Peer review of the pesticide risk assessment of the active substance *Metschnikowia fructicola* NRRL Y-27328

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**Abstract**

The conclusions of EFSA following the peer review of the initial risk assessments carried out by the competent authority of the rapporteur Member State, France, for the pesticide active substance *Metschnikowia fructicola* NRRL Y-27328 and the assessment of the application for inclusion in Annex IV of Regulation (EU) No 396/2005 are reported. The context of the peer review was that required by Regulation (EC) No 1107/2009 of the European Parliament and of the Council. The conclusions were reached on the basis of the evaluation of the representative uses of *Metschnikowia fructicola* NRRL Y-27328 as a fungicide on stone fruits, strawberries and grapes. The reliable endpoints, appropriate for use in regulatory risk assessment are presented. Missing information identified as being required by the regulatory framework is listed. Concerns are identified.

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Summary

*Metschnikowia fructicola* NRRL Y-27328 is a new active substance for which, in accordance with Article 7 of Regulation (EC) No 1107/2009 of the European Parliament and of the Council (hereinafter referred to as ‘the Regulation’), the rapporteur Member State (RMS), France, received an application from Koppert B.V. in September 2014 for approval. In accordance with Article 8(1)(g) of the Regulation, Koppert B.V. submitted an application for inclusion of the active substance in Annex IV of Regulation (EU) No 396/2005. Complying with Article 9 of the Regulation, the completeness of the dossier was checked by the RMS and the date of admissibility of the application was recognised as being 3 June 2015.

The RMS provided its initial evaluation of the dossier on *Metschnikowia fructicola* NRRL Y-27328 in the draft assessment report (DAR), which was received by the European Food Safety Authority (EFSA) on 17 October 2016. The DAR included a proposal to include the active substance in Annex IV of Regulation (EU) No 396/2005, in accordance with Article 11(2) of Regulation (EC) No 1107/2009. The peer review was initiated on 28 November 2016 by dispatching the DAR for consultation to the Member States and the applicant, Koppert B.V.

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

In accordance with Article 12 of the Regulation, EFSA should adopt a conclusion on whether *Metschnikowia fructicola* NRRL Y-27328 can be expected to meet the approval criteria provided for in Article 4 of the Regulation taking into consideration recital (10) of the Regulation. Furthermore, this conclusion also addresses the assessment required from EFSA under Article 12 of Regulation (EC) No 396/2005, provided the active substance will be approved under Regulation (EC) No 1107/2009 without restrictions affecting the residue assessment. The conclusions laid down in this report were reached on the basis of the evaluation of the representative uses of *Metschnikowia fructicola* NRRL Y-27328 as a fungicide on stone fruits, strawberries and grapes, as proposed by the applicant. Full details of the representative uses can be found in Appendix A of this report.

The data submitted showed low and variable efficacy levels of the uses of *Metschnikowia fructicola* NRRL Y-27328 according to the representative uses proposed at the European Union (EU) level.

A data gap was identified for a detailed reporting of the search of the scientific peer-reviewed open literature on the active substance and its relevant metabolites dealing with side effects on the environment and non-target species.

In the area of the identity of the active substance and physical and technical properties of the representative formulation, a data gap was identified to confirm the specificity of markers used in the method for identification of the strain.

*Metschnikowia fructicola* NRRL Y-27328 showed lack of significant toxicity, infectivity or pathogenicity in available studies. Concerning secondary metabolites/toxins, it is known that *Metschnikowia fructicola* NRRL Y-27328 produces pulcherrimin during manufacturing. Pulcherrimin is of unknown toxicological concern and a quantitative risk assessment cannot be done. No other secondary metabolites/toxins were investigated and a data gap was identified. Overall, the non-dietary risk assessment to secondary metabolites/toxins including pulcherrimin cannot be finalised.

It was not necessary to perform a consumer risk assessment for remaining viable cell colony forming units of *Metschnikowia fructicola* NRRL Y-27328, as the latter did not show harmful health effects at higher concentrations and is therefore of no concern. Information on concentrations of pulcherrimin and any other secondary metabolites/toxins potentially present on the agricultural commodity are not available and toxicological reference values for pulcherrimin are missing. Consequently, a quantitative dietary exposure assessment for this secondary metabolite cannot be carried out. Because of remaining uncertainties related to the presence of pulcherrimin and potential other metabolites/toxins, an inclusion of *M. fructicola* strain NRRL Y-27328 in Annex IV of Regulation (EC) No 396/2005 cannot be recommended.

