredient is used as biocide for control of ants and cockroaches in- and outdoors. Because it is considered unlikely that livestock consumes the biocidal product (either direct or indirect via feed of plant origin), no residues are expected in food and feed of animal origin. Therefore analytical methods for the analysis of abamectin residues in food or feed of animal origin are not required.

2.1.2 Intended Uses and Efficacy

The assessment of the biocidal activity of the active substance demonstrates that it has a sufficient level of efficacy against some of the target organisms (Pharaohs ants and cockroaches) and the evaluation of the summary data provided in support of the efficacy of the accompanying product, establishes that the product may be expected to be efficacious.

The efficacy of the different constituants was not examined separately in insects. The avermectins all consist of a similar molecular structure with only minor differences, and could possibly all act as an insecticide. The chemical differences are rather small, given the size and structure of the molecule, and are all situated on 3 positions of the molecule. The difference between avermectin B1a and avermectin B1b is on 1 position only, being either an ethyl or methyl functionality. Moreover, avermectin B1a and avermectin B1b were tested separately in a few vertebrate kinetics studies, where they turned out to have similar properties. From this it is taken that the efficacy of a mixture of 80/20 up to 100/0 avermectin B1a/avermectin B1b will be similar.

In addition, in order to facilitate the work of Member States in granting or reviewing authorisations, and to apply adequately the provisions of Article 5(1) of Directive 98/8/EC and the common principles laid down in Annex VI of that Directive, the intended uses of the substance, as identified during the evaluation process, are listed in Appendix II.

2.1.3 Classification and Labelling of the active substance

At 17th March 2010 the Committee for Risk Assessment (RAC) has adopted an opinion on the proposal for harmonised classification and labelling of abamectin:
Abamectin is the ISO common name for a mixture of ≥80 % avermectin B1a and ≤20 % avermectin B1b. The use of the word “mixture” in the ISO description is not in line with REACH and CLP terminology. Following the terminology of REACH and CLP Regulations, abamectin is a substance containing ≥80 % avermectin B1a and ≤20 % avermectin B1b.The material considered in this report fulfils the ISO definition.

According to the REACH guidance document on substance identification the substance is a monoconstituent substance with avermectin B1a (CAS Number 65195-55-3) as its main constituent (purity > 83%) and with avermectin B1b as an impurity. However, part 1.1.1.4 of Annex VI of Regulation (EC) 1272/2008 (CLP Regulation) states that whenever possible plant protection products and biocides are designated by their ISO names. As abamectin is used as both a plant protection product and as a biocide in this proposal preference is given to the use of the ISO name abamectin as the International Chemical Identifier for inclusion in Annex VI of the CLP Regulation.

Therefor, abamectin should not be considered as a monoconstituent, but as the mixture as defined by the ISO common name.

2.1.3.1 Proposed classification based on Directive 67/548/EEC

Physico-chemical properties

Based on the submitted information, classification and labelling for the active substance is not considered necessary.

Human toxicological properties

Classification of the active substance with T+ (very toxic).

R26 "very toxic by inhalation" because of LC50 > 0.034 and < 0.051 mg/kg in the rat.

R28 "very toxic if swallowed" because of LD50 rat 8.7 mg/kg bw.

R63 “possible risk of harm to the unborn child”.
Justification: increased number of resorptions, the occurrences of cleft palate, omphalocele, clubbed fore-feet and delayed ossification, sometimes with evidence of maternal toxicity (based on studies with non sensitive species, so excluding studies with the sensitive CF-1 mouse).

R48/23/25 "Toxic: danger of serious damage to health by prolonged exposure through inhalation and if swallowed".
Justification: There was clear neurotoxicity at 0.00269 mg/L which is below the guidance value for R48/23 in a 30 day inhalation study. In the oral 18-weeks dog study, neurotoxicity and mortality were observed at 0.5 mg/kg/day, a dose level clearly below the guidance value for R48/25 of 5 mg/kg bw/day in a 13-week study.

Because of being allocated the R26 and R28 phrases, abamectin is considered very toxic (T+).

Specific concentration limits:	**Cn ≥ 5%**	**T ; R48/23**
	0.5% < Cn <5%	**Xn; R48/20**

Environmental properties

Classification of the active substance with N (Dangerous to the environment).
The EC50 for invertebrates is lower than 1 mg a.s./L and the substance is not readily biodegradable. Therefore, abamectin should be classified as Very toxic to aquatic organisms (R50) and May cause long-term adverse effects in the aquatic environment (R53).Because of being allocated the R50/53 phrases, abamectin is considered dangerous for the environment (N).

Classification of the preparation		
N; R50-53	**N; R51-53**	**R52-53**
Cn > 0.0025%	**0.00025% < Cn <0.0025%**	**0.000025% < Cn <0.00025%**

2.1.3.2 Proposed classification based on Regulation EC 1272/2008

Signal word: Danger
Symbol: GHS06, GHS08, GHS09

Phys/Chem hazards:	-	
Health hazards:	Acute Tox. 2	H300
	Acute Tox. 1	H330
	Repr. 2	H361d
	STOT-RE 1	H372 (“Causes damage to the nervous system through prolonged or repeated exposure”)
Environment:	Aquatic Acute 1	H400
	Aquatic Chronic 1	H410

Specific concentration limits:

Cn ≥ 5%	**STOT-RE 1; H372 Causes damage to the nervous system through prolonged or repeated exposure**
0.5% ≤ Cn <5%	**STOT-RE 2; H373 May cause damage to the nervous system through prolonged or repeated exposure**

Classification of the mixture		
H400, H410	**H411**	**H412**
Cn > 0.0025%	**0.00025% < Cn <0.0025%**	**0.000025% < Cn <0.00025%**

M-factors: **10,000**

2.1.4 Classification and Labelling of the biocidal products

2.1.4.1 Proposed classification based on Directive 67/548/EEC

Raid Ant Bait
- Physico-chemical properties: no classification proposed.
- Human toxicological properties: R38: irritating to skin and R43: sensitizing to skin.
  Since the product contains peanut butter it is recommended to include a suitable warning like: “Attention, product contains peanuts”.
- Environmental properties: N; R50/53.

Raid Roach Bait
- Physico-chemical properties: no classification proposed.
- Human toxicological properties: R38: irritating to skin and R43: sensitizing to skin.
  Since the product contains peanut butter it is recommended to include a suitable warning like: “Attention, product contains peanuts”.
- Environmental properties: N; R50/53.

Avert Dry Flowable Cockroach Bait 310 A
- Physico-chemical properties: A classification cannot be proposed at present, because reliable data on flammability, auto-flammability and/or reaction with water are not available.
- Human toxicological properties: No classification proposed.
- Environmental properties: N; R50/53.

2.1.4.2 Proposed classification based on Regulation EC 1272/2008

Raid Ant Bait
- Physico-chemical properties: no classification proposed.
- Human toxicological properties: Skin Sens. 1, H317/May cause an allergic skin irritation.
  Since the product contains peanut butter it is recommended to include a suitable warning like: “Attention, product contains peanuts”.

– Environmental properties: Aquatic Acute 1, H400/Very toxic to aquatic life and Aquatic Chronic 1, H410/Very toxic to aquatic life with long lasting effects.

Raid Roach Bait
– Physico-chemical properties: no classification proposed.
– Human toxicological properties: Skin Sens. 1, H317/May cause an allergic skin irritation.
  Since the product contains peanut butter it is recommended to include a suitable warning like: “Attention, product contains peanuts”.
– Environmental properties: Aquatic Acute 1, H400/Very toxic to aquatic life and Aquatic Chronic 1, H410/Very toxic to aquatic life with long lasting effects.

Avert Dry Flowable Cockroach Bait 310 A
– Physico-chemical properties: A classification cannot be proposed at present, because reliable data on flammability, auto-flammability and/or reaction with water are not available.
– Human toxicological properties: No classification proposed.
– Environmental properties: Aquatic Acute 1, H400/Very toxic to aquatic life and Aquatic Chronic 1, H410/Very toxic to aquatic life with long lasting effects.

2.2 Summary of the risk assessment

2.2.1 Human health risk assessment

The present evaluation of the compound abamectin is completely based on the Abamectin 91/414/EEC Draft Assessment Report (DAR) issued October 2005 by the 91/414/EEC Rapporteur Member State The Netherlands (abamectin vol3B6 – Annex B – Tox section), the revised abamectin addendum (February 2008) and the EFSA conclusion (EFSA Scientific Report (2008) 147, 1-106; finalised 29 may 2008). The EFSA conclusion is written by EFSA after the PRAPeR expert meeting. For Plant Protection Products, abamectin was discussed by the experts in mammalian toxicology in December 2007 (PRAPeR meeting 39, round 8). No new information on this substance was provided by the notifier since the PRAPeR expert meeting. Based on the DAR, the addendum and the EFSA conclusion, abamectin is included in Annex I of 91/414/EEC.

Abamectin is an insecticide comprising of a mixture of avermectin B1a (minimum 80%) and avermectin B1b (maximum 20%). This evaluation contains studies performed with abamectin technical and specific aspects of the toxicological properties of the 8,9-Z isomer of abamectin, a product of abamectin photolysis. The metabolism and kinetic studies, and the 18-week toxicity study in the dog, were performed on avermectin B1a. A comparative metabolism and kinetic study was performed on avermectin B1b. All other studies were performed on abamectin technical comprising avermectins B1a and B1b.
An important aspect to consider in the risk assessment of abamectin is the role of p-glycoprotein polymorphism and its relevance for human risk assessment.

2.2.1.1 Hazard identification

The toxicological database indicates that the critical toxicological endpoints for abamectin and the 8,9-Z isomer are:
- Neurotoxicity
- Fetotoxicity

2.2.1.2 Effects assessment

For abamectin a complete toxicological dossier is available. For the 8,9-Z isomer the studies were restricted to acute oral toxicity studies and developmental toxicity studies (including maternal toxicity).

Toxicokinetics
Abamectin is almost completely absorbed in the gastrointestinal tract of the rat (calculated bioavailability was 86% based on compared excretion after intravenous and oral administration) and distributed throughout tissues and organs. Maximum concentrations in blood are achieved within 4-8 h after administration. It is rapidly eliminated from the body, almost exclusively in the faeces (mainly by non biliary excretion of the absorbed dose), and does not accumulate in tissues/organs after repeated exposure. The major reactions involved in the biotransformation of abamectin in the rat are demethylation, hydroxylation, cleavage of the oleandrosyl ring, and oxidation reactions. In the rat metabolism, the 8,9-Z isomer of avermectin B1a is not formed. Dermal penetration is very low, less than 1% is absorbed through human skin in vitro and through the skin of monkeys. For the inhalation route 100% absorption is assumed.

Acute toxicity
Abamectin is very toxic by the oral and inhalatory route, but is not toxic by dermal exposure. It is not irritating to skin or eyes and has no sensitizing properties.
Based on the acute toxicity results, the proposed classification is T+, R26/28 Very toxic by inhalation and if swallowed.

Repeated dose toxicity
The database contains oral and inhalation studies. Due to the low dermal penetration of the compound the lack of a short-term dermal toxicity study is not considered to constitute a data gap.

An 8-week dietary range-finding study in the rat and 12 (dietary), 18 (gavage) and 53-week (dietary) toxicity studies in the dog have been performed. The studies were performed using abamectin technical except the 18-week toxicity study in dogs which used avermectin B1a. A 90-day toxicity study in rats was not conducted. Since it is not likely that a 90-day toxicity study will give additional information to the information of the other toxicity studies and since the dog is clearly the most sensitive species, such a study with abamectin is not necessary.

In the 18 week oral toxicity study with dogs, a very steep dose-response relationship for avermectin B1a in the dog was observed, since the oral NOAEL by gavage is 0.25 mg/kg bw/day and death, clinical signs (ataxia, tremors, mydriasis and ptyalism),

reduced weight gain and histopathological changes in the liver occurred at 0.5 mg/kg bw/day.
In the 53-week oral toxicity study with abamectin technical in dogs, death occurred at the dose level of 1.0 mg/kg bw/day, and pupil reactivity was decreased or absent at the dose level of 0.5 mg/kg bw/day. Based on this effect on pupil reactivity, the NOAEL in this study is 0.25 mg/kg bw/day. The results of both these studies show that a similar steep dose response exists for abamectin technical. Target organ was the nervous system and the liver. The most appropriate NOAEL in the short-term toxicity studies is 0.25 mg/kg bw/day for both abamectin technical and avermectin B1a in the dog.
Based on the severity of the effects observed at a relatively low dose (one death at 0.5 mg/kg bw/day in the 18-week dog study), the classification T; R48/25 Toxic, Danger of serious damage to health by prolonged exposure if swallowed, is proposed.

