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Peer review of the pesticide risk assessment of the active substance *Beauveria bassiana* strain 147

European Food Safety Authority (EFSA)

Abstract

The conclusions of the European Food Safety Authority (EFSA) following the peer review of the initial risk assessments carried out by the competent authority of the rapporteur Member State France for the pesticide active substance *Beauveria bassiana* strain 147 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 147 as an insecticide on ornamental palm trees. 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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Key words: *Beauveria bassiana* strain 147, peer review, risk assessment, pesticide, insecticide

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Summary

Beauveria bassiana strain 147 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), France, received an application from Arysta Lifescience S.A.S. on 6 November 2012 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 5 February 2013.

The RMS provided its initial evaluation of the dossier on *Beauveria bassiana* strain 147 in the draft assessment report (DAR), which was received by the European Food Safety Authority (EFSA) on 2 October 2014. The peer review was initiated on 8 October 2014 by dispatching the DAR for consultation to the Member States and the applicant, Arysta Lifescience S.A.S.

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 area of ecotoxicology.

In accordance with Article 12 of the Regulation, EFSA should adopt a conclusion on whether *Beauveria bassiana* strain 147 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 147 as an insecticide on ornamental palm trees, as proposed by the applicant. Full details of the representative uses can be found in Appendix A of this report.

Sufficient efficacy data were provided to support the use of this material.

A data gap has been identified for a satisfactory search of the scientific peer-reviewed open literature relevant to the scope of the application, dealing with side-effects on the environment and non-target species in relation to *Beauveria bassiana* strain 147 and its secondary metabolites/toxins, published within the last 10 years before the date of submission of the dossier, completed in accordance with the Guidance of EFSA on the submission of scientific peer-reviewed open literature for the approval of pesticide active substances under Regulation (EC) No 1107/2009.

In the area of identity of the microorganism/biological properties/physical and technical properties and methods of analysis data gaps were identified for the validation of analytical methods for secondary metabolites and for a storage stability study for the formulation.

In the area of mammalian toxicology, a data gap was identified for addressing the toxicity of the microorganism after repeated dose via inhalation. Another data gap was identified in relation with the lack of data on the potential toxicity of the secondary metabolites/toxins. As a consequence of these two data gaps, the risk assessment for the operators, workers, bystanders and residents cannot be concluded.

As the use is only on ornamental palms there is no consumer exposure and residues data are not required.

No satisfactory information has been provided to demonstrate that, under the conditions of use, any secondary metabolites/toxins produced by *Beauveria bassiana* strain 147 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 contamination and soil and surface water exposure.

A high risk to honeybees was concluded for the representative field use to palm trees. The risk assessment for aquatic organisms, non-target arthropods and sewage treatment organisms could not be finalised with the available information. The risk assessment for non-target organisms from secondary metabolites and toxins in the environment following application is not finalised.

A low risk to birds, mammals, wild bees, non-target arthropods, earthworms, soil microorganisms and non-target plants was concluded for the representative use to palm trees in glasshouses, however, a data gap was identified to address the risk to aquatic organisms. A data gap for information to address the risk to sewage treatment organisms from the representative use in glasshouses was concluded. No assessment was available for pollinators which may be introduced to glasshouses. Given the concerns raised for honeybees, it cannot be excluded that *Beauveria bassiana* strain 147 poses a risk to pollinators if introduced to glasshouses.

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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 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 147 is a new active substance for which, in accordance with Article 7 of the Regulation, the RMS, France (hereinafter referred to as the 'RMS'), received an application from Arysta Lifescience S.A.S. on 6 November 2012 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 5 February 2013.

The RMS provided its initial evaluation of the dossier on *Beauveria bassiana* strain 147 in the DAR, which was received by EFSA on 2 October 2014 (France, 2014). The peer review was initiated on 8 October 2014 by dispatching the DAR to the Member States and the applicant, Arysta Lifescience S.A.S., 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, the RMS, and the European Commission on 30 January 2015. On the basis of the comments received, the applicant's response to the comments and the RMS's evaluation thereof, it was concluded that additional information should be requested from the applicant, and that EFSA should conduct an expert consultation in the area of 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 147 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 September 2015.

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 147 as an insecticide on ornamental palm trees, as proposed by the applicant. Furthermore, this conclusion also addresses the assessment required from EFSA under

[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.

Article 12 of Regulation (EC) No 396/2005. 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, 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 (EFSA, 2015) 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 (30 January 2015);
- the evaluation table (14 September 2015);
- the report 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 (France, 2015) 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 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

Efficacy data following the guidance document SANCO/10054/2013-rev. 3 (European Commission, 2013) were provided and are acceptable.

A data gap has been identified for a search of the scientific peer-reviewed open literature on the active substance and its relevant secondary metabolites/toxins, 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).

The strain under review is *Beauveria bassiana* strain 147. Strain 147 was originally isolated from populations of diapausing larvae of European corn borer (*Ostrinia nubilalis*) present in Levesville (Beauce - France).

The representative formulated product for the evaluation was 'ARY-0711a-01' containing 5 x 10^8 CFU/g. The formulation is a microgranule (MG).

The representative use evaluated was on ornamental palms in both indoor and outdoor conditions. Full details of the GAP can be found in the list of end points in Appendix A.

Conclusions of the evaluation

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

Strain 147 is deposited at CNCM (Collection Nationale de Culture de Microorganismes) – Institut Pasteur, Paris, France, I-2960

The strain is not able to grow at 37 °C and above.

The content of contaminating microorganisms was fully addressed and is in accordance with the OECD issue paper (OECD, 2011). It can be concluded that this strain does not produce significant secondary metabolites/toxins during the manufacturing process. However, a data gap was identified for further validation of the methods of analysis used.

The identification of the strain is based on sequencing of ITS region of rRNA and 2 intergenic regions of mt DNA. Other quantitative methods were provided which were acceptable. Analytical methods for plants, animals and the environment were not required.

For 'ARY-0711a-01' containing strain 147 a data gap was identified for further storage stability data including data on microbiological contaminants.

2. Mammalian toxicity

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 (or no information on the specific strain identified was available). 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, *Beauveria bassiana* strains show allergic potential and sensitising properties for both skin 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* 147 was not infective or pathogenic after oral exposure (rat LD_{50} > 1.8 x 10^9 CFU/kg bw), after intratracheal exposure (rat LD_{50} > 4.2 × 10^8 CFU/kg bw), and after intraperitoneal exposure (rat LD_{50} > 6.9 x 10^8 CFU/kg bw). Mild irritant effects were observed in dermal and eye irritation studies with rabbits.

