CONCLUSION ON PESTICIDES PEER REVIEW

EFSA Journal

ADOPTED: 4 January 2017

doi: 10.2903/j.efsa.2017.4693

Peer review of the pesticide risk assessment of the active substance bifenazate

European Food Safety Authority (EFSA)

Abstract

The conclusions of EFSA following the peer review of the initial risk assessments carried out by the competent authorities of the rapporteur Member State Sweden and co-rapporteur Member State Italy for the pesticide active substance bifenazate are reported. The context of the peer review was that required by Commission Implementing Regulation (EU) No 844/2012. The conclusions were reached on the basis of the evaluation of the representative uses of bifenazate as an acaricide on strawberry, fruiting vegetables (tomatoes, peppers, aubergines, cucumbers, courgettes, melons and watermelons), flowering and ornamental plants, and nursery ornamentals. The reliable end points, appropriate for use in regulatory risk assessment, are presented. Missing information identified as being required by the regulatory framework is listed. Concerns are identified.

Keywords: bifenazate, peer review, risk assessment, pesticide, acaricide

Requestor: European Commission

Question number: EFSA-Q-2014-00644

Correspondence: pesticides.peerreview@efsa.europa.eu

Amendment: An editorial correction was carried out that does not materially affect the contents or outcome of this scientific output. To avoid confusion, the older version has been removed from the EFSA Journal, but is available on request, as is a version showing all the changes made. In section 9.1 the correct code for the bifenazate-diazene metabolite is D3598 and not D9963 in relation to the consumer risk assessment issue.

Suggested citation: EFSA (European Food Safety Authority), 2017. Conclusion on the peer review of the pesticide risk assessment of the active substance bifenazate. EFSA Journal 2017;15(1):4693, 27 pp. doi:10.2903/j.efsa.2017.4693

ISSN: 1831-4732

The EFSA Journal is a publication of the European Food Safety Authority, an agency of the European Union.

Summary

Commission Implementing Regulation (EU) No 844/2012 (hereinafter referred to as 'the Regulation') lays down the procedure for the renewal of the approval of active substances submitted under Article 14 of Regulation (EC) No 1107/2009. The list of those substances is established in Commission Implementing Regulation (EU) No 686/2012. Bifenazate is one of the active substances listed in Regulation (EU) No 686/2012.

In accordance with Article 1 of the Regulation, the rapporteur Member State (RMS), Sweden, and co-rapporteur Member State (co-RMS), Italy, received an application from Arysta LifeScience Great Britain Limited for the renewal of approval of the active substance bifenazate. Complying with Article 8 of the Regulation, the RMS checked the completeness of the dossier and informed the applicant, the co-RMS (Italy), the European Commission and the European Food Safety Authority (EFSA) about the admissibility.

The RMS provided its initial evaluation of the dossier on bifenazate in the renewal assessment report (RAR), which was received by EFSA on 29 January 2016. In accordance with Article 12 of the Regulation, EFSA distributed the RAR to the Member States and the applicant, Arysta LifeScience Great Britain Limited, for comments on 5 February 2016. EFSA also provided comments. In addition, EFSA conducted a public consultation on the RAR. EFSA collated and forwarded all comments received to the European Commission on 10 May 2016.

Following consideration of the comments received on the RAR, 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, environmental fate and behaviour, and ecotoxicology.

In accordance with Article 13(1) of the Regulation, EFSA should adopt a conclusion on whether bifenazate can be expected to meet the approval criteria provided for in Article 4 of Regulation (EC) No 1107/2009 of the European Parliament and of the Council.

The conclusions laid down in this report were reached on the basis of the evaluation of the representative uses of bifenazate as an acaricide on strawberry, fruiting vegetables (tomatoes, peppers, aubergines, cucumbers, courgettes, melons and watermelons), flowering and ornamental plants, and nursery ornamentals, as proposed by the applicant. Full details of the representative uses can be found in Appendix A of this report.

Data were submitted to conclude that the uses of bifenazate according to the representative uses proposed at the European Union (EU) level result in a sufficient acaricidal efficacy against the target organisms.

A data gap was identified for a search of the scientific peer-reviewed open literature on the relevant metabolites and more details are needed concerning the available literature search for the active substance.

A data gap was identified for a monitoring method for body fluids. As the residue definitions for soil and groundwater for monitoring were concluded as bifenazate only, a data gap was identified for a monitoring method analysing just bifenazate.

For mammalian toxicology, data gaps are set for the analytical methods used in each of the toxicological studies that are not reported for a comparative *in vitro* metabolism study including human material and for the phototoxicity/photomutagenicity potential of bifenazate. In addition, further clarifications are required to assess the endocrine disrupting properties of bifenazate. Moreover, toxicological data are needed (repeated dose toxicity study and genotoxicity data) for three metabolites, D3598, A1530S and carbamate. Finally, some risks are noted for operators treating strawberries (downward applications) using manual hand-held sprayers, workers handling ornamentals outdoor, and operators and workers treating and handling any of the indoor representative crops.

A series of data gaps were identified in the residue section, and moreover, the finalisation of the toxicological assessment of metabolites including bifenazate-diazene, part of the residue definition for the risk assessment and monitoring, is pending. Therefore, the consumer risk assessment can only be preliminarily conducted for a limited number of crops (strawberry and tomato) and not on the full range of crops included in the representative uses.

A data gap was identified due to the unknown identity of soil and sediment water metabolites IMH/IBMHC (chromatographic retention time 38 min) and IBMHC/DDC (chromatographic retention time 37.3 min). Furthermore, for these two metabolites, a data gap was identified for the soil adsorption endpoints to be derived. The proposed structures of metabolites DPHPDD and hydroxylated D3598 were not confirmed against authentic reference standards; therefore, a data gap was identified. For

the surface water and sediment exposure assessments, several data gaps were identified. In particular, calculations for metabolites D9963 and D9472 were not acceptable; step 3 calculations for the representative use in strawberries, and step 2 and 3 calculations for the representative use in ornamental plants were not available for bifenazate and its metabolites. A data gap was identified for information on the effect of water treatment processes on the nature of residues of metabolites potentially present in surface water, when surface water is abstracted for drinking water. This gap leads to the consumer risk assessment from the consumption of drinking water being not finalised for all the representative uses.

In the area of ecotoxicology, data gaps were identified to further address the risk to birds and mammals, aquatic organisms, honeybees and other non-target arthropods, and soil microorganisms. Critical areas of concerns were identified for birds and mammals, and non-target arthropods; a high risk was identified for all representative uses. In the absence of suitable exposure estimates, the aquatic risk assessment for bifenazate and its pertinent metabolites (uses on ornamentals) and for metabolites D9963 and D9472 (uses on strawberries and fruiting vegetables) could not be finalised.

Table of contents

Background

Commission Implementing Regulation (EU) No 844/2012[1] (hereinafter referred to as 'the Regulation') lays down the provisions for the procedure of the renewal of the approval of active substances, submitted under Article 14 of Regulation (EC) No 1107/2009[2]. This regulates for the European Food Safety Authority (EFSA) the procedure for organising the consultation of the Member States, the applicant(s) and the public on the initial evaluation provided by the rapporteur Member State (RMS) and/or co-rapporteur Member State (co-RMS) in the renewal assessment report (RAR), and the organisation of an expert consultation where appropriate.

In accordance with Article 13 of the Regulation, unless formally informed by the European Commission that a conclusion is not necessary, EFSA is required to adopt a conclusion on whether the active substance can be expected to meet the approval criteria provided for in Article 4 of Regulation (EC) No 1107/2009 within 5 months from the end of the period provided for the submission of written comments, subject to an extension of up to 8 months where additional information is required to be submitted by the applicant(s) in accordance with Article 13(3).

In accordance with Article 1 of the Regulation, the RMS, Sweden, and co-RMS, Italy, received an application from Arysta LifeScience Great Britain Limited for the renewal of approval of the active substance bifenazate. Complying with Article 8 of the Regulation, the RMS checked the completeness of the dossier and informed the applicant, the co-RMS (Italy), the European Commission and EFSA about the admissibility.

The RMS provided its initial evaluation of the dossier on bifenazate in the RAR, which was received by EFSA on 29 January 2016 (Sweden, 2016a).

In accordance with Article 12 of the Regulation, EFSA distributed the RAR to the Member States and the applicant, Arysta LifeScience Great Britain Limited, for consultation and comments on 5 February 2016. EFSA also provided comments. In addition, EFSA conducted a public consultation on the RAR. EFSA collated and forwarded all comments received to the European Commission on 10 May 2016. At the same time, the collated comments were 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 13(3) of the Regulation were considered in a telephone conference between EFSA and the RMS on 28 June 2016. 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, environmental fate and behaviour, and ecotoxicology.

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 and the written consultation on the assessment of additional information, where these 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 the Member States via a written procedure in December 2016.

This conclusion report summarises the outcome of the peer review of the risk assessment of the active substance and the representative formulation, evaluated on the basis of the representative uses of bifenazate as an acaricide on strawberry, fruiting vegetables (tomatoes, peppers, aubergines,

[1] Commission Implementing Regulation (EU) No 844/2012 of 18 September 2012 setting out the provisions necessary for the implementation of the renewal procedure for active substances, as provided for in Regulation (EC) No 1107/2009 of the European Parliament and of the Council concerning the placing of plant protection products on the market. OJ L 252, 19.9.2012, p. 26–32.