The results of a recent 30-day inhalation study in rats (including a preliminary 5-day study) were presented in the revised addendum to Volume 3 (B.6) of February 2008. The NOAEL was 0.577 µg/L (0.11 mg/kg bw/day) based on clinical signs and reduced motor activity in females.

Chronic toxicity and carcinogenicity
There was no evidence of carcinogenicity in chronic studies in either rat or mouse at any of the dose levels employed (up to 2 mg/kg bw/day in rats and 8 mg/kg bw/day in mice). Although clinical signs of neurotoxicity were evident in rats and to a lesser extend in mice, no histopathological correlate was evident. The lowest NOAEL determined in long-term toxicity studies was 1.5 mg/kg bw/day in the rat carcinogenicity and toxicity study.

Genotoxicity
Abamectin technical did not induce gene mutations in either bacterial or mammalian cells at any of the tested concentrations either with or without metabolic activation. There was no evidence of a clastogenic effect at any tested concentration either in vitro or in vivo. It is concluded that abamectin technical and/or its metabolites are not genotoxic.

Reproductive toxicity
In the evaluation of the rat 2-generation study provided in the DAR (for Plant Protection Products), it was concluded that there were adverse effects on the reproductive parameters in the absence of maternal toxicity (increased duration of cohabitation in F0 generation, increased number of F0 dams with prolonged interoestrus during the second mating, decreased number of matings for the F1b litter). Therefore a classification for the reproductive toxicity was proposed. However, the notifier provided additional individual data, re-calculations and new information that were evaluated by the RMS in the addendum to B.6 (February 2008). Based on this, it was concluded that the findings were without dose-response relationship or statistical significance, and that there was an increased sensitivity of older animals showing an early onset of persistent oestrus. Overall, no strong reproductive effects were triggering a classification. Therefore the NOAEL for parental and reproduction toxicity was 0.4 mg/kg bw/day (the highest dose tested) whereas the NOAEL for the offspring was 0.12 mg/kg bw/day, based on an increased pup mortality and retarded weight gain in both generations.

Teratogenic and fetotoxic effects were observed in both rats and rabbits. In rabbits the effects were observed in presence of maternal toxicity. In rats, however, cleft palate, changed sex ratio and increased number of fetuses with lumbar rib and lumbar count variation was observed at 1.6 mg/kg bw/day in the absence of maternal toxicity, with a NOAEL of 0.8 mg/kg bw/day. Based on the malformations in rats and rabbits, sometimes with evidence of maternal toxicity, the compound should be classified as R63 “possible risk of harm to the unborn child”.

Neurotoxicity

An acute and a 90-day neurotoxicity study were performed in rats (by gavage) and described in the addendum (February 2008). The acute NOAEL was 0.5 mg/kg bw based on the reduced splay reflex observed on day 1 at 1.5 mg/kg bw, and the 90-day NOAEL was 1.6 mg/kg bw/day based on clinical signs, body weight loss and changes in the stomach at 4 mg/kg bw/day.

Abamectin does not belong to a chemical class which is suspected to cause delayed neurodegenerative effects (organophosphates, carbamates) and studies do not indicate histopathological evidence of central or peripheral nervous system damage. Therefore specific studies on delayed neurotoxicity are not required.

Additional studies with the 8,9-Z isomer of avermectin B1a

In a comparative study, the acute oral toxicity of the 8,9-Z isomer was higher in CF-1 male mice (LD_{50} between 10 and 20 mg/kg bw) than in CD-1 female mice (LD_{50} 217 mg/kg bw). In an Ames test, the 8,9-Z isomer was not mutagenic, with or without metabolic activation. In a one-generation reproductive study with rats, the maternal NOAEL was 0.40 mg/kg bw/day (the highest dose tested) and the offspring NOAEL was 0.12 mg/kg bw/day based on an increase in post-natal deaths and in sex ratio. No effect on female fertility or reproductive performance was observed (only the females were treated).

Developmental studies with the 8,9-Z isomer of avermectin B1a were performed in CF-1 mice, CD-1 mice and CD rats. The studies with CF-1 mice were not considered relevant for the human risk evaluation due to particular species sensitivity (see below, ‘relevance of the polymorphism’). However, in the developmental study with CD-1 mice, the maternal NOAEL was 3.0 mg/kg bw/day (the highest dose tested). Based on an increased incidence of cleft palates in all treated groups, considered substance-related by the experts, only a developmental LOAEL of 0.75 mg/kg bw/day could be derived. As last result for the 8,9-Z isomer, an embryotoxicity study with CD rats did not demonstrated neither maternal nor embryotoxic effects up to 1.0 mg/kg bw/day (maternal and developmental NOAEL).

Based on this limited database (since the data obtained with the CF-1 mouse have been considered non relevant), the experts in the PRAPeR expert meeting agreed that the 8,9-Z isomer has the same toxicological profile as abamectin.

Additional studies abamectin

A study with juvenile rhesus monkeys showed that the most sensitive indicator of abamectin toxicity was emesis, occurring at $\geq$ 2.0 mg/kg bw, and leading to a NOAEL of 1.0 mg/kg bw. Clinical signs of neurotoxicity occurred only at 24 mg/kg bw, and were limited to transient sedation and marked mydriasis. The maximum plasma concentrations of abamectin were increasing with the dose level, and were not accompanied by a markedly increased severity in clinical signs.

In an antidote study with dogs it was demonstrated that ipecac administered within 15 minutes of abamectin ingestion prevented coma and death and reduced the incidence and/or severity of the clinical signs.

Relevance of the polymorphism of the MDR-1 gene incoding for P-glycoprotein expression

It has been demonstrated that the CF-1 mouse was particularly sensitive to abamectin and 8,9-Z isomer toxicity and that this sensitivity was related to the genotype for the MDR-1 gene encoding for P-glycoprotein expression (which is a key constituent of the placental barrier and blood-brain barrier). Different investigative studies were performed with CF-1 mice, pregnant and non-pregnant, of known genotype for the MDR-1 gene, and with CF-1 and CD-1 mice of unknown genotype. The results showed that sensitive CF-1 individuals do not express P-glycoprotein in the cerebrum, cerebellum and jejunum whereas “non-sensitive” CF-1 mice and all CD-1 mice do express P-glycoprotein in these tissues.

In exploratory studies with rat foetuses, pups and adults, the expression of P-glycoprotein in the cerebrum and cerebellum was shown to be lower in neonates than in adults, first detected on postnatal day 7 and developed to full (adult) extent during the first 20 days after birth. There is evidence that P-glycoprotein expression is localized in the brain capillaries, suggesting a role for P-glycoprotein in the blood brain barrier. Furthermore the expression of P-glycoprotein in the jejunal border does not start before day 8 after birth. Therefore it is presumed that neonate rats, with limited or no Pglycoprotein expression, have an increased susceptibility to abamectin toxicity.

An extensive summary of the recent literature was provided in the addendum (November 2007; revised February 2008) and discussed by the experts in the PRAPeR meeting. They agreed with the conclusion that the studies with the unique polymorphic CF-1 mouse are not relevant for human risk assessment, since non-functional P-glycoprotein has not been identified in humans and only the homozygous CF-1 mouse with non functional P-glycoprotein was shown to be more sensitive to abamectin toxicity.

In rats, expression of P-glycoprotein in the brain develops to adult levels during the first 20 days after birth, and the expression of P-glycoprotein in the jejunum does not start before postnatal day 8. Since neonatal rats have limited P-glycoprotein expression (which is considered in contrast to man), it is suggested that neonatal rats are increased susceptible for abamectin toxicity. Since this susceptible period with limited P-glycoprotein expression after birth is not present in man, effects observed in neonatal rats during lactation are considered not appropriate for human risk evaluation of abamectin and the 8,9-Z isomer.

2.2.1.3 Exposure assessment

The use pattern of Avert Dry Flowable Cockroach bait indicates a long-term exposure of the professional user. Therefore the use of a long-term AEL and a long-term NOAEL, for estimation of the MOE is considered appropriate.

The two bait products (Raid Ant Bait and Raid Roach Bait) are not used by professionals, but only by non-professionals. The bait stations consist of a robust plastic cartridge and should be placed indoors in the path/tracks of ants or

cockroaches e.g. in corners between walls and the floor. Based on the use pattern for these products no exposure of the non-professional user is expected.
Exposure of the general population is specifically considered for children who can be exposed throughout the year to residues of the products on, or in the vicinity of the treated area, dermally by rubbing and orally as a result of hand-mouth contact. For this scenario a long-term exposure is considered.
The exposure estimates are presented in the tables in paragraph 2.2.1.4.

2.2.1.4 Risk characterisation

The human health risk characterisation is performed using both the AEL and the MOE approach. For both approaches the most relevant NOAEL is chosen.
A risk index of <100% and a MOE of greater than 100 is considered safe using in both cases a safety factor of 100 for acute, subacute or chronic exposure.

For all products indirect exposure to abamectin as a result of residues in food is considered negligible. Therefore, it is not necessary to determine an ADI and ARfD. However, these have already been set for the use of abamectin as a plant protection product.

ADI:
The calculation of the ADI is based on the highest dose at which no adverse effect is observed in the most appropriate study in the most sensitive species. Abamectin was tested in several toxicity studies in rats, mice, dogs and monkeys, providing the basis for the establishment of the ADI. The relevance of findings in animal studies for human risk assessment is also taken into account. Studies with abamectin technical and the 8,9-Z isomer of avermectin B1a have shown that sensitivity to abamectin and the 8,9-Z isomer toxicity is linked to the expression of P-glycoprotein. It has been demonstrated that the CF-1 mouse is particularly sensitive to abamectin and the 8,9-Z isomer toxicity and that this sensitivity is related to genotype for the mdr-1 gene encoding for P-glycoprotein expression. P-glycoprotein is the key constituent of the placental barrier and blood-brain barrier. Since polymorphism for the mdr-1 gene resulting in non-functional P-glycoprotein has not been detected (and if occurring it will be very rare) within the human population, the effects observed in CF-1 mice are considered not relevant for human risk evaluation (see also B.6.8.2 in this addendum).
The neonatal rat is also sensitive because the placental barrier and blood-brain barrier is incompletely formed at birth, which is considered in contrast to man. Since such a sensitive period with limited P-glycoprotein expression is not present in man, the effects observed in neonatal rats are considered not relevant for human risk evaluation.
For the present derivation of the ADI, the studies with the sensitive CF-1 mice are not taken into account.

Abamectin
Considering the studies performed with abamectin excluding those performed with CF-1 mice, the overall NOAEL of 0.25 mg/kg bw/day was obtained from two dog studies, an 18-weeks and a 53-weeks study, with a LOAEL of 0.52 mg/kg bw/day, based on clinical signs of toxicity (ataxia, tremors, mydriasis, ptyalism), mortality, reduced weight gain, histopathological changes in the liver and absent or decreased

pupil reflex. Application of a safety factor for inter- and intraspecies differences of 100 results in an ADI of 0.0025 mg/kg bw/day.

(Note: the revised ADI established by JMPR in 1997 was based on the fetal NOAEL of 0.12 mg/kg bw/day from the two-generation study. Accounting for neonatal hypersusceptibility in the rat, a reduced uncertainty factor of 50 was applied. In addition, the NOAEL from the one year dog study of 0.25 mg/kg bw/day was considered, with an uncertainty factor of 100. The ADI was rounded down to 0.002 mg/kg bw/day. The CVMP (2002; Committee for Veterinary Medicinal Products) recommended that a revised ADI for abamectin should be based on the NOAEL of 0.25 mg/kg bw/day from the one-year repeated dose study in dogs. Using a uncertainty factor of 100, this results in a value of 0.0025 mg/kg bw/day.)

8,9-Z isomer of avermectin B1a

Excluding the studies performed with the CF-1 mice results in a limited number of studies performed with the 8,9-Z isomer. Based on the available studies with the 8,9-Z isomer, excluding the CF-1 mice, it can be concluded that the toxicity of the 8,9-Z isomer of avermectin B1a is lower or comparable to the toxicity of abamectin, with regard to acute toxicity, developmental toxicity, reproduction toxicity and genotoxicity (only based on an Ames test). It has to be discussed in the expert meeting whether the available data is sufficient to conclude that the ADI of abamectin is also applicable to the 8,9-Z isomer of avermectin B1a (taking into account that the dog is the most sensitive species for abamectin).
PRAPeR 39 (Dec. 2007): The experts agreed, based on the comparability with the parent compound abamectin, that the ADI of the parent can be used for the 8,9-Z isomer.

