Peer review of the pesticide risk assessment of the active substances *Pepino Mosaic Virus*, EU strain, mild isolate Abp1 and *Pepino Mosaic Virus*, CH2 strain, mild isolate Abp2

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Abstract

The conclusions of the EFSA following the peer review of the initial risk assessments carried out by the competent authority of the rapporteur Member State, Spain, for the pesticide active substances *Pepino Mosaic Virus*, EU strain, mild isolate Abp1 and *Pepino Mosaic Virus*, CH2 strain, mild isolate Abp2 and the considerations as regards the inclusion of the substances in Annex IV of Regulation (EC) No 396/2005 are reported. The context of the peer review was that required by Regulation (EC) No 1107/2009 of the European Parliament and of the Council. The conclusions were reached on the basis of the evaluation of the representative use of *Pepino Mosaic Virus*, EU strain, mild isolate Abp1 and *Pepino Mosaic Virus*, CH2 strain, mild isolate Abp2 as an elicitor on tomato (permanent greenhouse production systems). The reliable endpoints, appropriate for use in regulatory risk assessment, are presented. Missing information identified as being required by the regulatory framework is listed.

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Summary

*Pepino Mosaic Virus*, EU strain, mild isolate Abp1 and *Pepino Mosaic Virus*, CH2 strain, mild isolate Abp2 are new active substances for which, in accordance with Article 7 of Regulation (EC) No 1107/2009 of the European Parliament and of the Council, the rapporteur Member State (RMS), Spain, received an application from Abiopep Plant Health S.L. on 27 November 2017 for approval. Complying with Article 9 of the Regulation, the completeness of the dossier was checked by the RMS and the date of admissibility of the application was recognised as being 15 February 2018.

An initial evaluation of the dossier on *Pepino Mosaic Virus*, EU strain, mild isolate Abp1 and *Pepino Mosaic Virus*, CH2 strain, mild isolate Abp2 was provided by the RMS in the draft assessment report (DAR) and subsequently, a peer review of the pesticide risk assessment on the RMS evaluation was conducted by EFSA in accordance with Article 12 of Regulation (EC) No 1107/2009. The following conclusions are derived.

The uses of *Pepino Mosaic Virus*, EU strain, mild isolate Abp1 and *Pepino Mosaic Virus*, CH2 strain, mild isolate Abp2 according to the representative uses as an elicitor in permanent greenhouse tomato production systems, as proposed at EU level, result in a sufficient efficacy against the infection of aggressive PepMV isolates.

The assessment of the data package revealed no issues that need to be included as critical areas of concern with respect to the identity of the microorganism/biological properties/physical and technical properties of the representative formulation.

Critical areas of concern on mammalian toxicology were not identified.

*Pepino Mosaic Virus*, EU strain, mild isolate Abp1 and *Pepino Mosaic Virus*, CH2 strain, mild isolate Abp2 are candidates for inclusion in Annex IV to Regulation (EC) 396/2005 and no maximum residue level (MRL) is needed. Since the product contains nicotine as an impurity, consumers may be exposed to non-viable residues. The consumer risk assessment for estimated nicotine residues related to the representative use alone did not lead to an exceedance of the toxicological reference values for nicotine. A risk assessment considering exposure to nicotine from other dietary sources was not conducted in the remit of the peer review.

Regarding fate, for the representative uses in permanent greenhouses *Pepino Mosaic Virus*, EU strain, mild isolate Abp1 and *Pepino Mosaic Virus*, CH2 strain, mild isolate Abp2 are not expected to persist above natural background levels in soil and in surface water, taking into account repeated applications over the years. Contamination of groundwater with nicotine at levels above 0.1 µg/L are not expected as a result of the proposed uses of *Pepino Mosaic Virus*, EU strain, mild isolate Abp1 and *Pepino Mosaic Virus*, CH2 strain, mild isolate Abp2.

Low risk is identified for all representative uses in permanent greenhouses as the exposure to non-target terrestrial organisms is expected to be negligible. Based on the available information, a low risk to aquatic organisms was also concluded for all representative uses in permanent greenhouses.
Background

Regulation (EC) No 1107/2009 of the European Parliament and of the Council1 (hereinafter referred to as 'the Regulation') lays down, inter alia, the detailed rules as regards the procedure and conditions for approval of active substances. This regulates for the European Food Safety Authority (EFSA) the procedure for organising the consultation of Member States and the applicant(s) for comments on the initial evaluation in the draft assessment report (DAR), provided by the rapporteur Member State (RMS), and the organisation of an expert consultation, where appropriate.

