CONCLUSION ON PESTICIDES PEER REVIEW

EFSA Journal

APPROVED: 11 April 2017

doi: 10.2903/j.efsa.2017.4831

Peer review of the pesticide risk assessment of the active substance *Beauveria bassiana* IMI389521

European Food Safety Authority (EFSA),
Maria Arena, Domenica Auteri, Stefania Barmaz, Giulia Bellisai, Alba Brancato, Daniela Brocca, Laszlo Bura, Harry Byers, Arianna Chiusolo, Daniele Court Marques, Federica Crivellente, Chloé De Lentdecker, Marcella De Maglie, Mark Egsmose, Zoltan Erdös, Gabriella Fait, Lucien Ferreira, Marina Goumenou, Luna Greco, Alessio Ippolito, Frederique Istace, Samira Jarrah, Dimitra Kardassi, Renata Leuschner, Christopher Lythgo, José Oriol Magrans, Paula Medina, Ileana Miron, Tünde Molnar, Alexandre Nougadere, Laura Padovani, Juan Manuel Parra Morte, Ragnor Pedersen, Hermine Reich, Angela Sacchi, Miguel Santos, Rositsa Serafimova, Rachel Sharp, Alois Stanek, Franz Streissl, Jürgen Sturma, Csaba Szentes, José Tarazona, Andrea Terron, Anne Theobald, Bénédicte Vagenende, Alessia Verani and Laura Villamar-Bouza

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* IMI389521 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 *Beauveria bassiana* IMI389521 as an insecticide in empty post-harvest storage facilities. 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.

Keywords: *Beauveria bassiana* IMI389521 peer review, risk assessment, pesticide, insecticide

Requestor: European Commission

Question number: EFSA-Q-2015-00362

Correspondence: pesticides.peerreview@efsa.europa.eu

Suggested citation: EFSA (European Food Safety Authority), Arena M, Auteri D, Barmaz S, Bellisai G, Brancato A, Brocca D, Bura L, Byers H, Chiusolo A, Court Marques D, Crivellente F, De Lentdecker C, De Maglie M, Egsmose M, Erdös Z, Fait G, Ferreira L, Goumenou M, Greco L, Ippolito A, Istace F, Jarrah S, Kardassi D, Leuschner R, Lythgo C, Magrans JO, Medina P, Miron I, Molnar T, Nougadere A, Padovani L, Parra Morte JM, Pedersen R, Reich H, Sacchi A, Santos M, Serafimova R, Sharp R, Stanek A, Streissl F, Sturma J, Szentes C, Tarazona J, Terron A, Theobald A, Vagenende B, Verani A and Villamar-Bouza L, 2017. Conclusion on the peer review of the pesticide risk assessment of the active substance *Beauveria bassiana* IMI389521. EFSA Journal 2017;15(9):4831, 16 pp. https://doi.org/10.2903/j.efsa.2017.4831

ISSN: 1831-4732

The EFSA Journal is a publication of the European Food Safety Authority, an agency of the European Union.

Summary

Beauveria bassiana IMI389521 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 Exosect Limited on 28 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* IMI389521 in the draft assessment report (DAR), which was received by the European Food Safety Authority (EFSA) on 22 February 2016. The peer review was initiated on 13 May 2016 by dispatching the DAR for consultation to the Member States and the applicant, Exosect Limited.

Following consideration of the comments received on the DAR, it was concluded that additional information should be requested from the applicant, and that there was no need to conduct an expert consultation.

In accordance with Article 12 of the Regulation, EFSA should adopt a conclusion on whether *Beauveria bassiana* IMI389521 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 use of *Beauveria bassiana* IMI389521 as an insecticide in empty post-harvest storage facilities, as proposed by the applicant. Full details of the representative uses can be found in Appendix A of this report.

A data gap is identified for information on the efficacy for the proposed uses following the guidance document SANCO/10054/2013-rev. 3

A data gap was identified for an updated literature search.