ARfD (acute reference dose):

The calculation of the acute reference dose is based on the highest dose at which no adverse effect is observed in the most appropriate acute toxicity study in the most sensitive species. In acute oral and inhalation toxicity studies, both abamectin and its 8,9-Z isomer appeared to be very toxic. Clinical signs of neurotoxicity and mortality were observed within a few hours after dosing. In repeated dose studies, these effects were also observed within a few hours after dosing. In teratogenicity studies, abamectin and 8,9-Z isomer exposure resulted in fetotoxicity. Since these effects are considered to be induced by a single exposure within a certain time window, these effects are considered relevant for the establishment of the ARfD.
For the present derivation of the ARfD, the studies with the sensitive CF-1 mice are not taken into account.

Abamectin

Considering the studies performed with abamectin excluding those performed with CF-1 mice, the lowest NOAEL of 0.5 mg/kg bw/day for acute effects was observed in the acute neurotoxicity study in rats, based on reduced splay reflex, with a LOAEL of 1.5 mg/kg bw. Application of a safety factor for inter- and intraspecies differences of 100 results in an ARfD of 0.005 mg/kg bw/day.

8,9-Z isomer of avermectin B1a

Excluding the studies performed with the CF-1 mice results in a limited number of studies performed with the 8,9-Z isomer. Based on the available studies with the 8,9-Z isomer, excluding the CF-1 mice, it can be concluded that the toxicity of the 8,9-Z isomer of avermectin B1a is lower or comparable to the toxicity of abamectin, with

regard to acute toxicity, developmental toxicity, reproduction toxicity and genotoxicity (only based on an Ames test). It has to be discussed in the expert meeting whether the available data is sufficient to conclude that the ARfD of abamectin is also applicable to the 8,9-Z isomer of avermectin B1a.
PRAPeR 39 (Dec. 2007): The experts agreed, based on the comparability with the parent compound abamectin, that the ARfD of the parent can be used for the 8,9-Z isomer.

AELs and MOEs
Conform normal practice three individual AELs will be derived: one acceptable exposure level for acute, one for a medium-term and one for a long-term exposure. It should be noted, however, that in this case the exposure is not only for abamectin itself, but can also be for the photolysis product (8,9-Z isomer), depending on the way of use.
For the present derivation of the AEL, the studies with the sensitive CF-1 mice are not taken into account. Although exposure of professionals is mainly via dermal contact and inhalation, the AELs will be based on oral studies. The 30-day inhalation study does not show route-specific effects and the effects observed at the LOAEL (0.52 mg/kg bw/day) are relatively marginal. Considering the dose selection and the relatively marginal effects at the LOAEL, the AELs should not be based on the 30-day inhalation study.
The different NOAELs for the three exposure scenarios that will be chosen as starting point for the MOE approach are the same as used for the AEL approach.

AEL acute
See ARfD:
$AEL_{systemic,\ acute\ for\ abamectin}$: 0.005 mg/kg bw.
$AEL_{systemic,\ acute\ for\ 8,9\text{-}Z\ isomer\ of\ avermectin\ B1a}$: 0.005 mg/kg bw.

AEL medium-term
A comparison of the toxicity of the 8,9-Z isomer of avermectin B1a with that of abamectin shows that they have similar toxicity. Therefore, it is appropriate to establish a single AEL for abamectin and its 8,9-Z isomer of avermectin B1a.
Considering the studies performed with abamectin excluding those performed with CF-1 mice, a NOAEL of 0.25 mg/kg bw/day was obtained from two dog studies, an 18-weeks and a 53-weeks study, with a LOAEL of 0.5 mg/kg bw/day, based on clinical signs of toxicity (ataxia, tremors, mydriasis, ptyalism), mortality, reduced weight gain, histopathological changes in the liver and absent or decreased pupil reflex. Metabolism studies in the rat showed that orally administered abamectin is almost completely absorbed (~86%) and therefore it is not necessary to adjust the systemic AEL. A safety factor of 100 can be applied.

The following medium-term AELs were established:
$AEL_{short\text{-}term}$: 0.0025 mg/kg bw/day
$AEL_{systemic,\ medium\text{-}term\ for\ 8,9\text{-}Z\ isomer\ of\ avermectin\ B1a}$: 0.0025 mg/kg bw.

AEL long-term:
The NOAEL that is relevant for long-term AEL, (i.e. the NOAEL of 0.25 mg/kg bw/day in the 18-week and 53-week dog studies) is the same as that used for the medium-term AEL.

The following long-term AELs were established:
$AEL_{systemic, long-term}$: 0.0025 mg/kg bw/day
$AEL_{systemic, long-term for 8,9-Z isomer of avermectin B1a}$: 0.0025 mg/kg bw.

In the tables below the risk assessment for the three formulations are shown. The risk assessment for direct exposure using Avert Dry Flowable Cockroach Bait 310A is presented in table 2.2.1-4.1 and table 2.2.1-4.2.

Table 2.2.1-4.1: Internal exposures and risk assessment of Avert Dry Flowable Cockroach Bait 310A for professional users; AEL approach

Route	Estimated internal exposure (mg a.s./ kg bw- day)		AEL-systemic (mg a.s./ kg bw- day)	Risk-index (% of AEL)	
	without PPE	with PPE		without PPE	with PPE
Avert Dry Flowable Cockroach Bait 310A					
Inhalation	2.1×10^{-5}	2.1×10^{-6}	2.5×10^{-3}	0.8	0.08
Dermal	2.2×10^{-5}	2.2×10^{-6}	2.5×10^{-3}	0.9	0.09
Total	4.3×10^{-5}	4.3×10^{-6}	2.5×10^{-3}	1.7	0.17

Table 2.2.1-4.2: Internal exposures and risk assessment of Avert Dry Flowable Cockroach Bait 310A for professional users; MOE approach

Route	Estimated internal exposure (mg a.s./ kg bw- day)		NOAEL-systemic (mg a.s./ kg bw- day)	MOE	
	without PPE	with PPE		without PPE	with PPE
Avert Dry Flowable Cockroach Bait 310A					
Inhalation	2.1×10^{-5}	2.1×10^{-6}	0.25	11,905	119,048
Dermal	2.2×10^{-5}	2.2×10^{-6}	0.25	11,363	113,636
Total	**4.3×10^{-5}**	**4.3×10^{-6}**	0.25	5813	58,139

Both risk assessment scenario's (AEL and MOE approach) indicate that there is no risk for the professional user when using Avert Dry Flowable Cockroach Bait 310A.

The risk assessment for indirect exposure using Avert Dry Flowable Cockroach Bait 310A is presented in table 2.2.1-4.3 and Table 2.2.1-4.4.
Risk assessment for indirect exposure using Raid Ant Bait or Raid Roach Bait is presented in table 2.2.1-4.5 and Table 2.2.1-4.6.

Table 2.2.1-4.3: Indirect exposure as a result of use of Avert Dry Flowable Cockroach Bait 310A; AEL approach

	Estimated internal exposure (mg a.s. / kg bw- day)	Long-term AEL-systemic; child (mg a.s./ kg bw- day)	Risk-index (% of AEL)

	Estimated internal exposure (mg a.s. / kg bw- day)	Long-term AEL-systemic; child (mg a.s./ kg bw- day)	Risk-index (% of AEL)
Avert Dry Flowable Cockroach Bait 310A			
Dermal	7.4×10^{-5}	0.0025	2.9
Oral	8.3×10^{-4}	0.0025	33
Total	**9.1×10^{-4}**	0.0025	**36**

Table 2.2.1-4.4: Indirect exposure as a result of use of Avert Dry Flowable Cockroach Bait 310A; MOE approach

	Estimated internal exposure (mg a.s. / kg bw- day)	NOAEL-systemic (mg a.s./ kg bw- day)	MOE
Avert Dry Flowable Cockroach Bait 310A			
Dermal	7.4×10^{-5}	0.25	3380
Oral	8.3×10^{-4}	0.25	301
Total	**9.1×10^{-4}**	0.25	**275**

Table 2.2.1-4.5: Indirect exposure of a child as a result of use of Raid Ant Bait and Raid Roach Bait; AEL approach

	Estimated acute internal exposure [1)] (mg a.s. / kg bw- day)	Long-term AEL-systemic; child (mg a.s./ kg bw- day)	Risk-index (% of AEL)
Raid Ant Bait			
Dermal	$<< 5.1 \times 10^{-7}$	0.0025	<< 0.02
Oral	$<< 5.8 \times 10^{-6}$	0.0025	<< 0.23
Total	**$<< 6.3 \times 10^{-6}$**	0.0025	**<< 0.25**
Raid Roach Bait			
Dermal	$<< 2.6 \times 10^{-6}$	0.0025	<< 0.1
Oral	$<< 2.9 \times 10^{-5}$	0.0025	<< 1.2
Total	**$<< 3.1 \times 10^{-5}$**	0.0025	**<< 1.2**

1): These exposures are the result of first tier worst case screening calculations, the real exposures will be much smaller than the calculated values.

Table 2.2.1-4.6: Indirect exposure of a child as a result of use of Raid Ant Bait and Raid Roach Bait; MOE approach

	Estimated acute internal exposure [1)] (mg a.s. / kg bw- day)	NOAEL-systemic (mg a.s./ kg bw- day)	MOE
Raid Ant Bait			
Dermal	<< 5.1 x 10^{-7}	0.25	>>490000
Oral	<< 5.8 x 10^{-6}	0.25	>>43000
Total	**<< 6.3 x 10^{-6}**	0.25	**>>39700**
Raid Roach Bait			
Dermal	<< 2.6 x 10^{-6}	0.25	>>96200
Oral	<< 2.9 x 10^{-5}	0.25	>>8620
Total	**<< 3.1 x 10^{-5}**	0.25	**>>8060**

1): These exposures are the result of first tier worst case screening calculations, the real exposures will be much smaller than the calculated values.

Both risk assessment scenario's (AEL and MOE approach) indicate that there is no risk for the children when they are orally (by hand-mouth contact) and/or dermally exposed to residues of either three bait products. The exposures are far below 100% of the AEL and the MOE amply exceeds the value of 100. The exposure to the 8,9-Z isomer cannot be quantified. However, if photodegradation of abamectin to the 8,9-Z isomer occurs, this means that part of the abamectin 'disappears'. Since the AEL for abamectin is the same as for the 8,9-Z isomer, the possible exposure to the 8,9-Z isomer is actually already taken into account in the above risk assessment for abamectin.

A reverse reference scenario using an AF of 100, showed that infants should ingest 3.3% of the contents of a baitbox containing Raid Ant Bait or 2.0% of the contents of a baitbox containing Raid Roach Bait, to achieve a body burden equivalent to the NOAEL. This can only be achieved when the child-resistant bait station is opened, because all bait stations are designed to prevent touching the bait formulation inside the station by an internal barrier wall. Furthermore, the label instructions clearly state that the bait station must be out of reach of children. The possible risk for infants/children relies on the robustness of the bait stations. Therefore, it will be included in the elements to be taken into account by Member State that the robustness of the bait station has to be assessed at product authorisation level.

2.2.1.5 Conclusion human health risk assessment

Using abamectin as baits against ants or cockroaches, safe use is expected for professional users when using a dry flowable bait (Avert Dry Flowable Cockroach

Bait 310A), even without PPE and it will not lead to an unacceptable risk for the general population (a.o. children).
Also the use of abamectin as a wax block by nonprofessionals for the control of ants (Raid Ant Bait) or cockroaches (Raid Roach Bait) will not lead to an unacceptable risk for the general population when risk mitigation measures are in place (a.o. children).

2.2.2 Environmental risk assessment

2.2.2.1 Fate and distribution in the environment

Biodegradation in water
Abamectin is not readily biodegradable.
In natural water/sediments systems, the dissipation of abamectin from the water phase was dominated by sorption, the $DT_{50,water}$ was 2.4 days. The average $DT_{50,system}$ was 89 days, the $DT_{50,sediment}$ 99 days at 20°C. The average $DT_{50,system}$ and $DT_{50,sediment}$ at 12 °C are 169 and 188 days, respectively.
Metabolites in the water phase all accounted for <1% of AR. In sediment, the following metabolites were detected:
- 8a-oxo-avermectin B_{1a} (NOA 448111): maximum 2.8% of AR on day 100
- 8a-hydroxy-avermectin B_{1a} (NOA 448112): maximum 1.9% of AR on day 70
- 4"-oxo-avermectin B_{1a} (NOA 426289): maximum 8.6% of AR on day 100
- 3"-demethyl-avermectin B_{1a} (NOA 445495): maximum 2.0% of AR on day 70

Bound residues increased to maximum 23.2% of AR at the end of the study after 100 days, mineralisation was low with a maximum of 3.2% of AR after 100 days.