In accordance with Article 12 of the Regulation, EFSA is required to adopt a conclusion on whether an active substance can be expected to meet the approval criteria provided for in Article 4 of the Regulation (also taking into consideration recital (10) of the Regulation) within 120 days from the end of the period provided for the submission of written comments, subject to an extension of 30 days where an expert consultation is necessary, and a further extension of up to 150 days where additional information is required to be submitted by the applicant(s) in accordance with Article 12(3).

*Pepino Mosaic Virus*, EU strain, mild isolate Abp1 and *Pepino Mosaic Virus, CH2 strain, mild isolate Abp2* are new active substances for which, in accordance with Article 7 of the Regulation, the RMS, Spain (hereinafter referred to as the ‘RMS’), received an application from Abiopep Plant Health S.L. on 27 November 2017 for approval of the active substances *Pepino Mosaic Virus*, EU strain, mild isolate Abp1 and *Pepino Mosaic Virus, CH2 strain, mild isolate Abp2*. Complying with Article 9 of the Regulation, the completeness of the dossier was checked by the RMS and the date of admissibility of the application was recognised as being 15 February 2018.

The RMS provided its initial evaluation of the dossier on *Pepino Mosaic Virus, EU strain, mild isolate Abp1* and *Pepino Mosaic Virus, CH2 strain, mild isolate Abp2* in the DAR, which was received by EFSA on 22 July 2019 (Spain, 2019). The peer review was initiated on 22 October 2019 by dispatching the DAR for consultation of the Member States and the applicant, Abiopep Plant Health S.L., for consultation and comments. EFSA also provided comments. In addition, EFSA conducted a public consultation on the DAR. The comments received were collated by EFSA and forwarded to the RMS for compilation and evaluation in the format of a reporting table. The applicant was invited to respond to the comments in column 3 of the reporting table. The comments and the applicant’s 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 applicant in accordance with Article 12(3) of the Regulation were considered in a telephone conference between EFSA and the RMS on 6 February 2020. On the basis of the comments received, the applicant’s response to the comments and the RMS’s evaluation thereof, it was concluded that additional information should be requested from the applicant, and that EFSA should conduct an expert consultation in the area of effects on human health.

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.

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.

In accordance with Article 12 of the Regulation, EFSA should adopt a conclusion on whether *Pepino Mosaic Virus, EU strain, mild isolate Abp1* and *Pepino Mosaic Virus, CH2 strain, mild isolate Abp2* can be expected to meet the approval criteria provided for in Article 4 of the Regulation, taking into consideration recital (10) of the Regulation.

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 November 2020.

This conclusion report summarises the outcome of the peer review of the risk assessment on the active substances and the representative formulation evaluated on the basis of the representative use of *Pepino Mosaic Virus*, EU strain, mild isolate Abp1 and *Pepino Mosaic Virus, CH2 strain, mild isolate Abp2* as elicitor on tomato (permanent greenhouse production systems) as proposed by the applicant.

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1 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.
In accordance with Article 12(2) of Regulation (EC) No 1107/2009, risk mitigation options identified in the DAR and considered during the peer review, if any, are presented in the conclusion. Furthermore, this conclusion also addresses the requirement for an assessment by EFSA under Article 12 of Regulation (EC) No 396/2005, provided that the active substances will be approved under Regulation (EC) No 1107/2009 without restrictions affecting the residue assessment. In the event of a non-approval of the active substances or an approval with restrictions that have an impact on the residue assessment, the Annex IV proposal from this conclusion might no longer be relevant and a new assessment under Article 12 of Regulation (EC) No 396/2005 will be required.

A list of the relevant endpoints for the active substances and the formulation is provided in Appendix A.

A key supporting document to this conclusion is the peer review report (EFSA, 2020), 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 DAR;
- the reporting table (11 February 2020);
- the evaluation table (30 November 2020);
- 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.

Given the importance of the DAR, including its revisions (Spain, 2020), 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 identity of the microorganism and the properties of the formulated product

_Pepino mosaic virus_ European (EU) strain, mild isolate Abp1 and _Pepino mosaic virus_ Chilean (CH2) strain, mild isolate Abp2 are deposited in the German Collection of Microorganisms and Cell Cultures Leibniz-Institut (DSMZ) in Braunschweig, Germany, under the reference numbers DSM32069 and DSM32070, respectively.