In the area of fate and behaviour into the environment, data gaps for information on the natural abundance of *M. fructicola* in the environment and/or further information on the persistence and multiplication of *M. fructicola* in the environment (soil and water compartments) have been identified. Furthermore, also the mobility of *M. fructicola* in the environment has not been addressed. A data gap for information to address the influence of natural/UV light on the persistence of *M. fructicola* in the environment was also identified. Finally, data gaps for information on the potential production of pulcherrimin and other secondary metabolites/toxins (e.g. chitinases) in the environment have been identified.
In the area of ecotoxicology, data gaps have been identified to further address the risk of *Metschnikowia fructicola* NRRL Y-27328 to fish, bees, non-target arthropods, earthworms and soil microorganisms. In addition, further data are needed on the toxicity to non-target organisms of the secondary metabolites/toxins pulcherrimin and chitinases.
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Background

Regulation (EC) No 1107/2009 of the European Parliament and of the Council1 (hereinafter referred to as ‘the Regulation’) lays down, *inter alia*, the detailed rules as regards the procedure and conditions for approval of active substances. This regulates for the European Food Safety Authority (EFSA) the procedure for organising the consultation of Member States and the applicant for comments on the initial evaluation in the draft assessment report (DAR), provided by the rapporteur Member State (RMS), and the organisation of an expert consultation, where appropriate.

In accordance with Article 12 of the Regulation, EFSA is required to adopt a conclusion on whether an active substance can be expected to meet the approval criteria provided for in Article 4 of the Regulation (also taking into consideration recital (10) of the Regulation) within 120 days from the end of the period provided for the submission of written comments, subject to an extension of 30 days where an expert consultation is necessary, and a further extension of up to 150 days where additional information is required to be submitted by the applicant in accordance with Article 12(3).

*Metschnikowia fructicola* NRRL Y-27328 is a new active substance for which, in accordance with Article 7 of the Regulation, the RMS, France (hereinafter referred to as the ‘RMS’), received a proposal to include the active substance in Annex IV of Regulation (EU) No 396/2005 as referred to in Article 7 of Regulation (EC) No 396/2005.2 Complying with Article 9 of the Regulation, the completeness of the dossier was checked by the RMS and the date of admissibility of the application was recognised as being 3 June 2015.

The RMS provided its initial evaluation of the dossier on *Metschnikowia fructicola* NRRL Y-27328 in the DAR, which was received by EFSA on 17 October 2016 (France, 2016). The DAR included a proposal to include the active substance in Annex IV of Regulation (EU) No 396/2005, in accordance with Article 11(2) of the Regulation. The peer review was initiated on 28 November 2016 by dispatching the DAR for consultation of the Member States and the applicant, Koppert B.V., for consultation and comments. EFSA also provided comments. In addition, EFSA conducted a public consultation on the DAR. The comments received were collated by EFSA and forwarded to the RMS for compilation and evaluation in the format of a reporting table. The applicant was invited to respond to the comments in column 3 of the reporting table. The comments and the applicant’s response were evaluated by the RMS in column 3.

The need for expert consultation and the necessity for additional information to be submitted by the applicant in accordance with Article 12(3) of the Regulation were considered in a telephone conference between EFSA and the RMS on 20 March 2017. On the basis of the comments received, the applicant’s response to the comments and the RMS’s evaluation thereof, it was concluded that additional information should be requested from the applicant, and that there was no need to conduct an expert consultation.

The outcome of the telephone conference, together with EFSA’s further consideration of the comments is reflected in the conclusions set out in column 4 of the reporting table. All points that were identified as unresolved at the end of the comment evaluation phase and which required further consideration, were compiled by EFSA in the format of an evaluation table.

The conclusions arising from the consideration by EFSA, and as appropriate by the RMS, of the points identified in the evaluation table, were reported in the final column of the evaluation table.

In accordance with Article 12 of the Regulation, EFSA should adopt a conclusion on whether *M. fructicola* NRRL Y-27328 can be expected to meet the approval criteria provided for in Article 4 of the Regulation, taking into consideration recital (10) of the Regulation. A final consultation on the conclusions arising from the peer review of the risk assessment took place with Member States via a written procedure in October 2017.

This conclusion report summarises the outcome of the peer review of the risk assessment on the active substance and the representative formulation evaluated on the basis of the representative uses of *Metschnikowia fructicola* NRRL Y-27328 as a fungicide on stone fruits, strawberries and grapes as

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1 Regulation (EC) No 1107/2009 of 21 October 2009 of the European Parliament and of the Council concerning the placing of plant protection products on the market and repealing Council Directives 79/117/EEC and 91/414/EEC. OJ L 309, 24.11.2009, p. 1–50.