In the intratracheal study, 3 deaths were observed during the first day post exposure. Considering also the localisation of lesions (lungs only), the lung clearance by day 3 (for surviving animals), the fact that the microorganism was not shown to grow at human body temperature, these mortalities are not consistent with an infection or a pathogenic effect. Although likely to be related to the mode of administration, a possible sensitisation and/or toxic effect by inhalation cannot be excluded. As a consequence, a data gap is identified for addressing the toxicity of the microorganism after repeated dose via inhalation. The RMS disagrees.

With regard to the genotoxicity assessment of *Beauveria bassiana* strain 147, Ames tests performed with culture juice and with DMSO extracts from pulverised mycelium in two different media gave negative results.

In a 90-day rat oral study with *Beauveria bassiana* strain 147, a dose of 4 × 10^8 CFU/kg bw per day did not induce neither toxic effects nor infectivity or pathogenicity. The test organism was not detected in any of the samples collected at the terminal necropsy.

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. Since no threshold can be assumed for a genotoxic compound, the assumption that the doses tested in genotoxicity studies are much higher than the level in the technical specification cannot be supported.

It is also noted that a recent EFSA opinion (EFSA, 2014) concluded that there are insufficient data to establish a tolerable daily intake (TDI) or/and an acute reference dose (ARfD) for beauvericin.

Due to insufficient current literature data on secondary metabolites/toxins and their potential toxicity, it is not possible at this stage to conclude on the hazard assessment for the secondary metabolites/toxins of *Beauveria bassiana* strain 147 (data gap).

Reference values and exposure

Considering the representative uses, the derivation of an ADI and ARfD was not necessary. Pending on further investigation/clarification of the repeat dose toxicity by inhalation, the risk assessment for the operator, worker, bystander and resident cannot be finalised.

3. Residues

The representative use is on ornamental palms and there will therefore be no consumer exposure. As this is the case no residue data have been submitted or required.

4. Environmental fate and behaviour

Information has not been provided in relation to potential interference of *Beauveria bassiana* strain 147 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[3]). However, as these methods require pathogenic bacteria to be identified and confirmed as

[2] Council Directive 98/83/EC of 3 November 1998 on the quality of water intended for human consumption. OJ L 330, 5.12.98, p.32-54

[3] Commission Regulation (EU) 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.

absent, it is probably unlikely that filamentous fungi or their conidia would interfere with methodologies used for such determinations.

The majority of the information available in the dossier of *Beauveria bassiana* strain 147 was extrapolated from published review or articles gathering relevant information on different strains of *Beauveria bassiana*. In particular, information available from the draft assessment reports of strains ATCC-74040 and GHA were considered (Germany, 2007a, 2007b, 2012a, 2012b). This was considered acceptable by the peer review.

4.1. Fate and behaviour in the environment of the microorganism

Strain specific data on *Beauveria bassiana* strain 147 to address the persistence and multiplication in soil were not provided. The information provided was generally from open literature. A number of recent persistency studies show that *Beauveria 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). It was estimated that the applied inoculum density decreases to upper natural background levels within 0.5-1.5 years. These values indicate that the fungi can be considered as persistent. Predicted environmental concentration (PEC) for *Beauveria bassiana* strain 147 in soil are presented in Appendix A. The calculations are based on the conservative assumption that there is no crop interception and without considering a decline of CFUs between applications. In situations where the palm trees are planted in pots in nurseries and the pots are positioned on hard surfaces, the soil exposure to *Beauveria bassiana* strain 147 following the application of 'ARY-0711a-01' can be considered as negligible.

Studies on persistence and multiplication in water of *Beauveria bassiana* strain 147 are not available. One study aiming at assessing fungal diversity in 3 untreated water sources (surface, spring and groundwater) found that less than 2% of the identified fungi belonged to the genus *Beauveria*. Literature information in the dossier indicates that conidia of *Beauveria bassiana* in water are unlikely to proliferate and will probably be rapidly degraded by bacteria and protozoa in natural non-sterile water bodies. Maximum initial PEC surface water values following applications of 'ARY-0711a-01' were calculated assuming 100% drift into water bodies, instant and complete homogenisation in the water body.

Specific study on the *Beauveria bassiana* strain 147 has not been conducted to evaluate its persistence and mobility in air. Its degradation in the air has been related in the literature to UV exposition and different technologies are even developed to protect the fungus from this kind of exposition. Overall, taking all the observations into consideration, it has been concluded that *Beauveria bassiana* is expected to be degraded rapidly in the air and no accumulation is expected.

With respect to the mobility of the microorganism, different studies showed that conidia of *Beauveria bassiana* are not very mobile in soil and generally remain on the soil surface. Insects can transport conidia which are subsequently dislodged through grooming and transferred to soil particles. Heavy rainfall can also potentially promote the horizontal movement of conidia. Presence of conidia in air or 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 'ARY-0711a-01' is not available. 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 544/2011[4] need to be fulfilled if all the following conditions are met:

- the relevant metabolite is stable outside the microorganism

[4] 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.

- a toxic effect of the relevant metabolite is independent of the presence of the microorganism, and
- the relevant metabolite is expected to occur in the environment in concentrations considerably higher than under natural conditions.

This data gap is pertinent in respect of the representative uses in the field and glasshouse assessed for *Beauveria bassiana* strain 147. In situations where the palm trees are planted in pots in nurseries and the pots are positioned on hard surfaces, the soil and groundwater exposures to the relevant metabolite(s) produced by *Beauveria bassiana* strain 147 can be considered as negligible.

A specific literature search was conducted by the applicant on the secondary metabolites/toxins detected in the spore powder and in the formulated product. Concerning background levels of *Beauveria bassiana* secondary metabolites/toxins, information was found only on natural occurrence and distribution in surface water of beauvericin and on its biodegradation. It was concluded that the amounts of beauvericin present in the formulated product will not occur in the surface water compartment in concentrations higher than under natural conditions.