Both _Pepino mosaic virus_ (PepMV) mild isolates Abp1 and Abp2 originate from natural, indigenous wild type viruses, isolated from samples taken in a commercial tomato crop in Murcia (Spain) in 2001 and 2007, respectively, and are not genetically modified.

The representative formulated product for the evaluation was ‘AbioProtect®’, a suspension concentrate (SC) (tomato plant extract), containing minimum 5 × 10^{11} viral genome copies per L, with equal amounts of PepMV, EU strain, mild isolate Abp1 and of PepMV, CH2 strain, mild isolate Abp2.

The representative uses evaluated comprise applications by low-volume spraying of tomato seedlings immediately before planting as an elicitor, to provide protection against infection of aggressive PepMV isolates in permanent greenhouse tomato production systems. Full details of the GAP can be found in the list of endpoints in Appendix A.

Data were submitted to conclude that the uses of _Pepino mosaic virus_ mild isolates Abp1 and Abp2 according to the representative uses proposed at EU level result in a sufficient plant elicitor effect against the targeted organisms, following the guidance document SANCO/10054/2013-rev. 3 (European Commission, 2013).

Conclusions of the evaluation

1. **Identity of the microorganism/biological properties/physical and technical properties and methods of analysis**

The following guidance documents were followed in the production of this conclusion: European Commission, 2012, 2013.
**Pepino Mosaic Virus** belongs to the family **Alphaflexiviridae**, genus **Potexvirus**.

The microbial pest control agents (MPCA) are technical concentrates (TK) of watery extracts of tomato leaves, with a high content of particles of PepMV, EU strain, mild isolate Abp1 and of PepMV, CH2 strain, mild isolate Abp2. The content of the pure microorganism PepMV, EU strain, mild isolate Abp1 and PepMV, CH2 strain, mild isolate Abp2 is set up to be at least $2.5 \times 10^{11}$ genome copies/L in the final formulation of the microbial pest control product (MPCP). Nicotine, originating from the tomato leaves, was considered relevant impurity (see Section 2). The maximum level of nicotine in the technical concentrates Abp1 and Abp2 was 0.005 mg/L for Abp1 and 0.007 mg/L for Abp2. The nicotine level depends on the amount of tomato leaves of the individual batches; as a consequence, it was proposed to limit the nicotine content of the MPCP instead of the MCPA. The maximum nicotine content of the MPCP was $3.87 \times 10^{-5}$ mg/kg.

There are several methods for detection, identification and differentiation of PepMV genotypes and identification of the isolates, including nucleotide sequence, real-time quantitative reverse transcription PCR (RT-qPCR), molecular hybridisation and a bioassay in tomato.

PepMV is closely related to Narcissus mosaic virus (NMV), Scallion virus X (SVX), Cymbidium mosaic virus (CymMV) and Potato aucuba mosaic virus (PAMV). It is not pathogenic to humans or animals. The analysis of contaminating microorganisms in commercially produced batches complies with the requirements of SANCO/12116/2012 rev.0 (European Commission, 2012).

RT-qPCR method and a bioassay are available for the qualitative and quantitative determination of Abp1 and Abp2 isolates in the formulation. Appropriate methods are available to test the presence of human pathogens in the MPCP.

### 2. Mammalian toxicity

From available medical data, no adverse reactions in personnel involved in research, production and application were reported as a result of exposure to **Pepino Mosaic virus**, EU strain, mild isolate Abp1 and **Pepino Mosaic virus**, CH2 strain, mild isolate Abp2. The family **Alphaflexiviridae**, as the highest taxonomic unit including Pepino Mosaic virus (genus **Potexvirus**), is recognised as having the qualified presumption of safety (QPS) status (EFSA BIOHAZ Panel, 2013).

As all other viruses, also **Pepino Mosaic virus**, EU strain, mild isolate Abp1 and **Pepino Mosaic Virus**, CH2 strain, mild isolate Abp2 does not produce antimicrobial substances, toxins or secondary metabolites and cannot become resistant to antibiotics or spread resistance.

