Peer review of the pesticide risk assessment of the active substance *Beauveria bassiana* strain PPRI 5339

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Abstract

The conclusions of EFSA following the peer review of the initial risk assessments carried out by the competent authority of the rapporteur Member State, the Netherlands, for the pesticide active substance *Beauveria bassiana* strain PPRI 5339 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 uses of *Beauveria bassiana* strain PPRI 5339 as an insecticide in protected Solanaceae (tomato, sweet pepper, aubergine, edible and processed fruits), in protected Cucurbitaceae (cucumber, edible and processed fruits) and in protected ornamentals. The reliable endpoints, appropriate for use in regulatory risk assessment are presented. Missing information identified as being required by the regulatory framework is listed. Concerns are identified.

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Summary

*Beauveria bassiana* strain PPRI 5339 is a new active substance for which, in accordance with Article 7 of Regulation (EC) No 1107/2009 of the European Parliament and of the Council (hereinafter referred to as 'the Regulation'), the rapporteur Member State (RMS), the Netherlands, received an application from BASF Corporation on 1 October 2014 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 2 June 2015.

The RMS provided its initial evaluation of the dossier on *Beauveria bassiana* strain PPRI 5339 in the draft assessment report (DAR), which was received by the European Food Safety Authority (EFSA) on 22 December 2016. The peer review was initiated on 3 March 2017 by dispatching the DAR for consultation to the Member States and the applicant, BASF Corporation.

Following consideration of the comments received on the DAR, it was concluded that additional information should be requested from the applicant and that EFSA should conduct an expert consultation in the areas of mammalian toxicology, residues and ecotoxicology.

In accordance with Article 12 of the Regulation, EFSA should adopt a conclusion on whether *Beauveria bassiana* strain PPRI 5339 can be expected to meet the approval criteria provided for in Article 4 of the Regulation taking into consideration recital (10) of the Regulation. Furthermore, this conclusion also addresses the assessment required from EFSA under Article 12 of Regulation (EC) No 396/2005, provided the active substance will be approved under Regulation (EC) No 1107/2009 without restrictions affecting the residue assessment. The conclusions laid down in this report were reached on the basis of the evaluation of the representative uses of *Beauveria bassiana* strain PPRI 5339 as an insecticide in protected Solanaceae (tomato, sweet pepper, aubergine, edible and processed fruits), in protected Cucurbitaceae (cucumber, edible and processed fruits) and in protected ornamentals, as proposed by the applicant. Full details of the representative uses can be found in Appendix A of this report.

Data were submitted to conclude that the uses of *Beauveria bassiana* strain PPRI 5339 according to the representative uses proposed at EU level result in a sufficient insecticidal efficacy against thrips and whitefly.

A data gap was identified for a search of the scientific peer-reviewed open literature on the active substance and its relevant metabolites.

In the area of identity, biological and technical properties of the active substance and the formulation, data gaps were identified for additional information on the method of identification at strain level, for the determination of dispersion stability, wet sieve test, pourability, accelerated storage stability and shelf life study of the formulation (including data on beauvericin content).

In the area of mammalian toxicology, two data gaps were identified. An appropriate growth temperature study for *Beauveria bassiana* PPRI 5339 should be provided to clear the need for further toxicological investigations of the microorganism. Additional data on secondary metabolites/toxins (the amounts produced and appropriate investigations of their potential toxicity to humans) should also be provided in order to conclude on the risk.

As there is no indication for the necessity of reference values for *Beauveria bassiana* strain PPRI 5339, further consideration might not need to be given to occurrence of viable residues of *Beauveria bassiana* PPRI 5339 on plant commodities. In terms of secondary metabolites, measured concentrations following treatment according to critical Good Agricultural Practice (cGAP) are not available, but should be provided. There is very high uncertainty with the theoretical estimates submitted for beauvericin, which in EFSA's view do not permit a reliable conclusion regarding consumer safety.

Reliable information was not provided to demonstrate that, under the conditions of use, any secondary metabolites/toxins produced by *Beauveria bassiana* PPRI 5339 will not occur in the environmental compartments in concentrations considerably higher than under natural conditions. Consequently, further data on the persistence, transformation and mobility of these compounds may be needed in order to assess the potential for groundwater exposure and soil and surface water exposure.

In the area of ecotoxicology pending on the finalisation of the exposure assessment for soil and surface water, further information may be needed to address the risk to soil and aquatic organisms for any secondary metabolites/toxins produced by *Beauveria bassiana* PPRI 5339. In addition, a data gap was identified to provide further details on the literature search.
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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).

Beauveria bassiana strain PPRI 5339 is a new active substance for which, in accordance with Article 7 of the Regulation, the RMS, the Netherlands (hereinafter referred to as the 'RMS'), received an application from BASF Corporation on 1 October 2014 for approval of the active substance Beauveria bassiana strain PPRI 5339. 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 2 June 2015.