5. Ecotoxicology

A data gap was identified (see Section 4) for further information to understand the possibility of *Beauveria bassiana* strain 147 to produce secondary metabolites/ toxins in the environment following application. Some ecotoxicological information was provided in the DAR for the known metabolites beauvericin and cyclosporine. However, the data were not included in the dossier and consequently not been evaluated by the RMS. Therefore, the information could not be validated for use in risk assessment. A data gap was therefore identified for further information to address the risk to non-target organisms from secondary metabolites and toxins including beauvericin and cyclosporine.

A suitable study demonstrating that *Beauveria bassiana* strain 147 is not infectious or pathogenic to birds was available. Furthermore, it was concluded that *Beauveria bassiana* strain 147 is not infectious or pathogenic to mammals.

In the available studies on fish and *Daphnia magna* mortality was observed, however, it was not clear the reasons for the mortality. The studies were discussed at the Pesticides Peer Review Expert, Teleconference 115. The experts considered that the mortality could have been due to a number of reasons such as a physical effect caused by the presence of the test material. However, the studies lacked sufficient information (e.g. assessment of turbidity or the use of attenuated control) to be able to reach such a conclusion. Therefore, with the information available it was concluded that the assessment of infectivity and pathogenicity could not be finalised. A data gap was therefore concluded for further information to address the potential for infectivity and pathogenicity to fish and aquatic invertebrates (relevant for all representative uses). On the basis of the available data a low risk to algae was concluded.

Two laboratory studies investigating the chronic effects on adult bees were available. In both studies mortality was observed. It was not clear the reason for the observed mortality and therefore, with the information available, it was considered that it cannot be excluded that the effects were caused by infectivity or pathogenicity. A bee brood semi-field study was available. No difference in forager mortality was observed. However, for the brood assessments, there was a severe problem in the control not performing as expected. The study was therefore not considered to be valid. Several literature papers were included in the revised DAR. None of the papers were performed with *Beauveria bassiana* strain 147. It is, however, noted that a study indicated that some strains can be infectious to honeybee larvae. A further study indicated mortality of honeybees when exposed to *Beauveria bassiana* strains Arkansas, GHA, London and NY under laboratory conditions. The study authors stated that there was a comparable level of mortality to the control under field conditions. However, the level of detail regarding the test methodology for the field experiments was severely lacking. Overall, it seems evident that some strains of *Beauveria bassiana* have the ability to be infectious and pathogenic to honeybees. Given that the strain specific data for *Beauveria bassiana* strain 147 indicates mortality of adult bees and the available bee brood study was not considered valid, it is considered that it cannot be excluded that *Beauveria bassiana* strain 147 poses a risk to honeybees from infectivity and pathogenicity. It is noted that the representative use as a microgranule to field grown palm trees may result in a low exposure to bees. Nevertheless, exposure

cannot be fully excluded and therefore it is necessary to demonstrate that *Beauveria bassiana* strain 147 is not infectious or pathogenic to bees. A high risk to honeybees was therefore concluded and a data gap for further information to address the risk to adult honeybees and honeybee brood was identified (relevant for the representative uses to field grown palm trees).

Studies investigating the effect of *Beauveria bassiana* strain 147 on non-target arthropods were available. However, one of the studies was not considered to be valid due to high levels of mortality in the control group. Some literature information was also summarised which indicated that some strains of *Beauveria bassiana* can be infectious to non-target arthropods. Overall, it is considered that the available information is not sufficient to demonstrate that *Beauveria bassiana* strain 147 will not be infectious or pathogenic to non-target arthropods. A data gap was therefore identified (relevant for the representative uses to field grown palm trees).

A chronic toxicity study with earthworms was available. No specific investigations of infectivity and pathogenicity were performed. However, due to a lack of effects observed in the study it was concluded that *Beauveria bassiana* strain 147 is unlikely to be infectious or pathogenic to earthworms. Literature information was available which indicated that applications of *Beauveria bassiana* did not affect the diversity of fungal communities over a 7 week period. A low risk to soil microorganisms was therefore concluded. A low risk to non-target plants was concluded on the basis of the available data.

For the representative use to palm trees in glasshouses, exposure to birds, mammals, wild bees, non-target arthropods, earthworms, soil microorganisms and non-target plants was considered unlikely. A low risk was therefore concluded. However, exposure to surface water cannot be excluded and therefore a data gap to address the risk to aquatic organisms from infectivity and pathogenicity and from secondary metabolites/toxins was concluded. Exposure to sewage treatment organisms cannot be excluded. No reliable information was available to address the risk and therefore a data gap was concluded (relevant only for the representative use to palm trees in glasshouses). No assessment was available for pollinators which may be introduced to glasshouses. Given the concerns raised for honeybees, it cannot be excluded that *Beauveria bassiana* strain 147 poses a risk to pollinators if introduced to glasshouses.

Some literature information was included in the DAR. However, it was not clear whether a systematic search of the literature was performed. Furthermore, an evaluation of the search methodology was not available. Consequently a data gap was identified for a search of the scientific peer-reviewed open literature on the microorganism and its relevant secondary metabolites/toxins.

6. Overview of the risk assessment of compounds listed in residue definitions triggering assessment of effects data for the environmental compartments

Table 1: Soil

Compound (name and/or code)	Persistence	Ecotoxicology
Beauveria bassiana strain 147	The applied inoculum density decreases to upper natural background levels within 0.5-1.5 years. These values indicate the fungi can be considered as persistent.	Low risk to soil organisms
Relevant toxins or secondary metabolites	Data gap pending on their identification and quantification	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 (at least one FOCUS scenario or relevant lysimeter)	Pesticidal activity	Toxicological relevance	Ecotoxicology
Relevant toxins or secondary metabolites	Data gap pending on their identification and quantification	Data gap pending on their identification and quantification	No data	Data gap	No reliable data.

Table 3: Surface water and sediment

Compound (name and/or code)	Ecotoxicology
Beauveria bassiana strain 147	Data gap
Relevant toxins or secondary metabolites	Data gap

Table 4: Air

Compound (name and/or code)	Toxicology
Beauveria bassiana strain 147	Data gap
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).

7.1. Data gaps identified for the representative uses evaluated

- A search of the scientific peer-reviewed open literature on the active substance and its relevant metabolites/toxins, 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; relevant for all representative uses evaluated; submission date proposed by the applicant unknown, see Sections 4 and 5).

- Validated analytical methods for the secondary metabolites. If the validated method is different to that used in the batch study then a new batch study should be provided (relevant for all representative uses evaluated; submission date proposed by the applicant unknown; see Section 1).

