European Food Safety Authority

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CONCLUSION ON PESTICIDE PEER REVIEW

Conclusion on the peer review of the pesticide risk assessment of the active substance cerevisane (cell walls of *Saccharomyces cerevisiae* strain LAS117)[1]

European Food Safety Authority[2]

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ABSTRACT

The conclusions of the European Food Safety Authority (EFSA) following the peer review of the initial risk assessments carried out by the competent authority of the rapporteur Member State France for the pesticide active substance cerevisane (cell walls of *Saccharomyces cerevisiae* strain LAS117), and the assessment of the proposal for inclusion of the substance in Annex IV of Regulation (EC) 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 the active substance as a systemic resistance inducer against fungi and bacteria in lettuce and other salad crops. The reliable endpoints concluded as being appropriate for use in regulatory risk assessment, derived from the available studies and literature in the dossier peer reviewed, are presented. Missing information identified as being required by the regulatory framework is listed. No concerns are identified.

KEY WORDS

cerevisane, cell walls of *Saccharomyces cerevisiae* strain LAS117, peer review, risk assessment, pesticide, systemic resistance inducer

[1] On request from the European Commission, Question No EFSA-Q-2013-00548, approved on 7 February 2014. Note: After the adoption of this Conclusion by EFSA the applicant decided to withdraw the application. In line with EFSA practices for transparency, EFSA has decided to publish, nevertheless, the adopted Conclusion for information.

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SUMMARY

Cerevisane (cell walls of *Saccharomyces cerevisiae* strain LAS117) 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, the rapporteur Member State (RMS) France received an application from Agro-Levures et Dérivés SAS on 5 March 2012 for approval. Complying with Article 9 of the Regulation, the completeness of the dossier was checked by the RMS and the date of admissibility of the application was recognised as being 14 May 2012.

The RMS provided its initial evaluation of the dossier on cerevisane (cell walls of *Saccharomyces cerevisiae* strain LAS117) in the Draft Assessment Report (DAR), which was received by the EFSA on 22 February 2013. The DAR included a proposal to include the substance in Annex IV of Regulation (EC) No 396/2005. The peer review was initiated on 5 March 2013 by dispatching the DAR for consultation of the Member States and the applicant Agro-Levures et Dérivés SAS.

Following consideration of the comments received on the DAR, it was concluded that additional information should be requested from the applicant, and that the EFSA should conduct an expert consultation in the area of mammalian toxicology.

In accordance with Article 12 of the Regulation, the EFSA should adopt a conclusion on whether cerevisane (cell walls of *Saccharomyces cerevisiae* strain LAS117) can be expected to meet the approval criteria provided for in Article 4 of the Regulation taking into consideration recital (10) of the Regulation.

The conclusions laid down in this report were reached on the basis of the evaluation of the representative uses of the active substance as a systemic resistance inducer against fungi and bacteria in lettuce and other salad crops, as proposed by the applicant. Full details of the representative uses can be found in Appendix A to this report.

A data gap was identified for a search of the scientific peer-reviewed open literature on the active substance and its relevant metabolites.

In the area of identity, physical/chemical/technical properties and methods of analysis a data gap was identified for a shelf-life study.

Human exposure to cerevisane (cell walls of *Saccharomyces cerevisiae* strain LAS117) can widely occur from exposure to *Saccharomyces cerevisiae*, and although a sensitisation potential by inhalation cannot be excluded, no human safety concerns are expected from the use of this substance as a plant protection product.

In the area of residues no food safety concern was identified for consumers from the use of this substance as a plant protection product.

Taking into account the nature of the substance, a specific environmental exposure assessment is not deemed necessary. No concern was identified with respect to potential groundwater contamination.

No areas of concern or data gaps were identified for ecotoxicology.

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BACKGROUND

Regulation (EC) No 1107/2009 of the European Parliament and of the Council[3] (hereinafter referred to as 'the Regulation') lays down, *inter alia*, the detailed rules as regards the procedure and conditions for approval of active substances. This regulates for the European Food Safety Authority (EFSA) the procedure for organising the consultation of Member States and the applicant(s) for comments on the initial evaluation in the Draft Assessment Report (DAR) provided by the rapporteur Member State (RMS), and the organisation of an expert consultation where appropriate.

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

Cerevisane (cell walls of *Saccharomyces cerevisiae* strain LAS117) is a new active substance for which in accordance with Article 7 of the Regulation, the rapporteur Member State France (hereinafter referred to as the 'RMS') received an application from Agro-Levures et Dérivés SAS on 5 March 2012 for approval of the active substance. 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 14 May 2012.

The RMS provided its initial evaluation of the dossier on cerevisane (cell walls of *Saccharomyces cerevisiae* strain LAS117) in the Draft Assessment Report (DAR) (France, 2012), which was received by the EFSA on 22 February 2013. The DAR included a proposal to include the substance in Annex IV of Regulation (EC) No 396/2005[4]. The peer review was initiated on 5 March 2013 by dispatching the DAR for consultation of the Member States and the applicant Agro-Levures et Dérivés SAS, for consultation and comments. EFSA also provided comments. 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 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 the EFSA, the RMS, and the European Commission on 20 June 2013. 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 the EFSA should conduct an expert consultation in the area of mammalian toxicology.

The outcome of the telephone conference, together with the EFSA's further consideration of the comments is reflected in the conclusions set out in column 4 of the Reporting Table. All points that were identified as unresolved at the end of the comment evaluation phase and which required further consideration, including those issues to be considered in an expert consultation, were compiled by the EFSA in the format of an Evaluation Table.

[3] 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.

[4] 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.

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 consultation where this took place, were reported in the final column of the Evaluation Table.

In accordance with Article 12 of the Regulation, the EFSA should adopt a conclusion on whether cerevisane (cell walls of *Saccharomyces cerevisiae* strain LAS117) 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 January 2014.

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 cerevisane (cell walls of *Saccharomyces cerevisiae* strain LAS117) as a systemic resistance inducer against fungi and bacteria in lettuce and other salad crops, as proposed by the applicant. 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 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, 2014) 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 June 2013),
- the Evaluation Table (4 February 2014),
- the report of the scientific consultation with Member State experts (where relevant),
- the comments received on the assessment of the additional information (where relevant),
- the comments received on the draft EFSA conclusion.