With respect to the identity and physic and chemical properties, available information on analysis of batches allows setting a specification for relevant secondary metabolite beauvericin at levels < 0.1 mg/kg. A data gap has been identified for analysis and specification of other known secondary metabolites. A data gap has been identified for a technique able to identify and distinguish *Beauveria bassiana* IMI389521 at strain level. For 'Bb38 DP' containing strain IMI389521, a data gap was identified for storage stability.

In the area of mammalian toxicity, the risk assessment for operators and workers cannot be finalised due to data gaps related to the potential secondary metabolites/toxins, and to the need to confirm the absence of growth of *Beauveria bassiana* IMI389521 at human body temperature.

Data gaps were identified in the residue section and it is currently not possible to conclude on the dietary exposure and risk assessment with regard to the use of *Beauveria bassiana* IMI389521 in grain stores, specifically in terms of potential secondary metabolites/toxins.

Sufficient and reliable information has not been provided in relation to the fate and behaviour of the organism in the environment and on the production of relevant secondary metabolites. However, no further information is required since the representative uses are restricted to treatment of empty post-harvest storage facilities and it is understood that exposure to the environment can be prevented by standard good application practices.

On the basis of the information provided and considering the representative use, non-target organisms are not expected to be exposed to *Beauveria bassiana* IMI389521. Therefore, the risk could be concluded as low.

Table of contents

Abstract 1
Summary 3
Background 5
The active substance and the formulated product 6
Conclusions of the evaluation 6
1. Identity of the microorganism/biological properties/physical and technical properties and methods of analysis 6
2. Mammalian toxicity 7
3. Residues 8
4. Environmental fate and behaviour of the microorganism 8
5. Ecotoxicology 9
6. Overview of the risk assessment of compounds listed in residue definitions triggering assessment of effects data for the environmental compartments (Tables 1–4) 10
7. Data gaps 11
8. Particular conditions proposed to be taken into account to manage the risk(s) identified 12
9. Concerns 12
9.1. Issues that could not be finalised 12
9.2. Critical areas of concern 12
9.3. Overview of the concerns identified for each representative use considered 12
References 13
Abbreviations 13
Appendix A – List of end points for the active substance and the representative formulation 15
Appendix B – Used compound codes 16

Background

Regulation (EC) No 1107/2009 of the European Parliament and of the Council[1] (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 (MSs) 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 IMI389521 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 Exosect Limited on 28 October 2014 for approval of the active substance *Beauveria bassiana* IMI389521. 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* IMI389521 in the DAR, which was received by EFSA on 22 June 2016 (Netherlands, 2016). The peer review was initiated on 13 May 2016 by dispatching the DAR for consultation of the MSs and the applicant, Exosect Limited, 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 1 September 2016. 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 there was no need to conduct an expert consultation.

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, 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 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* IMI389521 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 MSs via a written procedure in March–April 2017.

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 use of *Beauveria bassiana* IMI389521 as an insecticide in empty grain stores 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 substance or an approval with restrictions that have an impact on the residue assessment, 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.

[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 addition, a key supporting document to this conclusion is the peer review report (EFSA, 2017), 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 (1 September 2016);
the evaluation table (7 April 2017);
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 (Netherlands, 2017) 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

No information on the efficacy for the proposed uses following the guidance document SANCO/10054/2013-rev. 3 (European Commission, 2013) has been provided and peer reviewed. A data gap is identified.

During the literature review, data were retrieved which covered the metabolites tenellin, bassianolide, bassianin, beauvericin and vivotoxins, but did not cover the metabolites oosporein, oxalic acid and cyclosporine (also common to other microorganisms) (data gap). A new search of the scientific peer-reviewed open literature on these metabolites, dealing with side effects on health, published within 10 years before the date of submission of the dossier, should 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

Beauveria bassiana is a naturally occurring soil-borne entomopathogenic fungus. Strain *Beauveria bassiana* IMI389521 was isolated from and adult infected coleopteran in a grain store in the UK and deposited into the international tissue culture collection at CABI Bioscience Genetic Resource Collection (both as freeze dried and liquid-nitrogen stocks under accession number IMI389521.

