CONCLUSION ON PESTICIDES PEER REVIEW

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Peer review of the pesticide risk assessment of the active substance abamectin

European Food Safety Authority (EFSA)
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Abstract

The conclusions of EFSA following the peer review of the initial risk assessments carried out by the competent authorities of the rapporteur Member State Austria and co-rapporteur Member State Malta for the pesticide active substance abamectin are reported. The context of the peer review was that required by Commission Implementing Regulation (EU) No 844/2012, as amended by Commission Implementing Regulation (EU) No 2018/1659. The conclusions were reached on the basis of the evaluation of the representative uses of abamectin as an insecticide and acaricide on tomato and strawberry, and updated following the request from Commission to review the exposure and risk assessments as regards birds and mammals, aquatic organisms and soil macroorganisms. The risk assessment to bees and non-target arthropods was also updated. The reliable end points, appropriate for use in regulatory risk assessment are presented. Missing information identified as being required by the regulatory framework is listed. Concerns are identified.

Keywords: abamectin, peer review, risk assessment, pesticide, insecticide, acaricide

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Summary

Commission Implementing Regulation (EU) No 844/2012, as amended by Commission Implementing Regulation (EU) No 2018/1659, lays down the procedure for the renewal of the approval of active substances submitted under Article 14 of Regulation (EC) No 1107/2009. The list of those substances is established in Commission Implementing Regulation (EU) No 686/2012 as amended by Commission Implementing Regulation (EU) No 2016/183. Abamectin is one of the active substances listed in that Regulation.

In accordance with Article 1 of Regulation (EU) No 844/2012, the rapporteur Member State (RMS), Austria, and co-rapporteur Member State (co-RMS), Malta, received an application from the Abamectin Task Force comprising Industrias Afrasa, S.A., Lainco, S.A., Probelte S.A.U., Rotam Agrochem International Co Ltd and SAPEC Agro, S.A. for the renewal of approval of the active substance abamectin.

An initial evaluation of the dossier on abamectin was provided by the RMS in the renewal assessment report (RAR) and subsequently, a peer review of the pesticide risk assessment on the RMS evaluation was conducted by EFSA in accordance with Article 13 of Commission Implementing Regulation (EU) No 844/2012, as amended by Commission Implementing Regulation (EU) No 2018/1659.

The European Food Safety Authority (EFSA) published its conclusion on the peer review of the pesticide risk assessment of abamectin on 20 August 2020. On 1 February 2022, the European Commission sent a mandate to EFSA with a request to review the exposure and risk assessments as regards birds and mammals, aquatic organisms and soil macroorganisms. The risk assessment to bees and non-target arthropods was also updated.

The uses of abamectin according to the representative uses as an insecticide and acaricide on tomato and strawberry in permanent greenhouses and walk-in tunnels, as proposed at the European Union (EU) level result in a sufficient insecticidal and acaricidal efficacy against the target organisms.

The assessment of the data package revealed no issues that need to be included as critical areas of concern with respect to the identity, physical, chemical and technical properties of abamectin or the respective formulation.

In the area of mammalian toxicology and non-dietary exposure, no critical areas of concern were identified.

The assessment of the data package revealed no issues that could not be finalised or that need to be included as critical areas of concern with respect to residues in food and feed for the representative uses in southern Europe (SEU), besides the fact that consumer risk assessment cannot be finalised due to the data gap identified in the Fate section with respect of drinking water. Consumer risk assessment cannot be finalised for the representative uses in northern Europe (NEU) since a data gap has been identified for residue trials performed under these conditions. The maximum residue level (MRL) proposed in Article 12 of Regulation (EC) No 396/2005 (EFSA, 2014b) will need to be revised as for change of toxicological reference values (acceptable daily intake (ADI) and acute reference dose (ARfD)), since it is envisaged that acute risk may be identified for some of the crops.

The data available on environmental fate and behaviour are sufficient to carry out the required environmental exposure assessments at EU level, with the notable exception that a data gap was identified for information on the effect of water treatment processes on the nature of residues of both the active substance and its identified metabolites potentially present in surface water, when surface water is abstracted for the production of drinking water. This gap leads to the consumer risk assessment from the consumption of drinking water being not finalised for all the representative uses.

In the area of ecotoxicology, the risk to earthworms could not be finalised for the 1 $\times$ 2.7 g a.s./ha applications to tomatoes and strawberries in walk-in tunnels. High risk to several groups of non-target organisms were identified (not triggering though critical areas con concern since for each group of non-target organisms at least one safe use has been detected), i.e.:

- Mammals (all representative uses in walk-in tunnels),
- Birds (for the representative uses in walk-in tunnels at 3 $\times$ 18 g a.s./ha to tomatoes and 2 $\times$ 18 g a.s./ha to strawberries),
- Aquatic organisms (for the representative uses in walk-in tunnels and in permanent greenhouses at 3 $\times$ 18 g a.s./ha to tomatoes and 2 $\times$ 18 g a.s./ha to strawberries and for walk in tunnels on these crops at 1 $\times$ 2.7 g a.s./ha, unless when used in walk-in tunnels spray drift exposure could be mitigated by more than 95%),

- Honey bees (all representative uses in walk-in tunnels),
- Non-target arthropods other than bees (all representative uses in walk-in tunnels),
- Earthworms and soil macroorganisms (for the representative uses in walk-in tunnels at 3 × 18 g a.s./ha to tomatoes and 2 × 18 g a.s./ha to strawberries).

Based on the available information, abamectin does not meet the ED criteria for both humans and non-target organisms.

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Background

Commission Implementing Regulation (EU) No 844/2012[1], as amended by Commission Implementing Regulation (EU) No 2018/1659[2], (hereinafter referred to as 'the Regulation'), lays down the provisions for the procedure of the renewal of the approval of active substances, submitted under Article 14 of Regulation (EC) No 1107/2009[3]. This regulates for the European Food Safety Authority (EFSA) the procedure for organising the consultation of Member States, the applicant(s) and the public on the initial evaluation provided by the rapporteur Member State (RMS) and/or co-rapporteur Member State (co-RMS) in the renewal assessment report (RAR), and the organisation of an expert consultation where appropriate.

In accordance with Article 13 of the Regulation, unless formally informed by the European Commission that a conclusion is not necessary, EFSA is required to adopt a conclusion on whether the active substance can be expected to meet the approval criteria provided for in Article 4 of Regulation (EC) No 1107/2009 within 5 months from the end of the period provided for the submission of written comments, subject to an extension of an additional 3 months where additional information is required to be submitted by the applicant(s) in accordance with Article 13(3). Furthermore, in accordance with Article 13(3a), where the information available in the dossier is not sufficient to conclude the assessment on whether the approval criteria for endocrine disruption are met, additional information can be requested to be submitted in a period of minimum 3 months, not exceeding 30 months, depending on the type of information requested.

In accordance with Article 1 of the Regulation, the RMS Austria and co-RMS Malta received an application from the Abamectin Task Force comprising Industrias Afrasa, S.A., Lainco, S.A., Probelte S.A.U., Rotam Agrochem International Co Ltd and SAPEC Agro, S.A. for the renewal of approval of the active substance abamectin. Complying with Article 8 of the Regulation, the RMS checked the completeness of the dossier and informed the applicants, the co-RMS (Malta), the European Commission and EFSA about the admissibility.

The RMS provided its initial evaluation of the dossier on abamectin in the RAR, which was received by EFSA on 17 April 2019 (Austria, 2019).

In accordance with Article 12 of the Regulation, EFSA distributed the RAR to the Member States and the applicants, the Abamectin Task Force comprising Industrias Afrasa, S.A., Lainco, S.A., Probelte S.A.U., Rotam Agrochem International Co Ltd and SAPEC Agro, S.A., for consultation and comments on 29 May 2019. EFSA also provided comments. In addition, EFSA conducted a public consultation on the RAR. EFSA collated and forwarded all comments received to the European Commission on 29 July 2019. At the same time, the collated comments were forwarded to the RMS for compilation and evaluation in the format of reporting table. In addition, the applicants were invited to respond to the comments received. The comments and the applicants' response were evaluated by the RMS in column 3.

The need for expert consultation and the necessity for additional information to be submitted by the applicants in accordance with Article 13(3) of the Regulation were considered in a telephone conference between EFSA, the RMS and co-RMS on 11 October 2019. On the basis of the comments received, the applicants' response to the comments and the RMS's evaluation thereof, it was concluded that additional information should be requested from the applicants, and that EFSA should conduct an expert consultation in the areas of mammalian toxicology, residues, environmental fate and behaviour and ecotoxicology.

The outcome of the telephone conference, together with EFSA's further consideration of the comments, is reflected in the conclusions set out in column 4 of the reporting table. All points that were identified as unresolved at the end of the comment evaluation phase and which required further consideration, including those issues to be considered in an expert consultation, were compiled by EFSA in the format of an evaluation table.

[1] Commission Implementing Regulation (EU) No 844/2012 of 18 September 2012 setting out the provisions necessary for the implementation of the renewal procedure for active substances, as provided for in Regulation (EC) No 1107/2009 of the European Parliament and of the Council concerning the placing of plant protection products on the market. OJ L 252, 19.9.2012, p. 26–32.

[2] Commission Implementing Regulation (EU) No 2018/1659 of 7 November 2018 amending Implementing Regulation (EU) No 844/2012 in view of the scientific criteria for the determination of endocrine disrupting properties introduced by Regulation (EU) 2018/605.

[3] Regulation (EC) No 1107/2009 of 21 October 2009 of the European Parliament and of the Council concerning the placing of plant protection products on the market and repealing Council Directives 79/117/EEC and 91/414/EEC. OJ L 309, 24.11.2009, p. 1–50.

The conclusions arising from the consideration by EFSA, and as appropriate by the RMS, of the points identified in the evaluation table, together with the outcome of the expert consultation and the written consultation on the assessment of additional information, where these took place, were reported in the final column of the evaluation table.

A final consultation on the conclusions arising from the peer review of the risk assessment took place with Member States via a written procedure in June 2020.

EFSA published its conclusion on the peer review of the pesticide risk assessment of abamectin on 20 August 2020 (EFSA, 2020a) in which, *inter alia*, a critical area of concern was identified regarding the chronic risk to aquatic invertebrates from abamectin for all the uses in permanent greenhouses and in walk-in tunnels. In addition, a high risk was identified for walk-in tunnels uses for birds and mammals, aquatic invertebrates (for the metabolite 8-carboxy-6-hydroxy avermectin B_{1a} in permanent greenhouses as well), honeybees, non-target arthropods, earthworms and other soil macroorganisms.

In the Standing Committee on Plants, Animals, Food and Feed, discussions on a possible decision on the renewal of the active substance took place between March 2021 and May 2021. Decision-making could so far not be concluded because several issues, such as a lower range of the application/ uses proposed in the dossier (i.e. one application at a lower application rate), had not been specifically considered in the risk assessment. The RMS agreed to conduct such additional risk assessment. In order for the Commission to have the information required for decision making, on 1 February 2022 the European Commission sent a mandate to EFSA with a request to review, based on the updated RAR and List of end points (LoEP) that the RMS would provide to EFSA, the exposure and risk assessments for abamectin (avermectin B_{1a}/B_{1b}) and its relevant metabolites in the respective compartments for the uses in strawberries and tomatoes, in particular to update:

- exposure assessments in soil and surface water including the sediment compartment, for an application of 1 × 2.7 g a.s./ha (high-tech greenhouse, and low-tech greenhouse/walk-in tunnel);
- the risk assessment for aquatic invertebrates for an application of 1 × 2.7 g a.s./ha (high-tech greenhouse);
- the risk assessment for aquatic organisms, for an application of 1 × 2.7 g a.s./ha including risk mitigation measures (RMMs) beyond the 95% limit recommended by the FOCUS landscape and mitigation guidance (FOCUS, 2007) to reduce exposure (e.g. a combination of multiple RMMs such as no-spray buffer zones larger than 20 m, and drift reducing nozzles) (low-tech greenhouse/walk-in tunnel);
- the risk assessment for birds & mammals for an application of 1 × 2.7 g a.s./ha (low-tech greenhouse/walk-in tunnel);
- the risk assessment for earthworms and collembolan for an application rate of 1 × 2.7 g a.s./ ha (low-tech greenhouse/walk-in tunnel).

EFSA was requested to update its conclusion as the results of this mandate within five months from receiving the updated RAR and LoEP from the RMS, which were received by EFSA on 28 February 2022 (Austria, 2022). On 13 May 2022, the RMS submitted a new version of the updated RAR and LoEP including also new calculations of the lower application rate for bees and non-target arthropods, in agreement with Commission, as were missing from the mandate while a high risk in walk-in tunnels was identified in the previous conclusion (Austria, 2022).