The RMS provided its initial evaluation of the dossier on Beauveria bassiana strain PPRI 5339 in the DAR, which was received by EFSA on 22 December 2016 (the Netherlands, 2016). The peer review was initiated on 3 March 2017 by dispatching the DAR for consultation of the Member States and the applicant, BASF Corporation 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 of that table.

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 21 June 2017. 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 areas of mammalian toxicology, residues 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.

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 where this 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 Beauveria bassiana strain PPRI 5339 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 February 2018.

This conclusion report summarises the outcome of the peer review of the risk assessment on the active substance and the representative formulation evaluated on the basis of the representative uses of Beauveria bassiana strain PPRI 5339 as an insecticide in protected Solanaceae (tomato, sweet pepper, aubergine, edible and processed fruits), in protected Cucurbitaceae (cucumber, edible and processed fruits) and in protected ornamentals as proposed by the applicant. Furthermore, this conclusion also addresses the assessment required from EFSA under Article 12 of Regulation (EC) No 396/2005, provided the active substance 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

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.
substance or an approval with restrictions that have an impact on the residue assessment, the 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 end points for the active substance and the formulation is provided in Appendix A.

In addition, a key supporting document to this conclusion is the peer review report (EFSA, 2018), 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 (15 June 2017);
- the evaluation table (1 March 2018);
- the reports 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 (the Netherlands, 2018) and the peer review report, both documents are considered as background documents to this conclusion.

It is recommended that this conclusion report and its background documents would not be accepted to support any registration outside the European Union (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

*Beauveria bassiana* strain PPRI 5339 is a fungus deposited at the Agricultural Research Culture Collection (NRRL) International Depositary Authority, Peoria, Illinois, USA under accession number NRRL 50757. *Beauveria bassiana* strain PPRI 5339 is a naturally occurring strain not originally indigenous to Europe, initially isolated from the larva of a tortoise beetle, *Conchyloctenia punctata* (Coleoptera: Cassidinae) collected in KwaZulu Natal, South Africa. *Beauveria bassiana* strain PPRI 5339 is now naturally found across Europe.

The representative formulated product for the evaluation was 'BAS 480 00 I (Broadband)', an oil dispersion (OD) containing 43.9 g/kg (40 g/L) (nominal $4 \times 10^{12}$ CFU/L, minimum content $4 \times 10^{12}$ CFU/L, maximum $8 \times 10^{12}$ CFU/L) *Beauveria bassiana* strain PPRI 5339. An FAO specification does not exist for this product.

The representative uses evaluated comprise applications by spraying against thrips (*Frankliniella occidentalis* and *Thrips tabaci*) and whitefly (*Trialeurodes vaporariorum*, *Bemisia tabaci* and *Bemisia argentifoli* *i*) in protected Solanaceae (tomato, sweet pepper, aubergine, edible and processed fruits), in protected Cucurbitaceae (cucumber, edible and processed fruits) and in protected ornamentals. 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 *Beauveria bassiana* strain PPRI 5339 according to the representative uses proposed at EU level result in a sufficient insecticidal efficacy against thrips and whitefly, following the guidance document SANCO/10054/2013-rev. 3 (European Commission, 2013).

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 the environment and non-target species 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 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: Working Document on Microbial Contaminant Limits for Microbial Pest Control Products (European Commission, 2012) and Guidance on the assessment of bacterial susceptibility to antimicrobials of human and veterinary importance (EFSA, 2012).
The technical grade microbial pest control agent (MPCA) contains $1.0 \times 10^{14}$ viable CFU/kg.

Identification of *Beauveria bassiana* strain PPRI 5339 is based on ribosomal ribonucleic acid (rRNA) gene sequencing, by sequencing of the internal transcribed spacer (ITS) ribosomal region including the 3’ end of the 18S region, the ITS1 region, the 5.8S region and the ITS2 region. The resulting sequence is compared to the nucleotide sequences deposited in databases using Basic Local Alignment Search Tool (BLAST). It should be noted, however, that this method does not allow for an unequivocal identification at strain level. As a consequence, a data gap was identified for additional information on the method for identification of *Beauveria bassiana* strain PPRI 5339 at the strain level.

*B. bassiana* strains are able to synthesize metabolites with very different chemical and biological properties, like low molecular weight compounds, non-peptide pigments, cyclodepsipeptides, high molecular weight proteins. Potential effects on humans or the environment also differ between metabolites. Some of these metabolites are key determinants in pathogenicity for *B. bassiana* towards their host insects. Effects of metabolites on target hosts depend on both the *Beauveria* strains that differ in the production of metabolites and the target insects that differ in susceptibility towards metabolites. No detrimental *in vivo* effects of metabolites produced by *B. bassiana* are known so far on humans or non-target organisms. Most *Beauveria* strains were only assessed for a single type of secondary metabolites, and no specific information on the capacity to produce different groups of metabolites with potential impact on humans or the environment is available for any of the strains, including *Beauveria bassiana* strain PPRI 5339. *Beauveria bassiana* strain PPRI 5339 produces beauvericin, the maximum content was set at 0.5 mg/kg.