[2] 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.

cucumbers, courgettes, melons and watermelons), flowering and ornamental plants, and nursery of ornamentals, as proposed by the applicant. A list of the relevant end points for the active substance and the formulation is provided in Appendix A.

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

- the comments received on the RAR;
- the reporting table (28 June 2016);
- the evaluation table (6 December 2016);
- the reports of the scientific consultation with the 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 RAR, including its revisions (Sweden, 2016a,b), and the peer review report, both documents are considered as background documents to this conclusion and thus are made publicly available.

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

The active substance and the formulated product

Bifenazate is the ISO common name for isopropyl 3-(4-methoxybiphenyl-3-yl)carbazate or isopropyl 2-(4-methoxybiphenyl-3-yl)hydrazinoformate (IUPAC).

The representative formulated product for the evaluation was 'Floramite 240 SC (UBI 6704-06)', a suspension concentrate (SC) containing 240 g/L bifenazate.

The representative uses evaluated were foliar spray applications for the control of *Tetranychus urticae* in field and protected: strawberry, fruiting vegetables (tomatoes, peppers, aubergines, cucumbers, courgettes, melons and watermelons), flowering and ornamental plants, and nursery of ornamentals. 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 uses of bifenazate according to the representative uses proposed at the EU level result in a sufficient acaricidal efficacy against the target organisms, following the guidance document SANCO/10054/2013 – rev. 3 (European Commission, 2013).

A data gap has been identified for a search of the scientific peer-reviewed open literature on the relevant metabolites, dealing with side effects on health, the environment and non-target species, and published within the 10 years before the date of submission of the dossier, to be conducted and reported in accordance with the EFSA guidance on the submission of scientific peer-reviewed open literature for the approval of pesticide active substances under Regulation (EC) No 1107/2009 (EFSA, 2011a). Concerning the active substance, the data available are not reported in sufficient detail in the RAR.

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/3029/99-rev. 4 (European Commission, 2000a), SANCO/3030/99-rev. 4 (European Commission, 2000b) and SANCO/825/00-rev. 8.1 (European Commission, 2010).

The reference specification of the first approval was updated. The proposed specification is based on batch data from industrial scale production. The minimum purity of the active substance as manufactured is 980 g/kg. There is no FAO specification available.

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 bifenazate or the representative formulation. The main data regarding the identity of bifenazate and its physical and chemical properties are given in Appendix A.

Some of the methods for the generation of pre-approval data required for the risk assessment did not fully meet the requirements of the guidance document; however, they were considered fit for purpose. High-performance liquid chromatography-ultraviolet (HPLC-UV) methods are available for the determination of bifenazate in the technical material and in the representative formulation.

The sum of the residues of bifenazate and bifenazate-diazene (D3598), expressed as bifenazate can be monitored in food and feed of plant origin by liquid chromatography with tandem mass spectrometry (LC–MS/MS) with a limit of quantification (LOQ) of 0.01 mg/kg in all plant commodity groups, except hops in which the LOQ is 0.1 mg/kg. An analytical method for monitoring residues in food and feed of animal origin is not needed as no maximum residue levels (MRLs) were proposed for the animal matrices. A LC–MS/MS method is available for the determination of the residues of the sum of bifenazate and bifenazate-diazene, expressed as bifenazate in soil with a LOQ of 0.01 mg/kg. It should be noted, however, that the residue definition for monitoring was concluded as bifenazate only, meaning that a data gap was identified for a monitoring method analysing just bifenazate. The determination of bifenazate and bifenazate-diazene, expressed as bifenazate in drinking water and surface water can be done by LC–MS/MS with a LOQ of 0.1 μg/L. The residue definition for monitoring in ground water was concluded as bifenazate only, as a consequence, a data gap was identified for a monitoring method in groundwater. Monitoring of the residues of bifenazate in air can be done by LC–MS/MS with a LOQ of 0.4 $\mu g/m^3$.

The determination of residues of bifenazate and metabolites bifenazate-diazene (quantified as bifenazate), A1530 and A1530S (quantified as A1530) in bovine kidney, liver, milk and fat can be done by LC–MS/MS with a LOQ of 0.01 mg/kg for all commodities. A data gap was, however, identified for a monitoring method in body fluids.

2. Mammalian toxicity

The toxicological profile of the active substance bifenazate and its metabolites was discussed at the Pesticides Peer Review experts' TC 148 and assessed based on the following guidance documents: SANCO/221/2000-rev. 10-final (European Commission, 2003), SANCO/10597/2003-rev. 10.1 (European Commission, 2012) and Guidance on dermal absorption (EFSA PPR Panel, 2012).

To assess the toxicological profile of the **active substance**, the applicant submitted a complete set of valid toxicity studies. The toxicity studies were representative of the proposed technical specification for the active substance and associated impurities. Toluene is identified as relevant impurity (max of 0.7 g/kg). The analytical methods used in each of the toxicological studies are not reported, a data gap is set.

In the toxicokinetics studies, oral absorption is estimated to be 36%. Bifenazate is widely distributed (highest residues in the liver, kidney, whole blood, heart, spleen, red blood cells and lungs) and there is no evidence for accumulation. Excretion of substance is predominantly through the bile at low dose and via faeces for high dose. At low dose, it is extensively metabolised, less at high dose and the metabolites are formed following hydrazine oxidation demethylation, ring hydroxylation, elimination of hydrazine carboxylic acid part and conjugation with glucuronic acid or sulfate. A data gap is set for the comparative *in vitro* metabolism study including human material that should be performed as required in Regulation (EU) No 283/2013.

In the acute toxicity studies, the substance has a low acute toxicity when administered orally, dermally or by inhalation to rats. It is not a skin or an eye irritant but it is a skin sensitiser in guinea pig maximisation test. A harmonised classification Skin Sens. 1, H317[3] (may cause an allergic skin reaction) exists. The available OECD 3T3 NRU-PT test does not allow concluding properly on the phototoxicity potential of bifenazate (data gap) since the substance as its maximum UV/VIS absorption within UVB range. It is noted, however, that there is no validated test for UVB absorbers leading to a data gap. The photomutagenicity potential should be reconsidered once phototoxicity potential of bifenazate is addressed.

The most sensitive species is the dog. The relevant short- and long-term oral no observed adverse effect level (NOAEL) is 1 mg/kg body weight (bw) per day. This value is based on liver and haematological effects observed in the 90-day and 1-year dog studies (changes in the kidney and bone marrow are also observed in the 1-year study). In the 2-year rat study supported by the 18-month mice study, the NOAEL of 1 mg/kg bw per day is based on spleen and haematological effects. Based on the observed effects in the short-term studies, the harmonised classification STOT RE 2, H373[3] (may cause damage to organs through repeated exposure) is supported by the experts.

Bifenazate is unlikely to be genotoxic based on available genotoxicity studies: Ames test, mouse lymphoma mutagenesis assay, *in vitro* cytogenetic test and *in vivo* micronucleus test. In a chronic/carcinogenicity study in rat, liver tumours and haematopoietic neoplasia are observed but not dose related. In addition, further data on mammary tumours have been submitted after the Pesticide Peer Review experts' meeting. There is no dose–response for mammary carcinomas, multiple mammary carcinomas in unscheduled deaths, interim and terminally sacrificed animals. In addition, when considering the total number of mammary carcinomas, no dose response is observed. In a carcinogenicity study in mice, no treatment-related increased incidence in tumours is reported. An increase in adenoma in 10 out of 48 males at the highest dose is not statistically significant and is the only effect treatment related. The incidence of haematopoietic neoplasia (spleen, thymus and blood) in female mice is reported as not dose related. To conclude based on the available data, bifenazate does not show a carcinogenic potential.

In the two-generation study in rats, the agreed parental NOAEL is 1.5 mg/kg bw per day based bodyweight and bodyweight gain reduction. EFSA does not support the arguments presented by the RMS to disregard both the body weight effects and delay in vaginal opening as treatment-related effect relevant to the offspring and the reproduction, even if these effects are observed in the presence of parental toxicity. In EFSA's view, it is considered that the delay in vaginal opening should be taken into consideration for the setting of the reproduction NOAEL and the reduced bodyweight for the offspring's NOAEL. This does not change the risk assessment as parental toxicity is also observed

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

at the same dose level. EFSA proposes to set the both NOAELs at 6.1 mg/kg bw per day based on these effects.

In the developmental toxicity study in rat, developmental toxicity (retroesophageal aortic arch) was observed at a dose eliciting maternal toxicity. The relevant maternal and developmental NOAELs are 10 mg/kg bw per day and 100 mg/kg bw per day for the rat, respectively. In rabbits, no maternal or developmental toxicity were observed and both the maternal and developmental NOAELs are 200 mg/kg bw per day, the highest dose tested.

The substance does not show a neurotoxic potential in an acute neurotoxicity study in rats. The neurotoxicity NOAEL for the short-term neurotoxicity study is 13 mg/kg bw per day, based on reduced rearing at the lowest observable adverse effect level (LOAEL) of 35 mg/kg bw per day.

No alert on immunotoxicity is observed based on a 28-day immunotoxicity study in mice and based on the available data package.

