CONCLUSION ON PESTICIDE PEER REVIEW

Conclusion on the peer review of the pesticide risk assessment of the active substance *Metarhizium anisopliae* var. *anisopliae* BIPESCO 5/F52[1]

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SUMMARY

Metarhizium anisopliae var. *anisopliae* BIPESCO 5/F52 is one of the 295 substances of the fourth stage of the review programme covered by Commission Regulation (EC) No 2229/2004[3], as amended by Commission Regulation (EC) No 1095/2007[4].

Metarhizium anisopliae var. *anisopliae* BIPESCO 5/F52 was included in Annex I to Directive 91/414/EEC on 1 May 2009 pursuant to Article 24b of the Regulation (EC) No 2229/2004 (hereinafter referred to as 'the Regulation'), and has subsequently been deemed to be approved under Regulation (EC) No 1107/2009[5], in accordance with Commission Implementing Regulation (EU) No 540/2011[6], as amended by Commission Implementing Regulation (EU) No 541/2011[7]. In accordance with Article 25a of the Regulation, as amended by Commission Regulation (EU) No 114/2010[8], the European Food Safety Authority (EFSA) is required to deliver by 31 December 2012 its view on the draft review report submitted by the European Commission in accordance with Article 25(1) of the Regulation. This review report was established as a result of the initial evaluation provided by the designated rapporteur Member State in the Draft Assessment Report (DAR). The EFSA therefore organised a peer review of the DAR. The conclusions of the peer review are set out in this report.

The Netherlands being the designated rapporteur Member State submitted the DAR on *Metarhizium anisopliae* var. *anisopliae* BIPESCO 5/F52 in accordance with the provisions of Article 22(1) of the Regulation, which was received by the EFSA on 24 July 2007. The peer review was initiated on 11 June 2008 by dispatching the DAR for consultation of the Member States and on 24 April 2008 to the notifiers Agrifutur S.r.l. and Novozymes Biological Inc. Following consideration of the comments received on the DAR, it was concluded that EFSA should conduct a full peer review and deliver its conclusions on *Metarhizium anisopliae* var. *anisopliae* BIPESCO 5/F52.

The conclusions laid down in this report were reached on the basis of the evaluation of the representative uses of *Metarhizium anisopliae* var. *anisopliae* BIPESCO 5/F52 for the control of

[1] On request from the European Commission, Question No EFSA-Q-2009-00253, issued on 7 December 2011.
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[3] OJ L 379, 24.12.2004, p.13
[4] OJ L 246, 21.9.2007, p.19
[5] OJ L 309, 24.11.2009, p.1
[6] OJ L 153, 11.6.2011, p.1
[7] OJ L 153, 11.6.2011, p.187
[8] OJ L 37, 10.2.2010, p.12

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insects on a variety of crops, as proposed by the notifiers. Full details of the representative uses can be found in Appendix A to this report.

In the areas of identity of the micro-organism, biological properties, physical and technical properties and methods of analysis, the following data gaps remain: data on contaminating micro-organisms, pathogens and toxins, a method to unequivocally identify the micro-organism down to strain level, various other methods, storage stability data for the formulations and various physical and chemical properties of the formulation.

In the area of mammalian toxicology, no critical area of concern and no data gap were identified. However, the production of toxins cannot be excluded and therefore the risk assessment cannot be finalised for humans.

For the time being no critical area of concern is identified however, as the issue of toxins is not fully addressed for sections 1 and 2, the consumer risk assessment remains open for the edible crops.

Data available on fate and behaviour in soil show that *Metarhizium anisopliae* may be very high persistent at concentrations considerably higher than background natural conditions (after one single application it is estimated that it will take more than 10 years for levels to decline down to the upper background level). Data gaps have been identified to establish the accumulated plateau after repeated applications over the years and to address the persistence and multiplication of the fungi and the conidia in water. A critical area of concern has been identified with respect to the persistence and spread of the micro-organism in the environment. A data gap has been identified in the identity section to exclude the presence of swainsonine, destruxins and cytochalasin toxins by the notified strain of *Metarhizium anisopliae*. Depending on the outcome of the data gaps that have been identified in sections 1 and 5 to exclude the presence of swainsonine, destruxins and cytochalasin as toxins of *Metarhizium anisopliae* further information may be needed to assess the production and the fate and behaviour of these toxins in the environment.

The data available on ecotoxicology were not sufficient to carry out the required risk assessments for non-target organisms. Data gaps were identified for birds and mammals, aquatic organisms, pollinators, non-target arthropods, earthworms and soil non-target micro-organisms. The risk characterization for wild mammals, honey bees, earthworms and non-target soil micro-organisms for the representative uses, could not be finalised. The risk for epizootic infections within the wide range of host species including beneficial arthropods was identified as a critical area of concern.

KEY WORDS

Metarhizium anisopliae var. *anisopliae* BIPESCO 5/F52, peer review, risk assessment, pesticide, insecticide

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BACKGROUND

Metarhizium anisopliae var. *anisopliae* BIPESCO 5/F52 is one of the 295 substances of the fourth stage of the review programme covered by Commission Regulation (EC) No 2229/2004[9], as amended by Commission Regulation (EC) No 1095/2007[10].

Metarhizium anisopliae var. *anisopliae* BIPESCO 5/F52 was included in Annex I to Directive 91/414/EEC on 1 May 2009 pursuant to Article 24b of the Regulation (EC) No 2229/2004 (hereinafter referred to as 'the Regulation'), and has subsequently been deemed to be approved under Regulation (EC) No 1107/2009[11], in accordance with Commission Implementing Regulation (EU) No 540/2011[12], as amended by Commission Implementing Regulation (EU) No 541/2011[13]. In accordance with Article 25a of the Regulation, as amended by Commission Regulation (EU) No 114/2010[14] the European Food Safety Authority (EFSA) is required to deliver by 31 December 2012 its view on the draft review report submitted by the European Commission in accordance with Article 25(1) of the Regulation (European Commission, 2008a). This review report was established as a result of the initial evaluation provided by the designated rapporteur Member State in the Draft Assessment Report (DAR). The EFSA therefore organised a peer review of the DAR. The conclusions of the peer review are set out in this report.

The Netherlands being the designated rapporteur Member State submitted the DAR on *Metarhizium anisopliae* var. *anisopliae* BIPESCO 5/F52 in accordance with the provisions of Article 22(1) of the Regulation, which was received by the EFSA on 24 July 2007 (The Netherlands, 2007). The peer review was initiated on 11 June 2008 by dispatching the DAR for consultation and comments of the Member States and on 24 April 2008 to the notifiers Agrifutur S.r.l. and Novozymes Biological Inc. In addition, the EFSA conducted a public consultation on the DAR. The comments received were collated by the EFSA and forwarded to the RMS for compilation and evaluation in the format of a Reporting Table. The comments were evaluated by the RMS in column 3 of the Reporting Table.

The scope of the peer review was considered in a telephone conference between the EFSA, the RMS, and the European Commission on 18 April 2011. On the basis of the comments received and the RMS' evaluation thereof it was concluded that the EFSA should organise a consultation with Member State experts in all areas except for residues.

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 consultation with Member State experts, and additional information to be submitted by the notifiers, were compiled by the EFSA in the format of an Evaluation Table.

The conclusions arising from the consideration by the EFSA, and as appropriate by the RMS, of the points identified in the Evaluation Table, together with the outcome of the expert discussions where these took place, were reported in the final column of the Evaluation Table.

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 October - November 2011.

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 for the control of insects on a variety of crops, as proposed by the notifiers. A list of the relevant end points for the active substance as well as 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

[9] OJ L 379, 24.12.2004, p.13
[10] OJ L 246, 21.9.2007, p.19
[11] OJ L 309, 24.11.2009, p.1
[12] OJ L 153, 11.6.2011, p.1
[13] OJ L 153, 11.6.2011, p.187
[14] OJ L 37, 10.2.2010, p.12

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, 2011) comprises the following documents, in which all views expressed during the course of the peer review, including minority views, can be found:

- the comments received on the DAR,
- the Reporting Table (5 May 2009),
- the Evaluation Table (2 December 2011),
- the reports of the scientific consultation with Member State experts,
- the comments received on the assessment of the points of clarification,
- the comments received on the draft EFSA conclusion.

Given the importance of the DAR including its addendum (compiled version of June 2011 containing all individually submitted addenda (The Netherlands, 2011)) and the Peer Review Report, both documents are considered respectively as background documents A and B to this conclusion.

THE IDENTITY OF THE MICRO-ORGANISM AND THE PROPERTIES OF THE FORMULATED PRODUCT

The strains under review, BIPESCO 5 and F52, have both originally been isolated in Austria from *Cydia pomonella* or codling moth, a lepidopteran from the family of Tortricidae.