There is no evidence of direct relationships of *Beauveria bassiana* strain PPRI 5339 to known plant, animal or human pathogens.

The optimal growth temperature range for *B. bassiana* is from 22 to 28°C. A non-good laboratory practice (GLP) study was provided showing that *Beauveria bassiana* strain PPRI 5339 is not able to grow at temperatures of 32°C and above and that it is sensitive to UV light. Activity of *B. bassiana* towards target organisms is dependent on acidification and the activity increases below pH 4.5.

In the open literature, *B. bassiana* was found to be sensitive to posaconazole and to echinocandins. Two instances of potential resistance of *Beauveria bassiana* to antifungal agents, voriconazole, fluconazole and amphotericin B, have been identified in the literature. No specific information addressing the issue of resistance/sensitivity to antibiotics and other antimicrobial agents has been found in the open literature concerning strain PPRI 5339.

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 active substance, physical and technical properties of the representative formulation; however data gaps were identified for the determination of dispersion stability, wet sieve test, pourability, accelerated storage stability and shelf life study of the formulation (including data on beauvericin content). Label instructions might be needed for the formulation concerning low temperature storage.

Acceptable methods are available for the determination of the microorganism and beauvericin content in the formulation and for the determination of the content of contaminating microorganisms. No residue definition was applicable for *Beauveria bassiana* strain PPRI 5339; therefore, no post-registration monitoring methods are needed.

2. **Mammalian toxicity**

*Beauveria bassiana* PPRI 5339 has been discussed during the Pesticides Peer Review TC 157.

**General data**

*Beauveria bassiana* can be considered as a rare opportunistic human pathogen, isolated in very few cases from eye infection, pulmonary disease or disseminated infection in immunocompromised patients, but no case was demonstrated to be related to *Beauveria*-based biopesticides. No infection has been reported among manufacturing plant personnel during medical surveillance.

Being a fungus, *Beauveria* sp. is not expected to possess the potential for transfer of genetic material.

**Toxicity studies**

Based on information from the literature, *B. bassiana* strains show allergic potential and sensitising properties via both dermal and inhalatory contacts. As for other microorganisms based products, the warning phrase ‘Microorganisms may have the potential to provoke sensitising reactions’, can be applied taking into account that hazard statements applicable to chemicals (according to Regulation (EC) No 1272/2008) are not appropriate for microorganisms.
Basic acute studies showed that *Beauveria bassiana* strain PPRI 5339 was not infective or pathogenic after oral, intratracheal or intraperitoneal exposure. During acute inhalation studies with aerosols generated from the powdered test item, mortality and histopathological findings in the lungs included acute inflammation, necrosis, congestion and haemorrhage were observed. It was presumed that these effects are consistent with an allergic reaction and that mortality was caused by asphyxiation due to inflammation of the lungs. If it is confirmed that *Beauveria bassiana* PPRI 5339 does not grow at human body temperature (data gap for GLP compliant study), further investigations of its potential for repeat dose toxicity will not be needed. The RMS considers that the non-GLP study is sufficient to demonstrate the lack of growth at human body temperature.

The genotoxic potential of *Beauveria bassiana* strain PPRI 5339 was assessed using the bacterial reverse mutation assay, which gave negative results.

### Secondary metabolites/toxins

*Beauveria bassiana* has the potential to produce a range of different secondary metabolites after application or in contact with the target organism. Hazardous properties have been identified for some of them (e.g. beauvericin and pigments) whereas no information is available for others (e.g. bassianolide).

Literature data for beauvericin indicated negative results in Ames tests, but positive results for chromosomal aberrations, sister-chromatid exchanges and micronuclei were reported *in vitro* with eukaryotic cells, as well as apoptosis induction and cytotoxic effects.

In an EFSA Scientific Opinion on the risks to human and animal health related to the presence of beauvericin and enniatins in food and feed (EFSA CONTAM Panel, 2014), it is concluded that *in vitro* genotoxicity data are equivocal for beauvericin but some studies suggested a potential genotoxic effect, and taking into account the limited data available (e.g. no repeat dose study), it was not possible to establish a tolerable daily intake (TDI) or an acute reference dose (ARfD) for beauvericin. During the Pesticides Peer Review TC 157, the experts agreed that the threshold of toxicological concern (TTC) value for genotoxic compounds (0.0025 μg/kg body weight (bw) per day) could be used for beauvericin. If this value is exceeded by the exposure estimates (acute or chronic), further data will be needed to derive more specific reference values.