Bifenazate is not classified or proposed to be classified as carcinogenic category 2 and as toxic for reproduction category 2, in accordance with the provisions of Regulation (EC) No 1272/2008[3] and, therefore, the conditions of the interim provisions of Annex II, Point 3.6.5 of Regulation (EC) No 1107/2009 concerning human health for the consideration of endocrine disrupting properties are not met. During the Pesticide Peer Review experts' meeting, the majority of the experts did not see evidence for endocrine disrupting properties for bifenazate; however, some indications are observed for one main metabolite (uterotrophic assay from literature search) and delay in vaginal opening with the parent that may require further clarification (such as level 2/3 of the OECD conceptual Framework for the identification of endocrine disruptors).

The acceptable daily intake (ADI) is the same set during the first review (European Commission, 2005), of 0.01 mg/kg bw per day based on the NOAEL of 1 mg/kg bw per day for spleen, liver and haematological effects observed in the 1-year dog and 2-year rat studies, supported by the 18-month mice study, applying an uncertainty factor (UF) of 100. The acceptable operator exposure level (AOEL) is 0.0036 mg/kg bw per day based on the same effects recorded for the ADI from the 1-year dog study, applying an UF of 100 and correcting for the limited oral absorption by 36%. The AOEL has been changed compared to that set during the first peer review as the oral absorption value has been increased from 28% to 36%.

An acute reference dose (ARfD) was not set under the first review (European Commission, 2005). An ARfD of 0.1 mg/kg bw and also an acute AOEL (AAOEL) of 0.036 mg/kg bw per day are derived, based on the maternal NOAEL of 10 mg/kg bw per day for early reduced body weight gain from the rat developmental toxicity study and applying an UF of 100, corrected by the limited oral absorption value of 36% for AAOEL.

The RMS estimated **non-dietary exposure** (i.e. operator, worker, bystander and resident) as a first Tier with dermal absorption values derived from the *in vitro* dermal absorption study on human skin, i.e. 2.4% for the concentrate and 75% for the in-use field dilution. Using these dermal absorption values, all operator exposure estimates exceed the AOEL. As a refinement, it was agreed to derive dermal absorption using a triple pack approach, the resulting dermal absorption values are 1% for the concentrate and 24% for the in-use field dilutions. Considering these revised dermal absorption values, protective measures have to be followed to ensure that the level of operator and worker exposure does not exceed the AOEL. Even so, some exposure estimates remain above the AOEL: operators treating strawberries (downward applications) using a manual hand-held sprayer, workers handling ornamentals outdoor, and operators and workers treating and handling any of the indoor representative crops. Bystander exposure does not exceed the AOEL. Resident's exposure exceeds the AOEL according to the EFSA calculator, while according to Martin et al. calculations, residents exposure represents up to 14% of the AOEL.

Three **metabolites** (bifenazate-diazene (D3598), A1530S and carbamate) are found in residues for which data are needed (data gap).

More robust data to determine the toxicological profile of D3598 (also rat metabolite) should be submitted. Indeed, quantitative structure–activity relationship (QSAR) analysis has been performed but the full output file is not available. RMS has checked the presence of alerts for genotoxicity using the OECD Toolbox. The only alert found is observed in D3598 and bifenazate. Nevertheless, no data are available for the other endpoints and a toxicological reference value should be set in order to assess the risk for consumer. Therefore, further data are needed to derive a toxicological reference value. Concerning metabolite A1530S (biphenyl-4-yl sulfate) and carbamate (isopropyl (4-methoxybiphenyl-3-yl)carbamate), no toxicological data are available; therefore, data are required in order to assess the risk for consumer, a repeated dose toxicity study and genotoxicity data.

3. Residues

The assessment in the residue section is based on the OECD guidance document on overview of residue chemistry studies (OECD, 2009), the OECD publication on MRL calculations (OECD, 2011), the European Commission guideline document on MRL setting (European Commission, 2011).

Metabolism of bifenazate was investigated after foliar applications in the categories of fruit (oranges, apples and grapes), pulses and oilseeds (cotton), cereals and grass crops (maize), and root crops (radish) using bifenazate ^{14}C-labelled in the substituted phenyl ring.

In fruits, bifenazate was the main component of the total radioactive residue (TRR) (34–79% TRR) with bifenazate-diazene (D3598) present as the pertinent metabolite (up to 40% of the TRR). In radish, cotton and maize, low translocation of radioactivity to radish roots, cotton seed and maize grain was observed. No identification was attempted in radish roots. Radioactivity in cotton seeds was mostly incorporated into natural compounds. Analysis of radish tops and cotton gin trash confirmed that parent bifenazate was the major residue on the plant parts that were directly exposed to the treatment. Metabolism in maize resulted in a range of metabolites in the different commodities. It is noted that in cereals the metabolic breakdown of bifenazate had progressed further then in the other crops, so that in maize grain parent was not detected while A1530S was the only compound identified, and in maize stover, parent was not the major residue (2–6% TRR) but metabolites bifenazate-diazene (6–10% TRR), A1530S (8–12% TRR) and carbamate (isopropyl (4-methoxybiphenyl-3-yl)carbamate) (8–14% TRR) were the pertinent residues. However, overall the metabolite picture is consistent and qualitatively comparable across the different crop categories.

It is proposed to define the residue for both enforcement and risk assessment in fruits as the sum of bifenazate and bifenazate-diazene, expressed as bifenazate, pending confirmation that the same toxicological reference values can be used for bifenazate and bifenazate-diazene (see Section 2). Regarding the possibility of setting a global plant residue definition for risk assessment, it is necessary to take into account all commodities including feed items and thus to further consider the relevance of the major metabolites A1530S and carbamate in the cereal metabolism. For monitoring, the sum of bifenazate and bifenazate-diazene, expressed as bifenazate is considered containing compounds that are good markers across all plant commodities. The inclusion of bifenazate-diazene is also necessary in view of the available analytical method.

In a confined rotational crop study with ^{14}C-labelled bifenazate residues in succeeding carrots, lettuce and wheat at twice, the nominal rate the TRRs in mature food commodities (lettuce, carrot and wheat grain) were less than 0.02 mg/kg for all plant-back intervals, significant residue levels were only found in feed commodities. Identification attempts failed as neither bifenazate nor any of the primary crop plant metabolites could be identified in rotational crops. It is unknown whether the uptake of soil specific metabolites, e.g. with the carbazole structure such as IBMHC/DDC (DT_{90} up to 154.7 days) was investigated. However, in view of the representative uses under peer review, given the twofold application rate to bare soil in the available study, the data can be used to conclude that significant individual residue compounds are unlikely to be present in rotational crops, while for a more critical use pattern in terms of application rate the issue may have to be reconsidered.

Acceptable storage stability tests are only available with parent bifenazate for up to 6 months in strawberries, showing acceptable stability of residue analysed as the sum of bifenazate and bifenazate-diazene. Fortification with bifenazate-diazene was not conducted and thus storage stability of bifenazate-diazene was not tested over a reproducible period of time (data gap).

Significant degradation of both bifenazate and bifenazate-diazene was observed when studied separately in the fruiting vegetable/cucurbit commodity category, or the number of fortified stored samples was insufficient, respectively. Thus, storage stability of residues is insufficiently addressed. Pending the availability of guideline conforming storage stability studies for both the relevant analytes over the full storage period used in the magnitude-of-residue studies, only the residue trials with storage up to 1 month were considered for further assessment.

Under these circumstances, the number of residue trials was insufficient for protected tomatoes (six trials) and field tomatoes in northern Europe (NEU) (four trials) and southern Europe (SEU) (two trials) as a minimum number of eight trials is required. The data confirm that from a residue perspective the critical use is in protected tomatoes when a comparable good agricultural practice (cGAP) is followed for the protected and non-protected crop. Three trials each per crop and zone were submitted in peppers and courgettes/cucumbers conducted in the field, but the period of sample storage in these trials exceeded the period for which residue stability could be demonstrated. Given the representative

uses are in the whole fruiting vegetables category, complete data sets of residue trials (indoor and outdoor) supported by acceptable storage stability data are necessary in order to support the critical uses in the whole category of fruiting vegetables (tomatoes, peppers, cucurbits edible peel, cucurbits inedible peel and sweet corn).

For strawberries, the proportionality principle was inconsistently applied in the residue trials addressing the same representative use in the field. If considered an option, the principle should be applied to every relevant trial submitted for the representative use as defined in the GAP table, specifically if the assessment outcome would be more critical. Moreover, the full validity of the strawberry trials is pending confirmation of storage stability of metabolite bifenazate-diazene. Therefore, review of the strawberry trials assessment is deemed necessary (data gap).

A data gap was also set with regard to potential residue levels in pollen and bee products.

In a study simulating food processing conditions, bifenazate was hydrolytically stable under all the conditions tested in this study, with bifenazate-diazene less than 2% applied radioactivity (AR). The behaviour of bifenazate-diazene under processing was not tested (data gap).

The representative uses do not give rise to significant exposure of food-producing animals, and no studies with such animals were submitted and assessed during the peer review. Therefore, a peer-reviewed animal residue definition is not available.

In view of a series of issues identified in Section 3 that still need clarification or have to be addressed by further data and for the pending finalisation of the toxicological assessment of metabolite bifenazate-diazene, the consumer risk assessment can only be preliminarily conducted for a limited number of crops (tomato and strawberry), and this preliminary assessment does not indicate a dietary intake concern.