Due to the absence of a number of key reports on the confidential part of the dossier available to EFSA, EFSA cannot confirm the conclusions of the RMS with respect to the manufacturing process of *Beauveria bassiana* IMI389521 (see data gap in Section 7 for details).

Occasional cases of ocular keratitis caused by *B. bassiana* have been described in the medical literature; however, information on the specific strains involved is not available. Information available on growing temperature ranges of *Beauveria bassiana* IMI389521 has not been derived under good laboratory practice (GLP) and is not conclusive. Since this information is essential to finalise the human health risk assessment a data requirement has been identified for growth experiments performed with increments of temperature of 0.5°C in the range of 34–38°C with precise temperature control (and optimal moisture conditions) carried out in a GLP facility. During the commenting of the draft conclusion, the RMS expressed his disagreement on the need of these data for *Beauveria bassiana* IMI389521; however, another MS agreed that these data was needed. Information on antibiotic resistance of *Beauveria bassiana* IM1289521 needs to be provided.

It is possible that this strain produces some toxins; however, sufficient information on this issue has not been provided. On the basis of available data from scientific literature, the following metabolites are assumed to be produced by *B. bassiana*: beauvericin, bassianin, bassianolide, beauverolides, beauveriolides, tenellin, oosporein, oxalic acid, bassiacridin, cyclosporin A and vivo toxins. Available information on analysis of batches allows setting a specification for beauvericin < 0.1 mg/kg. A data gap has been identified for analysis and specification for other known secondary metabolites. During

the commenting of the draft conclusion, the RMS expressed his disagreement on the need of data on other metabolites produced by *Beauveria bassiana* IM1289521; no other MSs expressed their views on it. According to the information provided by the applicant, the currently provided methodology is not robust enough to confirm identity at species level (and therefore not capable to determine the identity at strain level), a more discriminatory method such as multilocus sequence typing, DNA fingerprinting or whole genome sequencing would need to be conducted. A data gap has therefore been identified for a technique able to identify and distinguish *Beauveria bassiana* IMI389521 at strain level.

For 'Bb38 DP' containing strain IMI389521, a data gap was identified for storage stability for the formulation.

2. Mammalian toxicity

General data

Medical surveillance on manufacturing plant personnel since 2008 did not reveal any infectivity, pathogenicity, toxicity or sensitisation effect caused by *Beauveria bassiana* IMI389521.

B. bassiana can be considered as a rare opportunistic pathogen, isolated in 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 (or no information on the specific strain identified was available). From this limited evidence, it can also be concluded that although *B. bassiana* infections in humans are in the majority of cases effectively treated with antibiotics, the possible occurrence of further antibiotic resistant strains of *B. bassiana* cannot be discounted (data gap).

Toxicity studies

A pulmonary toxicity study with *B. bassiana* IMI389521 indicated no toxicity, pathogenicity or infectivity. The test item cleared to below the limit of detection within 7 days. In the absence of histopathological examination of the lungs, and considering that other *B. bassiana* strains showed local effects on the lungs, a potential sensitisation reaction by inhalation of *Beauveria bassiana* IMI389521 cannot be excluded.

In an Ames test with *Beauveria bassiana* IMI389521, no toxicologically significant increases in the frequency of revertant colonies were observed.

Specific studies on oral, inhalatory and percutaneous toxicity with the plant protection product have not been conducted. Studies on skin and eye irritation have been provided where the plant protection product was demonstrated to be not a skin or eye irritant.

In a study from the literature, *B. bassiana* crude extracts have been demonstrated to contain numerous allergens capable of being recognised by human serum immunoglobulins E (IgEs), and intradermal skin testing resulted in allergenic reactions in several individuals. 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.

