CONCLUSION ON PESTICIDES PEER REVIEW

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Peer review of the pesticide risk assessment of the active substance 24-epibrassinolide

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Abstract

The conclusions of the European Food Safety Authority (EFSA) following the peer review of the initial risk assessments carried out by the competent authority of the rapporteur Member State, Austria, for the pesticide active substance 24-epibrassinolide and the considerations as regards the inclusion of the substance in Annex IV of Regulation (EC) No 396/2005 are reported. The context of the peer review was that required by Regulation (EC) No 1107/2009 of the European Parliament and of the Council. The conclusions were reached on the basis of the evaluation of the representative uses of 24-epibrassinolide as an elicitor on grapes, leafy vegetables, sugar beet and as plant activator on grapes and cucurbits. The reliable endpoints, appropriate for use in regulatory risk assessment are presented. Missing information identified as being required by the regulatory framework is listed. No concerns are identified.

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Keywords: 24-epibrassinolide, peer review, risk assessment, pesticide, elicitor

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Summary

24-epibrassinolide is a new active substance for which, in accordance with Article 7 of Regulation (EC) No 1107/2009 of the European Parliament and of the Council, the rapporteur Member State (RMS), Austria, received an application from Suntton GmbH on 28 April 2017 for approval. In addition, the applicant submitted an application for inclusion of the substance in Annex IV of Regulation (EC) No 396/2005. Complying with Article 9 of the Regulation, the completeness of the dossier was checked by the RMS and the date of admissibility of the application was recognised as being 30 May 2017.

An initial evaluation of the dossier on 24-epibrassinolide was provided by the RMS in the draft assessment report (DAR) and subsequently, a peer review of the pesticide risk assessment on the RMS evaluation was conducted by EFSA in accordance with Article 12 of Regulation (EC) No 1107/2009. The following conclusions are derived.

The uses of 24-epibrassinolide according to the representative uses as an elicitor on grapes, leafy vegetables and sugar beet result in a sufficient efficacy. On the other hand, it was concluded that the use as a plant activator on leafy vegetables and cucurbits is not supported by the efficacy data provided.

The assessment of the data package revealed no issues that could not be finalised or that need to be included as critical areas of concern with respect to identity, physical/chemical properties and analytical methods and in the mammalian toxicology section.

In the section on residues, the available information on uptake, metabolism and degradation of 24-epibrassinolide is sufficient and does not indicate the formation of compounds of potential concern for consumers. Toxicological reference values for dietary risk assessment were not allocated, and therefore, a quantitative consumer risk assessment was not considered necessary. No critical areas of concern or issues that could not be finalised were identified.

An maximum residue level (MRL) application for inclusion of 24-epibrassinolide into Annex IV of Regulation (EC) No 396/2005 was submitted. It is proposed to include 24-epibrassinolide into Annex IV of Regulation (EC) No 396/2005.

The data available on environmental fate and behaviour are sufficient to carry out the required environmental exposure assessments at EU level for the representative uses.

The assessment of the data package revealed no issues that could not be finalised or that need to be included as critical areas of concern with respect to ecotoxicology.

24-epibrassinolide does not meet the criteria for endocrine disruption for humans and non-target organisms as set out in points 3.6.5 and 3.8.2 of Annex II to Regulation (EC) No 1107/2009, as amended by Commission Regulation (EU) 2018/605.
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Background

Regulation (EC) No 1107/2009 of the European Parliament and of the Council\(^1\) (hereinafter referred to as ‘the Regulation’) lays down, inter alia, the detailed rules as regards the procedure and conditions for approval of active substances. This regulates for the European Food Safety Authority (EFSA) the procedure for organising the consultation of Member States and the applicant(s) for comments on the draft assessment report (DAR), provided by the rapporteur Member State (RMS), and the organisation of an expert consultation, where appropriate.

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

24-epibrassinolide is a new active substance for which, in accordance with Article 7 of the Regulation, the RMS, Austria (hereinafter referred to as the ‘RMS’), received an application from Sunutton GmbH on 28 April 2017 for approval of the active substance 24-epibrassinolide. In addition, the applicant submitted an application for inclusion of the substance in Annex IV of Regulation (EC) No 396/2005\(^2\). Complying with Article 9 of the Regulation, the completeness of the dossier was checked by the RMS and the date of admissibility of the application was recognised as being 30 May 2017.