Due to insufficient data on secondary metabolites/toxins, the insufficient information on the amounts produced and the lack of appropriate investigations of their potential toxicity to humans, it is not possible to conclude on the risk assessment from secondary metabolites/toxins of *Beauveria bassiana* strain PPRI 5339 or their groundwater relevance should this assessment ever be triggered (data gap, issue not finalised).

### Reference values and non-dietary exposure

It is considered unlikely that *Beauveria bassiana* strain PPRI 5339 is pathogenic or infective based on the first tier studies, not indicating the need of specific reference values. In the absence of reference values, no exposure estimates are required.

Considering the TTC value of 0.0025 μg/kg bw per day for beauvericin, the exposure of operators (below the limit of quantification (LOQ) in the technical material) does not raise a concern, whereas the exposure of re-entry workers cannot be concluded in the absence of validated analytical data for the levels of beauvericin produced after application in permanent greenhouse, the RMS does not agree and considers that the information is sufficient and does not raise concerns for re-entry workers. For this representative use, the exposure of bystanders and residents does not raise a concern.

### 3. Residues

As it concerns viable residues, *Beauveria bassiana* PPRI 5339 is not expected to persist on crops outside of an infected insect host, however actual data with direct counting after application to plants were not submitted to demonstrate a swift decline. Yet, as the section on mammalian toxicology can conclude that there is no indication of the need to derive reference values for the microorganism, further consideration might not need to be given to occurrence of viable residues of *Beauveria bassiana* PPRI 5339 on plant commodities.

In terms of toxins/secondary metabolites, only theoretical estimates regarding the residues on crops were provided for beauvericin for which a genotoxic effect cannot be excluded (see Section 2). As demonstrated by the five-batch analysis, beauvericin was detectable in the technical material (spore concentrate) but not accurately quantifiable at levels lower than the lowest validated concentration of
the analytical method (0.5 mg/kg). It is noted that the permitted maximum content of beauvericin in the formulation is approximately 10-fold higher than the beauvericin concentration used in the submitted calculation; in this sense, the assumptions used for the estimation of potential residues may not be worst case. Moreover, the provided calculations using typical crop yield values to estimate concentrations of beauvericin on crops is surrounded by very high uncertainty due to the variability of a number of factors influencing the calculation. In the view of the hazard potential of beauvericin, EFSA does not consider this approach appropriate to reliably address the consumer risk from dietary exposure to beauvericin (data gap and issue that could not be finalised).

In situ production of beauvericin in the insects infesting a treated crop and potential transfer of beauvericin from insects to the crops has negligible impact on the total concentrations of beauvericin according to the RMS. This conclusion is not reproducible by EFSA when concentrations reported for insects are compared to the ones calculated for treated crops and moreover considering that no specific information is available on the extent of transfer from infected insects to crops. Studies on plants with different genera of entomopathogenic fungi including Beauveria species were referenced in the DAR; none of them was conducted with the strain under assessment. The studies reported non-measurable residues of metabolites (e.g. destruxin A and B, oosporein) on the tested crops, however LOQ or limit of detection (LOD) were not given. These findings were extrapolated by the RMS to address the transfer on crops of in situ produced beauvericin, beauveriolides, beauverolides and oosporein from Beauveria bassiana strain PPRI 5339. It is noted that, e.g. the referenced study by Seger et al. (2005), in the Netherlands (2018) in potato tuber reports an LOD and LOQ for oosporein as 2.4 mg/kg and 8.0 mg/kg, respectively. In EFSA's view, these high limits do not permit any conclusion that the contribution of in situ produced metabolites to the residues resulting from the use of the technical material will be negligible.

While the estimated concentrations of beauvericin on crops applied with the technical material may possibly be an overestimation as based on the total number of annual applications and assuming no degradation in the field, the concentrations of beauvericin from in situ production by the microorganism and contamination of crops may have been underestimated as their potential contribution was not considered. Actual concentrations of beauvericin following the use of Beauveria bassiana strain PPRI 5339 could not be reliably assessed. Investigation of levels of beauvericin and moreover the analysis for other metabolites in critical GAP (cGAP) conform trials is recommended (data gap, issue not finalised).

In terms of consumer exposure to beauvericin that is not related to the representative uses in fruiting vegetables but to other crops (mainly cereals, tree nuts, coffee, legumes), EFSA (EFSA CONTAM Panel, 2014) concluded that for beauvericin the chronic and acute exposure estimates, respectively, already exceeded the TTC of 0.0025 μg/kg bw per day for genotoxic compounds, with toddlers having the highest exposure. These results indicated the need for additional compound-specific toxicity data for beauvericin to assess its potential health risks for humans. As these exposure estimates did not consider fruiting vegetables as a source of beauvericin contamination, levels of beauvericin from the representative uses are likely to contribute in addition to the consumer burden estimated in the EFSA opinion (EFSA CONTAM Panel, 2014). Further data is necessary on both occurrence and toxicity to finalise a reliable consumer risk assessment.