The residue definition for enforcement and monitoring has not been changed compared to those used in the review of the existing MRLs for bifenazate (EFSA, 2011b). Whether a global plant residue definition for risk assessment can be derived and whether it is confirmed as the sum of both compounds currently included is pending, finalisation of both the toxicological and the relevance assessment of major plant metabolites. Therefore, once sufficient data and information is available to finalise the assessment on metabolites with regard to their toxicological properties, a revision of the Article 12 reasoned opinion may be necessary. In addition, an ARfD has been derived during the peer review that was not available at the time of the review of the existing MRLs for bifenazate. On the basis of the uses assessed during the review of the existing maximum residue levels (Art. 12) and with the assumption that the toxicological reference values of bifenazate can be applied to bifenazate-diazene, an acute intake concern cannot be excluded for peppers.

4. Environmental fate and behaviour

Bifenazate was discussed at the Pesticides Peer Review TC 141 in October 2016.

The rates of dissipation and degradation in the environmental matrices investigated were estimated using the FOCUS (2006) kinetics guidance. In soil laboratory incubations under aerobic conditions in the dark, bifenazate exhibited very low to low persistence forming the major (> 10% applied radioactivity (AR) or > 5% AR in at least two sequential measurements) metabolites bifenazate-diazene (D3598, max. 85.5% AR), which exhibited very low to low persistence, D1989 (max. 33.3% AR), which exhibited low to moderate persistence, IMH/IBMHC (chromatographic retention time 38 min, max. 12.5% AR) and IBMHC/DDC (chromatographic retention time 37.3 min, max. 6.9% AR), which exhibited moderate persistence. Experts expressed their concerns on the identity of metabolites IMH/IBMHC (retention time 38 min) and IBMHC/DDC (retention time 37.3 min); however, they accepted the kinetic assessment and the pathway scheme proposed. Therefore, a data gap was identified (see Section 7) because the identity of metabolites IMH/IBMHC (retention time 38 min) and IBMHC/DDC (retention time 37.3 min) is unknown.

Mineralisation of the phenyl ring ^{14}C radiolabel to carbon dioxide accounted for 15.2–23.0% AR after 119 days and 4.0–9.1% AR after 30 days. The formation of unextractable residues (not extracted by acetonitrile/water) for this radiolabel accounted for 64.0–67.3% AR after 119 days and for 53.6–66.8% after 30 days.

In anaerobic soil incubations, bifenazate transformation was similar to that under aerobic conditions, forming the major (> 10% AR) metabolites D3598 (max. 50.2% AR) and D1989 (max. 30.6% AR). Additionally, the major metabolite A1530 (max. 20.7% AR) was formed. Metabolite A1530 was only detected under anaerobic conditions. Anaerobic conditions were not considered to be of major importance for the representative uses. The anaerobic DT_{50} will not be used for the present risk

assessment. However, for uses of bifenazate on other crops than the representative uses considered here and/or with altered application timings, the importance of anaerobic conditions would need to be re-evaluated and metabolites formed under anaerobic conditions (such as A1530) might need to be addressed further. Bifenazate is quickly photodegraded on the soil surface, but the degradation is similar under dark control and irradiated conditions. Photodegradation in soil is not a major transformation pathway of bifenazate.

Bifenazate exhibited medium to low mobility in soil. It was concluded that the adsorption of bifenazate was not pH dependent. Metabolite D3598 exhibited slight mobility or was immobile, metabolite D1989 exhibited slight mobility. It was concluded that the adsorption of these metabolites was not pH dependent. Metabolites IMH/IBMHC (retention time 38 min) and IBMHC/DDC (retention time 37.3 min) exhibited immobility, but adsorption values were obtained via QSAR and LOQ estimations. This approach was considered acceptable for completing the exposure assessment for the representative uses; however, a data gap was identified for deriving adsorption endpoints for both metabolites.

In laboratory incubations in dark aerobic natural sediment water systems, bifenazate exhibited very low persistence, forming metabolites D3598 (max. 33.6% AR in the total system after 100 days), IMH/IBMHC (retention time 38 min, max. 23.9% AR in the total system after 15 days), D9472 (max. 21.6% AR in the total system after 100 days), IBMHC/DDC (retention time 37.3 min, max. 12.7% AR in the total system after 15 days). The unextractable sediment fraction (not extracted by acetonitrile/water) accounted for 52.4–65.7% AR at study end (15 days) and for 46.9–65.2% AR at study end (100 days) for the phenyl ring ^{14}C radiolabel. Mineralisation accounted for 2.8–12.0% AR at study end (15 days) and for 18.9–33.7% AR at study end (100 days) for the phenyl ring ^{14}C radiolabel.

Chromatographically resolved components accounting for > 10% AR were D3598 (65.7% AR at study end (12 h)), D9963 (30.4% AR at study end (150 h)), D9472 (18.6% AR after 2 days), D1989 (13.1% AR after 54 h) and hydroxylated D3598 (18.0% AR after 4 days).

Metabolite DPHPDD is an unknown component formed in the sterile hydrolysis study and metabolite hydroxylated D3598 is an unknown component formed in the sterile aqueous photolysis study. A data gap was identified for metabolites DPHPDD and hydroxylated D3598 because the proposed structures were not confirmed against authentic reference standards. However, these metabolites were included in the surface water and sediment exposure assessment based on default parameters.

The necessary surface water and sediment exposure assessments (predicted environmental concentrations (PEC) calculations) were carried out for bifenazate and its metabolites D3598, D1989, IMH/IBMHC (retention time 38 min), IBMHC/DDC (retention time 37.3 min), D9963, D9472, hydroxylated D3598 and DPHPDD, using the FOCUS (FOCUS, 2001) step 1 and step 2 (version 3.2 of the Steps 1–2 in FOCUS calculator), and step 3 approach.

A data gap was identified for step 3 calculations for the representative use in strawberries and for steps 2 and 3 calculations for the representative use in ornamental plants for bifenazate and its metabolites D3598, D1989, IMH/IBMHC (retention time 38 min), IBMHC/DDC (retention time 37.3 min), hydroxylated D3598 and DPHPDD. This leads to the surface water and sediment exposure assessment being not finalised for representative use in ornamental plants (see Sections 5 and 9). A data gap was identified for surface water and sediment exposure assessment for all representative uses for metabolites D9963 and D9472, because in the absence of adsorption endpoints conservative values should be used. This leads to the surface water exposure assessment being not finalised for metabolites D9963 and D9472 (see Sections 5 and 9). Adsorption endpoints used for metabolites IMH/IBMHC (retention time 38 min), IBMHC/DDC (retention time 37.3 min), hydroxylated D3598 and DPHPDD were conservative, and thus, in this particular case, the choice of these values for the surface water exposure assessment is acceptable.

The necessary groundwater exposure assessments were appropriately carried out using FOCUS (FOCUS, 2009) scenarios and the models PEARL 4.4.4 and PELMO 5.5.3 for the active substance bifenazate and its metabolites D3598, D1989, IMH/IBMHC (retention time 38 min) and IBMHC/DDC (retention time 37.3 min). Two sets of calculations were performed for an early and a late application using two applications every year. Due to the uncertainty in their identification, for metabolites IMH/IBMHC (retention time 38 min) and IBMHC/DDC (retention time 37.3 min), simulations were carried out using adsorption values from the QSAR estimation and a worst-case estimate based on the LOQ for IBMHC/DDC (retention time 37.3 min) and from the worst-case estimate based on the LOQ for IMH/IBMHC (retention time 38 min). The potential for groundwater exposure from the representative uses by bifenazate above the parametric drinking water limit of 0.1 μg/L was concluded to be low in geoclimatic situations that are represented by all FOCUS groundwater scenarios for all the

representative uses. For metabolites D3598, D1989, IMH/IBMHC (retention time 38 min) and IBMHC/DDC (retention time 37.3 min), the potential for groundwater exposure above the parametric drinking water limit of 0.1 μg/L was concluded to be low in all geoclimatic situations that are represented by all the relevant FOCUS groundwater scenarios.

The applicant made the case that for the glasshouse uses the risk assessment will be covered by the field uses, and then no specific calculations were performed in accordance with the EFSA guidance (EFSA, 2014).

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

The applicant provided information to address the effect of water treatments processes on bifenazate and metabolite D3598 residues that might be present in surface water; however, appropriate information to address the effect of water treatments processes on metabolites D1989, IMH/IBMHC (retention time 38 min), IBMHC/DDC (retention time 37.3 min), D9963, D9472, hydroxylated D3598 and DPHPDD residues that might be present in surface water, when surface water is abstracted for drinking water were not provided. This has led to the identification of a data gap (see Section 7) and results in the consumer risk assessment not being finalised (see Section 9).

5. Ecotoxicology

The risk assessment was based on the following documents: European Commission (2002a,b), SETAC (2001), EFSA (2009), EFSA PPR Panel (2013) and EFSA (2013). According to Regulation (EU) No 283/2013, data should be provided regarding the acute and chronic toxicity to honeybees and data to address the development of honeybee brood and larvae. As the European Commission (2002a) does not provide a risk assessment scheme which is able to use the chronic toxicity data for adult honeybees and the honeybee brood, when performing the risk assessment according to European Commission (2002a), the risk to adult honeybees from chronic toxicity and the risk to bee brood, could not be finalised due to the lack of a risk assessment scheme. Therefore, EFSA (2013) was used for the risk assessment in order to reach a conclusion for the representative uses.