This conclusion report summarises the outcome of the peer review of the risk assessment of the active substance and the representative formulation, evaluated on the basis of the representative uses of abamectin as an insecticide and acaricide on tomato and strawberry, as proposed by the applicants, and updated following the request from Commission to review the exposure and risk assessments as regards birds and mammals, aquatic organisms and soil macroorganisms. The updated conclusions of the risk assessment as regards bees and non-target arthropods are also reported. In accordance with Article 12(2) of Regulation (EC) No 1107/2009, risk mitigation options identified in the RAR and considered during the peer review are presented in the conclusion.

A list of the relevant end points for the active substance and the formulation is provided in Appendix A.

A key supporting document to this conclusion is the peer review report (EFSA, 2020b, updated in 2022), which is a compilation of the documentation developed to evaluate and address all issues raised in the peer review, from the initial commenting phase to the conclusion. The peer review report comprises the following documents, in which all views expressed during the course of the peer review, including minority views, where applicable, can be found:

- the comments received on the RAR;
- the reporting table (17 October 2019);
- the evaluation table (23 June 2020; updated in June 2022);
- the report(s) of the scientific consultation with Member State experts (where relevant);
- the comments received on the assessment of the additional information (where relevant);
- the comments received on the draft EFSA conclusion and the updated EFSA conclusion.

Given the importance of the RAR, including its revisions (Austria, 2020, 2022), and the peer review report, both documents are considered as background documents to this conclusion and thus are made publicly available.

It is recommended that this conclusion and its background documents would not be accepted to support any registration outside the EU for which the applicant has not demonstrated that it has regulatory access to the information on which this conclusion report is based.

The active substance and the formulated product

Abamectin is the ISO common name for mixture of ≥ 80% avermectin B_{1a}: (10*E*,14*E*,16*E*)-(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 and ≤ 20% avermectin B_{1b}: (10*E*,14*E*,16*E*)-(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 (IUPAC).

The representative formulated product for the evaluation was 'Abamectin 1.8% EC', an emulsifiable concentrate (EC) containing 18 g/L abamectin.

The representative uses evaluated were spray applications as an insecticide and acaricide against dipteran leafminers and mites in permanent greenhouses and walk-in tunnels (that are closed at the time the application is made) with soil bound growing systems of tomato and strawberry. Full details of the Good Agricultural Practices (GAPs) can be found in the list of end points in Appendix A.

Data were submitted to conclude that the uses of abamectin according to the representative uses proposed at EU level result in a sufficient efficacy against the target organisms, following the guidance document SANCO/2012/11251-rev. 4 (European Commission, 2014b).

A data gap has been identified for a search of the scientific peer-reviewed open literature on the active substance and its relevant metabolites, dealing with side effects on health and published within the 10 years before the date of submission of the dossier, to be conducted and reported in accordance with EFSA guidance on the submission of scientific peer-reviewed open literature for the approval of pesticide active substances under Regulation (EC) No 1107/2009 (EFSA, 2011).

Conclusions of the evaluation

1. Identity, physical/chemical/technical properties and methods of analysis

The following guidance documents were followed in the production of this conclusion: European Commission (2000a,b, 2010, 2012).

The proposed specifications for the minimum purity are based on batch data from industrial scale production and on quality control (QC) data. The proposed minimum purity of abamectin was 850 g/kg (sum of avermectin B_{1a} and avermectin B_{1b}), containing minimum 800 g/kg avermectin B_{1a} and maximum 200 g/kg avermectin B_{1b}. It should be emphasised that based on the batch data a higher minimum purity could have been proposed (minimum 900 g/kg abamectin, with a minimum content of avermectin B_{1a} of 840 g/kg and maximum content of avermectin B_{1b} of 50 g/kg). FAO specification does not exist for this substance.

The main data regarding the identity of abamectin and its physical and chemical properties are given in Appendix A. A data gap was identified for the determination of the emulsion stability of the representative formulation according to MT 36.3.

Adequate analytical methods are available for risk assessment in plants and soil and for the determination of abamectin in the technical material and in the representative formulations as well as

for the determination of the respective impurities in the technical material. For the other matrices new methods used in risk assessment were not submitted.

The residue definition for monitoring in plant matrices was defined as sum of avermectin B_{1a}, [8,9-Z]-isomer of avermectin B_{1a} and avermectin B_{1b}, expressed as avermectin B_{1a}. The compounds of the residue definition can be determined by high-pressure liquid chromatography with tandem mass spectrometry (HPLC–MS/MS) (QuEChERS multi-residue method) with a limit of quantification (LOQ) of 0.002 mg/kg for each compound. The residue definition for food of animal origin is avermectin B_{1a}, covered by legal provisions in force for abamectin from veterinary uses. Avermectin B_{1a}, avermectin B_{1b} and [8,9-Z]-isomer of avermectin B_{1a} can be determined by HPLC–MS/MS (QuEChERS multi-residue method) in animal matrices (milk, eggs, muscle, fat and kidney) with a LOQ of 0.002 mg/kg for each compound.

The residue definition for monitoring in soil is defined as avermectin B_{1a}, avermectin B_{1b}, 8a-oxo-avermectin B_{1a} (NOA 448111), 8a-hydroxy-avermectin B_{1a} (NOA 448112), 4"-oxo-avermectin B_{1a} (NOA 426289), 4,8a-dihydroxy-avermectin B_{1a} (NOA 457464) and 8a-oxo-4-hydroxy-avermectin B_{1a} (NOA 457465). Adequate HPLC–MS/MS method exists for monitoring all the components of the residue definition with a LOQ of 0.002 mg/kg for each substance, except for NOA 426289, which is a metabolite that can be determined also by HPLC–MS/MS with a LOQ of 0.1 μg/kg.

The monitoring residue definition for water (drinking, ground and surface) was defined as avermectin B_{1a}, avermectin B_{1b}, 8a-oxo-avermectin B_{1a} (NOA 448111), 8a-hydroxy-avermectin B_{1a} (NOA 448112), 4"-oxo-avermectin B_{1a} (NOA 426289), 4,8a-dihydroxy-avermectin B_{1a} (NOA 457464) and 8a-oxo-4-hydroxy-avermectin B_{1a} (NOA 457465). All the compounds of the residue definition can be monitored by HPLC–MS/MS with a LOQ of 0.1 μg/L for each. A data gap was, however, identified for an analytical method for the enforcement of the relevant limits based on the lowest effect concentrations for aquatic invertebrates.

Avermectin B_{1a} and avermectin B_{1b} in air can be determined by HPLC–MS/MS with a LOQ of 0.05 $\mu g/m^3$ for each analyte.

The residue definition in body fluids and tissues was defined as sum of avermectin B_{1a}, [8,9-Z]-isomer of avermectin B_{1a} and avermectin B_{1b}, expressed as avermectin B_{1a}. The QuEChERS multi-residue analytical method can be used for monitoring the compounds of the residue definition with a LOQ of 0.002 mg/kg for all analytes in all matrices.

2. Mammalian toxicity

The toxicological profile of the active substance abamectin, sum of avermectin B_{1a} (min 800 g/kg) and avermectin B_{1b} (max 200 g/kg), was discussed at the Pesticides Peer Review Experts' Meetings PREV 25 in March 2020; and based on the following guidance documents: SANCO/221/2000 – rev. 10-final (European Commission, 2003), SANCO/10597/2003 – rev. 10.1 (European Commission, 2012), Guidance on Dermal Absorption (EFSA PPR Panel, 2017), Guidance on the assessment of exposure of operators, workers, residents and bystanders in risk assessment for plant protection products (EFSA, 2014c) and Guidance on the Application of the CLP Criteria (ECHA, 2017).

The toxicological profile of abamectin relied upon toxicity studies that were considered representative of the old technical specification for the active substance and associated impurities. The same technical specification was proposed for the renewal.

In the toxicokinetic studies in rats, the systemic bioavailability of avermectin B_{1a} was estimated to be 86% after oral administration and there was no evidence for accumulation. Avermectin B_{1a} was distributed throughout all major organs and tissues and excreted almost exclusively in the faeces (more than 92%). The main metabolic pathway included demethylation, hydroxylation, cleavage of the oleandrosyl ring and oxidation reactions. A comparative metabolism and kinetic study with avermectin B_{1b} showed the same toxicokinetic profile as avermectin B_{1a}. The evaluation of the *in vitro* public literature studies in human and rats microsomes lead to the conclusion that the metabolism of abamectin in human and rats is comparable.

With regard to acute toxicity, abamectin is very toxic to rat by oral and inhalation administration with a harmonised classification[4] as H300 'Fatal if swallowed' and H330 'Fatal if inhaled', with characteristic signs of toxicity ranging from tremors and ataxia to mortality. Based on a dermal LD_{50},

[4] Regulation (EC) No 1272/2008 of the European Parliament and of the Council of 16 December 2008 on classification, labelling and packaging of substances and mixtures, amending and repealing Directives 67/548/EEC and 1999/45/EC, and amending Regulation (EC) No 1907/2006. OJ L 353, 31.12.2008, p. 1–1355.

the criteria for classification as H312 'Harmful in contact with skin' may also be met. There was no evidence neither of skin or eye irritation nor of skin sensitisation.

In the short-term dietary studies with both abamectin and avermectin B_{1a}, all species showed characteristic signs of central nervous system (CNS) toxicity. The dog was the most sensitive species and showed a very steep dose response for clinical signs of neurotoxicity and mortality (maximum tolerated dose (MTD) was clearly exceeded at 2.0 mg/kg body weight (bw) per day, lowest observable adverse effect level (LOAEL) at 0.5 mg/kg bw per day), without histopathological findings correlating to the nervous tissues. A no observed adverse effect level (NOAEL) of 0.25 mg/kg bw per day was set for the dog 18-week (with avermectin B_{1a}) and dog 53-week studies (with abamectin) based on CNS toxicity. In a 30-day rat inhalation study, a NOAEL was set at 0.577 μg/L (0.11 mg/kg bw per day) based on the increased incidence in clinical signs and reduced motor activity in females. The harmonised classification of abamectin as STOT RE 1, H372 'Causes damage to the nervous system through prolonged or repeated exposure' also took these findings into account. The relevant long-term oral NOAEL is 1.5 mg/kg bw per day from the 2-year rat study, based on CNS toxicity. Abamectin showed no carcinogenic potential in rats or mice. Based on the available genotoxicity studies, abamectin is unlikely to be mutagenic or clastogenic. However, a data gap to address the aneugenicity potential was set based on the lack of micronucleus study *in vitro* and/or *in vivo*[5], without triggering a critical concern since aneugenicity is considered a threshold mechanism, and therefore the setting of reference values is possible.

With regard to the reproductive toxicity of abamectin, the parental and reproductive NOAEL in the rat multigeneration study was set at 0.4 mg/kg bw per day (highest dose) in the absence of treatment related effects; and an offspring NOAEL of 0.12 mg/kg bw per day was identified based on an increased pup mortality, retarded body weight gain and transient retinal anomalies. In the developmental toxicity studies, the developmental NOAEL was set at 0.8 mg/kg bw per day based on cleft palate, effects on the sex ratio, on lumbar rib and lumbar count variation in rats; and at 0.5 mg/kg bw per day based on an increased incidence clubbed forefoot and an increased number of resorptions, a delayed ossification and an excess of incidences of cleft palate and of omphalocele in rabbits. The maternal NOAELs were set at 1.6 mg/kg bw per day, based on the absence of effects in the highest dose group in rats and at 1.0 mg/kg bw per day, based on decreased water and food consumption and weight loss during gestation in rabbits. The harmonised classification[4] based on these teratogenic observations in rats and rabbits is Repr. 2, H361d 'Suspected of damaging the unborn child'.

In regard to neurotoxicity of abamectin, the NOAEL for acute neurotoxicity was 0.5 mg/kg bw, based on a reduced splay reflex in rat, while the NOAEL for chronic neurotoxicity was set at 1.6 mg/kg bw per day, based on clinical signs (i.e. irregular breathing, upward curvature of the spine, reduced righting reflex, reduced splay reflex and sides pinched observed in the combined 90-day with neurotoxicity study from short term toxicity). The maternal NOAEL for the two developmental neurotoxicity studies was 0.4 mg/kg bw per day, while an overall neurodevelopmental LOAEL was set at 0.12 mg/kg bw per day based on decrease in body weight and delay in vaginal opening in both studies.

