CONCLUSION ON PESTICIDE PEER REVIEW

Conclusion on the peer review of the pesticide risk assessment of the active substance benalaxyl-M[1]

European Food Safety Authority[2]

European Food Safety Authority (EFSA), Parma, Italy

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 Portugal, for the pesticide active substance benalaxyl-M are reported. The context of the peer review was that required by Commission Regulation (EU) No 188/2011. The conclusions were reached on the basis of the evaluation of the representative use of benalaxyl-M as a fungicide on grapes. 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.

KEY WORDS

benalaxyl-M, peer review, risk assessment, pesticide, fungicide

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[2] Correspondence: pesticides.peerreview@efsa.europa.eu

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SUMMARY

Benalaxyl-M is a new active substance for which in accordance with Article 6(2) of Council Directive 91/414/EEC Portugal (hereinafter referred to as the 'RMS') received an application from Isagro SpA for approval. Complying with Article 6(3) of Directive 91/414/EEC, the completeness of the dossier was checked by the RMS. The European Commission recognised in principle the completeness of the dossier by Commission Decision 2003/35/EC.

The RMS provided its initial evaluation of the dossier on benalaxyl-M in the Draft Assessment Report (DAR), which was received by the EFSA on 21 November 2003. The peer review was initiated on 4 December 2003 by dispatching the DAR for consultation of the Member States and the applicant Isagro SpA. Subsequently the comments received on the DAR were evaluated by the RMS and the need for additional data was agreed in an evaluation meeting in July 2004. Remaining issues, as well as further data made available by the applicant upon request, were evaluated in a series of scientific meetings with Member State experts in June and July 2005. A final discussion of the outcome of the expert consultation took place with representatives from the Member States in April 2007, leading to the conclusion laid down in EFSA Scientific Report (2007) 112, which was finalised on 27 July 2007.

Following the submission of additional information from the applicant, the RMS provided an updated evaluation of the dossier on benalaxyl-M in the form of Addenda to the DAR, which were received by the EFSA on 16 April 2012. The European Commission requested EFSA to organise a peer review of the updated evaluation and revise its conclusion on benalaxyl-M. The peer review was initiated on 26 July 2012 by dispatching the Addenda to the DAR for consultation of the Member States and the applicant Isagro SpA.

Following consideration of the comments received on the Addenda to the DAR, it was concluded that EFSA should conduct an expert consultation in the area of environmental fate and behaviour, and should adopt a conclusion on whether benalaxyl-M can be expected to meet the conditions provided for in Article 5 of Directive 91/414/EEC, in accordance with Article 8 of Commission Regulation (EU) No 188/2011.

The conclusions laid down in this report were reached on the basis of the evaluation of the representative use of benalaxyl-M as a fungicide on grapes, 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 in the analytical methods section.

No data gap or area of concern was identified in the section of mammalian toxicology.

No data gap or area of concern was identified in the section of residues.

No data gap or area of concern was identified in the environmental fate and behaviour section. New FOCUS $PEC_{SW/sed}$ and FOCUS PEC_{GW} following current guidelines have been provided in the updated assessment.

No data gap or area of concern was identified in the section of ecotoxicology.

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BACKGROUND

In accordance with Article 80(1)(a) of Regulation (EC) No 1107/2009,[3] Council Directive 91/414/EEC[4] continues to apply with respect to the procedure and conditions for approval for active substances for which a decision recognising in principle the completeness of the dossier was adopted in accordance with Article 6(3) of that Directive before 14 June 2011.

Commission Regulation (EU) No 188/2011[5] (hereinafter referred to as 'the Regulation') lays down the detailed rules for the implementation of Council Directive 91/414/EEC as regards the procedure for the assessment of active substances which were not on the market on 26 July 1993. 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 8 of the Regulation, EFSA is required to adopt a conclusion on whether the active substance is expected to meet the conditions provided for in Article 5 of Directive 91/414/EEC within 4 months from the end of the period provided for the submission of written comments, subject to an extension of 2 months where an expert consultation is necessary, and a further extension of upto 8 months where additional information is required to be submitted by the applicant(s) in accordance with Article 8(3).

In accordance with Article 6(2) of Council Directive 91/414/EEC Portugal (hereinafter referred to as the 'RMS') received an application from Isagro SpA for approval of the active substance benalaxyl-M. Complying with Article 6(3) of Directive 91/414/EEC, the completeness of the dossier was checked by the RMS. The European Commission recognised in principle the completeness of the dossier by Commission Decision 2003/35/EC.[6]

The RMS provided its initial evaluation of the dossier on benalaxyl-M in the Draft Assessment Report (Portugal, 2003), which was received by the EFSA on 21 November 2003. The peer review was initiated on 4 December 2003 by dispatching the DAR for consultation of the Member States and the applicant Isagro SpA. Subsequently the comments received on the DAR were evaluated by the RMS and the need for additional data was agreed in an evaluation meeting in July 2004. Remaining issues, as well as further data made available by the applicant upon request, were evaluated in a series of scientific meetings with Member State experts in June and July 2005. A final discussion of the outcome of the expert consultation took place with representatives from the Member States in April 2007, leading to the conclusion laid down in EFSA Scientific Report (2007) 112 (EFSA, 2007a), which was finalised on 27 July 2007.

Following the submission of additional information from the applicant, the RMS provided an updated evaluation of the dossier on benalaxyl-M in the form of Addenda to the DAR (Portugal, 2013), which were received by the EFSA on 16 April 2012. The European Commission requested EFSA to organise a peer review of the updated evaluation and revise its conclusion on benalaxyl-M.

[3] Regulation (EC) No 1107/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market and repealing Council Directives 79/117/EEC and 91/414/EEC. OJ No L 309, 24.11.2009, p. 1-50.
[4] Council Directive 91/414/EEC of 15 July 1991 concerning the placing of plant protection products on the market. OJ L 230, 19.8.1991, p. 1-32, as last amended.
[5] Commission Regulation (EU) No 188/2011 of 25 February 2011 laying down detailed rules for the implementation of Council Directive 91/414/EEC as regards the procedure for the assessment of active substances which were not on the market 2 years after the date of notification of that Directive. OJ No L 53, 26.2.2011, p. 51-55.
[6] Commission Decision 2003/35/EC of 10 January 2003 recognising in principle the completeness of the dossiers submitted for detailed examination in view of the possible inclusion of benalaxyl-M, benthiavalicarb, 1-methylcyclopropene, prothioconazole and fluoxastrobin in Annex I to Council Directive 91/414/EEC concerning the placing of plant-protection products on the market. OJ No L 11, 16.1.2003, p. 52-53.

The peer review of the updated evaluation was initiated on 26 July 2012 by dispatching the Addenda to the DAR for consultation of the Member States and the applicant Isagro SpA. 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 8(3) of the Regulation were considered in a telephone conference between the EFSA, the RMS, and the European Commission on 21 November 2012. On the basis of the comments received, the applicant's response to the comments and the RMS's evaluation thereof it was concluded that no additional information should be requested from the applicant, and that the EFSA should organise an expert consultation in the area of environmental fate and behaviour.

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, including those issues to be considered in an expert consultation, were compiled by the EFSA in the format of an Evaluation Table.

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

A final consultation on the conclusions arising from the peer review of the risk assessment took place with Member States via a written procedure in February – March 2013.

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 use as a fungicide on grapes, 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, 2013) comprises the following documents, in which all views expressed during the course of the peer review, including minority views, can be found:

- the comments received on the Addenda to the DAR,
- the Reporting Table (21 November 2012),
- the Evaluation Table (15 March 2013),
- the report of the scientific consultation with Member State experts (where relevant),
- the comments received on the draft EFSA conclusion.

Given the importance of the Addenda to the DAR (compiled version of February 2013 containing all individually submitted addenda (Portugal, 2013)) and the Peer Review Report, both documents are considered respectively as background documents A and B to this conclusion. The background documents of the Peer Review Report (EFSA, 2007b) and the Final Addendum (Portugal, 2007) developed and prepared during the course of the initial peer review process are made publicly available as part of the background documentation to the original conclusion, finalised on 27 July 2007 (EFSA, 2007a).

THE ACTIVE SUBSTANCE AND THE FORMULATED PRODUCT

Benalaxyl-M is the ISO common name for methyl *N*-(phenylacetyl)-*N*-(2,6-xylyl)-D-alaninate (IUPAC). The unresolved isomeric mixture of this substance has the common name benalaxyl.

The representative formulated product for the evaluation was 'IR6141 M', a wettable powder (WP) containing 40 g/kg benalaxyl-M and 650 g/kg mancozeb.

The representative uses evaluated comprise applications by spraying against various fungal diseases on grapes. Full details of the GAP can be found in the list of end points in Appendix A.

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 minimum purity of benalaxyl-M as manufactured should not be less than 950 g/kg. No FAO specification exists. The specification is based on industrial scale production.

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, chemical and technical properties of benalaxyl-M or the representative formulation. It should be noted however, that the representative formulation may contain ethylene thiourea, which is a toxicologically relevant impurity of mancozeb, the second active substance of the formulation.[7] The main data regarding the identity of benalaxyl-M and its physical and chemical properties are given in Appendix A.

Adequate analytical methods are available for the determination of benalaxyl-M in the technical material and in the representative formulation as well as for the determination of the respective impurities in the technical material.

Appropriate HPLC-MS/MS methods exist for monitoring benalaxyl-M in food of plant origin with LOQs of 0.01 mg/kg for all matrices, however data gaps were identified for further validation data for the additional fragment ion and for an ILV to confirm the LOQ. It should be noted that a fully validated HPLC-MS method exists for the determination of benalaxyl-M in grapes with a LOQ of 0.02 mg/kg. An analytical method for food of animal origin is not required due to the fact that no MRLs are proposed, however HPLC-MS methods exist for monitoring benalaxyl-M in fat, kidney and liver with LOQs of 0.01 mg/kg and in meat, eggs and milk with LOQs of 0.02 mg/kg, respectively.

Benalaxyl-M in soil can be monitored by HPLC-MS with chiral column with a LOQ of 0.02 mg/kg, while metabolites BM-M3, BM-M7 and BM-M9 can be determined by HPLC-MS/MS with chiral column, with LOQs of 0.05 mg/kg for each substance. Residues of benalaxyl-M in drinking water and surface water can be monitored by HPLC-MS/MS with a LOQ of 0.05 µg/l. Benalaxyl-M can be monitored in the air by HPLC-MS/MS with chiral column with a LOQ of 0.9 µg/m^3.

A method for residues in body fluids and tissues is not required as the active substance is not classified as toxic or very toxic.

2. Mammalian toxicity

The following guidance document was followed in the production of this conclusion: SANCO/221/2000 rev. 10 - final (European Commission, 2003).

[7]Commission Implementing Regulation (EU) No 540/2011 of 25 May 2011 implementing Regulation (EC) No 1107/2009 of the European Parliament and of the Council as regards the list of approved active substances, OJ L 153, 11.6.2011, p. 1–186.

Benalaxyl-M has a similar pattern of toxicity, toxicokinetics and metabolism as benalaxyl. Benalaxyl-M is rapidly and extensively absorbed from the gastro-intestinal tract, and extensively metabolised before elimination. The acute toxicity is low by the oral, dermal and inhalation route, it is not a skin or eye irritant, and no potential for skin sensitisation was found. On repeated exposure, the target organ is the liver, inducing increased liver weight and increased cytochrome P-450 (CYP2B) and UDP-glucuronosyltransferase activities. There is no evidence of genotoxicity or carcinogenic potential associated with the exposure to benalaxyl-M. In reproductive toxicity studies, no effects on fertility, reproductive performance or development were observed. The Acceptable Daily Intake (ADI) is 0.04 mg/kg bw per day and the Acceptable Operator Exposure Level (AOEL) is 0.06 mg/kg bw per day with a safety factor of 100. No Acute Reference Dose (ARfD) is set. The estimated operator and bystander exposure is below the AOEL for the proposed use of 'IR6141 M' in grapes (considering only the benalaxyl-M component of the formulation); exposure of workers entering crops treated with benalaxyl-M is acceptable only if long sleeved shirt and long trousers are worn.

It is noted that the potential for combined toxicity with a formulation containing two active substances (i.e. mancozeb and benalaxyl-M) has not been concluded and will need to be considered at Member State level.

With regard to the groundwater metabolites (B-M1, racemate of BM-M7; B-M2, racemate of BM-M3; B-F7 (including R-isomer); R-isomer of B-F4; B-F8, racemate of BM-M2), considering the available toxicity data and taking into account the toxicological profile of benalaxyl-M, none of them is considered toxicologically relevant and the reference values of benalaxyl-M are considered applicable to them as well.

3. Residues

The assessment in the residue section below is based on the guidance documents listed in the document 1607/VI/97 rev.2 (European Commission, 1999), and the JMPR recommendations on livestock burden calculations stated in the 2004 and 2007 JMPR reports (JMPR, 2004 and 2007).