2 Regulation (EC) No 396/2005 of the European Parliament and of the Council of 23 February 2005 on maximum residue levels of pesticides in or on food and feed of plant and animal origin and amending Council Directive 91/414/EEC. OJ L 70, 16.3.2005, p. 1–16.
proposed by the applicant. Furthermore, this conclusion also addresses the assessment required from EFSA under Article 12 of Regulation (EC) No 396/2005, provided the active substance will be approved under Regulation (EC) No 1107/2009 without restrictions affecting the residue assessment. In the event of a non-approval of the active substance or an approval with restrictions that have an impact on the residue assessment, the proposal from this conclusion might no longer be relevant and a new assessment under Article 12 of Regulation (EC) No 396/2005 will be required. A list of the relevant end points for the active substance and the formulation is provided in Appendix A.

In addition, a key supporting document to this conclusion is the peer review report (EFSA, 2017), which is a compilation of the documentation developed to evaluate and address all issues raised in the peer review, from the initial commenting phase to the conclusion. The peer review report comprises the following documents, in which all views expressed during the course of the peer review, including minority views where applicable, can be found:

- the comments received on the DAR;
- the reporting table (20 March 2017);
- the evaluation table (17 November 2017);
- the comments received on the assessment of the additional information (where relevant);
- the comments received on the draft EFSA conclusion.

Given the importance of the DAR including its revisions (France, 2017) and the peer review report, both documents are considered as background documents to this conclusion.

It is recommended that this conclusion report and its background documents would not be accepted to support any registration outside the European Union (EU) for which the applicant has not demonstrated that it has regulatory access to the information on which this conclusion report is based.

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**The active substance and the formulated product**

*Metschnikowia fructicola* NRRL Y-27328 is a fungus deposited at the Agricultural Research Service Culture Collection (NRRL), at the National Center for Agricultural Utilization Research in Peoria, Illinois, USA, under the accession number NRRL Y-27328. It is a wild-type strain originally isolated from table grapes in central Israel.

The strain is also deposited at the culture collection of CBS-KNAW Fungal Biodiversity Centre, the Netherlands, under the accession number CBS 8853, at the Belgian Co-ordinated Collections of Microorganisms BCCM/MUCL, under the accession number MUCL 49135T and at the National Collection of Yeast Cultures, the United Kingdom, under the accession number NCYC 3096T.

The representative formulated product for the evaluation was ‘SHEMER’, a water-dispersible granule (WG) containing 580–590 g/kg (nominal $2 \times 10^{13}$ colony forming units (CFU)/kg, minimum content of viable spores $1 \times 10^{13}$ CFU/kg) *M. fructicola* NRRL Y-27328.

The representative uses evaluated comprise applications by spraying in stone fruits against *Monilinia fructigena* and *Monilia laxa* and in strawberries and grapes against *Botrytis cinerea*. Full details of the GAPs can be found in the list of end points in Appendix A.

The data submitted showed low and variable efficacy levels of the uses of *Metschnikowia fructicola* NRRL Y-27328 according to the representative uses proposed at EU level following the guidance document SANCO/10054/2013-rev. 3 (European Commission, 2013).

A data gap has been identified for a detailed reporting of the search of the scientific peer-reviewed open literature on the active substance and its relevant metabolites, dealing with side effects on the environment and non-target species and published within the 10 years before the date of submission of the dossier, to be conducted and reported in accordance with EFSA guidance on the submission of scientific peer-reviewed open literature for the approval of pesticide active substances under Regulation (EC) No 1107/2009 (EFSA, 2011).

**Conclusions of the evaluation**

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

The following guidance document was followed in the production of this conclusion: SANCO/12116/2012-rev. 0 (European Commission, 2012).
The technical material of *Metschnikowia fructicola* NRRL Y-27328 is not isolated; it is used directly in the production process for the formulated product. The 5 batches were shown to be compliant with the microbial contaminant limits established in SANCO/12116/2012–rev. 0 (European Commission, 2012).

A micro/minisatellite-primed polymerase chain reaction (PCR) method is proposed for the identification of *Metschnikowia fructicola* NRRL Y-27328 at the strain level using specific markers of *Metschnikowia fructicola* NRRL Y-27328; however, a data gap was identified to confirm the specificity of markers using closely related strains.

There is no evidence of direct relationships of *Metschnikowia fructicola* NRRL Y-27328 to known plant, animal or human pathogens. The growth temperature range of *Metschnikowia fructicola* NRRL Y-27328 was between 6°C and 36°C, the optimal growth temperature range being 20–27°C. It should be mentioned that the determination of growth temperature range was not done under GLP.

*Metschnikowia fructicola* NRRL Y-27328 produces pulcherriminates during the manufacturing process. Based on the analysis for pulcherrinic acid and pulcherrimin in five batches of the representative formulation, a maximum content specification of total pulcherriminate level may need to be proposed if pulcherriminate is considered relevant. No information is available to prove the absence of secondary metabolites/toxins other than pulcherriminates (e.g. chitinases) during production.