The abamectin acceptable daily intake (ADI), the acute reference dose (ARfD) and (acute) acceptable operator exposure level ((A)AOEL) are 0.0012 mg/kg bw per day based on the neurodevelopmental LOAEL of the developmental neurotoxicity studies. All values were derived with applying an uncertainty factor of 100.[6]

For the non-dietary exposure estimates, the dermal absorption values of abamectin in 'Abamectin 1.8% EC' were 11% for the concentrate and of 4.8% for the dilution (1:10), based on an *in vitro* study with human skin combined with experts' judgement on the available evidence.[7] The majority of the experts agreed that the dermal absorption is not expected to increase with higher dilutions. During the written procedure on the draft conclusion, one expert noted that the evidence of non-increased dermal absorption with dilution was not sufficiently demonstrated.

For the representative uses of 'Abamectin 1.8% EC' in protected production systems (permanent greenhouse and walk in tunnels) of strawberry and tomato, the operator exposure estimates were below the AOEL with the Dutch model when including the use of coverall and gloves during mixing/loading and application, while these estimates were below the AOEL with the European Crop

[5] Experts' consultation 2.1 in the Report of Pesticides Peer Review Experts' meeting 25 (March 2020).
[6] Experts' consultation 2.7 in the Report of Pesticides Peer Review Experts' meeting 25 (March 2020).
[7] Experts' consultation 2.8 in the Report of Pesticides Peer Review Experts' meeting 25 (March 2020).

Protection Association (ECPA) greenhouse model without use of personal protective equipment. It is noted that neither of these two models have been validated at EU level. The worker exposure estimates with the EFSA calculator were below the AOEL with the use of gloves during re-entry activities. For bystanders and residents, the exposure from uses in permanent greenhouse or walk in tunnels (when closed during application) can be considered as limited to vapour and is below the AOEL for adults and children with the EFSA calculator. During the written procedure on the draft conclusion, one expert noted that the exposure pathways to spray drift (droplets) and surface deposits from emissions of aerosols should be also considered: as a result, according to this approach the exposure estimated for bystanders and residents are not expected to be above than the (A)AOEL.

The toxicological profile of metabolites found as food residues or reaching levels in soil triggering consideration for groundwater exposure was concluded during the experts' meeting, based on experimental data, QSAR analysis, grouping and read-across. Several studies were performed with the [8,9-*Z*]-isomer of avermectin B_{1a} and showed the same toxicological profile as the parent abamectin. For 24-hydroxymethyl-avermectin B1 and the monosaccharide of avermectin B1 [NOA 419150] genotoxicity and general toxicity were considered covered by the parent based on read-across analysis, considering thus that aneugenicity is a data gap for the metabolites as well.

3. Residues

The assessment in the residue section is based on the OECD following documents: OECD (2009, 2011), European Commission (2011) and JMPR (2004, 2007). Abamectin was discussed in Pesticides Peer Review Experts' Teleconference PREV 27.

Metabolism in primary crops was investigated in the fruit (tomato-under field and greenhouse conditions, citrus), leafy (celery) and pulses/oilseeds (cotton) crop groups using foliar applications only. Despite some deficiencies in relation to the complete characterisation of residue in cotton seed grain, and considering the prominent effect of photolysis in the transformation of abamectin, it was concluded that these three metabolism studies were sufficient to establish the residue definition for all plant commodities for foliar applications. The residue **definition for monitoring and risk assessment** is set as: sum of avermectin B_{1a}, avermectin B_{1b} and [8,9-Z]-isomer of avermectin B_{1a}, expressed as avermectin B_{1a}.

With regard to the representative uses, significant residues in rotational crops are not expected, provided that abamectin is used according to the supported GAPs. In the framework of the initial peer review, the residue definition derived from the metabolism studies conducted with foliar applications, was also considered applicable to rotational crops. However, due to the assumed role of photolysis in the available metabolism studies, a data gap[8] to confirm the residue definition for soil applied uses was identified in the previous peer review. This data gap was not addressed in the remit of the renewal review, since it is not relevant to the representative uses covered by the assessment in this EFSA's conclusion.

The residue definition, as derived for primary crops, also applies to processed commodities resulting from the representative uses. However, and on a case-by-case basis and pending upon the type of processing and type of crop, the contribution of processed commodities and toxicological burden contribution of the processed commodities, the metabolite NOA 419150 might become relevant and will need to be considered for the risk assessment of other uses of abamectin.

Regarding the representative uses, residue definitions are not required for livestock matrices. The peer review agreed to set the default residue definition in line with the veterinary uses as avermectin B_{1a} to be the suitable marker of the residues for products of animal origin. A dietary burden calculation for fish with the Fraunhofer Model 2.0.3, showed that the trigger will not be exceeded and residues in fish do not need to be further considered.

The representative uses in southern Europe (SEU) were fully supported by the available data. However, since photolysis is considered to play a significant role on the degradation of abamectin components and in order to cover the most critical situation for the consumer exposure assessment, which is the northern Europe (NEU) GAP, a data gap was identified for the submission of 4 additional residue trials on tomatoes and 4 additional residue trials on strawberries compliant with the NEU GAP.

[8] Data requirements were previously identified by EFSA for nematicide uses and seed treatment applications. In particular, for residues section, metabolism studies with seed applications to support the seed application uses in tomato, lettuce, soya bean, beet, corn, cotton and carrot were requested by EFSA (2016) and would be needed in case these uses were to be supported in the future.

In addition, due to the significant effect of photolysis on the residue levels, a particular condition for abamectin to be used only within the period of March to October is proposed.

It is noted that the representative GAP application rates for tomatoes and strawberries are below to the application rate of what was identified as critical EU-GAP in the framework of the review of the existing maximum residue levels (MRLs) of abamectin according to the Article 12 of Regulation (EC) No 396/2005[9] (EFSA, 2014b). New (lower) MRLs are proposed in this conclusion for tomato and strawberries (tomatoes 0.015 mg/kg vs. 0.09 in Commission Regulation (EU) 2018/1514[10]; strawberries 0.07 mg/kg vs. 0.15 mg /kg in Commission Regulation (EU) 2018/1514.

The chronic and acute exposure assessment for abamectin was performed with regard to the residues (STMR, HR, resp.) observed in supervised field trials available for the representative uses. The chronic consumer intake was calculated to be 2.71 of the ADI (PRIMo 2) or 3 % (tomatoes) of the ADI (PRIMo 3.1). The highest acute intake related to the crops under consideration was estimated to be 53.3% (PRIMo 2) or 56% (PRIMo 3.1) of the ARfD for strawberries.

Consumer risk assessment is not finalised as appropriate information to address the effect of water treatments processes on the nature of the residues that might be present in surface water, when surface water is abstracted for drinking water (see Section 4). In addition, the consumer risk assessment cannot be considered finalised regarding the NEU uses (see Section 9).

Following Commission Regulation (EU) No 283/2013[11] regarding the requirement to consider the exposure arising from sources other than the plant protection active substance it is noted that the pesticide emamectin (composed of derivatives of avermectin B_{1a} and B_{1b}) and the veterinary drug ivermectin (avermectin B_{1a} and B_{1b} in a different proportion than in abamectin) share some components and/or the same mode of action and similar routes of exposure are expected and will need to be taken into account when the overall exposure to these compounds is considered.

The MRL proposed in Article 12 of Regulation (EC) No 396/2005 (EFSA, 2014b) will need to be revised since it is envisaged that acute risk may be identified for some of the crops as for change of toxicological reference values (ADI and ARfD).

4. Environmental fate and behaviour

Abamectin was discussed at the Pesticides Peer Review Experts' Teleconference 12 in March 2020.

Due to the small difference in the structure the fate and behaviour of avermectin B_{1a} in soil, water and air is considered to cover avermectin B_{1b} and both their consequent [8,9-*Z*] isomers (EFSA, 2016) which are minor aqueous photolysis transformation products.

The rates of dissipation and degradation in the environmental matrices investigated were estimated using FOCUS (2006) kinetics guidance. In soil laboratory incubations under aerobic conditions in the dark, avermectin B_{1a} exhibited moderate persistence, forming the major (> 10% applied radioactivity (AR)) metabolites 8a-oxo-avermectin B_{1a} (NOA 448111, max. 17.0% AR) which exhibited moderate to medium persistence, 8a-hydroxy-avermectin B_{1a} (NOA 448112, max. 22.0% AR) which exhibited moderate persistence and 4"-oxo-avermectin B_{1a} (NOA 426289, max. 12% AR), which exhibited low to moderate persistence. However, for this metabolite soil degradation endpoints were available for only two soils, and then a data gap was identified for soil incubation to address the degradation rate of 4"-oxo-avermectin B_{1a} (NOA 426289) in one additional soil in accordance with the data requirements of Commission Regulation (EU) No 283/2013 (see Section 8). The metabolites 4,8-dihydroxy-avermectin B_{1a} (NOA 457464 or M6, max. 9.9 % AR) which exhibited moderate to medium persistence, 8a-oxo-4-hydroxy-avermectin B_{1a} (NOA 457465, max. 9.9% AR) which exhibited moderate to high persistence and 8-carboxy-6-hydroxy-avermectin B_{1a} (M4, max. 9.0% AR), which exhibited moderate persistence were all above 5% AR at two subsequent sampling points, so triggered further consideration in the exposure assessment. Mineralisation of the [23-^{14}C]-avermectin B_{1a} radiolabel to carbon dioxide

[9] Regulation (EC) No 396/2005 of the European Parliament and of the Council of 23 February 2005 on maximum residue levels of pesticides in or on food and feed of plant and animal origin and amending Council Directive 91/414/EEC. OJ L 70, 16.3.2005, p. 1–16.

[10] Commission Regulation (EU) 2018/1514 of 10 October 2018 amending Annexes II, III and IV to Regulation (EC) No 396/2005 of the European Parliament and of the Council as regards maximum residue levels for abamectin, acibenzolar-S-methyl, clopyralid, emamectin, fenhexamid, fenpyrazamine, fluazifop-P, isofetamid, *Pasteuria nishizawae* Pn1, talc E553B and tebuconazole in or on certain products. OJ L 256, 12.10.2018, p. 8–32.

[11] Commission Regulation (EU) No 283/2013 of 1 March 2013 setting out the data requirements for active substances, in accordance with Regulation (EC) No 1107/2009 of the European Parliament and of the Council concerning the placing of plant protection products on the market. OJ L 93, 3.4.2013, p. 1–84.

accounted for 4.1–14.0 % AR after 91 days. The formation of unextractable residues (not extracted by acetonitrile/water) for this radiolabel accounted for 17.0–39.1% AR after 91 days.

In anaerobic soil incubations, avermectin B_{1a} was essentially stable. In the laboratory soil photolysis study, novel photodegradation products were not identified.

In satisfactory field dissipation studies carried out at three sites in Germany and two in the France (spray application to the soil surface on bare soil plots in late spring and early summer) avermectin B_{1a} exhibited very low to low persistence. Sample analyses were carried out for avermectin B_{1a} in soil samples from all sites and for metabolites 8a-oxo-avermectin B_{1a} (NOA 448111), 8a-hydroxy-avermectin B_{1a} (NOA 448112), 4,8a-dihydroxy-avermectin B_{1a} (NOA 457464 or M6) and 8a-oxo-4-hydroxy-avermectin B_{1a} (NOA 457465) in soil samples from one site. None of the metabolites were found under field conditions at this trial site. The field data were not normalised to FOCUS reference conditions (20°C and pF2 soil moisture) and endpoints were not combined with lab values to derive modelling endpoints. A data gap was identified for metabolites 8a-oxo-avermectin B_{1a} (NOA 448111), 4,8a-dihydroxy-avermectin B_{1a} (NOA 457464) and 4-hydroxy-8a-oxo-avermectin B_{1a} (NOA 457465) for information from two more field trial sites (see Section 8). The EU level assessments for the metabolites for the representative uses assessed have been completed using the available laboratory soil degradation endpoints.

Avermectin B_{1a} was immobile in soil. It was concluded that the adsorption of avermectin B_{1a} was not pH dependent. Metabolites 8a-oxo-avermectin B_{1a} (NOA 448111) and 8a-oxo-4-hydroxy-avermectin B_{1a} (NOA 457465) exhibited slight mobility to immobility in soil. Metabolites 8a-hydroxy-avermectin B_{1a} (NOA 448112) and 4,8a-dihydroxy-avermectin B_{1a} (NOA 457464 or M6) exhibited low to slight mobility in soil. Metabolite 4"-oxo-avermectin B_{1a} (NOA 426289) exhibited low mobility to immobile in soil. It was concluded that the adsorption of all these metabolites was not pH dependent. Experimental batch sorption study was not available for metabolite 8-carboxy-6-hydroxy-avermectin B_{1a} (M4). Therefore, a data gap was identified for a batch sorption study to address the adsorption of this metabolite in at least three soils in accordance with the data requirements of Commission Regulation (EU) No 283/2013[10] (see Section 8).