Plant metabolism was studied with racemic benalaxyl in fruit crops (grape vines, tomato). Plant metabolism was also studied in root & tuber crops (potato) but this study was not relied upon for setting the residue definition since no identification was attempted in potato tubers. In addition, plant metabolism was investigated comparatively with racemic benalaxyl and the pure isomer benalaxyl-M in the leaves of grape vines, tomato and potato. Analysis of the main plant metabolites of benalaxyl-M and benalaxyl demonstrated the metabolic pathway was qualitatively comparable for both compounds across the tested plant matrices. A major component of the terminal residue in grape and tomato fruits (greater than 50% TRR) and leaves of grape, tomato and potato (from 12 to 43% TRR) was the unchanged parent compound benalaxyl-M or benalaxyl, respectively. The identified metabolites were resulting from hydroxylation of parent compound and subsequent conjugation with one or more molecules of glucose, or additionally with malonic acid. The proportions of long chained conjugates increased with time. Some of the conjugates were present in significant proportions in fruits (up to 25% TRR) and in leaves (up to 55% TRR). However, these metabolites were considered less toxic than the parent compound. Upon enantiomer specific analysis of residues of benalaxyl and benalaxyl-M on the leaves of tomato, potato and grape vines no significant changes in the isomer ratios were observed within 14 days after application. However, there is an indication from peer-reviewed public literature that significant stereo-selective degradation of racemic benalaxyl can occur on a variety of crops (fruiting vegetables, leafy and root crops), leading to relative enrichment of the benalaxyl R-isomer (benalaxyl-M). Since benalaxyl-M was the subject of evaluation by this peer review, the finding is not considered to impact on the risk assessment for the representative use, but is noted here for completeness.

For risk assessment, in terms of the representative use in grapes (fruit crop group) the residue definition was set as benalaxyl-M. For monitoring, benalaxyl-M was proposed as the residue definition, but it was acknowledged that risk managers may opt for a more comprehensive definition

as 'benalaxyl, including other mixtures of constituent isomers including benalaxyl-M (sum of isomers)' considering broader aspects.

A sufficient number of field trials with benalaxyl-M in grapes are available to estimate consumer exposure and propose MRLs. Processing trials demonstrated that residues of benalaxyl-M were decreased in grape processed products for human consumption, however data on the nature of residues in processed commodities are not available, and were also not triggered by current requirements. All results from the residue trials and processing studies were supported by validated analytical methods and storage stability data.

As the representative use is on a perennial crop, residue uptake by following crops was not evaluated. Since grape commodities are not relevant feed items, studies addressing the metabolism and residue levels in livestock were not required.

Chronic dietary intakes (TMDI) by consumers from the consumption of table and wine grapes did not exceed 2% (France, all population) of the ADI allocated to benalaxyl-M. As for the consumer exposure to metabolites in groundwater potentially used as drinking water, an assessment was conducted based on the updated evaluation in the section on environmental fate and behaviour. Consumer exposure to the R-isomers of metabolites B-F4 and B-F7 was estimated as being individually less than 1% of the ADI of benalaxyl-M for the consumer subgroups of adults, toddlers and infants.

As no ARfD was allocated, an acute consumer exposure and risk assessment is not necessary.

4. Environmental fate and behaviour

Codes for benalaxyl-M metabolites equivalent to benalaxyl metabolites (pure stereoisomer of) used in the DAR and addenda do not match and sometimes overlap. Special attention must be paid to the fact that benalaxyl-M metabolite M2 (BM-M2 hereafter) is not the same as benalaxyl metabolite M2 (racemate of BM-M3). The updated assessment of benalaxyl-M was discussed in the Pesticides Peer Review Teleconference 83 (January 2013). BM-M2 was tentatively identified as the R-isomer of the benalaxyl lysimeter metabolite F8 (B-F8 hereafter).

A new study on the degradation of BM-M2 under dark aerobic conditions in three soils was presented in the updated assessment. BM-M2 may be considered to exhibit medium to high persistence under these conditions.

In the assessment presented in the original DAR, formation fractions of metabolites were derived from route and rate studies with Model Maker assuming first order processes. During the first peer review, further details on the multi-compartment model used to fit the kinetic parameters employed in modelling (including formation fractions) were requested. Further details on this multi-compartment kinetic analysis were presented in the updated assessment. The kinetic parameters derived from this analysis were found not to be reliable during the peer review of the updated assessment. Therefore, environmental modelling of the metabolites has been performed on the basis of maxima observed in the laboratory studies and apparent degradation rates calculated from the maxima or with degradation end points derived from studies where metabolites were applied as parent (FOCUS, 2006).

A batch adsorption/desorption study in three soils for BM-M2 has been presented in the updated assessment. According to this study this metabolite may be considered to be medium to very highly mobile in soil.

Updated $PEC_{SW/sed}$ following FOCUS SW scheme up to Step 3 have been presented for the parent and the metabolites (FOCUS, 2001).

Updated FOCUS GW modelling has been presented following the recommendations of the experts' consultation. The annual average 20 years 80^{th} percentile leachate concentrations of benalaxyl-M and

its metabolites BM-M9, BM-M7, BM-M3 and BM-M2 have been calculated with models PELMO 4.4.3, PRZM 3.5.2 and PEARL 4.4.4 for the representative use in grapes. In this new modelling benalaxyl-M metabolites BM-M3 and BM-M2 reach or exceed the limit of 0.1 µg/L in 4-6 out of 7 and 7 out of 7 scenarios respectively.

The substance properties necessary to perform FOCUS GW (FOCUS, 2009) simulations for the R-isomers of benalaxyl lysimeter metabolites B-F4 and B-F7 are not available. These metabolites exceed the trigger of 0.75 µg/L of annual average concentration in the leachate the first year after application (the trigger of 0.1 µg/L is also exceeded the second year) under the conditions of the lysimeter study. During the first peer review of benalaxyl-M it was concluded that the toxicological and ecotoxicological relevance of the R-isomers of these metabolites needed to be adequately addressed. Values observed in the lysimeter study have been used to perform the risk assessment needed to assess the relevance of these metabolites.

5. Ecotoxicology

The risk assessment was based on the following documents: European Commission (2002a, 2002b, 2002c) and SETAC (2001).

A low risk to birds, mammals, aquatic organisms, bees, earthworms, soil macroorganisms, soil microorganisms, non-target plants and sewage treatment organisms was concluded for the representative use of the active substance benalaxyl-M. In addition, a low risk to aquatic organisms from surface water metabolites (BM-M3, BM-M7 and BM-M9) and additional groundwater metabolites (R-isomer of B-F7, R-isomer of B-F4 and BM-M2 (R-isomer of B-F8)) was also concluded. A low risk to earthworms, soil macroorganisms and soil microorganisms from soil metabolites (BM-M3, BM-M7 and BM-M9) was also concluded. A risk assessment for a formulated product containing benalaxyl-M only indicated a low risk to non-target arthropods. It should be noted that the representative formulation (‘IR6141 M’) contains an additional active substance (mancozeb) and the ecotoxicological risk assessment for the formulated product was not completed.

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
Benalaxyl-M	Moderately to highly persistent ($DT_{50lab\ 20^{o}\ C}$ = 44.6 – 145.9 d)	Low risk to soil organisms.
BM-M7 Data available for B-M1 (racemate of BM-M7).	Moderately to medium persistent (DT_{50} = 50.1 – 89.8 d)	Low risk to soil organisms.
BM-M3 Data available for benalaxyl metabolite B-M2 (racemate of BM-M3)	Medium to highly persistent (DT_{50} = 68.3 – 109.1 d)	Low risk to soil organisms.
BM-M9	Low to moderately persistent (DT_{50} = 4.8 – 15.1 d)	Low risk to soil organisms.
BM-M2. Only for GW assessment. Data available for B-F8 (lysimeter metabolite) tentatively identified as racemate of BM-M2 metabolite.	Medium to highly persistent (DT_{50} = 59.4 – 137.1 d)	-

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**
Benalaxyl-M	Slightly mobile to immobile (K_{oc} = 2005 - 12346 mL/g)	FOCUS GW: No Lysimeter: No	Yes	Yes	Low risk to aquatic organisms.
BM-M7 Data available for B-M1 (racemate of BM-M7).	Medium mobile (K_{oc} = 151 - 521 mL/g)	FOCUS GW: No Lysimeter: Yes, up to 4.7 µg/L parent's equivalent.	Based on the data available for B-M1, no pesticidal activity was observed	No	Low risk to aquatic organisms.
BM-M3 Data available for benalaxyl metabolite B-M2 (racemate of BM-M3)	Highly to low mobile (K_{oc} = 80 - 756 mL/g)	FOCUS GW: Yes, 4/7 - 7/7 scenarios exceed 0.1 µg/L Lysimeter: Yes, up to 8.22 µg/L parent's equivalent.	Based on the data available for benalaxyl metabolite B-M2, no pesticidal activity was observed	No	Low risk to aquatic organisms.
BM-M9	Medium to very highly mobile (K_{oc} = 43 - 436 mL/g)	FOCUS GW: No Lysimeter: No	No data available	No data available, not required	Low risk to aquatic organisms.

R isomer of lysimeter benalaxyl metabolite B-F7	No data available	FOCUS GW: No simulation available Lysimeter study: Yes, up to 0.9 µg/L parent's equivalent.	No pesticidal activity was observed	No	Low risk to aquatic organisms.
R isomer of lysimeter benalaxyl metabolite B-F4	No data available	FOCUS GW: No simulation available Lysimeter study: Yes, up to 1.9 µg/L parent's equivalent.	No pesticidal activity was observed	No	Low risk to aquatic organisms.
BM-M2 Data available for B-F8 (lysimeter metabolite) tentatively identified as racemate of BM-M2 metabolite.	Medium to very highly mobile (K_{Foc} = 22.7 – 228.55 mL/g)	FOCUS GW: Yes, 7/7 scenarios exceed 0.1 µg/L Lysimeter (B-F8): Yes, up to 1.93 µg/L parent's equivalent.	No pesticidal activity was observed	No	Low risk to aquatic organisms.

6.3. Surface water and sediment

Compound (name and/or code)	**Ecotoxicology**
Benalaxyl-M (water and sediment)	Low risk to aquatic organisms.
BM-M7	Low risk to aquatic organisms.
BM-M3 (from soil)	Low risk to aquatic organisms.

BM-M9	Low risk to aquatic organisms.

6.4. Air

Compound (name and/or code)	**Toxicology**
Benalaxyl-M	Acute inhalation study not technically feasible. Benalaxyl: LC_{50} >4.204 mg/L air (4h, nose only, highest technically achievable concentration)

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

This is a complete list of the data gaps identified during the peer review process, including those areas where a study may have been made available during the peer review process but not considered for procedural reasons (without prejudice to the provisions of Article 7 of Directive 91/414/EEC concerning information on potentially harmful effects).

- Validation data for the additional fragment ion and an ILV to confirm the LOQ for the residue monitoring method in food of plant origin (relevant for all representative uses evaluated; submission date proposed by the applicant: unknown, see section 1).

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

- Use of a minimal level of protection (long sleeved shirt and long trousers) by workers entering crops treated with benalaxyl-M to be considered for an exposure below the AOEL (see section 2).

9. Concerns

9.1. Issues that could not be finalised

An issue is listed as an issue that could not be finalised where there is not enough information available to perform an assessment, even at the lowest tier level, for the representative uses in line with the Uniform Principles of Annex VI to Directive 91/414/EEC and where the issue is of such importance that it could, when finalised, become a concern (which would also be listed as a critical area of concern if it is of relevance to all representative uses).

- None

9.2. Critical areas of concern

An issue is listed as a critical area of concern where there is enough information available to perform an assessment for the representative uses in line with the Uniform Principles of Annex VI to Directive 91/414/EEC, and where this assessment does not permit to conclude that for at least one of the representative uses it may be expected that a plant protection product containing the active substance will not have any harmful effect on human or animal health or on groundwater or any unacceptable influence on the environment.

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

- None

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 this table.)