The RMS provided its initial evaluation of the dossier on 24-epibrassinolide in the DAR, which was received by EFSA on 06 June 2018 (Austria, 2018). The peer review was initiated on 16 January 2019 by dispatching the DAR for consultation of the Member States and the applicant, Sunutton GmbH for consultation and comments. EFSA also provided comments. In addition, EFSA conducted a public consultation on the DAR. The comments received were collated by EFSA and forwarded to the RMS for compilation and evaluation in the format of a reporting table. The applicant was invited to respond to the comments in column 3 of the reporting table. The comments and the applicant response were evaluated by the RMS in column 3.

The need for expert consultation and the necessity for additional information to be submitted by the applicant in accordance with Article 12(3) of the Regulation were considered in a telephone conference between EFSA and the RMS on 14 May 2019. On the basis of the comments received, the applicant’s response to the comments and the RMS’s evaluation thereof, it was concluded that additional information should be requested from the applicant and that EFSA should conduct an expert consultation in the areas of mammalian toxicology and 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 EFSA in the format of an evaluation table.

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

In accordance with Article 12 of the Regulation, EFSA should adopt a conclusion on whether 24-epibrassinolide can be expected to meet the approval criteria provided for in Article 4 of the Regulation, taking into consideration recital (10) of the Regulation.

A final consultation on the conclusions arising from the peer review of the risk assessment and on the proposal for inclusion of the substance in Annex IV of Regulation (EC) No 396/2005 took place with Member States via a written procedure in April 2020.

This conclusion report summarises the outcome of the peer review of the risk assessment on the active substance and the representative formulation evaluated on the basis of the representative uses of 24-epibrassinolide as an elicitor on grapes, leafy vegetables, sugar beet and as plant activator on leafy vegetables and cucurbits, as proposed by the applicant. In accordance with Article 12(2) of

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

\(^{2}\) Regulation (EC) No 396/2005 of the European Parliament and of the Council of 23 February 2005 on maximum residue levels of pesticides in or on food and feed of plant and animal origin and amending Council Directive 91/414/EEC. OJ L 70, 16.3.2005, p. 1–16.
Regulation (EC) No 1107/2009, risk mitigation options identified in the DAR and considered during the peer review are presented in the conclusion.

Furthermore, this conclusion also addresses the requirement for an assessment by EFSA under Article 12 of Regulation (EC) No 396/2005, provided that the active substance will be approved under Regulation (EC) No 1107/2009 without restrictions affecting the residue assessment. In the event of a non-approval of the active substance or an approval with restrictions that have an impact on the residue assessment, the Annex IV proposal, if any, from this conclusion might no longer be relevant and a new assessment under Article 12 of Regulation (EC) No 396/2005 will be required.

A list of the relevant end points for the active substance and the formulation is provided in Appendix A.

In addition, a key supporting document to this conclusion is the peer review report (EFSA, 2020), which is a compilation of the documentation developed to evaluate and address all issues raised in the peer review, from the initial commenting phase to the conclusion. The peer review report comprises the following documents, in which all views expressed during the course of the peer review, including minority views where applicable, can be found:

- the comments received on the DAR;
- the reporting table (9 April 2019);
- the evaluation table (29 April 2020);
- the report(s) of the scientific consultation with Member State experts (where relevant);
- the comments received on the assessment of the additional information (where relevant);
- the comments received on the draft EFSA conclusion.

Given the importance of the DAR including its revisions (Austria, 2020) and the peer review report, both documents are considered as background documents to this conclusion.

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

The active substance and the formulated product

24-epibrassinolide is the common name (no ISO) for (3aS,5R,6S,7aR,7bS,9aS,10R,12aS,12bS)-10-((2S,3R,4R,5R)-3,4-dihydroxy-5,6-dimethylheptan-2-yl)-5,6-dihydroxy-7a,9a-dimethylhexadecahydro-3H-benzo[c]indeno[5,4-e]oxepin-3-one (IUPAC).

The representative formulated product for the evaluation was 'Sunergist', a soluble liquid (SL) containing 0.1 g/L 24-epibrassinolide.

The representative uses evaluated were spray application as an elicitor of plant’s self-defence mechanisms against fungal diseases on wine and table grapes, leafy vegetables (e.g. lettuce) and sugar beet and as a plant activator to protect plants against abiotic stresses in wine and table grapes and cucurbits. Greenhouse applications on leafy vegetables and cucurbits include permanent and non-permanent structures. Full details of the good agricultural practices (GAPs) can be found in the list of end points in Appendix A.