The representative formulated products for the evaluation were 'GranMet GR' containing 1 x 10^{10} CFU/kg, 'GranMet WP' containing 9 x 10^{10} CFU/kg, 'Bio 1020' containing 9 x 10^{11} CFU/kg, 'Taenure MET52' containing 9 x 10^{11} CFU/kg, 'TickEx G' containing 9 x 10^{11} CFU/kg, 'Taerain Met52EC' containing 5.5 x 10^{12} CFU/kg, 'TickEx EC' containing 5.5 x 10^{12} CFU/kg,

'Bio 1020', 'Taenure MET52' and 'TickEx G' are identical formulations. 'TickEx EC' and 'Taerain Met52EC' are also identical formulations.

The representative uses evaluated comprise indoor and outdoor application. The method of application depends on the formulation and is by soil incorporation, soil spray/drench or foliar spraying against various insect pests. 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 micro-organism/biological properties/physical and technical properties and methods of analysis.

It was concluded that the two strains BIPESCO 5 and F52 are similar enough to be considered together for the risk assessment. They are subcultures of an individual isolate M.a. 43. This isolate is present in several culture collections as follows BBA, Germany: M.a. 43; HRI, UK: 275-86 (acronyms V275 or KVL 275); KVL Denmark: KVL 99-112 (Ma 275 or V 275); Bayer, Germany: DSM 3884; ATCC, USA: ATCC 90448; USDA, Ithaca, USA: ARSEF 1095.

The strains are not human pathogens and are not related to known human pathogens. The strains are not able to grow at 37 °C and above.

It is possible that these strains produce some toxins namely swainsonine, destruxins and cytochalasin. The evidence so far produced was not convincing that the manufacturing methods for these strains will not result in the formation of these toxins. For this reason a data gap has been identified for a batch analysis where these toxins are analysed making sure that the spores are vigorously extracted. The content of contaminating micro-organisms was not fully addressed and a data gap has been identified. For these reasons the specification for toxins and contaminating micro-organisms is not finalised.

A method of analysis to unequivocally identify the organism down to strain level was not available to the peer review. None of the methods of analysis were validated for the micro-organism in the products, for contaminating and pathogenic micro-organisms and for toxins. It could not be concluded whether methods are required for residues.

Full storage stability data are needed for all formulations and several data gaps for the physchem properties of the formulations have been identified.

2. Mammalian toxicity

No detailed analysis of the batches used in the toxicological studies is available. However, further information is not required, provided that adequate quality control is undertaken on the batches produced, certifying that toxicologically relevant pathogenic microbial contaminants are kept below levels internationally recognised for microbial contaminants (e.g. OECD) (see data gap in section 1).

No information has been provided on the potential transfer of genetic material from *Metarhizium anisopliae* to other organisms. Since the fungus is not shown to be pathogenic, this is not a concern for human health.

Among the personnel having worked with *Metarhizium anisopliae* var. *anisopliae* strain F52 for 9 months in 1998 (during manufacture, laboratory testing and conduction of greenhouse/field trials), no case of hypersensitivity has been reported. Few clinical cases of human infection by *M. anisopliae* var. *anisopliae* (strain not mentioned) were described in the open literature (keratitis, rhinitis, and systemic infection in an immunocompromised boy) but not associated with the use of the fungus for insect control. Additionally, atopic humans living in the area of a sugar cane plantation (in which the fungus is used as a biological control agent) were shown to be more susceptible for allergic reactions when exposed to crude extract of *M. anisopliae*, than atopic patients from an urban area. However, none of the non-atopic individuals of the control group showed a positive response.

In the absence of a reliable test for sensitisation, as for other micro-organisms, the following warning phrase was agreed by the experts "**Micro-organisms may have the potential to provoke sensitising reactions**", taking into account that hazard statements applicable to chemicals (according to Regulation (EC) No 1272/2008 (European Commission, 2008b)) are not appropriate for micro-organisms.

M. anisopliae var. *anisopliae* strain F52 was not infective or pathogenic after acute oral, intraperitoneal or intratracheal exposure to rats.

Crude extracts and several purified toxins of different strains of *M. anisopliae* var. *anisopliae* were tested in two Ames tests and a Vitotox assay and gave negative results. If toxins (a.o. destruxins, cytochalasin and swainsonine) are shown to be present in the technical specification (see data gap in section 1), further toxicity tests might be needed.

No adverse effects were observed in mice exposed through inhalation for two weeks in closed chambers, with a complete clearance 10 days after the last exposure. Even though it is not clear which variety and/or strain of the fungus was tested, this has to be considered together with the results of the acute intratracheal study in rats (which showed no pathogenic effect). Consequently, no adverse effects are expected to occur after repeated inhalation exposure to *M. anisopliae* var. *anisopliae* strain BIPESCO 5/F52 and no further study is required.

The derivation of reference values was not considered needed as the micro-organism was not shown to be pathogenic or infective based on the available data and studies.

Taking into account the absence of pathogenicity and infectiveness of the colony forming units, no operator, worker and bystander exposure estimates were considered necessary. Due to the sensitisation potential of micro-organisms, the use of adequate personal protective equipment should be further considered for dermal and inhalatory exposure. For the bystanders, it appears that the exposure cannot be prevented. Nevertheless, taking into account the available human data (see above) and animal studies (showing positive results with intratracheal exposure, of limited relevance for humans), the weight of evidence shows a low concern for the bystander. However, due to the data gap in section 1 for analysis of the potential toxins, the operator, worker and bystander risk assessment cannot be formally concluded. Furthermore, an additional concern might be identified if worker exposure to toxins present in dead insects could not be excluded.

3. Residues

The micro-organism itself is not pathogenic and is not related to any known pathogens. The consumer risk assessment cannot be finalised until the outstanding issues on toxins are addressed and it is confirmed by the toxicological assessment that a quantitative consumer risk assessment is not necessary for the edible uses.

4. Environmental fate and behaviour

Available data with respect to the fate and behaviour of *Metarhizium anisopliae* were not necessarily obtained with the specific variant and strains notified. There is no indication that the facts reported with respect to the fate and behaviour of *Metarhizium anisopliae* are variant or strain specific.

Therefore, the use of data from other variants or strains of *Metarhizium anisopliae* for the assessment of *Metarhizium anisopliae* var. *anisopliae* BIPESCO 5/F52 has been considered acceptable by the peer review.

Fate and behaviour in the environment of the micro-organism

Viability and dynamics of *Metarhizium anisopliae* var. *anisopliae* (various strains) **in soil** have been extensively investigated under laboratory and field conditions and a number of publications may be found in the open scientific peer reviewed literature. In the DAR results of some of these publications, presented by the notifiers in the dossier, were reported in tabular form. Some of the typographic errors in the table have been corrected in the final addendum to the DAR, but a critical assessment of the studies listed is still missing. Based on the summary table B.8.1.1-2 (as amended in the addendum) experts in the PRAPeR M4 meeting expressed their concerns on the potential persistence of *Metarhizium anisopliae* in the environment. Available information indicates that once applied to a field the time taken for levels of *Metarhizium anisopliae* to return to background levels is in the range of years. Since no further clarification has been provided in the addendum received after the PRAPeR M4 experts' meeting, EFSA has examined some of the publications quoted. The RMS also indicated the existence of a recently published review on the subject (Scheepmaker, J.W.A and Butt, T.M., 2010). Most of the papers presented in the dossier are considered in this review, together with some additional publications. In this review the establishment and persistence of various commercial enthomopathogenic fungi is examined. Authors concluded that the upper 95th percentile background level for *Metarhizium anisopliae* is about 10^3 CFU / g soil. Experiments have been performed with application rates in the range of 10^4 to 10^{14} CFU / g soil. In some cases during the course of the experiments, the level of *Metarhizium anisopliae* increased at levels above the applied ones due to multiplication of the micro-organism in the infected hosts. *Metarhizium anisopliae* is not a host specific species and therefore can easily persist in the environment. At the end of these experiments *Metarhizium anisopliae* conidia levels remain approximately a factor of 100 higher than the upper natural background level even after 7.5 years. Also in arable fields, despite that a steady decrease is observed, fungal spore numbers remained up to a factor 300 – 1000 higher than the natural background levels after 42 months (3.5 years). Most of the available studies do not show a decline to the upper natural background level of 10^3 CFU / g soil within the time span of the experiments. Besides temporary increases due to reproduction in the host, fungal numbers show a steady but slow decline. By extrapolating the results of these experiments, it may be roughly estimated that it would take more than 10 years after a single treatment to reach the upper natural level. When compared to other entomopathogenic fungi, *Metarhizium anisopliae* is remarkably more persistent than *Beauveria bassiana.* Presence of suitable hosts seems to be a key factor maintaining the levels of *Metarhizium anisopliae* above natural background levels. Levels attained under repeated application have not been thoroughly investigated in any of the studies presented in the dossier; therefore it is not possible to estimate the potential for accumulation of *Metarhizium anisopliae* when it is repeatedly used over different seasons. The initial PEC_{soil} of conidia has been presented in the context of the ecotoxicological evaluation. Since the accumulated plateau needs to be established to apply the fate and behaviour specific decision making criteria for the approval of products containing micro-organisms, a data gap has been identified by EFSA for its determination. A critical area of concern has been identified with respect to the persistence and spread of the micro-organism in the environment.

