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CONCLUSION ON PESTICIDES PEER REVIEW

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

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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 authorities of the rapporteur Member State Sweden for the pesticide active substance pirimicarb are reported. The context of the peer review was that required by Commission Implementing Regulation (EU) No 844/2012, as amended by Commission Implementing Regulation (EU) No 2018/1659. The conclusions were reached on the basis of the evaluation of the representative use(s) of pirimicarb as an insecticide on winter and spring wheat and sugar beet via foliar spray application and on ornamental pot plants in permanent greenhouses. 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

insecticide, peer review, pesticide, pirimicarb, risk assessment

CONTENTS

SUMMARY

Commission Implementing Regulation (EU) No 844/2012, as amended by Commission Implementing Regulation (EU) No 2018/1659, 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. Pirimicarb is one of the active substances listed in Regulation (EU) No 686/2012.

In accordance with Article 1 of Regulation (EU) No 844/2012, the original rapporteur Member State (RMS), The United Kingdom and the co-rapporteur Member State, Sweden, received an application from Syngenta Crop Protection AG for the renewal of approval of the active substance pirimicarb. Following the departure of the United Kingdom from the EU, the co-RMS Sweden was designated as the RMS.

An initial evaluation of the dossier on pirimicarb was provided by the original RMS in the renewal assessment report (RAR) and subsequently, a peer review of the pesticide risk assessment on the RMS evaluation was conducted by EFSA in accordance with Article 13 of Commission Implementing Regulation (EU) No 844/2012, as amended by Commission Implementing Regulation (EU) No 2018/1659. The following conclusions are derived.

The uses of pirimicarb according to the representative uses as an insecticide foliar spray application on wheat (winter and spring) and sugar beet in the field and foliar spray application on ornamentals (pot plants) in greenhouses (permanent) as proposed at EU level result in a sufficient insecticidal efficacy against the target pests.

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 and technical properties** of the active substance and the formulation for representative uses and **analytical methods**.

In the area of **mammalian toxicology**, the developmental neurotoxicity potential of pirimicarb could not be finalised considering existing concern based on the neurotoxic mode of action of the active substance and the neurotoxicity findings observed in the dataset available for the present peer review; accordingly, a data gap was identified for a developmental neurotoxicity study. Pirimicarb potential for phototoxicity and photomutagenicity could not be finalised.

Several data gaps were identified in the **residue** section for: rotational crops, livestock assessment, residue trials, magnitude of residues in bee products, further assessment of the genotoxicity/toxicological profile of metabolites, leading to the consumer risk assessment being not finalised in relation to the representative uses for wheat and sugar beet. As regards the use on ornamentals, since the proposed use is only ornamentals grown in pots, it is not expected to have an impact on the consumer except when the pots are placed on soil. In this specific circumstance, the consumer risk assessment cannot be finalised considering the potential for residues in rotational crops. The consumer risk assessment was also not finalised with regard to the nature of residues potentially present in drinking water.

The data available on **environmental fate and behaviour** were sufficient to carry out the required environmental exposure assessments at EU level for the representative uses, with the notable exceptions that data gaps were identified for information on the effect of chlorination reagent water treatment processes, on the nature of residues of identified metabolites potentially present in surface water, when surface water is abstracted for the production of drinking water and for the calculation of predicted environmental concentration (PEC) in soil for uses on pot grown ornamentals. The consequence of this is indicated in the paragraph above regarding the consumer risk assessment and paragraph below regarding soil organisms.

In the area of **ecotoxicology**, a critical area of concern was identified for aquatic organisms since a high risk was identified in the majority of scenarios for all representative uses. It was not possible to finalise the risk assessment for honey bees for the representative uses to winter wheat, spring wheat and sugar beet whereas due to missing exposure assessment, the risk to soil organisms could not be finalised for the representative use to ornamentals in permanent greenhouses (only relevant when pots are placed directly on the soil and the greenhouse is removed). A high acute risk to birds and non-target arthropods was concluded for the representative uses to winter wheat, spring wheat and sugar beet. A high acute risk to mammals was also concluded for the use on sugar beet.

Based on the available information, pirimicarb is not an endocrine disruptor in humans according to point 3.6.5 of Annex II to Regulation (EC) No 1107/2009; for non-target organisms, the assessment of the **endocrine disruption potential** of pirimicarb according to point 3.8.2 of Annex II to Regulation (EC) No 1107/2009, as amended by Commission Regulation (EU) 2018/605, could not be finalised.

BACKGROUND

Commission Implementing Regulation (EU) No 844/2012,[1] as amended by Commission Implementing Regulation (EU) No 2018/1659,[2] (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.[3] This regulates for the European Food Safety Authority (EFSA) the procedure for organising the consultation of 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 an additional 3 months where additional information is required to be submitted by the applicant(s) in accordance with Article 13(3). Furthermore, in accordance with Article 13(3a), where the information available in the dossier is not sufficient to conclude the assessment on whether the approval criteria for endocrine disruption are met, additional information can be requested to be submitted in a period of minimum 3 months, not exceeding 30 months, depending on the type of information requested.

In accordance with Article 1 of the Regulation, the original RMS, The United Kingdom and co-RMS Sweden received an application from Syngenta Crop Protection AG for the renewal of approval of the active substance pirimicarb. Complying with Article 8 of the Regulation, the RMS checked the completeness of the dossier and informed the applicant, the co-RMS (Sweden), the European Commission and EFSA about the admissibility.

The RMS provided its initial evaluation of the dossier on pirimicarb in the RAR, which was received by EFSA on 04 December 2017 (The United Kingdom, 2017).

In accordance with Article 12 of the Regulation, EFSA distributed the RAR to the Member States and the applicant, Syngenta Crop Protection AG, for consultation and comments on 23 March 2018. 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 25 May 2018. 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 teleconference between EFSA and the RMS on 11 July 2018. 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, residues and ecotoxicology.

The outcome of the teleconference, 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.

In addition, following a consultation with Member States in the Pesticides Peer Review Expert meetings TC 190 session 2 (January 2019) and TC 192 (February 2019), it was considered necessary to apply an additional clock stop of 30 months in accordance with Commission Implementing Regulation (EU) No 2018/1659. Accordingly, in January 2020 the applicant was given the opportunity to submit, within a period of up to 30 months, additional information to address the approval criteria 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) No 2018/605, and/or documentary evidence demonstrating that pirimicarb may be used such that exposure is negligible, and/or the conditions for application of the derogation under Article 4(7) of Regulation (EC) No 1107/2009 are met.

Following the departure of the United Kingdom from the EU (in 2020), the co-RMS Sweden was designated as the RMS.

The additional information submitted by the applicant was subsequently evaluated by the RMS. Furthermore, the applicant also requested a derogation under Article 4(7) of Regulation (EC) No 1107/2009, submitting evidence regarding the necessity of pirimicarb as an insecticide to control a serious danger to plant health. The evaluation of the data regarding this derogation request is presented in Appendices E and F of this conclusion.

A public consultation on the draft Article 4(7) scientific report and the revised RAR on the ED made available after the 30-month clock stop was conducted between July and September 2023. All comments received, including the ones from the applicant and the Member States, were collated in the format of a commenting table (on the draft Art 4(7) scientific report) and of a reporting table (on the revised RAR on the assessment of the endocrine-disrupting properties). As a result of the public consultation, the need for an additional experts' consultation in the area of mammalian toxicology and ecotoxicology was identified.

[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]Commission Implementing Regulation (EU) No 2018/1659 of 7 November 2018 amending Implementing Regulation (EU) No 844/2012 in view of the scientific criteria for the determination of endocrine disrupting properties introduced by Regulation (EU) 2018/605.

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

In addition since there were indications that pirimicarb may no longer satisfy the approval criteria in Article 4 of Regulation (EC) No 1107/2009, pursuant to Article 21(1) of Regulation (EC) No 1107/2009, the European Commission informed the applicant about the concerns and invited it to provide comments or information. The applicant submitted further information in January 2022, which has been evaluated by the RMS who submitted its evaluation to the European Commission and EFSA on 16 June 2022. In August 2022, in accordance with Article 21(2) of Regulation (EC) No 1107/2009, EFSA was requested to provide scientific and technical assistance concerning the review of the approval of the active substance pirimicarb and to deliver a statement on whether the applicable approval criteria may still be considered fulfilled, taking into consideration the information submitted by the applicant and the assessment of the RMS and, where applicable, the results of a discussion with experts from Member States. In February 2023 EFSA issued a statement concerning the review of the approval of the active substance pirimicarb addressing specifically (i) the risks to consumers from the exposure to metabolites of pirimicarb through dietary intake, (ii) the risks to human health through non-dietary exposure and (iii) the acute risk to birds from the representative uses of pirimicarb assessed for the first approval and additionally, from the representative uses reflecting the currently authorised uses as submitted as part of the renewal of approval (EFSA, 2023a).