An antibiotic resistance study was performed on *Metschnikowia fructicola* NRRL Y-27328 showing sensitivity against azoles (fluconazole, itraconazole, ketoconazole, voriconazole), polyenes (amphotericin B) and nucleic acid analogues (flucytosine) and showed intermediate sensitivity against echinocandins (caspofungin).

The assessment of the data package revealed no issues that need to be included as critical areas of concern with respect to the identity, physical and technical properties the representative formulation. It should be mentioned that the preparation is stable for at least 24 months at 4°C.

Acceptable methods are available for the determination of the microorganism in the technical material, formulation and for the determination of the content of contaminating microorganisms. Validated method is also available for the determination of the total pulcherriminate content of the formulation.

### 2. Mammalian toxicity

Potential transfer of genetic material from *Metschnikowia fructicola* NRRL Y-27328 to other organisms is considered unlikely as long it is confirmed it does not contain plasmids.

In the literature, *Metschnikowia pulcherrima* a close relative to *M. fructicola* has been involved in rare cases of opportunistic infections in immunocompromised people. It cannot be excluded that the current *Metschnikowia fructicola* NRRL Y-27328 could be involved in clinical cases. However, in most of the cases, the route of exposure is not relevant for the use of *Metschnikowia fructicola* NRRL Y-27328 as a plant protection product.

The applicant submitted a basic set of valid acute toxicity studies to evaluate the risk of the microorganism *Metschnikowia fructicola* NRRL Y-27328. In these acute toxicity studies, there was no indication for acute toxicity of *Metschnikowia fructicola* NRRL Y-27328 following oral, intratracheal and subcutaneous administration of high dose levels to rats. *Metschnikowia fructicola* NRRL Y-27328 did not show the potential to invade the body of the rats and did not proliferate therein excluding the risk of infection. Based on general assumption for microorganism, the use of the warning phrase ‘Microorganism may have the potential to provoke sensitising reactions’ applies to *Metschnikowia fructicola* NRRL Y-27328. The product is neither a skin nor eye irritant.

Based on the lack of significant toxicity, infectivity or pathogenicity in the available toxicological studies, the setting of health-based reference values for the microorganism *Metschnikowia fructicola* NRRL Y-27328 is not needed. Therefore, operator, worker, resident and bystander exposure estimates to the microorganism are not needed.

Concerning secondary metabolites/toxins, it is known that *Metschnikowia fructicola* NRRL Y-27328 produces pulcherrimin during manufacturing (see Section 1). No other secondary metabolites/toxins were investigated (data gap). There is no evidence of human health concern of pulcherrimin from the public literature. However, no specific toxicity studies are available. Pulcherrimin is of unknown toxicological concern and a quantitative risk assessment cannot be done. There is no information from fate and behaviour whether it could be formed after application. Overall, the non-dietary risk assessment to secondary metabolites/toxins including pulcherrimin cannot be finalised.
3. Residues

*Metschnikowia fructicola* NRRL Y-27328 was observed to decline rapidly on cherry tomatoes. After application on day zero, $2.6 \times 10^5$ CFU per tomato were found which declined to $2.8 \times 10^3$ CFU after seven and to $1.7 \times 10^2$ CFU after 14 days under greenhouse conditions while under field conditions already after one week the yeast was not detected any more.

A study investigated the potential presence of *Metschnikowia fructicola* NRRL Y-27328 in the aquatic environment. However, the study did not find any evidence of *Metschnikowia fructicola* in the aquatic environment, even after 105 days of observation.

On grapes, highest yeast counts were reported directly after the third application ($4.89 \times 10^3$ CFU/g leaves; $1.62 \times 10^5$ CFU/g berries) which declined after three days to $1.24 \times 10^5$ CFU/g leaves and to $8.15 \times 10^4$ CFU/g berries, respectively. A measurement 3 weeks after the second application indicated counts of $1.7 \times 10^3$ CFU/g leaves and of $4 \times 10^2$ CFU/g berries. Growth of *Metschnikowia fructicola* NRRL Y-27328 on leaves or berries was not observed.

*M. fructicola* is described to be part of the natural microbial community on different grape varieties where total yeast plate counts of $10^3$–$10^4$ CFU/mL are reported in the literature. Considering the proposed application rate of $2.6 \times 10^5$ CFU/berry and the proposed preharvest interval (PHI) of 1 day in the good agricultural practice (GAP) table for stone fruits, strawberries and grapes, it has to be concluded that at the time of harvest around $10^5$ CFU/berri are still present.

It was not necessary to perform a consumer risk assessment for remaining viable cell colony forming units of the strain, as the latter did not show harmful health effects at higher concentrations and is therefore of no concern.