Biodegradation in soil
The geometric mean DT_{50} of avermectin B_{1a} in soil at 20 °C is 28.4 days. The overall geometric mean DT_{50} of avermectin B_{1a} is 54 days when converted to the average EU outdoor temperature of 12°C.
The highest formation of bound residues was 39.1% of AR after incubation for 91 days at 20 °C. Highest mineralisation accounted for 12.4% of AR after 91 days.
In soil, the following metabolites were detected:
- 8a-oxo-avermectin B_{1a} (NOA 448111): maximum 10.3% of AR after 28 days; DT_{50} 45.3 days at 20 °C (and 86 days converted to 12°C)
- 8a-hydroxy-avermectin B_{1a} (NOA 448112): maximum 15.7% of AR after 28 days; DT_{50} 35.8 days at 20 °C (and 68 days converted to 12°C)
- 4,8a-dihydroxy-avermectin B_{1a} (NOA 457464): maximum 9.9% of AR after 90 days; DT_{50} 65.9 days at 20 °C (and 125 days converted to 12°C)
- 8a-oxo-4-hydroxy-avermectin B_{1a} (NOA 457465): maximum 9.9% of AR after 126 days; DT_{50} 112 days at 20 °C (and 212 days converted to 12°C)

Field dissipation studies with abamectin were carried out in Switzerland, Southern Germany, Northern France and Italy. The $DT_{50,field}$ is <1 to 1.8 days.

Abiotic degradation
Both ^{14}C- and ^{3}H-avermectin B_{1a} are hydrolytically stable at environmental relevant pH (4 - 7) and temperature (25 °C).

The aqueous $DT_{50,photolysis}$ of avermectin B_{1a} is 1.3 to 2 days (. Photometabolites are 8a-oxo-avermectin B_{1a} (NOA 448111; max. 5.6% of AR) and [8,9-Z]-avermectin B_{1a} (NOA 427011; 8.2% of AR).
The soil $DT_{50,photolysis}$ is 13 days, equivalent to 22 days in summer at 30-50 °N.

Distribution
The average K_{oc} of avermectin B_{1a} is 5638 L/kg. Sorption of avermectin B_{1a} is related to organic carbon content (OC), linear regression of K_F versus % OC gives a regression coefficient r^2 of 0.919.

For the soil metabolites, the following average K_{oc}-values were determined:
- 8a-oxo-avermectin B_{1a} (NOA 448111): 3997 L/kg
- 8a-hydroxy-avermectin B_{1a} (NOA 448112): 1943 L/kg
- 4,8a-dihydroxy-avermectin B_{1a} (NOA 457464): 1732 L/kg
- 8a-oxo-4-hydroxy-avermectin B_{1a} (NOA 457465): 3908 L/kg

Accumulation
The experimental bioconcentration factor (BCF) for fish is 52 L/kg ww, based on the fitted uptake and elimination rate constants.
No experimental data are available on terrestrial bioconcentration. The BCF for earthworms, estimated according to the TGD, is 302 L/kg.

2.2.2.2 Effects assessment

Aquatic compartment
Based on the lowest NOEC of 0.0035 µg/L for *Mysidopsis bahia* with an assessment factor of 10, the $PNEC_{aquatic}$ for abamectin is 0.35 ng/L.

Applying an assessment factor of 100 to the NOEC of 3.3 µg/kg dw for *Chironomus riparius*, the $PNEC_{sediment}$ is 33 ng/kg dw (12.7ng/kg ww).

Applying an assessment factor of 1000 to the lowest EC_{50}-values for *Daphnia magna* (0.082, 1.6 and 0.28 µg/L, respectively), the following $PNEC_{aquatic}$ are derived for the metabolites:
[8,9-Z]-avermectin B_{1a} (NOA 427011): 0.082 ng/L
8a-hydroxy- avermectin B_{1a} (NOA 448112): 1.6 ng/L
Insufficient valid studies are available for PNEC derivation for 4”-oxo-avermectin B_{1a} (NOA 426289):. The available acute daphnia study indicates a comparative toxicity as the parent abamectin, therefore worst case the $PNEC_{aquatic}$ is set equal to the PNEC of
[8,9-Z]-avermectin B_{1a} (NOA 427011): 0.082 ng/L

Sewage Treatment Plant
As a worst-case estimate, the NOEC for respiration of activated sludge is set to the water solubility of 1.21 mg/L. Applying an assessment factor of 10 to this value, leads to a $PNEC_{stp}$ for abamectin of 0.12 mg/L.
No PNEC can be derived for the metabolites.

Atmosphere
In view of the volatility of the active substance ($< 3.7 * 10^{-6}$ Pa (at 25 ºC)), significant exposure of the environment via air is not expected.

Terrestrial compartment
The acute LC_{50} of abamectin for earthworms is 33 mg/kg dw soil at 10 % OM, equivalent to 11 mg/kg dw soil after correction to the default OM content of 3.4 %. Applying an assessment factor of 1000 to this value, the $PNEC_{soil}$ for abamectin is 11 µg/kg dw soil (9.7 µg/kg ww soil).

The $PNEC_{soil,EP}$ applying equilibrium partitioning to the $PNEC_{aquatic}$ of 0.35 ng/L, is 0.040 µg/kg dw soil (0.035 µg/kg ww soil).

The $PNEC_{soil,EP}$ is a factor of 275 lower than the $PNEC_{soil}$ based on experimental data. Since the experimental data do not cover soil insects, that are potentially the most sensitive group of soil organisms, the $PNEC_{soil}$ is set to the $PNEC_{soil,EP}$ of 0.040 µg/kg dw soil (0.035 µg/kg ww soil).

Non compartment specific effects relevant to the food chain (secondary poisoning)
The $PNEC_{oral}$ for secondary poisoning of mammals is derived by applying an assessment factor of 30 to the chronic NOEC of 1.20 mg/kg feed, resulting in a $PNEC_{oral,mammal}$ of 0.04 mg/kg feed.
The $PNEC_{oral}$ for secondary poisoning of birds is derived by applying an assessment factor of 30 to the chronic NOEC of 12 mg/kg feed, resulting in a $PNEC_{oral,bird}$ of 0.4 mg/kg feed.

Effects on bees and other non-target arthropods
There are no accepted methods to derive a PNEC for bees or other non-target arthropods. In the absence of environmental emissions, significant exposure of bees and other non-target arthropods is not expected.

Groundwater
There are no accepted methods to derive a $PNEC_{grw}$. In the absence of environmental emissions, no exposure of groundwater is expected.

2.2.2.3 PBT assessment

The $DT_{50,water}$ of abamectin as determined in freshwater water/sediment systems is 2.4 days, but this value is valid for dissipation by sorption rather than for degradation. The average $DT_{50,system}$ is 89 days at 20 °C, the $DT_{50,sediment}$ is 99 days. The average $DT_{50,system}$ and $DT_{50,sediment}$ at 12 °C are 169 and 188 days, respectively.
The experimentally derived BCF for fish is 52 L/kg ww, based on Total Radioactive Residues in whole fish. The lowest chronic NOEC is 0.01 µg/L.
Formation of metabolites in environmentally relevant concentrations in the water phase is not considered likely, except for the photolysis product [8,9-Z]-avermectin B_{1a}. Because the ecotoxicological (field) studies are all performed under light, it can be assumed that potential effects of the isomer on aquatic organisms are covered by the studies with the parent compound, and that the above-mentioned NOEC of 0.01 µg/L applies.

In conclusion, abamectin is considered as P and T, but not B, and is therefore not classified as PBT.

2.2.2.4 Exposure assessment

The environmental exposure assessment of abamectin in the representative products Raid Ant Bait, Raid Roach Bait and Avert Dry Flowable Cockroach Bait 310A was done in accordance with the approach and recommendations of the OECD Emission Scenario Document (ESD) for insecticides, acaricides and products to control other arthropods (PT 18) for household and professional users (July, 2008). Further calculations of the Predicted Environmental Concentrations (PEC) in various environmental compartments were done in accordance with the Technical Guidance Document on Risk Assessment (TGD, 2003).
At TM I 2010, the commission proposed to reduce the number of large buildings to 300 (in comparison to 1000 in OECD ESD No. 18). In addition, the default surface area for a large building was set to 609 m^2 (in comparison to 3280 in OECD ESD No. 18).
A proposal for default values for the surface area treated for several target applications in large buildings was prepared by the commission and industry and presented at TMII 2010. At this TM, it was proposed to use in case of spot (cracks and crevice) applications the following numbers for surfaces treated and subjected to wet cleaning; 2 m^2 for a private house (as described in the OECD ESD No.18) and 9.3 m^2 for a large building.

Raid Ant Bait and Raid Roach Bait
The products Raid Ant Bait and Raid Roach Bait are ready-to-use filled, sealed bait stations (plastic cartridges) with holes, for indoor application only. According to Section 2.4.9 of the ESD, environmental emissions from this use can be considered negligible. According to Table 3.3-8 of the ESD, the bait stations are not subjected to cleaning, and no emissions are considered. It is mentioned that the only possible emission is when the cartridges are disposed of via domestic waste. Disposal to domestic waste only applies to the empty cartridges; if bait is left, cartridges should be disposed of as chemical waste.

Avert Dry Flowable Cockroach Bait 310A
The product Avert Dry Flowable Cockroach Bait 310A is a ready-to-use powder on grain basis in “puffer pack” to be used in cracks and crevices in buildings for protection of public health and property (domestic premises, commercial premises, food storage areas, public buildings, industrial premises).
Potential exposure to surface water bodies is envisaged via surface water following the wet cleaning of indoor treated surfaces. This indirect exposure to surface waters will occur when waste water passes through a sewage treatment plant (STP), where it is processed, and then discharged into rivers and streams.
Indirect exposure of soil and groundwater can occur when sewage sludge is applied in agriculture. Any potential deposition from the atmosphere has been neglected since emissions to air are considered to be negligible.

The exposure routes were calculated for indoor uses of the product Avert Dry Flowable Cockroach Bait 310A for both private houses (domestic, 2 m^2) and large (commercial) buildings (9.3 m^2). Concentrations were calculated for general (4-6 baitpoint/10 m² floor area) and difficult (12-24 baitpoint/10 m² floor area) applications to control pests of cockroaches indoors.

In table 3.3-8 of the OECD ESD for PT 18 no cleaning efficiency is stated for the intended use pattern for cracks and crevice treatment against cockroaches with a powder formulation. Therefore, the exposure assessment is set up in line with the spray treatment in cracks and crevices with a default cleaning efficiency of 25%.

2.2.2.5 Risk characterisation

No major metabolites of abamectin were detected in the water phase or sediment phase in laboratory water/sediment studies. Therefore, risk ratios concerning aquatic exposure, are based on the parent.
Formation of metabolites in soil in environmentally relevant concentrations is not considered likely for the emission route being waste water-STP-activated sludge-distribution on soil. Temporal peak values in formation of metabolites observed in lab soil degradation studies, are considered an effect of the instantaneous dosage of the a.s. at the start of the experiment Formation percentages for major metabolites observed in an aerobic soil degradation study (20 °C) concerned 8a-hydroxy-avermectin B_{1a} (NOA 448112), with a maximum of 15.7% of AR after 28 days and 8a-oxo-avermectin B_{1a} (NOA 448111) with a maximum of 10.3% of AR after 28 days, which was followed by a gradual decline to the end of the experiment. Considering that in proposed application, the a.s. is exposed to aerobic degradation in the STP, anaerobic degradation during activated sludge processing, followed by degradation in soil, it is not likely that peak concentrations of metabolites > 10% will occur in the soil compartment. In addition it can be mentioned that degradation rates under field conditions are considered to be higher than observed in lab experiments performed in the dark. Therefore, risk ratios concerning terrestrial exposure (soil), are based on the parent.

2.2.2.5.1 Aquatic compartment

In the absence of emissions to STP, surface water and sediment, no risks are expected for the aquatic compartment upon use of Raid Ant Bait and Raid Roach Bait.

Sewage Treatment Plant (STP)
Since all PEC/PNEC ratios for microorganisms in STP are below 1, no risk was identified at the representative use of abamectin Avert Dry Flowable Cockroach Bait 310 A.
When a cumulative risk is calculated for simultaneous applications in private houses and large buildings the PEC/PNEC ratios for micro-organisms in STP are still below 1 for the general and difficult scenarios.

Surface water
Since all PEC/PNEC ratios for aquatic organisms are below 1, no risk is identified at the representative use of abamectin Avert Dry Flowable Cockroach Bait 310 A.
When a cumulative risk is calculated for simultaneous applications in private houses and large buildings the PEC/PNEC ratios for aquatic organisms are still below 1 for the general and difficult scenarios.