Given the importance of the DAR including its final addendum (compiled version of January 2014 containing all individually submitted addenda (France, 2014)) and the Peer Review Report, both documents are considered respectively as background documents A and B to this conclusion.

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

THE ACTIVE SUBSTANCE AND THE FORMULATED PRODUCT

The active substance is the cell walls of *Saccharomyces cerevisiae* strain LAS117; the applicant has called this material 'cerevisane', but this is not an accepted common name and it is not linked to the identity of this substance.

The representative formulated product for the evaluation was 'ROMEO', a wettable powder formulation (WP) containing 100 % technical active substance with a minimum purity of 92.4 %.

The representative uses of cerevisane (cell walls of *Saccharomyces cerevisiae* strain LAS117) evaluated as a systemic resistance inducer comprise indoor and outdoor foliar spraying against fungi and bacteria in lettuce and other salad crops. Full details of the GAP can be found in the list of end points in Appendix A.

The assessment of the efficacy has been conducted following the guidance document SANCO/10054/2013 - rev. 3 (European Commission, 2013). Data were provided to confirm the efficiency of cerevisane (cell walls of *Saccharomyces cerevisiae* strain LAS117) on downy mildew when applied on lettuce preventively, at the dose rate of 750 g/ha. However, in case of high infestation, the efficacy of this active substance is lower than that observed with the reference compounds.

Whereas a number of publications on the yeast *Saccharomyces cerevisiae* have been submitted in the dossier, no systematic search of scientific peer reviewed literature following the Guidance of EFSA (EFSA, 2011) has been provided for the active substance cerevisane (cell walls of *Saccharomyces cerevisiae* strain LAS117). Therefore, a data gap has been identified by EFSA for a search of the scientific peer-reviewed open literature on the active substance and its relevant metabolites, dealing with side-effects on health, the environment and non-target species and published within the last 10 years before the date of submission of dossier, to be conducted and reported in accordance with the Guidance of EFSA on the submission of scientific peer-reviewed open literature for the approval of pesticide active substances under Regulation (EC) No 1107/2009 (EFSA, 2011).

CONCLUSIONS OF THE EVALUATION

1. Identity, physical/chemical/technical properties and methods of analysis

The following guidance documents were followed in the production of this conclusion: SANCO/3030/99 rev.4 (European Commission, 2000), SANCO/10597/2003 – rev. 10.1 (European Commission, 2012) and SANCO/825/00 rev. 8.1 (European Commission, 2010).

The material contains no relevant impurities. The minimum purity of the substance as produced is 92.4 %. No information was given on the maintenance of microbial contamination in the formulation when stored.

The main data regarding the identity of the active substance and its physical and chemical properties are given in Appendix A.

For the formulation a data gap was identified for a 2-year shelf-life study.

Adequate analytical methods are available for the formulation and the technical material. Methods of analysis for residues are not available and are not required due to the nature of this substance. A method of analysis for body fluids and tissues is not required for this substance.

2. Mammalian toxicity

The active substance is an inert derivate of the yeast *Saccharomyces cerevisiae* strain LAS117 corresponding to the cell walls of the yeast. *Saccharomyces cerevisiae* is the most widely used yeast in industrial/commercial food and beverage production and it is consumed as a nutritional supplement.

EFSA considered *Saccharomyces cerevisiae* safe for consumers having a presumption of safety status (EFSA BIOHAZ Panel, 2013).

The applicant submitted only dermal and eye irritation, as well as skin sensitisation GLP-compliant studies with cerevisane (cell walls of *Saccharomyces cerevisiae* strain LAS117). These studies demonstrated that the substance was not irritating to the skin or eyes and it was not a skin sensitiser in the skin sensitisation test.

In the literature, positive cases of allergenic effects were described in humans exposed by inhalation to *Saccharomyces cerevisiae*. Allergenic effects might be caused by sensitisation to cereal flour and secondary to fungal enzymes used as food improvement agents. However, these allergenic effects might be also caused by sensitisation by inhalation to components that might be present in the cell wall of *Saccharomyces cerevisiae*, such as enolase. The relevance of these allergenic effects to cerevisane was discussed at the Pesticides Peer Review Experts' Teleconference 96: given the uncertainties the majority of experts (the RMS disagreed) did not exclude this hazard for cerevisane and proposed the risk phrases R42[5] "May cause sensitisation by inhalation" and H334 "May cause allergy or asthma symptoms or breathing difficulties if inhaled"[6].

Despite the limited number of toxicity studies, EFSA concludes that human exposure to the substance can widely occur from exposure to *Saccharomyces cerevisiae*, and although a sensitisation potential by inhalation cannot be excluded (which is however not expected to exceed that arising from exposure to ubiquitous inhalation allergens), no human safety concerns are expected from the use of this substance as a plant protection product. Based on the toxicological profile, no health based reference values need to be set.

3. Residues

EFSA concludes that consumer exposure to cerevisane (cell walls of *Saccharomyces cerevisiae* strain LAS117) can widely occur from exposure to *Saccharomyces cerevisiae*, a yeast that is commonly used in food production (e.g. baking, brewing), and ubiquitous in food such as fruits and vegetables. The active substance is a non-viable inert compound, and thus the generation of residues different from those commonly occurring during biological degradation processes is not expected.

In the absence of any hazardous potential for consumers, residue data on the active substance are not required, and the calculation of the potential exposure of consumers (such as the TMDI) is not necessary. Further to this, MRLs are not proposed, and the active substance may be considered as a candidate for inclusion in Annex IV of Regulation (EC) No 396/2005.

No food safety concerns for consumers are expected from the use of this substance as a plant protection product.

4. Environmental fate and behaviour

A number of scientific publications have been submitted in the dossier to show the ubiquitous presence of the yeast *Saccharomyces cerevisiae* in the different environmental compartments (soil, plant surface, surface water) around the world. However, these publications are irrelevant in relation to the quantification of the background levels of the dead *Saccharomyces cerevisiae* cell material expected to naturally occur in the environment.

