BioAct WG, 1 X 10^{10} spores/gram (60 g/kg)

of *Purpureocillium lilacinum (syn. Paecilomyces lilacinus)* 251

Microbial pest control product against plant parasitic nematodes

Dossier according to OECD guidance for industry data submissions for microbial pest control products and their microbial pest control agents – August 2006

Summary documentation, Tier II

Annex IIIM, Section 4

Point IIIM 8: Rationale to waive residue studies on MPCP

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Applicant

Bayer CropScience AG

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OWNERSHIP STATEMENT

Introduction

The company Bayer CropScience AG is submitting a dossier for the re-approval of the microorganism *Purpureocillium lilacinum* 251 as an active substance under regulation (EC) 1107/2009.

The Microbial Pest Control Agent *Paecilomyces lilacinus* strain 251 was included into Annex I of Directive 91/414/EEC on 01/08/2008 (Commission Directive 2008/44/EC) and then approved according to the Commission Implementing Regulation (EU) No 540/2011 of 25 May 2011, implementing Regulation (EC) No 1107/2009 of the European Parliament [1)]. *P. lilacinus* strain 251 was notified and defended by Prophyta GmbH. The active ingredient has been evaluated in Belgium according to Uniform Principles. The representative formulated product for the initial evaluation was the experimental formulation PBP-01001-I, containing 2 × 10^9 spores/g. PBP-01001-I, is comparable to the commercial formulation BioAct WG, containing 1 × 10^{10} spores/g, and the only changes between both formulations were slight adjustments of the content of two co-formulants, without any impact on the performance or physical properties of the formulated product. The recommended rate in terms of spores per hectare remained exactly the same. The data on PBP-01001-I can therefore be extrapolated to the formulated product BioAct WG, a wettable granule formulation (WG), the representative formulation in the present application for the renewal.

In 2013 Bayer CropScience AG acquired Prophyta Biologischer Pflanzenschutz GmbH, now named Bayer CropScience Biologics GmbH. Bayer CropScience AG is the notifier for the renewal of *P. lilacinus* strain 251 in the procedure of AIR 3.

The microorganism has been previously classified as *Paecilomyces lilacinus* until 18S rRNA gene, internal transcribed spacer (ITS) and partial translation elongation factor 1-α (TEF) sequencing revealed that *P. lilacinus* is not related to *Paecilomyces.* The new genus name *Purpureocillium* has been proposed for *P. lilacinus* and the new species name was assigned: *Purpureocillium lilacinum.* Therefore the strain is now identified as *Purpureocillium lilacinum*. In this dossier *Paecilomyces lilacinus* 251 and *Purpureocillium lilacinum* 251 are used as synonyms: *Paecilomyces lilacinus = Purpureocillium lilacinum*.

It has to be taken into account that data on *Paecilomyces lilacinus* from the open literature stated before 2011 may not necessarily provide reliable information due to insufficient classification methods used in these studies, especially, if the strain identification is not provided and/or identification methods used were based solely on morphological characteristics. However, they may provide relevant information transferrable to *Purpureocillium lilacinum*.

Purpureocillium lilacinum 251 is a ubiquitous, saprobic filamentous fungus commonly isolated from soil, decaying vegetation, insects and nematodes. Strains of *P. lilacinum* are used in plant protection products due to their nematicide activity. The mode of action against plant pathogenic nematodes of *P. lilacinum* strain 251 is principally based upon parasitism of nematode eggs as well as the vermiform stages of the nematodes, leading eventually to their death. With regard to the results of toxicity and ecotoxicity studies of the active substance *P. lilacinum* strain 251, it can be concluded that *P. lilacinum* strain 251 shows no risk for exposed humans, animals and environment.

P. lilacinum 251 is intended to be used in plant protection products to control plant pathogenic nematodes. The representative use presented in this dossier comprises applications of the formulation BioAct WG in protected and non-protected vegetable crops to control root know nematode, *Meloidogyne* spp.

Here we submit data that were previously evaluated by RMS Belgium as well as new data and information based on literature searches and studies.

[1] OJEU L94/13 Commission Directive 2008/44/EC of 4 April 2008 amending Council Directive 91/414/EEC to include benthiavalicarb, boscalid, carvone, fluoxastrobin, *Paecilomyces lilacinus* and prothioconazole as active substances

IIIM 8 Residues in/on food and feed products for the Microbial Pest Control Product (rationale to waive residue studies on MPCP)

It is referred to the information and studies submitted for the active substance, *Purpureocillium lilacinum* 251, in Annex II, Doc IIM, Section 4, Point 6. The inert ingredients of the preparation BioAct®WG, *P. lilacinum* 251 formulated as WG, are nutritional additives generally used in human food, which exert no health effects (see Doc. H, Safety Data Sheets for all inert ingredients). Therefore, studies and information on the active ingredient, i.e. spores of *P. lilacinum* 251, are considered applicable and relevant with regard to the evaluation of the formulated product.