If the lack of germination or growth at the human body temperature is not confirmed by a validated study (see Section 1), further assessment (e.g. of the lack of toxicity, pathogenicity or infectivity after oral or repeated exposure) might need to be reconsidered in order to conclude on the risk assessment for human health. During the commenting of the draft conclusion, the RMS expressed his disagreement on the need of confirming the growth temperature of *Beauveria bassiana* IMI389521; however, another MS supported the data gap.

Secondary metabolites/toxins

The major metabolites produced by *B. bassiana* are beauvericin, bassianin, bassianolide, beauverolides, beauveriolides, tenellin, oosporein, oxalic acid and bassiacridin. In addition, the secondary metabolite cyclosporin A is considered of concern for human health (used as immunosuppressive drug).

Beauvericin has insecticidal, antibiotic, cytotoxic and ionophoric properties. Reports show high *in vitro* toxicity towards murine and human cell lines. In turkeys, beauvericin may affect the immune system by suppressing proliferation and inducing apoptosis of peripheral blood lymphocytes. Some indications of a genotoxic potential of beauvericin are also available in the literature. It is noted that a recent EFSA opinion (EFSA CONTAM Panel, 2014) concluded that there are insufficient data to establish a tolerable daily intake (TDI) or/and an acute reference dose (ARfD) for beauvericin. In the technical specification of *Beauveria bassiana* strain IMI389521, the specification for beauvericin is < 0.1 mg/kg.

Oosporein is produced by many isolates of *B. bassiana*. It has both antibiotic and antiviral properties, but no antifungal or phytotoxic effects. Toxicity in mice and hamsters indicated an LD_{50} value of 0.5 mg/kg body weight (bw) after intraperitoneal injection.

Insufficient data are available about the hazardous properties of the metabolites of *Beauveria bassiana* strain IMI389521 for the setting of acceptable exposure levels for humans (data gap).

The RMS is of the opinion that the potential for toxins/metabolites to enter the food/feed chain via infected insects (since they are produced in the host) is extremely low, considering also treatment and processing of stored grain which would further breakdown any remaining potential metabolites present. However EFSA is of the opinion that the available data do not support this statement.

Reference values and exposure

The representative use is an indoor treatment of storage facilities, 2–4 weeks before the introduction of the harvested grain crops. On the basis of a dust monitoring study, the dust levels of the formulation (containing kaolin as a largest component) during application were very high and exceeding the workplace exposure limits for operators. The use of appropriate respiratory protective equipment by operators will have to be considered at MS level. For the workers, a 4-h re-entry period for the storage facilities is proposed. Pending on the confirmation of the growth temperature of *Beauveria bassiana* IMI389521, the (need of) derivation of an acceptable operator exposure level (AOEL) and the risk assessment for operators and workers cannot be concluded. During the commenting of the draft conclusion, the RMS expressed his disagreement on the fact that the risk assessment for operators and workers cannot be concluded.

3. Residues

Beauveria bassiana IMI389521 is intended for application to the surfaces of empty post-harvest storage facilities before harvest to prevent infestation of grain when stored. It is therefore deduced that the good agricultural practice (GAP) does not intend measures of removal of *Beauveria bassiana* IMI389521 from the surfaces of the structure before grain is placed in storage. Regarding the contamination of grain and resultant potential livestock and consumer exposure issues, it was argued by the RMS that *Beauveria bassiana* IMI389521 is not a storage fungi and that growth and germination of *Beauveria bassiana* IMI389521 are dependent on the presence of a suitable insect host; however, insufficient evidence is available demonstrating that the absence of a host was the pertinent limiting factor. Moreover, it cannot be excluded per se that under practical conditions grain being placed into storage is becoming infested. It was further claimed by the RMS that the conditions induced to maintain the quality of stored cereal grain, such as temperature and humidity control, would also control the germination and growth of *Beauveria bassiana* IMI389521. Data to sufficiently demonstrate which grain storage techniques can be considered representative across European countries and data investigating actual conditions that would control or inhibit the spore germination and/or growth of the specific strain *Beauveria bassiana* IMI389521 were not provided (data gap), and therefore, it is difficult to ascertain the justification provided by the RMS.