Whereas, under the current regulatory framework new information would not be admissible at this stage of the peer review, the conclusions reached in the Scheepmaker, J.W.A and Butt, T.M review may be considered as potentially adverse with respect to the environment and deserve further consideration. Additionally, these conclusions do not differ substantially from the ones reached by the meeting PRAPeR M4 and EFSA when examining the results reported in the papers presented in the dossier (however conclusions in the aforementioned review may be considered more robust because they are supported by more data).

With respect to the **mobility of the micro-organisms**, at least one of the studies available in the dossier has demonstrated the potential spread of *Metarhizium anisopliae* in the environment after one

single application from treated to non-treated pasture areas (Rath, A.C. and Bullard, G.K., 1997). In this study applied *Metarhizium anisopliae* persist at levels equivalent or higher than the ones initially applied (5.1 10^4 CFU/g soil) for over 7.5 years. No conidia of *Metarhizium anisopliae* were detected in the non-treated areas during the first two years after treatment. However, after 7.5 years *Metarhizium anisopliae* had spread from treated to non-treated areas and levels measured in both plots were not significantly different. Distance between treated and non-treated plots is not reported in the study. Authors considered that spores could have been transported by unaffected soil invertebrates or movement of adult target organism redheaded cockchafer.

No information has been provided on the potential transfer of genetic material from *Metarhizium anisopliae* to other organisms.

A scientific publication is available in the dossier that addresses the fate and effects of a different variant of *Metarhizium anisopliae* (var *acridum*) in the **aquatic environment** (Milner, R.J. *et al.* 2002). In this study conidia survive in water for at least 20 h when applied in a water based spray. In this case slow deposition of conidia is observed. Also some level of multiplication cannot be excluded from results of the field experiments since doubling the applied dose results in a 10 times higher contamination rate. When applied by an oil based spray, conidia remain in the surface of the water not causing significant exposure to aquatic organisms and being more susceptible to inactivation by sun radiation.

No information on viability/population dynamics in natural sediment/water systems under dark and irradiated conditions is available in the dossier for the strains of *Metarhizium anisopliae* var. *anisopliae* BIPESCO 5/F52. A data gap has been identified during the peer review for data to address the persistence and multiplication of the fungi and the conidia in water.

Since exposure to surface water resulting from the sprayed applications cannot be excluded, a low tier risk assessment based on initial PEC SW following FOCUS drift values, has been presented in the DAR as a conservative estimation of the level of exposure of surface water to *Metarhizium anisopliae*.

No information has been provided in relation to potential interferences of *Metarhizium anisopliae* with the analytical systems for the control of the quality of drinking water provided for in Directive 98/83/EC.

Potential exposure of **groundwater** to *Metarhizium anisopliae* is deemed to be very low or negligible on the basis of the low penetration observed in the soil experiments available. Furthermore, the micro-organism is considered to be non-pathogenic and non-toxic to humans. Depending on the outcome of the data gaps identified in relation to the presence and formation of toxic metabolites in the product or in infected insects (sections 1 and 5) further data could be needed to assess the potential groundwater contamination by these metabolites.

As *Metarhizium anisopliae* is a ubiquitous micro-organism it can clearly be concluded that *M. anisopliae* is continuously present in the **air**. However, no specific information on the background levels and on the change of levels as a result of its use as a pesticide is available. Some general information on the susceptibility of fungal spores to natural sunlight is presented in the dossier; however no specific data for *Metarhizium anisopliae* are available. Therefore, it is not possible to estimate the levels reached as a result of its use as pesticide and the time span these levels will remain above background levels. This information is however not required since *Metarhizium anisopliae* is not pathogenic, nor toxic to humans and the weight of evidence did not raise further concern with respect to sensitizing properties.

Fate and behaviour in the environment of any relevant metabolite formed by the micro-organism under relevant environmental conditions

No information has been provided on the production and persistence of metabolites of *Metarhizium anisopliae* in the environment. A data gap has been identified in the identity section to exclude the

presence of swainsonine, destruxins and cytochalasin toxins by the notified strain of *Metarhizium anisopliae.* Several data gaps have been identified to assess the risk for insectivorous birds and mammals consuming infected insects including the risk posed by the toxins formed in the insect. Depending on the outcome of these data gaps, further information may be needed to assess the production and the fate and behaviour of these toxins in the environment, and the validity of the initial PECs proposed in the context of the ecotoxicological assessment would need to be confirmed.

5. Ecotoxicology

Birds may be directly exposed to conidia via ingestion of granules, sprayed plants or insects, whereas they may be indirectly exposed to the hyphens of the fungi or the produced toxins via ingestion of infected arthropods or other host organisms. Considering the available data, a high risk to birds theoretically cannot be excluded (e.g. due to consumption of granules). However, it was concluded that the risk for toxicity, infectiveness or pathogenicity arising from the direct exposure is not likely to be high. This conclusion was mainly based on the results of the available study on birds and considering that the temperature preference of *M. anisopliae* is below the body temperature of the birds. Results from the open literature data indicated no pathogenic changes in birds after consuming infected insects. In these studies however, only large birds were tested with a different strain of *M. anisopliae*. The experts at the PRAPeR M4 meeting discussed this issue and agreed on a data gap for information to refine the risk assessment for small insectivorous birds.

It was concluded that *Metarhizium anisopliae* neither exhibits infectivity nor pathogenicity to different **mammalian species** (see section 2). No assessments regarding the possible risk of insect-eating mammals were available however EFSA considered this as a relevant concern (see relevant data gap in section 1 regarding the issue for the toxins). Therefore a data gap for risk assessment for insect-eating mammals was identified. As a consequence, the assessment for insect-eating terrestrial vertebrates could not be finalised.

Risk assessments for **aquatic organisms** based on data for the standard species (rainbow trout, *daphnia magna* and a green algae) and considering a worst case approach via spray drift exposure of the aquatic environment resulted in a low risk for the conidia of *M. anisopliae* (e.g. PECsw was significantly lower than the toxicological endpoints). It is noted however that in these studies no solvents were used for the hydrophobic conidia, therefore the toxicity might not be representative for the formulations.
High risk was however concluded for *Ceriodaphnia dubia* (crustacea), for which the available endpoints were below the relevant PECsw. However, these endpoints are for a different variety of *M. anisopliae*.
In a literature review (the original publications were not available therefore not verified) larvae of mosquitoes were reported to be susceptible to *M. anisopliae*. Therefore it was concluded that it cannot be excluded that the risk to non-target diptera larvae and the possibility of the survival of conidia in water under particular conditions may be larger than expected from the available data set (regarding the fate and behaviour of the conidia in water, see section 4). Therefore a data gap for data on daphnids or larvae of aquatic insects with a representative formulation (containing e.g. solvents, emulsifiers) was identified for the representative uses where the product is sprayed or drenched.
Based on the available data from the open literature, crude extract of *M. anisopliae* was found to be very toxic to daphnids. Risk assessment considering this endpoint indicated low risk (e.g. level of potential exposure is significantly lower than the toxicological endpoint). It is noted however, that the validity of the relevant PEC (level of potential exposure) used in this risk assessment would need to be confirmed (see also section 4). Further laboratory tests with crude culture extracts of some other strains of *M. anisopliae* showed also significant adverse effects to embryos of aquatic organisms and amphibians. The neutral extracts of actively growing cultures contained destruxins (mycotoxins), however exact specifications were not available. It also remained unclear whether the aforementioned test results on the other strains can be extrapolated to *M. anisopliae* var. *anisopliae* BIPESCO 5/F52.
No symptoms of infectiveness or pathogenicity were observed in the tests on aquatic organisms. Some data from the open literature however revealed that toxins in the gut systems of some mosquitoes were

found after ingestion of dry conidia. This might be an indirect indication of infectivity or of the fact that the conidia contain toxins.

Only a limited data set with some shortcomings was available regarding the potential effects (toxicity, infectiveness or pathogenicity) of *M. anisopliae* to honey**bees**. Available laboratory data with another strain of *M. anisopliae* on three species of bumblebees however revealed high susceptibility to *M. anisopliae*, whereas relevant field studies on bumblebees showed neither infections nor treatment-related mortalities. In these field studies the contact exposure of bumblebees was shorter than in the laboratory studies. No data were available with toxins or other metabolites of *M. anisopliae* or with any of the plant protection products. Since the extent of the risk to these pollinators could not be established with the available information, a data gap for an appropriate risk assessment for pollinators was identified. As a consequence, the assessment for honeybees or for other pollinators (i.e. bumblebees) could not be finalised. Risk mitigation measures have been proposed to mitigate the exposure to pollinators. However, it is considered that it may not be possible to achieve sufficient mitigation, in particular for soil-dwelling pollinators, as *M. anisopliae* can be applied directly to the soil.