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 Member States via a written procedure in August–September 2024.

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 pirimicarb as an insecticide on winter and spring wheat and sugar beet via foliar spray application and on ornamental pot plants in permanent greenhouses, as proposed by the applicant. In accordance with Article 12(2) of Regulation (EC) No 1107/2009, risk mitigation options identified in the RAR and considered during the peer review, if any, are presented in the conclusion.

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

A key supporting document to this conclusion is the peer review report (EFSA, 2024), 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:

a. the comments received on the RAR;
b. the reporting table (13 July 2018 and 24 October 2023[4]);
c. the evaluation table (12 August 2024);
d. the reports of the scientific consultation with Member State experts (where relevant);
e. the comments received on the assessment of the additional information (where relevant);
f. the comments received on the draft EFSA conclusion.

Given the importance of the RAR, including its revisions (Sweden, 2024), 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 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 FORMULATION FOR REPRESENTATIVE USES

Pirimicarb is the ISO common name of 2-(dimethylamino)-5,6-dimethylpyrimidin-4-yl dimethylcarbamate (IUPAC).

The formulation for representative uses for the evaluation was 'A10788A' (Pirimor)', a water-dispersible granule (WG) containing 500 g/kg pirimicarb.

The representative uses evaluated were foliar spray applications on wheat (winter and spring), sugar beet and ornamentals (pot plants in greenhouses (permanent)) for the control of aphids. Full details of the Good Agricultural Practices (GAPs) can be found in the list of end points in Appendix B.

The information on the active substance, the formulation for representative uses, including the co-formulants in these formulations, was considered in the overall assessments during the peer review. None of the co-formulants is an unacceptable co-formulant listed in Annex III of Regulation (EC) No 1107/2009,[5] however one of the co-formulants of 'A10788A' (Pirimor)' is a currently approved basic active substance and one component of a co-formulant is a not approved active

[4]Reporting Table following consultation on the revised RAR on the assessment of the endocrine disrupting properties made available after the long-term ED clock stop.

[5]Commission Regulation (EU) 2021/383 of 3 March 2021 amending Annex III to Regulation (EC) No 1107/2009 of the European Parliament and Council listing co-formulants which are not accepted for inclusion in plant protection products. OJ L 74, 4.3.2021, p. 7–26.

substance under Regulation (EC) 1107/2009.[6] Details on the composition of the formulations cannot be reported in conclusions because of the provisions in Article 63(2)(d) of Regulation (EC) No 1107/2009, however this information was fully available and evaluated during the peer review. A proposal for classification of the formulation(s) according to the Regulation (EC) 1272/2008 was provided by the applicant and assessed by the RMS (please see Volumes 3 CP of the RAR).

Data were submitted to conclude that the use of pirimicarb according to the representative uses proposed at EU level results in a sufficient insecticidal efficacy against the target organisms, following the guidance document SANCO/2012/11251-rev. 4 (European Commission, 2014b).

CONCLUSIONS OF THE EVALUATION

General aspects

With regard to the mammalian toxicity information available for the formulation for representative uses 'Pirimor' (A10788A), studies were performed for the acute toxicity endpoints. With regard to the co-formulants contained in 'Pirimor', sufficient toxicological data were available for most components, but two (present well below 10% in the final formulation). For these two co-formulants, the experts considered that the available toxicological information did not sufficiently address the genotoxicity, repeated dose toxicity (short- and long-term) of 'Pirimor' and that they might be considered for further assessment (see Section 10).[7]

The availability of ecotoxicity data with the formulation for representative uses was discussed at the experts' meeting[8] (refer to Section 5). Furthermore, the experts also discussed the data retrieval search which was updated by the RMS after the meeting. Overall, the experts noted a concern related to the lack of data for birds with the formulation for representative uses (see Section 5) but no additional concerns were identified for the co-formulants.

A data gap has been identified for a search of the scientific peer-reviewed open literature on the active substance and its relevant metabolites, dealing with side effects non-target species and published within the 10 years before the date of submission of the dossier, to be conducted and reported in accordance with EFSA guidance on the submission of scientific peer reviewed open literature for the approval of pesticide active substances under Regulation (EC) No 1107/2009 (EFSA, 2011).[9]

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, 2000b, 2010).

The new proposed reference specification for pirimicarb is based on batch data from industrial plant production. The minimum purity of the technical material is 970 g/kg. It should be noted that evaluation of the toxicological relevance of the impurities is open (see Section 2) and as a consequence, new data such as spectral data, content of the impurities before and after the storage of the formulation and methods for analysis of the relevant impurities in the formulation might be required. There is no Food and Agriculture Organization of the United Nations (FAO) specification available for pirimicarb. The batches used in the (eco)toxicological assessment support the proposed new reference specification (see Sections 2 and 5) but not the original reference specification. As a consequence, it is recommended to update the reference specification of the first approval.

The main data regarding the identity of pirimicarb and its physical and chemical properties are given in Appendix B.

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 formulation for representative uses and for the determination of the respective impurities in the technical material.

Pirimicarb residues can be monitored in food and feed of plant origin by the QuEChERS method using liquid chromatography with tandem mass spectrometry (LC–MS/MS) with a limit of quantification (LOQ) of 0.01 mg/kg in all main commodity groups and in difficult matrices – caraway dried seed and chamomile dried flower. However, an ILV and extraction efficiency for high-water content and dry commodities, in which residues above the LOQ were found, are missing (**data gap** see Section 10). Extraction efficiency for high acid and high-oil commodities was not addressed but are not needed whilst residues in these matrices above the LOQ, consequent to the representative uses, were not found. Pirimicarb residues in food of animal origin can be determined by the QuEChERS method using LC–MS/MS with a LOQ of 0.01 mg/kg in all animal matrices. The efficiency of the extraction procedure used in the method was not verified as residues in the animal matrices above the LOQ, as a result of the representative uses, are not expected. However, metabolite R34865 was included

[6]Please see Regulation (EC) No 1107/2009 for acceptability criteria for co-formulants and Section 2.13.6 of the Technical report on the outcome of the pesticides peer review meeting on general recurring issues in physical and chemical properties and analytical methods. EFSA supporting publication 2019:EN-1623. 32 pp. https://doi.org/10.2903/sp.efsa.2019.EN-1623

[7]See expert consultation 2.19 at Pesticides Peer Review Experts' TC 131, March 2024 (EFSA, 2024).

[8]See experts' consultation 5.11 at Pesticides Peer Review Experts' TC 134, March 2024 (EFSA, 2024).

[9]See evaluation table section 5 open point 5.63 (EFSA, 2024).

in the provisional residue definition for monitoring in animal products (ruminants, see Section 3), therefore a **data gap** for a validated method for monitoring of this metabolite in animal products was set (see Section 10).

Pirimicarb residues in soil can be monitored by LC–MS/MS with a LOQ 0.01 mg/kg. Based on the data submitted the method can be considered as fully validated according SANTE/825/00 rev. 8.1 (European Commission, 2010), however, the final report of the validation study is missing (**data gap**, see Section 10).

The residue definition for monitoring in drinking/ground water was set as pirimicarb and in surface water as pirimicarb and metabolites R34885, R34836 and R35140. Residues of pirimicarb and metabolite R34836 in surface, drinking and groundwater can be monitored by gas chromatography–mass spectrometry (GC–MS) with a LOQ 0.1 µg/L. However, selectivity of the method for surface water was not addressed (**data gap**, see Section 10). In addition, the method applies a hydrolysis step aimed at converting metabolite R34885 to R34836, however the efficacy of this step was not demonstrated (**data gap**, see Section 10), therefore the method cannot be considered sufficiently validated for metabolite R34885. It is also noted that an ILV of the method for determination of pirimicarb in drinking water is missing (**data gap**, see Section 10). Metabolite R35140 can be monitored in surface water by LC–MS/MS with a LOQ of 0.05 µg/L.