Sediment
The PEC/PNEC ratios for sediment organisms are below 1 for the private house - general scenario and the large building scenarios and no risk was identified for these uses of abamectin in Avert Dry Flowable Cockroach Bait 310 A. However, the

PEC/PNEC ratio for sediment organisms was above 1 for the private house – difficult scenario.
When a cumulative risk is calculated for simultaneous applications in private houses and large buildings the PEC/PNEC ratios for sediment organisms are also above 1 for the difficult scenarios.
With a PEC/PNEC ratio > 1 in the cumulative risk assessment, a risk is indicated for sediment organisms. Assessing the worst-case scenarios for both private houses and large buildings, can be criticized as being unrealistic. Given the fact that both private houses and large buildings discharge on a single STP, a risk for sediment organisms for the difficult scenario should not be ignored. Risk for the environment, however, can be excluded by e.g. narrowing or adjustment of the use pattern for the difficult scenario at product authorization. One other option is to provide further data on ecotoxicity tests with sediment organisms during product authorisation in order to refine $PNEC_{sediment}$ and thus to refine the risk assessment for the sediment.

2.2.2.5.2 Assessment of drinking water criterion and persistence in sediment
No specific limit value is established for abamectin under Directive 98/83/EC, and therefore the general limit of 0.1 µg/L for organic pesticides applies.
The PEC sw is in all scenarios < 0.1 µg/L. This means that abamectin in Avert Dry Flowable Cockroach Bait does comply with the drinking water criterion for all scenarios.
The average $DT_{50,system}$ and $DT_{50,sediment}$ at 20 °C are 89 and 99 days, respectively, which is < 6 months. The average $DT_{50,system}$ and $DT_{50,sediment}$ at 12 °C are 169 and 188 days, respectively, which is > 6 months.
Mineralisation was < 5 %, but non-extractable residues were never > 70%. This means that abamectin is not considered as persistent in sediment.

2.2.2.5.3 Air

No relevant emissions to air are expected.

2.2.2.5.4 Terrestrial compartment
In the absence of emissions to soil and groundwater, no risks are expected for the terrestrial compartment upon use of Raid Ant Bait and Raid Roach Bait.

Soil
The PEC/PNEC ratios for soil organisms are below 1 for all scenarios and no risk was identified for these uses of abamectin in Avert Dry Flowable Cockroach Bait 310 A.
When the cumulative risk is calculated for private house scenarios and large building scenarios, the PEC/PNEC ratios for soil organisms are still below 1 for the general and difficult scenarios.

Groundwater
For all scenarios the estimated concentrations in groundwater are below the threshold value of 0.1 $\mu g.L^{-1}$ for organic pesticides derived from the Drinking Water Directive indicating no risk for groundwater.

Assessment of persistence in soil

The geometric mean DT_{50} of avermectin B_{1a} in laboratory studies at 20 °C is 28.4 days at 20°C. The overall geometric mean DT_{50} of avermectin B_{1a} is 54 days when converted to the average EU outdoor temperature of 12°C.
Bound residues are < 70% and mineralisation is > 5%. The $DT_{50,field}$ is < 1 – 1.8 days. Therefore, abamectin is not considered to be persistent in soil and complies with the persistence criteria that are laid down in paragraph 85 of Annex VI to the Biocides Directive and in the TNsG on Annex I inclusion.

2.2.2.5.5 Non compartment specific effects relevant to the food chain (primary and secondary poisoning)

Raid Ant Bait and Raid Roach Bait are insecticides in ready filled, sealed bait stations with holes. Avert Dry Flowable Cockroach Bait 310 A is a powder insecticide. No primary poisoning is expected as direct contact of birds or mammals with the three products is not likely to occur.

The risks of secondary poisoning of birds and mammals are estimated for the food chains *water ➔ fish ➔ fish eating bird or mammal* and *soil ➔ earthworm ➔ worm-eating bird or mammal*.
The PEC/PNEC is < 1 for birds and mammals, and no risk for secondary poisoning via consumption of fish or earthworms is expected.

2.2.2.5.6 Effects on bees and other non-target arthropods

Exposure of bees is considered negligible, since foraging of bees can be excluded for private houses and large buildings treated indoors or on soil on which STP sludge is spread. Of the other non-target arthropods species, leaf dwelling species are also not considered relevant. Truly soil-inhabiting species, such as springtails, are assumed to be covered in the terrestrial risk assessment. However, soil-dwelling species such as beetles, may be exposed to residues of abamectin. The highest initial PEC_{soil} for abamectin is $2.29*10^{-6}$ mg/kg ww soil. Assuming a soil mixing depth of 20 cm for local soil respectively (see TGD, table 11), and a wet bulk density of 1700 kg/m^3, these values are equivalent to 7.8 mg/ha for local soil.
No effects were found for the ground beetle *Poecilus cupreus* at application rates up to 29 and 58 g as/ha. In view of the expected exposure for the proposed uses, no risk is expected.

2.2.2.5.7 PBT assessment

Abamectin should thus be considered as Persistent (water/sediment) and Toxic, but not as Bioaccumulative and is therefore not classified as PBT. Inclusion in Annex I is not restricted by these criteria.

2.2.2.6 Conclusions environmental risk assessment

The environmental risk assessment is performed according to the methods of the ESD for insecticides, acaricides and products to control other arthropods (PT 18) for household and professional users (July, 2008) and TGD.
Inclusion of abamectin in Annex I is feasible for the environmental aspect because several safe uses are identified.
In the absence of emissions to STP, surface water, sediment, air, soil and groundwater, no risks are expected upon use of Raid Ant Bait and Raid Roach Bait.

For the product Avert Dry Flowable Cockroach Bait 310A PEC/PNEC ratios were > 1 for the sediment compartment for the private building - difficult scenario.

Private houses
For application of powder in cracks and crevices (2 m^2) in private houses for the general scenario (4-6 baitpoints/10 m² floor area) no risk for the water, sediment and soil compartment was identified. For the difficult scenario (12-24 baitpoints/10 m² floor area) a risk for the sediment compartment was identified for application in private houses (PEC/PNEC=1.8). No risk was identified for the difficult scenario for the water and soil compartment, when the product was applied in private houses.
Reverse scenario calculation shows that no risk for sediment organisms is calculated for up to 12 baitpoints/10 m^2 floor area. (0.58 mg abamectine/m^2).

Large buildings
For application of powder in cracks and crevices (9.3 m^2) in large buildings for the general scenario (4-6 baitpoints/10 m² floor area) and difficult scenario (12-24 baitpoints/10 m² floor area) no risk for the water, sediment and soil compartment was identified.
Reverse scenario calculation shows that no risk for sediment organisms is calculated for up to 12 baitpoints/10 m^2 floor area. (0.58 mg abamectine/m^2).

Cumulative risk assessment for private houses and large buildings
When a cumulative risk is calculated for simultaneous applications in private houses and large buildings, the PEC/PNEC ratios for the difficult scenarios for sediment organisms is 2.4 and a risk is indicated for sediment organisms.
Reverse scenario calculation shows that no risk for sediment organisms is calculated for up to 9 baitpoints/10 m^2 floor area. (0.44 mg abamectine/m^2).

No risk was identified for secondary poisoning of wild birds and mammals of the aquatic and terrestrial food chain at the proposed use of Raid Ant Bait, Raid Roach Bait.and Avert Dry Flowable Cockroach Bait 310A. Also no risk was identified for bees and other non-target arthropods.
Finally, there was no risk identified for contamination of groundwater at levels of 0.1 µg/L or above from the use of Raid Ant Bait, Raid Roach Bait.and Avert Dry Flowable Cockroach Bait 310A.

2.2.3 List of endpoints

In order to facilitate the work of Member States in granting or reviewing authorisations, and to apply adequately the provisions of Article 5(1) of Directive 98/8/EC and the common principles laid down in Annex VI of that Directive, the most important endpoints, as identified during the evaluation process, are listed in Appendix I.

3 PROPOSAL FOR THE DECISION

3.1 Background to the decision

Abamectin has been evaluated as an insecticide against ants and cockroaches. Abamectin-based formulations are evaluated to be used in buildings (industrial

premises, domestic premises, commercial premises, food storage areas, public buildings, hospitals). Abamectin-based formulations have been evaluated for non-professional and/or professional use.

Inclusion of abamectin in Annex I is feasible because for all aspects several safe uses have been identified:

- Physical chemical properties
  Based on physico-chemical properties, there is no hazard identified for abamectin, and for 2 of the 3 evaluated products.
  A hazard identification for the third product based on physico-chemical properties cannot be performed at present, because reliable data on flammability, auto-flammability and/or reaction with water are not available.

- Efficacy
  Because the nature of the products is a bait, efficacy is demonstrated with the biocidal product rather than the active substance. Abamectin is shown to be effective against cockroaches and Pharaoh ants (*Monomorium pharaonis*) when applied as a 0.05% w/w bait. Insufficient data are provided to show efficacy against all target organisms. At product authorisation additional efficacy data will be required for other ant species (*Lasius* sp, *Myrmica* sp).

- Human Health
  Primary exposure
  A safe use is identified for abamectin-based baits against ants or cockroaches for professional users when using a dry flowable bait even without PPE.
  The use of abamectin as a wax block for the control of ants or cockroaches by nonprofessionals is also identified as a safe use.

  Secondary exposure
  Abamectin-based baits against ants or cockroaches when using a dry flowable bait will not lead to an unacceptable risk for the general population (a.o. children).
  The use of abamectin as a wax block for the control of ants or cockroaches will not lead to an unacceptable risk for the general population when risk mitigation measures are in place (a.o. children).

- Environment
  In the absence of emissions to STP, surface water, sediment, air, soil and groundwater, no risks are expected upon use of Raid Ant Bait and Raid Roach Bait.
  For the product Avert Dry Flowable Cockroach Bait 310A no risk for the water, sediment and soil compartment was indicated for the private house - general scenario and for the large building scenarios, considering the highest application rate. However, the PEC/PNEC ratio for sediment organisms was above 1 for the private house – difficult scenario.
  Considering simultaneous exposure from private houses and large buildings according to the difficult scenario for sediment organisms a PEC/PNEC ratio of 2.4 was calculated .
  With a PEC/PNEC ratio > 1 in the cumulative risk assessment, a risk is indicated for sediment organisms. Given the fact that both private houses and large buildings discharge on a single STP, a risk for sediment organisms for the difficult scenario

should not be ignored. Risk for the environment, however, can be excluded by refinement of the $PEC_{sediment}$ or $PNEC_{sediment}$ at the product authorisation stage.

Secondary poisoning
No risk was identified for secondary poisoning of wild birds and mammals of the aquatic and terrestrial food chain at the proposed use of Raid Ant Bait, Raid Roach Bait.and Avert Dry Flowable Cockroach Bait 310A. Also no risk was identified for bees and other non-target arthropods.
Finally, there was no risk identified for contamination of groundwater at levels of 0.1 µg/L or above from the use of Raid Ant Bait, Raid Roach Bait.and Avert Dry Flowable Cockroach Bait 310A.

3.2 Decision regarding Inclusion in Annex I

Abamectin with a minimum purity of 900 g/kg abamectin (sum of avermectin B1a and avermectin B1b) of which minimal 830 g/kg avermectin B1a and maximal 80 g/kg avermectin B1b shall be included in Annex I to Directive 98/8/EC as an active substance for use in product-type PT 18 (insecticides, acaricides and products to control other arthropods) with the following specific provisions:

- Preventive health protection measures shall be taken for infants and children. For example, the use of bait stations may be necessary. The robustness of the bait station should be assessed at product authorisation.
- Products applied in such a way that emission to a sewage treatment plant cannot be prevented shall not be authorised for those application rates for which the Union level risk assessment showed unacceptable risks, unless data are submitted demonstrating that the product will meet the requirements of Article 5 and Annex VI, if necessary by the application of appropriate risk mitigation measures.

Not all potential uses have been evaluated at the Community level. It is therefore appropriate that Member States assess those risks to the compartments and populations that have not been representatively addressed in the Community level risk assessment and, when granting product authorisations, ensure that appropriate measures are taken or specific conditions imposed in order to mitigate the identified risks to acceptable levels.