The information on optimum growth and germination conditions with regard to *B. bassiana* strains in general as reported by the RMS (e.g. optimum temperature range of 13–33°C, source unknown) plus the facts that lower temperatures than the optimum tend to reduce growth rates but do not necessarily prevent fungal growth and that *Beauveria bassiana* IMI389521 was isolated from insects in a grain store, do in EFSA's opinion not provide sufficient evidence that *Beauveria bassiana* IMI389521 will not germinate or grow under the conditions possible in view of the representative use applied for. Specifically, in the absence of strain specific information on germination and growth conditions it is also not possible to assess whether or not measures such as limitation of the use of *Beauveria bassiana* IMI389521 to grain stores with controlled atmospheres would be effectively preventing its growth or spore germination. Consequently, the opinion of the RMS that the potential for secondary metabolites/toxins of *Beauveria bassiana* IMI389521 entering the food/feed chain would be extremely low is not supported by data (data gap). In EFSA's view, it is not possible at this stage to conclude on the dietary exposure and risk assessment with regard to the use of *Beauveria bassiana* IMI389521 in grain stores, specifically in terms of potential secondary metabolites/toxins. It is noted that the RMS disagrees with this conclusion.

4. Environmental fate and behaviour of the microorganism

Information has not been provided in relation to potential interference of *Beauveria bassiana* strain IMI389521 with the analytical systems for the control of the quality of drinking water provided for in Directive 98/83/EC[2] (see specific Annex VI decision making criteria in Part II Commission Regulation (EU) No 546/2011). However, as these methods require pathogenic bacteria to be identified and confirmed as absent, it is probably unlikely that filamentous fungi or their conidia would interfere with methodologies used for such determinations.

No information has been provided on the potential transfer of genetic material from *Beauveria bassiana* strain IMI389521 to other organisms. Being a fungus, *Beauveria* sp. is not expected to possess plasmids in their cytoplasm (only mitochondrial plasmids are known). Consequently, it is not expected to possess the potential for transfer of genetic material.

Sufficient and reliable information has not been provided in relation to the fate and behaviour of the organism in the environment and on the production of relevant secondary metabolites. However, the intended uses are restricted to treatment of empty post-harvest storage facilities. Therefore, it is understood that exposure to the environment can be prevented by standard good application practices and no further information is required.

5. Ecotoxicology

On the basis of the information provided and considering the representative use, the non-target organisms are not expected to be exposed to *Beauveria bassiana* IMI389521. Therefore, the risk could be concluded as low.

[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, pp. 32 ff.

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 IMI389521	No data; not required for the representative use proposed	No data; not required for the representative use proposed
Relevant toxins or secondary metabolites	No data; not required for the representative use proposed	No data; not required for the representative use proposed

Table 2: Groundwater

Compound (name and/or code)	Mobility in soil	> 0.1 µg/L at 1 m depth for the representative uses[a]	Pesticidal activity	Toxicological relevance
Relevant toxins or secondary metabolites	No data; not required for the limited use proposed	No data; not required for the limited use proposed	No data, however assumed to be the responsible of the pesticidal effect	Data gap

(a): At least one FOCUS scenario or a relevant lysimeter.