Representative use		**Grapes**
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	
	Parametric value of 10µg/L[(a)] 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): Value for non-relevant metabolites prescribed in SANCO/221/2000-rev 10-final, European Commission, 2003

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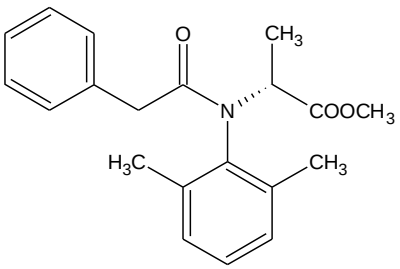
APPENDICES

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

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

Active substance (ISO Common Name) ‡	Benalaxyl-M
Function (*e.g.* fungicide)	Fungicide
Rapporteur Member State	Portugal

Identity (Annex IIA, point 1)

Chemical name (IUPAC) ‡	methyl *N*-(phenylacetyl)-*N*-(2,6-xylyl)-D-alaninate
Chemical name (CA) ‡	methyl *N*-(2,6-dimethylphenyl)-*N*-(phenylacetyl)-Dalaninate
CIPAC No ‡	766
CAS No ‡	98243-83-5
EEC No (EINECS or ELINCS) ‡	Not available
FAO Specification (including year of publication)‡	Not available
Minimum purity of the active substance as manufactured (g/kg) ‡	950 g/kg
Identity of relevant impurities (of toxicological, environmental and/or other significance) in the active substance as manufactured (g/kg)	No impurities of toxicological or environmental significance
Molecular formula ‡	$C_{20}H_{23}NO_3$
Molecular mass ‡	325.4 g/mol
Structural formula ‡	

Physical-chemical properties (Annex IIA, point 2)

Melting point (state purity) ‡	76 ± 0.5 ºC (100%)
Boiling point (state purity) ‡	No boiling point determined, compound decomposed (100%)
Temperature of decomposition	280 - 290 ºC
Appearance (state purity) ‡	White microcristalline solid (100%, 97.56%)
Vapour pressure (in Pa, state temperature) ‡	5.95×10^{-5} Pa (25 ºC) 2.36×10^{-5} Pa (20 ºC)
Henry's law constant (Pa m^3 mol^{-1}) ‡	2.33×10^{-4} Pa m^3 mol^{-1} (20 ºC)
Solubility in water (g/l or mg/l, state temperature) ‡	pH=4 33.07 ± 1.32 mg/l (20 ºC)
	pH=7 33.00 ± 1.82 mg/l (20 ºC)
	pH=9 37.05 ± 1.72 mg/l (20 ºC)
Solubility in organic solvents (in g/l or mg/l, state temperature) ‡	Readily soluble in most organic solvents (20 ºC). heptane 17074 mg/l xylene > 39 % w/w acetone > 49 % w/w ethyl acetate > 49 % w/w 1,2-dichloroethane > 50% w/w methanol > 50% w/w
Surface tension	59.82 ± 0.07 mN/m (conc. 29.6 mg/l) 60.84 ± 0.03 mN/m (conc. 28.5 mg/l) (20 ºC)
Partition co-efficient (log P_{OW}) (state pH and temperature) ‡	log P_{ow} = 3.87 (calculated value) Measured values: pH=4 log P_{ow} = 3.66 ± 0.05 (20 ºC) pH=7 log P_{ow} = 3.68 ± 0.19 (20 ºC) pH=9 log P_{ow} = 3.61 ± 0.06 (20 ºC)
Dissociation constant ‡	Dissociation in water does not occur (based on theoretical justification)
UV/VIS absorption (max.) (if absorption > 290 nm state ε at wavelength) ‡	max. at wavelengths: 252.7, 258.6, 264.6 and 274.1nm no absorption at $\lambda \geq 290$nm
Flammability (state purity) ‡	Not flammable
Explosive properties (state purity) ‡	Not explosive
Oxidising properties (state purity) ‡	Not oxidising

Summary of representative uses evaluated (benalaxyl-M)

Crop and/or situation (a)	Member State or Country	Product name	F G or I (b)	Pests or Group of pests controlled (c)	Formulation		Application				Application rate per treatment			PHI (days) (l)	Remarks: (m)
					Type (d-f)	Conc. of a.s. (i)	method kind (f-h)	growth stage & season (j)	number min max (k)	interval between applications (min)	kg as/hl min max	water l/ha min max	kg as/ha min max		
Grapes	Southern & Northern EUROPE	IR6141 M	F	*Plasmopara viticola* (Downy mildew) *Guignardia bidwellii* (Black rot) *Pseudopeziza tracheiphila* (Rot brenner) *Phomopsis viticola* (Excoriose)	WP	40 g/kg (*)	Spray	Pepper Grain Size Berries	4	10-14	0,01	1000	0,1(**)	40	(*) + mancozeb 650 g/kg (**) + 1,625 kg/ha of mancozeb

Remarks:

(a) For crops, the EU and Codex classifications (both) should be used; where relevant, the use situation should be described (*e.g.* fumigation of a structure)
(b) Outdoor or field use (F), glasshouse application (G) or indoor application (I)
(c) *e.g.* biting and suckling insects, soil born insects, foliar fungi, weeds
(d) *e.g.* wettable powder (WP), emulsifiable concentrate (EC), granule (GR)
(e) GCPF Codes - GIFAP Technical Monograph No 2, 1989
(f) All abbreviations used must be explained
(g) Method, *e.g.* high volume spraying, low volume spraying, spreading, dusting, drench
(h) Kind, *e.g.* overall, broadcast, aerial spraying, row, individual plant, between the plants - type of equipment used must be indicated
(i) g/kg or g/l
(j) Growth stage at last treatment (BBCH Monograph, Growth Stages of Plants, 1997, Blackwell, ISBN 3-8263-3152-4), including where relevant, information on season at time of application
(k) The minimum and maximum number of application possible under practical conditions of use must be provided
PHI - minimum pre-harvest interval
(l) Remarks may include: Extent of use/economic importance/restrictions
(m)

Methods of Analysis

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

Technical as (analytical technique)	HPLC-UV
Impurities in technical as (analytical technique)	GLC-FID
Plant protection product (analytical technique)	HPLC-UV

Analytical methods for residues (Annex IIA, point 4.2)

Residue definitions for monitoring purposes

Food of plant origin	benalaxyl-M
Food of animal origin	not applicable
Soil	benalaxyl-M
Water surface	benalaxyl-M
drinking/ground	benalaxyl-M
Air	benalaxyl-M

Monitoring/Enforcement methods

Food/feed of plant origin (analytical technique and LOQ for methods for monitoring purposes)	Benalaxyl-M: HPLC-MS with chiral column LOQ - 0.02 mg/kg (grape bunches and wine) (ILV) HPLC-MS/MS with chiral column LOQ - 0.01 mg/kg (all type of commodities) Open for confirmatory method and ILV
Food/feed of animal origin (analytical technique and LOQ for methods for monitoring purposes)	Not required as no MRLs are proposed HPLC-MS with chiral column LOQ - 0.01 mg/kg (fat, kidney. Liver) (confirmatory and ILV) LOQ - 0.02 mg/kg (meat, eggs, milk) (confirmatory and ILV)
Soil (analytical technique and LOQ)	Benalaxyl-M: HPLC-MS with chiral column LOQ - 0.02 mg/kg Metabolites BM-M3, BM-M7 and BM-M9: HPLC-MS/MS with chiral column LOQ - 0.05 mg/kg
Water (analytical technique and LOQ)	Benalaxy-M: HPLC-MS/MS with chiral column LOQ - 0.05 µg/l (drinking water, surface water)
Air (analytical technique and LOQ)	Benalaxyl-M: HPLC-MS/MS with chiral column LOQ - $9x10^{-4}$ mg/m^3
Body fluids and tissues (analytical technique and LOQ)	Not required

Classification and proposed labelling (Annex IIA, point 10)

with regard to physical/chemical data	Not classified

Impact on Human and Animal Health

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

Rate and extent of absorption ‡	Rapid and extensive absorption, > 80% within 8 h based on urinary (4–14%) and biliary (60–70%) excretion, benalaxyl
Distribution ‡	Widely distributed, benalaxyl and benalaxyl-M
Potential for accumulation‡	No evidence of accumulation, benalaxyl and benalaxyl-M
Rate and extent of excretion ‡	> 95% within 72 hours mainly by faeces (about 86%) with both compounds. $T_{1/2}$ = 18 h, benalaxyl-M
Metabolism in animals ‡	Extensive metabolism mainly by oxidation and hydroxylation. 12 metabolites found in both urine and faeces; parent compound found only in faeces. Same pathways with benalaxyl and benalaxyl-M
Toxicologically significant compounds (animals, plants and environment) ‡	Benalaxyl-M

Acute toxicity (Annex IIA, point 5.2)

Rat LD_{50} oral ‡	> 2000 mg/kg bw, benalaxyl-M
Rat LD_{50} dermal ‡	> 2000 mg/kg bw, benalaxyl-M
Rat LC_{50} inhalation ‡	Not technically feasible, benalaxyl-M > 4.204 mg/l air (4h, nose only, highest technically achievable concentration), benalaxyl
Skin irritation ‡	Non irritant, benalaxyl-M
Eye irritation ‡	Non irritant, benalaxyl-M
Skin sensitisation (test method used and result) ‡	Non sensitising (M&K test), benalaxyl-M

Short term toxicity (Annex IIA, point 5.3)

Target / critical effect ‡	Liver, benalaxyl and benalaxyl-M
Lowest relevant oral NOAEL / NOEL ‡	6.2 mg/kg bw per day (90d rat), benalaxyl-M
Lowest relevant dermal NOAEL / NOEL ‡	No data - not required
Lowest relevant inhalation NOAEL / NOEL ‡	No data - not required

Genotoxicity (Annex IIA, point 5.4) ‡	No genotoxic potential, benalaxyl and benalaxyl-M

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

Target/critical effect ‡	Heart weight and clinical chemistry, benalaxyl
Lowest relevant NOAEL / NOEL ‡	4.42 mg/kg bw per day (2-year rat), benalaxyl
Carcinogenicity ‡	No carcinogenic potential, benalaxyl

Reproductive toxicity (Annex IIA, point 5.6)

Reproduction target / critical effect ‡	No reproductive effects. Decreased pup body weight gain and increased liver weight at parental toxic dose levels, benalaxyl (rat).
Relevant reproductive NOAEL ‡	Parental and offspring: 5.33 mg/kg bw per day (rat), benalaxyl Reproductive toxicity: 275 mg/kg bw per day, benalaxyl (rat, highest dose tested)
Developmental target / critical effect ‡	No developmental effects, benalaxyl-M (rat) Delayed ossification (rat) and reduced bodyweight, benalaxyl (rabbit).
Relevant developmental NOAEL ‡	Maternal and developmental: 50 mg/kg bw per day, benalaxyl (rabbit) Maternal: 50 mg/kg bw per day, benalaxyl-M (rat)

	Developmental: 250 mg/kg bw per day, benalaxyl-M (rat)

Neurotoxicity / Delayed neurotoxicity (Annex IIA, point 5.7) ‡

	No data, no concern from other studies, not required

Other toxicological studies (Annex IIA, point 5.8) ‡

Metabolite B-M1 (racemate of BM-M7)	oral LD_{50} > 2000 mg/kg bw (rat) Ames test: negative Cell mutation assay in mouse lymphoma cells: negative Chromosome aberration test in Chinese Hamster Ovarian(CHO) cells: positive (-S9) Chromosome aberration test in human lymphocytes: positive (-S9) Micronucleus assay *in vivo*: negative 90-d oral study in rats: NOAEL = 922.8 mg/kg bw per day
Metabolite B-M2 (racemate of BM-M3)	oral LD_{50} > 2000 mg/kg bw (rat) Ames test: negative Cell mutation assay in mouse lymphoma cells: negative Chromosome aberration test in CHO cells: negative 90-d oral study in rats: NOAEL = 819.2 mg/kg bw per day
Metabolite B-F4 (R isomer)	Reverse mutation assay using *S. typhimurium* and *E. coli*: negative Chromosome aberration test in human lymphocytes with and without metabolic activation: negative Cell mutation assay in mouse lymphoma cells: negative
Metabolites B-F7 + B-F8 (racemate of BM-M2)	Reverse mutation assay using *S. typhimurium* and *E. coli*: negative Chromosome aberration test in human lymphocytes with and without metabolic activation: negative Cell mutation assay in mouse lymphoma cells: negative Mammalian micronucleus assay *in vivo*: negative

Medical data (Annex IIA, point 5.9) ‡

	No clinical cases of poisoning were notified since the beginning of the production of benalaxyl (early 80's)

Summary (Annex IIA, point 5.10)	Value	Study	Safety factor
ADI ‡	0.04 mg/kg bw per day	rat, 2y study, benalaxyl	100
AOEL ‡	0.06 mg/kg bw per day	rat, 90d study, benalaxyl-M	100
ARfD (acute reference dose) ‡	not allocated, not necessary		

Dermal absorption (Annex IIIA, point 7.3) ‡

Formulation: IR-6141 M	In vivo, rat: 2.5 % (undiluted product); 29 % (diluted), 6h exposure, benalaxyl-M

Acceptable exposure scenarios (including method of calculation)

For benalaxyl-M component of IR6141M (4% benalaxyl-M and 65% of mancozeb). Possible interaction between benalaxyl-M and mancozeb not considered.

Operator	Estimated exposures (in % of AOEL): UK POEM: no PPE / with PPE Tractor-mounted 66.6 / 60 Hand-held 33.3 / 23.3 German model: no PPE / with PPE Tractor-mounted 68.3 / 61 Hand-held 33.6 / 23.4
Workers	Estimated exposure is 49% of AOEL when long sleeved shirt and long trousers are used.
Bystanders	Estimated exposure is 0.36% of AOEL.