3.3 Elements to be taken into account by Member States when authorising products

Elements, which were not mentioned under the specific provisions of the decision but which need be taken into account at product authorisation level:

3.3.1 Identity and physical chemical properties

1. A shelf life study (2 years, ambient) is required where the active ingredient content, palatability, appearance, pH, and resistance of the packaging material before and after storage are verified for the formulations "Raid Ant Bait", "Raid Roach Bait" and "Avert Dry Flowable Cockroach Bait 310A". In addition particle size distrubution (and/or dry sieve test), and dustability need

to be verified for "Avert Dry Flowable Cockroach Bait 310A" before and after storage.
2. A palatability test and a palatability criterion for the formulations "Raid Ant Bait", "Raid Roach Bait" and "Avert Dry Flowable Cockroach Bait 310A" is required to be able to verify palatibility before and after storage.
3. Appearance, acidity/alkalinity or pH and bulk/tap density for the formulation “Avert Dry Flowable Cockroach Bait 310A” are not available.
4. Studies on Flammability (EEC A10), auto-flammability (EEC A16) and reaction with water (EEC A12) are not available for the the formulation “Avert Dry Flowable Cockroach Bait 310A”.

3.3.2 Analytical methods

None

3.3.3 Efficacy

1. Laboratory efficacy data and field efficacy data with the product Raid Ant Bait according to the intended use on other ant species than Pharaoh ants are required to support the claim "ants".
2. The majority of queen ants survived tests with bait containing 0.05% abamectin. Test data with the product Raid Ant Bait are required to verify whether the colony is totally killed.
3. Test conditions for cockroaches with the products Raid Roach Bait and Avert Dry Flowable Cockroach Bait 310A were between 24 en 29 °C. The average temperatures expected to be found in homes in northern Europe (and air-conditioned homes in southern Europe) would vary between approximately 19 and 22 °C. In southern Europe temperatures can be much higher. This should be taken into consideration at product authorisation.
4. Efficacy data for the product Raid Roach Bait have not been presented verifying the claim “kills eggs”. Results on German cockroach do not cover all cockroach species. The German cockroach differs from other target cockroach species when making the claim “kills eggs”. The German cockroach carries its egg capsule until the nymphs are ± ready to leave the capsule. Many other species drop their egg capsules in relatively damp areas for a length of time before the nymphs leave the capsule. These capsules are less prone to desiccation.

3.3.4 Classification and Labelling

None.

3.3.5 Human toxicology

The possible risk for infants/children relies on the robustness of the bait stations. Therefore, the robustness of the bait station has to be assessed at product authorisation level by Member States to ensure that they are child-resistant and exposure to the active substance will not occur.

Also if risks from the use of a biocidal product to companion animals are foreseen within the Member state, the Member State can - at the product authorisation stage- introduce risk mitigation measures to alleviate the risk.

Disposal of completely empty bait stations is to domestic waste. Bait stations that may contain biocidal product should be disposed in accordance with local waste regulations.

3.3.6 Environment

Risks for sediment organisms were identified for the product Avert Dry Flowable Cockroach Bait 310A and these need to be considered when products are authorised at MS level.
All other areas of use/scenarios than those covered by this CA report need to be carefully assessed with regard to environmental risks in case of future product registrations.
During authorisation of biocidal products at MS level, the environmental exposure assessment needs to be carried out on the basis of the actual emission scenarios for insecticides for household and professional use (i.e. OECD ESD No. 18 with additional guidance mutually agreed upon in the TM)..
The need to address any specific national conditions and/or undertake regional assessments should be considered, as only local environmental risk assessments have been carried out in this evaluation.
When evaluating products containing abamectin, Member States should take into account cumulative exposure from the biocidal uses of abamectin (in accordance with Art. 10.1 to Directive 98/8/EC) using agreed EU guidance where possible.

3.4 Requirement for further information

It is considered that the evaluation has shown that sufficient data have been provided to verify the outcome and conclusions, and permit the proposal for the inclusion of abamectin for use in product-type PT 18 (insecticides, acaricides and products to control other arthropods) in Annex I to Directive 98/8/EC.

3.5 Updating this Assessment Report

This assessment report may need to be updated periodically in order to take account of scientific developments and results from the examination of any of the information referred to in Articles 7, 10.4 and 14 of Directive 98/8/EC. Such adaptations will be examined and finalised in connection with any amendment of the conditions for the inclusion of abamectin in Annex I to the Directive.

APPENDIX I: LIST OF ENDPOINTS

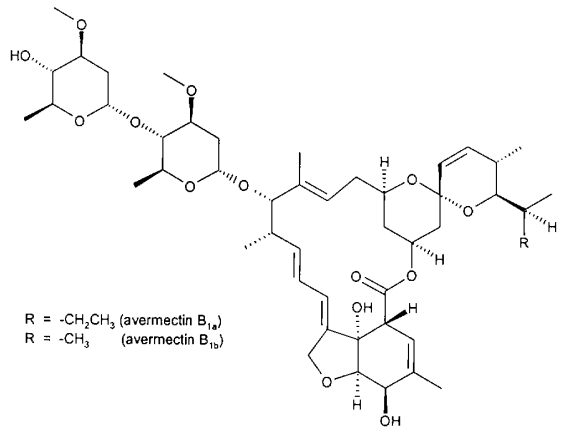
Active substance (ISO Common Name)	Abamectin (consisting of a mixture of >80% butyl (B1a) and <20% isopropyl (B1b)*
Product-type	PT 18 (insecticide)

***according to ISO, name of abamectin is changed since EFSA scientific report (2008) 147, 1-106 29 may 2008 was finisehed. In EFSA scientific report this box is left open.**

Chapter 1: Identity, Physical and Chemical Properties, Classification and Labelling

Identity

Chemical name (IUPAC)	**Avermectin B_{1a}** (10*E*,14*E*,16*E*,22*Z*)-(1*R*,4*S*,5'*S*,6*S*,6'*R*,8*R*,12*S*,13*S*,20*R*,21*R*,24*S*)-6'-[(*S*)-*sec*-butyl]-21,24-dihydroxy-5',11,13,22-tetramethyl-2-oxo-3,7,19-trioxatetracyclo[15.6.1.$1^{4,8}$.$0^{20,24}$]pentacosa-10,14,16,22-tetraene-6-spiro-2'-(5',6'-dihydro-2'*H*-pyran)-12-yl 2,6-dideoxy-4-*O*-(2,6-dideoxy-3-O-methyl-*α*-L-*arabino*-hexopyranosyl)-3-*O*-methyl-*α*-L-*arabino*-hexopyranoside **Avermectin B_{1b}** (10*E*,14*E*,16*E*,22*Z*)-(1*R*,4*S*,5'*S*,6*S*,6'*R*,8*R*,12*S*,13*S*,20*R*,21*R*,24*S*)-21,24-dihydroxy-6'-isopropyl-5',11,13,22-tetramethyl-2-oxo-3,7,19-trioxatetracyclo[15.6.1.$1^{4,8}$.$0^{20,24}$]pentacosa-10,14,16,22-tetraene-6-spiro-2'-(5',6'-dihydro-2'*H*-pyran)-12-yl 2,6-dideoxy-4-*O*-(2,6-dideoxy-3-*O*-methyl-*α*-L-*arabino*-hexopyranosyl)-3-*O*-methyl-*α*-L-*arabino*-hexopyranoside
Chemical name (CA)	abamectin: avermectin B_1 avermectin B_{1a}: 5-O-demethyl-avermectin A_{1a} avermectin B_{1b}: 5-O-demethyl-25-de(1- methylpropyl)-25-(1-methylethyl)-avermectin A_{1a}
CAS No	71751-41-2 (abamectin) 65195-55-3 (avermectin B_{1a}) 65195-56-4 (avermectin B_{1b})
EC No	265-610-3 (avermectin B_{1a}) 265-611-9 (avermectin B_{1b})
Other substance No.	CIPAC no 495 (abamectin)
Minimum purity of the active substance as manufactured (g/kg or g/l)	min. 900g/kg abamectin (sum of avermectin B_{1a} and avermectin B_{1b}) min. 830g/kg avermectin B_{1a} max. 80g/kg avermectin B_{1b}
Identity of relevant impurities and additives (substances of concern) in the active substance as manufactured (g/kg)	Based on environmental and (eco)toxicological information, there are no relevant impurities
Molecular formula	$C_{48}H_{72}O_{14}$ (avermectin B_{1a})

	$C_{47}H_{70}O_{14}$ (avermectin B_{1b})
Molecular mass	873.1 (avermectin B_{1a}) 859.1 (avermectin B_{1b})
Structural formula	

Physical and chemical properties

Melting point (state purity)	161.8-169.4 ºC (chemical purity 96.7%)
Boiling point (state purity)	Not determined, due to thermal decomposition during melting of abamectin.
Temperature of decomposition	thermal decomposition during melting of abamectin.
Appearance (state purity)	Technical: white powder (chemical purity 96.7%)
Relative density (state purity)	1.18 at 22 °C (chemical purity 96.7%)
Surface tension	52.4 mN/m at 20°C (90% saturated solution)(96.7%)
Vapour pressure (in Pa, state temperature)	$< 3.7 * 10^{-6}$ Pa (at 25 ºC)
Henry's law constant (Pa m^3/mol)	$\leq 2.7 * 10^{-3}$ Pa m^3 mol^{-1}
Solubility in water (g/L or mg/L, state temperature)	1.21 ± 0.15 mg/L; pH 7.57 (25 ºC) No pH dependence expected because of no dissociation
Solubility in organic solvents (in g/l or mg/l, state temperature)	acetone(25 ºC): 72 g/L dichloromethane (25 ºC): 470 g/L ethyl acetate (25 ºC): 160 g/L hexane (25 ºC): 0.110 g/L methanol (25 ºC): 13 g/L octanol (25 ºC): 83 g/L toluene (25 ºC): 23 g/L
Stability in organic solvents used in biocidal products including relevant breakdown products	not required: the active substance abamectin as manufactured does not include an organic solvent
Partition coefficient (log P_{OW}) (state temperature)	4.4 ± 0.3; pH 7.2 ±0 .1 (in aqueous phase), 20 ºC No pH dependence expected because of no dissociation
Dissociation constant	no dissociation in the pH-range from 1 to 12
UV/VIS absorption (max.) (if absorption > 290 nm state ε at wavelength)	no absorption maximum observed between 280 and 750 nm At 244 nm: e=30717 l/mol*cm 239 nm: e=28332

	253 nm: e=20156 (purity: not stated)
Flammability	not highly flammable no self-ignition before melting point (96.7%)
Explosive properties	not thermally, shock or friction sensitive
Oxidising properties	No oxidising properties (96.7%)

Classification and proposed labelling

with regard to physical/chemical data	none
with regard to toxicological data	Symbol : T+ Risk phrase : R26, R28, R48/R25, R63
with regard to fate and behaviour data	none
with regard to ecotoxicological data	Symbol N Risk phrases: R50, R53

Chapter 2: Methods of Analysis

Analytical methods for the active substance

Technical active substance (principle of method)	**avermectin B_{1a}, avermectin B_{1b}**: HPLC-UV at 254 nm
Impurities in technical active substance (principle of method)	HPLC-UV at 254 nm GC-FID

Analytical methods for residues

Soil (principle of method and LOQ)	HPLC-MS/MS after extraction with acetonitrile/water and clean-up on HLB SPE columns. Method validated on two soils. LOQ 0.5 µg/kg for individual compounds µg/kg (avermectin B1a, avermectin B1b, [8,9-Z]-avermectin B1a, 8a-oxo-avermectin B1a, 8a-hydroxy-avermectin B1a, 4,8a-dihydroxy-avermectin B1a and 4-hydroxy-8a-oxo-avermectin B1a)
Air (principle of method and LOQ)	Determination by HPLC-UV (243 nm) after extraction with methanol. Method validated at spiking levels 0.1 and 10 µg/m^3. LOQ for individual compounds 0.1 µg/m^3 (avermectin B1a, avermectin B1b)
Water (principle of method and LOQ)	Determination by LC-MS/MS after dilution with acetonitrile and clean-up on HLB SPE columns. Method validated on river water, ground water and drinking water. LOQ for individual compounds 0.05 µg/L (avermectin B1a, avermectin B1b, [8,9-Z]-avermectin B1a, 4"-oxo-avermectin B1a, 3"-demethyl-avermectin B1a)
Body fluids and tissues (principle of method and LOQ)	Relevant residues for monitoring human body fluids and tissues are avermectin B_{1a}, 8,9-Z isomer of avermectin B_{1a} and avermectin B_{1b}. HPLC-MS/MS method REM 198.02 with separate quantification of avermectin B_{1a}, avermectin B_{1a} 8,9-Z isomer, and avermectin B_{1b}. LOQ 0.002 mg/kg for meat and whole blood

Food/feed of plant origin (principle of method and LOQ for methods for monitoring purposes)	No methods required.
Food/feed of animal origin (principle of method and LOQ for methods for monitoring purposes)	No methods required.