As the available methods for testing dermal sensitisation are not suitable for testing microorganisms and there are no validated test methods for sensitisation by inhalation, **Pepino Mosaic virus**, EU strain, mild isolate Abp1 and **Pepino Mosaic Virus**, CH2 strain, mild isolate Abp2 may have the potential to provoke sensitising reactions.

All the basic studies indicated that **Pepino Mosaic virus**, EU strain, mild isolate Abp1 and **Pepino Mosaic Virus**, CH2 strain, mild isolate Abp2 are unlikely to have a potential of toxicity, infectivity and pathogenicity. In cultures of human alveolar epithelial cells type 2, there were no indications of infectivity or intracellular replication for both isolates.

Considering all the available information, it would not be necessary to derive reference values for **Pepino Mosaic virus**, EU strain, mild isolate Abp1 and **Pepino Mosaic Virus**, CH2 strain, mild isolate Abp2, as well as no quantitative operator, worker, resident and bystander risk assessment would be needed. In the absence of a quantitative risk assessment, the use of protective equipment might be considered to reduce the exposure in order to prevent the risk of adverse effects by dermal and/or inhalation exposure for operators and workers (sensitisation potential). Furthermore, nicotine is considered a relevant impurity. From the toxicological point of view, the maximum nicotine level of $3.87 \times 10^{-5}$ mg/kg in the MPCP is acceptable since the non-dietary exposure has been demonstrated to be very low when taking into account the toxicological reference values and dermal absorption value agreed for nicotine.

### 3. Residues

The assessment in the residue section is based on the following guidance documents: OECD (2009), European Commission (2011) and JMPR (2004, 2007).

Since it was not considered necessary to set reference values for **Pepino Mosaic Virus**, EU strain, mild isolate Abp1 and **Pepino Mosaic Virus**, CH2 strain, mild isolate Abp2 (see Section 2), it is concluded that **Pepino Mosaic Virus**, EU strain, mild isolate Abp1 and **Pepino Mosaic Virus**, CH2 strain,
mild isolate Abp2 is a candidate for inclusion in Annex IV to Regulation (EC) 396/2005 and that no maximum residue level (MRL) is needed.

As the product contains nicotine as an impurity, consumers may be exposed to non-viable residues. No residue trials to quantify impurity nicotine in tomato commodity are available. Residues of impurity nicotine were estimated by EFSA using worst-case assumptions of maximum content of nicotine of $3.87 \times 10^{-7}$ mg/kg in the MPCP (resulting on an application rate of nicotine of 0.033 mg of nicotine/ha) is transferred (no degradation assumed) on minimum yield of tomato reported in FAOstat data (2016) for EU countries 8,686 kg/ha. These considerations resulted in an estimated maximum nicotine concentration of 0.004 g nicotine/kg tomatoes. This concentration is in the range of the reported natural nicotine contents in tomato (Domino, 1993) and below the default MRL of 0.01* mg/kg for nicotine in tomato (European Commission, 2005).

Since the expected residue of nicotine in tomatoes as result of the application of MPCP is not exceeding the expected natural levels in tomatoes, a consumer risk assessment is not strictly necessary. Nevertheless, a worst-case consumer risk assessment was performed by the RMS and presented in Appendix A.

**Pepino Mosaic Virus**, EU strain, mild isolate Abp1 and **Pepino Mosaic Virus**, CH2 strain, mild isolate Abp2 are proposed for inclusion in Annex IV to Regulation (EC) 396/2005 and no maximum residue level (MRL) is needed.

### 4. Environmental fate and behaviour

Information regarding the potential interference of PepMV mild isolates Abp1 and Abp2 with the analytical systems for the control of the quality of drinking water provided for in Directive 98/83/EC was not included in the applicant's dossier. This is a specific decision-making criterion for the authorisation of plant protection products containing microorganisms (see uniform principles in Commission Regulation (EU) No 546/2011). However, as the viruses PepMV mild isolates Abp1 and Abp2 are unlikely to interfere with the analytical systems which have bacteria as their target, further information or data have not been requested.

Information was not provided on the potential transfer of genetic material from PepMV mild isolates Abp1 and Abp2 to other organisms. However, for PepMV mild isolates Abp1 and Abp2 infection and replication is known to be very specific to plants and has not been reported to occur in other organisms, including humans or animals (EFSA BIOHAZ Panel, 2013, 2020).