[5] According to the agreed procedures, the EFSA Conclusions include, among other elements, a proposal for classification and labelling. Proposals for classification made in the context of the evaluation procedure under Regulation (EC) No 1107/2009 are not formal proposals. In this particular case the applicant and the Rapporteur Member State disagreed with the EFSA proposal. The classification of the substance and the harmonisation of the classification, if required, should be established according to the provisions of Article 4 and Article 37 of Regulation (EC) No 1272/2008, respectively.

[6] Considering that the substance is regarded as a chemical, the usual warning sentence for sensitisation potential for microorganisms would not be applicable.

The degradation of *Saccharomyces cerevisiae* by two fungi species when incubated at 30 °C with and without 2-mercaptoethanol has been reported. Without 2-mercaptoethanol losses of 25 – 30 % were observed after 6 d. However, the relevance of these experimental conditions to the environmental conditions occurring in soil and surface water, and the natural occurrence of the fungi species used in these experiments have not been assessed. Therefore, this study does not provide further insight as regards the persistence of the active substance components in the natural environment.

An estimation of soil exposure resulting from a single application of 0.75 kg a.s./ha is presented in the DAR (France, 2012) and compared with the estimated mass resulting from the natural occurrence reported for the total yeast CFU concentration in agricultural soils. As indicated by the RMS, the assumptions, on which this calculation is based, are not sufficiently supported by data. If the calculation was performed following standard assumptions for 5 cm, the background levels of the yeast cell material may be expected to be exceeded by a single application of cerevisane (cell walls of *Saccharomyces cerevisiae* strain LAS117), and may be expected to be significantly exceeded by the maximum 8 applications proposed as representative uses. However, the dead cell biological material contained in the active substance (see section 1) does not only occur as residues of this yeast but also originates from other living matter and thereby contributing to background levels. Therefore, the background level of the dead cell material of solely *Saccharomyces cerevisiae* strain LAS117 is not considered relevant in the risk assessment.

An estimation of surface water exposure was compared with the amount of yeast released to water by a yeast production company. However, the relevance of these point source releases in relation to the agricultural use is not assessed. In particular, the comparison seems to ignore possible effects of the sewage plant treatments on the industrial residual yeast material.

Nevertheless, despite the lack of specific reliable information on the fate of cerevisane (cell walls of *Saccharomyces cerevisiae* strain LAS117) in the environment, it can be concluded that:

- dead cell biological materials contained in the active substance (see section 1) can be common not only to the residues of this yeast, but also to the residues originating from other living organisms,

- as *Saccharomyces cerevisiae* has already been considered to have a presumption of safety status with respect to consumer health (EFSA BIOHAZ Panel, 2013), it may be reasonably expected that the active substance (cell walls of *Saccharomyces cerevisiae* strain LAS117) should not contain any compound or impurity that would be considered to be of concern.

Overall, it can be concluded that no further information or assessment is needed to address the environmental risk assessment from the representative uses of this substance as a plant protection product.

5. Ecotoxicology

No toxicity studies were performed with the active substance (i.e. the cell walls of *Saccharomyces cerevisiae* strain LAS117) on non-target organisms, except on *Daphnia magna* and algae, but several literature data were provided with *Saccharomyces cerevisiae.* Some data showed that *Saccharomyces cerevisiae* is used as probiotics for birds and fish, or as a food supplement for bees with no harmful effects.

Overall, it can be concluded that no harmful effects are expected to occur for non-target organisms, considering the identity and the nature of the active substance. Therefore the risk to non-target organisms can be concluded as low.

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	Ecotoxicology
cerevisane (cell walls of *Saccharomyces cerevisiae* strain LAS117)	Not known, not relevant	Low risk

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
cerevisane (cell walls of *Saccharomyces cerevisiae* strain LAS117)	Not known, not relevant	Not known, not relevant	Yes	No	Low risk

6.3. Surface water and sediment

Compound (name and/or code)	Ecotoxicology
cerevisane (cell walls of *Saccharomyces cerevisiae* strain LAS117)	Low risk

6.4. Air

Compound (name and/or code)	**Toxicology**
cerevisane (cell walls of *Saccharomyces cerevisiae* strain LAS117)	No data. A sensitisation potential by inhalation cannot be excluded.

7. Data gaps

This is a complete list studies to be generated, still ongoing or available but not peer reviewed that were 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 56 of the Regulation concerning information on potentially harmful effects).

7.1. Data gaps identified for the representative uses evaluated

- A search of the scientific peer-reviewed open literature on the active substance and its relevant metabolites, dealing with side-effects on health, the environment and non-target species and published within the last 10 years before the date of submission of dossier, to be conducted and reported in accordance with the Guidance of EFSA on the submission of scientific peer-reviewed open literature for the approval of pesticide active substances under Regulation (EC) No 1107/2009 (EFSA, 2011; relevant for all representative uses evaluated; submission date proposed by the applicant: unknown).

- Two-year shelf-life study (relevant for all representative uses evaluated; submission date proposed by the applicant: unknown; see section 1).

7.2. Data gaps identified for the maximum residue level applications

Not applicable.

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

8.1. Particular conditions proposed for the representative uses evaluated

- None.

8.2. Particular conditions proposed for the maximum residue level applications

Not applicable.

9. Concerns

9.1. Concerns for the representative uses evaluated

9.1.1. 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 in accordance with Article 29(6) of the Regulation and as set out in Commission Regulation (EU) No 546/2011[7] 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).

None identified.

9.1.2. 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 in accordance with

[7] 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.

Article 29(6) of the Regulation and as set out in Commission Regulation (EU) No 546/2011, 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.

No critical areas of concerns were identified.

9.1.3. Overview of the concerns identified for each representative use considered

(If a particular condition proposed to be taken into account to manage an identified risk, as listed in section 8, has been evaluated as being effective, then 'risk identified' is not indicated in this table.)