4. Environmental fate and behaviour

Information has been provided in relation to potential interference of Beauveria bassiana strain PPRI 5339 with the analytical systems for the control of the quality of drinking water provided for in Directive 98/83/EC11 (see specific Annex VI decision making criteria in Directive 2005/25/EC12). As these methods require pathogenic bacteria to be identified and confirmed as absent, it is unlikely that filamentous fungi or their conidia would interfere with methodologies used for such determinations.

Information has been provided on the potential transfer of genetic material from Beauveria bassiana strain PPRI 5339 to other organisms. Beauveria spp. are not expected to possess plasmids in their cytoplasm (only mitochondrial plasmids are known). Consequently they are not expected to possess the potential to transfer genetic material.

4.1. Fate and behaviour in the environment of the microorganism

Strain specific data on Beauveria bassiana strain PPRI 5339 to address the persistence and multiplication in soil were not provided. The information provided was generally related to Beauveria bassiana species from the open literature. B. bassiana exists naturally at a background level
of ca. 830 CFU/g soil, which is based on the 95th percentile of the geometric mean of 13 field studies. Several investigations showed that *B. bassiana* populations decreased gradually in time due to many factors: frequency of application, pest densities, ecological fitness of inoculum and agricultural practices (e.g. ploughing). After inoculation the population of *B. bassiana* gradually declines until reaching the background level 0.5–1.5 years after treatment. These values indicate the fungal spores can be considered as persistent. In general, the persistent microbial pest control agent (MCPA) may be present in an inactive state and activated under very specific conditions. Germination of *B. bassiana* conidia and subsequent multiplication only occurs in the presence of a host. Predicted environmental concentration (PEC) in soil were not calculated as *Beauveria bassiana* strain PPRI 5339 is intended for application in permanent greenhouses only, and therefore according to the OECD (2012) and EFSA (2014) guidance the soil exposure following the application of 'BAS 480 00 I’ is not considered relevant.

A study on **persistence and multiplication in water** of *Beauveria bassiana* strain PPRI 5339 showed that the rate of reduction of viable conidia is influenced by biotic and abiotic factors, being faster in non-sterile water maintained in sunlight than in sterile water maintained in darkness. Maximum initial PEC surface water values following applications of 'BAS 480 00 I’ have been presented in Appendix A. PEC surface water were calculated using a standard FOCUS ditch scenario taking into account the non-rectangular dimensions of the ditch 1 m wide and a water depth of 0.3 m assuming standard emission of 0.1% from glasshouses.

Specific investigations on the *Beauveria bassiana* strain PPRI 5339 were conducted to evaluate its **persistence and mobility in air**. It was demonstrated that a rapid inactivation of *Beauveria bassiana* spores occurs following exposure to UV-C light. Furthermore, a general study on *Beauveria bassiana* photoprotection showed that *B. bassiana* spores were inactivated by exposure to direct sunlight or UV light. Overall, taking all the observations into consideration, it was concluded that only propagules of *Beauveria bassiana* emitted from protected cropping systems are expected to be degraded rapidly in the air and no accumulation outside the glasshouse is expected.

With respect to the **mobility** of the microorganism, different studies showed that conidia of *B. bassiana* are not very mobile in soil and generally remain on the soil surface. The movement of conidia vertically through the soil profile was correlated with high infiltration rate in soil. Furthermore, the horizontal movement is possible via insects and heavy rainfall. However, no groundwater assessment is necessary since *B. bassiana* is neither pathogenic nor toxic to humans. Presence of conidia in air outside of greenhouses or in water is low and survival of the fungus in these environments is limited.

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

Strain specific information on secondary metabolites/toxins production in the environment following applications of ‘BAS 480 00 I’ is not available. Information from scientific literature was provided indicating that secondary metabolites/toxins are only present in the cadavers of host insects. Cases were made considering information from scientific literature (Skrobek et al., 2008; Schenzel, 2016) on concentration and fate of beauvericin in the environment in order to demonstrate that the release into the environment of any metabolites formed as part of the infection process is considered unlikely, because metabolites will degrade quickly due to the action of lytic enzymes present in the insect cadavers. Following this argumentation, the risk of environmental contamination by secondary metabolites was considered by the applicant to be negligible. Only if, under the conditions of use, relevant secondary metabolites/toxins are produced by the microorganism, the data requirement and the corresponding risk assessment as outlined in Part B point 7 of Commission Regulation (EU) No 544/2011² need to be fulfilled. Accepting that exposure is negligible, the first and the third condition below would not be met:

1) the relevant metabolite is stable outside the microorganism

2) a toxic effect of the relevant metabolite is independent of the presence of the microorganism, and

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² Commission Regulation (EU) 544/2011 of 10 June 2011 implementing Regulation (EC) No 1107/2009 of the European Parliament and of the Council as regards the data requirements for active substances. OJ L 155, 11.6.2011, p. 1–66.
3) the relevant metabolite is expected to occur in the environment in concentrations considerably higher than under natural conditions.