- An additional stability study including data on microbiological contaminants (according to European Commission, 2012) after storage of the preparation at 4°C during 1 year or under other optimum condition of storage in its commercial package (relevant for all representative uses evaluated; submission date proposed by the applicant unknown; see Section 1).

- Further characterisation of the toxicity of the microorganism after repeated exposure via inhalation (relevant for all representative uses evaluated; submission date proposed by the applicant unknown; see Section 2).

- Further information in order to conclude on the hazard and risk assessment for the secondary metabolites/toxins of *Beauveria bassiana* strain 147 (relevant for all representative uses evaluated; submission date proposed by the applicant unknown; see Section 2).

- Satisfactory information to demonstrate that, under the conditions of use, any relevant secondary metabolites/toxins that are produced by *Beauveria bassiana* strain 147 will not occur in the environmental compartments in concentrations considerably higher than under natural conditions (with the exception for the aquatic compartment exposed to beauvericin present in the formulated product). Further data on the persistence, transformation and mobility of these compounds may be needed in order to assess the potential level of environmental exposure including groundwater (relevant for all representative uses evaluated; submission date proposed by the applicant: unknown; see Section 4).

- Further information to address the risk to non-target organisms from secondary metabolites and toxins, including beauvericin and cyclosporine (relevant for all representative uses; submission date proposed by the applicant unknown; see Section 5).

- Information to demonstrate that *Beauveria bassiana* strain 147 is not infectious or pathogenic to fish, aquatic invertebrates and non-target arthropods (relevant for the representative uses to field grown palm trees; submission date proposed by the applicant unknown; see Section 5).

- Further information to address the observed effects on honeybees and to demonstrate that *Beauveria bassiana* strain 147 is not infectious or pathogenic to adult honeybees and honeybee brood (relevant for the representative uses to field grown palm trees; submission date proposed by the applicant unknown; see Section 5).

- Information to address the risk to sewage treatment organisms relevant for the representative uses to palm trees in glasshouses; 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

8.1. Particular conditions proposed for the representative uses evaluated

No particular conditions are proposed for the representative uses evaluated.

9. Concerns

9.1. Concerns for the representative uses evaluated

9.1.1. 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[5] 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 therefore the risk assessment cannot be finalised for humans (including operators, workers, bystanders and residents) and the environment including the assessment of potential groundwater contamination and the potential risk to non-target organisms.
2. The assessment of infectivity and pathogenicity for fish, aquatic invertebrates, non-target arthropods and sewage treatment organisms could not be finalised with the available data.

9.1.2. 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 a 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.

[5] 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.

3. None identified for the representative uses evaluated

9.1.3. 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		Ornamental palm trees Max 5 applications to control Paysandisi archon (14 days interval)		Ornamental palm trees Max 7 applications to control Rhynchophorus ferrugineus (21 days interval)	
		field	glasshouse	field	glasshouse
Operator risk	Risk identified				
	Assessment not finalised	X[1]	X[1]	X[1]	X[1]
Worker risk	Risk identified				
	Assessment not finalised	X[1]	X[1]	X[1]	X[1]
Bystander/resident risk	Risk identified				
	Assessment not finalised	X[1]		X[1]	
Consumer risk	Risk identified				
	Assessment not finalised				
Risk to wild non-target terrestrial vertebrates	Risk identified				
	Assessment not finalised	X[1]		X[1]	
Risk to wild non-target terrestrial organisms other than vertebrates	Risk identified	X		X	
	Assessment not finalised	X[1,2]		X[1,2]	
Risk to aquatic organisms	Risk identified				
	Assessment not finalised	X[1,2]	X[1,2]	X[1,2]	X[1,2]
Groundwater exposure to active substance	Legal parametric value breached				
	Assessment not finalised				
Groundwater exposure to metabolites	Legal parametric value breached				
	Parametric value of 10µg/L(a) breached				
	Assessment not finalised	X[1]	X[1]	X[1]	X[1]

Columns are grey if no safe use can be identified. The superscript numbers in this table relate to the numbered points indicated in Sections 9. Where there is no superscript number, see Sections 2 to 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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Abbreviations

ε	decadic molar extinction coefficient
1/*n*	slope of Freundlich isotherm
a.s.	active substance
AChE	acetylcholinesterase
ADE	actual dermal exposure
ADI	acceptable daily intake
AF	assessment factor
AOEL	acceptable operator exposure level
AP	alkaline phosphatase
AR	applied radioactivity
ARfD	acute reference dose
AST	aspartate aminotransferase (SGOT)
AV	avoidance factor
BCF	bioconcentration factor
BUN	blood urea nitrogen
bw	body weight
CAS	Chemical Abstracts Service
CFU	colony-forming units
ChE	cholinesterase
CI	confidence interval
CIPAC	Collaborative International Pesticides Analytical Council Limited
CL	confidence limits
d	day
DAA	days after application
DAR	draft assessment report
DAT	days after treatment
DDD	daily dietary dose
DM	dry matter
DMSO	dimethyl sulfoxide
DT_{50}	period required for 50% dissipation (define method of estimation)
DT_{90}	period required for 90% dissipation (define method of estimation)
dw	dry weight
EbC_{50}	effective concentration (biomass)
EC_{50}	effective concentration
ECHA	European Chemicals Agency
EEC	European Economic Community

EINECS	European Inventory of Existing Commercial Chemical Substances
ELINCS	European List of New Chemical Substances
EMDI	estimated maximum daily intake
ER_{50}	emergence rate/effective rate, median
ErC_{50}	effective concentration (growth rate)
EU	European Union
EUROPOEM	European Predictive Operator Exposure Model
f(twa)	time-weighted average factor
FAO	Food and Agriculture Organization of the United Nations
FID	flame ionisation detector
FIFRA	Federal Insecticide, Fungicide, and Rodenticide Act
FIR	food intake rate
FOB	functional observation battery
FOCUS	Forum for the Co-ordination of Pesticide Fate Models and their Use
GAP	good agricultural practice
GC	gas chromatography
GCPF	Global Crop Protection Federation (formerly known as International Group of National Associations of Manufacturers of Agrochemical Products (GIFAP))
GGT	gamma glutamyl transferase
GM	geometric mean
GS	growth stage
GSH	glutathione
Hb	haemoglobin
Hct	haematocrit
HPLC	high-pressure liquid chromatography or high-performance liquid chromatography
HPLC-MS	high-pressure liquid chromatography–mass spectrometry
HQ	hazard quotient
IEDI	international estimated daily intake
IESTI	international estimated short-term intake
IOBC	International Organisation Biological Control
IPM	integrated pest management
ISO	International Organization for Standardization
ITS	internal transcribed spacer
IUPAC	International Union of Pure and Applied Chemistry
JMPR	Joint Meeting on the FAO Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Expert Group on Pesticide Residues (Joint Meeting on Pesticide Residues)
K_{doc}	organic carbon linear adsorption coefficient