Only dietary tests on three **non-target arthropod species** were available. The mortality rate in the *M. anisopliae* treated groups was not significantly different compared to the results of the concurrent control groups. No symptoms of infectiveness or pathogenicity were observed in these tests. Arthropods living in or on the soil are more likely to be exposed to *M. anisopliae* however no soil-dwelling arthropods were tested. The contact route of exposure of non-target arthropods was also not addressed by testing however this route of exposure was considered to be more relevant than the other potential routes of infection. Summaries of laboratory and field studies from the open literature where the contact route of exposure on some ground-dwelling arthropods was also considered, were however available. These studies revealed that *M. anisopliae* has a wide range of host species. A summary document with comparison of the impact of chemical insecticides to the impact of *M. anisopliae* used as a pesticide on non-target arthropods was also available for the peer review. The overall conclusion in this document was that chemical insecticides have a more significant impact to non-target arthropods than the use of *M. anisopliae*, therefore the risk might be considered as low. This quantitative risk characterisation to non-target arthropods was discussed and found to be appropriate by the experts at PRAPeR M4. It was however noted that no relevant guidance was available for such a risk assessment following a quantitative approach. It was also noted that in case of epizootic infections in the host range of arthropod species the decrease of the density of *M. anisopliae* is a slow process. It was concluded that *M. anisopliae* is persistent in soil (see section 4) and appropriate long-term studies (e.g. that consider reproductive effects) were not available. Therefore a data gap was identified to further address the risk to non-target arthropods considering the persistence of *M. anisopliae* in soil. Considering this data gap, the risk of epizootic infections within the wide range of host species, including beneficial arthropods (see also issues regarding bumblebees), was identified as a critical area of concern.

A standard acute effect study was available for **earthworms**. No signs of toxicity, infectiveness or pathogenicity were observed in this test. The risk to earthworms based on this study was considered to be low (e.g. PECsoil inital was significantly lower than the available endpoint). Effect data on long-term scale were not available. Moreover the micro-organisms accumulated over years (e.g. PEC plateau) might be much higher than the initial PECs used in this assessment. Therefore a data gap was identified to further address the risk to earthworms considering the persistence of *M. anisopliae* in soil (regarding the persistence in soil and requirement for PEC plateau, see also section 4). As a consequence, the assessment for earthworms could not be finalised.

No specific data were available for **soil micro-organisms**. Therefore a data gap for the potential impact of the use of *M. anisopliae* as a pesticide on nitrogen transformation and carbon mineralization was identified. In general, it was anticipated that the application of *M. anisopliae* var. *anisopliae* BIPESCO 5/F52 will have repercussions on the ecology of the soil ecosystem, as would have any intervention in the soil compartment. The scale of possible repercussions due to the application of *M.*

anisopliae var. *anisopliae* BIPESCO 5/F52 in time or space was however not clarified. Therefore the assessment for soil micro-organisms could not be finalised.

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

6.1. Soil

Compound (name and/or code)	**Persistence, viability and dynamics**	**Ecotoxicology**
Metarhizium anisopliae var *anisopliae*	Very high persistent at concentrations considerably higher than background natural conditions (after one single application it is estimated that it will take more than 10 years for levels to decline below the upper background level).	The acute risk to earthworms was considered to be low. Data gaps were identified for long-term risk assessment for earthworms and for data for non-target soil micro-organisms.
Potential exogenous metabolites A data gap has been identified in the identity section to exclude the presence of swainsonine, destruxins and cytochalasin toxins by the notified strain of *Metarhizium anisopliae.* Depending on the outcome of these data gaps, further information may be needed to assess the production and the fate and behaviour of these toxins in the environment		

6.2. Ground water

Compound (name and/or code)	**Mobility in soil**	**>0.1 µg/L 1m depth for the representative uses (at least one FOCUS scenario or relevant lysimeter)**	**Pesticidal activity**	**Toxicological relevance**	**Ecotoxicological activity**
Metarhizium anisopliae is considered non-pathogenic and non-toxic to humans.	-	-	-	-	-

Potential exogenous metabolites A data gap has been identified in the identity section to exclude the presence of swainsonine, destruxins and cytochalasin toxins by the notified strain of *Metarhizium anisopliae.* Depending on the outcome of these data gaps, further information may be needed to assess the production and the fate and behaviour of these toxins in the environment.					

6.3. Surface water and sediment

Compound (name and/or code)	**Ecotoxicology**
Metarhizium anisopliae var *anisopliae*	Data gap identified regarding potential effects of relevant representative formulations to aquatic organisms. Crude extract (including mycotoxins) of *M. anisopliae* was found to be very toxic to daphnids. Risk assessment considering this endpoint indicated low risk. Crude culture extracts of some other strains of *M. anisopliae* showed significant adverse effects to embryos of aquatic organisms and amphibians.

Potential exogenous metabolites A data gap has been identified in the identity section to exclude the presence of swainsonine, destruxins and cytochalasin toxins by the notified strain of *Metarhizium anisopliae*. Depending on the outcome of these data gaps, further information may be needed to assess the production and the fate and behaviour of these toxins in the environment	

6.4. Air

Compound (name and/or code)	**Toxicology**
Metarhizium anisopliae var *anisopliae*	No infectivity or pathogenicity after acute intratracheal exposure in rats.
Potential exogenous metabolites A data gap has been identified in the identity section to exclude the presence of swainsonine, destruxins and cytochalasin toxins by the notified strain of *Metarhizium anisopliae*. Depending on the outcome of these data gaps, further information may be needed to assess the production and the fate and behaviour of these toxins in the environment	

7. List of studies to be generated, still ongoing or available but not peer reviewed

This is a complete list of the data gaps identified during the peer review process, including those areas where 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 7 of Directive 91/414/EEC concerning information on potentially harmful effects).

- Method of analysis that unequivocally identifies the organism to strain level (relevant for all representative uses evaluated; submission date proposed by the notifier: submitted and evaluated but not eligible for consideration in the peer review; see section 1)
- A specification for microbial contamination with supporting batch data and validated methods of analysis (relevant for all representative uses evaluated; submission date proposed by the notifier: unknown; see section 1)
- Batch analysis data for swainsonine, destruxins and cytochalasin (relevant for all representative uses evaluated; submission date proposed by the notifier: unknown; see section 1)
- Storage stability study for all formulations (relevant for all representative uses evaluated; submission date proposed by the notifier: unknown; see section 1)
- Wettability, persistent foam, suspensibility, wet sieve, particle size distribution for the WP formulation (relevant for the WP formulation; submission date proposed by the notifier: unknown; see section 1)
- Persistent foam for the OD (formerly described as an EC) formulation (relevant for the OD formulation; submission date proposed by the notifier: unknown; see section 1)
- Particle size distribution for the GR formulations (relevant for all representative uses evaluated; submission date proposed by the notifier: unknown; see section 1)
- Pourability and dispersion stability for the OD formulation (formerly described as an EC) (relevant for the OD formulation; submission date proposed by the notifier: unknown; see section 1)
- Validated methods for contaminating micro-organisms including pathogens (relevant for all representative uses evaluated; submission date proposed by the notifier: unknown; see section 1)
- Validated methods of analysis for destruxins, cytochalasin and swainsonine (relevant for all representative uses evaluated ; submission date proposed by the notifier: unknown; see section 1)
- Validation for the formulations methods of analysis (relevant for all representative uses evaluated ; submission date proposed by the notifier: unknown; see section 1)
- Data to establish the accumulated plateau in soil after repeated applications over the years (relevant for all representative uses evaluated; submission date proposed by the notifier: unknown; see section 4)
- Data to address the persistence and multiplication of the fungi and the conidia in water (relevant for all representative uses evaluated; submission date proposed by the notifier: unknown; see section 4)
- Further information to refine the risk assessment for small insectivorous birds consuming infected insects, including the risks caused by the hyphens and of the fungi toxins (relevant for all representative uses evaluated; submission date proposed by the notifier: unknown; see section 5)

- Risk assessment for insect-eating mammals due to the consumption of infected insects, including the risks caused by the hyphens and of the fungi toxins (relevant for all representative uses evaluated; submission date proposed by the notifier: unknown; see section 5)

- Data on daphnids or larvae of aquatic insects with relevant representative formulation(s) where the direct contamination of the aquatic environment (e.g. spray drift) is a route of exposure to aquatic organisms (relevant for all representative uses evaluated where the formulation is sprayed or drenched; submission date proposed by the notifier: unknown; see section 5)

- An appropriate risk assessment for pollinators (i.e. honeybees, bumblebees) (relevant for all representative uses evaluated; submission date proposed by the notifier: unknown; see section 5)

- An appropriate risk assessment for non-target arthropods considering the persistence of *M. anisopliae* in soil (relevant for all representative uses evaluated; submission date proposed by the notifier: unknown; see section 5)

- An appropriate risk assessment for earthworms considering the persistence of *M. anisopliae* in soil (relevant for all representative uses evaluated; submission date proposed by the notifier: unknown; see section 5)

- Data on nitrogen transformation and carbon mineralization (relevant for all representative uses evaluated; submission date proposed by the notifier: unknown; see section 5)

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

- Use of personal protective equipment by operators and workers due to the sensitization potential of micro-organisms

- Mitigation measures to mitigate the exposure of pollinators is recommended (see section 5)

9. Concerns

9.1. Issues that could not be finalised

An issue is listed as an issue that could not be finalised where 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 of Annex VI to Directive 91/414/EEC and where 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).