Data were submitted to conclude that the use of 24-epibrassinolide according to the representative uses proposed at EU level results in a sufficient elicitor efficacy following the guidance document SANCO/10054/2013 - rev. 3 (European Commission, 2013). It was concluded that the use as a plant activator is not supported by the efficacy data provided (data gap).

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: European Commission (2000a,b, 2010).

   The proposed specification for 24-epibrassinolide is based on batch data from industrial scale production. The proposed minimum purity of the technical material is 900 g/kg. The batches used in the (eco)toxicological assessment support the proposed reference specification (see Sections 2 and 5). There is no FAO specification available for 24-epibrassinolide.

   The main data regarding the identity of 24-epibrassinolide and its physical and chemical properties are reported in Appendix A.
Adequate methods are available for the generation of data required for the risk assessment. Methods of analysis are available for the determination of the active substance in the technical material and in the representative formulations and the impurities in the technical material.

No monitoring methods were needed since MRLs in food/feed of plant origin and animal products were not set. Methods for monitoring in air and for biomonitoring in body fluids and tissues were also considered not needed. Residue definition for monitoring in soil and water was set as 24-epibrassinolide, and as a consequence a data gap for monitoring methods in these two compartments was set.

2. Mammalian toxicity

24-epibrassinolide was discussed in the Pesticides Peer Review Meeting 18 in October 2019. Available toxicity studies indicated that 24-epibrassinolide is poorly absorbed by the oral route and it is of low acute toxicity by the oral, dermal and inhalation routes to rats. It is not a skin sensitiser and it is not an irritant to the skin or eyes. 24-epibrassinolide is unlikely to be genotoxic. The no observed adverse effect level (NOAEL) in the 90-day rat study is 300 mg/kg body weight (bw) per day based on decreased body weight and food consumption at 1,000 mg/kg bw per day. The developmental and maternal NOAEL in the rat developmental toxicity study is 1,000 mg/kg bw per day (the highest dose level tested). The batches used in toxicity studies were in line with the technical specification and relevant impurities were not identified.

24-epibrassinolide is considered similar to the plant sterols used as cholesterol-lowering substances in food supplements. Their efficacy as cholesterol-lowering substances in food supplements has been assessed by EFSA NDA Panel (2012). Owning to the nature of the active substance, data waivers for certain toxicological endpoints were accepted. Overall, it is not expected that the use of 24-epibrassinolide as a plant protection product will pose a risk to human health when compared to the use of similar plant sterols as food supplements.

The applicant did not submit further toxicity studies on 24-epibrassinolide such as reproductive toxicity or carcinogenicity studies. Likewise, data waiving on those endpoints was considered acceptable. Toxicological reference values were not allocated and a quantitative human risk assessment was not deemed necessary.

3. Residues

24-epibrassinolide is a brassinosteroid that is naturally occurring in higher and lower plants and some fungi.

According to the available scientific literature, the metabolism of exogenously applied and endogenous 24-epibrassinolide is similar and includes hydrogenation, hydroxylation, esterification and glycosylation steps. However, a uniform metabolism pathway cannot be established, and the pattern of compounds formed and the degradation time of 24-epibrassinolide can vary depending on the plant species, plant organ and the developmental stage. In addition, it is known that brassinosteroids are metabolised by some microorganisms into their corresponding 12β-hydroxylated brassinosteroid compounds.

In tests in wheat and cucumber, 14C-24-epibrassinolide was readily taken up and swiftly transported throughout plants when applied to the roots, while transport was generally very slow or not observed when 14C-24-epibrassinolide was applied to leaves. However, a difference in the metabolism steps and the resulting metabolites is not expected. The concentration of brassinosteroids in plants is regulated by a complex system of feedback pathways and brassinosteroids are constantly synthesised, metabolised, activated and inactivated depending on the plant’s needs as well as environmental cues. Consideration of uptake and fate of exogenously applied 24-epibrassinolide by plants via their roots was triggered by the DT90 of 24-epibrassinolide in soil (see Section 4) and could be addressed by the available information.

Altogether, the available information on uptake, metabolism and degradation of 24-epibrassinolide is sufficient and does not indicate the formation of compounds with the potential for concern to consumers.