In laboratory incubations in dark aerobic natural sediment water systems, avermectin B_{1a} exhibited moderate to medium persistence partitioning to sediment forming three major metabolites 8a-oxo-Avermectin B_{1a} (NOA 448111, max. 9% AR in sediment after 117 days and max. 8% AR in water after 7 days), 8a-hydroxy-avermectin B_{1a} (NOA 448112, max. 7% AR in sediment after 97 days and only max. 3% AR in water after 62 days) and 4"-oxo-Avermectin B_{1a} (NOA 426289, max. 7% AR in sediment and max. 6% AR in water after 29 days). The unextractable sediment fraction accounted for 16–23.2% AR at the study end. Mineralisation of abamectin accounted for 3.0–7% AR at the end of the study. The rate of decline of avermectin B_{1a} in a laboratory sterile aqueous photolysis experiment showed a significant degradation process relative to that occurred in the aerobic sediment water incubations. Avermectin B_{1a} was photolytically degraded in sterile aqueous media forming no major transformation products. [8,9-Z]-avermectin B_{1a} (NOA 427011) was a minor sterile aqueous transformation product. The strong and expected rapid adsorption capacity of the precursor abamectin components to sediment would mean that it is expected that there would be negligible opportunity for [8,9-Z]-avermectin B_{1a} or [8,9-Z]-avermectin B_{1b} to be formed in natural water systems.

The necessary surface water and sediment exposure assessments (predicted environmental concentrations (PECs)) were carried out for abamectin and its metabolites 8a-oxo-avermectin B_{1a} (NOA 448111), 8a-hydroxy-avermectin B_{1a} (NOA 448112), 4"-oxo-avermectin B_{1a} (NOA 426289), 4,8-dihydroxy-avermectin B_{1a} (NOA 457464, M6), 4-hydroxy-8-oxo-avermectin B_{1a} (NOA 457465) and 8-carboxy-6-hydroxy-avermectin B_{1a} (M4) using the FOCUS (FOCUS, 2001) step 1 and step 2 approach (version 3.2 of the steps 1–2 in FOCUS calculator) for all representative uses.

For the representative uses in walk-in tunnels step 3 (FOCUS, 2001) and step 4 calculations were available[12] for abamectin and its metabolites, for the drainage scenarios as recommended by the EFSA guidance (EFSA, 2014a). The step 4 calculations appropriately followed the FOCUS (FOCUS, 2007) guidance, with 10 m no-spray drift buffer zones (distance between a tunnel and a water body) plus 50% drift reducing nozzles and 20 m spray drift buffer zones being implemented for the drainage scenarios (representing an 86–93% spray drift reduction). A MS Excel spreadsheet was appropriately used to implement these mitigation measures in the simulations. The experts at the meeting discussed the applicants' proposed exposure assessment where it was proposed that the walk-in tunnels were closed at the time of application. The applicant suggested that such mitigation would reduce the

[12] Simulations utilised the agreed Q10 of 2.58 (following EFSA, 2008) and Walker equation coefficient of 0.7.

exposure to surface water and therefore suggested that there would be no input via spray drift. Although the experts agreed that such mitigation would reduce the exposure to surface water via spray drift, it was considered that the available exposure estimates did not account for other mechanisms of emission from the field to the surface water which are inexplicitly accounted for in the 'spray-drift' values (which would be better termed off-field emission values). As such, the experts did not agree that the available exposure assessment, assuming no emission via 'spray-drift' was appropriate.[13] In line with the mandate from the European Commission the RMS presented step 4 calculations taking into account risk mitigation measures greater than the limit of 95% that is recommended by the FOCUS landscape and mitigation guidance (FOCUS, 2007) usually used for risk assessment. For the representative uses on tomatoes and strawberries, the combined mitigations measures result in a total reduction of 98.6% (90% drift reducing nozzles + 10 m no-spray buffer zone) and in a total reduction of 99.3% (90% drift reducing nozzles + 20 m no-spray buffer zone). The results of these calculations are reported in the Volume 3 – B.8 (CP) (Austria, 2022).

For the representative uses in permanent greenhouses calculations were available for abamectin and its metabolites using the GEM model (Greenhouse Emission Model - version 3.3.2) (Step 3, EFSA, 2014a). It should be noted that the GEM model and scenario definition used were an EU guidance agreed example scenario reflecting Dutch conditions for high technology (permanent) greenhouses. However, it also needs to be noted that it may not be representative for the range of these structure types present in all EU territories.

The necessary groundwater exposure assessments, for the representative uses, were carried out using FOCUS (European Commission, 2014a) scenarios and the models PEARL 4.4.4, PELMO 5.5.3 and MACRO 5.5.4.[14] The potential for groundwater exposure from the representative uses by avermectin B_{1a} and its metabolites above the parametric drinking water limit of 0.1 μg/L was concluded to be low in geoclimatic situations that are represented by all 9 FOCUS groundwater scenarios.

The applicant did not provide appropriate information to address the effect of water treatments processes on the nature of the residues that might be present in surface water, when surface water is abstracted for drinking water. This has led to the identification of a data gap (see Section 8) and results in the consumer risk assessment not being finalised (see Section 9).

The PEC in soil, surface water, sediment, and groundwater covering the representative uses assessed can be found in Appendix A of this conclusion.

5. Ecotoxicology

The risk assessment was based on the following documents: European Commission (2002a,b), SETAC (2001), EFSA (2009), EFSA PPR Panel (2013) and EFSA (2013). According to Regulation (EU) No. 283/2013 data should be provided regarding the acute and chronic toxicity to honeybees and data to address the development of honeybee brood and larvae. As the European Commission (2002a) does not provide a risk assessment scheme which is able to use the chronic toxicity data for adult honeybees and the honeybee brood, when performing the risk assessment according to European Commission (2002a), the risk to adult honeybees from chronic toxicity and the risk to bee brood, could not be finalised due to the lack of a risk assessment scheme. Therefore, the EFSA (2013) was used for risk assessment in order to reach a conclusion for the representative uses.

Abamectin has been discussed by the experts in ecotoxicology during the Pesticides Peer Review Experts' Meeting PREV 26 (March 2020).

The batches used in the ecotoxicity studies were considered sufficiently representative of the proposed (and old) technical specification.

Abamectin is a mixture of two compounds, avermectin B_{1a} and B_{1b}, with avermectin B_{1a} purity $\geq$ 80%. Most of the ecotoxicity studies were conducted with this mixture and it was considered that the potential differences in ecotoxicity between the two compounds are not significant.

For the representative uses in permanent greenhouses, by considering that the exposure is expected to be negligible, low risk was concluded to birds, mammals, bees, non-target arthropods other than bees, earthworms and other soil macroorganisms, soil microorganisms and non-target terrestrial plants. A high risk to introduced pollinators was indicated with the available data.

Acute and long-term oral toxicity data for **birds and mammals** were available with the active substance abamectin.

[13] Experts' consultation 4.6 of the Report of the Pesticide Peer Review TC 12.
[14] Simulations utilised the agreed Q10 of 2.58 (following EFSA, 2008) and Walker equation coefficient of 0.7.

Based on the available data and risk assessment, low acute risk from dietary exposure to **birds** was concluded for the uses in walk-in tunnels (tier 1). High long-term risk to birds was concluded at tier 1 for the uses in walk-in tunnels[15] (3 × 18 g a.s./ha to tomatoes and 2 × 18 g a.s./ha to strawberries), with the exception of small granivorous and omnivorous birds (BBCH ≥ 50) in tomato and small omnivorous birds (BBCH ≥ 40) in strawberries. Reliable refinements were not available for the scenarios for which high risk was indicated.

A low acute risk was indicated for **mammals** for the uses in walk-in tunnels, with the exception of frugivorous and small herbivorous mammals in tomatoes and for small (BBCH ≥ 40) and large (BBCH: 10-39) herbivorous mammals in strawberries for which a high acute risk was indicated (tier 1). High long-term risk to mammals was also concluded at tier 1 for the uses in walk-in tunnels.

A low risk to birds and mammals from secondary poisoning was concluded for abamectin and the metabolite 8-carboxy-6-hydroxy-avermectin B_{1a} for the uses in walk-in tunnels. Assuming that the metabolite is 10-time of higher toxicity than the parent, the risk to the fish-eating birds and mammals from the metabolite 4″-oxo-avermectin B_{1a} was assessed as low while for the risk to earthworm-eating birds and mammals from this metabolite this screening was not sufficient to indicate low risk (data gap).

With regard to the representative uses for which low risk for abamectin could not be concluded for birds and mammals, refined risk assessments were not available. Instead, it was proposed by the applicant that risk mitigation measures should be established, i.e. closing the walk-in tunnels and keeping them closed for 15 days. However, the experts considered that the exact period could not be established due to the lack of suitable data and needs to be further decided at MS level. For the metabolite 4″-oxo-avermectin B_{1a}, the experts[15] noted that mitigation of closing the tunnels for 15 days would not address the risk via secondary poisoning to birds and mammals from 4″-oxo-avermectin B_{1a} when exposure could occur sometime after application.

The risk to birds and mammals from consumption of contaminated water was low for all the representative uses.

A risk assessment for birds and mammals was not available for plant metabolites (data gap).

Table 1 summarises the outcome of the risk assessment for terrestrial vertebrates for a single application of 2.7 g a.s./ha.

Table 1: Outcome of the risk assessment for terrestrial vertebrates for a single application of 2.7 g a.s./ha to strawberries and tomatoes in walk-in tunnels

Taxa	Type of assessment	Strawberries	Tomatoes
Birds	Acute, dietary	Low risk at the screening step	Low risk at the screening step
	Reproductive, dietary	Low risk at the screening step	Low risk at the screening step
	Secondary poisoning, fish-eating birds	Low risk for abamectin and both pertinent metabolites[(a)]	Low risk for abamectin and both pertinent metabolites[(a)]
	Secondary poisoning Earthworm-eating birds	Low risk for abamectin and metabolite 8-carboxy-6-hydroxy-avermectin B_{1a} (M4) **Metabolite 4″-oxo-avermectin B_{1a} – screening assessment did not exclude a risk**	Low risk for abamectin and metabolite 8-carboxy-6-hydroxy-avermectin B_{1a} (M4) **Metabolite 4″-oxo-avermectin B_{1a} – screening assessment did not exclude a risk**
	Consumption of contaminated water	Low risk	Low risk
Mammals	Acute, dietary	Low risk at the screening step	Low risk at the screening step
	Reproductive, dietary	**High risk at tier 1 (small herbivorous)[(b)]**	**High risk at tier 1 (fruit-eating, small herbivorous)[(b)]**
	Secondary poisoning, fish-eating mammals	Low risk for abamectin and both pertinent metabolites[(a)]	Low risk for abamectin and both pertinent metabolites[(a)]
	Secondary poisoning Earthworm-eating mammals	Low risk for abamectin and metabolite 8-carboxy-6-hydroxy-avermectin B_{1a} (M4)	Low risk for abamectin and metabolite 8-carboxy-6-hydroxy-avermectin B_{1a} (M4)

[15] Experts' consultation 5.1 of the Report of the Pesticides Peer Review Experts' Meeting 26 (March 2020).

Taxa	Type of assessment	Strawberries	Tomatoes
		Metabolite 4”-oxo-avermectin B_{1a} – screening assessment did not exclude a risk	**Metabolite 4”-oxo-avermectin B_{1a} – screening assessment did not exclude a risk**
	Consumption of contaminated water	Low risk	Low risk

a.s.: active substance.
(a): Metabolites 8-carboxy-6-hydroxy-avermectin B_{1a} (M4) and 4”-oxo-avermectin B_{1a}.
(b): No suitable refinements were available.

Reliable refinements were not available to resolve the reproductive risk to mammals nor to perform a tier 1 risk assessment for earthworm-eating birds and mammals for metabolite 4”-oxo-avermectin B_{1a} (data gap).

Acute and chronic toxicity studies were conducted with **aquatic organisms** (fish, aquatic invertebrates and algae) for the active substance abamectin, the pertinent surface-water and sediment metabolites, and the representative formulation.

A low acute risk to **fish** was indicated at (FOCUS) Step 3 for all the representative uses of abamectin. The chronic risk to fish from abamectin was assessed as low (Step 3, using the GEM model and representative scenario) for the uses in permanent greenhouses. Low chronic risk to fish was indicated for the uses in walk-in tunnel at FOCUS Step 4 provided that suitable mitigation measures (i.e. 10 m no-spray zone between a tunnel and water body) are employed.

The acute risk to **aquatic invertebrates** from abamectin was assessed as high at tier 1 and therefore it was refined based on a refined endpoint (Hazard Concentration 5, HC_5) derived from species sensitivity distribution.[16] The outcome of the risk assessment for aquatic invertebrates is summarised in Table 2.