A GC–MS method exists for monitoring pirimicarb residue in air with a LOQ of 6 µg/m^3, however the retention capacity of the sorbent was not demonstrated (**data gap**, see Section 10).

Liquid chromatography- ultraviolet (LC-UV) and QuEChERS using LC–MS/MS can be used for monitoring of pirimicarb residues in body fluids with LOQs of 0.05 mg/L and 0.01 mg/kg. Pirimicarb residues in body tissues can be determined by QuEChERS using LC–MS/MS with a LOQ of 0.01 mg/kg. However, a **data gap** for a validated method for monitoring of metabolite R34865 in body fluids and tissues was identified (see Section 10).

2 | MAMMALIAN TOXICITY

The toxicological profile of the active substance pirimicarb and its metabolites was discussed at the Pesticides Peer Review Experts' meeting 190, session 2, in January 2019; at the Pesticide Peer Review Meeting 07, session 1, in June 2019 and at the Pesticide Peer Review TC 89 in September 2022 (resulting in an EFSA Statement concerning the review of the approval of the active substance, EFSA, 2023a); the toxicological reference values and co-formulants were discussed at the Pesticides Peer Review TC 131 in March 2024.

The assessment is based on the following guidance documents: European Commission (2003, 2012), EFSA (2015, 2022); EFSA PPR Panel (2012) and ECHA (2017).

Regarding the original and newly proposed **reference specification** (RS), insufficient data are provided to conclude on the toxicological relevance of the impurities (**data gap**, see Section 10). The test material used in toxicity studies is not representative of the original RS, while the newly proposed RS is supported by the test material used in the toxicological studies, based on at least two key studies (the 1-year study in dogs and long-term study in mice).

Pirimicarb belongs to the carbamate group of insecticides, its mechanism of action being through inhibition of the acetylcholinesterase (AChE) enzyme activity.

The oral **absorption** of pirimicarb is estimated to account for > 80% of the administered low (1 mg/kg bw) and high (50 mg/kg bw) dose administered. **Excretion** occurs predominantly through the urine route. The main **metabolic** pathway identified involves the loss of the carbamate moiety to produce a range of substituted hydroxypyrimidines. A sex difference was evident in the metabolic profile, with males showing a more extensive range of 4-hydroxypyrimidines than females. Based on comparative in vitro metabolism study, no unique human metabolites have been identified compared to rats; quantitative metabolic inter-species differences were not addressed but considered covered by the uncertainty factor of 10 for inter-species variability applied in deriving toxicological reference values.

The **residue definition** for body fluids and tissues includes pirimicarb and R34865 metabolite.

Pirimicarb has moderate **acute** toxicity by the oral and inhalation routes and no toxicity by the dermal route, it is not irritant to eyes and skin but is a skin sensitiser (harmonised classifications: Acute Tox 3, H301, Acute Tox 3, H331 and Skin Sens 1, H317[10]); (ECHA, 2014)

Based on its UV–vis absorption spectra, phototoxicity and photomutagenicity testing is required for pirimicarb. In the absence of agreed methodology to address photomutagenicity, phototoxicity is considered a surrogate for photomutagenicity. Pirimicarb was tested positive in an in vitro phototoxicity assay (according to OECD TG 432) and a hazard concern for phototoxicity and photomutagenicity is identified. Further data to address the phototoxicity and photomutagenicity (i.e. OECD TG 498 assay[11] and/or agreed methodology to assess the risk to phototoxic and photomutagenic pesticide active substances) are needed to conclude on the phototoxicity potential, leading to a data gap and an **issue not finalised** (see Section 9.1.1).

Short-term oral toxicity studies were provided for rats and dogs, both species presenting as critical effects inhibition of AChE activity and related clinical signs. Additional adverse effects were observed in dogs on the haematological system indicative of anaemia. The resulting relevant no observed adverse effect level (NOAEL) is 3.5 mg/kg body weight (bw) per day based on tremors and increased haemosiderin deposition in the spleen in female dogs at 10 mg/kg bw per day (1-year dog study).

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

[11]According to the current state of the art, the newly available OECD TG 498 assay could be considered a proper follow up for substances positive in the OECD TG 432. This follow up was not discussed at the time of the experts' meetings in 2019 (EFSA, 2024).

Based on the available **genotoxicity** data package, the substance is unlikely to be genotoxic in vivo.[12]

After **long-term exposure**, target organs for toxicity included the kidneys; clinical chemistry changes such as increased cholesterol and triglycerides were also observed in rats. The relevant NOAEL is 3.7 mg/kg bw per day (from the 2-year toxicity and carcinogenicity study in rats), based on decreased body weight gain, pelvic transitional cell hyperplasia and pelvic ectasia in the kidneys, increased plasma cholesterol and triglycerides observed at 12.3 mg/kg bw per day.

Treatment-related increased incidence of tumours/neoplasia was observed in rats and mice and included uterine stromal cell polyps and thymoma in female rats, and pulmonary adenoma, benign keratising squamous epithelioma and ovary tumours (papillary cystadenoma) in female mice with a relevant carcinogenicity NOAEL of 15.6 mg/kg bw per day (from the 2-year rat study). Accordingly, the harmonised classification Carc Cat 2 H351 was established under the CLP Regulation[13] (ECHA, 2014).

Regarding **reproductive toxicity** studies, effects on fertility and sperm count were observed in the recent two-generation reproductive toxicity study in rats submitted to assess the endocrine disrupting potential of pirimicarb. In this study, the parental toxicity NOAEL is 24 mg/kg bw per day based on reduced body weight and body weight gain observed at 81.5 mg/kg bw per day. The offspring toxicity NOAEL is 24 mg/kg bw per day based on reduced pup body weights and absolute brain weight at 81.5 mg/kg bw per day. Finally, the reproductive toxicity NOAEL is also 24 mg/kg bw per day based on effects on fertility and sperm count at 81.5 mg/kg bw per day.[14]

With regard to foetal **development,** increased skeletal variants were observed in rats and rabbits. In the rat teratogenicity study, the maternal toxicity NOAEL is 25 mg/kg bw per day based on decreased body weight gain observed at 75 mg/kg bw per day and the developmental toxicity NOAEL is 25 mg/kg bw per day based on reduced foetal body weight and increased skeletal variants observed at 75 mg/kg bw per day. In the rabbit teratogenicity study, the maternal toxicity NOAEL is 10 mg/kg bw per day based on death, reduced body weight gain and reduced food consumption observed at 60 mg/kg bw per day and the developmental toxicity NOAEL is 10 mg/kg bw per day based on increased skeletal variants at 60 mg/kg bw per day.

The substance was concluded unlikely to be a reproductive toxicant in humans.

With respect to **neurotoxicity**, reduced overall activity was induced at 40 mg/kg bw in an acute neurotoxicity study in rats, triggering a NOAEL of 10 mg/kg bw. In a sub-chronic neurotoxicity study, no neurotoxic effects were observed and a NOAEL of 5.6 mg/kg bw per day was set, based on changes in body weight and reduced food utilisation. This NOAEL was identified as relevant to address short-term toxicity of pirimicarb in rats. Considering the chemical structure of the active substance, existing concern based on its mode of action (MoA), the recurrent neurotoxicity findings observed in the dataset available for the peer review and the lack of a comparative cholinesterase assay for this active substance, a data gap for a developmental neurotoxicity (DNT) study is set leading to an **issue not finalised** (see Section 9.1.1).[15]

The substance was concluded unlikely to be **immunotoxic** in humans based on the standard toxicological data package.

The **acceptable daily intake** (**ADI**) is 0.0035 mg/kg bw per day, based on the 1-year dog study (supported by the 2-year rat study), applying an increased uncertainty factor (UF) of 1000. The additional UF of 10 was applied due to the data gap for a DNT study. The ADI value differs from the previous peer review where the ADI of 0.035 mg/kg bw per day was based on the same NOAEL from the 1-year dog study but applying the standard UF of 100 (EFSA, 2005).