However, the studies by Skrobek et al. (2008) and Schenzel (2016), which were the basis of the cases made to demonstrate that risk of environmental contamination by secondary metabolites was negligible, were not available in the dossier. Therefore, a data gap was identified and this results in an assessment not finalised.

5. Ecotoxicology

It is noted that the representative use was exclusively in permanent greenhouses, therefore, exposure of birds, mammals, wild bees, non-target arthropods, earthworms, soil microorganisms and non-target terrestrial plants to *Beauveria bassiana* strain PPRI 5339 was considered unlikely, and the risk was considered as low.

The effects on fish of *Beauveria bassiana* strain PPRI 5339 were discussed at the Pesticides Peer Review TC 157. A study addressing the effects on fish of *Beauveria bassiana* strain PPRI 5339 was available which was deemed questionable and not sufficient to draw a conclusion. Two studies from literature performed with *B. bassiana* were available indicating effects on fish embryos in some of the tested concentrations. A study demonstrating the rapid inactivation of the spores of *Beauveria bassiana* strain PPRI 5339 under direct sunlight or UV light was available (see Section 4). On the basis of this study, and considering that the suspension of the microorganism, being extremely hydrophobic, is expected to stay on the surface of the water, a limited exposure to the active microorganism in surface water is expected. Overall, a low risk to fish was concluded for the representative uses assessed.

A study on grass shrimp was available. In this study, infection and pathogenicity in adults was observed only via direct injection whilst no infection was observed for exposure via water (most relevant exposure route). While it is acknowledged that the available study on aquatic invertebrates was not performed with a standard species, a low risk to aquatic invertebrates was concluded considering the available information.

In the available study on algae, no effects were observed at the highest tested concentration. Overall, considering the available studies and information a low risk to algae was concluded.

A low risk to the organisms used in biological methods for sewage treatment was concluded.

Effects to pollinators which may be introduced in glasshouses following exposure to *B. bassiana* cannot be fully excluded from the available data, although effects were seen only with a formulation different than the representative one and with the strain GHA; this may need to be further addressed at Member States level.

Pending on the finalisation of the exposure assessment for soil and surface water further information might be needed to address the risk to soil and aquatic organisms for any secondary metabolites/toxins produced by *Beauveria bassiana* PPRI 5339 (data gap, see also Section 4). The RMS is of opinion that the risk assessment for soil and aquatic organisms for metabolites formed in the insects’ cadavers is not necessary.

A search of scientific peer-reviewed open literature was provided. However, a detailed justification for excluding some of the retrieved studies was not provided (data gap). It is noted that the RMS considered this data requirement as addressed.
6. Overview of the risk assessment of 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)                  | Persistence                                                                 | Ecotoxicology |
|---------------------------------------------|-----------------------------------------------------------------------------|---------------|
| *Beauveria bassiana* strain PPRI 5339       | The applied inoculum density decreases to upper natural background levels within 0.5 –1.5 years. These values indicate the fungal spores can be considered as persistent | Low risk      |
| Relevant toxins or secondary metabolites    | Data gap                                                                   | Data gap      |

Table 2: Groundwater

| Compound (name and/or code)                  | Mobility in soil | > 0.1 µg/L at 1 m depth for the representative uses\(\textsuperscript{(a)}\) | Pesticidal activity | Toxicological relevance |
|---------------------------------------------|------------------|-----------------------------------------------------------------|--------------------|------------------------|
| Relevant toxins or secondary metabolites    | Data gap         | Data gap                                                        | No data            | Data gap               |

\(\textsuperscript{(a)}\): At least one FOCUS scenario or a relevant lysimeter.

Table 3: Surface water and sediment

| Compound (name and/or code)                  | Ecotoxicology   |
|---------------------------------------------|-----------------|
| *Beauveria bassiana* strain PPRI 5339     | Low risk        |
| Relevant toxins or secondary metabolites    | Data gap        |