Chapter 3: Impact on Human Health

Absorption, distribution, metabolism and excretion in mammals

Rate and extent of oral absorption:	Maximum blood concentration within 4-8 h. Approximately 86% of oral dose is absorbed (based on urinary excretion after oral or intravenous administration).
Rate and extent of dermal absorption:	1% of applied dose (*in vivo* study with monkey, confirmed by *in vitro* study with human skin)
Distribution:	Distributed throughout all major organs and tissues
Potential for accumulation:	No potential for accumulation upon repeated oral administration
Rate and extent of excretion:	Rapidly eliminated, almost exclusively via non-biliary excretion back into the intestine and eliminated with the faeces
Toxicologically significant metabolite	Parent and 8,9-Z isomer of avermectin B1a (photodegradation product)

Acute toxicity

LD50 oral	oil vehicle: 8.7 mg/kg bw (m), 12.8 mg/kg bw (f) aqueous vehicle: 232 mg/kg bw (m), 214 mg/kg bw (f)
LD50 dermal	> 330 mg/kg bw; (rabbit, > 2000 mg/kg bw)
LC50 inhalation	>0.051 mg/L (m), >0.034 mg/L and <0.051 mg/L (f)
Skin irritation	Not irritating
Eye irritation	Not irritating
Skin sensitization (test method used and result)	Non-sensitizing (M&K)

Repeated dose toxicity

Species/ target / critical effect	Dog/tremors, ataxia and mydriasis, liver, absent or decreased pupil reflex
Lowest relevant oral NOAEL / LOAEL	0.25 mg/kg bw/day (18 and 53 week dog)
Lowest relevant dermal NOAEL / LOAEL	No data available; not required
Lowest relevant inhalation NOAEL / LOAEL	0.577 µg/L (30-d, rat)

Genotoxicity	No genotoxic potential, in *in vitro* and *in vivo* genotoxicity studies

Carcinogenicity

Species/type of tumour	No carcinogenic potential in rats nor mice
lowest dose with tumours	

Reproductive toxicity

Species/ Reproduction target / critical effect	Parent: no treatment-related effects Fertility: no effects Offspring: increased pup mortality, retarded

	pup growth, total litter loss, decreased lactation index
Lowest relevant reproductive NOAEL / LOAEL	Parental and reproductive: 0.4 mg/kg bw/day (highest dose tested) Offspring: 0.12 mg/kg bw per day (findings in young rats, not relevant for human risk assessment)
Species/Developmental target / critical effect	Rat: Cleft palate, lumbar rib and lumbar count varation (in the absence of maternal toxicity) Rabbit: Cleft palate, omphaloceles, clubbed fore-feet and delayed ossification (at maternally toxic dose)
Lowest relevant developmental NOAEL / LOAEL	0.8 mg/kg bw/day (rat; maternal NOAEL 1.6 mg/kg bw/day); 1.0 mg/kg bw/day (rabbit; also maternal NOAEL)

Neurotoxicity / Delayed neurotoxicity

Species/ target/critical effect	Acute neurotoxicity: rat / reduced splay relfex Repeated neurotoxicity: 90-day rat / clinical signs, body weight loss, macroscopy and histology stomach Delayed neurotoxicity: not required, not performed
Lowest relevant NOAEL / LOAEL.	Acute neurotoxicity: 0.5 mg/kg bw Repeated neurotoxicity: 1.6 mg/kg bw/day

Other toxicological studies

P-glycoprotein deficient animals (CF-1 mouse, neonatal rat) are more sensitive to abamectin.

Since non-functional p-glycoprotein has not been identified in humans, and the supplementary studies show that only the –/– CF-1 mouse is more sensitive to abamectin toxicity, the studies with the unique polymorphic CF-1 mouse are not relevant for human risk assessment.

Toxicity of the 8,9-Z isomer of avermectin B1a is lower or comparable to abamectin:

oral LD_{50} 217 mg/kg bw (CD-1 mice)

Developmental study with CD-1 mice: maternal NOAEL 3.0 mg/kg bw/d (highest dose), foetal NOAEL <0.75 mg/kg bw/d (cleft palate)

Developmental study with rats: maternal NOAEL 1.0 mg/kg bw/day, foetal NOAEL 1.0 mg/kg bw/day (no effects at the highest dose)

One generation study with rats: maternal and reproductive NOAEL 0.40 mg/kg bw/d (highest dose), offspring NOAEL 0.12 mg/kg bw/d (postnatal death)

Ames test negative.

The reference values derived for abamectin are applicable also for the 8,9-Z isomer.

Medical data

No adverse health effects from manufacturing

Severely poisoned patients showed an uneventful recovery from typical symptoms of avermectin toxicity

Summary

Non-professional user	Value	Study	Safety factor
ADI (acceptable daily intake, external long-term reference dose)	0.0025 mg/kg bw/day	18 and 53-week dog study	100
AEL acute	0.005 mg/kg bw/day	Acute neurotoxicity rat	100
AEL medium- and long-term	0.0025 mg/kg bw/day	18 and 53-week dog study	100
ARfD (acute reference dose)	0.005 mg/kg bw/day	Acute neurotoxicity rat	100
Professional user			
Reference value for inhalation (proposed OEL)	-		
Reference value for dermal absorption	1%		

Acceptable exposure scenarios (including method of calculation)

Professional users	No adverse health effects due to abamectin exposure are expected
Production of active substance:	No data
Formulation of biocidal product	No data
Intended uses	Control of ants or cockroaches
Secondary exposure	Acceptable for proposed uses
Non-professional users	Use pattern indicates no exposure

Chapter 4: Fate and Behaviour in the Environment

The fate and behaviour of the B1b component of abamectin in soil water and air is expected to be comparable to that of the B1a component due to the small difference in the structure resulting from an ethyl or a methyl functional group substitution in a compound with a molecular mass of >850 (assessment of B1a is considered to cover B1b and both their consequent [8,9-Z] isomers).

Route and rate of degradation in water

Hydrolysis of active substance and relevant metabolites (DT_{50}) (state pH and temperature)	**avermectin B_{1a}**: No hydrolysis at pH 4 -7, 25 °C pH 9, 60 °C: 4.9 d pH 9, 50 °C: 9.9 d pH 9, 25 °C: 213 d (extrapolated) pH 9, 20 °C: 380 d (calculated with Arrhenius equation) metabolites: 2-epi-avermectin B_{1a}: 25 % of AR at 50 and 60 °C 1,18 hydrolysed avermectin B_{1a}: 17.5 % of AR at 60 °C unknown: 15.6 % of AR at 60 °C
Photolytic / photo-oxidative degradation of active substance and resulting relevant metabolites	**avermectin B_{1a}**: Xenon: 2 d, equivalent to 1.5 sunlight days at 30 – 50 °N natural summer sunlight 40 °N: 1.3 d metabolites: NOA 448111: 5.6 % of AR [8,9-Z]-avermectin B_{1a}: 8.2 % of AR, $DT_{50,photo}$ 5.8 sunlight days at 30 - 50 °N
Readily biodegradable (yes/no)	No
Biodegradation in seawater	No information supplied
Degradation in water/sediment (range or median, with n value, with r^2 value, state temperature)	$DT_{50,\ water}$: **avermectin B_{1a}**: mean 2.4 d (20 °C; range 1.8 - 2.9 d; n = 2, first-order, r^2 0.945 - 0.953). mean 4.6 d (when converted to 12°C) Decline of concentrations in water column determined by rapid initial sorption. Value represents dissipation rather than degradation.
	$DT_{50,\ whole\ system}$: **avermectin B_{1a}**: mean 89 d (20 °C; range 87 - 91 d; n = 2, first-order, r^2 0.965 - 0.991) mean 169 d (when converted to 12°C)
	$DT_{50,sediment}$: **avermectin B_{1a}**: mean 99 d (87 - 111 d; n = 2, first-order, r^2 0.942 - 0.987) mean 188 d (when converted to 12°C)
	$DT_{90,\ water}$: calculation from DT_{50} not applicable as DT_{50} is determined by sorption
	$DT_{90,\ whole\ system}$: calculated as 3.3 x $DT_{50,system}$

	avermectin B_{1a}: mean 294 d
	$DT_{90,\ sediment}$: calculated as 3.3 x $DT_{50,sediment}$ **avermectin B_{1a}**: mean 327 d
Mineralisation	max. 0.1 – 3.2 % of AR (study end 100 d; n = 2)
Non-extractable residues	max. 20.4 – 23.2 % of AR (study end 100 d; n = 2)
Distribution in water / sediment systems (active substance)	**avermectin B_{1a}**: sediment: max. 78.1 - 82.8 % of AR after 14 d, 44.3 - 45.3 % of AR at study end after 100 d
Distribution in water / sediment systems (metabolites)	water: metabolites < 1 % of AR sediment: 8a-oxo-avermectin B_{1a} (NOA 448111): max. 1.9-2.8 % of AR (70 - 100 d) 8a-hydroxy-avermectin B_{1a} (NOA 448112): max. 1.5-1.9 % of AR (35/70 - 70 d) 4"-oxo-avermectin B_{1a} (NOA 426289): max. 6.9 - 8.6 % of AR (70 - 100 d) 3"-demethyl-avermectin B_{1a} (NOA 445495): max. 1.7 - 2.0 % of AR (day 70)

Route and rate of degradation in soil

Mineralisation (aerobic)	12.4 % of AR (91 d) [23-^{14}C] -avermectin B_{1a} 3.2% of AR (21weeks); [3,7,11,13,23-^{14}C]-avermectin B_{1a} (25ºC biometer flask)
Non-extractable residues after 100 days	39.1 % of AR (91 d) max. 44.1% after 196 d [23-^{14}C] -avermectin B_{1a}
Relevant metabolites - name and/or code, % of applied a.i. (range and maximum)	8a-hydroxy-avermectin B_{1a} (NOA 448112): 15.7 % of AR 8a-oxo-avermectin B_{1a} (NOA 448111):10.3 % of AR 4,8a-dihydroxy-avermectin B_{1a} (NOA 457464):9.9 % of AR 8a-oxo-4-hydroxy-avermectin B_{1a} (NOA 457465): 9.9 % of AR unknown metabolite U8 > 5 % of AR on > 2 consecutive time points

Laboratory studies (range or median, with number of measurements, with regression coefficient)	$DT_{50, lab}$ (20°C, aerobic): **avermectin B_{1a}**: geometric mean 28.4 d[4] (range 11.2 - 65.7 d; n = 8; r^2 0.9471 - 0.9970) **NOA 448111**: geometric mean 45.3 d (range 40.5 - 50.6 d; n = 4; r^2 0.86 - 0.94) **NOA 448112**: geometric mean 35.8 d (range 26.8 - 75.4 d; n = 4; r^2 0.93 - 0.98) **NOA 457464**: geometric mean 65.9 d (range 48.5 - 99.0 d; n = 3; r^2 0.97 - 0.99) **NOA 464457**: geometric mean 112 d (range 59.8 - 173 d; n = 3; r^2 0.97 - 0.98) $DT_{50, lab}$ (when converted to 12°C, aerobic): **avermectin B_{1a}**: geometric mean 54 d **NOA 448111**: geometric mean 86 d **NOA 448112**: geometric mean 68 d **NOA 457464**: geometric mean 125 d **NOA 464457**: geometric mean 212 d
	$DT_{90, lab}$ (20°C, aerobic): calculated as DT_{50} x 3.3 **avermectin B_{1a}**: 95.3 d **NOA 448111**: 150 d **NOA 448112**: 119 d **NOA 457464**: 219 d **NOA 464457**: 372 d
	$DT_{50, lab}$ (10°C, aerobic): **avermectin B_{1a}**: 50.6 d, calculated with Arrhenius equation from DT_{50} at 8.6, 20 and 30 °C
	degradation in the saturated zone: no information available
Field studies (state location, range or median with number of measurements)	$DT_{50, field}$: **avermectin B_{1a}**: Vouvry, CH: 1.8 d (grass cover after application on bare soil, average temperature 16 °C); [8,9-Z]-avermectin B_{1a} detected shortly after appl but no longer after 1 day Bavaria, D: < 1 d (grass cover after application on bare soil, average temperature 17 °C); [8,9-Z]-avermectin B_{1a} analysed <LOQ

[4] In the List of Endpoints of the DAR from March 2008, the mean DT_{50} is given as 28.7 days, but this is most likely a typing error, because the same data range and r^2 are used and the text of Annex B gives 28.4 days.