The **acute reference dose** (**ARfD**) is 0.01 mg/kg bw, based on the acute neurotoxicity study supported by the rabbit developmental toxicity study, applying an increased uncertainty factor (UF) of 1000 due to the data gap for a DNT study. This value differs from the previous peer review where the ARfD of 0.1 mg/kg bw was based on the same acute neurotoxicity study, applying the standard UF of 100 (EFSA, 2005).

The **acceptable operator exposure level** (**AOEL**) is 0.0035 mg/kg bw per day, based on the 1-year dog study (supported by the 2-year study in rats), applying an increased UF of 1000 due to the data gap for a DNT study, as well as no correction for oral absorption. This value differs from the previous peer review where the AOEL of 0.035 mg/kg bw per day was based on the same NOAEL from the 1-year dog study, applying the standard UF of 100 (EFSA, 2005).

The **acute AOEL** (**AAOEL**) is 0.01 mg/kg bw, based on the acute neurotoxicity study supported by the rabbit developmental toxicity study, applying an increased UF of 1000 due to the data gap for a DNT study, as well as no correction for oral absorption.

During the running of the current peer review, new information (in vitro data for AChE enzyme inhibition and in vivo data with pirimicarb) submitted by the applicant and assessed by the RMS (Sweden, 2022) resulted in a request by the European Commission for EFSA to deliver a statement on whether the applicable approval criteria may still be considered fulfilled, taking into consideration the information submitted by the applicant and the assessment of the rapporteur Member State, Sweden.[16] In this statement, an ADI/AOEL of 0.007 mg/kg bw per day were set based on the 1-year dog study supported by the 2-year rat study and applying an overall UF of 500 (and no correction of the AOEL for oral absorption); an additional UF of 5 was agreed due to the lack of specific data addressing DNT or the pup sensitivity to AChE inhibition.[17]

[12]See experts' consultation 2.4 at Pesticides Peer Review Meeting 190 (session 2), January 2019 (EFSA, 2024).

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

[14]See experts' consultation 2.18 at Pesticides Peer Review TC 131, March 2024 (EFSA, 2024).

[15]See experts' consultation 2.6 at Pesticides Peer Review Meeting 190, session 2 in January 2019, experts' consultation 2.1 at Pesticides Peer Review TC 89 in September 2022 and 2.18 at Pesticides Peer Review TC 131 in March 2024 (EFSA, 2024).

[16]See provisions of article 21 of Regulation (EC) No 1107/2009.

[17]See experts' consultation 2.1 at the Pesticides Peer Review TC 89 in September 2022 (EFSA, 2024).

It is noted that the agreed additional UF of 10 in the present renewal peer review, due to lack of DNT assessment, is in line with the current approach for this data gap for cholinesterase inhibitor insecticides.

Dermal absorption of pirimicarb in the formulation for representative uses 'A10788A' (Pirimor) has been assessed in a 'triple pack' approach (in vivo/in vitro rat, in vitro human skin). Based on the EFSA guidance (EFSA PPR Panel, 2012), the dermal absorption values to be used for risk assessment are 1% for the concentrate and range from 14% (for the dilution 0.375 g/L in sugar beet) to 22% (for the dilution 0.25 g/L in ornamentals) for the representative uses.

The **non-dietary exposure** estimates for **operators** (based on EFSA, 2022) are below the (A)AOEL for use on ornamentals in greenhouse, in case of downward spraying only (i.e. for low crops) and with the use of appropriate personal protective equipment (PPE) (i.e. workwear and gloves during mixing, loading and application) and drift reduction measures. It is noted that in case of dense crop scenario, additional impermeable clothing during application would also be required. For the other uses in winter and spring wheat and sugar beet, use of PPE is necessary to ensure exposure below (A)AOEL (see Table 7).

For **workers**, during activities on ornamentals in greenhouse, the exposure estimates are above the AOEL even with use of gloves. The predicted exposure is below the AOEL when re-entry is at minimum 3 days for activities of limited duration (2 h, after one application) up to 16 days for longer duration activities (8h, after three applications). For the representative uses in sugar beet and winter wheat (one application), worker exposure estimates are below the AOEL while for the use in spring wheat (two applications), the estimates are above the AOEL for inspection activities (based on EFSA, 2022).

Exposure estimates for **residents and bystanders** (based on EFSA, 2022) are above the (A)AOEL for all representative uses (even including all available risk mitigation measures) with exception of the use on **ornamentals** in case of downward spraying, with the use of a 5 m buffer zone and drift reduction technology.

Toxicological studies and information have been provided for the **carbamate metabolites** R34836, R34885 and R35140; for the **hydroxypirimidine metabolites** R31680, R31805, R34865; for the **guanidine metabolites** R12378, R16192, R16210 and for other metabolites, SYN548582, as reported in Appendix B. Metabolites of pirimicarb found in groundwater and/or in animals/plants were discussed at peer review experts' meetings.[18] A genotoxicity potential could be excluded for R34836, R31680 and SYN548582. Toxicological reference values of the parent pirimicarb apply to metabolites R34836 and R31680. The ones relevant to consumer risk assessment are presented and discussed in the following table. Further assessment of the toxicological profile of metabolites R31805, R34865, R34885 (relevant to establish the residue definition for risk assessment), R406405 (major metabolite in milk) and R16210 (only genotoxicity profile) is needed (data gaps leading to an **issue not finalised**, see Sections 3 and 9.1.1) (Table 1).

TABLE 1 Summary of the toxicological profile of the metabolites relevant to consumer risk assessment.

Metabolite	Genotoxicity	General toxicity reference values (RV)	Source of human exposure[a]
R34836	Unlikely to be genotoxic in vivo	RV of pirimicarb apply	Residues
R31805	Positive gene mutation in mammalian cells in vitro (mouse Lymphoma test), follow up needed in vivo (**data gap**) Negative for clastogenicity and aneugenicity	This metabolite might be covered by the parent for general toxicity and if specific reference values should be set, these might be derived from the 90-day study No conclusion, pending data gap in genotoxicity	Residues
R34865	Positive gene mutation in mammalian cells in vitro (mouse lymphoma test), follow up needed in vivo (**data gap**) Negative for clastogenicity and aneugenicity	Loss of carbamate moiety and general toxicity data indicate that it might be of lower toxicity than the parent This metabolite might be covered by the parent for general toxicity No conclusion, pending data gap in genotoxicity	Residues
R34885	Equivocal gene mutation in bacteria (Ames test) Clarification (new test) needed (**data gap**) Negative for clastogenicity and aneugenicity	No conclusion, pending data gap in genotoxicity	Residues
R31680	Unlikely to be genotoxic	RV of pirimicarb apply (worst case)	None under the representative uses
R406405	QSAR analysis showing an alert for Ames test. Inconclusive for genotoxicity (**data gap**)	ToxTree: same alerts as for the parent; inconclusive for general toxicity, a toxicological assessment is not possible (**data gap**)	Residues
SYN548582	Unlikely to be genotoxic	No data, general toxicity cannot be assessed	Residues
R16210	No data (**data gap**)	Acute oral LD_{50}: 1445 mg/kg bw based on testing dimethyl guanidine hydrochloride; no data on repeated dose toxicity	Residues

[a]As groundwater metabolite please refer to the assessment summarised under Section 7.

[18]Refer to experts' consultations 2.10 and 2.2 in the Report of Pesticides Peer Review Experts' Meeting TC 190 session 2 (January 2019) and TC 89 (September 2022) (EFSA, 2024).

3 | RESIDUES

The assessment in the residue section is based on the following guidance documents: OECD (2009, 2011), European Commission (2011) and JMPR (2004, 2007).

Pirimicarb was discussed at the Pesticides Peer Review Experts' meeting 191 in January–February 2019.

Metabolism studies on lettuce, potatoes, apples and wheat, were conducted through foliar application on pyrimidine ring and they showed pirimicarb being the predominant residue in lettuce (52% total radioactive residue (TRR)), apple fruits (30% TRR) and wheat grains (25% TRR), with a limited presence in potatoes (1.7% TRR). Metabolite **R34836** was detected in significant quantities in lettuce (21% TRR), whereas in other crops it remained below 10% TRR. Although metabolites **R34885** and **R31805** were generally recovered at levels below 10% TRR across most of the investigated crops, their absolute amounts were relevant (0.14 mg/kg and 1 mg/kg respectively in lettuce). Metabolite **R34865** was observed at levels up to 0.72 mg/kg, exclusively in lettuce. In potato tubers at less exaggerated application (approx. 3N), metabolite **R16210** was recovered at 15% TRR, despite the overall low total radioactivity of residues (0.04 mg/kg). Notably, the genotoxic profile of R16210 remains unresolved (see Section 2).