Classification and proposed labelling (Annex IIA, point 10)

with regard to toxicological data	none

Residues

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

Plant groups covered	Fruits (grapes, tomato)
Rotational crops	Not relevant
Plant residue definition for monitoring	Benalaxyl-M; optional Benalaxyl including other mixtures of constituent isomers including benalaxyl-M (sum of isomers)
Plant residue definition for risk assessment	Benalaxyl-M
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	Lactating goats and laying hens
Animal residue definition for monitoring	Not required for representative use
Animal residue definition for risk assessment	Not required for representative use
Conversion factor (monitoring to risk assessment)	Not applicable
Metabolism in rat and ruminant similar (yes/no)	Not applicable
Fat soluble residue: (yes/no)	Yes, according to log P_{ow}

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

Not required for representative use

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

The stability of racemic benalaxyl was tested on several vegetal substrates (grapes, wine, potatoes and tomatoes) stored in the dark, at a temperature below -20ºC over 3 years of storage. During this period no appreciable degradation occurred.The racemic benalaxyl demonstrated to remain stable for up to 3 years. It was assessed that the R-isomer (Benalaxyl-M) does not degrade in the same storage conditions: in fact the percentages at the last sampling time show that even if the R-isomer only is assumed to be responsible for the observed variations (i.e. apparent degradation), anyhow these are not statistically significant.

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

Intakes by livestock ≥ 0.1 mg/kg diet/day:	Ruminant: no	Poultry: no	Pig: no
Muscle			
Liver			
Kidney			
Fat			
Milk			
Eggs			

Summary of critical residues data (Annex IIA, point 6.3, Annex IIIA, point 8.2)

Crop	Northern or Mediterranean Region	Trials results relevant to the critical GAP (a)	Recommendation/comments	MRL	STMR (b)
Grapes	N/S	2x <0.020, 2x0.027, 0.028, 0.030, 0.033, 0.034, 0.044, 0.046, 0.048, 0.055, 0.070, 0.071, 0.090, 0.096		0.2	0.039

(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 critical GAP

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

ADI	0.04 mg/kg bw per day
TMDI (% ADI) EFSA PRIMo	2 % FR all population; 1 % WHO Cluster diet B
NEDI (% ADI)	Not required
Factors included in NEDI	Not applicable
ARfD	Not allocated
Acute exposure (% ARfD)	Not required

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

Crop/processed crop	Number of studies	Transfer factor	% Transference *
Grapes/must	1	0.4	Not calculated
Grapes/juice	4	0.2-0.4	Not calculated
Grapes/young wine	3	0.2-0.4	Not calculated
Grapes/bottled wine	4	0.2-0.4	Not calculated

* Calculated on the basis of distribution in the different portions, parts or products as determined through balance studies

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

grapes	0.2 mg/kg

Fate and Behaviour in the Environment

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

Mineralisation after 100 days ‡	Benalaxyl-M (^{14}C-U-aniline ring): evolved CO_2: 3,62% at 100 days (n=4) BM-M7 (^{14}C-U-aniline ring): 14.96-24.47% at 100 DAT (n=3) BM-M3 (^{14}C-U-aniline ring): 18.54-26.38% at 100 DAT (n=3) BM-M9 (^{14}C-U-aniline ring): 2.06-5.94% at 15-43 DAT (n=3)
Non-extractable residues after 100 days ‡	Benalaxyl-M (^{14}C-U-aniline ring): 21.51% at 100 days; 5.75-25.59% at 130-150 DAT (n=4) BM-M7 (^{14}C-U-aniline ring): 12.91-16.62% at 100 DAT (n=3) BM-M3: (^{14}C-U-aniline ring): 10.36-15.70% at 100 DAT (n=3) BM-M9 (^{14}C-U-aniline ring): 9.47-14.04% at 15-43 DAT (n=3)
Relevant metabolites - name and/or code, % of applied (range and maximum) ‡	BM-M7: 10.46-24.12% at 45-130 DAT (n=4) BM-M3: 7.57-28.46% at 70-150 DAT (n=4) BM-M9: 15.20-33.32% at 45-150 DAT (n=4) BM-M12: 0.51 - 7.2 % AR at 150 d (n=4)

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

Anaerobic degradation ‡	Available study for benalaxyl does not comply with current standards; however, gives indications of slower degradation under anaerobic conditions. No further data required for representative uses supported for EU risk assessment.
Soil photolysis ‡	Data for Benalaxyl-M: Soil photolysis followed the same pattern as observed under aerobic soil degradation (in the dark) although slower; the main degradation product was BM-M9 (max. 7.97% at 29 DAT).

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

Laboratory studies ‡

Benalaxyl-M	Dark aerobic conditions						
Soil type	%oc	pH[a)]	t. °C / % MWHC	DT_{50} /DT_{90} (d)	DT_{50} (d) 20 °C pF2/10kPa[b)]	St. r^2	Method of calculation
loam	2.05	7.9	20ºC/40%	44.6/148.1	48.97	0.98	1st order
2.1	0.56	6.0	20ºC/40%	145.9 / 484,39	68.57	0.80	1st order
2.2	2.19	5.8	20ºC/40%	70 / 232	135.8	0.79	1st order
2.3	1.18	6.6	20ºC/40%	94.4 /-313.4	206.74	0.96	1st order
Geometric mean					**98.53**		

a) Measured in [medium to be stated, usually calcium chloride solution or water]

b) Normalised using a Q10 of 2.58 and Walker equation coefficient of 0.7

BM-M9	Dark aerobic conditions							
Soil type	%oc	pH[a)]	t. °C / % MWHC	DT_{50}/ DT_{90} (d)	f. f.	DT_{50} (d) 20 °C pF2/10kPa[b)]	St. (χ^2)	Method of calculation
SP-2.1	0.81	5.7	20ºC/40-60%	7.2		7.2		SFO
SP-2.2	2.16	5.7	20ºC/40-60%	4.8		4.8		SFO
SP-2.3	0.98	6.5	20ºC/40-60%	15.1		15.1		SFO
Geometric mean						8.05		

a) Measured in [medium to be stated, usually calcium chloride solution or water]

b) Normalised using a Q10 of 2.58 and Walker equation coefficient of 0.7

BM-M9	Dark aerobic conditions Derived from decline after maxima in parent's study							
Soil type	%oc	pH[a)]	t. °C / % MWHC	DT_{50}/ DT_{90} (d)	f. f. k_f / k_{dp}	DT_{50} (d) 20 °C pF2/10kPa[b)]	St. (χ^2)	Method of calculation
Z-1				NA		**31.57***	3.9	SFO
SP-2.1	0.81	5.7	20ºC/40-60%	NC		NC		
SP-2.2	2.16	5.7	20ºC/40-60%	NC		33.5	7.3	SFO
SP-2.3	0.98	6.5	20ºC/40-60%	NC		NC		
Geometric mean						Not applicable		

* with correction factor => loam = 0.94

B-M1 (as surrogate of BM-M7)	Dark aerobic conditions							
Soil type	%oc	pH[a)]	t. °C / % MWHC	DT_{50}/ DT_{90} (d)	f. f.	DT_{50} (d) 20 °C pF2/10kPa[b)]	St. (r^2)	Method of calculation
SP-2.1	0.59	6.0	20±2ºC/40%	50.1		50.1	0.99	SFO
SP-2.2	2.27	6.1	20±2ºC/40%	84.0		84.0	0.99	SFO
SP-2.3	1.24	6.6	20±2ºC/40%	89.8		89.8	0.98	SFO
Geometric mean						67.67		

a) Measured in [medium to be stated, usually calcium chloride solution or water]

b) Normalised using a Q10 of 2.58 and Walker equation coefficient of 0.7

BM-M7	Dark aerobic conditions. Derived from decline after maxima in parent's study							
Soil type	%oc	pH[a)]	t. °C / % MWHC	DT_{50}/ DT_{90} (d)	f. f.	DT_{50} (d) 20 °C pF2/10kPa[b)]	St. (χ^2)	Method of calculation
Z-1				NA		77	1.7	SFO
SP-2.1	0.59	6.0	20±2ºC/40%	NC		NC		
SP-2.2	2.27	6.1	20±2ºC/40%	NC		**157***	4.5	SFO
SP-2.3	1.24	6.6	20±2ºC/40%	NC		54	6.7	SFO
Geometric mean						86.75		

* with correction factor => loamy sand = 1

B-M2 (as surrogate of BM-M3)	Dark aerobic conditions							
Soil type	%oc	pH[a)]	t. °C / % MWHC	DT_{50}/ DT_{90} (d)	f. f.	DT_{50} (d) 20 °C pF2/10kPa[b)]	St. (r^2)	Method of calculation
SP-2.1	0.59	6.0	20±2ºC/40%	68.3		68.3	0.92	SFO
SP-2.2	2.27	6.1	20±2ºC/40%	100.0		100.0	0.9	SFO

B-M2 (as surrogate of BM-M3)	Dark aerobic conditions							
Soil type	%oc	pH[a)]	t. °C / % MWHC	DT_{50}/ DT_{90} (d)	f. f.	DT_{50} (d) 20 °C pF2/10kPa[b)]	St. (r^2)	Method of calculation
SP-2.3	1.24	6.6	20±2ºC/40%	109.1		109.1	0.9	SFO
Geometric mean						**84.85**		
Arithmetic mean				90.66				

a) Measured in [medium to be stated, usually calcium chloride solution or water]

b) Normalised using a Q10 of 2.58 and Walker equation coefficient of 0.7

BM-M3	Dark aerobic conditions. Derived from decline after maxima in parent's study							
Soil type	%oc	pH[a)]	t. °C / % MWHC	DT_{50}/ DT_{90} (d)	f. f. k_f / k_{dp}	DT_{50} (d) 20 °C pF2/10kPa[b)]	St. (χ^2)	Method of calculation
Z-1				NA		NC		
SP-2.1	0.59	6.0	20±2ºC/40%	NC		117	7.2	SFO
SP-2.2	2.27	6.1	20±2ºC/40%	NC		NC		
SP-2.3	1.24	6.6	20±2ºC/40%	NC		NC		
Geometric mean								

B-F8 (as surrogate of BM-M2)	Dark aerobic conditions							
Soil type	%oc	pH[a)]	t. °C / % MWHC	DT_{50}/ DT_{90} (d)	f. f.	DT_{50} (d) 20 °C pF2/10kPa[b)]	St. (χ^2)	Method of calculation
SP-2.1	0.74	5.1	20±2ºC/60%	137.1/455.3		137	2.8	SFO
SP-2.2	2.09	5.5	20±2ºC/60%	122.2/406.0		122.2	2.3	SFO
SP-2.3	0.97	6.6	20±2ºC/60%	59.4/197.2		59.4	2.5	SFO
Geometric mean						**99.84**		

a) Measured in [medium to be stated, usually calcium chloride solution or water]

b) Normalised using a Q10 of 2.58 and Walker equation coefficient of 0.7

BM-M2	Dark aerobic conditions Derived from decline after maxima in parent's study							
Soil type	%oc	pH[a)]	t. °C / % MWHC	DT_{50}/ DT_{90} (d)	f. f. ~~k_f / k_{dp}~~	DT_{50} (d) 20 °C pF2/10kPa[b)]	St. (χ^2)	Method of calculation
Z-1				NA		NC		
SP-2.1	0.74	5.1	20±2ºC/60%	NC		17.1	8.6	SFO
SP-2.2	2.09	5.5	20±2ºC/60%	NC		NC		
SP-2.3	0.97	6.6	20±2ºC/60%	NC		NC		
Geometric mean						Not applicable		

Field studies ‡

Benalaxyl (as a surrogate of benalaxyl-M)	Aerobic conditions								
Soil type (indicate if bare or cropped soil was used).	Location (country or USA state).	X[1] MWC (%)	pH[a)]	Depth (cm)	DT_{50} (d) actual	DT_{90}(d) actual	St. (χ^2) r^2	DT_{50} (d) Norm[b)].	Method of calculation
Loam (bare;3.3kg as/ha)	Linate (Italy)	35.5% FC	6.75	7.5	49	NC	0.99		SFO

Field studies ‡

Benalaxyl (as a surrogate of benalaxyl-M)	Aerobic conditions								
Soil type (indicate if bare or cropped soil was used).	Location (country or USA state).	X[1] MWC (%)	pH[a)]	Depth (cm)	DT_{50} (d) actual	DT_{90}(d) actual	St. (χ^2) r^2	DT_{50} (d) Norm[b)].	Method of calculation
Loam (bare;241g as/ha)	Bad Oldesloe (Germany)	52.5	6.8	-	20	67			SFO
Clay loam (bare;241g as/ha)	Moorfleet (Germany)	61.95	6.7	-	25	84			SFO
Sandy loam (bare;241g as/ha)	Klein Offenseth (Germany)	51.2	4.4		98	326			SFO
Silt loam (bare;241g as/ha)	Verliehausen (Germany)	51.1	5.3		71	235			SFO
Geometric mean					44.3				
The active substance (benalaxyl) remained confined in the top 0-10 cm soil layer. The compounds B-M2 were found down to 20 cm depth.									

a) Measured in [medium to be stated, usually calcium chloride solution or water]

b) Normalised using a Q10 of 2.58 and Walker equation coefficient of 0.7

pH dependence (yes / no) (if yes type of dependence)	‡	No
Soil accumulation and plateau concentration ‡		Benalaxyl-M and BM-M9 are not expected to accumulate in soil based on the respective degradation rates. Plateau maximum concentrations of Benalaxyl-M has been estimated by EFSA just after last application of benalaxyl-M in each year is 0.26 mg a.s. /kg soil BM-M3 are not expected to accumulate in soil based on the calculation of the accumulation potential for these metabolites. Plateau maximum concentrations of BM-M7 and BM-M3 estimated just after last application of benalaxyl-M in each year are 0.0552 and 0.0632 mg/Kg soil