It is noted that the representative uses included uses in greenhouse. Since the use in non-permanent greenhouse could not be excluded, a risk envelope approach was taken considering the fact that the application pattern is the same for both field and greenhouse uses.

In addition, it must be noted that concerns on the identity of soil and surface water metabolites IMH/IBMHC (retention time 38 min) and IBMHC/DDC (retention time 37.3 min) were raised (see Section 4).

At the tier 1 level, a high risk to **birds** and **mammals** via long-term exposure via the diet was concluded for all the representative uses (data gap) while a low acute risk could be concluded. A low risk to birds and mammals for bifenazate was concluded also for the other exposure routes. Further information is needed to address the risk to bird and mammals via exposure to the plant metabolites, in particular for metabolites bifenazate-diazene (D3598), carbamate, A1530S, D9472, D9963 and A1530, and to address the risk via exposure through the food chain to the soil metabolites D3598, D1989, IMH/IBMHC (retention time 38 min) and IBMHC/DDC (retention time 37.3 min), and for the surface water metabolites D3598, D1989, DPHPDD, IBMHC/DDC (retention time 37.3 min), IMH/IBMHC (retention time 38 min) and hydroxylated D3598 (data gap).

A low acute and chronic risk to **aquatic organisms** could be concluded for bifenazate for the uses on fruiting vegetables and strawberries. For the use on ornamental, only Step 1 FOCUS exposure estimates were available and a high risk for bifenazate and its pertinent surface water metabolites could not be excluded (data gap), see also Section 4.

The following metabolites were identified as relevant for surface water: D3598 (relevant also for sediment), D1989, D9963, D9472, DPHPDD, IBMHC/DDC (retention time 37.3 min), IMH/IBMHC (retention time 38 min) and hydroxylated D3598. Reliable acute toxicity endpoints were available for metabolite D3598 (all trophic levels) and for metabolite D1989 (aquatic invertebrates only). Chronic toxicity endpoints were not available for these metabolites while both acute and chronic toxicity endpoints were not available for the remaining surface water metabolites. Information to address the risk for the pertinent sediment metabolite D3598 was not available (data gap). Using the available toxicity endpoints and the available FOCUS exposure estimates, a high acute risk to aquatic invertebrates and fish, and a low risk to algae were concluded for metabolite D3598 for the uses on strawberries and fruiting vegetables (data gap). For metabolite D1989, a high acute risk, for fish only, was concluded for the use on strawberries while a low acute risk for all trophic levels was concluded

for the uses on fruiting vegetables. By assuming the metabolites as 10 times more toxic than the parent compound, a high acute risk could not be excluded for metabolites DPHPDD (aquatic invertebrates only), hydroxylated D3598 (aquatic invertebrates only), IBMHC/DCC (fish and aquatic invertebrates) and IMH/IBMHC (fish and aquatic invertebrates), and a high chronic risk to fish could not be excluded for metabolites D3598, D1989, DPHPDD and OH D3598 for the uses on strawberries (data gap). For the uses on fruiting vegetables, a high acute risk to aquatic invertebrates and fish could not be excluded for metabolite IMH/IBMHC and for DPHPDD (aquatic invertebrates) while a high chronic risk to fish could not be excluded for D3598, DPHPDD and hydroxylated D3598. A low chronic risk could be concluded for metabolites D1989 and a low acute risk could be concluded for metabolite IBMHC/DDC (with mitigation measures to reduce the run off). A low risk to algae was concluded for all metabolites for all representative uses assessed. Suitable exposure estimates were not available for metabolites D9963 and D9472; therefore, the aquatic risk assessment could not be performed (data gap).

Reliable acute contact and oral toxicity studies for honey**bees** performed with the active substance and the representative formulation were available. Using these data in a screening risk assessment in accordance with EFSA (2013), a low acute risk was concluded for all the representative uses. At the tier 1 level, a high chronic risk for honeybees was identified for the uses on strawberries and fruiting vegetables for the treated crop scenario (BBCH < 70), weeds and the succeeding crop scenario (data gap). Considering that the use on ornamentals can cover a high variety of plants and include flowering ornamentals, the risk assessment for this use was performed using the 'oilseed rape' and 'orchard 1' crop categories of EFSA (2013). For the orchard category, a high risk was concluded for all scenarios except the treated crop (BBCH higher or equal to 70) while for the 'oilseed rape category' a high risk was concluded for the treated crop (BBCH < 70), the weeds and the succeeding crop scenario (data gap).

A low acute and chronic risk to honeybees was concluded on the basis of the screening assessment for exposure to residues of bifenazate in guttation fluids and surface water. An assessment of the exposure via residues in puddle water was not available. Nevertheless, considering all the available data and assessments including the assessments on guttation fluid and on surface water, a low acute and chronic risk was concluded also for the puddle scenario.

The risk assessment for larvae could not be performed due to the lack of a suitable endpoint (data gap). Other assessments that were not available included sublethal effects (i.e. hypopharyngeal glands (HPG), data gap), accumulative effects, and metabolites occurring in pollen and nectar (data gap).

Data to perform a risk assessment for solitary bees were not available. A literature study on the effects of Floramite 240 mg/L SC on bumblebees (*Bombus terrestris*) was available (Besard et al., 2010). In this study, three different exposure routes were assessed: contact, oral via treated sugar solution and oral via treated pollen. Following oral exposure, especially via treated sugar solutions, effects on mortality and reproduction (no drones produced during the entire exposure period, 11 weeks) at concentrations of 96 mg a.s./L were observed. An individual dose cannot be estimated since no measurements of consumed sugar solutions were reported. Therefore, the potential use of this study in the risk assessment is limited.

A high in-field risk to **non-target arthropods** was concluded for all representative uses at the tier 1 level for the standard species *Typhlodromus pyri*. The available higher tier studies were not sufficient to address the identified risk (data gap).

A low risk for **earthworms** and other **soil macroorganisms** was concluded for bifenazate and its pertinent metabolites. A low risk for **soil microorganisms** was concluded for bifenazate while further data are needed to address the risk for its pertinent soil metabolites (data gap).

A low risk to **non-target terrestrial higher plants** was concluded for all the representative uses assessed.

A low risk to **biological methods for sewage treatment** could be concluded.

With regard to the endocrine disruption potential, it is noted that in the available avian reproduction test on mallard duck, the pathological examinations revealed inactive ovaries in 6/16 female birds in all concentrations tested. No effects on the ovaries were observed in the controls. No other studies were available to address the potential endocrine activity of bifenazate. Pending on the outcome of the data gap in Section 2, further ecotoxicological tests might be necessary to address the potential endocrine disrupting properties of bifenazate.

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

Table 1: Soil

Compound (name and/or code)	Persistence	Ecotoxicology
Bifenazate	Very low to low persistence Single first order and biphasic kinetics DT_{50} 0.09–0.40 days (DT_{90} 0.3–12.3 days; laboratory conditions at 20°C, pF2 soil moisture)	Low risk
Bifenazate-diazene (D3598)	Very low to low persistence Single first order and biphasic kinetics DT_{50} 0.21–1.45 days (DT_{90} 0.68–28.4 days; laboratory conditions at 20°C, pF2 soil moisture)	Data gap
D1989	Low to moderate persistence Single first order kinetics DT_{50} 2.12–11.0 days (DT_{90} 7.04–53.2 days; laboratory conditions at 20°C, pF2 soil moisture)	Data gap
IMH/IBMHC (retention time 38 min)	Moderate persistence Single first order kinetics DT_{50} 15.4–23.9 days (DT_{90} 51.1–79.2 days; laboratory conditions at 20°C, pF2 soil moisture)	Data gap
IBMHC/DDC (retention time 37.3 min)	Moderate persistence Single first order kinetics DT_{50} 22.4–46.6 days (DT_{90} 74.3–154.7 days; laboratory conditions at 20°C, pF2 soil moisture)	Data gap

DT_{50}: period required for 50% dissipation; DT_{90}: period required for 90% dissipation.

Table 2: Groundwater

Compound (name and/or code)	Mobility in soil	> 0.1 µg/L at 1 m depth for the representative uses[a]	Pesticidal activity	Toxicological relevance
Bifenazate	Medium to low mobility K_{Foc} 243–628 mL/g	No	Yes	Yes
Bifenazate-diazene (D3598)	Slight mobility to immobile K_{Foc} 4,795–22,303 mL/g	No	No	No data, data not required
D1989	Slight mobility K_{Foc} 3,725–3,962 mL/g	No	No	No data, data not required
IMH/IBMHC (retention time 38 min)	Immobile K_{Foc} 61,170 mL/g (a worst-case estimated adsorption based on the LOQ)	No	No	No data, data not required

Compound (name and/or code)	Mobility in soil	> 0.1 µg/L at 1 m depth for the representative uses[a]	Pesticidal activity	Toxicological relevance
IBMHC/DDC (retention time 37.3 min)	Immobile K_{Foc} 61,170 mL/g (a worst-case estimated adsorption based on the LOQ, if identified as IBMHC)	No	No	No data, data not required
	Immobile K_{Foc} 71,540 mL/g (QSAR estimation, if identified as DDC)	No	No	No data, data not required

K_{Foc}: Freundlich organic carbon adsorption coefficient; LOQ: limit of quantification; QSAR: quantitative structure–activity relationship.
(a): At least one FOCUS scenario or a relevant lysimeter.