Representative use		**Lettuce and other salad crops** **Field uses**	**Lettuce and other salad crops** **Glasshouse uses**
Operator risk	Risk identified		
	Assessment not finalised		
Worker risk	Risk identified		
	Assessment not finalised		
Bystander risk	Risk identified		
	Assessment not finalised		
Consumer risk	Risk identified		
	Assessment not finalised		
Risk to wild non target terrestrial vertebrates	Risk identified		
	Assessment not finalised		
Risk to wild non target terrestrial organisms other than vertebrates	Risk identified		
	Assessment not finalised		
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[(a)]		
	Parametric value of 10µg/L[(b)] breached		
	Assessment not finalised		
Comments/Remarks			

The superscript numbers in this table relate to the numbered points indicated in sections 9.1 and 9.2. Where there is no superscript number see sections 2 to 6 for further information.
(a): When the consideration for classification made in the context of this evaluation under Regulation (EC) No 1107/2009 is confirmed under Regulation (EC) No 1272/2008 of the European Parliament and of the Council of 16 December.
(b): Value for non relevant metabolites prescribed in SANCO/221/2000-rev 10-final, European Commission, 2003.

9.2. Concerns for the maximum residue level applications

Not applicable.

REFERENCES

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European Commission, 2000. Technical Material and Preparations: Guidance for generating and reporting methods of analysis in support of pre- and post-registration data requirements for Annex II (part A, Section 4) and Annex III (part A, Section 5) of Directive 91/414. SANCO/3030/99 rev.4, 11 July 2000.

European Commission, 2010. Guidance Document on residue analytical methods. SANCO/825/00 rev. 8.1, 16 November 2010.

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European Commission, 2013. Guidance Document on data requirements on efficacy for the dossier to be submitted for the approval of new active substances contained in plant protection products. SANCO/10054/2013 - rev. 3, 11 July 2013.

France, 2012. Draft Assessment Report (DAR) on the active substance cerevisane (cell walls of *Saccharomyces cerevisiae* strain LAS117) prepared by the rapporteur Member State France in the framework of Regulation (EC) No 1107/2009, November 2012. Available at www.efsa.europa.eu

France, 2014. Final Addendum to the Draft Assessment Report (DAR) on cerevisane (cell walls of *Saccharomyces cerevisiae* strain LAS117), compiled by EFSA, January 2014. Available at www.efsa.europa.eu

APPENDICES

APPENDIX A – LIST OF END POINTS FOR THE ACTIVE SUBSTANCE AND THE REPRESENTATIVE FORMULATION

Identity, Physical and Chemical Properties, Details of Uses, Further Information

Active substance (ISO Common Name)	Cerevisane (cell walls of *Saccharomyces cerevisiae* strain LAS117)
Function (*e.g.* fungicide)	Systemic resistance inducer on plants
Rapporteur Member State	France
Co-rapporteur Member State	N.A.

Identity (Annex IIA, point 1)

Chemical name (IUPAC)	Not relevant
Chemical name (CA)	Not relevant
CIPAC No	Not relevant
CAS No	Not relevant
EC No (EINECS or ELINCS)	Not relevant
FAO Specification (including year of publication)	Not relevant
Minimum purity of the active substance as manufactured	Minimum certified value for cerevisane (cell walls of *Saccharomyces cerevisiae* strain LAS117) in technical active substance: 92.4 % (w/w) Specification of the major components of the active substance:

		Certified values rounded off by RMS
Carbohydrates		Min 50.1 % Max 58.4 %
Carbohydrates	**Mannans**	Min 20.2 % Max 28.7 %
	Glucans	Min 17.2 % Max 31.5 %
Crude Fat		Min 11.0 % Max 21.0 %
Crude proteins		Min 16.8 % Max 28.9 %

Identity of relevant impurities (of toxicological, ecotoxicological and/or environmental concern) in the active substance as manufactured	No relevant impurity
Molecular formula	N.A.
Molecular mass	N.A.
Structural formula	N.A.

Physical and chemical properties (Annex IIA, point 2)

Melting point (state purity)	Not relevant
Boiling point (state purity)	Not relevant
Temperature of decomposition (state purity)	Not relevant
Appearance (state purity)	Beige powder
	Not relevant
Vapour pressure (state temperature, state purity)	Not relevant
Henry's law constant	Not relevant
Solubility in water (state temperature, state purity and pH)	Not relevant
Solubility in organic solvents (state temperature, state purity)	Not relevant
Surface tension (state concentration and temperature, state purity)	Not relevant
Partition co-efficient (state temperature, pH and purity)	Not relevant
Dissociation constant (state purity)	Not relevant
UV/VIS absorption (max.) incl. ε (state purity, pH)	Not relevant
Flammability (state purity)	Not highly flammable
Explosive properties (state purity)	No explosive properties
Oxidising properties (state purity)	No oxidising properties

Summary of representative uses evaluated (Cerevisane **(**cell walls of *Saccharomyces cerevisiae* strain LAS117)**)**

Crop and/ or situation (a)	Product Name	F, G or I (b)	Pests or Group of pests controlled (c)	Formulation		Application				Application rate per treatment			PHI (days) (m)	Remarks
				Type (d-f)	Conc. of MPCA (i)	Method Kind (f-h)	Growth stage & season (j)	Number min max (k)	Interval between applications (min)	kg /hL min max	water L/ha min max	kg /ha (l)		
Lettuce/ All Europe	ROMEO	G	Downy mildew	WP	1000*	Foliar spray	At any stage & season. Preventive treatment Not in strong pressure	1 - 8	7 days	0.075 – 0.75	100-1000	0.75*	1	0.75 kg product/ha
Lettuce/ All Europe	ROMEO	F	Downy mildew	WP	1000*	Foliar spray	At any stage & season. Preventive treatment Not in strong pressure	1 - 8	7 days	0.075 – 0.75	100-1000	0.75*	1	0.75 kg product/ha
Lettuce and other salads/ All Europe	ROMEO	G	Systemic Resistance Inducer (downy mildew, botrytis, rhizoctonia)	WP	1000*	Foliar spray	At any stage & season. Preventive treatment Not in strong pressure	1 - 8	7 days	0.05-0.5	100-1000	0.5*	1	0.5 kg product/ha
Lettuce and other salads / All Europe	ROMEO	F	Systemic Resistance Inducer (downy mildew, botrytis, rhizoctonia)	WP	1000*	Foliar spray	At any stage & season. Preventive treatment Not in strong pressure	1 - 8	7 days	0.05-0.5	100-1000	0.5*	1	0.5 kg product/ha

* Concentrations and doses are expressed in technical active ingredient minimum purity 92.4 %.