Table 3: Surface water and sediment

Compound (name and/or code)	Ecotoxicology
Beauveria bassiana IMI389521	No data; not required for the limited use proposed
Relevant toxins or secondary metabolites	No data; not required for the limited use proposed

Table 4: Air

Compound (name and/or code)	Toxicology
Beauveria bassiana IMI389521	Not toxic, pathogenic or infective by inhalation
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 new search of the scientific peer-reviewed open literature on the metabolites oosporein, oxalic acid and cyclosporine A (also common metabolites to other microorganisms), dealing with side effects on health, published within the 10 years before the date of submission of the dossier, should 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; submission date proposed by the applicant unknown; see Sections 1 and 2).
- Information of the efficacy for the proposed uses following the guidance document SANCO/10054/2013-rev. 3 (European Commission, 2013) needs to be provided (relevant for all representative uses; submission date proposed by the applicant unknown; see Section 1).
- Applicant to ensure that the reports of SOP IMI521 Inoc-001, SOP IMI521 Inoc-002, SOP IMI521 Prod-001, SOP IMI521 Prod-002, SOP IMI521 Prod-003, SOP IMI521 Prod-004, SOP IMI521 Prod-005(1), SOP IMI521 Prod-005 (2), SOP IMI521 Prod-006, SOP QC-Sup-001, SOP IMI521 Inoc-003 are added to the confidential part of the dossier made available to EFSA and the competent authorities of the MSs other than the RMS that already received the documents (relevant for all representative uses; submission date proposed by the applicant unknown; see Section 1).
- Applicant to provide appropriate product storage stability data using product stored in the commercial packaging. The announced ongoing studies for storage stability & shelf life at 4 and 25°C might be appropriate to address this requirement (relevant for all representative uses; submission date proposed by the applicant unknown; see Section 1).
- Applicant to provide a specification for secondary metabolites which may be produced by *Beauveria bassiana*. The specification to be based on an analysis of batches of pure spore material following the applied for method of manufacturer for this strain. IMI389521 (relevant for all representative uses; submission date proposed by the applicant unknown; see Section 1).
- A technique able to identify and distinguish *Beauveria bassiana* IMI389521 at strain level needs to be proposed and validated (relevant for all representative uses; submission date proposed by the applicant unknown; see Section 1).
- Applicant to provide clear evidence that conidia of *Beauveria bassiana* IM1289521 do not germinate above 35°C. The study to be performed under GLP to allow its use for the human health assessment (relevant for all representative uses; submission date proposed by the applicant unknown; see Section 2).
- Applicant to provide data to characterise the production and persistence of beauvericin and other mycotoxins found to be produced by *Beauveria bassiana* strain IM1289521 in the plant products (stored grain) and the grain store environment (relevant for all representative uses; submission date proposed by the applicant unknown; see Sections 1 and 3).
- Information on the antibiotic resistance of *Beauveria bassiana* IMI389521 (relevant for all representative uses; submission date proposed by the applicant unknown; see Sections 1 and 2).
- Further data should be provided to conclude on the hazard and risk assessment for the secondary metabolites/toxins of *Beauveria bassiana* strain IMI389521 (relevant for all representative uses; submission date proposed by the applicant unknown; see Section 2).
- Data investigating actual conditions that would control or inhibit the spore germination and/or growth of the specific strain *Beauveria bassiana* IMI389521 and data to sufficiently demonstrate which grain storage techniques can be considered representative across European countries (relevant for all representative uses; submission date proposed by the applicant unknown; see Section 3).
- Data to assess the potential for secondary metabolites/toxins of *Beauveria bassiana* IMI389521 entering the food/feed chain and the resulting dietary exposure and risk (relevant for all representative uses; submission date proposed by the applicant unknown; see Section 3).

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

Intended uses are restricted to treatment of empty post-harvest storage facilities, standard good application practices to prevent environmental exposure should be applied. Further information to address environmental risk assessment would need to be required if uses are to be extended to field or greenhouse applications.

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[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 cannot be excluded and their hazard assessment cannot be finalised for humans (including operators and workers for the representative use). As a consequence, the risk assessment cannot be concluded.

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 a 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.

- None.

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.)

[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.