Table 3: Surface water and sediment

Compound (name and/or code)	Ecotoxicology
Bifenazate	Data gap
Bifenazate-diazene (D3598)	Data gap[a]
D1989	Data gap
IMH/IBMHC (retention time 38 min)	Data gap[a]
IBMHC/DDC (retention time 37.3 min)	Data gap[a]
D9963	Data gap
D9472	Data gap
Hydroxylated D3598	Data gap
DPHPDD	Data gap

(a): Only for fruiting vegetables, FOCUS STEP 3 estimates were available, low risk for ¼ scenarios.

Table 4: Air

Compound (name and/or code)	Toxicology
Bifenazate	**Rat acute inhalation study:** LC_{50} > 4.4 mg/L air per 4 h (no classification required)

LC_{50}: lethal concentration, median.

7. Data gaps

This is a list of data gaps identified during the peer review process, including those areas in which a study may have been made available during the peer review process but not considered for procedural reasons (without prejudice to the provisions of Article 56 of Regulation (EC) No 1107/2009 concerning information on potentially harmful effects).

- A data gap has been identified for a search of the scientific peer-reviewed open literature on the relevant metabolites, dealing with side effects on health, the environment and non-target species and published within the 10 years before the date of submission of the dossier, to be conducted and reported in accordance with EFSA guidance on the submission of scientific peer-reviewed open literature for the approval of pesticide active substances under Regulation (EC) No 1107/2009 (EFSA, 2011a). Concerning the active substance, the data available are not reported in sufficient detail in the RAR.
- The monitoring method for the determination of bifenazate in soil and ground water (relevant for all representative uses evaluated; submission date proposed by the applicant: unknown, see Sections 1, 4 and 5).
- The monitoring method for the determination of the compounds of the residue definition in body fluids (relevant for all representative uses evaluated; submission date proposed by the applicant: end of 2016, see Section 1).
- Analytical methods used in each of the toxicological studies are not reported (relevant for all representative uses evaluated, submission date proposed by the applicant: unknown; see Section 2).
- A comparative *in vitro* metabolism study including human material should be performed as required in Regulation (EU) No 283/2013 (relevant for all representative uses evaluated, submission date proposed by the applicant: unknown; see Section 2).
- Phototoxicity potential of bifenazate and photomutagenicity are unknown (relevant for all representative uses evaluated, submission date proposed by the applicant: unknown; see Section 2).
- Further clarification regarding the endocrine disrupting properties are needed (such as level 2/3 of the OECD conceptual Framework for the identification of EDs) (relevant for all representative uses evaluated, submission date proposed by the applicant: unknown; see Section 2).
- Toxicological data (repeated dose toxicity study and genotoxicity data) on metabolites A1530S, carbamate and D3598 are needed to assess the consumer risk (relevant for uses on strawberries and fruiting vegetables, submission date proposed by the applicant: unknown; see Section 2).
- Guideline conforming storage stability data over the full period of sample storage under frozen conditions for bifenazate and D3598 in the relevant crops from the category of fruiting vegetables (relevant for uses on fruiting vegetables, submission date proposed by the applicant: unknown; see Section 3).
- Guideline conforming storage stability data over the full period of sample storage under frozen conditions for D3598 in strawberries (relevant for uses on strawberries, submission date proposed by the applicant: unknown; see Section 3).
- Applicant to provide a rational for the observation in the citrus metabolism study that in acidic samples (juice, pulp) there is a significant decrease of the per cent polar compounds after 14 months of storage and in increase of per cent D3598, that is not observed in the non-acidic peel samples (relevant for uses on strawberries and fruiting vegetables, submission date proposed by the applicant: unknown; see Section 3).
- A reasoned proposal regarding a global plant residue definition for risk assessment, taking into account the relevance of the major metabolites on the basis of the available plant metabolism studies (relevant for uses on strawberries and fruiting vegetables, submission date proposed by the applicant: unknown; see Section 3).
- Hydrolysis study simulating processing conditions for metabolite D3598 (relevant for uses on strawberries and fruiting vegetables, submission date proposed by the applicant: unknown; see Section 3).

- A full data set of acceptable residue trials in tomato (outdoor) supported by demonstration of acceptable storage stability for NEU and SEU (relevant for uses on fruiting vegetables, submission date proposed by the applicant: unknown; see Section 3).
- A full data set of acceptable residue trials in peppers (outdoor) supported by demonstration of acceptable storage stability for NEU and SEU (relevant for uses on fruiting vegetables, submission date proposed by the applicant: unknown; see Section 3).
- A full data set of acceptable residue trials in cucurbits with edible peel (outdoor) supported by demonstration of acceptable storage stability for NEU and SEU (relevant for uses on fruiting vegetables, submission date proposed by the applicant: unknown; see Section 3).
- A full data set of acceptable residue trials in cucurbits with inedible peel (outdoor) supported by demonstration of acceptable storage stability for NEU and SEU (relevant for uses on fruiting vegetables, submission date proposed by the applicant: unknown; see Section 3).
- A full data set of acceptable residue trials in sweet corn (outdoor) supported by demonstration of acceptable storage stability for NEU and SEU (relevant for uses on fruiting vegetables, submission date proposed by the applicant: unknown; see Section 3).
- A full data set of acceptable residue trials in tomato (indoor) supported by demonstration of acceptable storage stability for NEU and SEU (relevant for uses on fruiting vegetables, submission date proposed by the applicant: unknown; see Section 3).
- A full data set of acceptable residue trials in peppers (indoor) supported by demonstration of acceptable storage stability for NEU and SEU (relevant for uses on fruiting vegetables, submission date proposed by the applicant: unknown; see Section 3).
- A full data set of acceptable residue trials in cucurbits with edible peel (indoor) supported by demonstration of acceptable storage stability for NEU and SEU (relevant for uses on fruiting vegetables, submission date proposed by the applicant: unknown; see Section 3).
- A full data set of acceptable residue trials in cucurbits with inedible peel (indoor) supported by demonstration of acceptable storage stability for NEU and SEU (relevant for uses on fruiting vegetables, submission date proposed by the applicant: unknown; see Section 3).
- Clarification on the indoor GAP on fruiting vegetables concerning growing of sweet corn, and if applicable a full data set of acceptable residue trials in sweet corn (indoor) supported by demonstration of acceptable storage stability for NEU and SEU (relevant for uses on fruiting vegetables, submission date proposed by the applicant: unknown; see Section 3).
- A review of the strawberry residues trials assessment with consistent application of the proportionality approach for the same use (relevant for uses on strawberries EU outdoor, submission date proposed by the applicant: unknown; see Section 3).
- Submission of data or information against the data requirement on residue levels in pollen and in bee products for human consumption resulting from residues taken up by honeybees from crops at blossom, or in order to support the requested waiver, evidence for the statement that bees are not foraging on flowers of fruiting vegetables and strawberries should be submitted (relevant for uses on strawberries and fruiting vegetables, submission date proposed by the applicant: unknown; see Section 3).
- The identity of metabolites IMH/IBMHC (retention time 38 min) and IBMHC/DDC (retention time 37.3 min) is unknown (relevant for all representative uses evaluated, submission date proposed by the applicant: unknown; see Sections 4 and 5).
- Adsorption endpoints to be derived for metabolites IMH/IBMHC (retention time 38 min) and IBMHC/DDC (retention time 37.3 min) (relevant for all representative uses evaluated, submission date proposed by the applicant: unknown; see Section 4).
- The proposed structures of metabolites DPHPDD and hydroxylated D3598 were not confirmed against authentic reference standards (relevant for all representative uses evaluated, submission date proposed by the applicant: unknown; see Section 4).
- Step 3 calculations for the representative use in strawberries and step 2 and 3 calculations for the representative use in ornamental plants were not performed for bifenazate and its metabolites D3598, D1989, IMH/IBMHC (retention time 38 min), IBMHC/DDC (retention time 37.3 min), D9963, D9472, hydroxylated D3598 and DPHPDD (relevant for representative uses in strawberries and ornamental plants, submission date proposed by the applicant: unknown; see Sections 4 and 5).
- The surface water exposure assessment for metabolites D9963 and D9472 is not acceptable (relevant for all representative uses evaluated, submission date proposed by the applicant: unknown; see Section 4).