(a) For crops, the EU and Codex classifications (both) should be taken into account; 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 sucking insects, soil born insects, foliar fungi, weeds (d) e.g. wettable powder (WP), emulsifiable concentrate (EC), granule (GR) (e) CropLife International Technical Monograph no 2, 6th Edition. Revised May 2008. Catalogue of pesticide (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) g/kg or g/L. Normally the rate should be given for the active substance (according to ISO) and not for the variant in order to compare the rate for same active substances used in different variants (e.g. fluoroxypyr). In certain cases, where only one variant is synthesised, it is more appropriate to give the rate for the variant (e.g. benthiavalicarb-isopropyl). (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 applications possible under practical conditions of use (l) The values should be given in g or kg whatever gives the more manageable number (e.g. 200 kg/ha instead of 200 000 g/ha or 12.5 g/ha instead of 0.0125 kg/ha (m) PHI - minimum pre-harvest interval

Methods of Analysis

Analytical methods for the active substance (Annex IIA, point 4.1)

Technical a.s. (analytical technique)	Crude fat: method adapted from Regulation (EC) No. 152/2009 Mannans and Glucans: enzymatic method using spectrophotometric detection Carbohydrates: calculated by difference according to the Arrêté JORF (08/09/77) Crude protein: method ISO 5983 – 2
Impurities in technical a.s. (analytical technique)	Confidential, see Vol. 4
Plant protection product (analytical technique)	Methods are identical to the ones used for the technical active substance.

Analytical methods for residues (Annex IIA, point 4.2)

Residue definitions for monitoring purposes

Food of plant origin		N.A.
Food of animal origin		N.A.
Soil		N.A.
Water	surface	N.A.
	drinking/ground	N.A.
Air		N.A.

Monitoring/Enforcement methods

Food/feed of plant origin (analytical technique and LOQ for methods for monitoring purposes)	Not required
Food/feed of animal origin (analytical technique and LOQ for methods for monitoring purposes)	Not required
Soil (analytical technique and LOQ)	Not required
Water (analytical technique and LOQ)	Not required
Air (analytical technique and LOQ)	Not required
Body fluids and tissues (analytical technique and LOQ)	Not required

Classification and proposed labelling with regard to physical and chemical data (Annex IIA, point 10)

	RMS/peer review proposal
Active substance	-

Impact on Human and Animal Health

Absorption, distribution, excretion and metabolism (toxicokinetics) (Annex IIA, point 5.1)

Rate and extent of oral absorption	No data, considered not necessary
Distribution	No data, considered not necessary
Potential for accumulation	No data, considered not necessary
Rate and extent of excretion	No data, considered not necessary
Metabolism in animals	No data, considered not necessary
Toxicologically relevant compounds (animals and plants)	None
Toxicologically relevant compounds (environment)	None

Acute toxicity (Annex IIA, point 5.2)

Rat LD_{50} oral	No data. No human safety concerns are known or expected.	
Rat LD_{50} dermal	No data, considered not necessary	
Rat LC_{50} inhalation	No data, considered not necessary	
Skin irritation	Non irritant	
Eye irritation	Non irritant	
Skin sensitisation	Non sensitizer (LLNA)	
Inhalation sensitisation	Positive cases of respiratory sensitisation reported in humans exposed to *Saccharomyces cerevisiae.*	Resp. Sens.1. H334

Short term toxicity (Annex IIA, point 5.3)

Target / critical effect	No data. No human safety concerns are known or expected.	
Relevant oral NOAEL	No data, considered not necessary	
Relevant dermal NOAEL	No data, considered not necessary	
Relevant inhalation NOAEL	No data, considered not necessary	

Genotoxicity (Annex IIA, point 5.4)

No data. No human safety concerns are known or expected.	

Long term toxicity and carcinogenicity (Annex IIA, point 5.5)

Target/critical effect	No data. No human safety concerns are known or expected.	
Relevant NOAEL	No data, considered not necessary	
Carcinogenicity	No data, considered not necessary	

Reproductive toxicity (Annex IIA, point 5.6)

Reproduction toxicity

Reproduction target / critical effect	No data. No human safety concerns are known or expected.	
Relevant parental NOAEL	No data, considered not necessary	
Relevant reproductive NOAEL	No data, considered not necessary	
Relevant offspring NOAEL	No data, considered not necessary	

Developmental toxicity

Developmental target / critical effect	No data, considered not necessary	
Relevant maternal NOAEL	No data, considered not necessary	
Relevant developmental NOAEL	No data, considered not necessary	

Neurotoxicity (Annex IIA, point 5.7)

Acute neurotoxicity	No data, considered not necessary	
Repeated neurotoxicity	No data, considered not necessary	
Delayed neurotoxicity	No data, considered not necessary	

Other toxicological studies (Annex IIA, point 5.8)

Mechanism studies	No data, considered not necessary
Studies performed on metabolites or impurities	No data, considered not necessary

Medical data (Annex IIA, point 5.9)

Positive cases of respiratory sensitisation reported in humans exposed to *Saccharomyces cerevisiae*.

Summary (Annex IIA, point 5.10)	Value	Study	Safety factor
ADI	Not relevant		
AOEL	Not relevant		
ARfD	Not relevant		

Dermal absorption ‡ (Annex IIIA, point 7.3)

Formulation (e.g. name 50 % EC)	Not relevant

Exposure scenarios (Annex IIIA, point 7.2)

Operator	Exposure assessment not needed
Workers	Exposure assessment not needed
Bystanders/Residents	Exposure assessment not needed

Classification and proposed labelling with regard to toxicological data (Annex IIA, point 10)

Substance classified	Cerevisane (cell walls of *Saccharomyces cerevisiae* strain LAS117).
Classification according to Council Directive 67/548/EEC / Regulation (EC) No 1272/2008:	No harmonised classification and labelling.
Peer review proposal[8]	Under Council Directive 67/548/EEC[9] R42 Under Regulation (EC) No 1272/2008[10] Resp. Sens. 1. H334.

[8] It should be noted that harmonised classification and labelling is formally proposed and decided in accordance with Regulation (EC) No 1272/2008. Proposals for classification made in the context of the evaluation procedure under Regulation (EC) No 1107/2009 are not formal proposals.

[9] Council Directive 67/548/EEC of 27 June 1967 on the approximation of laws, regulations and administrative provisions relating to the classification, packaging and labelling of dangerous substances. OJ 196, 16.08.1967, p. 001-0098.