Table 5: Overview of concerns

Representative use		Empty stores
Operator risk	Risk identified	
	Assessment not finalised	X[1]
Worker risk	Risk identified	
	Assessment not finalised	X[1]
Resident/bystander risk	Risk identified	
	Assessment not finalised	
Consumer risk	Risk identified	
	Assessment not finalised	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	
	Assessment not finalised	
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 μg/L breached	
	Assessment not finalised	

The superscript numbers in this table relate to the numbered points indicated in Section 9.1.

References

EFSA (European Food Safety Authority), 2011. Submission of scientific peer-reviewed open literature for the approval of pesticide active substances under Regulation (EC) No 1107/2009. EFSA Journal 2011;9(2):2092, 49 pp. https://doi.org/10.2903/j.efsa.2011.2092

EFSA (European Food Safety Authority), 2017. Peer review report to the conclusion regarding the peer review of the pesticide risk assessment of the active substance *Beauveria bassiana* IMI389521.

EFSA CONTAM Panel (EFSA Panel on Contaminants in the Food Chain), 2014. Scientific Opinion on the risks to human and animal health related to the presence of beauvericin and enniatins in food and feed. EFSA Journal 2014;12(8):3802, 174 pp. https://doi.org/10.2903/j.efsa.2014.3802

European Commission, 2013. Guidance document on data requirements on efficacy for the dossier to be submitted for the approval of new active substances contained in plant protection products.

Netherlands, 2016. Draft Assessment Report (DAR) on the active substance *Beauveria bassiana* IMI389521 prepared by the rapporteur Member State the Netherlands in the framework of Regulation (EC) No 1107/2009, February 2016. Available online: www.efsa.europa.eu

Netherlands, 2017. Revised Draft Assessment Report (DAR) on *Beauveria bassiana* IMI389521 prepared by the rapporteur Member State the Netherlands in the framework of Regulation (EC) No 1107/2009, February 2017. Available online: www.efsa.europa.eu

Abbreviations

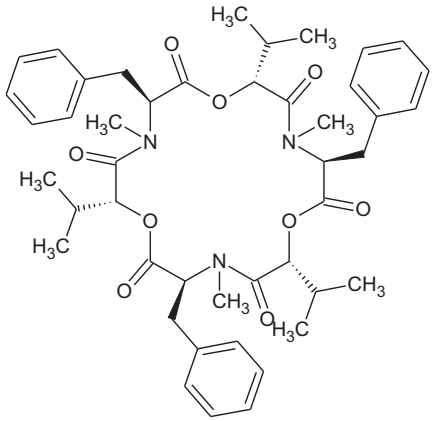
AOEL	acceptable operator exposure level
ARfD	acute reference dose
bw	body weight
DAR	draft assessment report
EEC	European Economic Community
FOCUS	Forum for the Co-ordination of Pesticide Fate Models and their Use
GAP	good agricultural practice
GLP	good laboratory practice
IgE	immunoglobulin E
LD_{50}	lethal dose, median; dosis letalis media
MS	Member State
RMS	rapporteur Member State

SMILES	simplified molecular-input line-entry system
TDI	tolerable daily intake

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.2017.4831

Appendix B – Used compound codes

Code/trivial name[(a)]	Chemical name/SMILES notation	Structural formula
Beauvericin	(3*S*,6*R*,9*S*,12*R*,15*S*,18*R*)-3,9,15-Tribenzyl-6,12,18-triisopropyl-4,10,16-trimethyl-1,7,13-trioxa-4,10,16-triazacyclooctadecane-2,5,8,11,14,17-hexone CC(C)[C@H]4OC(=O)[C@H](Cc1ccccc1)N(C)C(=O)[C@H](OC(=O)[C@H](Cc2ccccc2)N(C)C(=O)[C@H](OC(=O)[C@H](Cc3ccccc3)N(C)C4=O)C(C)C)C(C)C	

SMILES: simplified molecular-input line-entry system.
(a): The metabolite name in bold is the name used in the conclusion.