#### 4.1. Fate and behaviour in the environment of the microorganism

Information on persistence and multiplication of PepMV mild isolates Abp1 and Abp2 in soil is not needed for representative uses on soil-less protected cropping systems (e.g. hydroponic systems) (EFSA, 2014). However, information of the fate and behaviour in soil is relevant for the representative soil-bound cropping systems. In a greenhouse study completed by an officially recognised testing facility, PepMV mild isolates Abp1 and Abp2 were not detected in soil 200 days after the crop was treated with the viruses. Scientific peer-reviewed literature data indicate that Pepino mosaic virus is persistent to a certain extent outside its host and infection of some weed species has been reported for wild strains of Pepino mosaic virus in the vicinity of greenhouses. For the representative uses in soil-bound cropping systems in permanent greenhouse PepMV mild isolates Abp1 and Abp2 are not expected to persist and be present above natural background levels in soil, taking into account repeated applications over the years. Consequently, EFSA concluded that the information is sufficient to address the uniform principles criterion associated with persistence and accumulation in the environment regarding soil. Predicted environmental concentrations (PECs) in soil for PepMV mild isolates Abp1 and Abp2 were calculated and reported in the DAR and in Appendix A.

Exposure of surface water through drainage water by PepMV mild isolates Abp1 and Abp2 is not expected for the representative uses in hydroponic systems (soil-less cultivation). However, exposure to surface water through drainage from the representative protected soil-bound cropping cannot be excluded. A scientific publication observed stability and transmission of Pepino mosaic virus in water.

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2 Council Directive 98/83/EC of 3 November 1998 on the quality of water intended for human consumption. OJ L 330, 5.12.1998, p. 32–54.

3 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.
According to this paper, Mild \textit{Pepino Mosaic Virus} may remain infectious in water for up to 3 weeks. In a greenhouse study from a recognised testing facility, PepMV mild isolates Abp1 and Abp2 were not detected in tomato crops 12, 19 and 21 days after each inoculation of the crops with leachate from tomatoes treated with the viruses. For the representative protected soil-bound cropping PepMV mild isolates Abp1 and Abp2 are not expected to persist and be present above natural background levels in surface water, taking into account repeated applications over the years. Consequently, EFSA concluded that the information is sufficient to address the uniform principles criterion associated with persistence and accumulation in the environment regarding surface water for the representative uses. PECs in surface water for PepMV mild isolates Abp1 and Abp2 were calculated on the basis of there being 0.1% emission from permanent greenhouses. These calculations are reported in the DAR and in Appendix A.

4.2. Fate and behaviour in the environment of any relevant metabolite formed by the microorganism under relevant environmental conditions and an impurity

Viruses do not produce metabolites, they can only modify host cell metabolism, as they self-replicate within host organisms. It is considered that no further information is required at EU level since a qualified presumption of safety has been found to be applicable to Alphaflexiviridae viruses such as PepMV mild isolates Abp1 and Abp2 (EFSA BIOHAZ Panel, 2013, 2020). PepMV mild isolates Abp1 and Abp2 contain the relevant impurity nicotine resulting from the manufacturing process (see Section 1). During the peer review, the nicotine was considered a relevant impurity in PepMV mild isolates Abp1 and Abp2 and further information was requested from the applicant for updating the PECs in the environmental compartments.

The applicant provided information on the fate and behaviour of nicotine based on endpoints found in the public domain (mostly peer-reviewed scientific literature). These endpoints were used to perform an exposure assessment of nicotine as result of the representative uses of PepMV mild isolates Abp1 and Abp2. Both the endpoints and the exposure assessment are considered acceptable for the purpose of assessing the fate and behaviour of nicotine as an impurity of PepMV mild isolates Abp1 and Abp2 (See Appendix A). Contamination of ground water with nicotine at levels above 0.1 \( \mu \text{g/L} \) is not expected as a result of the proposed uses of PepMV mild isolates Abp1 and Abp2 (See Appendix A).

5. Ecotoxicology

5.1. Infectiveness and pathogenicity of \textit{Pepino Mosaic Virus}, EU strain, mild isolate Abp1 and \textit{Pepino Mosaic Virus}, CH2 strain, mild isolate Abp2

PepMV mild isolates Abp1 and Abp2 are naturally occurring plant virus strains. Its host plants are mainly from the \textit{Solanaceae} family. \textit{Pepino mosaic virus} infection and replication are known to be very specific to plants and has not been reported to occur in other organisms (see Section 4).