Field trials submitted in support of the representative uses and analysing for pirimicarb and R34836 were sufficient only for wheat grain. For wheat straw, only six trials were submitted for the Northern EU (NEU) use, resulting in a **data gap** for additional two GAP compliant trials (see Section 10). Additionally, no residue trials were available for sugar beet leaves in the NEU (data gap and **issue not finalised,** see Section 9.1.1). Despite in sugar beet roots only five trials were available for NEU this could be considered sufficient based on low residue situation found in sugar beet roots from Southern EU (SEU).

In the two rotational crop metabolism studies conducted in lettuce, radish, wheat and millet, a similar metabolic pattern was observed as in primary crops. Pirimicarb was detected in radish roots up to 20% TRR and in the other crops in limited quantities (< 4% TRR), while metabolites **R34836, R31805, R34865** and **R34885** were recovered in significant (mainly in absolute) amounts of TRR in most crops (e.g. 0.13 mg/kg in radish leaves for R34865). Additionally, R31805, R34865 and R34885 are very highly persistent compounds in soil (see Section 4).

Two rotational crop field trials conducted in the US covering the application rate and soil plateau concentration of pirimicarb with regard to the cGAP were submitted. These trials were analysed for pirimicarb, R34836 and R238177, confirming the presence of pirimicarb and R34836 residues in rotational crops. R31805, R34865 and R34885 were not investigated in the field rotational crop studies. Nevertheless, based on results from metabolism studies and their persistence in soil (see Section 4), these compounds are expected to be found in rotational crops. Consequently, **a data gap** was identified for sufficient rotational crop field trials analysing pirimicarb and the metabolites R31805, R34865, R34836 and R34885, supported by storage stability and validated analytical methods. Moreover, the genotoxic profile of several metabolites, including R31805, R34865 and R34885 expected as residues in rotational crops, was not ruled out (see Section 2), leading to the consumer risk assessment not finalised (see Section 9.1.1).

Considering the information from primary and rotational crops metabolism studies, the outstanding data from field rotational trials and the findings from the mammalian toxicology section, a **provisional residue definition for risk assessment** for plants was proposed as the sum of pirimicarb and R34836, expressed as pirimicarb. Storage stability data for R34885 were also not available and they would be needed in case this metabolite will be included finally in the risk assessment residue definition for plants (**data gap**, see Section 10). **For enforcement** the residue definition in plants is proposed as pirimicarb.

Regarding the assessment of livestock, four metabolism studies were submitted in laying hens and lactating goats. In laying hens, pirimicarb underwent extensive metabolism, yielding R34865 (up to 48% TRR in egg white) and R31680 (up to 50% TRR in muscle). In ruminants, R34865, R31680 and R406405 were detected in milk, with levels reaching up to 29%, 16% and 16% TRR, respectively. Currently, the **residue definition for risk assessment** in **ruminants provisionally** includes R34865 and R31680, expressed as pirimicarb. For the major metabolite R406405 in milk, no genotoxicity data were available (see Section 2) and its significance for the risk assessment may have to be reassessed pending clarification of its genotoxicity profile. The **enforcement residue definition** for ruminant commodities is also provisionally proposed as R34865 expressed as pirimicarb, pending the conclusion on the genotoxicity potential of R34865. It is highlighted that the fate of R34836 in animal matrices was not investigated, despite being triggered by the dietary burden resulting from the representative uses for ruminants, thus a **data gap** is identified leading to an **issue not finalised** (see Section 9.1.1). In poultry, the investigation of R34836 is currently not needed, as residues above 0.01 mg/kg are not expected in poultry matrices. Consequently, the **residue definitions for risk assessment** and **enforcement** in poultry matrices was proposed as pirimicarb by default.

Standard hydrolysis studies were submitted for pirimicarb and metabolite R34836. The results showed no significant degradation (lower than 10% TRR) of either compound under the tested hydrolytic conditions. The same residue definitions as for primary crops could be applied also for processed commodities on a provisional basis. The stability of pirimicarb residues and metabolite R34836 was demonstrated in several commodities for up to 18 months when stored at –15°C. Although storage stability data were provided for cabbage and lettuce (high-water content), sugar beet leaves are not covered by the available data (**data gap,** see Section 10).

As regards the fish metabolism, the waiving based on the fat solubility of pirimicarb does not cover all the relevant metabolites included in the risk assessment residue definition; therefore, fish metabolism studies covering all the metabolites are needed (**data gap**, see Section 10). Regarding the magnitude of residues in pollen and bee's products for human

consumption, no data were submitted. Therefore, trials analysing for all compounds included in the plant risk assessment residue definition are needed (**data gap**, see Section 10).

An indicative consumer risk assessment was conducted using the new toxicological reference values: an ADI of 0.0035 mg/kg bw per day and an ARfD of 0.01 mg/kg bw, which were derived during the renewal peer review process. Residue trials on wheat, sugar beet root and leaves were used in the PRIMo rev. 3.1 tool. The theoretical maximum daily intake (TMDI) resulted in a maximum of 13% of the ADI (GEMs/Food G06 diet), while the acute intake international estimated short-term intake (IESTI) was calculated at 11% of the ARfD. However, the overall consumer risk assessment is not finalised pending the finalisation of the residue definitions in plant and livestock due to the identified data gaps in plants and animals alongside the pending assessment of the genotoxicity potential of relevant metabolites (see Sections 2 and 9.1.1). Regarding the use on ornamentals grown in pots where they are placed on the soil and could be grown into rotation with food crops, the exposure to consumers via dietary intake cannot be excluded and consequently the risk assessment cannot be finalised (see Section 9.1.1).

The consumer risk assessment from the consumption of drinking water is not finalised considering the lack of appropriate information to address the effect of water treatment processes with chlorination reagents on the nature of residues, potentially present in surface water when surface water is abstracted for drinking water (see Sections 4 and 9.1.1).

In the context of the renewal of the approval of pirimicarb, as toxicological reference values were lowered and the residue definitions for risk assessment were amended, a screening assessment considering the maximum residue levels (MRLs) derived for the authorised uses under the Article 12 of Regulation (EC) No 396/2005 (Art 12 MRL review) (EFSA, 2014) was carried out using, where appropriate, the provisional residue definitions from the current peer review and the amended toxicological reference values. Both the chronic and acute dietary intake exceeded the toxicological reference values, resulting in a consumer risk. The international estimated daily intake (IEDI) was calculated **to 219% of the ADI** while the maximum IESTI was calculated for peaches **1244% of the ARfD.** For 33 raw commodities and 11 processed commodities the IESTI exceed 100% of the ARfD. **Considering these results indicating consumer intake concerns a revision of the assessment of existing MRLs is recommended.**

4 | ENVIRONMENTAL FATE AND BEHAVIOUR

The rates of dissipation and degradation in the environmental matrices investigated were estimated using FOCUS (2006) kinetics guidance. In soil laboratory incubations under aerobic conditions in the dark, pirimicarb exhibited low to high persistence, forming the major (> 10% applied radioactivity (AR)) metabolites **R31805** (max. 27% AR, exhibiting moderate to very high persistence**), R34865** (max. 31% AR, high to very high persistence), **R34885** (max. 12% AR, moderate to very high persistence) and **R34836** (max. 19% AR, low to high persistence). The metabolite **R35140** was also formed and concluded to need assessment as it contains the carbamate moiety, it exhibited low persistence. Mineralisation of the 2-^{14}C pyrimidinyl ring radiolabel to carbon dioxide accounted for 0.3%–62% AR after 90–112 days. The formation of unextractable residues (not extracted by acetone: ammonium acetate) for this radiolabel accounted for 7%–36% AR after 90–112 days. In an anaerobic soil incubation, pirimicarb degraded more slowly than under aerobic conditions with **R31805** being the only metabolite formed at levels needing consideration. In a soil photolysis investigation, pirimicarb degradation was faster than in the dark control, but novel metabolites were not formed. Pirimicarb exhibited very high to low mobility in soil. **R34885** exhibited high to low soil mobility, **R34836** exhibited very high to slight soil mobility, **R34865** exhibited medium to slight soil mobility or was immobile and **R35140** exhibited very high to high soil mobility. It was concluded that the adsorption of pirimicarb and these metabolites was not pH dependent. **R31805** exhibited high to slight soil mobility or was immobile, with high mobility being exhibited under alkaline soil conditions. Exposure assessments therefore accounted for the pH dependent adsorption behaviour of R31805. Reliable field dissipation trial kinetic dissipation and degradation endpoints were unavailable for pirimicarb (four geographical locations needed) and its soil metabolites R31805, R34885 and R34865 (three geographical locations needed), that, based on their laboratory DT endpoints, trigger their investigation under field conditions. This is therefore identified as a **data gap** (see Section 10). The EU level assessment therefore had to be completed with just the degradation kinetic endpoints that were available from the laboratory incubations.