1. The production of toxins cannot be excluded and therefore the risk assessment cannot be finalised for humans and the environment including the assessment of potential groundwater contamination.

2. The risk characterization for wild mammals could not be finalised.

3. The risk characterization for honeybees or for other pollinators could not be finalised.

4. The risk characterization for earthworms could not be finalised.

5. The risk characterization for soil micro-organisms could not be finalised.

9.2. Critical areas of concern

An issue is listed as a critical area of concern where there is enough information available to perform an assessment for the representative uses in line with the Uniform Principles of Annex VI to Directive 91/414/EEC, and where this assessment does not permit to conclude 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 where the assessment at a higher tier level could not be finalised due to a lack of information, and where the assessment performed at the lower tier level does not permit to conclude 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.

6. Persistence and spread (mobility) of the micro-organism in the environment. Soil background levels of *Metarhizium anisopliae* may not be recovered even after 7.5 years after treatment, and spread from treated to non-treated areas has been observed.

7. The risk of epizootic infections within the wide range of host species, including beneficial arthropods. The decrease of the density of *M. anisopliae* was indicated as slow in the host range of arthropod species. Moreover *M. anisopliae* was considered as persistent in soil (see section 5).

9.3. Overview of the concerns 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 this table.)

Representative use		**Edible uses**	**Non-Edible uses**
Operator risk	Risk identified		
	Assessment not finalised	X[1]	X[1]
Worker risk	Risk identified		
	Assessment not finalised	X[1]	X[1]
Bystander risk	Risk identified		
	Assessment not finalised	X[1]	X[1]
Consumer risk	Risk identified		
	Assessment not finalised	X[1]	
Risk to wild non target terrestrial vertebrates	Risk identified		
	Assessment not finalised	X[1,2]	X[1,2]
Risk to wild non target terrestrial organisms other than vertebrates	Risk identified	X[7]	X[7]
	Assessment not finalised	X[1,3,4,5]	X[1,3,4,5]
Risk to aquatic organisms	Risk identified		
	Assessment not finalised		
Groundwater exposure active substance	Legal parametric value breached		
	Assessment not finalised		
Groundwater exposure metabolites	Legal parametric value breached		
	Parametric value of 10µg/L[(a)] breached		
	Assessment not finalised	X[1]	X[1]
Comments/Remarks			

The superscript numbers in this table relate to the numbered points indicated as concerns

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

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APPENDICES

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	*Metarhizium anisopliae* var. *anisopliae* BIPESCO 5/F52
Function (e.g. control of fungi)	control of insects

Identity of the micro-organism (Annex IIM 1)

Name of the organism	*Metarhizium anisopliae* var. *anisopliae*
Taxonomy	**Kingdom:** Fungi **Sub-Kingdom:** Neomycota **Phylum:** Ascomycota **Sub-Phylum:** Euascomycotina **Class:** Pyrenomycetes **Order:** Hypocreales **Family:** Clavicipitaceae **Genus:** *Metarhizium* **Species:** *anisopliae* **Variety:** *anisopliae* **Isolate:** BIPESCO 5/F 52
Species, subspecies, strain:	*Metarhizium anisopliae* var. *anisopliae* strains BIPESCO 5 and F52
Identification	A unique identification of BIPESCO 5/F52 (referred to as M.a. 43) is based on group-I introns at three different positions within the 28S rDNA gene of *Metarhizium anisopliae* var. *anisopliae*. Open for an unequivocal method
Culture collection	BBA, Germany : M.a. 43 HRI, UK: 275-86 (acronyms V275 or KVL 275) KVL, Denmark: KVL 99-112 (Ma 275 or V 275) Bayer, Germany: DSM 3884 ATCC, USA: ATCC 90448 USDA, Ithaca, USA: ARSEF 1095
Minimum and maximum concentration of the micro-organism used for manufacturing of the formulated product (CFU/g; CFU/L, etc.):	Agrifutur: approx. 3 x 10^9 CFU/g MPCP powder. Novozymes Biological Inc: 1.0 x 10^{10} CFU/g with upper limits of 5.0-6.0 x 10^{10} CFU/g and lower limits of 9.0 x 10^9 CFU/g.
Identity and content of relevant impurities in the technical grade micro-organism:	Open
Is the MPCA genetically modified; if so provide type of modification	No

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

Origin and natural occurrence,	The strains under review, BIPESCO 5 and F52, have both originally been isolated in Austria from *Cydia pomonella* or codling moth, a lepidopteran

background level	from the family of Tortricidae.
Target organism(s)	Insect pests susceptible to *M. anisopliae* var. *anisopliae* include aphids, thrips, whitefly, scarabs (Coleoptera, Melolonthidae), weevils (Coleoptera: Curculionidae), mites, and gnats.
Mode of action	BIPESCO 5/F52 produces toxins destruxins A, B and E; the quantitative role of these toxins in the infection process is not completely known. If not by paralysis, insect death probably occurs due to various processes including depletion of nutrients, physical obstruction or invasion of organs and toxicosis.
Host specificity	*M. anisopliae* var. *anisopliae* BIPESCO 5/F52 has a wide host range which is confined primarily to the order of the insects but also includes some species of the Acarina. The most common hosts of *M. anisopliae* var. *anisopliae* BIPESCO 5/F52 under 'natural' or 'agricultural' conditions are probably some subtaxa within the Coleoptera insect order (scarabs and weevils) found in and on soils.
Life cycle	Entomopathogenic fungi such as *Metarhizium* var. *anisopliae* BIPESCO 5/F52 invade their host by direct penetration of the host exoskeleton or cuticle. Conidia germinate on the host surface and may differentiate to form an appressorium. An infection hypha penetrates down through the host cuticle and eventually emerges into the haemocoel of the insect. Inside the body of the insect, the fungus produces free-floating cells which are passively transported throughout the haemocoel. At this stage toxins may be produced. Following the death of the insect, under humid conditions, the mycelium penetrates the insect cuticle, again mostly at the intersegmental joints, and produces infectious conidia on the outside of the cadaver. Under dry conditions, the fungus may survive in the hyphal stage, but fail to produce conidia on the outside of the body. The production of conidia requires water potentials above – 100 bars, but below 10 ºC and above 35 ºC no sporulation occurs. The optimal temperature for sporulation is 25-30 ºC. M. anisopliae can grow in vitro in the pH range 3.3 – 8.5.
Infectivity, dispersal and colonisation ability	*Metarhizium* spores can be dispersed by a wide range of organisms such as adult cockchafers, earthworms, phoretic mites, Acari, Collembola, dipteran and coleopteran larvae. Optimal growth of *M. anisopliae* var. *anisopliae* BIPESCO 5/F52 occurs between 22 and 30 °C.
Relationships to known pathogens	There are no relationships to plant, animal or human pathogens
Genetic stability	*M. anisopliae* var. *anisopliae* BIPESCO 5/F52 are genetically stable.
Production of relevant metabolites/toxins	Open
Resistance/sensitivity to antibiotics/anti-microbial agents used in human or veterinary medicine	No reports.

Classification and proposed labelling

with regard to the micro-organism:	The active substance should be classified as potentially sensitising by inhalation and skin contact. No classification and labelling for the micro-organism regarding the environment is proposed.