- Information on the effect of water treatment processes on the nature of residues of identified metabolites potentially present in surface water (D1989, IMH/IBMHC (retention time 38 min), IBMHC/DDC (retention time 37.3 min), hydroxylated D3598 and DPHPDD), when surface water is abstracted for drinking water, were not sufficient in order to assess the consumer risk from the consumption of drinking water (relevant for all representative uses evaluated, submission date proposed by the applicant: unknown; see Section 4).
- Further information to address the long-term risk to birds and mammals (relevant for all representative uses evaluated; submission date proposed by the applicant: unknown; see Section 5).
- Further information to address the risk to bird and mammals via exposure to the plant metabolites, in particular for metabolites D3598, carbamate, A1530S, D9472, D9963 and A1530 and to address the risk via exposure through the food chain to the soil metabolites D3598, D1989, IMH/IBMHC (retention time 38 min) and IBMHC/DDC (retention time 37.3 min) and for the surface water metabolites D3598, D1989, DPHPDD, IBMHC/DDC (retention time 38 min), IMH/IBMHC (retention time 37.3 min), hydroxylated D3598 (relevant for all representative uses evaluated; submission date proposed by the applicant: unknown; see Section 5).
- An aquatic risk assessment for the use on ornamentals for bifenazate and its pertinent surface water metabolites (relevant for the uses on ornamentals; submission date proposed by the applicant: unknown; see Sections 4 and 5).
- Further information to address the risk to aquatic organisms for metabolites D9963 and D9472 and the risk to sediment dwellers for metabolite D3598 (relevant for all representative uses evaluated; submission date proposed by the applicant: unknown; see Section 5).
- Further information to address the risk to aquatic organisms for metabolites D3598 (acute and chronic), D1989 (acute and chronic), IMH/IBMHC (retention time 38 min) (acute), IBMHC/DDC (retention time 37.3 min) (acute), DPHPDD (acute and chronic) and hydroxylated D3598 (acute and chronic) (relevant for the uses on strawberries). Further information to address the risk to aquatic organisms for metabolites D3598 (acute and chronic), IMH/IBMHC (retention time 38 min) (acute), DPHPDD (acute and chronic) and hydroxylated D3598 (chronic) (relevant for the uses on fruiting vegetables, submission date proposed by the applicant: unknown; see Section 5).
- Further information to address the chronic risk to honeybees (adult) (relevant for all representative uses evaluated; submission date proposed by the applicant: unknown; see Section 5).
- Further information to address the chronic risk to honeybees (larvae) for all exposure routes (relevant for all representative uses evaluated; submission date proposed by the applicant: unknown; see Section 5).
- Based on EFSA (2013), suitable data to address the risk of sublethal effects (e.g. HPG development effects) to honeybees due to exposure to bifenazate (relevant for all representative uses evaluated; submission date proposed by the applicant: unknown; see Section 5).
- Information to assess the risk to honeybees due to plant metabolites occurring in pollen and nectar (relevant for all representative uses evaluated; submission date proposed by the applicant: unknown; see Section 5).
- Further information to address the risk to non-target arthropods (relevant for all representative uses evaluated; submission date proposed by the applicant: unknown; see Section 5).
- Further information to address the risk to soil microorganisms for soil metabolites D3598, D1989, IMH/IBMHC (retention time 38 min), IBMHC/DDC (retention time 37.3 min) (relevant for all representative uses evaluated; submission date proposed by the applicant: unknown; see Section 5).

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

- Gloves and work wear have to be worn by operators during mixing and loading and application in field applications in strawberries to ensure that the AOEL is not exceeded (see Section 2).
- Work wear, gloves, hood and visor have to be worn by operators during mixing and loading and application in field applications in fruiting vegetables and ornamentals to ensure that the AOEL is not exceeded (see Section 2).
- Working clothing and gloves have to be worn by workers re-entering treated strawberries and fruiting vegetables fields to ensure that the AOEL is not exceeded (see Section 2).

9. Concerns

9.1. Issues that could not be finalised

An issue is listed as 'could not be finalised' if there is not enough information available to perform an assessment, even at the lowest tier level, for the representative uses in line with the uniform principles in accordance with Article 29(6) of Regulation (EC) No 1107/2009 and as set out in Commission Regulation (EU) No 546/2011[4] 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 Regulation (EC) No 1107/2009.

1) The consumer risk assessment from the consumption of water could not be finalised, while satisfactory information was not available to address the effect of water treatment processes on the nature of the residues that might be present in surface water, when surface water is abstracted for drinking water (see Section 4).
2) The aquatic risk assessment could not be finalised for metabolites D9963 and D9472 (see Sections 4 and 5).
3) The aquatic risk assessment for bifenazate and its pertinent metabolites could not be finalised for representative use in ornamental plants (see Sections 4 and 5).
4) The consumer risk assessment is not finalised due to a number of data gaps that likely have an impact on the assessment residue levels in the different crops and due to the pending issue whether the toxicological reference values of bifenazate can be applied to metabolite D3598 included in the residue definition for both monitoring and risk assessment (see Section 3).

9.2. Critical areas of concern

An issue is listed as a critical area of concern if there is enough information available to perform an assessment for the representative uses in line with the uniform principles in accordance with Article 29 (6) of Regulation (EC) No 1107/2009 and as set out in Commission Regulation (EU) No 546/2011, and if this assessment does not permit the conclusion that, for at least one of the representative uses, it may be expected that a plant protection product containing the active substance will not have any harmful effect on human or animal health or on groundwater, or any unacceptable influence on the environment.

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

An issue is also listed as a critical area of concern if, in the light of current scientific and technical knowledge using guidance documents available at the time of application, the active substance is not expected to meet the approval criteria provided for in Article 4 of Regulation (EC) No 1107/2009.

5) A high risk to **birds** and **mammals** via long-term exposure was concluded for all the representative uses (see Section 5).
6) A high risk to **non-target arthropods** was concluded for all the representative uses (see Section 5).

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

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

[4] 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		Strawberries (Field)	Strawberries (green house)	Fruiting vegetables (field)	Fruiting vegetables (green house)	Ornamentals (field)	Ornamentals (green house)
Operator risk	Risk identified	For manual hand-held sprayer only	X		X		X
	Assessment not finalised						
Worker risk	Risk identified		X		X	X	X
	Assessment not finalised						
Resident/ bystander risk	Risk identified						
	Assessment not finalised						
Consumer risk	Risk identified						
	Assessment not finalised	X[1,4]	X[4]	X[1,4]	X[4]	X[1]	
Risk to wild non-target terrestrial vertebrates	Risk identified	X[5]	X[5]	X[5]	X[5]	X[5]	X[5]
	Assessment not finalised						
Risk to wild non-target terrestrial organisms other than vertebrates	Risk identified	X[6]	X[6]	X[6]	X[6]	X[6]	X[6]
	Assessment not finalised						
Risk to aquatic organisms	Risk identified						
	Assessment not finalised	X[2]	X[2]	X[2]	X[2]	X[2,3]	X[2,3]
Groundwater exposure to active substance	Legal parametric value breached						
	Assessment not finalised						
Groundwater exposure to metabolites	Legal parametric value breached						
	Parametric value of 10 μg/L breached						
	Assessment not finalised						

Columns are grey if no safe use can be identified. The superscript numbers relate to the numbered points indicated in Sections 9.1 and 9.2. Where there is no superscript number, see Sections 2–6 for further information.

References

Besard L, Mommaerts V, Vandeven J, Cuvelier X, Sterk G and Smagghe G, 2010. Compatibility of traditional and novel acaricides with bumblebees (Bombus terrestris): a first laboratory assessment of toxicity and sublethal effects. Pest Management Science, 66, 786–793. doi:10.1002/ps.1943

EFSA (European Food Safety Authority), 2009. Guidance on Risk Assessment for Birds and Mammals on request from EFSA. EFSA Journal 2009;7(12):1438, 358 pp. doi:10.2903/j.efsa.2009.1438

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

EFSA (European Food Safety Authority), 2011b. Reasoned opinion of EFSA: Review of the existing maximum residue levels (MRLs) for bifenazate according to Article 12 of Regulation (EC) No 396/2005. EFSA Journal 2011;9(12):2484, 48 pp. doi:10.2903/j.efsa.2011.2484

EFSA (European Food Safety Authority), 2013. EFSA Guidance Document on the risk assessment of plant protection products on bees (*Apis mellifera, Bombus* spp. and solitary bees). EFSA Journal 2013;11(7):3295, 268 pp. doi:10.2903/j.efsa.2013.3295

EFSA (European Food Safety Authority), 2014. EFSA Guidance Document on clustering and ranking of emissions of active substances of plant protection products and transformation products of these active substances from protected crops (greenhouses and crops grown under cover) to relevant environmental compartments. EFSA Journal 2014;12(3):3615, 43 pp. doi:10.2903/j.efsa.2014.3615

EFSA (European Food Safety Authority), 2017. Peer review report to the conclusion regarding the peer review of the pesticide risk assessment of the active substance bifenazate. Available online: www.efsa.europa.eu

EFSA PPR Panel (EFSA Panel on Plant Protection Products and their Residues), 2012. Guidance on dermal absorption. EFSA Journal 2012;10(4):2665, 30 pp. doi:10.2903/j.efsa.2012.2665

EFSA PPR Panel (EFSA Panel on Plant Protection Products and their Residues), 2013. Guidance on tiered risk assessment for plant protection products for aquatic organisms in edge-of-field surface waters. EFSA Journal 2013;11(7):3290, 186 pp. doi:10.2903/j.efsa.2013.3290

European Commission, 2000a. Residues: guidance for generating and reporting methods of analysis in support of pre-registration data requirements for Annex II (Part A, Section 4) and Annex III (Part A, Section 5) of Directive 91/414. SANCO/3029/99-rev. 4, 11 July 2000.

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

European Commission, 2002a. Guidance Document on Terrestrial Ecotoxicology Under Council Directive 91/414/EEC. SANCO/10329/2002-rev. 2 final, 17 October 2002.

European Commission, 2002b. Guidance Document on Aquatic Ecotoxicology Under Council Directive 91/414/EEC. SANCO/3268/2001-rev. 4 final, 17 October 2002.