In laboratory incubations in dark aerobic natural sediment water systems, pirimicarb exhibited high persistence, forming no metabolites/chromatographic peaks > 5% AR (max. 3.5% AR, which had the retention time of R34885) in water or sediment. So, from these incubations no component other than pirimicarb triggered the need for identification or exposure assessment. The unextractable sediment fraction (not extracted via Soxhlet using acetone then acetone/water) was a sink for the 2-^{14}C pyrimidinyl ring radiolabel, accounting for 10–13% AR at study end (100 days). Mineralisation of this radiolabel was minimal accounting for a maximum 1.5% at study end. The rate of decline of pirimicarb in a laboratory sterile aqueous photolysis experiment indicated very low to moderate persistence (half-life of 1.9 hours at pH 7 30° N summer sunlight 5-cm light path length, estimated from the quantum yield to be 0.5 days for a 30-cm deep water column at ca. 50° N summer sunlight increasing to 12 days for winter sunlight). Chromatographically resolved components accounting for > 10% AR were R31805 (max. 28% AR), R34885 (max. 18% AR) and R16210 (max. 14% AR).

The necessary surface water and sediment exposure assessments (predicted environmental concentrations (PEC) calculations) were carried out for pirimicarb and the metabolites R31805, R34885, R34836, R34865, R35140 and R16210 using the FOCUS (FOCUS, 2001) step 1 and step 2 approach (version 3.2 of the Steps 1–2 in FOCUS calculator). For the active substance pirimicarb and metabolites R34885, R34836 and R35140, appropriate step 3 (FOCUS, 2001) and step 4 calculations were

available based on the daily sum of these compounds with this being defined in the assessment as the 'holistically assessed carbamate moiety' (HAM).[19] FOCUS Step 3 and Step 4 calculations were also available for the non-carbamate metabolites R31805 and R34865.[20] The step 4 calculations appropriately followed the FOCUS (FOCUS, 2007) guidance, with no-spray drift buffer zones of 20 m being implemented for the drainage scenarios (representing a 91%–93% spray drift reduction), and combined no-spray buffer zones with vegetative buffer strips of 20 m (reducing solute flux in run-off by 80% and erosion run-off of mass adsorbed to soil by 95%) being implemented for the run-off scenarios. The SWAN tool (version 4.0.1) was appropriately used to implement these mitigation measures in the simulations. However, risk managers and others may wish to note that whilst run-off mitigation is included in the step 4 calculations available, the FOCUS (FOCUS, 2007) report acknowledges that for substances with K_{Foc} < 2000 mL/g (i.e. pirimicarb and R31805, R34885, R34836, R34865 and R35140), the general applicability and effectiveness of run-off mitigation measures had been less clearly demonstrated in the available scientific literature, than for more strongly adsorbed compounds.

For the representative protected use on pot grown ornamentals in greenhouses (permanent), a surface water exposure assessment was based on PEC where 0.1% and 0.2% emission of pirimicarb from greenhouses is re-deposited on an adjacent surface water body with a water volume of 300 L/m^2. This approach has been accepted by Member State experts as an assumption that can be used in EU level surface water exposure assessments for greenhouse uses and is referred to in FOCUS (2008) air guidance as being appropriate. It is noted that this only covers part of the use in greenhouses (permanent) when the pots are on a sealed hard standing such as concrete and does not cover the situation where the pots might be placed on soil. Consequently, a **data gap** has been identified for the missing surface water exposure assessments for uses on pot plants (ornamentals) in greenhouses (permanent) where pots stand on soil (see Section 10). For these exposure assessments, in addition to emission via condensate, they also need to cover the drainage route to surface water. It is noted (see Section 5) that a high long-term risk to aquatic invertebrates was already indicated from 0.1% emission (i.e. via condensate moving to surface water). High risk might therefore also be expected for the representative uses where pots stand on soil.

The necessary groundwater exposure assessments were appropriately carried out using FOCUS (European Commission, 2014a) scenarios and the models PEARL 4.4.4, PELMO 5.5.3 and MACRO 5.5.4.[21] The potential for groundwater exposure from the representative field uses by pirimicarb and its soil metabolites R31805, R34885, R34836, R34865 and R35140 above the parametric drinking water limit of 0.1 µg/L was concluded to be low in geoclimatic situations that are represented by all nine FOCUS groundwater scenarios.

The RMS provided appropriate information to address the effect of the water treatment process of ozonation on the nature of the residues that might be present in surface water, when surface water is abstracted for producing drinking water. The conclusion of consideration of peer-reviewed scientific publications was that neither pirimicarb nor any of its degradation products that trigger assessment (R31805, R34885, R34836, R34865, R35140 and R16210) would be expected to undergo any transformation due to oxidation to nitrosamines with ozone. However, as upon request, the applicant did not provide appropriate information to address the effect of water treatment with chlorination reagents, this has led to the identification of a **data gap** and results in the consumer risk assessment not being finalised (see Sections 3 and 9.1.1).

The PEC in soil, surface water, sediment and groundwater covering the representative uses assessed (except the PEC soil for pot grown ornamentals in greenhouses (permanent)) can be found in Appendix B of this conclusion.[22] The provision of the PEC soil for pot grown ornamentals in greenhouses where pots are placed on soil has been identified as a **data gap** leading to an assessment not finalised (see Sections 3, 5 and 9.1.1). A key to the wording used to describe the persistence and mobility of the compounds assessed can be found in Appendix C of this conclusion.

5 | ECOTOXICOLOGY

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

Some aspects of the environmental risk assessment of the representative uses of pirimicarb were discussed at the Pesticides Peer Review experts' meeting TC 192 (11–15 February 2019).

The batches used in the ecotoxicity studies were considered to be sufficiently representative of the proposed specification. However, no assessment of whether the batches were comparable to the existing specification was available.

For the representative use to ornamentals grown in pots in permanent greenhouses, minimal exposure to birds, mammals, bees, non-target arthropods and non-target terrestrial plants is expected. Consequentially, a low risk to these groups of organisms was concluded.

Suitable acute toxicity data for **birds** and **mammals** were available for the active substance. Furthermore, two acute toxicity studies were available for mammals which were performed using comparable formulations to the formulation for representative uses. Acute toxicity data for mammals were also available for metabolite R34836. Furthermore, an avian

[19]Simulations utilised the agreed Q10 of 2.58 (following EFSA, 2008) and Walker equation coefficient of 0.7.

[20]Simulations utilised the agreed Q10 of 2.58 (following EFSA, 2008) and Walker equation coefficient of 0.7.

[21]Simulations utilised the agreed Q10 of 2.58 (following EFSA, 2008) and Walker equation coefficient of 0.7.

[22]The applicant was requested to provide PEC soil for pot grown ornamentals and no data were provided. The applicant stated that pots would be placed on concrete, tables or benches precluding soil exposure (see reporting table comment 4(89) and evaluation table section 4 data requirement 4.5 (EFSA, 2024)). This was considered not in line with the representative uses applied for in the dossier that made no reference to the fact that pots were to only be placed on concrete, tables or benches and should not be placed on soil.

reproduction study was available and the endpoint was agreed during the experts' meeting.[23] The suitable long-term endpoint for the assessment of wild mammals was also agreed during the experts' meeting.[24]

When expressed in terms of active substance, the toxicity endpoint from the acute toxicity studies with mammals performed using comparable formulations to the formulation for representative uses, was three times lower than that of the pirimicarb. An acute risk assessment for mammals was presented using this endpoint in addition to a risk assessment with the active substance (see below). No toxicity study was available for birds with the formulation for representative uses. The experts at the meeting noted that a high acute risk to birds is already identified for the representative field uses (see below) and therefore it was agreed that the lack of information regarding the toxicity of the formulation for representative uses to birds should be reflected as an additional uncertainty that should be addressed in future assessments.