With regard to potential toxins/secondary metabolites, it was shown that the pigment pulcherrimin was present in the technical product at low levels. Nevertheless, it has to be noted that no information on concentrations of pulcherrimin and any other secondary metabolites/toxins potentially present on the agricultural commodity are available. Toxicological reference values for pulcherrimin are not available which would permit to carry out a quantitative dietary exposure assessment for this secondary metabolite. Because of remaining uncertainties related to the presence of pulcherrimin and potential other metabolites/toxins, an inclusion of *Metschnikowia fructicola* strain NRRL Y-27328 in Annex IV of Regulation (EC) No 396/2005 cannot be recommended (European Commission, 2015).

4. Environmental fate and behaviour

4.1. Fate and behaviour in the environment of the microorganism

Specific studies on the fate of *Metschnikowia fructicola* NRRL Y-27328 in soil are not available. A number of scientific published papers on different aspects of other species of yeasts and including few ones on other strains of *M. fructicola* are available. These studies do not allow fulfilling the information required by the Regulation (EC) No 1107/2009 with respect to persistence and multiplication in soil of *Metschnikowia fructicola* NRRL Y-27328. The peer review confirms that insufficient data/information is available to confirm the claim on the ubiquity of *Metschnikowia fructicola* NRRL Y-27328 in the soil. Additional information on the natural abundance of *M. fructicola* in the environment and its 'temporary fluctuations', especially in soil would need to be provided. If such information was not available, further information on the persistence and multiplication of *M. fructicola* in the environment measured in experiments where it is introduced according good agricultural practices for its use as a plant protection product and the time needed to recover background levels would need to be provided. Therefore, a data gap is identified for data/information on the natural abundance of *Metschnikowia fructicola* NRRL Y-27328 in soil and its persistence and multiplication. Initial predicted environmental concentrations (PECs) soil, based on updated application rates, are available in the DAR. Furthermore, also the mobility of *M. fructicola* in the environment has not been addressed.

Specific studies on the fate of *Metschnikowia fructicola* NRRL Y-27328 in water are not available. A number of scientific published papers on different aspects of other species of yeasts and including some few ones on other strains of *M. fructicola* are available. The information available cannot be considered representative of natural water/sediment systems. One published scientific study observed the potential stability of *M. pulcherrima*, sister species of *M. fructicola*, in water of at least 9 days. Therefore, further information on the persistence and multiplication of *Metschnikowia fructicola* NRRL Y-27328 in aquatic environment would be needed to finalise the risk assessment. For the representative use in greenhouse, the risk to aquatic organisms can be characterised as low only on
the basis of the assumption that any significant exposure can be precluded for the representative uses proposed, which has not been demonstrated by the information presented in the DAR. The RMS proposed a label phrase tailored to local practice and legislation would be needed, to control the waste disposal of spent application solution and to prevent accidental spillage entering sewers or surface water drains in relation to the use in greenhouses. Exposure to surface water from disposal of spent application solution or spillage is not the subject of risk assessment according to the data requirements and available guidance.

Information provided by the applicant is not sufficient to address the influence of natural/UV light on the persistence of \textit{M. fructicola} in the environment. Persistence of \textit{Metschnikowia fructicola} NRRL Y-27328 in the environment under wave lengths and intensities comparable to environmental conditions need to be investigated.

4.2. Fate and behaviour in the environment of any relevant metabolite formed by the microorganism under relevant environmental conditions

\textit{Metschnikowia fructicola} NRRL Y-27328 is known to produce cyclic dipeptide-based metabolite pulcherrimin under the conditions of production (in contrast to other strains of the species \textit{M. fructicola} that do not produce this metabolite). Additional information on the potential production of pulcherrimin by \textit{Metschnikowia fructicola} NRRL Y-27328 after application of the formulated product according to the intended uses and on the fate and behaviour of pulcherrimin in the environment should be provided.

In addition, applicant needs to provide additional information on the production of other secondary metabolites/toxins (other than pulcherrimin) by \textit{Metschnikowia fructicola} strain NRRL Y-27328 under environmental conditions. In particular, the production of chitinases should be investigated (see Section 5).

5. Ecotoxicology

No data on the toxicity, infectivity and pathogenicity of \textit{Metschnikowia fructicola} NRRL Y-27328 to \textit{birds} are available. However, considering the growth temperature range of \textit{Metschnikowia fructicola} NRRL Y-27328 (6–36°C) and the optimal growth temperature range being 20–27°C, low risk to birds is concluded for all the representative uses.

Based on the available toxicological studies, showing any significant toxicity, infectivity or pathogenicity, low risk to \textit{mammals} is concluded for all the representative uses.

No data are available addressing the toxicity, infectivity and pathogenicity of \textit{Metschnikowia fructicola} NRRL Y-27328 to \textit{fish} (data gap). Toxicity data on \textit{aquatic invertebrates} (21-day study) and \textit{algae} with the representative formulation are available showing no adverse effects, potential for infectivity and pathogenicity of \textit{Metschnikowia fructicola} NRRL Y-27328. No data are available on \textit{aquatic plants} and no information was retrieved from the literature. However, considering that the substance has no herbicidal property, the risk to aquatic plants is considered low.