K_{Foc}	Freundlich organic carbon adsorption coefficient
LC	liquid chromatography
LC_{50}	lethal concentration, median
LC-MS	liquid chromatography–mass spectrometry
LC-MS-MS	liquid chromatography with tandem mass spectrometry
LD_{50}	lethal dose, median; dosis letalis media
LDH	lactate dehydrogenase
LOAEL	lowest observable adverse effect level
LOD	limit of detection
LOQ	limit of quantification (determination)
M/L	mixing and loading
MAF	multiple application factor
MCH	mean corpuscular haemoglobin
MCHC	mean corpuscular haemoglobin concentration
MCV	mean corpuscular volume
mm	millimetre (also used for mean measured concentrations)
mN	milli-newton
MRL	maximum residue level
MS	mass spectrometry
MSDS	material safety data sheet
MTD	maximum tolerated dose
mtDNA	mitochondrial DNA
MWHC	maximum water-holding capacity
NESTI	national estimated short-term intake
NOAEC	no observed adverse effect concentration
NOAEL	no observed adverse effect level
NOEC	no observed effect concentration
NOEL	no observed effect level
NPD	nitrogen–phosphorus detector
OECD	Organisation for Economic Co-operation and Development
OM	organic matter content
Pa	pascal
PD	proportion of different food types
PEC	predicted environmental concentration
PEC_{air}	predicted environmental concentration in air
PEC_{gw}	predicted environmental concentration in groundwater
PEC_{sed}	predicted environmental concentration in sediment

PEC_{soil}	predicted environmental concentration in soil
PEC_{sw}	predicted environmental concentration in surface water
PHED	pesticide handler's exposure data
PHI	pre-harvest interval
PIE	potential inhalation exposure
pK_a	negative logarithm (to the base 10) of the dissociation constant
P_{ow}	partition coefficient between *n*-octanol and water
PPE	personal protective equipment
ppm	parts per million (10^{-6})
PT	proportion of diet obtained in the treated area
PTT	partial thromboplastin time
QSAR	quantitative structure–activity relationship
r^2	coefficient of determination
rRNA	ribosomal ribonucleic acid
REACH	Registration, Evaluation, Authorisation of Chemicals Regulation
RPE	respiratory protective equipment
RUD	residue per unit dose
SC	suspension concentrate
SD	standard deviation
SFO	single first-order
SMILES	simplified molecular-input line-entry system
SSD	species sensitivity distribution
STMR	supervised trials median residue
$t_{1/2}$	half-life (define method of estimation)
TER	toxicity exposure ratio
TER_A	toxicity exposure ratio for acute exposure
TER_{LT}	toxicity exposure ratio following chronic exposure
TER_{ST}	toxicity exposure ratio following repeated exposure
TK	technical concentrate
TLV	threshold limit value
TMDI	theoretical maximum daily intake
TRR	total radioactive residue
TSH	thyroid-stimulating hormone (thyrotropin)
TWA	time-weighted average
UDS	unscheduled DNA synthesis
UV	ultraviolet
W/S	water/sediment

w/v	weight per unit volume
w/w	weight per unit weight
WBC	white blood cell
WG	water dispersible granule
WHO	World Health Organization
wk	week
yr	year
λ	wavelength

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

Identity, Biological properties, Details of Uses, Further Information

Active micro-organism	*Beauveria bassiana* strain 147
Function (e.g. control of fungi)	Insecticide

Identity of the micro-organism (Annex IIM 1)

Name of the organism	*Beauveria bassiana* strain 147
Taxonomy	Species: *bassiana* First description: Vuillemin Strain: 147 Genus: *Beauveria* Family: *Clavicipitaceae*
Species, subspecies, strain:	*Beauveria bassiana* strain 147
Identification	Identification based on sequencing of ITS region of rRNA and 2 intergenic regions of mt DNA
Culture collection	Deposited at CNCM (Collection Nationale de Culture de Microorganismes) – Institut Pasteur, Paris, France, I-2960

Biological properties of the micro-organism (Annex IIM 2)

Origin and natural occurrence	*Beauveria bassiana* is a telluric, ubiquitous fungus. It is not host specific but an opportunistic entomopathogen capable of attacking a wide range of insect taxa. This conclusion is reinforced by evidence that closely related isolates originating from the same geographic region were isolated from taxonomically distant insect hosts. Strain 147 was isolated from populations of diapausing larvae of European corn borer (*Ostrinia nubilalis*) present in Levesville (Beauce - France).
Target organism(s)	The Palm Borer, *Paysandia archon* The red palm weevil, *Rhynchophorus ferrugineus*
Mode of action	*Beauveria bassiana* 147 acts by contact-action. Spores (also called conidia (= asexual spores)) adhere to the host cuticle and then germinate. The cuticle is penetrated and the fungus grows by vegetative growth in the host haemocoel. External spores are produced upon the death of the host in order to propagate the fungus to new hosts.
Host specificity	*Beauveria bassiana* has a large host range, most commonly being found in the insect orders Lepidoptera, Coleoptera and Hemiptera.

Life cycle	Parasitic phase: Adhesion and germination of spores on the cuticle Penetration of the tegument: recognition (production of different enzymes) and infection Colonisation: toxic substance emission, multiplication (production of blastospores), haemocoel invasion Saprophytic phase: Total colonisation Exit of the hyphae through the tegument in favourable environmental conditions Sporulation Survival in the soil Dissemination
Infectivity, dispersal and colonisation ability	*Beauveria bassiana* is a naturally occurring, ubiquitous fungus. Conidia are poorly mobile in soil, being dispersed predominantly by leaching and by the activity of soil micro fauna.
Relationships to known plant, animal or human pathogens	*Beauveria bassiana* strain 147 is not related to any known human pathogens.
Genetic stability	Natural non modified organisms can change by mutation or recombination. 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.
Production of relevant metabolites/toxins	Strains of *Beauveria bassiana* have the potential to produce a range of different secondary metabolites. Beauvericin is specified at very low amount. Other secondary metabolites were looked for but not detected. Validation of the method for the other secondary metabolites: pending.
Resistance/sensitivity to antibiotics used in human or veterinary medicine	In clinical cases linked to *Beauveria bassiana* reported in the open literature, the use of some fungicides has proved efficiency: amphotericin B +/- itraconazole in the case of systemic infections, topical natamycin + oral fluconazole in the case of keratitis. Nevertheless, two cases of keratitis showed resistance to amphotericin B and fluconazole, whereas concerned strains (not specified) were sensitive to posaconazole, itraconazole, miconazole and voriconazole.