Summary of representative uses evaluated (*Metarhizium anisopliae* var. *anisopliae* 'Bipesco 5/F52')

Crop and / or situation	Member State or Country	Product name	F G or I	Pests or Group of pests controlled	Formulation		Application				Application rate per treatment			PHI (days)	Remarks
					Type	Conc. of MPCA	Method Kind	Growth stage & Season	Number min max	Interval between applications (days, min)	kg MPCP/ hL min max	Water L/ha min max	kg MPCP/ha [CFU /ha] min max		
(a)			(b)	(c)	(d-f)	(i)	(f-h)	(j)	(k)					(l)	(m)
Meadows, Grassland Sports fields Golf courses Football grounds	EU-member states	**GranMet GR**	F	*Phyllopertha horticola* *Amphimallon solstitialis*	GR	3.3 g/kg = 10^{10} CFU/kg MPCP	overall drilling	all growth stages	1 x min 2 x max per year	7	no water	no water	15-30 kg MPCP/ha = [1.5-3 x 10^{11} CFU/ha]	one day	no restrictions
Vineyards Grapes	EU-member states	**GranMet GR**	F G	*Otiorhynchus sulcatus* *Daktulosphaira vitifoliae*	GR	3.3 g/kg = 10^{10} CFU/kg MPCP	drilling in rows or individual plant drilling	all growth stages	1 x min 2 x max per year	7	no water	no water	15-30 kg MPCP/ha = [1.5-3 x 10^{11} CFU/ha]	one day	no restrictions

Crop and / or situation	Member State or Country	Product name	F G or I	Pests or Group of pests controlled	Formulation		Application				Application rate per treatment			PHI (days)	Remarks
					Type	Conc. of MPCA	Method Kind	Growth stage & Season	Number min max	Interval between applications (days, min)	kg MPCP/hL min max	Water L/ha min max	kg MPCP/ha [CFU/ha] min max		
Horticulture Grass, Ornamentals etc.	EU-member states	**GranMet GR**	F G	*Otiorhynchus sulcatus* *Phylloperth a horticola* *Amphimallon solstitialis*	GR	3.3 g/kg = 10^{10} CFU/kg MPCP	overall – or individual plant drilling	all growth stages	1 x min 2 x max per year	28	no water	no water	15-30 kg MPCP/ha = [1.5-3 x 10^{11} CFU/ha]	one day	no restrictions
Fruit plantations Trees, shrubs, etc.	EU-member states	**GranMet GR**	F G	*Otiorhynchus sulcatus*	GR	3.3 g/kg = 10^{10} CFU/kg MPCP	overall – or individual plant drilling	all growth stages	1 x min 2 x max per year	7	no water	no water	15-30 kg MPCP/ha = [1.5-3 x 10^{11} CFU/ha]	one day	no restrictions
Crop	EU-	**GranM**	F	*Diabrotica*	GR	3.3 g/kg =	overall – or	all	1 x	7	no	no water	15-30 kg	one day	no

Crop and / or situation	Member State or Country	Product name	F G or I	Pests or Group of pests controlled	Formulation		Application				Application rate per treatment			PHI (days)	Remarks
					Type	Conc. of MPCA	Method Kind	Growth stage & Season	Number min max	Interval between applications (days, min)	kg MPCP/hL min max	Water L/ha min max	kg MPCP/ha [CFU/ha] min max		
Maize etc. (susceptible arable and vegetable crops)	member states	**et GR**	G	*virgifera* *Phyllopertha horticola* *Amphimallon solstitialis*		10^{10} CFU/kg	drilling in rows	growth stages	min 2 x max per year		water		MPCP/ha = [1.5-3 x 10^{11} CFU/ha]		restrictions
Forest Trees etc.	EU-member states	**GranMet GR**	F	*Otiorhynchus sulcatus* *Strophosoma melanogrammum* and *S. capitatum*	GR	3.3 g/kg = 10^{10} CFU/kg	individual plant drilling	all growth stages	1 x min 2 x max per year	7	no water	no water	15-30 kg MPCP/ha = [1.5-3 x 10^{11} CFU/ha]	one day	no restrictions
Meadows, Grassland	EU-member states	**GranMet WP**	F	*Phyllopertha horticola*	WP	30 g / kg MPCP =	overall drench	all growth stages	1 x min 2 x	7	min 0.1- max 0.5	min 1000	1-5 kg MPCP/ha 9 x 10^{10} –	one day	no restrictions

Crop and / or situation	Member State or Country	Product name	F G or I	Pests or Group of pests controlled	Formulation		Application				Application rate per treatment			PHI (days)	Remarks
					Type	Conc. of MPCA	Method Kind	Growth stage & Season	Number min max	Interval between applications (days, min)	kg MPCP/ hL min max	Water L/ha min max	kg MPCP/ha [CFU /ha] min max		
Sports fields Golf courses Football grounds				*Amphimallon solstitialis*		9×10^{10} CFU / kg MPCP			max per year			max 1500	4.5×10^{11} CFU / ha		
Vineyards Grapes	EU-member states	**GranMet WP**	F G	*Otiorhynchus sulcatus* *Daktulosphaira vitifoliae*	WP	30 g / kg MPCP = 9×10^{10} CFU / kg MPCP	drench in rows or individual plant drench	all growth stages	1 x min 2 x max per year	7	min 0.1 max 0.5	min 1000 max 1500	1-5 kg MPCP/ha 9×10^{10} – 4.5×10^{11} CFU / ha	one day	no restrictions
Horticulture Grass, Ornamental	EU-member states	**GranMet WP**	F G	*Otiorhynchus sulcatus* *Phyllopertha horticola*	WP	30 g / kg MPCP = 9×10^{10} CFU / kg	overall – or individual plant drench	all growth stages	1 x min 2 x max per	28	min 0.1 max 0.5	min 1000 max 1500	1-5 kg MPCP/ha 9×10^{10} – 4.5×10^{11} CFU / ha	one day	no restrictions

Crop and / or situation	Member State or Country	Product name	F G or I	Pests or Group of pests controlled	Formulation		Application				Application rate per treatment			PHI (days)	Remarks
					Type	Conc. of MPCA	Method Kind	Growth stage & Season	Number min max	Interval between applications (days, min)	kg MPCP/hL min max	Water L/ha min max	kg MPCP/ha [CFU /ha] min max		
s etc.				*Amphimallon solstitialis*		MPCP			year						
Fruit plantations Trees, scrubs, etc.	EU-member states	**GranMet WP**	F G	*Otiorhynchus sulcatus*	WP	30 g / kg MPCP = 9×10^{10} CFU / kg MPCP	overall – or individual plant drench	all growth stages	1 x min 2 x max per year	7	min 0.1 max 0.5	min 1000 max 1500	1-5 kg MPCP/ha 9×10^{10} – 4.5×10^{11} CFU / ha	one day	no restrictions
Crop Maize etc. (susceptible arable and	EU-member states	**GranMet WP**	F G	*Diabrotica virgifera* *Phyllopertha horticola* *Amphimallo*	WP	30 g / kg MPCP = 9×10^{10} CFU / kg MPCP	overall – or drench in rows	all growth stages	1 x min 2 x max per year	7	min 0.1 max 0.5	min 1000 max 1500	1-5 kg MPCP/ha 9×10^{10} – 4.5×10^{11} CFU / ha	one day	no restrictions

Crop and / or situation	Member State or Country	Product name	F G or I	Pests or Group of pests controlled	Formulation		Application				Application rate per treatment			PHI (days)	Remarks
					Type	Conc. of MPCA	Method Kind	Growth stage & Season	Number min max	Interval between applications (days, min)	kg MPCP/hL min max	Water L/ha min max	kg MPCP/ha [CFU /ha] min max		
vegetable crops)				*n solstitialis*											
Forest Trees etc.	EU-member states	**GranMet WP**	F	*Otiorhynchus sulcatus* *Strophosoma melanogrammum* and *S. capitatum*	WP	30 g / kg MPCP = 9×10^{10} CFU / kg MPCP	individual plant drench	all growth stages	1 x min 2 x max per year	7	min 0.1 max 0.5	min 1000 max 1500	1-5 kg MPCP/ha 9×10^{10} – 4.5×10^{11} CFU/ ha	one day	no restrictions
Nursery, greenhouses Perennials, trees, shrubs, fruit, annuals	EU-member states	**Bio 1020®**	G/I	*Otiorhyncus sultacus* *Exomala orientalis, Fungus gnats, Sciaridae*	GR	2% = 9×10^{11} CFU/kg MPCP	soil incorporation	all growth stages	1x min 2x max per year	7	No water	N/A	500-1500 g/m^3 or 50-150 kg/ha = $4{,}5 \times 10^{13}$ - $1{,}35 \times 10^{14}$ CFU /ha	None	no restrictions incorporated to 1cm depth

Crop and / or situation	Member State or Country	Product name	F G or I	Pests or Group of pests controlled	Formulation		Application				Application rate per treatment			PHI (days)	Remarks
					Type	Conc. of MPCA	Method Kind	Growth stage & Season	Number min max	Interval between applications (days, min)	kg MPCP/ hL min max	Water L/ha min max	kg MPCP/ha [CFU /ha] min max		
Nursery, greenhouses Perennials, trees, shrubs, fruit, annuals	EU-member states	**Taenure® Met 52®**	G/ I	*Otiorhyncus sultacus Exomala orientalis, Fungus gnats, Sciaridae*	GR	2% = $9x10^{11}$ CFU/kg MPCP	soil incorporation	all growth stages	1x min 2x max per year	7	No water	N/A	500-1500 g/m^3 or 50-150 kg/ha = $4,5x10^{13}$-$1,35 x10^{14}$ CFU /ha	None	no restrictions incorporated to 1cm depth
Horticulture Landscape, Lawns, golfs, athletic fields, gardens	EU-member states	**TickExG®**	F	*Otiorhyncus sultacus Exomala orientalis, Fungus gnats, Sciaridae*	GR	2% = $9x10^{11}$ CFU/kg MPCP	Application to soil	all growth stages	1x min 3x max per year	7	No water	N/A	25 to 150 kg/ha = $2x10^{13}$ to $1.3x10^{14}$ CFU /ha	None	no restrictions