Soil adsorption/desorption (Annex IIA, point 7.1.2)

Benalaxyl-M‡							
Soil Type	OC %	Soil pH	K_d (mL/g)	K_{doc} (mL/g)	K_F (mL/g)	K_{Foc} (mL/g)	1/n
B-1 sandy loam	1.32	6.6	70.88	-	74.91	5675	1.04
PC-3 silt loam	1.71	7.47	100.15	-	72.26	4226	0.92
SP-2.1 sand	0.59	6.0	86.49	-	72.84	12346	0.98
VM-1	2.27	8.04	53.03	-	45.51	2005	0.96
Arithmetic mean						6063	0.98
pH dependence, Yes or No			No				

B-M1 (as surrogate of BM-M7)							
Soil Type	OC %	Soil pH	K_d (mL/g)	K_{fads} (mL/g)	K_{foc} (mL/g)	K_{oc} (mL/g)	1/n
AR-1 loamy sand (USDA class)	14.42	3.38	21.741	18.148	126	151	0.915
Roncadello silty clay (USDA class)	1.35	6.61	7.039	13.104	971	455	0.763

G-2 silt loam (USDA class)	2.13	5.58	9.691	8.414	395	521	0.892
Arithmetic mean					**497**	375	0.86
pH dependence (yes or no)							

B-M2 (as a surrogate of BM-M3)							
Soil Type	OC %	Soil pH	K_d (mL/g)	K_{fads} (mL/g)	K_{foc} (mL/g)	K_{oc} (mL/g)	1/n
AR-1 loamy sand (USDA class)	14.42	3.38	11.563	12.285	85.19	80	0.983
Roncadello silty clay (USDA class)	1.35	6.61	1.712	1.224	90.67	127	1.049
G-2 silt loam (USDA class)	2.13	5.58	16.104	9.391	440.83	756	0.821
Arithmetic mean					**206**	321	0.95
pH dependence (yes or no)							

BM-M9							
Soil Type	OC %	Soil pH	K_d (mL/g)	K_{fads} (mL/g)	K_{fdes} (mL/g)	K_{oc} (mL/g)	1/n
B-1 sandy loam (USDA class)	1.33	6.29	4.071			285	0.957
SP-2.1 sand (USDA class)	0.50	5.7	2.280			436	0.961
SP-2.2 loamy sand (USDA class)	2.12	5.7	2.562			110	0.957
VM-1 clay loam (USDA class)	6.27	7.91	2.618			43	1.067
Arithmetic mean						218.5	0.99
pH dependence (yes or no)							

B-F8 (as a surrogate of BM-M2)							
Soil Type	OC %	Soil pH	K_d (mL/g)	K_{fads} (mL/g)	K_{foc} (mL/g)	K_{oc} (mL/g)	1/n
PV-1 loamy sand	1.827	6.1	0.777	0.438	23.97	42.502	0.977
Stir-2 clay	0.534	7.7	0.245	0.121	22.70	45.787	1.013
G-2 loam	2.158	5.4	9.519	4.932	228.55	581.846	0.994
Arithmetic mean					91.74		0.99
pH dependence (yes or no)			No				

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

Column leaching ‡	Three formulations of benalaxyl were tested (GALBEN OE 20, GALBEN 25 WP and GALBEN 5 GR) on standard soils (BBA 2.1, BBA 2.2 and BBA 2.3). In all the studies less than 2% of the applied amount (corresponding to levels below the LOD - 25.6 μg/l) were found in the soil leachates. Metabolites were not analysed in this study.
Aged residues leaching ‡	30 days aged benalaxyl was applied to silty loam soil. 86% AR was found in the soil columns with more than 70% AR in the upper 0-15 cm soil; 14% AR was found in leachate and was characterised as B-M1(7.86%AR), B-M2 (5.56% AR) and benalaxyl acid (racemate of BM-M9)with 0.29% AR.
Lysimeter/ field leaching studies ‡	No lysimeter study available for benalaxyl-M. A lysimeter study is available for benalaxyl. Two lysimeters (I and II) with undisturbed sandy (1.77% c.o. at

0-30 cm; 0.3% c.o. at 30-60 cm) soil monoliths (depth 1.2 m, surface area 1.0 m2).

Application: 4x 0.240 kg s.a./ha (14C-benalaxyl formulated as GALBEN M 8-65) on May 30 to July, 15, 2002, on tomatoes at stage BBCH 21 to 22. Product was only applied first year.

Leachate samples were taken on a weekly basis. Reference compounds used were B-M1 (98.5% purity), B-M2 (97.4% purity) and benalaxyl acid (> 98% purity, racemate of BM-M9). All other radioactive fractions detected were identified by LC-MS.

Analysis of the leachates

Leachate from year 1: Lys I 10.98%AR (17.71 µg a.s. equiv./L) and Lys II 9.39% AR (14.04 µg a.s equiv/L)

Leachate from year 2: Lys I 1.19%AR (3.36 µg a.s. equiv./L) and Lys II 1.87% AR (5.14 µg a.s equiv/L)

No benalaxyl or benalaxyl-acid were detected in the leachates.

Metabolite B-M1 (racemate of BM-M7): max.: 9.30 µg a.s.equiv./L (160DA1T) (1.6%AR) in both Lysimeters.

Year 1 annual average: 4.7 µg a.s equiv./L also in both Lysimeters

Year 2 annual average: 0.09 µg a.s. equiv./L (Lys I) and 0.18 µg a.s. equiv./L (Lys II)

Metabolite M2 (racemate of BM-M3):

Max.: 20.25 µg a.s. equiv./L (220DA1T) (1.0%AR).

Year 1 annual average: 8.22 µg a.s. equiv./L (Lys I)

and 5.11 µg a.s. equiv./L (Lys II)

Year 2 annual average: 2.72 µg a.s. equiv./L (Lys I) and 3.6 µg a.s. equiv./L (Lys II).

Benalaxyl lysimeter metabolite B-F4

Year 1 annual average: 1.90 µg a.s. equiv./L (Lys I) and 1.71 µg a.s. equiv./L (Lys II).

Year 2 annual average: 0.15 µg a.s. equiv./L (Lys I) and 0.43 µg a.s. equiv./L(Lys II).

Benalaxyl lysimeter metabolite B-F7

Year 1 annual average: 0.9 µg a.s.equiv./L (Lys I and II)

Year 2 annual average: 0.3 µg a.s.equiv./L (Lys I and II)

Benalaxyl lysimeter metabolite B-F8 (tentatively identified as the racemate of BM-M2)

Year 1 annual average: 1.93 µg a.s. equiv./L (Lys I) and 1.38 µg a.s. equiv./L (Lys II).

	Year 2 annual average: 0.34 µg a.s. equiv./L (Lys I) and 0.57 µg a.s. equiv./L (Lys II) **Soil analysis** At the end of the 2 years 27% to 30% AR still remained associated to soil. The top soil layer itself accounted for ca 6%AR. HPLC analysis of the extracts from the 1st experimental year showed the presence of benalaxyl, B-M1, B-M2 and B-F8, however none of them exceeded 0.026 mg/kg soil.

PEC (soil) (Annex IIIA, point 9.1.3)

Parent: Benalaxyl-M

Method of calculation	DT_{50}: 98 days First-order kinetics Representative worst-case from field studies
Application rate	Crop: grape % plant interception: 50% number of applications: 4 Interval: 10 days Application rate: 100 g as/ha

$PEC_{(s)}$ (mg/kg)		Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application Time weighted average
Initial		0.0667	---	0.2407	---
Short term	24h	0.0662	0.0665	0.2390	0.2399
	2d	0.0658	0.0662	0.2373	0.2390
	4d	0.0648	0.0658	0.2340	0.2373
Long term	7d	0.0635	0.0651	0.2291	0.2348
	28d	0.0547	0.0605	0.1975	0.2184
		0.0468	0.0562	0.1690	0.2027
	50d	0.0329	0.0478	0.1187	0.1725
	100d				

Plateau maximum concentrations of Benalaxyl-M has been estimated by EFSA just after last application of benalaxyl-M in each year is 0.26 mg a.s. /kg soil

Metabolite: BM-M7 (Annex IIIA, point 9.1.3)

Method of calculation	DT_{50}: 90 days First-order kinetics Representative worst-case from laboratory studies
Application rate	Crop: grapes % plant interception: 50% number of applications: 4 Interval: 10 days Application rate: 100 g as/ha (assumed BM-M7 is formed at a maximum of 24.12% of the applied dose) Molar fraction 0.9 relative to the a.s.

PEC$_{(s)}$ (mg/kg)		Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application Time weighted average
Initial		0.0145	-	0.0519	-
Short term	24h	0.0144	0.0144	0.0515	0.0517
	2d	0.0143	0.0144	0.0511	0.0515
	4d	0.0141	0.0143	0.0503	0.0511
Long term	7d	0.0137	0.0141	0.0492	0.0505
	28d	0.0117	0.0130	0.0418	0.0467
	50d	0.0099	0.0120	0.0353	0.0431
	100d	0.0067	0.0101	0.0240	0.0362

Plateau maximum concentrations of BM-M7 estimated just after last application of benalaxyl-M after consecutive yearly application is 0.0552 mg/Kg soil

Metabolite: BM-M3 (Annex IIIA, point 9.1.3)

Method of calculation	DT_{50}: 98 days First-order kinetics Representative worst-case from laboratory studies
Application rate	Crop: grape % plant interception: 50% number of applications: 4 Interval: 10 days Application rate: 100 g as/ha (assumed BM-M3 is formed at a maximum of 28.46% of the applied dose) Molar fraction 0.86 relative to the a.s.

PEC$_{(s)}$ (mg/kg)		Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application Time weighted average
Initial		0.0163	---	0.0588	---
Short term	24h	0.0162	0.0162	0.0584	0.0586
	2d	0.0161	0.0162	0.0580	0.0584
	4d	0.0158	0.0161	0.0572	0.0580
Long term	7d	0.0155	0.0159	0.0560	0.0574
	28d	0.0134	0.0148	0.0482	0.0533
	50d	0.0114	0.0137	0.0413	0.0495
	100d	0.0080	0.0117	0.0290	0.0422

Plateau maximum concentrations of BM-M3 estimated just after last application of benalaxyl-M after consecutive yearly application is 0.0632 mg/kg soil

Metabolite: BM-M9 (Annex IIIA, point 9.1.3)

Method of calculation	DT_{50}: 13.4 days First-order kinetics Representative worst-case from laboratory studies
Application rate	Crop: grape % plant interception: 50% number of applications: 4 Interval: 10 days Application rate: 100 g as/ha (assumed BM-M9 is formed at a maximum of 33.32% of the applied dose) Molar fraction 0.96 relative to the a.s.

PEC$_{(s)}$ (mg/kg)		Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application Time weighted average
Initial		0.0213	---	0.0461	---
Short term	24h	0.0202	0.0208	0.0438	0.0449
	2d	0.0192	0.0202	0.0416	0.0438
	4d	0.0173	0.0192	0.0375	0.0416

Long term	7d	0.0148	0.0179	0.0321	0.0387
	28d	0.0050	0.0113	0.0108	0.0244
	50d	0.0016	0.0076	0.0034	0.0165
	100d	0.0001	0.0041	0.0003	0.0089

Metabolite: BM-M2 (Annex IIIA, point 9.1.3)

Method of calculation	DT_{50}: 137.1 days SFO kinetics Representative worst-case from laboratory studies
Application rate	Crop: grape % plant interception: 50% number of applications: 4 Interval: 10 days Application rate: 100 g as/ha (assumed BM-M2 is formed at a maximum of 7.17% of the applied dose) Molar fraction 0.99 relative to the a.s.