Summary of intended uses

Crop and /or situation (a)	Member State or Country	Product name	F G or I (b)	Pest or Group of pests controlled (c)	Formulation		Application				Application rate per treatment			PHI (day) (l)	Remarks (m)
					Type (d-f)	Conc. of MPCA (i)	method kind (f-h)	growth stage & season (j)	Number min max	interval between applications (min)	CFU MPCA/ hl min max	water l/ha min max	CFU MPCA/ ha min max		
Ornemental Palm trees	Southern Europe	ARY-0711a-01 (*Beauveria bassiana* 147)	F G	*Paysandisia archon*	MG	$5x10^8$CFU / g of dry matter	Direct application of the granules between the rachis with an atomizer equipped for micro-granule or with a little applicator	During the flight period of *Paysandisia archon* adults	1-5	14 d	Not relevant	Not relevant	Max 106 kg/ha Formulated Product (5.3 x 10^{13} CFU/ha) *	NA	
Ornemental Palm trees	Southern Europe	ARY-0711a-01 (*Beauveria bassiana* 147)	F G	*Rhynchophorus ferrugineus*	MG	$5x10^8$CFU / g of dry matter	Direct application of the granules between the rachis with an atomizer equipped for micro-granule or with a little applicator	During the flight period of *Rhynchophorus ferrugineus*	7 applications max	21d	Not relevant	Not relevant	Max 106 kg/ha Formulated Product (5,3 x 10^{13} CFU/ha) *	NA	

Explanation of a -m

a: The EU classification for crops (90/642/EEC).
b: Outdoor or field use (F), glasshouse application (G) or indoor application (I)
c: e.g. biting and sucking insects, soil born insects, foliar fungi, weeds
d: e.g. wettable powder (WP), emulsifiable concentrate (EC), granule (GR), water soluble powder (SP)
e: GCPF Codes - GIFAP Technical Monograph No 2, 1989
f: all abbreviations used must be explained
g: Method, e.g. high volume spraying, low volume spraying, spreading, dusting, drench,
h: Kind, e.g. overall, broadcast, aerial spraying, row, individual plant, between the plants - type of equipment used must be indicated.
i: g/kg, g/l or appropriate term for micro-organisms
j: Growth stage at last treatment (BBCH Monograph, Growth stage of plants, 1997, Blackwell, ISBN 3-8263-3152-4)
k: The minimum and maximum number of application possible under practical conditions of use must be provided
l: PHI - minimum pre-harvest interval
m: Remarks may include: Extent of use/economic importance/restrictions

Application rates (max = 300g per palm tree)	**Height < 1 m**	**Height > 1 m**
Phoenix spp.	8 g/palm	10 g/palm
Washingtonia spp and other palm trees	3 g/palm	10 g/palm
Trachycapus spp., *Chamaerops* spp. and other palm trees with fibrous stipe	35 g/meter of stipe	100 g/meter of stipe

Further information

Production control	Confidential, see vol. 4 for more details
Proposal for classification and labelling	'Micro-organisms may have the potential to provoke sensitizing reactions'

Analytical Methods

Analytical methods for the micro-organism (Annex IIM 4.2.8; 4.3; IIIM 5.3)

Manufactured micro-organism (principle of method)	Not applicable. The production process of the end-use product is continuous, therefore the technical grade of *Beauveria bassiana* 147 is obtained by liquid fermentation from a mother culture stock of *Beauveria bassiana* 147.
Impurities and contaminating micro-organisms in manufactured material (principle of method)	Microbial contaminants determined according to standards methods
Plant protection product (principle of method)	Quantification of viable *Beauveria bassiana* strain 147 spores performed by plating on potato dextrose agar. Open for validated method for secondary metabolites.

Analytical methods for residues (viable and non-viable) in exposed compartments and organisms (Annex IIM 4.5)

of the active micro-organism (principle of method)	Not required
of relevant metabolites/toxins (principle of method)	Not required

Effects on Human Health

Effects on human health (Annex IIM 5; IIIM 7)

Medical data and direct observation, e.g. clinical cases (Annex IIM 5.2)	Like any micro-organism, *Beauveria bassiana* can potentially act as an opportunistic pathogen. However, despite a 30-year history of research and commercial use, infections in humans in which *Beauveria bassiana* is identified are extremely rare, consisting of eye infections after mechanical damage to the cornea and lung diseases and disseminated infections in profoundly immunocompromised patients.
Medical surveillance on manufacturing plant personnel	No adverse health effect attributed to *Beauveria bassiana* was recorded on manufacturing plant workers from 2007 till now.
Sensitisation/allergenicity observations, if appropriate	Microorganisms may have the potential to provoke sensitizing reactions. Based on literature data, *Beauveria bassiana* strains show allergic potential and sensitizing properties to both skin and inhalatory contact.
Acute toxicity, pathogenicity and infectiveness	
Acute oral toxicity, pathogenicity and infectiveness	Rat, LD_{50} > 1.8x10^9 CFU/kg bw) (*Beauveria bassiana* 147 Technical). No evidence of toxicity or infectivity. Total clearance at day 3.
Acute inhalation toxicity, pathogenicity and infectiveness	Rat, LD_{50} > 4.2x10^8 CFU/kg bw) (*Beauveria bassiana* 147 Technical), 3/18 deaths on day 1, treatment-related lung lesions probably linked to a sensitization and/or toxic effect by inhalation. No evidence of infectivity. Total clearance at day 3.
Intraperitoneal/subcutaneous single dose	Rat, LD_{50} > 6.9x10^8 CFU/kg bw) (*Beauveria bassiana* 147 Technical). No evidence of toxicity or infectivity.
Genotoxicity (Annex IIM 5.3.5)	Negative in four Ames tests performed on culture juices of *Beauveria bassiana* 147 and DMSO extracts from pulverized *Beauveria bassiana* 147 mycelium, both in two different media.
	Beauvericin: negative results in Ames test; *in vitro* positive results for chromosomal aberrations, sister-chromatid exchanges and micronuclei in eukaryotic cells.
	Pigments (oosporein, bassianin, tenellin): cytotoxic properties reported in the open literature
Cell culture studies (Annex IIM, point 5.3.6)	No data – not required.
Information on short term toxicity and pathogenicity (Annex IIM, point 5.3.7)	Rat, 90-day, NOAEL > 4x10^8 CFU/kg bw per day (*Beauveria bassiana* 147 Technical). Total clearance.
First aid measures, medical treatment (Annex IIM, point 5.2.5)	In case of skin contact, wash with water. In the unlikely case of eye, lung or disseminated infection following contact with *Beauveria bassiana*, specialist´s expertise and treatment with anti-mycotic drugs will be needed.
Specific toxicity, pathogenicity and infectiveness studies (Annex IIM, point 5.5)	Dermal irritation study, rabbit (*Beauveria bassiana* 147 Technical): mild irritant Dermal irritation study, rabbit (*Beauveria bassiana* 147 Formulation): not irritant Eye irritation study, rabbit (*Beauveria bassiana* 147 Formulation): mild irritant Open literature data - local corneal infections reported after experimental ocular infection of rabbits with *Beauveria bassiana* (strain not specified)