Table 2: Outcome of the risk assessment for aquatic invertebrates to abamectin

Representative use	Acute	Chronic
3 × 18 g a.s./ha to tomatoes in walk-in tunnels and 2 × 18 g a.s./ha to strawberries in walk-in tunnels	High risk at FOCUS Step 3 High risk at FOCUS Step 4 (20 m no-spray buffer zone) Additional mitigation required to achieve a low risk was not calculated but is not required since the chronic risk to aquatic invertebrates defines the required level of mitigation.	High risk at FOCUS step 3 High risk at FOCUS Step 4 (20 m no-spray buffer zone) > 99.4% drift reduction would be needed to achieve low risk (numerical value not mathematically achieved combining 20 m no-spray buffer zone and 90% drift-reduction technology)
1 × 2.7 g a.s./ha to strawberries and tomatoes in walk-in tunnels	High risk at FOCUS Step 3 Low risk at FOCUS step 4 (10 m no-spray buffer zone)	High risk at FOCUS Step 3 High risk at FOCUS Step 4 (20 m no-spray buffer zone). Low risk with 96.26% drift reduction (numerical value for 20 m no-spray buffer zone and 50% drift-reduction technology).
3 × 18 g a.s./ha to strawberries and tomatoes in permanent greenhouses	High risk at Step 3 EFSA, (2014a) (GEM (Greenhouse Emission Model - version 3.3.2))	High risk at Step 3 EFSA, (2014a) (GEM (Greenhouse Emission Model - version 3.3.2))
1 × 2.7 g a.s./ha to strawberries and tomatoes in permanent greenhouses	Low risk at Step 3 EFSA, (2014a) (GEM (Greenhouse Emission Model - version 3.3.2))	Low risk at Step 3 EFSA, (2014a) (GEM (Greenhouse Emission Model - version 3.3.2))

a.s.: active substance; FOCUS: Forum for the Co-ordination of Pesticide Fate Models and their Use.

[16] Experts’ consultation 5.2 of the Report of the Pesticides Peer Review Experts’ Meeting 26 (March 2020).

It should be noted that the risk mitigation measures needed to protect aquatic organisms for uses in walk-in tunnels are greater than the limit of 95% that is recommended by the FOCUS landscape and mitigation guidance (FOCUS, 2007) usually used for risk assessment.

The risk to **algae** from abamectin was assessed to be low for all the representative uses.

Low risk to **sediment-dwelling organisms** from abamectin and the pertinent sediment metabolites was indicated for all the representative uses.

The acute and chronic risk to fish as well as the risk to algae from all the pertinent surface-water metabolites was assessed to be low for all the representative uses. The acute and chronic risk to aquatic invertebrates from the surface-water metabolites of abamectin for all the representative uses, was low at Step 3, except for the metabolite 8-carboxy-6-hydroxy-avermectin B_{1a}. Considering a single application of 2.7 g a.s./ha, to both strawberries and tomatoes, in permanent greenhouses, a low risk for the metabolite 8-carboxy-6-hydroxy-avermectin B_{1a} was concluded. For the uses in walk-in tunnels, low (acute and chronic) risk can be concluded for 8-carboxy-6-hydroxy-avermectin B_{1a} (FOCUS Step 4 (10 m no-spray buffer zone) for the maximum application rates and FOCUS Step 3 for a single application of 2.7 g a.s./ha).

Sufficient acute oral and chronic adult toxicity data were available with adult **honey bees** and abamectin. There were also toxicity data (8 days) on honey bee larvae with the representative formulation. Based on this, and considering additional information, RMS concluded the data requirement to be sufficiently addressed. However, available data were not reliable or sufficient in EFSA view to address effects on larvae development, i.e. 22 days (data gap). Valid data were not available on acute contact toxicity to honey bees (data gap).

The acute oral risk to honeybees in accordance with European Commission (2002a) was high for all representative uses in walk-in tunnels. The risk to honey bees was also assessed in accordance with EFSA (2013), and a high acute oral and chronic risk to and honey bee adults' larvae (chronic oral) was concluded at tier 1 for all representative uses of abamectin in walk-in tunnels.

Available data (i.e. aged residue studies, field study with honey bees and greenhouse study with bumblebee) indicated that toxicity decreases with increasing aging time of residues but were not sufficiently reliable for specifying risk mitigation measures (i.e. waiting periods for opening following application) for the uses in walk-in tunnels.

Data on the assessment of sublethal effects on honeybees (hypopharyngeal glands (HPG)) were not available (data gap).

An assessment of the accumulative effects was not available.

A high acute oral and chronic risk to (adults and larvae) honeybees, on the basis of the screening assessment for exposure to residues of abamectin in guttation fluids, could not be excluded (data gap relevant for all representative uses in walk-in tunnels). A low acute oral and chronic risk to adult honey bees from exposure to residues of abamectin in surface water was indicated. Owing to the data gap for a 22-day larva study, a low chronic risk to honey bee larvae from exposure via surface water was not demonstrated for any of the representative uses. An assessment of the exposure via residues in puddle water was not available. However, considering all the available data and assessments, a high risk to adult honey bees (acute oral and chronic) and to honey bee larvae (chronic) could not be excluded for the puddle scenario (data gap).

Metabolites of abamectin are present in vegetative plant parts mainly on leaves. Toxicity data were not provided to address the risk to bees from exposure to metabolites (data gap). Based on worst-case assumptions and assessment, high risk from exposure of bees to plant metabolites of abamectin could not be excluded.

Standard toxicity data were not available for bumblebees and solitary bees. An extended laboratory study with bumblebees exposed to dry residues of the representative formulation applied as foliar spray to apple leaves addressed only contact toxicity. Although it also showed a decreased mortality with the aging of residues, the study was considered insufficient to exclude risk to beneficial pollinators introduced to permanent greenhouses.

For **non-target terrestrial arthropods** other than bees, extended laboratory studies with fresh and aged residues for the two standard test species *Typhlodromus pyri* and *Aphidius ropalosiphi* and two additional species (*Orius laevigatus* and *Poecilus cupreus*) were available with the representative formulation.

For the uses in walk-in tunnels, the risk assessment for non-target arthropods was assessed in the same manner as would be done for a field use, i.e. a consideration of the risk to in-field and off-field populations of non-target arthropods. On the basis of the available tier 2 risk assessment, the outcome of the in-field and off-field risk assessment us summarised in the Table 3 below.

Table 3: Outcome of the risk assessment for non-target arthropods, other than bees, to abamectin

Representative use	In-field risk	Off-field risk
3 × 18 g a.s./ha to tomatoes in walk-in tunnels	High risk	Crop height < 50 cm: Low risk with mitigation (10 m no-spray buffer zones or 90 % drift-reducing nozzles or closing the tunnels at the time of application). Crop height > 50 cm: High risk unless the tunnels are closed at the time of application.
2 × 18 g a.s./ha to strawberries in walk-in tunnels	High risk	Low risk with mitigation (10 m no-spray buffer zones or 90 % drift-reducing nozzles or closing the tunnels at the time of application)
1 × 2.7 g a.s./ha to strawberries walk-in tunnels	High risk	Low risk
1 × 2.7 g a.s./ha and tomatoes in walk-in tunnels	High risk	Crop height < 50 cm: Low risk Crop height > 50 cm: Low risk with mitigation (5 m no-spray buffer zone, 75 % drift reducing nozzles or closing the tunnels at the time of application)
3 × 18 g a.s./ha to strawberries and tomatoes in permanent greenhouses	Low risk	Low risk
1 × 2.7 g a.s./ha to strawberries and tomatoes in permanent greenhouses	Low risk	Low risk

a.s.: active substance.

For **earthworms** and **other soil macroorganisms**, experimental data were available with the representative formulation and *Eisenia foetida*,[17] *Folsomia candida* and *Hypoaspis aquleifer*. Three chronic earthworm studies were available, however two of them were considered as not reliable.[17] In the third study, effects on reproduction were observed in all tested concentrations meaning that no no observed effect concentration (NOEC) values could be obtained.[17] The risk to earthworm (using the lowest observed effect concentration (LOEC) value) and soil macroorganisms from abamectin was assessed to be high for the representative uses in walk-in tunnels at the maximum application rates (3 × 18 g a.s./ha to tomatoes and 2 × 18 g a.s./ha to strawberries). Suitable higher-tier data or refinements were not available.[17] Considering a single application of 2.7 g a.s./ha a low risk to soil macroorganisms was concluded. Since no NOEC value was obtained in the available chronic earthworm study, a high risk to earthworms could not be excluded[18] (data gap and assessment not finalised).

For the use in walk-in tunnels, there are six soil metabolites for which a risk assessment for soil organisms is needed (8a-hydroxy-avermectin B_{1a}, 8a-oxo-avermectin B_{1a}, 4"-oxo-avermectin B_{1a}, 4,8a-dihydroxy-avermectin B_{1a}, 8a-oxo-4-hydroxy-avermectin B_{1a}, 8-carboxy-6-hydroxy avermectin B_{1a}). There were toxicity data and risk assessment with earthworms and other soil macroorganisms and the metabolite 8a-hydroxy-avermectin B_{1a} that indicated low risk for all representative uses. Toxicity data were not available with the remaining five pertinent soil metabolites of abamectin.

No screening assessment could be performed for earthworms since no NOEC value was obtained in the available chronic earthworm study (data gap and assessment not finalised for uses in walk-in tunnel). The screening assessment for soil macroorganisms (collembolan) did not exclude a risk for the maximum application rate (data gap) but a low risk was concluded for applications of 1 × 2.7 g a.s./ha.

Experimental data were available for the representative formulation with **soil microorganisms** and low risk from abamectin was concluded for the uses in walk-in tunnels. For metabolites, data and risk assessment were available only with the metabolite 8a-hydroxy-avermectin B_{1a} and a low risk was also indicated. No data were available with the remaining pertinent soil metabolites. Based on screening-level assessment, a low risk was indicated, for the use in walk-in tunnels.

For the use to permanent greenhouses, the exposure assessment indicated that there may be exposure to the persistent soil metabolite 8a-oxo-4-hydroxy-avermectin B_{1a} (in the case the greenhouse is removed). A low risk to soil organisms was concluded on the basis of the available assessments.

A vegetative vigour study was available with the representative formulation and the risk to **non-target terrestrial plants** was assessed as low for all the representative uses.

[17] Experts' consultation 5.3 of the Report of the Pesticides Peer Review Experts' Meeting 26 (March 2020).
[18] The TER values for earthworms were higher than the trigger using a LOEC value; hence, this is not considered to show a high risk.

Reliable data were not available with abamectin regarding effects on **biological methods in sewage treatment plants** (data gap relevant for the permanent greenhouses).

6. Endocrine disruption properties

With regard to the assessment of the endocrine disruption potential of abamectin **for humans** according to the ECHA/EFSA guidance (2018), for the T-modality the data set is complete and no adversity has been observed and no T-related endocrine activity has been detected. All the experts agreed that abamectin is not an endocrine disruptor (ED) for the T-modality. Regarding the Estrogen, androgen, steroidogenic (EAS)-modalities, the majority of the experts concluded that based on the lack of adversity in an incomplete data set and lack of endocrine activity in a complete data set, this substance is not ED for the EAS-modalities.

For wild mammals as non-target organisms, the conclusion drawn for humans based on mammalian studies also applies.

For non-target organisms other than mammals, for the T-modality, a level 3 test according to OECD 231 (Amphibian Metamorphosis Assay) was available. No effects were observed on parameters like developmental stage and thyroid histopathology. As a result, the endocrine activity through the T-modality is considered negative and therefore T-mediated adversity is unlikely.

For the EAS-modalities, a Fish Short-Term Reproduction Assay (FSTRA) according to OECD 229 was available. No statistically significant effects were observed in any of the measured parameters. Although the study presented some deficiencies,[19] considering all the available information (i.e. level 2 studies negative, outcome of the ED assessment for humans and mammals) EAS-mediated adversity is considered unlikely based on the lack of endocrine activity through the EAS-modalities.

Based on the available information on humans and non-target organisms, abamectin does not meet the ED criteria according to points 3.6.5 and 3.8.2 of Annex II to Regulation (EC) No 1107/2009.