Application rates of 24-epibrassinolide in crops are very low (less than 1 g/ha) and a calculation of hypothetical residues showed that for all representative uses, the possible residues would be well below 0.01 mg/kg and the natural endogenous brassinosteroid content in plant tissues.
Toxicological reference values for dietary risk assessment were not allocated (see Section 2), and a quantitative consumer risk assessment was considered unnecessary.

It is proposed to include 24-epibrassinolide into Annex IV of Regulation (EC) No 396/2005 since the inclusion criteria according to guidance document European Commission, 2015 are met.

4. Environmental fate and behaviour

24-epibrassinolide was discussed in the Pesticides Peer Review Meeting 19 in October 2019.

Brassinosteroids, including 24-epibrassinolide, are naturally occurring and ubiquitous plant constituents. Information on the natural existence of the substance in the environment and on the possible route and rate of degradation were found in the published scientific literature. Due to the natural occurrence of 24-epibrassinolide in plant tissues, exposure assessment for metabolites was considered unnecessary as the levels of active substance being applied were considered to be covered by the naturally present levels of brassinosteroids in terrestrial and aquatic plant organs, including leaves, that following the normal plant growth cycles reach soil and are naturally present in aquatic systems.

Although not much is known on the exact degradation pathway of brassinosteroids in soil, it is considered that the degradation pathway for synthesised 24-epibrassinolide will be the same as for the natural sources. Furthermore, as only low amounts of the synthesised molecule are proposed to be applied, the artificial release will only influence natural background levels to a limited extent.

In soil laboratory incubations from the public literature, 24-epibrassinolide exhibited moderate to medium persistence. Though the DT50 in soil triggered soil dissipation studies, these were considered not needed based on the ubiquitous presence of brassinosteroids in the soil environment consequent to their natural addition from decaying plant organs such as leaves and subsequent decomposition.

Experimental studies were not available for the determination of the mobility of 24-epibrassinolide in soil. However, quantitative structure-activity relationship (QSAR) estimations of the adsorption of 24-epibrassinolide were performed with KocWin 2.01. Two methods were used (MCI and Kow), resulting in the estimation of two different values. These values would indicate that 24-epibrassinolide might exhibit very high mobility or be immobile in soil. For the exposure assessment, it was decided to use the worst case of the two available estimated values depending on the environmental compartment investigated.

Degradation rates in natural sediment water systems could not be derived from the available scientific literature so the degradation rate resulting from a sterile hydrolysis experiment at pH 7 following normalisation to 20°C was used for the surface water and sediment exposure assessment.

The necessary surface water and sediment exposure assessments (Predicted environmental concentrations (PEC) calculations) were carried out for 24-epibrassinolide, using the FOCUS (FOCUS, 2001) step 1 and step 2 approach (version 3.2 of the Steps 1–2 in FOCUS calculator). The surface water and sediment exposure assessments for the representative protected uses were considered covered by the available calculations for the field uses.

The necessary groundwater exposure assessments were appropriately carried out using FOCUS (European Commission, 2014) scenarios and the models PEARL 4.4.4, PELOM 5.5.3 and MACRO 5.5.4. The potential for groundwater exposure from the representative uses by 24-epibrassinolide above the parametric drinking water limit of 0.1 μg/L (that might be applicable should managers consider that 24-epibrassinolide acts as a fungicide) was concluded to be low in geoclimatic situations that are represented by all nine FOCUS groundwater scenarios.

As PEC in groundwater and surface water for 24-epibrassinolide were calculated to be below 0.1 μg/L for the representative uses assessed and transformation products were assessed as being lower than natural background levels, residues that might be present in surface water and groundwater, when surface water or groundwater is abstracted for drinking water were considered too low to trigger the need to assess the effect of drinking water treatment processes on raw water residues.

The PEC in soil, surface water, sediment and groundwater covering the representative uses assessed can be found in Appendix A of this conclusion.

5. Ecotoxicology

The risk assessment was based on the following documents: European Commission (2002), SETAC (2001), EFSA (2009), EFSA PPR Panel (2013) and EFSA (2013).

