Final Review report for the active substance *Isaria fumosorosea* strain Apopka 97 (formerly *Paecilomyces fumosoroseus* Apopka strain 97, PFR 97 or CG 170, ATCC20874) finalised in the Standing Committee on Plants, Animals, Food and Feed at its meeting on 12 December 2014 in view of the renewal of the approval of *Isaria fumosorosea* strain Apopka 97 as active substance in accordance with Regulation (EC) No 1107/2009

1. **Procedure followed for the re-evaluation process**

This review report has been established as a result of the evaluation of *Isaria fumosorosea* strain Apopka 97, in accordance with Regulation (EC) No 1107/2009\(^2\) and Commission Regulation (EU) No 1141/2010\(^3\) following the submission of an application to renew the approval of this active substance expiring in December 2015. *Isaria fumosorosea* strain Apopka 97 is the new name of the species formerly known as *Paecilomyces fumosoroseus* Apopka strain 97.


*Paecilomyces fumosoroseus* Apopka strain 97 is a substance that was included in Annex I to Council Directive 91/414/EEC concerning the placing of plant protection products on the market, by Commission Directive 2001/47/EC\(^6\). *Paecilomyces fumosoroseus* Apopka strain 97 is deemed to have been approved under Regulation (EC) No 1107/2009 and is listed in Part A of the Annex to Commission Implementing Regulation (EU) No 540/2011\(^7\).

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1. Does not necessarily represent the views of the Commission.
In accordance with the provisions of Article 5 of Directive 91/414/EEC, Mitsui Agriscience notified to the Commission of their wish to renew the approval of the active substance *Isaria fumosorosea* strain Apopka 97 in Annex I to the Directive.

Commission Directive 2010/77/EU\(^8\) extended until 31 December 2015 the period of approval of *Isaria fumosorosea* strain Apopka 97 to allow the completion of its review.

Commission Regulation (EU) No 1141/2010 designated the rapporteur Member States and the co-rapporteur Member States which had to submit the relevant renewal assessment reports and recommendations to the European Food Safety Authority (EFSA).

For *Isaria fumosorosea* strain Apopka 97 the rapporteur Member State was Belgium and the co-rapporteur Member State was the Netherlands.

Belgium finalised in June 2013 its examination, in the form of a renewal assessment report. This Report was sent to the Commission and the European Food Safety Authority on 3 June 2013 and included a recommendation concerning the decision to be taken with regard to the renewal of the approval of *Isaria fumosorosea* strain Apopka 97 for the supported uses.

In accordance with Article 16 of Commission Regulation (EU) No 1141/2010, the Commission requested the EFSA to arrange an expert consultation on the rapporteur Member State's renewal assessment report and to deliver its conclusions.

Therefore, the EFSA organised an intensive consultation of technical experts from Member States, to review the renewal assessment report and the comments received thereon (peer review).

The EFSA sent to the Commission its conclusion on the risk assessment (Conclusions regarding the peer review of the pesticide risk assessment of the active substance)\(^9\). This conclusion refers to background document A (renewal assessment report and additional report) and background document B (EFSA peer review report).

According to the provisions of Article 17 of Regulation (EU) No 1141/2010, the Commission referred a draft review report on the renewal of approval to the Standing Committee on Plants, Animals, Food and Feed, for final examination. The draft review report on renewal of approval was finalised in the meeting of the Standing Committee on 12 December 2014.

The present review report on renewal of approval contains the conclusions of the final examination by the Standing Committee. Given the importance of the conclusion of the EFSA, and the comments and clarifications submitted after the conclusion of the EFSA (part of background document C), these documents are also considered to be part of this review report.

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\(^8\) OJ L 293, 11.11.2010, p. 48.

2. **Purposes of this review report**

This review report, including the background documents and appendices hereto, has been developed and finalised in support of **Commission Implementing Regulation (EU) 2015/306** concerning the renewal of approval of *Isaria fumosorosea* strain Apopka 97 as active substance under Regulation (EC) No 1107/2009, and to assist the Member States in decisions on individual plant protection products containing *Isaria fumosorosea* strain Apopka 97 they have to take in accordance with the provisions of that Regulation, and in particular the provisions of Article 29(1) of Regulation (EC) No 1107/2009 and the uniform principles laid down in Regulation (EU) No 546/2011.