For the representative uses to winter wheat, spring wheat and sugar beet the tier 1 risk assessment for birds indicated a high acute risk but a low long-term risk. Several refinements were discussed during the experts' meeting[25] (focal species and body weight, refined deposition value, the proportion of diet obtained in the treated area (PT) values and body-burden modelling). The experts agreed with the refined deposition values and with the suggested focal species but did not accept the other refinements. However, even considering the agreed refinements, a high acute risk to birds was concluded for the representative uses to winter wheat, spring wheat and sugar beet.

The acute risk to mammals was presented using both the endpoint from the study with pirimicarb and the endpoint for the formulation for representative uses. For the representative uses to winter wheat, spring wheat and sugar beet, using the endpoint from the study with pirimicarb a low acute risk to mammals was indicated. However, using the formulation endpoint, a high acute risk to mammals was indicated in the tier 1 risk assessment. A refined deposition value was agreed and applied to the risk assessment which result in a low acute risk for the representative uses in winter and spring cereals. However, no suitable refinement was available for the large herbivorous mammals in sugar beet and therefore a high acute risk to mammals was concluded for that use.

For the representative uses to winter wheat, spring wheat and sugar beet, a low long-term risk to mammals was indicated with the exception of the small herbivorous mammal for the representative use to spring wheat. A refined deposition value was agreed and applied to the risk assessment which result in a low risk.

A secondary poisoning assessment was not triggered for pirimicarb, aquatic metabolites (R31805, R34885, R34836, R34865, R35140, R16210) and soil metabolites (R31805, R34885, R34836, R34865, R35140). A low risk to birds and mammals from consumption of contaminated water was concluded for both pirimicarb and the previously mentioned soil metabolites.

A low risk to mammals from plant metabolite R34836 was concluded with the available information. However, insufficient information was available to address the risk to birds from this metabolite (**data gap**, see Section 10).

For pirimicarb, suitable toxicity data were available for the acute and chronic assessment of **aquatic organisms** (fish, aquatic invertebrates, algae). Several additional toxicity data were available for aquatic invertebrates; such studies were evaluated to be supportive by the experts during the peer review meeting.[26] Furthermore, data were available giving the toxicity to aquatic invertebrates for the formulation for the representative uses. No data with the formulation for the representative uses were available for fish and algae. However, considering the toxicity of the parent to these taxa, no further data were considered necessary.

Acute toxicity data were available for **aquatic invertebrates** for surface water metabolites R34836, R34885, R34865, R35140 and R31805. For fish (acute) and algae toxicity data for metabolites R31805 and R34865 were available. No toxicity data were provided for metabolite R16210; however, considering the argumentation provided by the applicant regarding its structure, this was considered as acceptable and a low risk could be concluded without a quantitative assessment.

Metabolites R34836, R34885 and R35140 contain the carbamate toxophore in their chemical structure. Furthermore, their toxicity towards aquatic invertebrates was noted to be in the same order of magnitude to the parent substance. As a result, the risk assessment for pirimicarb and these metabolites was performed using exposure estimates based on the daily sum of these compounds referred to as the 'holistically assessed carbamate moiety' (HAM, see Section 4). The combined PEC value was then compared to the lowest available toxicity endpoint. This approach was agreed by the experts during the expert meeting.[27]

Several refinements for the acute and chronic risk assessment for aquatic invertebrates were discussed during the experts' meeting.[23] Considering that the acute toxicity data for additional species were only considered as supportive, the experts agreed that they should not be used to plot species sensitivity distribution nor use a geometric mean in the risk assessment. Nevertheless, accounting for the higher sensitivity of *Daphnia magna* relative to the other tested species, the experts agreed to lower the assessment factor for the acute assessment to 50. No suitable refinements were available for the chronic assessment.

Considering the exposure to HAM, the risk to fish (acute and chronic) and algae from pirimicarb and metabolites R34836, R34885 and R35140, was shown to be low, for all representative uses, based on FOCUS step 1 exposure estimates. The acute assessment for aquatic invertebrates was presented only considering the refined assessment factor. For the uses to winter

[23]See experts' consultation 5.2 at Pesticides Peer Review Meeting 192 (session 2), February 2019 (EFSA, 2024).
[24]See evxperts' consultation 5.3 at Pesticides Peer Review Meeting 192 (session 2), February 2019 (EFSA, 2024).
[25]See experts' consultation 5.1 at Pesticides Peer Review Meeting 192 (session 2), February 2019 (EFSA, 2024).
[26]See experts' consultation 5.4 at Pesticides Peer Review Meeting 192 (session 2), February 2019 (EFSA, 2024).
[27]See experts' consultation 5.4 at Pesticides Peer Review Meeting 192 (session 2), February 2019 (EFSA, 2024).

wheat, spring wheat and sugar beet, a high acute and chronic risk to aquatic invertebrates was indicated at FOCUS step 3 for pirimicarb and metabolites R34885, R34836 and R35140. Using the available FOCUS step 4 exposure estimates, which consider maximum risk mitigation measures in line with FOCUS (2007) guidance as set out in Section 4, a high risk to aquatic invertebrates was indicated in:

- 6/9 FOCUS scenarios for the representative use to winter wheat;
- 4/5 FOCUS scenarios for the representative use to spring wheat (two applications)[28];
- 3/4 FOCUS scenarios for the representative use to sugar beet.

For the representative use to ornamental plants in greenhouses, a high risk was indicated.[29] Consequently, a high risk to aquatic invertebrates was included in the majority of the scenarios for all representative uses (**critical area of concern**, see Section 9.1.2).

A low acute risk to aquatic invertebrates for metabolites R34865 and R31805 was indicated for all representative uses at FOCUS step 1. However, since these metabolites still contain the carbamate moiety a chronic risk assessment for aquatic invertebrates was performed considering the toxicity was equal to pirimicarb. For metabolite R31805, a low risk was indicated in 6/9 FOCUS surface water scenarios for winter wheat, 3/5 for spring wheat and 4/4 for sugar beet. For metabolite R34865, a low chronic risk to aquatic invertebrates was indicated for all representative uses. The risk assessment was deemed also to conclude a low risk to fish and algae. Toxicity data, for sediment dwelling organisms, for pirimicarb and sediment metabolites (R34885, R34836, R35140) were not available and therefore a **data gap** was concluded (see Section 10). The risk to sediment dwelling organisms for metabolites R31805, R34865, R16210 was considered to be covered by the risk assessments for aquatic invertebrates from HAM.

No fully reliable acute oral toxicity endpoint for pirimicarb or the formulation for representative uses were available for **honey bees** (**data gap**, see Section 9.1.1). A reliable acute contact endpoint for honeybees from a study with a comparable formulation to the formulation for representative uses was available but none for pirimicarb. A chronic toxicity endpoint for honeybees was available for both pirimicarb and the formulation for representative uses, whereas for honeybee larvae only the endpoint with the formulation for representative uses was reliable. In addition, there were four semi-field studies and two field studies with honey bees available. No data were available for sublethal effects (**data gap**, see Section 9.1.1) or accumulative effects. Furthermore, no toxicity data were available for bumble bees or solitary bees.

Information was presented to demonstrate that spring and winter wheat are not attractive to honeybees; this is aligned to the state-of-the-art considerations on the attractiveness of crops to honeybees (EFSA, 2023b). It was also noted that sugar beet is usually harvested before flowering which would mean that bees would not be exposed to residues on the treated crop. It is noted, however, that the GAP table does not restrict the use to sugar beet harvested before flowering. Furthermore, for all field crops, exposure to bees can occur via weeds in the field, plants in the field margin, flowering adjacent crops and residues in the succeeding crop. The RMS also raised a concern that honeybees may be exposed via consumption of over-sprayed insect honey dew which is considered to be relevant for cereals.