[10] Regulation (EC) No 1272/2008 of the European Parliament and of the Council of 16 December 2008 on classification, labelling and packaging of substances and mixtures, amending and repealing Directives 67/548/EEC and 1999/45/EC, and amending Regulation (EC) No 1907/2006. OJ L 353, 31.12.2008, 1-1355.

Residues

Metabolism in plants (Annex IIA, point 6.1 and 6.7, Annex IIIA, point 8.1 and 8.6)

Plant groups covered	No data (not required)
Rotational crops	No data (not required)
Metabolism in rotational crops similar to metabolism in primary crops?	No data (not required)
Processed commodities	No data (not required)
Residue pattern in processed commodities similar to residue pattern in raw commodities?	No data (not required)
Plant residue definition for monitoring	None
Plant residue definition for risk assessment	None
Conversion factor (monitoring to risk assessment)	None

Metabolism in livestock (Annex IIA, point 6.2 and 6.7, Annex IIIA, point 8.1 and 8.6)

Animals covered	No data (not required)
Time needed to reach a plateau concentration in milk and eggs	No data (not required)
Animal residue definition for monitoring	None
Animal residue definition for risk assessment	None
Conversion factor (monitoring to risk assessment)	None
Metabolism in rat and ruminant similar (yes/no)	No data (not required)
Fat soluble residue: (yes/no)	No data (not required)

Residues in succeeding crops (Annex IIA, point 6.6, Annex IIIA, point 8.5)

No data (not required)

Stability of residues (Annex IIA, point 6 introduction, Annex IIIA, point 8 Introduction)

No data (not required)

Residues from livestock feeding studies (Annex IIA, point 6.4, Annex IIIA, point 8.3)

	Ruminant:	Poultry:	Pig:
	Conditions of requirement of feeding studies		
Expected intakes by livestock ≥ 0.1 mg/kg diet (dry weight basis) (yes/no - If yes, specify the level)	No data (not required)	No data (not required)	No data (not required)
Potential for accumulation (yes/no):	No	No	No

Metabolism studies indicate potential level of residues ≥ 0.01 mg/kg in edible tissues (yes/no)	No data (not required)	No data (not required)	No data (not required)
	Feeding studies (Specify the feeding rate in cattle and poultry studies considered as relevant) Residue levels in matrices : Mean (max) mg/kg		
Muscle	/	/	/
Liver	/	/	/
Kidney	/	/	/
Fat	/	/	/
Milk	/		
Eggs		/	

Summary of residues data according to the representative uses on raw agricultural commodities and feedingstuffs (Annex IIA, point 6.3, Annex IIIA, point 8.2)

Crop	**Northern or Mediterranean Region, field or glasshouse, and any other useful information**	**Trials results relevant to the representative uses** **(a)**	**Recommendation/comments**	**MRL estimated from trials according to the representative use**	**HR** **(c)**	**STMR** **(b)**
Lettuce and other salads	All Europe	None, not required	No further data required	No MRL is required. The active substance is a candidate for Annex IV of Regulation (EC) No 396/2005	N.A.	N.A.

(a) Numbers of trials in which particular residue levels were reported *e.g.* 3 x <0.01, 1 x 0.01, 6 x 0.02, 1 x 0.04, 1 x 0.08, 2 x 0.1, 2 x 0.15, 1 x 0.17
(b) Supervised Trials Median Residue *i.e.* the median residue level estimated on the basis of supervised trials relating to the representative use
(c) Highest residue

Consumer risk assessment (Annex IIA, point 6.9, Annex IIIA, point 8.8)

ADI	Not required, QPS
TMDI (% ADI) according to WHO European diet	Not necessary
TMDI (% ADI) according to national (to be specified) diets	Not necessary
IEDI (WHO European Diet) (% ADI)	Not necessary
NEDI (specify diet) (% ADI)	Not necessary
Factors included in IEDI and NEDI	Not applicable
ARfD	Not required, QPS
IESTI (% ARfD)	Not necessary
NESTI (% ARfD) according to national (to be specified) large portion consumption data	Not necessary
Factors included in IESTI and NESTI	Not applicable

Processing factors (Annex IIA, point 6.5, Annex IIIA, point 8.4)

Crop/ process/ processed product	Number of studies	Processing factors		Amount transferred (%) (Optional)
		Transfer factor	Yield factor	
None, not required				

Proposed MRLs (Annex IIA, point 6.7, Annex IIIA, point 8.6)

.....	No MRL is proposed. The active substance is a candidate for Annex IV of Regulation (EC) No 396/2005 for products for which no MRL are required.
.....	
.....	
.....	
.....	

When the MRL is proposed at the LOQ, this should be annotated by an asterisk after the figure.

Environmental fate and behaviour

Route of degradation (aerobic) in soil (Annex IIA, point 7.1.1.1.1)

Mineralization after 100 days	No data, not required.
Non-extractable residues after 100 days	No data, not required.
Metabolites requiring further consideration - name and/or code, % of applied (range and maximum)	No data, not required.

Route of degradation in soil - Supplemental studies (Annex IIA, point 7.1.1.1.2)

Anaerobic degradation

Mineralization after 100 days	No data, not required.
Non-extractable residues after 100 days	No data, not required.
Metabolites that may require further consideration for risk assessment - name and/or code, % of applied (range and maximum)	No data, not required.

Soil photolysis

Metabolites that may require further consideration for risk assessment - name and/or code, % of applied (range and maximum)	No data, not required.

Rate of degradation in soil (Annex IIA, point 7.1.1.2, Annex IIIA, point 9.1.1)

Laboratory studies

Parent	Aerobic conditions						
Soil type	X[11]	pH	t. °C / % MWHC	DT_{50} /DT_{90} (d)	DT_{50} (d) 20 °C pF2/10kPa	St. (r^2)	Method of calculation
No data, not required.							

Field studies

Parent	Aerobic conditions								
Soil type (indicate if bare or cropped soil was used).	Location (country or USA state).	X[11]	pH	Depth (cm)	DT_{50} (d) actual	DT_{90}(d) actual	St. (r^2)	DT_{50} (d) Norm.	Method of calculation
No data, not required.									