Acute toxicity data (contact and oral) on \textit{honeybees} are available with the representative formulation. No signs of toxicity were reported. A valid toxicity study on the non-target arthropod species \textit{Phytoseiulus persimilis} is available, showing no adverse effects of the representative formulation. Several literature studies were reported in the DAR demonstrating that yeasts including \textit{Metschnikowia} species are naturally occurring in plants and nectar and have been isolated from bees and insects. However, none of the studies was specific to \textit{M. fructicola}. Therefore, the information is not considered suitable to address the potential for infectivity and pathogenicity of \textit{Metschnikowia fructicola} NRRL Y-27328 to bees and non-target arthropods (data gap).

Suitable studies addressing the toxicity, infectivity and pathogenicity of \textit{Metschnikowia fructicola} NRRLY-27328 to \textit{earthworms} and effects on \textit{soil microorganisms} were not available (data gap). The available literature studies are not deemed sufficient considering that, as reported in Section 4, the available information in the DAR is not considered sufficient to confirm that \textit{Metschnikowia fructicola} NRRLY-27328 is ubiquitous in soil.

No information is available on the potential toxicity to non-target organisms of the secondary metabolites/toxins pulcherrimin and chitinases (data gap).
6. Overview of the risk assessment of compounds listed in residue definitions triggering assessment of effects data for the environmental compartments (Tables 1–4)

**Table 1:** Soil

| Compound (name and/or code) | Persistence | Ecotoxicology |
|-----------------------------|-------------|---------------|
| Metschnikowia fructicola NRRL Y-27328 | Data gap | Data gap |
| Secondary metabolites/toxins, including pulcherrimin | No data | Data gap |

**Table 2:** Groundwater

| Compound (name and/or code) | Mobility in soil | > 0.1 μg/L at 1 m depth for the representative uses<sup>(a)</sup> | Pesticidal activity | Toxicological relevance |
|-----------------------------|------------------|-------------------------------------------------|-------------------|------------------------|
| Secondary metabolites/toxins, including pulcherrimin | No data | No data | No data | Unknown toxicological concern |

<sup>(a)</sup>: At least one FOCUS scenario or a relevant lysimeter.

**Table 3:** Surface water and sediment

| Compound (name and/or code) | Ecotoxicology |
|-----------------------------|---------------|
| Metschnikowia fructicola strain NRRL Y-27328 | Data gap (fish) |
| Secondary metabolites/toxins, including pulcherrimin | Data gap |

**Table 4:** Air

| Compound (name and/or code) | Toxicology |
|-----------------------------|------------|
| Metschnikowia fructicola strain NRRL Y-27328 | Low acute inhalation toxicity (the LC₅₀ is > 6.52 mg/L (equivalent to 2.05 × 10⁶ CFU/L)) |
| Secondary metabolites/toxins, including pulcherrimin | Data gap |

LC₅₀: lethal concentration, median; CFU: colony forming unit.
7. Data gaps

This is a list of data gaps identified during the peer review process, including those areas in which a study may have been made available during the peer review process but not considered for procedural reasons (without prejudice to the provisions of Article 56 of the Regulation concerning information on potentially harmful effects).