$PEC_{(s)}$ (mg/kg)		Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application Time weighted average
Initial		0.0047	---	0.0176	---
Short term	24h	0.0047	0.0047	0.0175	0.0176
	2d	0.0047	0.0047	0.0175	0.0175
	4d	0.0047	0.0047	0.0173	0.0175
Long term	7d	0.0046	0.0047	0.0170	0.0173
	28d	0.0041	0.0044	0.0153	0.0164
	50d	0.0037	0.0042	0.0137	0.0156
	100d	0.0029	0.0037	0.0106	0.0138

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

Hydrolysis of active substance and relevant metabolites (DT_{50}) (state pH and temperature) ‡	pH 4 : stable (50ºC)
	pH 7 : stable (50ºC)
	pH 9 : DT_{50} = 11 days (50ºC) DT_{50} = 6.54 days (55ºC) DT_{50} = 1.96 days (65ºC) DT_{50} = 301.3 days (25ºC extrapolated - Arrhenius). Main hydrolysis product at pH 9 is BM-M9.
Photolytic degradation of active substance and relevant metabolites ‡	Not performed as no absorption at wavelenghts > 290 nm (benalaxyl-M).
Readily biodegradable (yes/no) ‡	No
Degradation in water/sediment - $DissT_{50}$ water ‡ - $DissT_{90}$ water ‡ - DT_{50} whole system ‡ - DT_{90} whole system ‡	Study performed with benalaxyl 17 days (Pond) and 58 days (River) (r2 = 0.96) 57 days (Pond) and 190 days (River) (r2 = 0.96) 127 days (Pond) and 197 days (River) 406 days (Pond) and 630 days (River)
Degradation in water/sediment - $DissT_{50}$ water ‡ - $DissT_{90}$ water ‡ - DT_{50} whole system ‡ - DT_{90} whole system ‡	Study performed with benalaxyl-M 35.5 days (Pond) and 40.8 days (River) 118.0 days (Pond) and 135.4 days (River) 85.1 days (Pond) and 163.9 days (River) 282.7 days (Pond) and 544.4 days (River)
Mineralization	max. 0.38%AR (pond) at 100DAT max. 53.53%AR (river) at 100DAT (benalaxyl-M)
Non-extractable residues	max. 8.13%AR (pond) at 100DAT max. 7.77%AR (pond) at 100DAT (benalaxyl-M)
Distribution in water / sediment systems (active substance) ‡	Benalaxyl study Pond: 0 h until day 2, main portion in water phase, then active substance remains adsorbed to the sediment with 53% at the end of the study (100d). River: 0 h until day 30, main portion in water phase. At day 100, 25.8% in water phase and 43% adsorbed to the sediment. there were no metabolites > 10 % in water Benalaxyl-M study Pond: surface water – 48.84% AR at the end of the study (100d). River: surface water – 33.94% AR at the end of the study (100d).
Distribution in water / sediment systems (metabolites) ‡	Benalaxyl study B-M1 (racemic of BM-M7) was preferentially in water with a maximum of 7.3% AR at day 100 (River); benalaxyl acid (racemic of BM-M9) were preferentially in the sediment with maximums of 1.38% AR (Pond) and 5.38% AR (Pond), respectively at day 100. There were no metabolites > 10 % in sediment. Benalaxyl-M study: The main degradation compounds, identified by co-TLC were BM-M9 and BM-M7. (R isomer of B-M1) BM-M9 reached the maximum amount of 11.13% and 16.93% of AR in Pond and River systems, respectively. BM-M7 reached the maximum amount of 35.75% and 1.06% of AR in Pond and River systems, respectively. It also reaches a maximum of 32.41 % in the water phase after 100d. Compound BM-M3 (R isomer of B-M2) was also identified by co-TLC: it reached the maximum amount of 1.72% and 0.22% of AR in Pond and River systems, respectively. None of the other compounds ever reached levels higher than

3% AR.

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

Benalaxyl-M

FOCUS SW/sed simulation

Crop	Region	Run-off/drainage input into surface water		Application			crop interception	
		Season	% of soil residue	Max rate (kg as/ha)	Max number	Min interval	category	%
grapes	North EU	Oct - Feb	5	0.100	4	10	full canopy	70

data	Benalaxyl-M	BM-M7	BM-M3	BM-M9	BM-M2
soil DT_{50} (days)	98	not used in the model			
MW	325	293	279	311	323
Koc	6063	not used in the model			
water-sediment study DT_{50} (days) $DT_{50whole\ system}$ $DT_{50water}$ max. % of metabolite (% AR)	 164 164 -	 - - 36	 - - 2	 - - 17	 - - 1
water solubility (mg/L)	33	-	-		
max. % of metabolite in soil (% AR)	-	24	28	33	7

Highest PECsw and PECsed of Benalaxyl-M and its metabolites calculated using FOCUS STEP 1-2

compound	Highest PECsw and PECsed (µg/L)	
	PEC_{sw}	PEC_{sed}
Benalaxyl-M	3.22	170.9
BM-M7	1.03	42.6
BM-M3	0.48	28.7
BM-M9	0.81	45.2
BM-M2	0.15	8.6

PEC_{SW} (as µg/L) and PEC_{SED} (as µg/kg) of benalaxyl-M and its degradation compounds BM-M9, BM-M7, BM-M3 and BM-M2 estimated with simulation model of Step 3

compound	Scenario	PEC_{SW} ini	PEC_{SW} 28 d TWA	PEC_{SED} ini	PEC_{SED} 28 d TWA
benalaxyl-M	D6 ditch	**1.7600**	0.9970	**9.7920**	8.4070
	R1 pond	0.1400	0.1140	1.5230	1.5200
	R1 stream	1.0300	0.0158	0.2960	0.1970
	R2 stream	1.3810	0.0165	0.8210	0.7750
	R3 stream	1.4520	0.0550	3.3650	2.8230
	R4 stream	1.0300	0.0318	0.9470	0.6860
BM-M9	D6 ditch	0.5720	0.3680	**0.7750**	0.6510
	R1 pond	0.0526	0.0468	0.1350	0.1340
	R1 stream	0.3300	0.0051	0.0417	0.0115
	R2 stream	0.4430	0.0053	0.0337	0.0094
	R3 stream	**0.5850**	0.0400	0.1990	0.0722
	R4 stream	0.4390	0.0196	0.1440	0.0354
BM-M7	D6 ditch	0.393	0.238	**1.316**	1.131
	R1 pond	0.0328	0.028	0.245	0.245
	R1 stream	0.224	0.00345	0.0507	0.0267
	R2 stream	0.301	0.00361	0.067	0.051
	R3 stream	0.317	0.0242	0.313	0.192
	R4 stream	**0.574**	0.0287	0.467	0.203
BM-M3	D6 ditch	0.439	0.281	**0.741**	0.635
	R1 pond	0.0399	0.0354	0.122	0.122
	R1 stream	0.253	0.00389	0.0356	0.0109
	R2 stream	0.339	0.00608	0.0609	0.017
	R3 stream	**0.555**	0.0453	0.227	0.0954
	R4 stream	0.485	0.0261	0.161	0.0577
BM-M2	D6 ditch	0.127	0.0828	**0.132**	0.113
	R1 pond	0.0119	0.0107	0.0202	0.0202
	R1 stream	0.0735	0.00113	0.00701	0.00172
	R2 stream	0.0986	0.00145	0.0101	0.00225
	R3 stream	**0.21**	0.0149	0.0483	0.0173
	R4 stream	0.193	0.0075	0.0418	0.00913

The highest estimated PECsw and PECsed from STEP 1-2 and STEP 3

compound	Highest PECsw and PECsed in STEP 1-2		Highest PECsw and PECsed in STEP 3	
	PEC_{sw} (µg/L)	**PEC_{sed} (µg/kg)**	**PEC_{sw} (µg/L)**	**PEC_{sed} (µg/kg)**
Benalaxyl-M	**3.22**	**170.9**	1.76	9.8
BM-M7	**1.03**	42.6	0.57	1.3
BM-M3	0.48	28.7	**0.56**	0.7
BM-M9	**0.81**	45.2	0.58	0.77
BM-M2	0.15	8.6	**0.21**	0.13

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

Method of calculation and type of study (*e.g.* modelling, monitoring, lysimeter)	Model PELMO 4.4.3, PRZM 3.5.2 and PEARL 4.4.4 Crop: Grapes The leachate concentration was estimated in all FOCUS scenarios (Chateaudun, Hamburg, Kremsmunster, Piacenza, Porto, Sevilla and Thiva) for the use in vine according to the following scheme: Simulation period: 20 years Mean annual concentration at 1m soil depth. PECgw is represented by 80th percentile. DT50 values of 59.6*, 157, 31.96, 84.85 and 99.84 days, were used resp for benalaxyl-M, BM-M7, BM-M9, BM-M3 and BM-M2 (R isomer of B-F8). Mean Koc values of 6063, 497.0, 219, 206.0 and 91.74 mL/g resp. for benalaxyl-M, BM-M7, BM-M9, BM-M3 and BM-M2 (R isomer of B-F8). (PELMO & PRZM). Mean Kom values of 3525, 288.28, 127.03, 119.0 and 53 mL/g resp. for benalaxyl-M, BM-M7, BM-M9, BM-M3 and BM-M2 (R isomer of B-F8). (PEARL). 1/n = 0.98, 0.86, 0.99, 0.95 and 0.99 resp. for benalaxyl-M, BM-M7, BM-M9, BM-M3 and BM-M2 (R isomer of B-F8). Metabolites BM-M9, BM-M7, BM-M3 and BM-M2 (R isomer of B-F8) were applied as a Test Item at a dose depending on their maximum occurrence of 33.32%, 24.12%, 28.46% and 7.17%, respectively, found in soil metabolism studies of the parent Benalaxyl-M. TSCF (plant uptake) = 0.0 Q_{10} = 2.58 * First order value derived by EFSA for benalaxyl-M is DT_{50} = 98.53d. No significant impact expected on the parent calculated concentration due to the high adsorption. The use of a shorter half life for the parent is expected to result on more worst case results for the metabolites
Application rate	4 x 0.1 kg a.s./ha (4 treatments with soil incorporation of metabolites)

70% interception

$PEC_{(gw)}$

Four Treatments – With Soil Incorporation

Concentration of metabolites in the percolate at 1 m soil depth (80th percentile) – 4 treatments in vines – **with soil incorporation** - (data are expressed as µg/L)

Compound	Scenari	PELMO	PRZM	PEAR
BM-M9	Châteaudun	0.015	0.009	0.029
	Hamburg	0.047	0.032	0.055
	Kremsmünster	0.044	0.019	0.057
	Piacenz	0.046	0.032	0.053
	Port	0.020	0.010	0.012
	Sevill	0.002	0.000	0.012
	Thiv	0.003	0.001	0.007
BM-M7	Châteaudun	0.000	0.000	0.001
	Hamburg	0.002	0.000	0.004
	Kremsmünster	0.002	0.000	0.005
	Piacenz	0.003	0.001	0.004
	Port	0.000	0.000	0.000
	Sevill	0.000	0.000	0.000
	Thiv	0.000	0.000	0.000
BM-M3	Châteaudun	0.221	0.155	0.266
	Hamburg	0.293	0.223	0.291
	Kremsmünster	0.271	0.164	0.265
	Piacenz	0.295	0.215	0.304
	Port	0.146	0.095	0.117
	Sevill	0.037	0.007	0.122
	Thiv	0.078	0.028	0.114
BM-M2	Châteaudun	0.636	0.554	0.604
	Hamburg	0.704	0.639	0.575
	Kremsmünster	0.547	0.492	0.430
	Piacenz	0.532	0.456	0.598
	Port	0.346	0.318	0.284
	Sevill	0.444	0.258	0.437
	Thiv	0.524	0.381	0.456

-Lysimeter study

On basis of the lysimeter study available for benalaxyl, the meeting of experts (EPCO 26) concluded that it cannot be excluded that under realistic worst case situations the trigger of 0.1 µg / L (and 0.75 µg / L) will be exceeded by metabolites BM-M3 and BM-M7 and the enantiomeric pure equivalents of B-F4, B-F7 and B-F8 when benalaxyl-M is applied according the proposed GAP.

No groundwater modelling is available for metabolites B-F4 and B-F7 therefore the maximum values of **1.90 µg a.s. equiv./L** and **0.9 µg a.s. equiv./L** should be used for the relevance assessment of the R-isomers of metabolites B-**F4** and B-**F7** resulting from the application of benalaxyl-M.

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

Direct photolysis in air ‡	no data submitted
Quantum yield of direct phototransformation	not available for air
Photochemical oxidative degradation in air ‡	DT_{50}: 4.174 h and 12.523 h, assuming OH-radical concentrations of 1.5 x 10^6/cm^3 and 0.5 x 10^6/cm^3 (Atkinson estimation)
Volatilization ‡	from plant surfaces: no data, not required
	from soil: no data, not required

PEC (air)

Method of calculation	no data, not required

$PEC_{(a)}$

Maximum concentration	no data, not required

Definition of the Residue (Annex IIA, point 7.3)

Relevant to the environment	Soil: benalaxyl-M, BM-M3, BM-M7, BM-M9 Surface water and sediment: benalaxyl-M, BM-M3, BM-M7, BM-M9 Groundwater: benalaxyl-M, BM-M7, BM-M3, BM-M9, R isomer of B-F7, R isomer of B-F4, BM-M2 (R isomer of B-F8). Air: benalaxyl-M

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

Soil (indicate location and type of study)	no data, not required.
Surface water (indicate location and type of study)	no data, not required.
Ground water (indicate location and type of study)	no data, not required.
Air (indicate location and type of study)	no data, not required.