This review report provides also for the evaluation required under part II, Section A.2(b) of the above mentioned uniform principles, as well as under several specific sections of chapter B of these principles. In these sections it is provided that Member States, in evaluating applications and granting authorisations, shall take into account the information concerning the requirements of Regulation (EU) No 544/2011, submitted for the purpose of (renewal of) approval of the active substances, as well as the result of the evaluation of those data.

In accordance with the provisions of Article 18 of Regulation (EU) No 1141/2010, this review report will be made available to the public.

The information in this review report is, at least partly, based on information which is confidential and/or protected under the provisions of Regulation (EC) No 1107/2009. It is therefore recommended that this review report would not be accepted to support any registration outside the context of that Regulation, e.g. in third countries, for which the applicant has not demonstrated to have regulatory access to the information on which this review report is based.

3. **Overall conclusion in the context of Regulation (EC) No 1107/2009**

The overall conclusion from the evaluation is that it may be expected that plant protection products containing *Isaria fumosorosea* strain Apopka 97 will still fulfil the safety requirements laid down in Article 4(1) to (3) of Regulation (EC) No 1107/2009. This conclusion is however subject to compliance with the particular requirements in sections 4, 5, 6 and 7 of this report, as well as to the implementation of the provisions of Article 29(1) of Regulation (EC) No 1107/2009 and the uniform principles laid down in Regulation (EU) No 546/2011, for each *Isaria fumosorosea* strain Apopka 97 containing plant protection product for which Member States will grant or review the authorisation.

Furthermore, these conclusions were reached within the framework of the uses which were proposed and supported by the applicant and mentioned in the list of uses supported by available data (attached as Appendix II to this review report).

Extension of the use pattern beyond those described above will require an evaluation at Member State level in order to establish whether the proposed extensions of use can satisfy the requirements of Article 29(1) of Regulation (EC) No 1107/2009 and of the uniform principles laid down in Regulation (EU) No 546/2011.

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The review has identified several acceptable exposure scenarios for operators, workers and bystanders, which require however to be confirmed for each plant protection product in accordance with the relevant sections of the above mentioned uniform principles. In particular, Member States shall pay particular attention to the protection of operators and workers, taking into account that all microorganisms should be regarded as potential sensitizers.

The review has also concluded that under the proposed and supported conditions of use there are no unacceptable effects on the environment, as provided for in Article 4(3)(e) of Regulation (EC) No 1107/2009, provided that certain conditions are taken into account as detailed in section 6 of this report.

The following point were considered as open by the EFSA (2013) for *Isaria fumosorosea* strain Apopka 97, however their risk is considered low or negligible for the following reasons:

– The production of toxins/secondary metabolites of unknown toxicity cannot be excluded and therefore the risk assessment cannot be considered finalised for humans (including operators, workers and consumers) and the environment, including the assessment of potential groundwater contamination and residues in plants. *Isaria fumosorosea* strain Apopka 97 was screened for the presence of well-known mycotoxins such as aflatoxins and beauvericins, which were not detected. The substances which are produced by the strain, which are beauverolides, have been clearly identified, and the review clearly demonstrated that they are not of toxicological concern. The toxicology dossier of *Isaria fumosorosea* strain Apopka 97, as well as the studies performed with the beauverolides themselves, and existing open literature data clearly indicate that this strain does not produce secondary metabolites which could have adverse effects to mammals. Moreover, *Isaria fumosorosea* strain Apopka 97 is not expected to occur in groundwater as it is not released into the environment and exposure levels to blastopores containing them is considered negligible due to use in greenhouses only. The same applies to all other environmental compartments. This would indicate a low or even negligible risk for operators, workers, consumers and the environment.

– The surface water exposure assessment and consequently the risk assessment for aquatic organisms, is not considered finalised. The review confirmed the low persistence / viability of *Isaria fumosorosea* strain Apopka 97 in aquatic environments. It can be assumed that the decrease in the populations is even much stronger in a natural environment, as factors like exposure to sun light, grazing activity by aquatic micro- and macrofauna, dilution effects due to water flow and competition with indigenous microorganisms were not considered in the available laboratory studies. Anyhow within 4-6 days after use in greenhouses, the blastospores of *Isaria fumosorosea* strain Apopka 97 will completely disappear from surface water bodies even if worst case conditions are assumed. In addition, the strain is not related to any known fish or daphnid pathogen and there exists no case report in the scientific literature indicating that the genus *Isaria* exhibits pathogenic properties in fish or daphnids. Hence, from an overall point of view the risk for aquatic non-target organisms due to the intended use of *Isaria fumosorosea* strain Apopka 97 in greenhouses is considered negligible.