3 Simulations utilised the agreed Q10 of 2.58 (following EFSA, 2008) and Walker equation coefficient of 0.7.
Toxicity data were not available for birds. Acute and long-term toxicity data (90-day chronic oral toxicity study) were available for the active substance, 24-epibrassinolide, for mammals. Furthermore, an acute toxicity study with mammals was also available for the representative product, Sunergist. As toxicity data were not available for birds, a quantitative risk assessment could not be performed. Instead, a weight-of-evidence assessment was performed which accounted for the natural occurrence of brassinosteroids in the diet of birds (and mammals) and an illustrative risk assessment assuming that the substance is 10 times more toxic to birds than mammals (which resulted in a high margin of safety being indicated). The available acute risk assessment for mammals indicated a low risk for all representative uses. A risk assessment was also presented using the endpoint from the available 90-day chronic oral toxicity study. This type of endpoint does not account for reproductive effects and therefore is not normally selected for risk assessment. Nevertheless, a low long-term (including reproductive effects) was concluded given that brassinosteroids naturally occur in the diet of mammals. A low risk to birds and mammals was also concluded for secondary poisoning and for intake via contaminated water.

Acute toxicity data were available for fish and aquatic invertebrates. Toxicity data were not available for algae or aquatic plants. Furthermore, chronic toxicity data were not available. Based on the available quantitative risk assessment, a low acute risk was concluded for fish and aquatic invertebrates for all representative uses. Owing to the lack of toxicity data, a quantitative chronic risk assessment for algae and aquatic plants was not available. Nevertheless, a low risk was concluded given that the application of 24-epibrassinolide, according to the representative use, is not likely to increase the natural background level of brassinosteroids.

Acute contact and oral toxicity data for honey bees were available. Data were not available for the chronic oral toxicity to honey bees, toxicity to honey bee larvae, sublethal effects to honey bees or accumulated effects to honey bees. Furthermore, toxicity data were not available for bumble bees or solitary bees.

Acute risk assessments, in accordance with both European Commission (2002) and EFSA (2013), were available. Both risk assessments indicated a low acute contact and oral risk to honeybees with a high margin of safety. Owing to the lack of toxicity data, a quantitative risk assessment could not be performed to cover the chronic risk to honeybees, risk to honeybee larvae or risk from sublethal effects. However, a low risk to bees was concluded based on a weight-of-evidence assessment which considered the natural background concentrations of brassinosteroids in plants and pollen and information from the scientific literature.

Tier 1 toxicity studies with the two standard species of non-target arthropods were available. A low risk to non-target arthropods was concluded based on the available tier 1 risk assessment.

Toxicity studies were not available for earthworms, other soil macroorganisms and soil microorganisms. Consequently, a quantitative risk assessment for soil organisms was not available. However, as discussed in Section 4, the representative use of 24-epibrassinolide is not likely to result in soil concentrations which are greater than the background level of brassinosteroids. Consequently, a low risk to earthworms, other soil macroorganisms and soil microorganisms was concluded.

Toxicity studies with non-target terrestrial plants were not available, so a quantitative risk assessment could not be carried out. It is stated that 24-epibrassinolide acts by activating and enhancing the defence and immune system of plants which would infer that no adverse effects on non-target plants are anticipated. Furthermore, literature information was provided which indicated that brassinosteroids, including 24-epibrassinolide, are naturally occurring plant growth promoting molecules found in plant tissues. Other studies indicated that exposure to brassinosteroids results in higher crop yield. Consequently, accounting for the available weight-of-evidence, a low risk to non-target terrestrial plants was concluded.

For the representative uses, a low risk to organisms involved in biological sewage treatment processes was concluded.

6. Endocrine disruption properties

An assessment of the endocrine-disrupting properties of 24-epibrassinolide was discussed at the Peer Review Experts’ meeting PREV 22 (January 2020).

24-Epibrassinolide is a plant hormone belonging to the brassinosteroid class of compounds and it is considered similar to the plant sterols used as cholesterol-lowering substances in food supplements.

Regarding human health, a complete data package according to data requirements is not available for 24-epibrassinolide. However, the overall weight of evidence indicates that based on lack of
any estrogen, androgen, thyroid, steroidogenesis (EATS) mediated adverse effect in the available data set, the expected low absorption of the substance and the similarity with plant sterols for which the absence of endocrine effects via the oral route was concluded (SCF, 2000) an assessment of endocrine-disrupting properties for human health in line with ECHA/EFSA Guidance (2018) did not appear necessary from a scientific point of view. This conclusion is further supported by an exposure through the representative uses is not expected to impact on the overall human exposure to naturally occurring brassinosteroids.