Crop and / or situation	Member State or Country	Product name	F G or I	Pests or Group of pests controlled	Formulation		Application				Application rate per treatment			PHI (days)	Remarks
					Type	Conc. of MPCA	Method Kind	Growth stage & Season	Number min max	Interval between applications (days, min)	kg MPCP/hL min max	Water L/ha min max	kg MPCP/ha [CFU /ha] min max		
Nursery, greenhouses Perennials, trees, shrubs, fruit, annuals	EU-member states	**Taerain® Met52EC**	G/I	*Tetranychus urticae* *Bemisia argentifolii* *Trialeurodes vaporariorum* *Franklinieallia occidentalis*	OD	11.0% = $5.5x10^{12}$ CFU/L MPCP	Full cover foliage or soil incorporation	all growth stages	1x min 4x max per year	5-10	0.12 to 0.52L EC/hL	1000-1500L	1.25-5L/ha = $7.3x10^{12}$ to $3x10^{13}$ CFU /ha	4 hours	no restrictions
Horticulture Landscape, Lawns, golfs, athletic fields, gardens	EU-member states	**TickEx EC®**	F	*Otiorhyncus sultacus* *Exomala orientalis,* *Fungus gnats, Sciaridae*	OD	11.0% = $5.5x10^{12}$ CFU/L MPCP	Soil directed spray applications	all growth stages	1x min 3x max per year	7	0.7-1 L EC/hL	500-1000L	6.5-9.5 L/ha = $3.6x10^{13}$ to $5.3x10^{13}$ CFU /ha	none	no restrictions

Crop and / or situation	Member State or Country	Product name	F G or I	Pests or Group of pests controlled	Formulation		Application				Application rate per treatment			PHI (days)	Remarks
					Type	Conc. of MPCA	Method Kind	Growth stage & Season	Number min max	Interval between applications (days, min)	kg MPCP/hL min max	Water L/ha min max	kg MPCP/ha [CFU/ha] min max		

(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), greenhouse application (G) or indoor application (I)
(c) *e.g.* biting and suckling insects, soil born insects, foliar fungi, weeds
(d) *e.g.* wettable powder (WP), emulsifiable concentrate (EC), granule (GR)
(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 plant - type of equipment used must be indicated
(i) Cfu=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) Indicate the minimum and maximum number of application possible under practical conditions of use
(l) PHI - minimum pre-harvest interval
(m) Remarks may include: Extent of use/economic importance/restrictions

Analytical Methods

Analytical methods for the micro-organism (Annex IIM 4.2; 4.3; IIIM 5.4)

Manufactured micro-organism (principle of method)	Open
Impurities and contaminating micro-organisms in manufactured material (principle of method)	Open
Microbial plant protection product (principle of method)	Open

Analytical methods for residues (viable and non-viable) (Annex IIM 4.5)

of the active micro-organism (principle of method)	Open
of relevant metabolites/toxins (principle of method)	Open

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

Medical data, surveillance and observations	Based on the total toxicological package of the active substance *M. anisopliae* var. *anisopliae* BIPESCO 5/F52, it is concluded that the active substance and its products do not exhibit infectivity or pathogenicity. There are only a few case studies of human infections reported in the open literature, however, none of these cases were associated with the use of *M. anisopliae* for insect control. No adverse effects on human health were reported to have occurred in the laboratories and the production facilities of the applicant.
Toxicity	
after acute oral exposure:	No adverse effects. Rat oral LD_{50} >1 x 10^8 spores/animal
after acute inhalation exposure:	Slight reversible effects in lungs after intratracheal administration. Rat inhalation LD_{50} >1 x 10^8 spores/animal
after acute intraperitoneal/subcutaneous exposure:	Slight reversible effects on spleen weight. Rat intraperitoneal LD_{50} >1 x 10^7 spores/animal
Infectivity	
after acute oral exposure:	Not infective
after acute inhalation exposure:	Not infective
after acute intraperitoneal/subcutaneous exposure:	Intraperitoneal: not infective
Pathogenicity	
after acute oral exposure:	not pathogenic
after acute inhalation exposure:	not pathogenic
after acute intraperitoneal/subcutaneous exposure:	Intraperitoneal: not pathogenic
Genotoxicity	No genotoxic potential
Cell culture study	Not required
Short term toxicity/pathogenicity	No adverse effects in mice after repeated inhalation exposure to *M. anisopliae* (strain unknown)
Specific toxicity, pathogenicity and infectiveness studies	No further testing required.
AOEL:	Not applicable, lack of adverse effects due to *M. anisopliae* var. *anisopliae* BIPESCO 5/F52 in studies performed.
ADI:	Not applicable, lack of adverse effects due to *M. anisopliae* var. *anisopliae* BIPESCO 5/F52 in studies

	performed.

Exposure scenarios (including method of calculation)

Application method:	Soil application/incorporation, soil directed spray application and/or foliar application, overall or individual plant drench
Operator:	Open. Use of adequate PPE to be considered, due to the sensitisation potential of micro-organisms
Workers:	Open. Use of adequate PPE to be considered, due to the sensitisation potential of micro-organisms
Bystanders:	Open. Low concern based on the weight of evidence

Residues

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

Viable residues	Open
Non-viable residues	Open

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

Persistence and multiplication in soil	*Metarhizium anisopliae* var. *anisopliae* may be very high persistent at concentrations considerably higher than background natural conditions (after one single application it is estimated that it will take more than 10 years for levels to decline down to the upper background level) Data gap to determine the accumulated plateau in soil after repeated applications.
Persistence and multiplication in water	Data gap
Persistence and multiplication in air	Fungal spores in general, are susceptible to solar radiation. *Metarhizium anisopliae* var. *anisopliae* is expected to be present in the air. No specific information on the background levels and on the change of levels as a result of its use as pesticide is available No further information is required since *Metarhizium anisopliae* is not pathogenic or toxic to humans and low concern for bystanders has been identified with respect to sensitizing properties.
Mobility	*Metarhizium* spores can be dispersed by a wide range of organisms (adult cockchafers, earthworms, phoretic mites, Acari, Collembola, dipteran and coleopteran larvae).

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

Effects on birds and other non-target terrestrial vertebrates	No evidence of pathogenicity or replication of strains BIPESCO 5/F52 of *Metarhizium anisopliae* var. *anisopliae* in birds. Toxicity of the microorganism to birds: 5-d LD_{50} of >3.5x10^8 CFU/g bw/day (>5000 mg a.s./kg bw/day) Data on metabolites of the microorganisms: - Level of Dtx A found in infected insects: 5.5 µg/insect cadaver - Level of Dtx B found in infected insects: 1.1 µg/insect cadaver - Toxicity of the metabolites to mammals: $LD_{50,dtx\ A}$: 1 mg/kg bw $LD_{50,dtx\ B}$: 13.2 mg/kg bw

Effect on aquatic organisms

Substance	Species	Method	Duration [d]	Criterion	Value [CFU/L]
FISH					
Strain F52	*Oncorhynchus mykiss*	renewal	30	NOEC	>3.7x10^9
additional experiments					
ARSEF 2575	*Gambusa affinis* embryos	static	4	LC_{50}	141 mg/L (extract)
ARSEF 1080	*Menidia beryllina* embryos	static	4	mortality	significant at 8.2 x 10^8 CFU/L (12 mg a.s./L)
ARSEF 2575	*Gambusa affinis* adults	static	1	$NOEC_{reproduction}$	>200 mg/L (extract)
ARSEF 2575	*Gambusa affinis* adults	dietary	90	$NOEC_{dietary}$	>2.2x10^4 CFU/mg feed dw
INVERTEBRATES					
Strain F52	*Daphnia magna*	renewal	21	NOEC MATC	3.5x10^8 5x10^8
M.anisopliae var.acridium	*Ceriodaphnia dubia*	renewal	7	LC_{50}	<1.2x10^5
M.anisopliae var.acridium	*Ceriodaphnia dubia*	static	72 h.	NOEC	6.7x10^3
additional experiments					
ARSEF 2575	*Mysidopsis bahia*		4	LC_{50}	2.4 mg/L (extract)
ARSEF 2575	*Palaemonetes pugio* embryos		4	LC_{50}	52 mg/L (extract)