– The risk assessment for organisms involved in biological methods for sewage treatment is not considered finalised. However, given that *Isaria fumosorosea* strain Apopka 97 is used in greenhouse applications as a foliar spray and as highly diluted aqueous solutions and
no concentrated quantities of the microbe are released into the sewages which in general do contain huge quantities of various microorganisms and other waste products would indicate a low risk to biological methods of sewage treatment.

From the review, it can be concluded that under the proposed and supported conditions of use Isaria fumosorosea strain Apopka 97 complies with the criteria provided for in Article 4 of Regulation (EC) No 1107/2009. The criteria as listed in point 5 of Annex II as regards the classification of an active substance in accordance with Regulation (EC) No 1272/2008 do not apply to Isaria fumosorosea strain Apopka 97 as microorganisms in general are not covered by this Regulation.

With regard to the other criteria the following can be stated:

– 'Persistence' is not an appropriate term to be used for microorganisms as they are in general naturally occurring. Isaria fumosorosea is widely distributed throughout the world and can be isolated from many arthropods, mainly Lepidoptera from the air, water, plants, and other fungi and often from soil. Isaria fumosorosea strain Apopka 97 can be found in various soil types at very low densities. In this respect it is more appropriate to consider the multiplication and the mobility. No viable conidia were detected by colony counts after 38 days. In addition the fungus Isaria fumosorosea has no self-mobility and the blastospores are short living. It is also expected that the mobility of the strain Isaria fumosorosea strain Apopka 97 is limited as the only intended uses are in glasshouses. Therefore, Isaria fumosorosea strain Apopka 97 is not considered to be 'persistent'.

– 'Bioconcentration' -where the amount of pesticide residue is measured in an organism's tissue relative to the concentration in the organism's environment- is a property not applicable to an entomopathogenic fungus like Isaria fumosorosea strain Apopka 97 which has shown no toxicity, pathogenicity or infectivity to mammals and only intended to be used against greenhouse whitefly (Trialeurodes vaporariorum).

– Isaria fumosorosea strain Apopka 97 does not fulfil the interim criteria to be considered as an endocrine disruptor. Isaria fumosorosea strain Apopka 97 is not classified (microorganisms in general are not covered by Regulation (EC) No 1272/2008) and no toxic effects to endocrine organs have been observed as a result of the use of plant protection products containing Isaria fumosorosea strain Apopka 97.

– No neurotoxic or immunotoxic effects have been observed as a result of the use of plant protection products containing Isaria fumosorosea strain Apopka 97.

Therefore, Isaria fumosorosea strain Apopka 97 can be considered a low risk active substance in accordance with Article 22 of Regulation (EC) No 1107/2009.

4. Identity

The main properties of Isaria fumosorosea strain Apopka 97 are given in Appendix I. The strain is deposited in the American Type Culture Collection (ATCC) under the name Paecilomyces fumosoroseus Apopka ATCC 20874.
The minimum and maximum concentration of the micro-organism used for manufacturing of the formulated product is $1.0 \times 10^8$ CFU/ml and $2.5 \times 10^9$ CFU/ml.

It has been established that for the active substance notified by the applicant none of the manufacturing impurities considered are, on the basis of information currently available, of toxicological or environmental concern. However, strict maintenance of environmental conditions and quality control analysis during the manufacturing process shall be assured by the producer, in order to ensure the fulfilment of the limits on microbiological contamination as referred to in the Working Document SANCO/12116/2012.

5. **Endpoints and related information**

In order to facilitate Member States, in granting or reviewing authorisations, to apply adequately the provisions of Article 29(1) of Regulation (EC) No 1107/2009 and the uniform principles laid down in Regulation (EU) No 546/2011, the most important endpoints were identified during the re-evaluation process. These endpoints are listed in the conclusion of the EFSA.

6. **Particular conditions to be taken into account on short term basis by Member States in relation to the granting of authorisations of plant protection products containing *Isaria fumosorosea* strain Apopka 97**

On the basis of the proposed and supported uses (as listed in Appendix II), the following issues have been identified as requiring particular and short term attention from all Member States, in the framework of any authorisations to be granted, varied or withdrawn, as appropriate:

- Protection of operators and workers, taking into account that *Isaria fumosorosea* strain Apopka 97 is to be considered, as any microorganisms, a potential sensitizer.