7. Overview of the risk assessment of compounds listed in residue definitions triggering assessment of effects data for the environmental compartments (Tables 4–7)

Table 4: Soil

Compound (name and/or code)	Persistence	Ecotoxicology
Avermectin B_{1a}	Moderate persistence Single first-order and FOMC DT_{50} 12.4–49.3 days (DT_{90} 52.7 – 164 days, 20°C 40–45% MWHC soil moisture) Very low to low persistence Field dissipation studies single first-order and biphasic kinetics DT_{50} 0.32–1.7 days (DT_{90} 0.86–15.5 days)	High risk to earthworm and collembolan for uses in walk-in tunnels for the maximum application rates. Low risk to other soil macroorganisms (collembolan) for uses in walk-in tunnels (single application of 2.7 g a.s./ha). Data gap for earthworms for uses in walk-in tunnels (single application of 2.7 g a.s./ha).
8a-oxo-avermectin B_{1a} (NOA 448111)	Moderate to medium persistence Single first-order kinetics DT_{50} 43.9–68.4 days (DT_{90} 146 – 237 days, 20°C 40–45% MWHC soil moisture)	Data gap for earthworms (relevant for all representative uses in walk-in tunnels) Data gap for soil macroorganisms (collembolan) for uses in walk-in tunnels (maximum application rates). Low risk to other soil macroorganisms (collembolan) for uses in walk-in tunnels (single application of 2.7 g a.s./ha)
8a-hydroxy-avermectin B_{1a} (NOA 448112)	Moderate persistence Single first-order kinetics DT_{50} 16.9–57.3 days (DT_{90} 56–190 days, 20°C 40–45% MWHC soil moisture)	Low risk to soil organisms for all representative uses

[19] See experts' consultation 5.4 of the report of the Pesticide Peer Review meeting 26.

Compound (name and/or code)	Persistence	Ecotoxicology
4,8-dihydroxy-avermectin B_{1a} (NOA 457464, M6)	Moderate to medium persistence Single first-order kinetics DT_{50} 44.5–74 days (DT_{90} 148–246 days, 20°C 40% MWHC soil moisture)	Data gap for earthworms (relevant for all representative uses in walk-in tunnels) Data gap for soil macroorganisms (collembolan) for uses in walk-in tunnels (maximum application rates). Low risk to other soil macroorganisms (collembolan) for uses in walk-in tunnels (single application of 2.7 g a.s./ha)
8a-oxo-4-hydroxy-avermectin B_{1a} (NOA 457465)	Moderate to high persistence Single first-order kinetics DT_{50} 50.5–181 days (DT_{90} 168–602 days, 20°C 40% MWHC soil moisture)	Data gap for earthworms (relevant for all representative uses in walk-in tunnels) Data gap for soil macroorganisms (collembolan) for uses in walk-in tunnels (maximum application rates). Low risk to other soil macroorganisms (collembolan) for uses in walk-in tunnels (single application of 2.7 g a.s./ha)
4"-oxo-avermectin B_{1a} (NOA 426289)	Low to moderate persistence Single first-order kinetics DT_{50} 5.5–35.0 days (DT_{90} 18.2–116 days, 20°C 45% MWHC soil moisture)	Data gap for earthworms (relevant for all representative uses in walk-in tunnels) Data gap for soil macroorganisms (collembolan) for uses in walk-in tunnels (maximum application rates). Low risk to other soil macroorganisms (collembolan) for uses in walk-in tunnels (single application of 2.7 g a.s./ha)
8-carboxy-6-hydroxy-avermectin B_{1a} (M4)	Moderate persistence Single first-order kinetics DT_{50} 31.3–31.9 days (DT_{90} 104–106 days, 20°C 45% MWHC soil moisture)	Data gap for earthworms (relevant for all representative uses in walk-in tunnels) Data gap for soil macroorganisms (collembolan) for uses in walk-in tunnels (maximum application rates). Low risk to other soil macroorganisms (collembolan) for uses in walk-in tunnels (single application of 2.7 g a.s./ha)

DT_{50}: period required for 50% dissipation: DT_{90}: period required for 90% dissipation; MWHC: maximum water-holding capacity; a.s.: active substance.

Table 5: Groundwater

Compound (name and/or code)	Mobility in soil	> 0.1 µg/L at 1 m depth for the representative uses[(a)]	Pesticidal activity	Toxicological relevance
Avermectin B_{1a}	Immobile K_{FOC} 5701-7893 mL/g	No	Yes	Yes
8a-oxo-avermectin B_{1a} (NOA 448111)	Slight mobile to immobile K_{FOC} 3027-5052 mL/g	No	Assessment not triggered for the representative uses	Not triggered
8a-hydroxy-avermectin B_{1a} (NOA 448112)	Low to slight mobility K_{FOC} 1098-3104 mL/g	No	Assessment not triggered for the representative uses	Not triggered
4,8-dihydroxy-avermectin B_{1a} (NOA 457464, M6)	Low to slight mobility K_{FOC} 1082-2423 mL/g	No	Assessment not triggered for the representative uses	Not triggered
8a-oxo-4-hydroxy-avermectin B_{1a} (NOA 457465)	Slight mobile to immobile K_{FOC} 2573-5813 mL/g	No	Assessment not triggered for the representative uses	Not triggered

Compound (name and/or code)	Mobility in soil	> 0.1 µg/L at 1 m depth for the representative uses[a]	Pesticidal activity	Toxicological relevance
4"-oxo-avermectin B_{1a} (NOA 426289)	Low mobility to immobile K_{FOC} 1427-6142 mL/g	No	Assessment not triggered for the representative uses	Not triggered
8-carboxy-6-hydroxy-avermectin B_{1a} (M4)	Data gap	No	Assessment not triggered for the representative uses	Not triggered

K_{FOC}: Freundlich organic carbon adsorption coefficient.
(a): FOCUS scenarios or a relevant lysimeter.

Table 6: Surface water and sediment

Cozpound (name and/or code)	Ecotoxicology
Avermectin B_{1a}	High risk, with risk mitigation reducing spray drift by 95%, to aquatic invertebrates (maximum application rates in walk-in tunnels)[a] High risk, with risk mitigation reducing spray drift by 95%, to aquatic invertebrates (1 × 2.7 g a.s./ha in walk-in tunnels[b] High risk to aquatic invertebrates (maximum application rates in permanent greenhouse) Low risk to aquatic invertebrates (1 × 2.7 g a.s./ha in permanent greenhouse) Low risk to fish (acute), algae, and sediment-dwelling organisms (all uses) Low chronic risk to fish in permanent greenhouse and with mitigation for the walk-in tunnels uses
8a-oxo-Avermectin B_{1a} (NOA448111) (soil, water/sediment)	Low risk to fish, aquatic invertebrates, algae, and sediment-dwelling organisms (all uses)
8a-hydroxy-Avermectin B_{1a} (NOA448112) (soil, water/sediment)	Low risk to fish, aquatic invertebrates, algae, and sediment-dwelling organisms (all uses)
4,8-dihydroxy-Avermectin B_{1a} (NOA457464, M6) (soil)	Low risk to fish, aquatic invertebrates, algae, and sediment-dwelling organisms (all uses)
8a-oxo-4-hydroxy-Avermectin B_{1a} (NOA457465) (soil)	Low risk to fish, aquatic invertebrates, algae, and sediment-dwelling organisms (all uses)
4"-oxo-Avermectin B_{1a} (NOA426289) (soil, water/sediment)	Low risk to fish, aquatic invertebrates, algae, and sediment-dwelling organisms (all uses)
8-carboxy-6-hydroxy-Avermectin B_{1a} (M4) (soil)	Low risk to aquatic invertebrates (1 × 2.7 g a.s./ha in permanent greenhouse) Low risk with mitigation to aquatic invertebrates for uses in walk-in tunnels (maximum application rates) Low risk to aquatic invertebrates for uses in walk-in tunnels (1 × 2.7 g a.s./ha) Low risk to fish, algae, and sediment-dwelling organisms (all uses)

a.s.: active substance.
(a): Low risk would only be indicated if a drift reduction > 99.4% could be achieved, if this might be achieved in practice is uncertain.
(b): Low risk only indicated with a combination a 20 m spray drift buffer zone with 50% drift reduction nozzle which numerically was calculated to represent a 96.26% drift reduction, if this might be achieved in practice is uncertain.

Table 7: Air

Compound (name and/or code)	Toxicology
Abamectin	LC_{50} less than 0.21 mg/L

LC_{50}: lethal concentration, median.

8. Data gaps

This is a list of data gaps identified during the peer review process, including those areas in which a study may have been made available during the peer review process but not considered for procedural reasons (without prejudice to the provisions of Article 56 of Regulation (EC) No 1107/2009 concerning information on potentially harmful effects).

- A search of the scientific peer-reviewed open literature on the active substance and its relevant metabolites, dealing with side effects on health and published within the 10 years before the date of submission of the dossier, to be conducted and reported in accordance with EFSA guidance on the submission of scientific peer-reviewed open literature for the approval of pesticide active substances under Regulation (EC) No 1107/2009 (EFSA, 2011; relevant for all representative uses evaluated).
- Determination of the emulsion stability of the representative formulation according to MT 36.3 (relevant for all representative uses evaluated; see Section 1).
- Analytical method for the enforcement of the relevant limits based on the lowest effect concentrations for aquatic invertebrates (relevant for all representative uses evaluated; see Sections 1 and 5).
- Toxicological assessment of abamectin aneugenicity potential (relevant for all representative uses evaluated; see Section 2).
- Toxicological assessment of aneugenicity potential of [8,9-*Z*]-isomer of avermectin B1, 24-hydroxymethyl-avermectin B1 and monosaccharide of avermectin B1 [NOA 419150] metabolites (relevant for all representative uses evaluated; see Section 2).
- In order to cover the most critical situation for the consumer exposure assessment, 4 additional residue trials on tomatoes and 4 additional residue trials on strawberries compliant with the NEU GAP (relevant for all representative uses in NEU; see Section 3).
- An aerobic soil degradation study to address the degradation rate of metabolite 4”-oxo-avermectin B_{1a} (NOA 426289) in one additional soil (relevant for all representative uses evaluated; see Section 4).
- Field dissipation studies measuring metabolites 8a-oxo-avermectin B_{1a} (NOA 448111), 4,8a-dihydroxy-avermectin B_{1a} (NOA 457464) and 4-hydroxy-8a-oxo-avermectin B_{1a} (NOA 457465) in two field trial sites (relevant for all representative uses evaluated; see Section 4).
- A batch sorption study to address the adsorption of metabolite 8-carboxy-6-hydroxy-avermectin B_{1a} (M4) in at least 3 soils (relevant for all representative uses evaluated; see Section 4).
- The effect of water treatment processes on the nature of residues present in surface, when surface water is abstracted for drinking water (Article 4 (approval criteria for active substances) 3. (b) of Regulation (EC) No 1107/2009) has not been assessed (relevant for all representative uses evaluated; see Section 4).
- A proper summary and evaluation of the study by Stamm (1998) in reference to Austria, 2020 and more information on the transport via air were not provided in the amended RAR (data gap not relevant to finalise the risk assessment for the representative uses; see Section 4, Open point 4.48 in Evaluation table (EFSA, 2020b)).
- Data to address the risk to earthworm-eating birds and mammals from the metabolite 4”-oxo-avermectin B_{1a} (relevant for all representative uses in walk-in tunnels evaluated; see Section 5).
- Data to address the risk to birds and mammals from plant metabolites (relevant for the representative uses in walk-in tunnels evaluated; see Section 5).
- Data to address the risk to honey bee larvae (relevant for the representative uses in walk-in tunnels evaluated; see Section 5).
- Data on acute contact toxicity to honey bees (relevant for the representative uses in walk-in tunnels evaluated; see Section 5).
- Data on the assessment of sublethal effects on honey bees (hypopharyngeal glands (HPG)) (relevant for the representative uses in walk-in tunnels evaluated; see Section 5).
- Data to address the risk to bees from exposure to metabolites (relevant for the representative uses in walk-in tunnels evaluated; see Section 5).
- Data to address the risk to bees from exposure to guttation fluid and puddle water (relevant for the representative uses in walk-in tunnels evaluated; see Section 5).

- Data to address the risk to earthworms from abamectin (relevant for single application of 2.7 g a.s./ha in walk-in tunnels; see Section 5).
- Data to address the risk to earthworms from the pertinent soil metabolites: 8a-oxo-avermectin B_{1a}, 4″-oxo-avermectin B_{1a}, 4,8a-dihydroxy-avermectin B_{1a}, 8a-oxo-4-hydroxy-avermectin B_{1a}, 8-carboxy-6-hydroxy avermectin B_{1a} (relevant for all representative uses in walk-in tunnels evaluated; see Section 5).
- Data to address the risk to other soil macroorganisms (collembolan) from the pertinent soil metabolites: 8a-oxo-avermectin B_{1a}, 4″-oxo-avermectin B_{1a}, 4,8a-dihydroxy-avermectin B_{1a}, 8a-oxo-4-hydroxy-avermectin B_{1a}, 8-carboxy-6-hydroxy avermectin B_{1a} (relevant for the maximum application rates of the representative uses in walk-in tunnels evaluated; see Section 5).
- Data on effects on biological methods in sewage treatment plants (relevant for the representative uses in permanent greenhouses evaluated; see Section 5).