	Open literature data – long-term inhalatory exposure (18-month), rats and mice (*Beauveria bassiana*, strain not specified): allergic lung reactions

Reference values

Acceptable operator exposure level	Open, pending further clarification of repeated dose toxicity by inhalation
Acute reference dose	Not established, not needed for the representative uses
Acceptable daily intake	Not established, not needed for the representative uses

Exposure scenarios

Operators	Not finalized (pending further characterization of the toxicity by inhalation and of the hazard assessment of toxins/metabolites) Appropriate PPE/RPE needed considering the potential sensitising properties and the mild eye irritant effects of *Beauveria bassiana.*
Workers	Not finalized (pending further characterization of the toxicity by inhalation and of the hazard assessment of toxins/metabolites)
Bystanders and residents	Not finalized (pending further characterization of the toxicity by inhalation and of the hazard assessment of toxins/metabolites)

Residues

Residues in or on treated products, food and feed (Annex IIM 6; IIIM 8)

Viable residues Non-viable residues	Since a risk to consumers is not expected arising from the assessed representative use of *Beauveria bassiana* 147 neither a residue definition nor an MRL are considered necessary

Fate and Behaviour in the Environment (Annex IIM 7; IIIM 9)

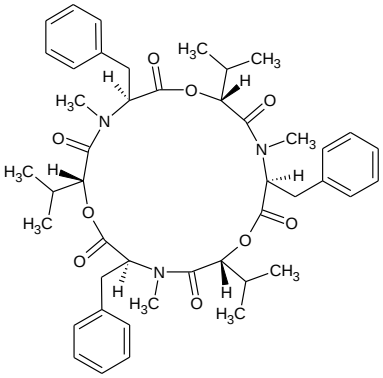
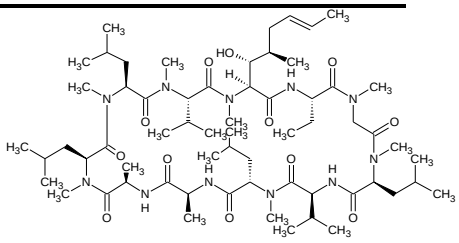
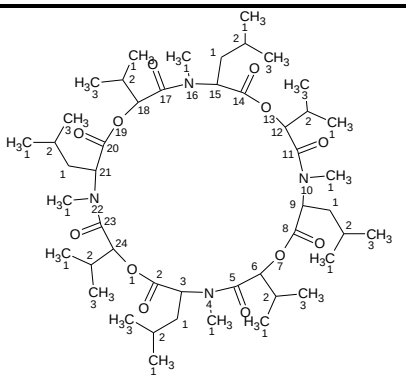
Persistence and multiplication in soil	Information on persistence and multiplication in soil was available for *Beauveria* sp. Conservative PECsoil values were calculated: Following 1 application of 106 kg Ostrinil®/ha (5.3 × 10^{13} cfu/ha), the initial PECsoil (in 5 cm) values without considering crop interception are: 141.33 mg of Ostrinil®/kg soil, and 7.07 x 10^{7} cfu/kg soil Following 7 applications of 106 kg Ostrinil®/ha (5.3 × 10^{13} cfu/ha), the initial PECsoil (in 5 cm) values without considering crop interception are: 989.33 mg of Ostrinil®/kg soil, and 4.95 x 10^{8} cfu/kg soil The applied inoculum density decreases to upper natural background levels within 0.5-1.5 years. These values indicate the fungi can be considered as persistent.
Persistence and multiplication in water	Information on persistence and multiplication in water was available for *Beauveria* sp. Conservative PECsw values were calculated. Following 1 application of 106 kg Ostrinil®/ha (5.3 × 10^{13} cfu/ha), the initial PECsw values (drift of 100%) are: 35.3 mg of Ostrinil®/L, and 1.77 × 10^{7} cfu/L. Following 7 applications of 106 kg Ostrinil®/ha (5.3 × 10^{13} cfu/ha), the initial PECsw values (drift of 100%) are: 247.33 mg of Ostrinil®/L, and 1.24 × 10^{8} cfu/L.
Persistence and multiplication in air	Information on persistence and multiplication in air was available for *Beauveria* sp.: it has been concluded *that Beauveria bassiana* is expected to be degraded rapidly in the air and no accumulation is envisaged.
Mobility	Information on mobility was available for *Beauveria* sp. Conidia of *Beauveria bassiana* are not very mobile in soil and generally remain on the soil surface. Presence of conidia in air or water is low and survival of the fungus in these environments is limited.