The nature of the product and its active substance are not adequately described and assessed by applying the term 'residue', or by quantifying 'residues', since this definition commonly implies a toxicological concern of the residual deposit of a plant protection product, which is not attributable to BioAct WG and *P. lilacinum* 251, for following reasons:

- *P. lilacinum* is a wide-spread, ubiquitous and common soil-born fungus, living mainly on decay of organic matter. Strain 251 is of natural origin, and is not genetically modified. Despite natural long-term exposure of the human population in the Philippines and the exposed personnel of the applicant there is no evidence for any infectivity, toxicity and pathogenicity of this strain.
- This strain is not an opportunistic human pathogen. Lack of infectivity, toxicity and pathogenicity is confirmed by results of acute toxicological studies, showing 100% clearance of spores from all tissues and body fluids, and no treatment related adverse effects in test animals signs at a single oral dose of 2000 mg/kg bw upon different routes of exposure (see Annex II, Doc IIM, Section 3).
- Infectivity of *P. lilacinum* 251 is ruled out by the inability of this strain to grow at temperatures of the human body (>36°C no growth was recorded, see Annex II, Doc IIM, Section 1, Point IIM 2.8).
- Further, *P. lilacinum* 251 does not act via toxins in nematode control, and does not produce the well-known paecilotoxin, or secondary metabolites of toxicological concern, as evidenced by its extremely low acute toxicity (see Annex II, Doc IIM, Section 1, Point IIM 2.3.2 and IIM 2.6, and Section 3, respectively).
- The production process for BioAct WG ensures that no secondary metabolites but only purified spores of the biocontrol strain are found in the end-use product.
- The inert ingredients of BioAct WG are natural organic compounds, used in human food, which present no health risk for consumers either.
- In most of the crops envisaged for use of BioAct WG no deposit is likely to occur, since soil drench applications rule out a direct contact between the applied product and the fruit. This applies to all crops with above ground harvest, such as tomatoes.
- After harvest any remaining fungal spores on potato, celery and carrots will be exposed to unfavourable conditions (e.g. dryness), and are not likely to germinate and grow on the harvested crop.
- Any potentially occurring residual deposits on these crops are not relevant as a human health concern in view of the toxicological profile of this strain and likely to be minimal in amount due to the low environmental concentration in soil predicted from maximum field use of BioAct WG ($PEC_{soil} = 32 \times 10^7$ CFU/kg dry weight soil in top 5 cm, see calculation in Annex III, Doc IIIM, Section 6, Point IIIM 11.1).
- *P. lilacinum* is not able to enter plants and infest them, as evidenced from its beneficial effect on plant health and growth. As a saprophytic fungus it would use the resources of the plant host in case access was possible.

In summary, the lack of infectivity and a treatment related effect upon exposure to *P. lilacinum* 251 indicate that residual deposits of this fungus will not impose a health risk for consumers. In this case, there is no need and no scientifically justified value to define an Acceptable Daily Intake (ADI). Therefore, calculation of the potential exposure of consumers in terms of the Theoretical Maximum Daily Intake (TMDI) and its relation to the ADI is not relevant, and conclusively a Maximum Residue Level (MRL) need not be proposed.

According with the EFSA conclusions (*EFSA Scientific Report* (2007, M-496430-01-1) 103, 1-35 Conclusion on the peer review of *Paecilomyces lilacinus* strain 251),

"*Humans and animals can be commonly exposed to P. lilacinus strain 251, an organism found in soil. No toxicological or pathological endpoints were identified for P. lilacinus strain 251, as demonstrated in chapter 2 of this document.*

Dietary exposure from use P. lilacinus strain 251 is likely to be minimal. Any potentially remaining fungal spores on harvested crop parts are not likely to germinate and grow, and moreover will be exposed to unfavorable conditions. Furthermore, residues of the microbial pesticide are likely to be removed from treated

food by washing and processing. Thus, the amount of residues the consumer will be exposed, if any, is likely to be very low.

Even if residues are not removed, however, it is believed that dietary exposure to the microbial agent will result in negligible risk to consumers as in view of the toxicological profile of this strain no hazard to human health has been identified. Because of the low toxicity and the low exposure of P. lilacinus strain 251 expected from the proposed uses, there is no concern for acute and chronic risks for the general population or sensitive subpopulations, such as infants and children.

Based on the risk assessment for the consumer it was concluded that MRLs for P. lilacinus strain 251 on food commodities are not required. Thus, P. lilacinus strain 251 is considered eligible for inclusion in the Annex VI of Regulation 396/2005."

References

Annex point / reference number	Author(s)	Year	Title Source *(where different from company)* Company name, Report No., Date, GLP/GEP status *(where relevant)*, published or not	Data protect. claimed	Owner
KIIIM 8 /01	Anon.	2007	Conclusion regarding the peer review of the pesticide risk assessment of the active substance - Paecilomyces lilacinus strain 251 EFSA, European Food Safety Authority -public data-, Report No.: M-496430-01-1, Edition Number: M-496430-01-1 Date: 2007-07-13 GLP/GEP: n.a., unpublished	Yes	-public data-