Likewise, for non-target organisms, an assessment of the endocrine properties in line with ECHA and EFSA (2018) was not available. However, the use of 24-epibrassinolide is not considered to increase the natural exposure of non-target organisms to brassinosteroids, based on the natural occurrence of brassinosteroids in environment considering the low application rate of 24-epibrassinolide according to the representative uses assessed. Additionally, there is no evidence in the literature that brassinosteroids may lead endocrine-mediated adversity in non-target organisms. Therefore, an assessment of endocrine-disrupting properties for non-target organisms in line with ECHA and EFSA (2018) did not appear necessary from a scientific point of view.

Considering the above, it can be concluded that 24-epibrassinolide does not meet the criteria for endocrine disruption for humans and non-target organisms according to points 3.6.5 and 3.8.2 of Annex II to Regulation (EC) No 1107/2009, as amended by Commission Regulation (EU) 2018/605⁴.

7. Overview of the risk assessment of compounds listed in residue definitions triggering assessment of effects data for the environmental compartments (Tables 1–4)

Table 1: Soil

| Compound (name and/or code) | Persistence | Ecotoxicology          |
|-----------------------------|-------------|------------------------|
| 24-epibrassinolide          | Moderate to medium persistence Single first-order DT50 22–70 days (laboratory conditions at 20°C, 60% MWHC soil moisture) | Low risk to soil organisms |

Table 2: Groundwater

| Compound (name and/or code) | Mobility in soil | > 0.1 µg/L at 1 m depth for the representative uses⁵ | Pesticidal activity | Toxicological relevance |
|-----------------------------|------------------|----------------------------------------------------|---------------------|------------------------|
| 24-epibrassinolide          | Very high mobility to immobile K<sub>Foc</sub> 27–82420 mL/g (estimated via QSAR) | No                     | Yes           | Low toxicity            |

(a): At least one FOCUS scenario or relevant lysimeter. Note that the parametric drinking water limit might be applicable should managers consider that 24-epibrassinolide acts as a fungicide. If just considered an elicitor of the plants defence mechanism, the parametric drinking water limit of the legislation might not apply.

Table 3: Surface water and sediment

| Compound (name and/or code) | Ecotoxicology |
|-----------------------------|---------------|
| 24-epibrassinolide          | Low risk to aquatic organisms |

Table 4: Air

| Compound (name and/or code) | Toxicology |
|-----------------------------|------------|
| 24-epibrassinolide          | Low acute toxicity by inhalation to rats |

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⁴ Commission Regulation (EU) 2018/605 of 19 April 2018 amending Annex II to Regulation (EC) No 1107/2009 by setting out scientific criteria for the determination of endocrine disrupting properties. OJ L 101, 20.4.2018, p. 33–36.
8. **Data gaps**

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

- Additional efficacy studies (relevant for plant activator use in wine and table grapes and cucurbits; see Section 1).
- Analytical methods for monitoring of 24-epibrassinolide in soil and water (relevant for all representative uses evaluated; see Section 1).

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

No particular conditions are proposed for the representative uses evaluated.

10. **Concerns**

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

An issue is listed as ‘could not be finalised’ if there is not enough information available to perform an assessment, even at the lowest tier level, for the representative uses in line with the uniform principles in accordance with Article 29(6) of the Regulation and as set out in Commission Regulation (EU) No 546/2011\(^5\) and if the issue is of such importance that it could, when finalised, become a concern (which would also be listed as a critical area of concern if it is of relevance to all representative uses).

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

None.

10.2. **Critical areas of concern**

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

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

An issue is also listed as a critical area of concern if, in the light of current scientific and technical knowledge using guidance documents available at the time of application, the active substance is not expected to meet the approval criteria provided for in Article 4 of the Regulation.

No critical areas of concern have been identified.