No specific data on infectiveness or pathogenicity of PepMV mild isolates Abp1 and Abp2 were available for the assessments of birds and mammals. PepMV, potex viruses or other members of the family Alphaflexiviridae are not known to have effects on mammals (see Section 2). Low risk is identified for all representative uses in permanent greenhouses as the exposure to birds and mammals is expected to be negligible.

No specific data on infectiveness or pathogenicity of PepMV mild isolates Abp1 and Abp2 were available for the assessments of fish and aquatic invertebrates. Effects were not observed in studies on algae and aquatic plants exposed to PepMV mild isolates Abp1 and Abp2. Based on the available information and opinions of the EFSA BIOHAZ Panel (2013, 2020), a low risk to aquatic organisms was concluded for all representative uses in permanent greenhouses.

No specific data were available to address infectivity and pathogenicity to bees and non-target arthropods. Some information was available on whiteflies and bumble bees from literature studies, where whiteflies and bumble bees were investigated for their potential as vectoring agents. These studies indicated no visible effects on whiteflies and bumble bees after foraging on tomato plants infected by some \textit{Pepino mosaic virus} strains. Low risk is identified for all representative uses in
permanent greenhouses as the exposure to bees and non-target arthropods is expected to be negligible.

For the representative uses in soil-bound cropping systems in permanent greenhouse Pepino Mosaic Virus, EU strain, mild isolate Abp1 and Pepino Mosaic Virus, CH2 strain, mild isolate Abp2 are not expected to persist and be present above natural background levels in soil, taking into account repeated applications over the years (see Section 4). Therefore, for representative uses in permanent greenhouses a quantitative risk assessment to earthworms, other soil macro-organisms and soil microorganisms is not requested according to EFSA guidance document on protected crops (EFSA, 2014).

No specific data on infectiveness or pathogenicity were available for the assessments of non-target terrestrial plants. Low risk is identified for all representative uses in permanent greenhouses as the exposure to non-target terrestrial plants is expected to be negligible.

5.2. Risk from impurity nicotine

The exposure to birds, mammals, bees, non-target arthropods, earthworms, soil microorganisms and non-target plants to the impurity nicotine was not considered relevant for the representative uses in permanent greenhouses. Therefore, a low risk was concluded for these non-target terrestrial organisms. However, some information for the toxicity of bees and other non-target arthropods was available from the open literature. Using this information, the RMS has concluded a low risk to bees and other non-target arthropods for the representative uses, including bumble bees introduced into the permanent greenhouse. In addition, application of the product for the representative use is intended at an early growth stage before flowering (see Section 3).

The impurity nicotine was present at very low levels in the MPCP Abp1 and Abp2 (see Section 1). For the representative uses in permanent greenhouse with one application per season, the exposure to surface water resulted in a PEC of $0.1032 \times 10^{-10}$ µg nicotine/L water (see Appendix A). Limited information was provided in the DAR in respect to possible effect of the impurity nicotine to aquatic organisms. Endpoints (mainly acute or short term) for fish, aquatic invertebrates and algae were derived from published literature and these endpoints were considered suitable for a risk assessment as they had been used in recent EFSA conclusion (EFSA, 2017a,b). MPCA Abp1 and Abp2 will be applied once per growing season resulting in very low PEC surface water concentrations. Nicotine is ready degradable and will not persist in water. Effect endpoints for aquatic organisms are presented in the list of endpoints from open literature (see Appendix A). Using these endpoints, a low risk is indicated to aquatic organisms. Overall, considering all the data and assessments that were available, a low risk from nicotine to aquatic organism was concluded for the representative uses in permanent greenhouses.
6. Overview of the risk assessment of the organism or metabolite compounds listed in residue definitions triggering assessment of effects data for the environmental compartments (Tables 1–4)

**Table 1: Soil**

| Compound (name and/or code)                                                                 | Ecotoxicology                                                                                                                                 |
|------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------|
| *Pepino Mosaic Virus, EU strain, mild isolate Abp1 and Pepino Mosaic Virus, CH2 strain, mild isolate Abp2* | As the virus is not expected to persist in soil for the representative uses in soil-bound crops in permanent greenhouses, no assessment is required (EFSA, 2014) |
| Nicotine (relevant impurity)                                                              | Nicotine is not expected to persist in soil. For the representative uses in soil-bound crops in permanent greenhouses, no assessment is required (EFSA, 2014) |