9. Particular conditions proposed to be taken into account to manage the risk(s) identified

- Use of gloves by workers during re-entry activities is necessary to have exposure estimates below the AOEL (see Section 2).
- A particular condition of use to apply only within the period of March to October is proposed. In addition, until the data gap for additional residue trials performed under NEU conditions is fulfilled, the use is proposed to be restricted to SEU (see Section 3).

10. Concerns

10.1. Issues that could not be finalised

An issue is listed as 'could not be finalised' if there is not enough information available to perform an assessment, even at the lowest tier level, for the representative uses in line with the uniform principles in accordance with Article 29(6) of Regulation (EC) No 1107/2009 and as set out in Commission Regulation (EU) No 546/2011[20] and if the issue is of such importance that it could, when finalised, become a concern (which would also be listed as a critical area of concern if it is of relevance to all representative uses).

An issue is also listed as 'could not be finalised' if the available information is considered insufficient to conclude on whether the active substance can be expected to meet the approval criteria provided for in Article 4 of Regulation (EC) No 1107/2009.

Consumer risk assessment not finalised as appropriate information to address the effect of water treatments processes on the nature of the residues that might be present in surface water, when surface water is abstracted for drinking water, is missing (see Sections 3 and 4).

Consumer risk assessment not finalised for uses in NEU (see Section 3).

The risk assessment for earthworms could not be finalised for the use to strawberries and tomatoes in walk-in tunnels at 1 × 2.7 g a.s./ha (see Section 5).

10.2. Critical areas of concern

An issue is listed as a critical area of concern if there is enough information available to perform an assessment for the representative uses in line with the uniform principles in accordance with Article 29(6) of Regulation (EC) No 1107/2009 and as set out in Commission Regulation (EU) No 546/2011, and if this assessment does not permit the conclusion that, for at least one of the representative uses, it may be expected that a plant protection product containing the active substance will not have any harmful effect on human or animal health or on groundwater, or any unacceptable influence on the environment.

An issue is also listed as a critical area of concern if the assessment at a higher tier level could not be finalised due to lack of information, and if the assessment performed at the lower tier level does not permit the conclusion that, for at least one of the representative uses, it may be expected that a

[20] Commission Regulation (EU) No 546/2011 of 10 June 2011 implementing Regulation (EC) No 1107/2009 of the European Parliament and of the Council as regards uniform principles for evaluation and authorisation of plant protection products. OJ L 155, 11.6.2011, p. 127–175.

plant protection product containing the active substance will not have any harmful effect on human or animal health or on groundwater, or any unacceptable influence on the environment.

An issue is also listed as a critical area of concern if, in the light of current scientific and technical knowledge using guidance documents available at the time of application, the active substance is not expected to meet the approval criteria provided for in Article 4 of Regulation (EC) No 1107/2009.

Critical areas of concern were not identified, since at least one safe use has been detected for each group of non-target organisms.

10.3. Overview of the concerns identified for each representative use considered (Table 8)

(If a particular condition proposed to be taken into account to manage an identified risk, as listed in Section 8, has been evaluated as being effective, then 'risk identified' is not indicated in Table 8)

Table 8: Overview of concerns

Representative use		Use on tomato (3 ×) and strawberry (2 ×) in walk in tunnels Maximum application rate (18 g a.s./ha)	Use on tomato and strawberry in walk in tunnels (1 × 2.7 g a.s./ha)	Use on tomato (3 ×) and strawberry (2 ×) in permanent greenhouses Maximum application rate (18 g a.s./ha)	Use on tomato and strawberry in permanent greenhouses (1 × 2.7 g a.s./ha)
Operator risk	Risk identified				
	Assessment not finalised				
Worker risk	Risk identified				
	Assessment not finalised				
Resident/bystander risk	Risk identified				
	Assessment not finalised				
Consumer risk	Risk identified				
	Assessment not finalised	X[1,2]*	X[1,2]*	X[1,2]*	X[1,2]*
Risk to wild non-target terrestrial vertebrates	Risk identified	X	X[(e)]		
	Assessment not finalised				
Risk to wild non-target terrestrial organisms other than vertebrates	Risk identified	X[(g)]	X[(h)]		
	Assessment not finalised		X[3]		
Risk to aquatic organisms	Risk identified	X[(d)]	X[(c)]	X[(f)]	
	Assessment not finalised				
Groundwater exposure to active substance	Legal parametric value breached				
	Assessment not finalised				
Groundwater exposure to metabolites	Legal parametric value breached[(a)]				
	Parametric value of 10 µg/L[(b)] breached				
	Assessment not finalised				

a.s.: active substance.
The superscript numbers relate to the numbered points indicated in Sections 10.1 and 10.2. Where there is no superscript number, see Sections 2–7 for further information.
*: the superscript '2' refers only to assessment not finalised of NEU uses meaning that for SEU uses, the assessment is finalised (with respect to residue in crops, only drinking water pending).
(a): When the consideration for classification made in the context of this evaluation under Regulation (EC) No 1107/2009 is confirmed under Regulation (EC) No 1272/2008 of the European Parliament and of the Council of 16 December 2008.
(b): Value for non-relevant metabolites prescribed in SANCO/221/2000-rev. 10 final, European Commission (2003).
(c): Low risk only indicated with a combination a 20m spray drift buffer zone with 50% drift-reduction nozzle which numerically was calculated to represent a 96.26% drift reduction, if this might be achieved in practice is uncertain.
(d): Low risk would only be indicated if a drift reduction > 99.4% could be achieved, if this might be achieved in practice is uncertain.
(e): Reliable refinements were not available to resolve the reproductive risk to mammals nor to perform a tier 1 risk assessment for earthworm-eating birds and mammals for metabolite 4"-oxo-avermectin B_{1a}.
(f): High risk at Step 3 EFSA (2014a) scenario (GEM (Greenhouse Emission Model - version 3.3.2)).
(g): High risk to honey bees; high in-field risk to NTAs and macroorganisms.
(h): High risk to honey bees for abamectin and high in-field risk to NTAs.

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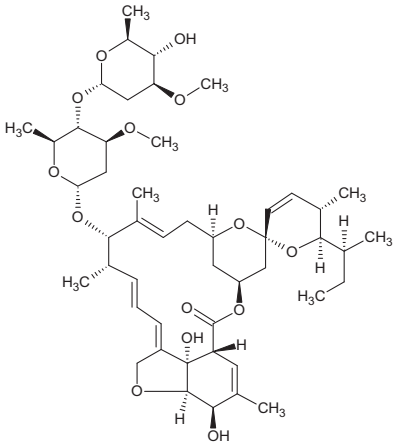
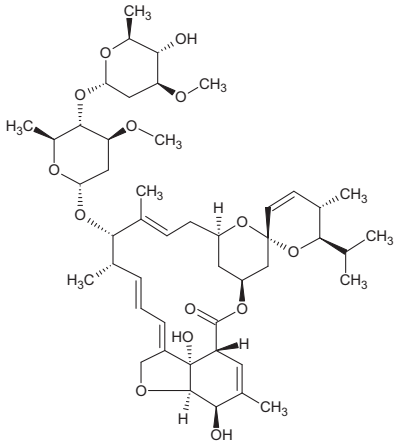
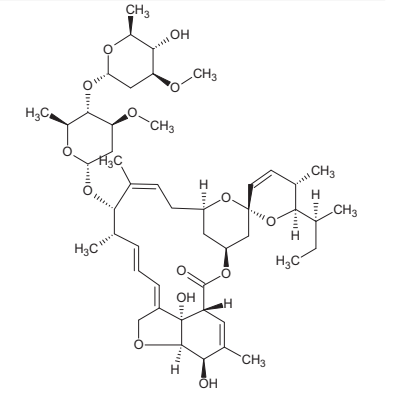
Abbreviations

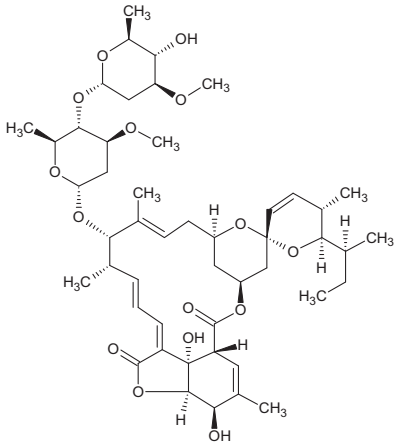
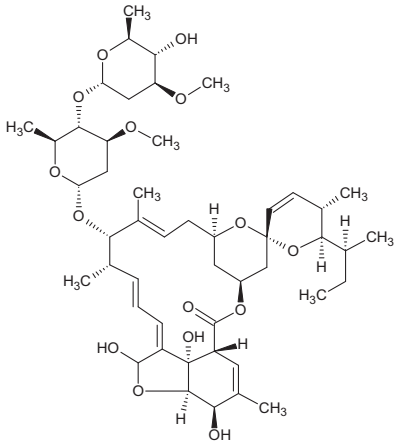
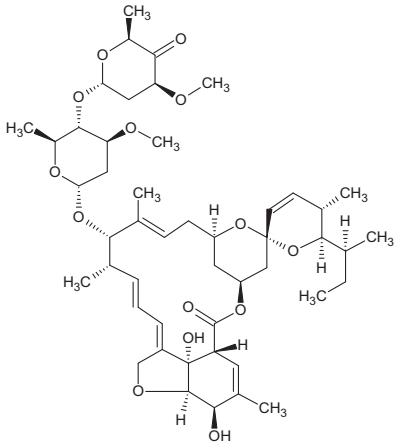
a.s.	active substance
AAOEL	acute acceptable operator exposure level
ADI	acceptable daily intake
AOEL	acceptable operator exposure level
AR	applied radioactivity
ARfD	acute reference dose
bw	body weight
CNS	central nervous system
DT_{50}	period required for 50% dissipation (define method of estimation)
DT_{90}	period required for 90% dissipation (define method of estimation)
EAS	Estrogen, androgen, steroidogenic
ECHA	European Chemicals Agency
ECPA	European Crop Protection Association
EEC	European Economic Community
ED	endocrine disruptor
FAO	Food and Agriculture Organization of the United Nations
FOCUS	Forum for the Co-ordination of Pesticide Fate Models and their Use
FSTRA	Fish Short-Term Reproduction Assay
GAP	Good Agricultural Practice
GEM	Greenhouse Emission Model
HPLC–MS/MS	high-pressure liquid chromatography with tandem mass spectrometry
HPG	hypopharyngeal glands
HR	hazard rate
InChiKey	International Chemical Identifier Key
ISO	International Organization for Standardization
IUPAC	International Union of Pure and Applied Chemistry
JMPR	Joint Meeting of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Expert Group on Pesticide Residues (Joint Meeting on Pesticide Residues)
K_{FOC}	Freundlich organic carbon adsorption coefficient
LC_{50}	lethal concentration, median
LD_{50}	lethal dose, median; dosis letalis media
LOAEL	lowest observable adverse effect level
LOEC	lowest observed effect concentration
LoEP	List of end points
LOQ	limit of quantification
MRL	maximum residue level
MTD	maximum tolerated dose
MWHC	maximum water-holding capacity
NEU	northern Europe
NOAEL	no observed adverse effect level
NOEC	no observed effect concentration
OECD	Organisation for Economic Co-operation and Development
PEC	predicted environmental concentration
QC	quality control
QSAR	quantitative structure–activity relationship
RAR	Renewal Assessment Report
RMM	risk mitigation measure
SEU	southern Europe
SMILES	simplified molecular-input line-entry system
STMR	supervised trials median residue
WHO	World Health Organization

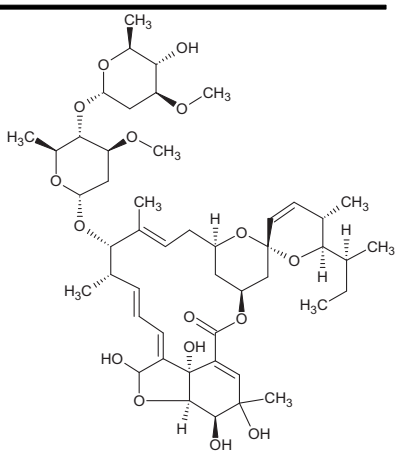
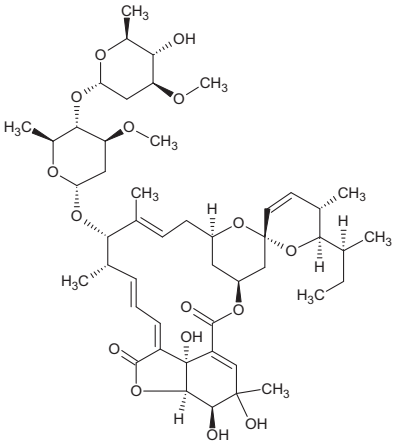
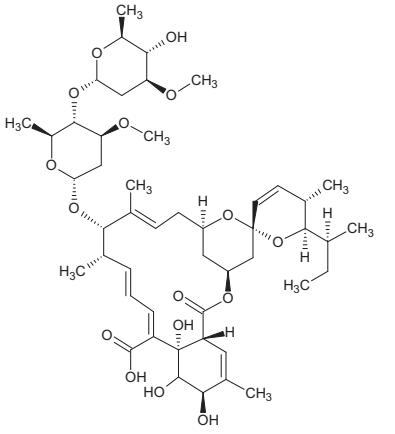
Appendix A – List of end points for the active substance and the representative formulation