10.3. **Overview of the concerns identified for each representative use considered**

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

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\(^5\) Commission Regulation (EU) No 546/2011 of 10 June 2011 implementing Regulation (EC) No 1107/2009 of the European Parliament and of the Council as regards uniform principles for evaluation and authorisation of plant protection products. OJ L 155, 11.6.2011, p. 127–175.
Table 5: Overview of concerns

| Representative use                  | Wine grapes and table grapes (BBCH 15–85) | Wine grapes and table grapes (BBCH 71–79) | Leafy vegetables (field, greenhouse) | Sugar beet (field) | Cucurbits (greenhouse) |
|-------------------------------------|-------------------------------------------|-------------------------------------------|-------------------------------------|--------------------|------------------------|
| Operator risk                       | Risk identified                           |                                           |                                     |                    |                        |
|                                     | Assessment not finalised                  |                                           |                                     |                    |                        |
| Worker risk                         | Risk identified                           |                                           |                                     |                    |                        |
|                                     | Assessment not finalised                  |                                           |                                     |                    |                        |
| Resident/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 to active substance | Legal parametric value breached            |                                           |                                     |                    |                        |
|                                     | Assessment not finalised                  |                                           |                                     |                    |                        |
| Groundwater exposure to metabolites | Legal parametric value breached\(^{(a)}\)  | Parametric value of 10 µg/L\(^{(b)}\) breached | Assessment not finalised |                    |                        |

\(^{(a)}\): When the consideration for classification made in the context of this evaluation under Regulation (EC) No 1107/2009 is confirmed under Regulation (EC) No 1272/2008 of the European Parliament and of the Council of 16 December 2008.

\(^{(b)}\): Value for non-relevant metabolites prescribed in SANCO/221/2000-rev. 10 final, European Commission, 2003.

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**Abbreviations**

1/n slope of Freundlich isotherm

λ wavelength

ε decadic molar extinction coefficient

bw body weight

DAR draft assessment report

DT50 period required for 50% dissipation (define method of estimation)

DT90 period required for 90% dissipation (define method of estimation)

ECHA European Chemicals Agency

FAO Food and Agriculture Organization of the United Nations

FIR food intake rate
| Acronym | Definition |
|---------|------------|
| FOB     | functional observation battery |
| FOCUS   | Forum for the Co-ordination of Pesticide Fate Models and their Use |
| GAP     | Good Agricultural Practice |
| GM      | geometric mean |
| GS      | growth stage |
| ISO     | International Organization for Standardization |
| IUPAC   | International Union of Pure and Applied Chemistry |
| iv      | intravenous |
| K_{Foc} | Freundlich organic carbon adsorption coefficient |
| MCI     | molecular connectivity indices |
| mm      | millimetre (also used for mean measured concentrations) |
| mN      | milli-newton |
| MOA     | mode of action |
| MRL     | maximum residue level |
| MS      | mass spectrometry |
| MWHC    | maximum water-holding capacity |
| NOAEL   | no observed adverse effect level |
| 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 groundwater |
| PEC_{sed} | predicted environmental concentration in sediment |
| PEC_{soil} | predicted environmental concentration in soil |
| PEC_{sw} | predicted environmental concentration in surface water |
| pK_{a}  | negative logarithm (to the base 10) of the dissociation constant |
| P_{ow}  | partition coefficient between n-octanol and water |
| ppm     | parts per million (10^{-6}) |
| QSAR    | quantitative structure-activity relationship |
| SC      | suspension concentrate |
| SD      | standard deviation |
| SL      | soluble liquid |
| SMILES  | simplified molecular-input line-entry system |
| t_{1/2} | half-life (define method of estimation) |
| WHO     | World Health Organization |
Appendix A – List of end points for the active substance and the representative formulation

Appendix A can be found in the online version of this output ('Supporting information' section): https://doi.org/10.2903/j.efsa.2020.6132
## Appendix B – Used compound codes

| Code/trivial name<sup>(a)</sup> | IUPAC name/SMILES notation/InChiKey<sup>(b)</sup> | Structural formula<sup>(c)</sup> |
|-------------------------------|------------------------------------------------|---------------------------------|
| 24-epibrassinolide            | (3aS,5R,6S,7aR,7bS,9aS,10R,12aS,12bS)-10-((2S,3R,4R,5R)-3,4-dihydroxy-5,6-dimethylheptan-2-yl)-5,6-dihydroxy-7a,9a-dimethylhexadecahydro-3H-benzo[c]indeno[5,4-e]oxepin-3-one | ![Structural formula](image) |

<sup>(a)</sup>: The metabolite name in bold is the name used in the conclusion.

<sup>(b)</sup>: ACD/Name 2018.2.2 ACD/Labs 2018 Release (File version N50E41, Build 103230, 21 July 2018).

<sup>(c)</sup>: ACD/ChemSketch 2018.2.2 ACD/Labs 2018 Release (File version C60H41, Build 106041, 7 December 2018).