**Table 2: Groundwater**

| Compound (name and/or code)                                                                 | > 0.1 μg/L at 1 m depth for the representative uses<sup>(b)</sup> | Biological (pesticidal) activity/relevance Step 3a. | Hazard identified Steps 3b and 3c | Consumer RA triggered Steps 4 and 5 | Human health relevance |
|------------------------------------------------------------------------------------------|------------------------------------------------------------------|----------------------------------------------------|---------------------------------|----------------------------------|------------------------|
| Nicotine (relevant impurity)                                                              | No                                                               | Yes (insecticidal activity)                         | Not triggered                   | No                               | Not triggered           |

<sup>(a): Assessment according to European Commission guidance of the relevance of groundwater metabolites (2003).</sup>

**Table 3: Surface water and sediment**

| Compound (name and/or code)                                                                 | Ecotoxicology                                                                                                                                 |
|------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------|
| *Pepino Mosaic Virus, EU strain, mild isolate Abp1 and Pepino Mosaic Virus, CH2 strain, mild isolate Abp2* | The risk for infectiveness and pathogenicity to aquatic organisms was assessed as low for the representative uses |
| Nicotine (relevant impurity)                                                              | The risk to aquatic organisms was assessed as low for the representative uses                                                               |

**Table 4: Air**

| Compound (name and/or code)                                                                 | Toxicology                                                                                                                                                              |
|------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| *Pepino Mosaic Virus, EU strain, mild isolate Abp1 and Pepino Mosaic Virus, CH2 strain, mild isolate Abp2* | LC₅₀ > 5.02 mg/L air that corresponds with 3.39 × 10⁸ PepMV genome copies/L air (1.46 × 10⁹ genome copies/L air of Abp1 and 1.93 × 10⁹ genome copies/L air of Abp2) |
| Nicotine (relevant impurity)                                                              | Regarding the specification the maximum content of 3.87 × 10⁻⁷ mg/kg in the MPCP is acceptable from toxicological point of view |

7. Particular conditions proposed to be taken into account by risk managers

Risk mitigation measures (RMMs) identified following consideration of Member State (MS) and/or applicant's proposal(s) during the peer review, if any, are presented in this section. These measures applicable for human health and/or the environment leading to a reduction of exposure levels of operators, workers, bystanders/residents, environmental compartments and/or non-target organisms for the representative uses are listed below. The list may also cover any RMMs as appropriate, leading to an acceptable level of risks for the respective non-target organisms.

It is noted that final decisions on the need of RMMs to ensure the safe use of the plant protection product containing the concerned active substance will be taken by risk managers during the decision-making phase. Consideration of the validity and appropriateness of the RMMs remains the responsibility of Member States (MSs) at product authorisation, taking into account their specific agricultural, plant health and environmental conditions at national level (Table 5).

Table 5: Risk mitigation measures proposed for the representative uses assessed

| Representative use | Tomato (soil-bound) (permanent greenhouse) | Tomato (hydroponic) (permanent greenhouse) |
|--------------------|-------------------------------------------|-------------------------------------------|
| Foliar spray       | Use of PPE/RPE might be considered to reduce dermal and inhalation exposure (for the sensitisation potential) | Use of PPE/RPE might be considered to reduce dermal and inhalation exposure (for the sensitisation potential) |
| Operator risk      | Use of PPE/RPE might be considered to reduce dermal and inhalation exposure (for the sensitisation potential) | Use of PPE/RPE might be considered to reduce dermal and inhalation exposure (for the sensitisation potential) |
| Worker exposure    | Use of PPE might be considered to reduce dermal exposure (for the sensitisation potential) | Use of PPE might be considered to reduce dermal exposure (for the sensitisation potential) |

8. Concerns and related data gaps

8.1. 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 one or more of 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 546/2011⁴ 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.

No issues or assessments that could not be finalised including associated data gaps have been identified.

8.2. 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

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⁴ 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.
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, 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.

No critical areas of concern, including associated data gaps have been identified.

8.3. Overview of the concerns identified for each representative use considered (Table 6)

(If a particular condition proposed to be taken into account to manage an identified risk, as listed in Section 7, has been evaluated as being effective, then ‘risk identified’ is not indicated in Table 6.)