[11] X This column is reserved for any other property that is considered to have a particular impact on the degradation rate.

pH dependence ‡ (yes / no) (if yes type of dependence)	
Soil accumulation and plateau concentration ‡	No calculations are required.

Laboratory studies ‡

Parent	Anaerobic conditions						
Soil type	X[12]	pH	t. °C / % MWHC	DT_{50} / DT_{90} (d)	DT_{50} (d) 20 °C pF2/10kPa	St. (r^2)	Method of calculation
No data, not required.							

Soil adsorption/desorption (Annex IIA, point 7.1.2)

Parent ‡							
Soil Type	OC %	Soil pH	Kd (mL/g)	Koc (mL/g)	Kf (mL/g)	Kfoc (mL/g)	1/n
No data, not required.							
pH dependence, Yes or No							

Mobility in soil (Annex IIA, point 7.1.3, Annex IIIA, point 9.1.2)

Column leaching	No data, not required.
	No data, not required.
Aged residues leaching	No data, not required.
Lysimeter/ field leaching studies	No data, not required.

PEC (soil) (Annex IIIA, point 9.1.3)

Parent Method of calculation	No calculation required.
Application data	No calculation required.

Route and rate of degradation in water (Annex IIA, point 7.2.1)

Hydrolytic degradation of the active substance and metabolites > 10 %	No data, not required.
	No data, not required.
	No data, not required.

[12] X This column is reserved for any other property that is considered to have a particular impact on the degradation rate.

Photolytic degradation of active substance and metabolites above 10 %	No data, not required.
Quantum yield of direct phototransformation in water at Σ > 290 nm	No data, not required.
Readily biodegradable (yes/no)	No data, not required.

Degradation in water / sediment

Parent	Distribution (eg max in water *x* after *n* d. Max. sed x % after *n* d)									
Water / sediment system	pH water phase	pH sed	t. °C	DT_{50}-DT_{90} whole sys.	St. (r^2)	DT_{50}-DT_{90} water	St. (r^2)	DT_{50}- DT_{90} sed	St. (r^2)	Method of calculation
No data, not required.										
Metabolite 1	Distribution (eg max in water *x* after *n* d. Max. sed x % after *n* d)									
Water / sediment system	pH water phase	pH sed	t. °C	DT_{50}-DT_{90} whole sys.	St. (r^2)	DT_{50}-DT_{90} water	r^2	DT_{50}- DT_{90} sed	St. (r^2)	Method of calculation
No data, not required.										

Mineralization and non extractable residues					
Water / sediment system	pH water phase	pH sed	Mineralization x % after n d. (end of the study).	Non-extractable residues in sed. max x % after n d	Non-extractable residues in sed. max x % after n d (end of the study)
No data, not required.					

PEC (surface water) and PEC sediment (Annex IIIA, point 9.2.3)

Parent	No FOCUS modelling required.
Parameters used in FOCUSsw step 1 and 2	
Parameters used in FOCUSsw step 3 (if performed)	
Application rate	Following 8 cumulative applications of 0.75 kg a.s./ha: PECsw (overload) = 2 mg/L

PEC (ground water) (Annex IIIA, point 9.2.1)

Method of calculation and type of study (*e.g.* modelling, field leaching, lysimeter)	No calculation required.
Application rate	No calculation required.

$PEC_{(gw)}$ From lysimeter / field studies

Parent	1st year	2nd year	3rd year
Annual average (µg/L)	No data, not required.		

Fate and behaviour in air (Annex IIA, point 7.2.2, Annex III, point 9.3)

Direct photolysis in air	No data, not required.
Quantum yield of direct phototransformation	No data, not required.
Photochemical oxidative degradation in air	No data, not required.
Volatilisation	No data, not required.
	No data, not required.
Metabolites	No data, not required.

PEC (air)

Method of calculation	No data, not required.

$PEC_{(a)}$

Maximum concentration	No calculation required.

Residues requiring further assessment

Environmental occurring metabolite requiring further assessment by other disciplines (toxicology and ecotoxicology) or for which a groundwater exposure assessment is triggered.	Cerevisane (cell walls of *Saccharomyces cerevisiae* strain LAS117).

Monitoring data, if available (Annex IIA, point 7.4)

Soil (indicate location and type of study)	None
Surface water (indicate location and type of study)	None
Ground water (indicate location and type of study)	None
Air (indicate location and type of study)	None

Points pertinent to the classification and proposed labelling with regard to fate and behaviour data

None.

Ecotoxicology

Effects on terrestrial vertebrates (Annex IIA, point 8.1, Annex IIIA, points 10.1 and 10.3)

Species	Test substance	Time scale	End point (mg/kg bw/day)	End point (mg/kg feed)
Birds *Saccharomyces cerevisiae* cell walls are used in bird feeding with no harmful effect.				
Indicate species	a.s./preparation	Acute Short-term Long-term	No data, not required	
Mammals *Saccharomyces cerevisiae* is included in the QPS list proposed by EFSA.				
Indicate species	a.s./preparation	Acute Long-term	No data , not required	
Additional higher tier studies				
Not required				

Toxicity/exposure ratios for terrestrial vertebrates (Annex IIIA, points 10.1 and 10.3)

TER calculations are not applicable (no data). The risk to terrestrial vertebrates is considered as low.

Toxicity data for aquatic species (most sensitive species of each group) (Annex IIA, point 8.2, Annex IIIA, point 10.2)

Group	Test substance	Time-scale (Test type)	End point	Toxicity[1] (mg/L)
Laboratory tests ‡				
Fish *Saccharomyces cerevisiae* cell walls are used in fish feeding with no harmful effect.				
Indicate species	a.s./preparation	96 hr (flow-through)	Mortality, EC_{50}	No data, not required
	a.s./preparation	28 d (static)	Growth NOEC	
Aquatic invertebrate				
Daphnia magna	a.s.	48 h (static)	Mortality, EC_{50}	> 200 mg/L[2] (nom)
	a.s./preparation	21 d (static)	Reproduction, NOEC	No data, not required
Sediment dwelling organisms				
Indicate species	a.s./preparation	28 d (static)	NOEC	No data, not required

Group	Test substance	Time-scale (Test type)	End point	Toxicity[1] (mg/L)
Algae				
Pseudokirchneriella subcapitata	a.s.	72 h (static)	Yield: E_yC_{50} Growth rate: E_rC_{50}	E_yC_{50} (72-h) = 81.6 mg/L (nom) E_rC_{50} (72-h) = 194.4 mg/L (nom)
Higher plant				
Indicate species	a.s./preparation	14 d (static)	Fronds, EC_{50}	No data, not required
Microcosm or mesocosm tests				
Not required				

[1] indicate whether based on nominal ($_{nom}$) or mean measured concentrations ($_{mm}$). In the case of preparations indicate whether end points are presented as units of preparation or a.s.