Classification and proposed labelling (Annex IIA, point 10)

with regard to fate and behaviour data	Possible candidate for R53

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

Acute toxicity to mammals ‡	rat: LD_{50} > 2000 mg/kg bw
Long term toxicity to mammals	5000 mg/kg (275.01 mg/kg for males and 401.2 mg/kg for females) data for benalaxyl
Acute toxicity to birds ‡	LD_{50} > 2000 mg/kg bw (benalaxyl-M) LD_{50} > 5000 mg formulation (IR6142 M)/kg bw
Dietary toxicity to birds ‡	LC_{50} > 5000 ppm (775.2 mg/kg bw) (benalaxyl-M)
Reproductive toxicity to birds ‡	NOEC = 1000 ppm (90 mg a.s./kg bw) (benalaxyl)

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

4 applications of 0.1 kg a.s./ha to vineyards

Application rate (kg as/ha)	Crop	Category (*e.g.* insectivorous bird)	Time-scale	TER	Annex VI Trigger
0.100 x 4	vineyard	small insectivorous bird	acute	>369.8	10
		small insectivorous bird	short-term	>257.03	10
		small insectivorous bird	long-term	29.84	5
		Earthworm eating bird	long-term	279.5	5
		Fish eating bird	long-term	964.6	5

Worst case Toxicity/exposure ratios for terrestrial vertebrates (mammals) exposed through contaminated food (Annex IIIA, points 10.1 and 10.3)

4 applications of 0.1 kg a.s./ha to vineyards

Application rate (kg as/ha)	Crop	Category (*e.g.* insectivorous bird)	Time-scale	TER	Annex VI Trigger
0.100 x 4	vineyard	small herbivorous mammal	acute	105.8	10
		small herbivorous mammal	long-term	42.71	5
		Fish eating mammal	long-term	4758	5
		Earthworm eating mammal	long-term	1429	5

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	Endpoint	Toxicity (mg/l)
Laboratory tests				
Rainbow Trout (*O. mykiss)*	benalaxyl-M	acute	LC_{50}	4.9
Rainbow Trout (*O. mykiss)*	benalaxyl	chronic	NOEC	0.49
Rainbow Trout (*O. mykiss)*	Formulation IR6141 M 4-65*	acute	LC_{50}	1.5
Rainbow Trout (*O. mykiss)*	R isomer of B-F4	acute	LC_{50}	>100
Rainbow Trout (*O. mykiss)*	B-F7 + B-F8	acute	LC_{50}	>100
Rainbow Trout (*O. mykiss)*	BM-M9	acute	LC_{50}	>100
Rainbow Trout (*O. mykiss)*	B-M1	acute	LC_{50}	>100
Rainbow Trout (*O. mykiss)*	B-M2	acute	LC_{50}	>100
D. magna	benalaxyl-M	acute	EC_{50}	22.8
D. magna	benalaxyl-M	chronic	NOEC	0.2
D. magna	Formulation IR6141 M 4-65	acute	EC_{50}	1.8

Group	Test substance	Time-scale	Endpoint	Toxicity (mg/l)
D. magna	Formulation GALBEN M 8-65**	chronic	NOEC	0.0332
D. magna	R isomer of B-F4	acute	EC_{50}	>100
D. magna	B-F7 + B-F8	acute	EC_{50}	>100
D. magna	BM-M9	acute	EC_{50}	>100
D. magna	B-M1	acute	EC_{50}	>100
D. magna	B-M2	acute	EC_{50}	>100
Scenedesmus subspicatus	benalaxyl-M	-	E_rC_{50}	16.5
			E_bC_{50}	17.0
Selenastrum capricornutum	Formulation IR6141 M 4-65	-	E_rC_{50}	0.260
			E_bC_{50}	0.101
Desmodesmus subspicatus	R isomer of B-F4	-	E_bC_{50}	10.1[1]
			E_yC_{50}	40.8
			E_rC_{50}	7.9[1]
Desmodesmus subspicatus	B-F7 + B-F8	-	E_bC_{50}	>100
			E_yC_{50}	>100
			E_rC_{50}	>100
Desmodesmus subspicatus	BM-M9	-	E_rC_{50}	>200
			E_yC_{50}	149.78
Scenedesmus subspicatus	B-M1	-	E_rC_{50}	>100
			E_bC_{50}	62.5
Scenedesmus subspicatus	B-M2	-	E_rC_{50}	>100
			E_bC_{50}	64.5
C. riparius	benalaxyl	chronic	NOEC	3.13

* Contains 4% benalaxyl-M and 65% mancozeb
** Contains 8% benalaxyl and 65% mancozeb
[1] It should be noted that due to very steep dose response between the effects observed on the inhibition of biomass and yield between the test doses at 6.4 mg/L and 16 mg/L the endpoints should only be considered as approximate

Microcosm or mesocosm tests
No data submitted. Not necessary

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

FOCUS SURFACE WATER STEP 1 – 2 (maximum PEC value used for risk assessment)

4 applications of 0.1 kg a.s./ha to vineyards

Substance	Organisms	Toxicity Values			PECsw max. (mg as/L or mg as/ kg sediment) FOCUS Step 1 - 2	TER		Trigger Value
Benalaxyl-M	Fish	LC_{50} (96h)	4.9	mg as/L	0.00322	TERa	1522	100
		NOEC:	0.49	mg as/L		TERlt	152	10
	Aquatic Invertebrates	EC_{50} (48h)	22.8	mg as/L		TERa	7081	100
		NOEC (21d)	0.2	mg as/L		TERlt	62	10
	Green Algae	E_rC_{50} (72h)	16.5	mg as/L		TER	5124	10
	Sediment dwelling organisms	LC_{50} (28 d) as water concentration	17.7	mg/L		TERlt	5496.9	10
		LC_{50} (28 d) as sediment concentration	56.9	mg/kg	0.1709	TERlt	333	10
BM-M7	Fish	LC_{50} (96h[1] >	50[1]	mg/L	0.00103	TERa	>12500000	100
	Aquatic Invertebrates	EC_{50}(48h)[1] >	50[1]	mg/L		TERa	>12500000	100
	Green Algae	E_bC_{50}(72h)[1]	31.25[1]	mg/L		TER	7812500	10
BM-M3	Fish	LC_{50} (96h)[1] >	50[1]	mg/L	0.00048	TERa	>164474	100
	Aquatic Invertebrates	EC_{50}(48h)[1] >	50[1]	mg/L		TERa	>164474	100
	Green Algae	E_bC_{50}(72h)[1]	32.25[1]	mg/L		TER	106086	10
BM-M9	Fish	LC_{50} (96h) >	100	mg/L	0.00081	TERa	>123457	100
	Aquatic Invertebrates	EC_{50}(48h) >	100	mg/L		TERa	>123457	100
	Green Algae	E_rC_{50}(72h) >	200	mg/L		TER	>246914	10
		E_yC_{50}(72h)	148.78				183679	

[1]Toxicity endpoint taken from a study performed with the racemic mixture (B-M1 or B-M2). Therefore, the endpoint has been corrected by 50% according to the content of the pure R-enantiomer (BM-M7 or BM-M3).

RISK ASSESSMEMT FOR GROUNDWATER RETURNING TO SURFACE WATER (maximum PEC value used for risk assessment)

4 applications of 0.1 kg a.s./ha to vineyards

Substance	Organisms	Toxicity Values			PECgw max. (µg as/L)[1, 2]	TER		Trigger Value
BM-M7	-	-			0.005	See surface water risk assessment		-
BM-M3	-	-			0.304	See surface water risk assessment		-
BM-M9	-	-			0.057	See surface water risk assessment		-
R isomer of B-F7,	-	-			0.9	Aquatic toxicity data performed with a mixture of B-F7 + B-F8 indicated low toxicity.		-
R isomer of B-F4	Fish	LC_{50} (96h): >	100	mg/L	1.9	TERa	>52632	100
	Aquatic Invertebrates	EC_{50}(48h):>	100	mg/L		TERa	>52632	100
	Green Algae	E_bC_{50}(72h):	7.9	mg/L		TER	4158	10
BM-M2 (R isomer of B-F8)[3]	-	-			0.704	Aquatic toxicity data performed with a mixture of B-F7 + B-F8[3] indicated low toxicity.		-

[1] no dilution factor applied
[2] Maximum ground water PEC value from all scenarios used for risk assessment
3 B-F8 is the racemic mixture of BM-M2 and therefore contains 50% BM-M2.

Bioconcentration

Bioconcentration factor (BCF) ‡	57 (Benalaxyl)
Annex VI Trigger:for the bioconcentration factor	100
Clearance time (CT_{50})	< 6 h
(CT_{90})	< 14 d
Level of residues (%) in organisms after the 14 day depuration phase	2.0%

Effects on honeybees (Annex IIA, point 8.3.1, Annex IIIA, point 10.4)

Acute oral toxicity ‡	(Benalaxyl-M)	>104 µg a.s./bee
	Formulation IR6141 M	>162.9 µg IR6141 M/bee
Acute contact toxicity ‡	(Benalaxyl-M)	>100 µg a.s./bee
	Formulation IR6141 M	>141.3 µg IR6141 M/bee

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

4 applications of 0.1 kg a.s./ha to vineyards

Application rate (kg as/ha)	Crop	Route	Hazard quotient	Annex VI Trigger
Laboratory tests				
0.1	grapes	oral	0.96	50
0.1	grapes	oral	1.0	50
Field or semi-field tests: No data submitted. Not considered necessary				

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

Species	Stage	Test Substance and substrate	Dose (kg as/ha)	Endpoint	Effect	Annex VI Trigger
Laboratory tests						
‡ *P. persimilis*	adult	lab. Benalaxyl fresh residues on bean leaf disc	0.16 and 0.48	mortality	0%	30%
‡ *P. cupreus*	adult	lab. GALBEN M 8—65 quatz sand	0.240	mortality food consumption	0% 13.6%	30%
‡ *P. cupreus*	adult	Lab. IR6141 M 4—65 quatz sand	0.120 and 0.240	Mortality food consumption	3.3% and 0%	30%
‡ *C. carnea*	larvae	Lab. IR6141 M 4—65 Glass plate	0.120 and 0.240	mortality reproduction	2.2% and -4.3%	30%
‡ *T. cacoeciae*	pupae adult	lab. GALBEN M 8—65 Glass plate	0.240	parasitation efficiency	91% 99.9%	30%
‡ *S. corollae*	larvae	lab. GALBEN M 8—65 Glass plate	0.240	reproduction (fecundity and larval hatching rate)	61.4%	30%
‡ *T. cacoeciae*	adult	ex-lab. GALBEN M 8—65 fresh residues on bean leaf disc	0.0064 and 0.160 four treatments	parasitisation efficiency	0% and 44%	30%
‡ *A. rhopalosiphi*	adult	ex-lab. IR6141 M 4—65 fresh residues on vines leaves	0.004 and 0.100 four treatments	mortality parasitation efficiency	20% and 7.5% max 24.4%	30%
‡ *C. carnea*	larvae and pupae	ex-lab. GALBEN M 8—65 fresh residues on vines leaves	0.240 and 0.480	mortality reproduction	-2.2 and –4.4% 0.9%	30%

Effects on non-target arthropods

Species	Test substance and study design	Dose-range tested	Results
Typhlodromus pyri	'IR6141 M' (4 % IR6141 and 65% mancozeb (glass plate)	1000, 500, 250, 125, 62.5 and 31.25 g product/ha	7-day LR_{50}> 172.2 g product/ha Reproduction: >50 % effects at all treatments
Typhlodromus pyri	'IR6141 M mancozeb free' (glass plate)	10000, 5000, 2500, 1250 and 625 g product/ha	7-day LR_{50}> 10000 g product/ha Reproduction: Maximum of 39% reduction compared to the control (5000 g product/ha)[1]
Aphidius rhopalosiphi	'IR6141 M' (4 % IR6141 and 65% mancozeb) (glass plate-part1; barley seedlings-part2)	10000, 4000, 1600, 640 and 256 g product/ha	48-hour LR_{50}> 2745.6 g product/ha Reproduction: affected at all treatments (effects <50% at doses tested: 1600, 640 and 256 g product/ha)
Aphidius rhopalosiphi	'IR6141 M mancozeb free' (glass plate)	10000, 8000, 6400, 5120 and 4096 g product/ha	48-hour LR_{50}> 10000 g product/ha Reproduction: Maximum of 26.5% reduction compared to the control (6400 g product/ha)

[1] Effects on reproduction did not follow a dose response.