- As mentioned in Section 4 of this report, strict maintenance of environmental conditions and quality control analysis during the manufacturing process shall be assured by the producer, in order to ensure the fulfilment of the limits on microbiological contamination as referred to in the Working Document SANCO/12116/2012.

7. **List of studies to be generated**

No further studies were identified which were at this stage considered necessary in relation to the approval of *Isaria fumosorosea* strain Apopka 97 under the current approval conditions.

Some endpoints however may require the generation or submission of additional studies to be submitted to the Member States in order to ensure authorisations for use under certain conditions.

A complete list of studies to be generated, still ongoing or available but not peer reviewed can be found in the relevant part of the EFSA Conclusion (page 12-13).
8. **Information on studies with claimed data protection**

For information of any interested parties, the rapporteur Member State will keep available a document which gives information about the studies for which the applicant has claimed data protection and which during the re-evaluation process were considered as essential with a view to approval under Regulation (EC) No 1107/2009. This information is only given to facilitate the operation of the provisions of Article 62 of Regulation (EC) No 1107/2009 in the Member States. It is based on the best information available but it does not prejudice any rights or obligations of Member States or operators with regard to its uses in the implementation of the provisions of Article 62 of Regulation (EC) No 1107/2009 and neither does it commit the Commission.

9. **Updating of this review report**

The information in this report may require to be updated from time to time in order to take account of technical and scientific developments as well as of the results of the examination of any information referred to the Commission in the framework of Articles 13, 21, 38, 44, 56 of Regulation (EC) No 1107/2009. Any such adaptation will be finalised in the Standing Committee on Plants, Animals, Food and Feed, in connection with any amendment of the approval conditions for *Isaria fumosorosea* strain Apopka 97.
# APPENDIX I

## Identity and biological properties

**ISARIA FUMOSOROSEA STRAIN APOPKA 97**

<table>
<thead>
<tr>
<th>Active micro-organism:</th>
<th><em>Isaria fumosorosea</em> strain Apopka 97</th>
</tr>
</thead>
<tbody>
<tr>
<td>Known or new organisms:</td>
<td>Known, Revision of genus <em>Paecilomyces</em> : species included into <em>Isaria</em> clade followed by change of genera name (<em>Isaria</em>) and partially also in species name (<em>fumosorosea</em> instead of <em>fumosoroseus</em>). New name <em>Isaria fumosorosea</em></td>
</tr>
<tr>
<td>Known opportunistic:</td>
<td>No</td>
</tr>
<tr>
<td>Toxin production</td>
<td>Secondary metabolites such as beauverolides have been detected.</td>
</tr>
<tr>
<td>Resistance:</td>
<td>Not applicable to fungi</td>
</tr>
<tr>
<td>Resting stages:</td>
<td>Production of conidia or resting spores in/or on the host</td>
</tr>
</tbody>
</table>
| Production control: | - Check of product quality  
- Determination of pathogenicity on whiteflies.  
- Absence of secondary metabolites must be checked in each fermentation broth by HPLC. The quality of the HPLC method must be checked.  
New method for quantification of secondary metabolite beauverolide I is provided. |

<table>
<thead>
<tr>
<th>Name of the organism:</th>
<th><em>Isaria fumosorosea</em></th>
</tr>
</thead>
</table>
| Taxonomy: | Kingdom: Fungi  
Subkingdom: Dikarya  
Division/phylum: Ascomycota  
Subphylum: Pezizomycotina  
Class: Sordariomycetes  
Subclass: Hypocreomycetidae  
Order: Hypocreales  
Family: Cordycipitaceae  
Section: Isarioidea  
Genus: *Isaria*  
Species: *Isaria fumosorosea* Wize 1904 |
| Species, subspecies, strain | *Isaria fumosorosea* (Wize) Brown & Smith strain Apopka 97; PFR 97 or CG 170 or ATCC20874 |
| Identification: | Morphological criteria seen by classical microscopy methods;  
RAPD analysis: *Isaria fumosorosea* strain PFR97 Apopka is characterised with eight 10-mer primers from a RAPD kit and six 10-mer primers from another RAPD kit. These primers revealed a total of 167 repeatable bands that were used to construct strain specific RAPD patterns. |
| Culture collection: | American Type Culture Collection (ATCC) under the name *Paecilomyces fumosoroseus* Apopka ATCC 20874. |
| Minimum and maximum concentration of the micro-organism used for manufacturing of the formulated product (cfu/g; cfu/L, etc.): | 1.0 x 10⁸ CFU/mL and 2.5 x 10⁹ CFU/mL |
| Identity and content of relevant impurities in the technical grade micro- | The technical grade material does not contain relevant impurities |
**organism:**