Effects on Non-target Species (Annex IIM 8; IIIM 10)

Effects on birds	*Anas platyrhynchos* and *Colinus virginianus* (test item: OSTRINIL, 5-day dosing, 30-day observation): NOEL = 4 g/kg bw per day (4.4 x 10^8 CFU/kg bw per day) No indications of infectivity and pathogenicity.
Risk assessment	No indications of infectivity and pathogenicity at concentrations relevant to the likely exposure of birds for the representative use.
Effects on mammals	NOEL = 1.8 x 10^9 CFU/kg bw (technical, acute oral toxicity, pathogenicity and infectivity study in rat) NOEL = 1.88 x 10^9 CFU/kg bw (OSTRINIL, acute oral toxicity in rat) No toxic, pathogenic or infective effect has been observed after a daily administration of 10^8 CFU/animal of *Beauveria bassiana* on male and female rats.
Risk assessment	No indications of infectivity and pathogenicity at concentrations relevant to the likely exposure of mammals for the representative use.
Effect on aquatic organisms - fish	No reliable data.
Risk assessment	Open
Effect on aquatic organisms – freshwater invertebrates	No reliable data.
Risk assessment	Open
Effect on aquatic organisms – algae	*Pseudokirchneriella subcapitata* (test item: OSTRINIL 5 x 10^8 CFU/g, 3-day static test): NOEC = 2 g/L (1 x 10^9 CFU/L, nominal concentration) NOEC = 1.13 x 10^9 CFU/mL (measured concentration)
Risk assessment	TER_{LT} > 8-56 based on weight data, for 7 and 1 applications TER_{LT} > 0.9-3.4 based on cfu data, for 7 and 1 applications

Effects on bees	*Beauveria bassiana* 147 (Technical) 23 days - oral LC_{50} = 9285 mg product/L feed, equivalent to 1.0 x 10^6 CFU/mL feed 23 days - oral NOEC = 4.0 x 10^5 CFU/mL feed 23 days - oral LD_{50} = 185.7 µg product/bee or 2 x 10^4 CFU/bee *Beauveria bassiana* 147 (pure conidia powder) - ARY-0711a: 48-hour oral LD_{50} > 10µg formulated *Beauveria bassiana* 147 spores /bee 48-hour contact LD_{50} > 1µg formulated *Beauveria bassiana* 147 spores /bee 10-day oral NOEL = 0.338 µg *Beauveria bassiana* 147 conidia per bee per day
Risk assessment	Mortality observed in both the 23-day and 10-day chronic bee studies. With the information available, it cannot be excluded that this was due to infectivity and pathogenicity. No reliable information to address risk to bee brood available.
Effects on arthropods other than bees	Acute toxicity studies according to FIFRA guidelines: *Hippodamia convergens*, NOEC-4 day contact = 5 g OSTRINIL/ beetle *Chrysoperla carnea*, NOEC-3 day contact = 0.3 g OSTRINIL/larvae *Brachymeria intermedia*, NOEC-4 day contact = 5 g OSTRINIL/ wasps Extended laboratory study according to IOBC: *Typhlodromus pyri,* 14 day exposure to OSTRINIL (measured 1.5 x 10^{11} spores/g) sprays on potted bean plants: Corrected mortality between 8.0 and 15.9%, no dose response. Extended laboratory study according to OECD: *Folsomia candida*, 28 day exposure to OSTRINIL (>5 x 10^8 spores/g, measured 1.5 x 10^{11} spores/g) in natural soil: NOEC = 1 g OSTRINIL/kg dry soil
Risk assessment	Open
Effects on earthworms	*Eisenia foetida*, 56 day exposure to OSTRINIL (>5 x 10^8 spores/g, measured 1.5 x 10^{11} spores/g) in artificial soil: NOEC = 1 g OSTRINIL/kg dry soil
Risk assessment	TER_{LT} =1.11-7.07, for 7 and 1 applications Risk to soil organisms is low.
Effects on non-target soil micro-organisms	Literature study indicating that *Beauvaria bassiana* did not affect the diversity of fungal communities.
Risk assessment	Risk to soil microorganisms is low.
Additional studies	No data.

Appendix B – Used compound code(s)

Code/trivial name	Chemical name/SMILES notation*	Structural formula*
beauvericin	(3*S*,6*R*,9*S*,12*R*,15*S*,18*R*)-3,9,15-tribenzyl-4,10,16-trimethyl-6,12,18-tri(propan-2-yl)-1,7,13-trioxa-4,10,16-triazacyclooctadecane-2,5,8,11,14,17-hexone O=C([C@H](CC1=CC=CC=C1)N(C)C([C@@H](C(C)C)OC([C@H](CC2=CC=CC=C2)N(C)C([C@@H](C(C)C)OC([C@H](CC3=CC=CC=C3)N4C)=O)=O)=O)=O)O[C@H](C(C)C)C4=O	
cyclosporine	(3S,6S,9S,12R,15S,18S,21S,24S,30S,33S)-30-ethyl-33-[(1R,2R,4E)-1-hydroxy-2-methylhex-4-en-1-yl]-1,4,7,10,12,15,19,25,28-nonamethyl-6,9,18,24-tetrakis(2-methylpropyl)-3,21-di(propan-2-yl)-1,4,7,10,13,16,19,22,25,28,31-undecaazacyclotritriacontane-2,5,8,11,14,17,20,23,26,29,32-undecone C[C@H](C\C=C\C)[C@@H](O)[C@H]1C(=O)N[C@@H](CC)C(=O)N(C)CC(=O)N(C)[C@@H](CC(C)C)C(=O)N[C@H](C(=O)N(C)[C@@H](CC(C)C)C(=O)N[C@@H](C)C(=O)N[C@H](C)C(=O)N(C)[C@@H](CC(C)C)C(=O)N(C)[C@@H](CC(C)C)C(=O)N(C)[C@@H](C(C)C)C(=O)N1C)C(C)C	
bassianolide	4,10,16,22-tetramethyl-3,9,15,21-tetrakis(2-methylpropyl)-6,12,18,24-tetra(propan-2-yl)-1,7,13,19-tetraoxa-4,10,16,22-tetraazacyclotetracosane-2,5,8,11,14,17,20,23-octone CC(C)CC1C(=O)OC(C(=O)N(C)C(CC(C)C)C(=O)OC(C(=O)N(C)C(CC(C)C)C(=O)OC(C(C)C)C(=O)N(C)C(CC(C)C)C(=O)OC(C(C)C)C(=O)N1C)C(C)C)C(C)C	

*ACD/ChemSketch, Advanced Chemistry Development, Inc. ACD/Labs Release: 12.00. Product version: 12.00 (Build 29305, 25 Nov 2008)