Field or semi-field tests					
T. pyri	natural population	Field test IR6141 M 4-65	0.0075 and 0.100 four treatments	mites abundance	Recovery 84 dd. after last treatment No effects at drift rate
T. pyri	natural population	Field test GALBEN M 8--65	0.200 four treatments	mites abundance	Recovery 56 dd. after last treatment

4 applications of 2.5 kg formulation/ha to late vines (10 day interval between applications)

Test substance	Species	Effect (LR_{50} g/ha)	HQ in-field (4 applic.)	HQ off-field[1] (4 applic.) 3 m distance, 6.71 % spray-drift	Trigger
IR6141 M	*Typhlodromus pyri*	> 172.2	**<39**	<2.63	2
IR6141 M	*Aphidius rhopalosiphi*	> 2745.6	<**2.45**	<0.16	2
'IR6141 M mancozeb free'	*Typhlodromus pyri*	> 10000	<0.68	<0.05	2
'IR6141 M mancozeb free'	*Aphidius rhopalosiphi*	> 10000	<0.68	<0.05	2

Effects on earthworms (Annex IIA, point 8.4, Annex IIIA, point 10.6)

Acute toxicity ‡	Benalaxyl-M	LC_{50CORR} = 236.4 * mg as/kg soil
	B-M1	LC_{50CORR} = >500 * mg as/kg soil
	B-M2	LC_{50CORR} = >500* mg as/kg soil
	BM-M9	LC_{50CORR} = >500* mg as/kg soil
	Formulation IR6141 M:	LC_{50CORR} = >500 * mg form./kg soil
	B-F4:	LC_{50} = >1000 mg/kg soil
	B-F7 + B-F8:	>1000 mg/kg soil
Reproductive toxicity ‡	Benalaxyl-M	$NOEC_{CORR}$ = 26* mg as/kg soil
	B-M1	$NOEC_{CORR}$ = 125* mg/kg soil
	B-M2	$NOEC_{CORR}$ = 25* mg/kg soil
	Formulation IR6141 M:	$NOEC_{CORR}$ = 228* mg form./kg soil
	B-F7 + B-F8:	$NOEC_{CORR}$ = 16* mg F7+F8./kg soil

* values corrected to take in account of differences in o.c. between natural and artificial soils

Effects on other soil macro-organisms (Annex IIA, point 8.6)

Reproductive toxicity ‡	*Folsomia candida* B-M1 $NOEC_{mortality}$ = 31.25* mg/kg soil $NOEC_{reprod}$ = 500* mg/kg soil B-M2 $NOEC_{mortality}$ = 500* mg/kg soil $NOEC_{reprod}$ = 62.5* mg/kg soil BM-M9 $NOEC_{mortality}$ = 250* mg/kg soil $NOEC_{reprod}$ = 500* mg/kg soil B-F7 + B-F8 EC_{50} (28d) > 2.13~~33~~ mg/kg NOEC (28d) = 2.13~~33~~ mg/kg

* values corrected to take in account of differences in o.c. between natural and artificial soils

Toxicity/exposure ratios for soil organisms

4 applications of 0.1 kg a.s./ha to vineyards

Test organism	Test substance	Time scale	Soil PEC mg/kg soil	TER	Trigger
Earthworms					
Eisenia fetida	Benalaxyl-M	Acute	0.2407	982	10
Eisenia fetida	Benalaxyl-M	Chronic	0.2407	108	5
Eisenia fetida	BM-M3	Acute	0.0588	>4252[1]	10
Eisenia fetida	BM-M3	Chronic	0.0588	213[1]	5
Eisenia fetida	BM-M9	Acute	0.0461	>10846	10
Eisenia fetida	BM-M9	Chronic	0.0461	56[2]	5
Eisenia fetida	BM-M7	Acute	0.0519	>4817[1]	10
Eisenia fetida	BM-M7	Chronic	0.0519	1204[1]	5
Other soil macroorganisms					
Folsomia candida	BM-M3	Chronic	0.0588	531[1]	5
Folsomia candida	BM-M9	Chronic	0.0461	5423	5
Folsomia candida	BM-M7	Chronic	0.0519	301[1]	5

[1]Toxicity endpoint taken from a study performed with the racemic mixture (B-M1 or B-M2). Therefore, the endpoint has been corrected by 50% according to the content of the pure R-enantiomer (BM-M7 or BM-M3).
[2] No chronic data available for BM-M9 and therefore the TER was calculated assuming toxicity 10 times greater than the parent (i.e. assuming a NOEC of 2.6 mg/kg soil)

Effects on soil microorganisms (Annex IIA, point 8.5, Annex IIIA, point 10.7)

Nitrogen mineralization ‡	Benalaxyl: No prolonged adverse effects of benalaxyl at soil concentrations up to 1.65 mg a.s./kg; B-M1 no prolonged adverse effects of B-M1 at soil concentrations up to 0.5mg/kg; B-M2 no prolonged adverse effects of B-M2 at soil concentrations up to 0.5 mg a.s./kg; BM-M7 no prolonged adverse effects of BM-M7 at soil concentrations up to 0.4 mg a.s./kg; B-F7 + B-F8 no prolonged adverse effects of B-F7+ B-F8 at soil concentrations up to 0.4 mg a.s./kg; BM-M9 no prolonged adverse effects of BM-M9 at soil concentrations up to 0.56 mg/kg; Formulation FANTIC M: no prolonged adverse effects of the formulation at soil concentrations up to 33 mg form./kg;
Carbon mineralization ‡	Benalaxyl: no prolonged adverse effects of benalaxyl at soil concentrations up to 1.65 mg a.s./kg; B-M1 no prolonged adverse effects of B-M1 at soil concentrations up to 0.5mg/kg; B-M2 no prolonged adverse effects of B-M2 at soil concentrations up to 0.5 mg a.s./kg; BM-M7 no prolonged adverse effects of BM-M7 at soil concentrations up to 0.4 mg a.s./kg; B-F7 + B-F8 no prolonged adverse effects of B-F7+ B-F8 at soil concentrations up to 0.4 mg a.s./kg; BM-M9 no prolonged adverse effects of BM-M9 at soil concentrations up to 0.56 mg/kg; Formulation FANTIC M: no prolonged adverse effects of the formulation at soil concentrations up to 33 mg form./kg;

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

Several non-target plant species, 7 different plant species were selected, 3 Monocotyledonae: *Avena sativa*, *Triticum aestivum*, *Zea mays* and 4 Dicotiledonae: *Phaseolus vulgaris*, *brassica napus*, *Cucumis sativus*, *Lycopersicum esculetum*, were tested at the maximum dose rate of 0.5 kg/ha and no adverse effects were observed.

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

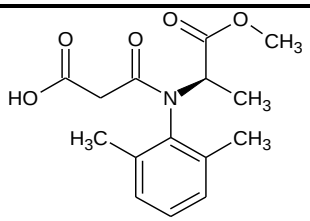
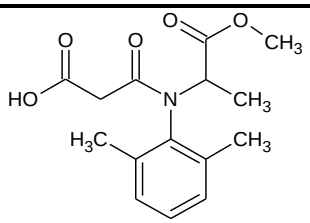
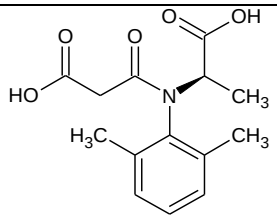
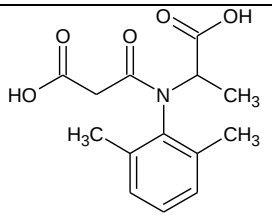
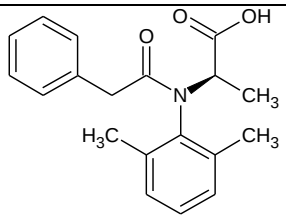
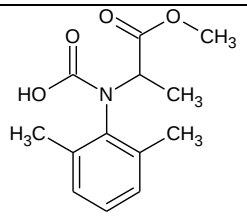
Compartment	
soil	Benalaxyl-M
water	Benalaxyl-M
sediment	Benalaxyl-M
groundwater	Benalaxyl-M

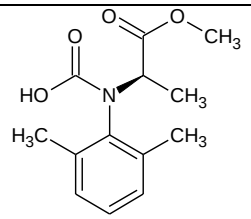
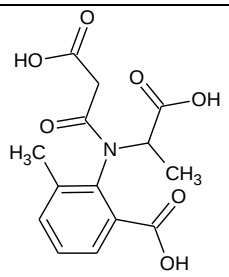
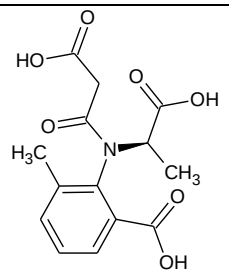
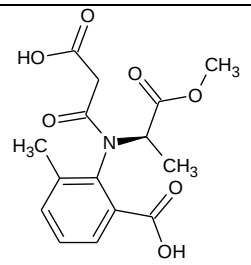
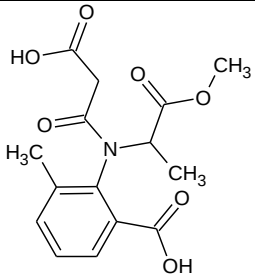
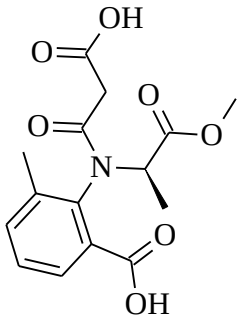
Classification and proposed labelling* (Annex IIA, point 10)

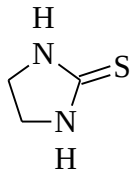
with regard to ecotoxicological data	N: Harmful R51/R53: Toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment

* It should be noted that classification 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.

APPENDIX B – USED COMPOUND CODE(S)

Code/Trivial name*	Chemical name**	Structural formula**
BM-M7 (benalaxyl-M metabolite, M7)	methyl *N*-(malonyl)-*N*-(2,6-xylyl)-D-alaninate or methyl *N*-(carboxyacetyl)-*N*-(2,6-dimethylphenyl)-D-alaninate	
B-M1 (benalaxyl metabolite, M1)	methyl *N*-(malonyl)-*N*-(2,6-xylyl)-DL-alaninate or methyl *N*-(carboxyacetyl)-*N*-(2,6-dimethylphenyl)-DL-alaninate	
BM-M3 (benalaxyl-M metabolite, M3)	*N*-(malonyl)-*N*-(2,6-xylyl)-D-alanine or *N*-(carboxyacetyl)-*N*-(2,6-dimethylphenyl)-D-alanine	
B-M2 (benalaxyl metabolite, M2)	*N*-(malonyl)-*N*-(2,6-xylyl)-DL-alanine or *N*-(carboxyacetyl)-*N*-(2,6-dimethylphenyl)-DL-alanine	
BM-M9 (benalaxyl-M metabolite, M9, benalaxyl-M acid)	*N*-(phenylacteyl)-*N*-(2,6-xylyl)-D-alanine *N*-(2,6-dimethylphenyl)-*N*-(phenylacetyl)-D-alanine	
B-F4 (benalaxyl metabolite, F4)	methyl *N*-(formyl)-*N*-(2,6-xylyl)-DL-alaninate methyl *N*-(2,6-dimethylphenyl)-*N*-(formyl)-DL-alaninate	

R-isomer of B-F4 (benalaxyl-M metabolite)	methyl *N*-(formyl)-*N*-(2,6-xylyl)-D-alaninate methyl *N*-(2,6-dimethylphenyl)-*N*-(formyl)-D-alaninate	
B-F7 (benalaxyl metabolite, F7)	2-{(carboxyacetyl)[(1*RS*)-1-carboxyethyl]amino}-3-methylbenzoic acid Or 2-(carboxyacetyl)-(2-hydroxy-1-methyl-2-oxoethylamino))-3-methylbenzoic acid	
R-isomer of B-F7 (benalaxyl-M metabolite)	2-{(carboxyacetyl)[(1*R*)-1-carboxyethyl]amino}-3-methylbenzoic acid	
BM-M2 (benalaxyl-M metabolite, M2)	2-{(carboxyacetyl)[(2*R*)-1-methoxy-1-oxo-2-propanyl]amino}-3-methylbenzoic acid	
B-F8 (benalaxyl metabolite, F8)	2-{(carboxyacetyl)[(2*RS*)-1-methoxy-1-oxo-2-propanyl]amino}-3-methylbenzoic acid Or 2-(2-(1-methoxycarboxy)ethylcarbamoyl)acetyl)-3-methylbenzoic acid	
R-isomer of B-F8	2-{(carboxyacetyl)[(2*R*)-1-methoxy-1-oxo-2-propanyl]amino}-3-methylbenzoic acid	

Ethylene thiourea		

* The metabolite name in bold is the name used in the conclusion.
** ACD/ChemSketch, Advanced Chemistry Development, Inc., ACD/Labs Release: 12.00 Product version: 12.00 (Build 29305, 25 Nov 2008)

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
CHO	Chinese hamster ovarian cell
CI	confidence interval
CIPAC	Collaborative International Pesticides Analytical Council Limited
CL	confidence limits
cm	centimetre
d	day
DAA	days after application
DAR	draft assessment report
DAT	days after treatment
DM	dry matter
DT_{50}	period required for 50 percent disappearance (define method of estimation)
DT_{90}	period required for 90 percent disappearance (define method of estimation)
dw	dry weight
EbC_{50}	effective concentration (biomass)
EC_{50}	effective concentration
ECHA	European Chemical Agency
EEC	European Economic Community
EINECS	European Inventory of Existing Commercial Chemical Substances
ELINCS	European List of New Chemical Substances
EMDI	estimated maximum daily intake
ER_{50}	emergence rate/effective rate, median
ErC_{50}	effective concentration (growth rate)
EU	European Union
EUROPOEM	European Predictive Operator Exposure Model
f(twa)	time weighted average factor
FAO	Food and Agriculture Organisation of the United Nations
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
MCH	mean corpuscular haemoglobin
MCHC	mean corpuscular haemoglobin concentration
MCV	mean corpuscular volume
mg	milligram
mL	millilitre
mm	millimetre
mN	milli-newton
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
PTT	partial thromboplastin time
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
TSH	thyroid stimulating hormone (thyrotropin)
TWA	time weighted average
UDP	uridine 5'-diphospho-glucuronosyltransferase
UDS	unscheduled DNA synthesis
UV	ultraviolet
W/S	water/sediment
w/v	weight per volume
w/w	weight per weight
WBC	white blood cell
WG	water dispersible granule
WHO	World Health Organisation

wk	week
yr	year