- A detailed reporting of the search of the scientific peer-reviewed open literature on the active substance and its relevant metabolites, dealing with side effects on the environment and non-target species and published within the 10 years before the date of submission of the dossier, to be conducted and reported in accordance with EFSA guidance on the submission of scientific peer-reviewed open literature for the approval of pesticide active substances under Regulation (EC) No 1107/2009 (EFSA, 2011; relevant for all representative uses evaluated; submission date proposed by the applicant unknown, see Sections 4 and 5).
- To confirm the specificity of markers used in the identification at strain level using closely related strains (relevant for all representative uses evaluated; submission date proposed by the applicant: unknown; see Section 1).
- Information to prove the absence of secondary metabolites/toxins other than pulcherriminates (e.g. chitinases) during production (relevant for all representative uses evaluated; submission date proposed by the applicant: unknown; see Sections 1 and 2).
- Information to prove the absence or address the toxicity of potential secondary metabolites/toxins including pulcherrimin on the raw agricultural commodity (RAC) after application of the microbial pest control product (MPCP) (relevant for all representative uses evaluated; submission date proposed by the applicant: unknown; see Sections 2 and 3).
- Additional information on the natural abundance of *M. fructicola* in the environment and its "temporary fluctuations"; especially in soil should be provided. If such information is not available further information on the persistence and multiplication of *M. fructicola* in the environment where it will be introduced as result of its use as plant protection product and the time needed to recover background levels would need to be provided (relevant for all representative uses evaluated; submission date proposed by the applicant: unknown; see Section 4).
- Additional information on the potential production and toxicity to non-target organisms of pulcherrimin by *Metschnikowia fructicola* NRRL Y-27328 after application of the formulated product according to the intended uses and on the fate and behaviour of pulcherrimin in the environment should be provided (relevant for all representative uses evaluated; submission date proposed by the applicant: unknown; see Sections 4 and 5).
- Applicant to provide additional information on the potential production and toxicity of other secondary metabolites/toxins (other than pulcherrimin) by *Metschnikowia fructicola* strain NRRL Y-27328 under environmental conditions. In particular, the production of chitinases should be investigated (relevant for all representative uses evaluated; submission date proposed by the applicant: unknown; see Section 4).
- Applicant to provide data to address the influence of natural light/UV light on the persistence of *Metschnikowia fructicola* NRRLY-27328 in the environment. This should be investigated with light of a wave range and intensity comparable to environmental conditions (relevant for all representative uses evaluated; submission date proposed by the applicant: unknown; see Section 4).
- Applicant to provide more information on the persistence and multiplication of *Metschnikowia fructicola* NRRL Y-27328 reaching aquatic environments after application (relevant for all field representative uses evaluated; submission date proposed by the applicant: unknown; see Section 4).
- Applicant to provide information on mobility of *Metschnikowia fructicola* strain NRRL Y-27328 in the environment (relevant for all representative uses evaluated; no submission date proposed by the applicant; see Section 4).
- Further information to address the potential for infectivity and pathogenicity of *Metschnikowia fructicola* NRRL Y-27328 on fish, bees and non-target arthropods (relevant for all representative uses evaluated; no submission date proposed by the applicant; see Section 5).
- Further information to address the toxicity, infectivity and pathogenicity of *Metschnikowia fructicola* NRRL Y-27328 on earthworms as well as effects on soil microorganisms (relevant for all representative uses evaluated; no submission date proposed by the applicant; see Section 5).
8. **Particular conditions proposed to be taken into account to manage the risk(s) identified**

- No particular conditions are proposed for the representative uses evaluated. The RMS proposed the use of a label phrase for the greenhouse uses related to the disposal of spent application solution and to preventing accidental spillage entering sewers or surface water drains. This route of exposure is not the subject of risk assessment according to the data requirements and available guidance.

9. **Concerns**

9.1. **Issues that could not be finalised**

An issue is listed as ‘could not be finalised’ if there is not enough information available to perform an assessment, even at the lowest tier level, for the representative uses in line with the uniform principles in accordance with Article 29(6) of the Regulation and as set out in Commission Regulation (EU) No 546/2011 and if the issue is of such importance that it could, when finalised, become a concern (which would also be listed as a critical area of concern if it is of relevance to all representative uses).

An issue is also listed as ‘could not be finalised’ if the available information is considered insufficient to conclude on whether the active substance can be expected to meet the approval criteria provided for in Article 4 of the Regulation.

1) The information available was insufficient to demonstrate that *Metschnikowia fructicola* NRRL Y-27328 would respect the uniform principles criterion of not being expected to persist in soil other plant growing media or natural water systems in concentrations considerably higher than the natural background levels, taking into account repeated applications over the years and should this not be the case, satisfy the uniform principles associated unless clause (see Section 4).

2) The presence and production of secondary metabolites/toxins (including pulcherrimin) cannot be excluded. Therefore, the risk assessment could not be finalised for human health (non-dietary and consumer risk assessment, including the assessment of potential groundwater exposure) and for non-target organisms (see Sections 2, 3, 4 and 5).

9.2. **Critical areas of concern**

An issue is listed as a critical area of concern if there is enough information available to perform an assessment for the representative uses in line with the uniform principles in accordance with Article 29 (6) of the Regulation and as set out in Commission Regulation (EU) No 546/2011, and if this assessment does not permit the conclusion that, for at least one of the representative uses, it may be expected that a plant protection product containing the active substance will not have any harmful effect on human or animal health or on groundwater or any unacceptable influence on the environment.

An issue is also listed as a critical area of concern if the assessment at the higher tier level could not be finalised due to lack of information, and if the assessment performed at the lower tier level does not permit the conclusion that, for at least one of the representative uses, it may be expected that a plant protection product containing the active substance will not have any harmful effect on human or animal health or on groundwater or any unacceptable influence on the environment.

An issue is also listed as a critical area of concern if, in the light of current scientific and technical knowledge using guidance documents available at the time of application, the active substance is not expected to meet the approval criteria provided for in Article 4 of the Regulation. None identified for the representative uses assessed.