Appendix A can be found in the online version of this output ('Supporting information' section): https://doi.org/10.2903/j.efsa.2022.7544

Appendix B – Used compound codes

Code/trivial name[a]	IUPAC name/SMILES notation/InChiKey[b]	Structural formula[c]
avermectin B_{1a}	(10*E*,14*E*,16*E*)-(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 CO[C@H]1C[C@@H](O[C@@H](C)[C@@H]1O)O[C@@H]1[C@@H](OC)C[C@@H](O[C@H]1C)O[C@@H]1C(C)=CC[C@@H]2C[C@H](OC(=O)[C@@H]3C=C(C)[C@@H](O)[C@H]4OCC(=CC=C[C@@H]1C)[C@@]34O)C[C@@]1(O2)C=C[C@H](C)[C@H](O1)[C@@H](C)CC RRZXIRBKKLTSOM-XPNPUAGNSA-N	
avermectin B_{1b}	(10*E*,14*E*,16*E*)-(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 CO[C@H]1C[C@@H](O[C@@H](C)[C@@H]1O)O[C@@H]1[C@@H](OC)C[C@@H](O[C@H]1C)O[C@@H]1C(C)=CC[C@@H]2C[C@H](OC(=O)[C@@H]3C=C(C)[C@@H](O)[C@H]4OCC(=CC=C[C@@H]1C)[C@@]34O)C[C@@]1(O2)C=C[C@H](C)[C@H](O1)C(C)C ZFUKERYTFURFGA-PVVXTEPVSA-N	
[8,9-Z]-isomer of avermectin B_{1a} (NOA427011)	[2′*S*,2a(3)*E*,4*E*,5′*S*,6*S*,6′*R*,7*S*,8*Z*,11*R*,15*S*,17a*R*,20*R*,20a*R*,20b*S*]-6′-[(2*S*)-butan-2-yl]-20,20b-dihydroxy-5′,6,8,19-tetramethyl-17-oxo-5′,6,6′,10,11,14,15,17,17a,20,20a,20b-dodecahydro-2*H*,7*H*-spiro[11,15-methanofuro[4,3,2-*pq*][2,6]benzodioxacyclooctadecine-13,2′-pyran]-7-yl 2,6-dideoxy-4-*O*-(2,6-dideoxy-3-*O*-methyl-α-L-*arabino*-hexopyranosyl)-3-*O*-methyl-α-L-*arabino*-hexopyranoside CO[C@H]1C[C@@H](O[C@@H](C)[C@@H]1O)O[C@@H]1[C@@H](OC)C[C@@H](O[C@H]1C)O[C@@H]1C(C)=CC[C@@H]2C[C@H](OC(=O)[C@@H]3C=C(C)[C@@H](O)[C@H]4OCC(=CC=C[C@@H]1C)[C@@]34O)C[C@@]1(O2)C=C[C@H](C)[C@H](O1)[C@@H](C)CC RRZXIRBKKLTSOM-RVQYPMJNSA-N	

Code/trivial name[a]	IUPAC name/SMILES notation/InChiKey[b]	Structural formula[c]
8a-oxo-avermectin B_{1a} (NOA448111)	[2′*S*,2a(3)*Z*,4*E*,5′*S*,6*S*,6′*R*,7*S*,8*E*,11*R*,15*S*,17a*R*,20*R*,20a*R*,20b*S*]-6′-[(2*S*)-butan-2-yl]-20,20b-dihydroxy-5′,6,8,19-tetramethyl-2,17-dioxo-5′,6,6′,10,11,14,15,17,17a,20,20a,20b-dodecahydro-2*H*,7*H*-spiro[11,15-methanofuro[4,3,2-*pq*][2,6]benzodioxacyclooctadecine-13,2′-pyran]-7-yl 2,6-dideoxy-4-*O*-(2,6-dideoxy-3-*O*-methyl-α-L-*arabino*-hexopyranosyl)-3-*O*-methyl-α-L-*arabino*-hexopyranoside CO[C@H]1C[C@@H](O[C@@H](C)[C@@H]1O)O[C@@H]1[C@@H](OC)C[C@@H](O[C@H]1C)O[C@@H]1C(C)=CC[C@@H]2C[C@H](OC(=O)[C@@H]3C=C(C)[C@@H](O)[C@H]4OC(=O)C(=CC=C[C@@H]1C)[C@@]34O)C[C@@]1(O2)C=C[C@H](C)[C@H](O1)[C@@H](C)CC XDZJLYBYTBXNKA-NZWFHOADSA-N	
8a-hydroxy-avermectin B_{1a} (NOA448112),	[2′*S*,2a(3)*Z*,4*E*,5′*S*,6*S*,6′*R*,7*S*,8*E*,11*R*,15*S*,17a*R*,20*R*,20a*R*,20b*S*]-6′-[(2*S*)-butan-2-yl]-2,20,20b-trihydroxy-5′,6,8,19-tetramethyl-17-oxo-5′,6,6′,10,11,14,15,17,17a,20,20a,20b-dodecahydro-2*H*,7*H*-spiro[11,15-methanofuro[4,3,2-*pq*][2,6]benzodioxacyclooctadecine-13,2′-pyran]-7-yl 2,6-dideoxy-4-*O*-(2,6-dideoxy-3-*O*-methyl-α-L-*arabino*-hexopyranosyl)-3-*O*-methyl-α-L-*arabino*-hexopyranoside CO[C@H]1C[C@@H](O[C@@H](C)[C@@H]1O)O[C@@H]1[C@@H](OC)C[C@@H](O[C@H]1C)O[C@@H]1C(C)=CC[C@@H]2C[C@H](OC(=O)[C@@H]3C=C(C)[C@@H](O)[C@H]4OC(O)C(=CC=C[C@@H]1C)[C@@]34O)C[C@@]1(O2)C=C[C@H](C)[C@H](O1)[C@@H](C)CC ORIHAMOZRDYFCM-UIPRHDOASA-N	
4″-oxo-avermectin B_{1a} (NOA426289),	[2′*S*,2a(3)*E*,4*E*,5′*S*,6*S*,6′*R*,7*S*,8*E*,11*R*,15*S*,17a*R*,20*R*,20a*R*,20b*S*]-6′-[(2*S*)-butan-2-yl]-20,20b-dihydroxy-5′,6,8,19-tetramethyl-17-oxo-5′,6,6′,10,11,14,15,17,17a,20,20a,20b-dodecahydro-2*H*,7*H*-spiro[11,15-methanofuro[4,3,2-*pq*][2,6]benzodioxacyclooctadecine-13,2′-pyran]-7-yl 2,6-dideoxy-4-*O*-(2,6-dideoxy-3-*O*-methyl-α-L-*threo*-hexopyranosyl-4-ulose)-3-*O*-methyl-α-L-*arabino*-hexopyranoside CO[C@H]1C[C@@H](O[C@@H](C)C1=O)O[C@@H]1[C@@H](OC)C[C@@H](O[C@H]1C)O[C@@H]1C(C)=CC[C@@H]2C[C@H](OC(=O)[C@@H]3C=C(C)[C@@H](O)[C@H]4OCC(=CC=C[C@@H]1C)[C@@]34O)C[C@@]1(O2)C=C[C@H](C)[C@H](O1)[C@@H](C)CC GPAWMCYJUHBIBY-JMQJWMQBSA-N	

Code/trivial name[a]	IUPAC name/SMILES notation/InChiKey[b]	Structural formula[c]
4,8a-dihydroxy-avermectin B_{1a} (NOA457464)	[2′*S*,2a(3)*Z*,4*E*,5′*S*,6*S*,6′*R*,7*S*,8*E*,11*R*,15*S*,20*S*,20a*R*,20b*R*]-6′-[(2*S*)-butan-2-yl]-2,19,20,20b-tetrahydroxy-5′,6,8,19-tetramethyl-17-oxo-5′,6,6′,10,11,14,15,17,19,20,20a,20b-dodecahydro-2*H*,7*H*-spiro[11,15-methanofuro[4,3,2-*pq*][2,6]benzodioxacyclooctadecine-13,2′-pyran]-7-yl 2,6-dideoxy-4-*O*-(2,6-dideoxy-3-*O*-methyl-α-L-*arabino*-hexopyranosyl)-3-*O*-methyl-α-L-*arabino*-hexopyranoside CO[C@H]1C[C@@H](O[C@@H](C)[C@@H]1O)O[C@@H]1[C@@H](OC)C[C@@H](O[C@H]1C)O[C@@H]1C(C)=CC[C@@H]2C[C@H](OC(=O)C3=CC(C)(O)[C@@H](O)[C@H]4OC(O)C(=CC=C[C@@H]1C)[C@@]34O)C[C@@]1(O2)C=C[C@H](C)[C@H](O1)[C@@H](C)CC OMBXABPRGJUCIC-LJCFFTHASA-N	
8a-oxo-4-hydroxy-avermectin B_{1a} (NOA457465)	[2′*S*,2a(3)*Z*,4*E*,5′*S*,6*S*,6′*R*,7*S*,8*E*,11*R*,15*S*,20*S*,20a*R*,20b*R*]-6′-[(2*S*)-butan-2-yl]-19,20,20b-trihydroxy-5′,6,8,19-tetramethyl-2,17-dioxo-5′,6,6′,10,11,14,15,17,19,20,20a,20b-dodecahydro-2*H*,7*H*-spiro[11,15-methanofuro[4,3,2-*pq*][2,6]benzodioxacyclooctadecine-13,2′-pyran]-7-yl 2,6-dideoxy-4-*O*-(2,6-dideoxy-3-*O*-methyl-α-L-*arabino*-hexopyranosyl)-3-*O*-methyl-α-L-*arabino*-hexopyranoside CO[C@H]1C[C@@H](O[C@@H](C)[C@@H]1O)O[C@@H]1[C@@H](OC)C[C@@H](O[C@H]1C)O[C@@H]1C(C)=CC[C@@H]2C[C@H](OC(=O)C3=CC(C)(O)[C@@H](O)[C@H]4OC(=O)C(=CC=C[C@@H]1C)[C@@]34O)C[C@@]1(O2)C=C[C@H](C)[C@H](O1)[C@@H](C)CC ZYBQZTRBRQQAOX-ISFARDRNSA-N	
8-carboxy-6-hydroxy-avermectin B_{1a} (M4)	(2′*S*,3*S*,5′*S*,6′*R*,7*R*,9*E*,11*S*,12*S*,13*E*,15*Z*,16a*S*,18*R*,20a*R*)-6′-[(2*S*)-butan-2-yl]-11-{[2,6-dideoxy-4-*O*-(2,6-dideoxy-3-*O*-methyl-α-L-*arabino*-hexopyranosyl)-3-*O*-methyl-α-L-*arabino*-hexopyranosyl]oxy}-16a,17,18-trihydroxy-5′,10,12,19-tetramethyl-1-oxo-3,4,5′,6′,7,8,11,12,16a,17,18,20a-dodecahydro-1*H*-spiro[3,7-methano[2,6]benzodioxacyclooctadecine-5,2′-pyran]-16-carboxylic acid CO[C@H]1C[C@@H](O[C@@H](C)[C@@H]1O)O[C@@H]1[C@@H](OC)C[C@@H](O[C@H]1C)O[C@H]1[C@@H](C)C=CC=C(C(=O)O)[C@@]2(O)[C@@H](C=C(C)[C@@H](O)C2O)C(=O)O[C@H]2C[C@H](O[C@]3(C2)C=C[C@H](C)[C@H](O3)[C@@H](C)CC)CC=C1C IPJDARSZWCALRL-DSJCMUTNSA-N	

IUPAC: International Union of Pure and Applied Chemistry; SMILES: simplified molecular-input line-entry system; InChiKey: International Chemical Identifier Key.
(a): The metabolite name in bold is the name used in the conclusion.
(b): ACD/Name 2019.1.1 ACD/Labs 2019 Release (File version N05E41, Build 110555, 18 July 2019).
(c): ACD/ChemSketch 2019.1.1 ACD/Labs 2019 Release (File version C05H41, Build 110712, 24 July 2019).