	avermectin B_{1a} + [8,9-Z]-avermectin B_{1a}: Bavaria, D: < 1 d (bare soil, average temperature 17 °C); analytical method UV detection, no distinction between parent and isomer Alsace, F: < 1 d (bare soil, average temperature 17 °C); analytical method does not distinguish between parent and isomer Po Valley, I: < 1 d (bare soil, average temperature 13 °C); analytical method does not distinguish between parent and isomer Champagne, F: < 1 d (bare soil, average temperature 13 °C); analytical method does not distinguish between parent and isomer
	$DT_{90, field}$: < 1 d
Anaerobic degradation	$DT_{50, lab}$ (20°C, anaerobic): No reliable anaerobic study supplied. Information from partly aerobic/anaerobic experiments indicate that additional degradation under anaerobic conditions is negligible as compared to preceding aerobic degradation
Soil photolysis	$DT_{50,photolysis}$: 13 d at 12 h L:D, 24.5 °C, corresponding with 21.7 d at 30 - 50 °N in summer
Mineralisation	7.6 % after 28 d
Non-extractable residues	25.9 % after 28 d
Relevant metabolites - name and/or code, % of applied a.i. (range and maximum)	**metabolites**: 8a-oxo-avermectin B_{1a} (NOA 448111): 5.7 % of AR 8a-hydroxy-avermectin B_{1a} (NOA 448112): 4.0 % of AR [8,9-Z]-avermectin B_{1a} (NOA 427011) is supposed to be formed under light
Soil accumulation and plateau concentration	Not relevant

Adsorption/desorption

Ka , Kd	K_F: **avermectin B_{1a}**: arith. mean 129 L/kg (range 18.2 - 334 L/kg; 7 soils) **NOA 448111**: arith. mean 81.7 L/kg (range 38.3 - 128 L/kg; 3 soils) **NOA 448112**: arith. mean 41.1 L/kg (range 15.9 - 78.9 L/kg; 3 soils) **NOA 457464**: arith. mean 35.4 L/kg (range 16.9 - 61.3 L/kg; 3 soils) **NOA 464457**: arith. mean 82.3 L/kg (range 32.7 - 148 L/kg; 3 soils)
Ka_{oc} , Kd_{oc}	K_{OC}: **avermectin B_{1a}**: arith. mean 5638 L/kg (range 1495 - 7893 L/kg; 1/n 0.789 - 1.01; 7 soils)

	NOA 448111: arith. mean 3997 L/kg (range 3027 - 5052 L/kg; 1/n 0.826 - 0.835; 3 soils) **NOA 448112**: arith. mean 1943 L/kg (range 1098 - 3104 L/kg; 1/n 0.796 - 0.961; 3 soils) **NOA 457464**: arith. mean 1732 L/kg (range 1082 - 2423 L/kg; 1/n 0.890 - 0.944; 3 soils) **NOA 464457**: arith. mean 3908 L/kg (range 2573 - 5813 L/kg; 1/n 0.791 - 1.01; 3 soils)
pH dependence (yes / no) (if yes type of dependence)	no

Fate and behaviour in air

Direct photolysis in air	no information supplied
Quantum yield of direct photolysis	0.0347 (summer); 0.0316 (fall); 0.0287 (winter)
Photo-oxidative degradation in air	$DT_{50,air}$ < 1 h estimated by Atkinson method
Volatilisation	from plant surfaces: no information supplied
	from soil: no information supplied

Monitoring data, if available

Soil (indicate location and type of study)	No information supplied
Surface water (indicate location and type of study)	No information supplied
Ground water (indicate location and type of study)	No information supplied
Air (indicate location and type of study)	No information supplied

Chapter 5: Effects on Non-target Species

Toxicity data for aquatic species (most sensitive species of each group for fresh- and saltwater)

Species	Substance	Time-scale (test type)	Endpoint	Toxicity [µg a.i./L]
Fish				
Oncorhynchus mykiss	abamectin	96 h (flow-through; modified exposure)	LC_{50}	8.7 (nom)[a]
Oncorhynchus mykiss	[8,9-Z]-avermectin B_{1a}	96 h (flow-through)	LC_{50}	5.1 (mm)[b]
Oncorhynchus mykiss	8a-hydroxy-avermectin B_{1a}	96 h (semi-static)	LC_{50}	520 (mm)
Oncorhynchus mykiss	abamectin	28 d (flow-through)	NOEC	0.52 (mm)
Invertebrates				
Daphnia pulex	abamectin	48 h (static)	EC_{50}	0.12 (mm)
Daphnia magna	[8,9-Z]-avermectin B_{1a}	48 h (static)	EC_{50}	0.082 (mm)

Daphnia magna	8a-hydroxy-avermectin B_{1a}	48 h (static)	EC_{50}	1.6 (mm)
Daphnia magna	4"-oxo-avermectin B_{1a}	48 h (static)	EC_{50}	0.28 (nom)
Daphnia magna	abamectin	21 d (flow-through)	NOEC	0.021 (nom, anal. verified)[c]
Mysidopsis bahia	abamectin	96 h (flow-through)	LC_{50}	0.020 (mm)
Mysidopsis bahia	abamectin	28 d (flow-through)	NOEC	0.0035 (mm)
Algae				
Pseudokirchneriella subcapitata	Vertimec 018 EC[d]	72 h (static)	E_rC_{50} NOE_rC	> 1590 (mm) ≥ 1590
Pseudokirchneriella subcapitata	[8,9-Z]-avermectin B_{1a}	72 h (static)	E_rC_{50}	> 9000 (mm)
Pseudokirchneriella subcapitata	8a-hydroxy-avermectin B_{1a}	72 h (static)	E_rC_{50}	> 6100 (mm)
Sediment organisms				
Chironomus riparius	avermectin B_{1a}	28 d (static; water spiked)	NOEC	0.081 µg/L (nom)
Chironomus riparius	avermectin B_{1a}	28 d (static; sediment spiked)	NOEC	3.3 µg/kg dw (nom, anal. verified)
Micro-organisms				
respiration activated sludge	abamectin	acute	NOEC	1.21 mg/L (water sol.)
Mesocosm studies				
Vertimec 018 EC, single application, recirculation started after 14 d: $NOEC_{community}$ 0.066 µg a.i./L (nominal) Vertimec 018 EC, 3 applications, interval 7 d, no recirculation: $NOEC_{community}$ 0.016 µg a.i./L (actual) Note that endpoints differ from those in the PPP-assessment, because recovery is not taken into account. Test can be considered an acute test.				

a: nom = nominal, as the actually tested concentrations were not analytically determined. The toxicity might be underestimated The endpoints from these studies can therefore only provide an indication of the toxicity.
b: mm = mean measured
c: nom, anal. verified = nominal data. Analytical verification was carried out. Test results can be used for risk assessment
d: no reliable test with active substance available

Effects on earthworms or other soil non-target organisms

Acute toxicity to *Eisenia foetida*	**abamectin**: LC_{50} 33 mg/kg (10 % OM) equivalent to 11 mg/kg at default OM content of 3.4 % **NOA 427011 ([8,9-Z]-avermectin B_{1a})**: LC_{50} 50 mg/kg (10 % OM) equivalent to 17 mg/kg at default OM content of 3.4 % **NOA 448112 (8a-hydroxy-avermectin B_{1a})**: LC_{50} 321 mg/kg (10 % OM) equivalent to 109 mg/kg at default OM content of 3.4 %
Reproductive toxicity to *Eisenia foetida*	**Vertimec 0.18 EC**: NOEC ≥ 0.72 mg as/kg (10 % OM, 56 d) equivalent to ≥ 0.24 mg/kg at default OM content of 3.4 %

Effects on soil micro-organisms

Nitrogen mineralization	**abamectin**: < 25 % effect after 28 days at 0.347 mg/kg dw (2.4 % OM) **NOA 427011 ([8,9-Z]-avermectin B_{1a})**: < 25 % effect after 28 days at 0.40 mg/kg dw **NOA 448112 (8a-hydroxy-avermectin B_{1a})**: < 25 % effect after 28 days at 0.66 mg/kg dw
Carbon mineralization	**abamectin**: < 25 % effect after 28 days at 0.347 mg/kg dw (2.4 % OM) **NOA 427011 ([8,9-Z]-avermectin B_{1a})**: < 25 % effect after 28 days at 0.40 mg/kg dw **NOA 448112 (8a-hydroxy-avermectin B_{1a})**: < 25 % effect after 28 days at 0.66 mg/kg dw

Effects on terrestrial vertebrates

Acute toxicity to mammals	LD_{50} 8.7 mg/kg bw
Long term toxicity to mammals	NOAEL 0.12 mg/kg bw.d (rat)
Acute toxicity to birds	$LD_{50} \leq$ 77 mg/kg bw (*Anas platyrhynchos*)
Dietary toxicity to birds	LC_{50} 48.6 mg/kg bw.d (*A. platyrhynchos*)
Reproductive toxicity to birds	NOEC 1.33 mg/kg bw.d (*A. platyrhynchos*, males)

Effects on honeybees

Acute oral toxicity	no reliable information available
Acute contact toxicity	**abamectin**: 0.0022 µg/bee

Effects on other beneficial arthropods

Acute oral toxicity	Residual effects of abamectin on non-target arthropods other than bees were determined for several species after spray application of formulated products in laboratory tests. Effects > 50% on survival and/or reproduction were found on the parasitic wasp *Aphidius rhopalosiphi* at ≥ 0.14 g as/ha, on the predatory mite *Typhlodromus pyri* at ≥ 0.20 g as/ha and on the predatory bug *Orius laevigatus* at ≥ 1.2 g as/ha. No effects were found for the ground beetle *Poecilus cupreus* at application rates up to 29 and 58 g as/ha.
Acute contact toxicity	
Acute toxicity to …	

Bioconcentration

Bioconcentration factor (BCF)	52 L/kg wwt in whole fish, derived by kinetic modelling, based on total radioactive residues (69 L/kg wwt in whole fish, based on measured total radioactivity) 302 L/kg wwt in earthworms, estimated
Depuration time (DT_{50})	CT_{50}: 3.3 d, based on k_2 = 0.21/d
(DT_{90})	CT_{90}: 11 d, based on k_2 = 0.21/d

Level of metabolites (%) in organisms accounting for > 10 % of residues	not determined

APPENDIX II: LIST OF INTENDED USES

Table II.1 Intended uses for abamectin containing products as proposed by the RMS

	Raid Ant Bait	Raid Roach Bait	Avert Dry Flowable Cockroach Bait 310A
Product description	"ready filled, sealed" Bait station (plastic cartridge) with holes (6x6 mm).	"ready filled, sealed " Bait station (plastic cartridge) with holes (15x8mm) for cockroaches to take the bait.	A ready-to-use powder 99% on grain basis in "puffer pack"
Organism to be controlled	Ants	cockroaches	cockroaches 7 species are mentioned.
Objects to be protected	In buildings	In buildings, industrial, homes and hospitals	In buildings, protection of public health and property: Domestic premises, Commercial premises, Food storage areas, Public buildings Industrial premises
Application aim (claim)	The following claims are included: Control of ants - continous control for 3 months, including carbamate, organophosphate, organochloride, and pyrethroid resistant ant strains. - halts egg production. - Provides chain kill. - Destroys queen and colony.	The following claims are included: Control of cockroaches - continuous control for 2 months of carbamate, organophosphate, organochloride and pyrethroid resistant cockroach strains - halts egg production - Provides chain kill - one roach feeds and many die	The following claims are included: effective against: 7 species of cockroaches
Dosage	2 baits/room of 12 m² 1.5 g product/bait 0.05% a.s.	4 baits/room of 12 m² 2.5 g product/bait 0.05 % a.s.	baitpoint: 2 cm diameter x 0.5 cm weight per baitpoint: 0.15 g. general: 4-6 baitpoint/10 m² floor area difficult: 12-24 baitpoint/10 m² floor area product: 0.05% a.s.
Frequency	Replace at 3 months interval	Replace at 2 months interval	Re-inspected after 2-4 weeks. A second application may be required in case of heavy infestation. Effective for up to 3 months after application.

	Raid Ant Bait	Raid Roach Bait	Avert Dry Flowable Cockroach Bait 310A
Season/period for use	not indicated	not indicated	not indicated
Indoors/outdoors use	Indoors	Indoors	indoors in crack and crevice
(Non) professional	non-professional	non-professional	professional
Instruction for use	Bait station should be placed in corners between walls and floor in the path of tracks of ants indoors. Keep out of reach of children and pets	Bait should be placed along base boards, in corners, under sinks, in cabinets and neat plumbing fixtures Preferably on horizontal surfaces touching corner walls. Keep out of reach children and pets	In cracks, crevice and voids no waiting period required Avoid application to excessively dusty, damp or greasy locations or situations where air movement may displace the bait. Do not apply where the product may be removed by routine cleaning. Do not use the product in areas where insecticidal sprays have been recently used. Do not use any other insecticides on or around the bait points as this may discourage cockroaches from feeding on them. Do not contaminate foodstuffs, eating utensils or food contact surfaces