Table 4: Air

| Compound (name and/or code)                  | Toxicology   |
|---------------------------------------------|--------------|
| *Beauveria bassiana* strain PPRI 5339     | Low risk     |
| Relevant toxins or secondary metabolites    | Data gap     |
7. **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 the Regulation 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, the environment and non-target species 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; submission date proposed by the applicant unknown)
- Additional information on the method for identification of *Beauveria bassiana* strain PPRI 5339 confirming the possibility of unequivocal identification at strain level (relevant for all representative uses evaluated; submission date proposed by the applicant unknown; see Section 1).
- Determination of dispersion stability, wet sieve test, pourability, accelerated storage stability of the formulation is missing (relevant for all representative uses evaluated; submission date proposed by the applicant unknown; see Section 1).
- Shelf life study of the formulation including data on beauvericin content is missing (relevant for all representative uses evaluated; submission date proposed by the applicant unknown; see Section 1).
- An appropriate study (GLP or from GLP-accredited laboratory) on the growth temperature of *Beauveria bassiana* PPRI 5339 should be provided in order to demonstrate the absence of growth at human body temperature (relevant for all representative uses evaluated; submission date proposed by the applicant unknown, see Section 2)
- Further data should be provided to conclude on the hazard and risk assessment for the secondary metabolites/toxins of *Beauveria bassiana* strain PPRI 5339, including relevant exposure assessment to beauvericin (relevant for all representative uses evaluated; submission date proposed by the applicant: unknown; Sections 2, 3 and 4).
- Investigation of levels of secondary metabolites/toxins (beauvericin and other metabolites) in cGAP conform trials is recommended (relevant for all representative uses evaluated; submission date proposed by the applicant: unknown; see Section 3).
- References (Skrobek et al., 2008; Schenzel, 2016) demonstrating that the release into the environment of any secondary metabolites/toxins is considered unlikely, or comparable evidence should be provided (relevant for all representative uses evaluated; submission date proposed by the applicant: unknown; see Sections 4 and 5).
- A detailed justification for excluding some of the studies retrieved via the literature search (i.e. Castrillo et al. (2010), Kirkland et al. (2006), Leland J.E. and Behle R.W (2005), Quesada-Moraga E. and Vey A (2004), Rehner S.A. Buckley E. (2005) and Middaugh, DP, Genthner, FJ 1994) and the study summaries from Castrillo et al. (2004), Krauss et al. (2004) (relevant for all representative uses evaluated, submission date proposed by the applicant unknown; see Section 5).

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

No particular conditions are proposed for the representative uses evaluated.

9. **Concerns**

9.1. **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 the Regulation and as set out in Commission Regulation
(EU) No 546/2011\textsuperscript{3} 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 the Regulation.

1) The production of relevant toxins/secondary metabolites could not be excluded and therefore the risk assessment could not be finalised for humans (via their diet and other exposure routes for re-entry workers). Pending on the finalisation of the exposure assessment for soil and surface water further information might be needed to address the risk to soil and aquatic organisms for any secondary metabolites/toxins produced by Beauveria bassiana PPRI 5339.

2) The production of relevant toxins/secondary metabolites could not be excluded, so with the available information, the assessment of potential groundwater exposure could not be finalised.

9.2. 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 the Regulation 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 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 the Regulation.

No critical areas of concern were identified for the representative uses evaluated.

9.3. Overview of the concerns identified for each representative use considered

(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 5.)

Table 5: Overview of concerns

| Representative use | Protected Solanaceae (tomato, sweet pepper, aubergine, edible and processed fruits) | Protected Cucurbitaceae (cucumber, edible and processed fruits) | Protected ornamentals |
|--------------------|-------------------------------------------------------------------------------------|-------------------------------------------------------------|----------------------|
| Operator risk      | Risk identified                                                                     |                                                              |                      |
|                    | Assessment not finalised                                                            |                                                              |                      |
| Worker risk        | Risk identified                                                                     |                                                              |                      |
|                    | Assessment not finalised                                                            |                                                              |                      |
|                    | X\textsuperscript{1}                                                                | X\textsuperscript{1}                                        | X\textsuperscript{1} |

\textsuperscript{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.
| Representative use                                      | Protected Solanaceae (tomato, sweet pepper, aubergine, edible and processed fruits) | Protected Cucurbitaceae (cucumber, edible and processed fruits) | Protected ornamentals |
|-------------------------------------------------------|-----------------------------------------------------------------------------------|-----------------------------------------------------------------|---------------------|
| **Resident/bystander risk**                           | Risk identified                                                                  | Assessment not finalised                                         |                     |
| **Consumer risk**                                     | Risk identified                                                                  | X\(^1\)                                                         | X\(^1\)             |
| **Risk to wild non-target terrestrial vertebrates**   | Risk identified                                                                  | Assessment not finalised                                         |                     |
| **Risk to wild non-target terrestrial organisms other than vertebrates** | Risk identified                                                                  | X\(^1\)                                                         | X\(^1\)             | X\(^1\)             |
| **Risk to aquatic organisms**                         | Risk identified                                                                  | Assessment not finalised                                         |                     |
| **Groundwater exposure to active substance**          | Legal parametric value breached                                                  | Assessment not finalised                                         |                     |
| **Groundwater exposure to metabolites**               | Legal parametric value breached                                                  | Parametric value of 10 \(\mu\)g/L\(^{(a)}\) breached          |                     |
|                                                       | Assessment not finalised                                                         | X\(^2\)                                                         | X\(^2\)             | X\(^2\)             |

Columns are grey if no safe use can be identified. The superscript numbers in this table relate to the numbered points indicated in Section 9.1. Where there is no superscript number, see Sections 2–6 for further information.