Substance	Species	Method	Duration [d]	Criterion	Value [CFU/L]
ARSEF 1080	*Palaemonetes pugio* embryos			mortality	44 and 77% (sign.) at 8.2 x 10^7 CFU/L and 8.2 x 10^8 CFU/L (1.2 and 12 mg a.s./L)
dry conidia	*Culex quinquefasciatus*	ingestion		physiological effects	toxin release in the gut
dry conidia	*Anopheles gambiae*	ingestion		physiological effects	toxin release in the gut
Crude extract	*Daphnia magna*		48 h	LC_{50}	0.04 mg/L
ALGAE					
Strain F52	*Pseudokirchneriella subcapitata*	static	10	ErC50 EbC50 NOEbC NOErC	>$8.8x10^{10}$ >$8.8x10^{10}$ $4.4x10^{10}$ $8.8x10^{10}$

Effects on other aquatic organisms	*Xenopus laevis*, 4-d LC_{50} of 32 mg/L (extract from 1 x 10^9 CFU ARSEF 2575/L) *Xenopus laevis*, NOEC > 8.2 x 10^8 CFU ARSEF 1080/L) (highest concentration)
Effect on plants other than algae	No data available; not required
Effects on bees and other arthropods	bees oral LD_{50} > 6000 CFU/bee larvae. Tested amount too low compared to use rate. other arthropods open *Bombus spp.* exposed to *M. anisopliae* var. *anisopliae* SF86-47: 73-77% infection rates and 86-90% mortality in 'maximum challenge' tests (contact exposure); 47-63% infection rates and 48-65% mortality after direct spraying with 8 mL of a conidial suspension of 10^8 CFU/mL

Laboratory experiments

Substance	**Species**	**Method**	**Dose [CFU/g feed]**	**Exposure duration [d]**	**Parameter**	**Adverse effect/value**
Strain F52	*Chrysoperla carnea*	dietary exposure	$4.2x10^5$	12	mortality	37 %

Substance	Species	Method	Dose [CFU/g feed]	Exposure duration [d]	Parameter	Adverse effect/value
			$4.2x10^6$	12	mortality	27 %
			$4.2x10^7$	12	mortality	33 %
Strain F52	*Hippodamia convergens*	dietary exposure	$4.2x10^5$	22	mortality	17 %
			$4.2x10^6$	22	mortality	20 %
			$4.2x10^7$	22	mortality	31 %
Strain F52	*Nasonia vitripennis*	dietary exposure	$4.2x10^5$	26	mortality	17 %
			$4.2x10^6$	26	mortality	17 %
			$4.2x10^7$	26	mortality	20 %
Strain F52	*Orius majusculus*	dripping on insect	10^9 CFU/mL	7	mortality	70 %
Strain F52	*Orius majusculus* imagos			7	LC_{50}	5.1 x 10^8 CFU/mL
	Orius majusculus nymphs			7	LC_{50}	3.9 x 10^7 CFU/mL
	Orius insidiosus imagos			7	LC_{50}	4.5 x 10^7 CFU/mL
	Orius insidiosus nymphs			7	LC_{50}	9.7 x 10^7 CFU/mL

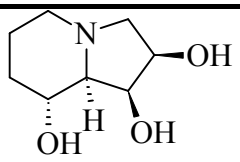
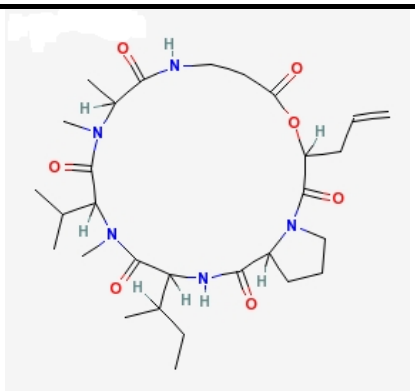
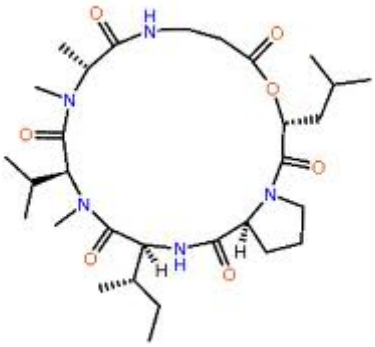
Field experiments

Substance	Species	Method	Dose [CFU/ha]	Exposure duration	Parameter	Adverse effect [%]
Strain F52	Coleoptera, Staphylinidae	single application in lucerne fields	10^{13}		mortality	0 0
Strain F52	Carabidae, Staphylinidae		10^{13}		mortality	0-0.4 0-4
Strain F52	Staphylinidae		6 x 10^{15}		mortality	16
Strain 5	Psocoptera[1]	single application in greenery	1 x 10^{14}	7 d	infection[9]	40
	Cicadellidae[2]			7 d		75
	Miridae[3]			7 d		52
	Pentatomidae[4]			7 d		50
	Coccinellidae[5]			277 d		10
	Ixodidae[6]			14 d		57
	Opiliones[7]			7 d		6
	Curculioniidae[8]			14 d		77

1: bark lice; 2: leafhoppers; 3: capsid bugs; 4: shield bugs; 5: ladybirds; 6: hard ticks; 7: harvest-men; 8: target weevils (*Strophosoma* spec.); 9: maximal infection obtained at the exposure duration given in the adjacent column. Infection rate further decreased rapidly in time.

Effects on earthworms	No signs of infectivity or pathogenicity to earthworms of the F52 strain of *Metarhizium anisopliae* var. *anisopliae* at concentration ≤ 7.0 x 10^{10} CFU/kg soil dw (1000 mg a.s./kg soil dw).
Effects on non-target soil micro-organisms	No data available; data gap
Additional studies	Destruxins have a relatively low toxicity to the frogs *Xenopus laevis* and *Rana temporaria*.

APPENDIX B – USED COMPOUND CODE(S)

Code/Trivial name	Chemical name	Structural formula
swainsonine	(1*S*,2*R*,8*R*,8a*R*)-octahydroindolizine-1,2,8-triol	
DMSO	(methylsulfinyl)methane dimethyl sulfoxide	
Destruxin A	16-butan-2-yl-10,11,14-trimethyl-13-propan-2-yl-3-prop-2-enyl-4-oxa-1,8,11,14,17-pentazabicyclo[17.3.0]docosane-2,5,9,12,15,18-hexone	
Destruxin B	(3*R*,10*R*,13*S*,16*S*,19*S*)-16-[(2*S*)-butan-2-yl]-10,11,14-trimethyl-3-(2-methylpropyl)-13-propan-2-yl-4-oxa-1,8,11,14,17-pentazabicyclo[17.3.0]docosane-2,5,9,12,15,18-hexone	

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ABBREVIATIONS

1/n	slope of Freundlich isotherm
λ	wavelength
ε	decadic molar extinction coefficient
°C	degree Celsius (centigrade)
µg	microgram
µm	micrometer (micron)
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
cm	centimetre
d	day
DAA	days after application
DAR	draft assessment report
DAT	days after treatment
DM	dry matter
DT_{50}	period required for 50 percent disappearance (define method of estimation)
DT_{90}	period required for 90 percent disappearance (define method of estimation)
dw	dry weight
EbC_{50}	effective concentration (biomass)
EC_{50}	effective concentration
ECHA	European Chemical 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 Organisation of the United Nations
fd	feed
FIR	Food intake rate
FOB	functional observation battery
FOCUS	Forum for the Co-ordination of Pesticide Fate Models and their Use
g	gram

GAP	good agricultural practice
GC	gas chromatography
GCPF	Global Crop Protection Federation (formerly known as GIFAP)
GGT	gamma glutamyl transferase
GM	geometric mean
GS	growth stage
GSH	glutathion
h	hour(s)
ha	hectare
Hb	haemoglobin
Hct	haematocrit
hL	hectolitre
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
ISO	International Organisation for Standardisation
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
kg	kilogram
K_{Foc}	Freundlich organic carbon adsorption coefficient
L	litre
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	metre
M/L	mixing and loading
MAF	multiple application factor
MATC	maximum allowable toxicant concentration
MCH	mean corpuscular haemoglobin
MCHC	mean corpuscular haemoglobin concentration
MCV	mean corpuscular volume
mg	milligram
mL	millilitre
mm	millimetre
mN	milli-newton
MPCA	microbial pest control agent
MPCP	microbial pest control product
MRL	maximum residue limit or level
MS	mass spectrometry
MSDS	material safety data sheet
MTD	maximum tolerated dose
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
OD	oil dispersion
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 ground water
PEC_{sed}	predicted environmental concentration in sediment
PEC_{soil}	predicted environmental concentration in soil
PEC_{sw}	predicted environmental concentration in surface water
pH	pH-value
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})
ppp	plant protection product
PT	proportion of diet obtained in the treated area
PTT	partial thromboplastin time
QSAR	quantitative structure-activity relationship
r^2	coefficient of determination
RPE	respiratory protective equipment
RUD	residue per unit dose
SC	suspension concentrate
SD	standard deviation
SFO	single first-order
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
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 volume
w/w	weight per weight
WBC	white blood cell
WG	water dispersible granule
WHO	World Health Organisation
wk	week
yr	year