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3 Commission Regulation (EU) No 546/2011 of 10 June 2011 implementing Regulation (EC) No 1107/2009 of the European Parliament and of the Council as regards uniform principles for evaluation and authorisation of plant protection products. OJ L 155, 11.6.2011, p. 127–175.
9.3. Overview of the concerns identified for each representative use considered

(If a particular condition proposed to be taken into account to manage an identified risk, as listed in Section 8, has been evaluated as being effective, then ‘risk identified’ is not indicated in Table 5.)

Table 5: Overview of concerns

| Representative use                        | Stone fruits | Protected strawberries | Grapes |
|------------------------------------------|--------------|------------------------|--------|
| Operator risk                            | Risk identified |                        |        |
|                                          | Assessment not finalised | X² |        |
| Worker risk                              | Risk identified |                        |        |
|                                          | Assessment not finalised | X² |        |
| Resident/bystander risk                   | Risk identified |                        |        |
|                                          | Assessment not finalised | X² |        |
| Consumer risk                            | Risk identified |                        |        |
|                                          | Assessment not finalised | X² |        |
| Risk to wild non-target terrestrial vertebrates | Risk identified |                        |        |
|                                          | Assessment not finalised | X² |        |
| Risk to wild non-target terrestrial organisms other than vertebrates | Risk identified |                        |        |
|                                          | Assessment not finalised | X² |        |
| Risk to aquatic organisms                | Risk identified |                        |        |
|                                          | Assessment not finalised | X² |        |
| Groundwater exposure to active substance  | Legal parametric value breached |        |        |
|                                          | Assessment not finalised |        |        |
| Groundwater exposure to metabolites       | Legal parametric value breached |        |        |
|                                          | Parametric value of 10 \(\mu\)g/L breached |        |        |
|                                          | Assessment not finalised |        |        |

Columns are grey if no safe use can be identified. The superscript numbers in this table relate to the numbered points indicated in Section 9.1. Where there is no superscript number, see Sections 2-6 for further information.

References

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

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European Commission, 2012. Working Document on microbial contaminant limits for microbial pest control products. SANCO/12116/2012 –rev. 0, September 2012.

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France, 2017. Revised Draft Assessment Report (DAR) on Metschnikowia fructicola NRRL Y-27328 prepared by the rapporteur Member State France in the framework of Regulation (EC) No 1107/2009, September 2017. Available online: www.efsa.europa.eu
### Abbreviations

| Abbreviation | Description |
|--------------|-------------|
| a.s.         | active substance |
| BCCM/MUCL    | Belgian Co-ordinated Collections of Microorganisms |
| CFU          | colony forming units |
| DAR          | draft assessment report |
| EEC          | European Economic Community |
| FOCUS        | Forum for the Co-ordination of Pesticide Fate Models and their Use |
| GAP          | good agricultural practice |
| LC₅₀         | lethal concentration, median |
| MPCP         | microbial pest control product |
| NRRL         | Agricultural Research Service Culture Collection |
| PCR          | polymerase chain reaction |
| PEC          | predicted environmental concentration |
| PECsoil      | predicted environmental concentration in soil |
| PHI          | preharvest interval |
| RAC          | raw agricultural commodity |
| RMS          | rapporteur Member State |
| SMILES       | simplified molecular-input line-entry system |
| UV           | ultraviolet |
| WG           | water-dispersible granule |
Appendix A – List of end points for the active substance and the representative formulation

Appendix A can be found in the online version of this output ('Supporting information' section): https://doi.org/10.2903/j.efsa.2017.5084
## Appendix B – Used compound codes

| Code/trivial name       | Chemical name/SMILES notation                                                                 | Structural formula |
|-------------------------|-----------------------------------------------------------------------------------------------|-------------------|
| Pulcherriminic acid     | 3,6-bis(2-methylpropyl)-1,4-dioxo-1\(\lambda^5\),4\(\lambda^5\)-pyrazine-2,5-diol             | ![Structural formula](image) |
|                         | Oc1[n+]([O-])c(CC(C)C)c(O)[n+]([O-])c1CC(C)C                                                |                   |
| Pulcherrimin            | {\(\mu\)-[1,2-di(hydroxy-1xO)-4,5-di(hydroxy-2xO)-3,6-bis(2-methylpropyl)pyrazine-1,4-diiumato(4-)]diiron(2\+)} | ![Structural formula](image) |
|                         | CC(C)c2[n+]3O[Fe]Oc3c(CC(C)C)[n+]1O[Fe]Oc12                                                    |                   |
| Pulcherriminate         | 3,6-bis(2-methylpropyl)-1,4-dioxo-1\(\lambda^5\),4\(\lambda^5\)-pyrazine-2,5-bis(olate)       | ![Structural formula](image) |
|                         | [O-]c1[n+]([O-])c(CC(C)C)c([O-])[n+]([O-])c1CC(C)C                                         |                   |

SMILES: simplified molecular-input line-entry system.