European Commission, 2003. Guidance Document on Assessment of the Relevance of Metabolites in Groundwater of Substances Regulated under Council Directive 91/414/EEC. SANCO/221/2000-rev. 10 final, 25 February 2003.

European Commission, 2005. Review report for the active substance bifenazate. Finalised in the Standing Committee on the Food Chain and Animal Health at its meeting on 3 June 2005 in view of the inclusion of bifenazate in Annex I of Council Directive 91/414/EEC. SANCO/10158/2005-rev.3, 3 June 2005, 27 pp.

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

European Commission, 2011. Guidelines on comparability, extrapolation, group tolerances and data requirements for setting MRLs. SANCO 7525/VI/95-rev. 9. March 2011. p.1–46

European Commission, 2012. Guidance document on the assessment of the equivalence of technical materials of substances regulated under Regulation (EC) No 1107/2009. SANCO/10597/2003-rev. 10.1, 13 July 2012.

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

FOCUS (Forum for the Co-ordination of Pesticide Fate Models and their Use), 2001. FOCUS surface water scenarios in the EU evaluation process under 91/414/EEC. Report of the FOCUS Working Group on Surface Water Scenarios. EC Document Reference SANCO/4802/2001-rev. 2, 245 pp., as updated by Generic guidance for FOCUS surface water scenarios, v. 1.1, March 2012.

FOCUS (Forum for the Co-ordination of Pesticide Fate Models and their Use), 2006. Guidance document on estimating persistence and degradation kinetics from environmental fate studies on pesticides in EU Registration Report of the FOCUS Work Group on Degradation Kinetics. EC Document Reference SANCO/10058/2005-v. 2.0, 434 pp., as outlined in Generic guidance for estimating persistence and degradation kinetics from environmental fate studies on pesticides in EU Registration, v. 1.0, November 2011.

FOCUS (Forum for the Co-ordination of Pesticide Fate Models and their Use), 2009. Assessing potential for movement of active substances and their metabolites to ground water in the EU. Report of the FOCUS Workgroup. EC Document Reference SANCO/13144/2010-v. 1, 604 pp., as outlined in Generic guidance for tier 1 FOCUS groundwater assessment, v. 2.0, January 2011.

OECD (Organisation for Economic Co-operation and Development), 2009. Guidance document on overview of residue chemistry studies. ENV/JM/MONO(2009)31, 28 July 2009.

OECD (Organisation for Economic Co-operation and Development), 2011. OECD MRL calculator: spreadsheet for single data set and spreadsheet for multiple data set, 2 March 2011. In: Pesticide Publications/Publications on Pesticide Residues. Available online: www.oecd.org

SETAC (Society of Environmental Toxicology and Chemistry), 2001. Guidance document on regulatory testing and risk assessment procedures for plant protection products with non-target arthropods. ESCORT 2.

Sweden, 2016a. Renewal Assessment Report (RAR) on the active substance bifenazate prepared by the rapporteur Member State Sweden, in the framework of Commission Implementing Regulation (EU) No 844/2012, January 2016. Available online: www.efsa.europa.eu

Sweden, 2016b. Revised Renewal Assessment Report (RAR) on bifenazate prepared by the rapporteur Member State Sweden in the framework of Commission Implementing Regulation (EU) No 844/2012, November 2016. Available online: www.efsa.europa.eu

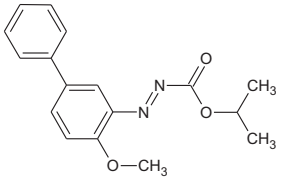
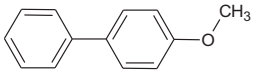
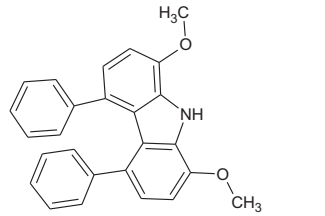
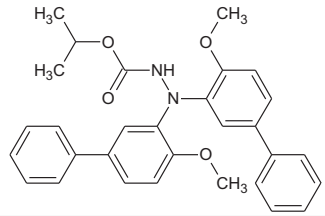
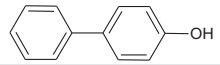
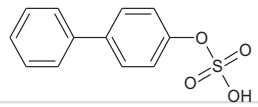
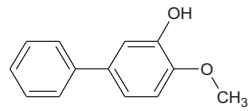
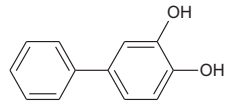
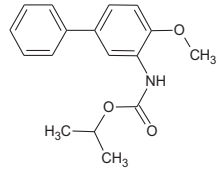
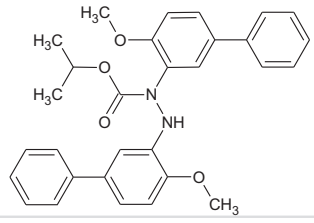
Abbreviations

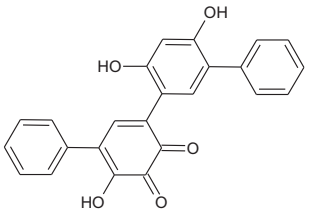
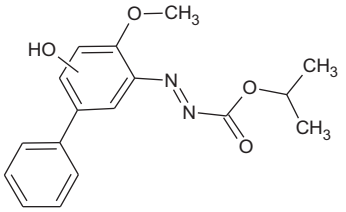
a.s.	active substance
AAOEL	acute acceptable operator exposure level
ADI	acceptable daily intake
AOEL	acceptable operator exposure level
AR	applied radioactivity
ARfD	acute reference dose
bw	body weight
DT_{50}	period required for 50% dissipation (define method of estimation)
DT_{90}	period required for 90% dissipation (define method of estimation)
EEC	European Economic Community
FAO	Food and Agriculture Organization of the United Nations
FOCUS	Forum for the Co-ordination of Pesticide Fate Models and their Use
GAP	Good Agricultural Practice
HPLC	high-pressure liquid chromatography or high-performance liquid chromatography
HPG	hypopharyngeal glands
ISO	International Organization for Standardization
IUPAC	International Union of Pure and Applied Chemistry
K_{Foc}	Freundlich organic carbon adsorption coefficient
LC_{50}	lethal concentration, median
LC–MS/MS	liquid chromatography with tandem mass spectrometry
LOAEL	lowest observable adverse effect level
LOQ	limit of quantification
MRL	maximum residue level
NEU	northern Europe
NOAEL	no observed adverse effect level
OECD	Organisation for Economic Co-operation and Development
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
QSAR	quantitative structure–activity relationship
RAR	renewal assessment report
RMS	rapporteur Member State
SC	suspension concentrate
SEU	southern Europe
SFO	single first order
SMILES	simplified molecular-input line-entry system
UF	uncertainty factor
UV	ultraviolet

Appendix A – List of end points for the active substance and the representative formulation

Appendix A can be found in the online version of this output ('Supporting information' section): https://doi.org/10.2903/j.efsa.2017.4693

Appendix B – Used compound codes

Code/trivial name[a]	Chemical name/SMILES notation	Structural formula
Bifenazate-diazene D3598	isopropyl (*E*)-(4-methoxybiphenyl-3-yl) diazenecarboxylate COc1ccc(cc1/N=N/C(=O)OC(C)C)c2ccccc2	
D1989	4-methoxybiphenyl COc1ccc(cc1)c2ccccc2	
DDC IBMHC/DDC (retention time 37.3 min)	1,8-dimethoxy-4,5-diphenyl-9*H*-carbazole COc4ccc(c1c4nc2c1c(ccc2OC)c3ccccc3)c5ccccc5 or isopropyl 2,2-bis(4-methoxybiphenyl-3-yl) hydrazinecarboxylate COc3ccc(cc3N(NC(=O)OC(C)C)c1cc(ccc1OC)c2ccccc2)c4ccccc4	 
A1530	biphenyl-4-ol Oc1ccc(cc1)c2ccccc2	
A1530S	biphenyl-4-yl hydrogen sulfate OS(=O)(=O)Oc1ccc(cc1)c2ccccc2	
D9963	4-methoxybiphenyl-3-ol Oc1cc(ccc1OC)c2ccccc2	
D9472	biphenyl-3,4-diol Oc1ccc(cc1O)c2ccccc2	
Carbamate	isopropyl (4-methoxybiphenyl-3-yl)carbamate COc1ccc(cc1NC(=O)OC(C)C)c2ccccc2	
IMH/IBMHC (retention time 38 min) IMH	isopropyl 1,2-bis(4-methoxybiphenyl-3-yl) hydrazinecarboxylate COc3ccc(cc3NN(c1cc(ccc1OC)c2ccccc2)C(=O)OC(C)C)c4ccccc4	

Code/trivial name[(a)]	Chemical name/SMILES notation	Structural formula
DPHDD	4″,6′,6″-trihydroxy-1,1′:3′,1″:3″,1‴-quaterphenyl-4′,5′-dione O=C1C(=CC(=C(O)C1=O)c2ccccc2)c4cc(c3ccccc3)c(O)cc4O	
Hydroxylated D3598 OH-D3598	isopropyl (*E*)-(x-hydroxy-4-methoxybiphenyl-3-yl) diazenecarboxylate x: 2, 5, 6	

SMILES: simplified molecular-input line-entry system.
(a): The compound name in bold is the name used in the conclusion.