Table 6: Overview of concerns reflecting the issues not finalised, critical areas of concerns and the risks identified that may be applicable for some but not for all uses or risk assessment scenarios

| Representative use | Tomato (soil-bound) (permanent greenhouse) | Tomato (hydroponic) (permanent greenhouse) |
|--------------------|---------------------------------------------|---------------------------------------------|
| Operator risk      | Risk identified                             | Risk identified                             |
| Worker risk        | Risk identified                             | Risk identified                             |
| Resident/bystander risk | Risk identified                        | Risk identified                             |
| Consumer risk      | Risk identified                             | Risk identified                             |
| Risk to wild non-target terrestrial vertebrates | Risk identified                          | Risk identified                             |
| Risk to wild non-target terrestrial organisms other than vertebrates | Risk identified                          | Risk identified                             |
| Risk to aquatic organisms | Risk identified                        | Risk identified                             |
| Groundwater exposure to active substance | Legal parametric value breached           | Legal parametric value breached(a)         |
| Groundwater exposure to metabolites | Legal parametric value breached(a)          | Parametric value of 10 μg/L(b) breached      |

(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).

9. List of other outstanding issues

Remaining data gaps not leading to critical areas of concern or issues not finalised but considered necessary to comply with the data requirements, and which are not relevant for some or all of the representative uses assessed at EU level. Although not critical, these data gaps may lead to uncertainties in the assessment and are considered relevant.

These data gaps refer only to the representative uses assessed and are listed in the order of the sections:

No outstanding issues.
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Abbreviations

1/n slope of Freundlich isotherm
λ wavelength
e decadic molar extinction coefficient
ADE actual dermal exposure
AF assessment factor
CHO Chinese hamster ovary cells
CI  confidence interval
CL  confidence limits
DAR  draft assessment report
DAT  days after treatment
DM  dry matter
EEC  European Economic Community
FAO  Food and Agriculture Organization of the United Nations
FID  flame ionisation detector
FIR  food intake rate
FOB  functional observation battery
FOCUS  Forum for the Co-ordination of Pesticide Fate Models and their Use
GAP  Good Agricultural Practice
GC  gas chromatography
ISO  International Organization for Standardization
IUPAC  International Union of Pure and Applied Chemistry
iv  intravenous
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)
LC_{50}  lethal concentration, median
M/L  mixing and loading
mm  millimetre (also used for mean measured concentrations)
mN  milli-Newton
MOA  mode of action
MRL  maximum residue level
MS  mass spectrometry
NOEL  no observed effect level
OECD  Organisation for Economic Co-operation and Development
Pa  Pascal
PD  proportion of different food types
PEC  predicted environmental concentration
PHI  preharvest interval
PIE  potential inhalation exposure
PPE  personal protective equipment
ppm  parts per million (10^{-6})
PT  proportion of diet obtained in the treated area
PTT  partial thromboplastin time
QPS  qualified presumption of safety
RBC  red blood cells
REACH  Registration, Evaluation, Authorisation of Chemicals Regulation
RPE  respiratory protective equipment
SC  suspension concentrate
SMILES  simplified molecular-input line-entry system
TWA  time-weighted average
UV  ultraviolet
W/S  water/sediment
w/v  weight per unit volume
w/w  weight per unit weight
WBC  white blood cell
WHO  World Health Organization
Appendix A – List of endpoints 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.2021.6388
### Appendix B – Used compound codes

| Code/trivial name<sup>(a)</sup> | IUPAC name/SMILES notation/InChiKey<sup>(b)</sup> | Structural formula<sup>(c)</sup> |
|--------------------------------|-------------------------------------------------|----------------------------------|
| nicotine                      | 3-[(2S)-1-methylpyrrolidin-2-yl]pyridine CN1CCC[C@H]1c1cnccc1 SNICXCGAKADSCV-JTQLQIEISA-N | ![Nicotine Structural Formula](image) |

<sup>(a)</sup> The metabolite name in bold is the name used in the conclusion.

<sup>(b)</sup> ACD/Name 2019.1.1 ACD/Labs 2019 Release (File version N05E41, Build 110555, 18 July 2019).

<sup>(c)</sup> ACD/ChemSketch 2019.1.1 ACD/Labs 2019 Release (File version C05H41, Build 110712, 24 July 2019).