<table>
<thead>
<tr>
<th>Is the MCPA genetically modified; if so provide type of modification</th>
<th>No modification</th>
</tr>
</thead>
</table>

| Origin and natural occurrence, background level:                     | - Isolated from *Phenococcus solani* Ferris (mealy bug), on gynura in a greenhouse located in Apopka.  
|                                                                      | - Widely distributed throughout the world.  
|                                                                      | - Isolated from many arthropods, mainly *Lepidoptera* from the air, water, plants, and other fungi and often from soil.  
|                                                                      | - Found in various soil types at very low densities. |

<table>
<thead>
<tr>
<th>Target organism(s):</th>
<th>Greenhouse whitefly (<em>Trialeurodes vaporariorum</em>)</th>
</tr>
</thead>
</table>

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<thead>
<tr>
<th>Mode of action:</th>
<th>Hyper parasitism; production of enzymes to penetrate insect cuticle and internal growth within insect and mechanical disruption of host.</th>
</tr>
</thead>
</table>

| Host specificity: | Very wide range of hosts. Intended use against *Trialeurodes vaporariorum*.  
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<tr>
<th></th>
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<tbody>
<tr>
<td></td>
<td><em>Isaria fumosorosea</em> is a fungus found in soil worldwide.</td>
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</tbody>
</table>

<table>
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<tr>
<th>Life cycle:</th>
<th>Asexual life cycle; infective unit is blastospore</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Infectivity, dispersal and colonisation ability:</th>
<th>Whitefly is most susceptible to infection in the N1 and N4 nymph stage. The infection cycle is rapid and symptoms of infection are apparent within 24-48 h after the conidia contact the insect. Hyphal bodies are formed in the host hemocoele followed by mycelium formation on the dorsum of the insect body within 48 h.</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Relationship to known pathogens:</th>
<th>The genus <em>Isaria</em> belongs to the group of opportunistic pathogens. They are of inherently low virulence and produce disease when the host resistance to infection is diminished (immunosuppressed people)</th>
</tr>
</thead>
</table>

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<tr>
<th>Genetic stability:</th>
<th>Stable</th>
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<tr>
<th>Production of relevant metabolites/toxins:</th>
<th>The level of secondary metabolites such as beauverolides has to be in line with the proposed OECD levels (see Working Document SANCO/12116/2012).</th>
</tr>
</thead>
</table>

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<tr>
<th>Resistance/sensitivity to antibiotics/anti-microbial agents used in human or veterinary medicine:</th>
<th><em>Isaria fumosorosea</em> shows variable resistance to amphotericine B, flucytosine and the triazole based drugs as well as terbinafine and voriconazole.</th>
</tr>
</thead>
</table>
APPENDIX II
List of uses supported by available data

*ISARIA FUMOSOROSEA STRAIN APOPKA 97*

<table>
<thead>
<tr>
<th>Crop and/or situation</th>
<th>Member State or Country</th>
<th>Product name</th>
<th>F or G</th>
<th>Pests or Group of pests controlled</th>
<th>Preparation</th>
<th>Application</th>
<th>Application rate per treatment</th>
<th>PHI (days)</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tomato/cucumber/glasshouse</td>
<td>Europe</td>
<td>Preferal ®</td>
<td>G</td>
<td>Whitefly in IPM</td>
<td>WG</td>
<td>2x10⁹ CFU/g ~ 200g/kg</td>
<td>spraying first whitefly larvae</td>
<td>7 days</td>
<td>1000 to 3000</td>
</tr>
</tbody>
</table>

(a) For crops, the EU and Codex classifications (both) should be used; where relevant, the use situation should be described (e.g. fumigation of a structure)
(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)
(e) GCPF Codes – Crop Life 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) viable granules = colony forming units and g/kg or g/L
(j) Growth stage at last treatment (BBCH Monograph, Growth Stages of Plants, 1997, Blackwell, ISBN 3-8263-3152-4), including where relevant, information on season at time of application
(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