(a): Value for non-relevant metabolites prescribed in SANCO/221/2000 rev-10. final, European Commission, 2003.

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OECD (Organisation for Economic Co-operation and Development), 2012. OECD guidance to the environmental safety evaluation of microbial biocontrol agents. ENV/JM/MONO(2012)1, 17 February 2012.

**Abbreviations**

ARfD acute reference dose  
BLAST Basic Local Alignment Search Tool  
bw body weight  
CFU colony forming units  
DAR draft assessment report  
EEC European Economic Community  
FAO Food and Agriculture Organization of the United Nations  
FOCUS Forum for the Co-ordination of Pesticide Fate Models and their Use  
GAP good agricultural practice  
GLP good laboratory practice  
ITS internal transcribed spacer  
IUPAC International Union of Pure and Applied Chemistry  
LOD limit of detection  
LOQ limit of quantification (determination)  
MPCA microbial pest control agent (active agent of the microbial pest control product)  
NRRL Northern Regional Research Laboratory  
OD oil dispersion  
OECD Organisation for Economic Co-operation and Development  
PEC predicted environmental concentration  
RMS rapporteur Member State  
rRNA ribosomal ribonucleic acid  
SMILES simplified molecular-input line-entry system  
TDI tolerable daily intake  
TTC threshold of toxicological concern  
UV ultraviolet  
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.2018.5230
### Appendix B – Used compound codes

| Code/trivial name(a) | IUPAC name/SMILES notation/ InChIKey(b) | Structural formula(c) |
|---------------------|----------------------------------------|-----------------------|
| **Beauvericin**     | (3S,6R,9S,12R,15S,18R)-3,9,15-tribenzyl-6,12,18-trisopropyl-4,10,16-trimethyl-1,7,13-trioxa-4,10,16-triazacyclododecane-2,5,8,11,14,17-hexone | ![Beauvericin structural formula](image) |
|                     | CC(C)(C@H)4OC(-O)(C@H)(C1cccc1)N(C)(C(-O))(C@H) (OC(-O))(C@H)(C2cccc2)N(C)(C(-O))(C@H)(OC(-O)) [C@H](C3cccc3)N(C)C4=O)O(C(C)(C(C)C)C(C)C CZOSYWGOOCPAP-UHFFFAOYNA-N | ![Beauvericin structural formula](image) |
| **Destruxin A**     | 3-(butan-2-yl)-5,8,9-trimethyl-6-(propan-2-yl)-16-(propan-2-en-1-yl)dodecahydropyrrolo[1,2-d][1,4,7,10,13,16]oxapentaazacyclononadecine-1,4,7,10,14,17(11H,16H)-hexone | ![Destruxin A structural formula](image) |
|                     | CC(C)C1C(-O)N(C)(C)(C(-O))NCC(-O)OC(C-C)C(-O) N2CCCCC2(-O)NC(C)(C)(C-C)C(-O)N1C | ![Destruxin A structural formula](image) |
|                     | HHYAVTAYHIVBEP-UHFFFAOYNA-N | ![Destruxin A structural formula](image) |
| **Destruxin B**     | 3-(butan-2-yl)-5,8,9-trimethyl-16-(2-methylpropyl)-6-(propan-2-yl)dodecahydropyrrolo[1,2-d][1,4,7,10,13,16]oxapentaazacyclononadecine-1,4,7,10,14,17(11H,16H)-hexone | ![Destruxin B structural formula](image) |
|                     | CC(C)C1C(-O)N(C)(C)(C(-O))NCC(-O)OC(C-C)C(-O) N2CCCCC2(-O)NC(C)(C)(C-C)C(-O)N1C | ![Destruxin B structural formula](image) |
|                     | RALCKLBQCSOW-UHFFFAOYNA-N | ![Destruxin B structural formula](image) |
| **Oosporein**       | (1Z)-3',5,5',6'-tetrahydroxy-4,4'-dimethyl[1,1'-bi(cyclohexane)-1',1',3',4',5'-tetraine]-2,2',3,6-tetrone | ![Oosporein structural formula](image) |
|                     | O=C2C(-C1/C(O) – C(O)(C=C(O)C=O) – C(O)=O) – C(C) C2=O | ![Oosporein structural formula](image) |
|                     | VWGQFPYHHEABM-UHFFFAOYNA-N | ![Oosporein structural formula](image) |

IUPAC: International Union of Pure and Applied Chemistry; SMILES: simplified molecular-input line-entry system.

(a): The metabolite name in bold is the name used in the conclusion.

(b): ACD/Name 2015 ACD/Labs 2015 Release (File version N20E41, Build 75170, 19 Dec 2014)

(c): ACD/ChemSketch 2015 ACD/Labs 2015 Release (File version C10H41, Build 75059, 17 Dec 2014)