[2] this endpoint was based on loss of dissolved oxygen (concentrations were below the trigger) at the highest tested concentrations.

Toxicity/exposure ratios for the most sensitive aquatic organisms (Annex IIIA, point 10.2)

FOCUS modelling: Not relevant

A very worst-case concentration is calculated assuming 100 % overload in a static water pond (30 cm-depth) giving a PECsw of 2 mg/L for 8 cumulative applications at 750 g/ha.

Test substance	Organism	Toxicity end point (mg/L)	Time scale	PEC_i	PEC_{twa}	TER	Annex VI Trigger
a.s.	Aquatic invertebrates	>200	Acute	2 mg/L	-	>100	100
a.s.	Algae	81.6	Chronic	2 mg/L	-	40.8	10

Bioconcentration				
	Active substance	Metabolite1	Metabolite2	Metabolite3
$logP_{O/W}$	Not determined, not required, unlikely to be > 3			
Bioconcentration factor (BCF)[1]	X*			
Annex VI Trigger for the bioconcentration factor				
Clearance time (days) (CT_{50})				
(CT_{90})				

Bioconcentration				
Level and nature of residues (%) in organisms after the 14 day depuration phase				

[1] only required if log $P_{O/W}$ >3.
* based on total ^{14}C or on specific compounds

Effects on honey bees (Annex IIA, point 8.3.1, Annex IIIA, point 10.4)

The parent yeast *Saccharomyces cerevisiae* is a well known yeast strain (Baker's Yeast or Brewer's Yeast), already used as food supplement for bees.

Test substance	Acute oral toxicity (LD_{50} µg/bee)	Acute contact toxicity (LD_{50} µg/bee)
a.s. / preparation	No data, not required	No data, not required
Field or semi-field tests		
Not required		

Hazard quotients for honey bees (Annex IIIA, point 10.4)

HQ calculations are not applicable (no data). The risk to honey bees is considered as low.

Effects on other arthropod species (Annex IIA, point 8.3.2, Annex IIIA, point 10.5)

Laboratory tests with standard sensitive species

Species	Test Substance	End point	Effect (LR_{50} g/ha[1])
Typhlodromus pyri		Mortality	No data, not required
Aphidius rhopalosiphi		Mortality	No data, not required

[1] for preparations indicate whether end point is expressed in units of a.s. or preparation

HQ calculations
HQ calculations are not applicable (no data). The risk to non-target arthropods is considered as low.

Further laboratory and extended laboratory studies
Not required

Field or semi-field tests
Not required

Effects on earthworms, other soil macroorganisms and soil microorganisms (Annex IIA points 8.4 and 8.5. Annex IIIA, points, 10.6 and 10.7)

Test organism	Test substance	Time scale	End point[1]
Earthworms			
	a.s. /preparation	Acute Chronic	No data, not required

Test organism	Test substance	Time scale	End point[1]
Other soil macroorganisms			
Soil mite	a.s. /preparation	Chronic	No data, not required
Collembola	a.s. /preparation	Chronic	No data, not required
Soil microorganisms			
Nitrogen mineralisation	a.s. /preparation		No data, not required
Carbon mineralisation	a.s. /preparation		No data, not required
Field studies[2]			
Not required			

[1] indicate where end point has been corrected due to log Pow >2.0 (e.g. LC_{50corr})
[2] litter bag, field arthropod studies not included at 8.3.2/10.5 above, and earthworm field studies

Toxicity/exposure ratios for soil organisms

TER calculations are not applicable (no data). The risk to soil macro- and microorganisms is considered as low.

Effects on non target plants (Annex IIA, point 8.6, Annex IIIA, point 10.8)

Preliminary screening data

No data, not required

Laboratory dose response tests

No data, not required

Additional studies (e.g. semi-field or field studies)

Not required

Effects on biological methods for sewage treatment (Annex IIA 8.7)

Test type/organism	end point
Activated sludge	No data, not required
Pseudomonas sp	No data, not required

Ecotoxicologically relevant compounds (consider parent and all relevant metabolites requiring further assessment from the fate section)

Compartment	
soil	None
water	None
sediment	None
groundwater	None

Classification and proposed labelling with regard to ecotoxicological data (Annex IIA, point 10 and Annex IIIA, point 12.3)

	Peer review
Active substance	Not classified. (EC_{50} > 100 mg/L for *Daphnia magna* and algal growth rate)

APPENDIX B – USED COMPOUND CODE(S)

Not applicable.

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
DDD	daily dietary dose
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
FID	flame ionisation detector
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
mg	milligram
mL	millilitre
mm	millimetre
mN	milli-newton
MPCA	microbial pest control agent
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
ng	nanogram
NOAEC	no observed adverse effect concentration
NOAEL	no observed adverse effect level
NOEC	no observed effect concentration

NOEL	no observed effect level
NPD	nitrogen phosphorous detector
OECD	Organisation for Economic Co-operation and Development
OM	organic matter content
Pa	pascal
PD	proportion of different food types
PEC	predicted environmental concentration
PEC_{air}	predicted environmental concentration in air
PEC_{gw}	predicted environmental concentration in 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
QPS	Qualified presumption of safety
QSAR	quantitative structure-activity relationship
r^2	coefficient of determination
REACH	Registration, Evaluation, Authorisation of CHemicals
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
TLV	threshold limit value
TMDI	theoretical maximum daily intake
TRR	total radioactive residue
TWA	time weighted average
UV	ultraviolet
W/S	water/sediment
w/v	weight per volume
w/w	weight per weight
WP	wettable powder
WHO	World Health Organization
wk	week
yr	year