Owing to the lack of suitable acute oral toxicity endpoint for honeybees, no tier 1 acute risk assessment could be performed using either the European Commission (2002a) or the EFSA (2013) guidance document (data gap leading to an **issue not finalised**, see Section 9.1.1). The available acute contact risk assessment, performed in accordance with European Commission (2002a), indicated a low risk to honeybees for contact exposure. Furthermore, the available chronic risk assessments for honeybees were not evaluated by the RMS and EFSA noted that it was not fully in line with the EFSA (2013) methodology (**data gap**).

The applicant provided a risk assessment for honey bees from plant metabolites, however, this has not been evaluated by the RMS (**data gap**, see Section 9.1.1).

The available higher tier studies were discussed in the experts' meeting.[30] Two of the semi-field studies and both of the field studies were performed on attractive crops and at a higher application rate than those in the representative uses; they were therefore not considered further for the assessment. The two other semi-field studies were performed with winter wheat over sprayed with sugar solution to mimic insect honey dew before the application of the test item. Effects on the honey bees were observed in both studies when applications were made during and outside of the bee flight period. However, both studies were performed at higher application rates than those considered for the representative uses under assessment and therefore it was not possible to conclude whether such effects are relevant for the representative uses. With the information available the experts' agreed that it is not possible to exclude a high risk to honey bees from this route of exposure[27] (data gap leading to an **issue not finalised**, see Section 9.1.1).

Tier 2 toxicity studies were available for **non-target arthropods.** Furthermore, several peer-reviewed publications identified in the literature search were evaluated and discussed in the RAR. For all representative field uses, the available tier 2 risk assessment indicated a low off-field risk to non-target arthropods provided risk mitigation measures equivalent to a 5 m no-spray buffer zone are used. However, a high in-field risk to non-target arthropods was indicated with the tier 2 risk assessment for all representative field uses. The refined risk assessment proposed by the applicant, using a refined

[28]For a single application to spring cereals, 3/5 FOCUS scenarios indicated a high risk for early and late applications.

[29]The aquatic risk assessment for the representative use in ornamentals considered three applications to ornamentals. No exposure assessment was available for one application.

[30]See experts' consultation 5.3 at Pesticides Peer Review Meeting 192 (session 2), February 2019 (EFSA, 2024).

degradation estimate, was discussed during the experts' meeting.[31] The experts concluded that such refinement, alone, was not sufficient to address the in-field risk to non-target arthropods. Therefore, a high in-field risk to non-target arthropods was concluded for the representative uses to winter wheat, spring wheat and sugar beet.

Chronic toxicity studies for **earthworms** and the **soil macro-organisms**, *Folsomia candida and Hypoaspis aculeifer*, were available for the formulation for representative uses. Based on the available risk assessment a low risk to earthworms and other soil macro-organisms was concluded for all representative field uses. A screening level assessment for soil metabolites R31805, R34885, R34836, R34865 and R35140 indicated a low risk to earthworms and other soil macro-organisms. Furthermore, suitable toxicity data and risk assessment were available indicating a low risk to **soil microorganisms**, for all representative field uses, for the formulation for representative uses, metabolite R31805 and metabolite R34865. A screening level assessment also indicated a low risk to soil micro-organisms for metabolites R34885, R34836 and R35140.

As discussed in Section 4, the exposure assessment for the representative use to ornamentals grown in pots placed on soil inside permanent greenhouses could not be finalised with the available information. As a result, a risk assessment for soil organisms could not be performed for this representative use (**issue not finalised**,[32] see Section 9.1.1).

Screening data were considered sufficient to indicate a low risk to **non-target terrestrial plants** for all representative uses. A low risk to **biological methods for sewage treatment** was concluded based on the available data.

6 | ENDOCRINE DISRUPTION PROPERTIES

The endocrine disruption properties of pirimicarb were discussed at the Pesticides Peer Review Experts' teleconferences (TCs) 190 (mammalian toxicology, 28–31 January 2019), 192 (ecotoxicology, 11–15 February 2019) and 131 (joint session mammalian toxicology and ecotoxicology, 4–8 March 2024).

With regard to the assessment of the endocrine disruption (ED) potential of pirimicarb for humans according to the ECHA/EFSA guidance (2018), in determining whether pirimicarb interacts with the oestrogen, androgen and steroidogenesis (EAS) and thyroid (T) mediated pathways, the number and type of effects induced; and the magnitude and pattern of responses observed across studies were considered. Additionally, the conditions under which effects occur were considered, in particular, whether or not endocrine-related responses occurred at dose(s) that also resulted in overt toxicity. The assessment is therefore providing a weight-of-evidence analysis of the potential interaction of pirimicarb with the EAS and T signalling pathways using the available evidence in the dataset.

Pirimicarb shows anti-androgenic activity in vitro at high concentrations and not reproducible. However, a pattern of A-activity is not observed in vivo in level 3 or level 5 studies in a complete dataset. It is concluded that there is no evidence for a pattern of adversity related to EAS-modalities. The ED criteria for EATS-modalities are not met for pirimicarb since a pattern for EATS-mediated adversity has not been observed in a complete dataset, including a series of studies submitted following the ED clock stop (Scenario 1a of the ECHA/EFSA (2018) ED Guidance applies).[33]

The outcome of the assessment reported above for humans also applies to **wild mammals as non-target organisms**.

For non-target organisms other than mammals, an amphibian metamorphosis assay (AMA, OECD TG 231) and a 21-day fish screening assay (OECD TG 230) were available to sufficiently investigate the endocrine activity through the T and EAS-modalities, respectively. Level 2 in vitro assays for A- and S- modalities were also available and showed positive evidence for androgen antagonistic activity and increase in estradiol, respectively.

The AMA was deemed valid and did not show any positive evidence for T-mediated endocrine activity. Therefore, pirimicarb is not considered to meet the ED criteria for the T-modality for non-target organisms other than mammals.

The available 21-day fish screening assay showed some drawbacks questioning its reliability, e.g. choice of the concentration not in line with the recommendations of the OECD TG 230, although not triggering systemic toxicity; older animals than suggested in the pertinent OECD guideline (i.e. 35-week old compared to the suggested 20 ± 2 weeks in the OECD TG 230); low number of spawning days in the control, although fecundity was not formally assessed; high prevalence of histopathological change (i.e. oocyte atresia in control ovaries). It has also to be noted that this kind of tests are not considered fully suitable to detect activity and adverse effects related to exposure to a potential anti-androgen. Nevertheless, a dose-dependent decrease in female vitellogenin (VTG) was observed in absence of signs of systemic toxicity. EFSA acknowledged the submission by the applicant of a technical statement reporting a summary of a rapid androgen disruption activity reporter (RADAR) assay (study in line with OECD TG 251) after the long-term ED clock stop period.[34] Preliminary results did seem to show a potential androgenic activity. However, no raw data were submitted and the study was not eligible for being considered by the peer review as provided outside the set regulatory deadline for providing additional information. Overall, in light of:

[31] See experts' consultation 5.6 at Pesticides Peer Review Meeting 192 (session 2), February 2019 (EFSA, 2024).

[32] Only relevant when the greenhouse is removed and land is returned to open field agricultural/horticultural production.

[33] See Experts' consultation 2.13 and 2.14 at the Pesticides Peer Review Experts' TC 131, March 2024 (EFSA, 2024).

[34] According to Article 13(3a) of Commission Implementing Regulation (EU) No 844/2012 as amended by Commission Implementing Regulation (EU) No 2018/1659 in view of the scientific criteria for the determination of endocrine disrupting properties introduced by Regulation (EU) 2018/605.

(i) positive in vitro evidence both in HTRA for androgen receptor antagonism (OECD TG 458) and H295R (OECD TG 456),[35]
(ii) dose-dependent decreased VTG in females observed in the 21-day screening assay,
(iii) drawback identified in the available 21-d screening assay (OECD TG 230), e.g. age of the animals, poor control performance in terms of spawning days,[36]
(iv) Fish short-term reproduction assay (FSTRA)-like studies not fully appropriate to detect potential androgen antagonists,
(v) lack of additional information, e.g. MoA analysis,

the available information, weight of evidence with its related uncertainties[37] were deemed as not sufficient to exclude/confirm the concerns identified and to draw a firm conclusion on the potential for endocrine disruption of pirimicarb in non-mammalian species for EAS-modalities.

Based on the available information, pirimicarb is not an endocrine disruptor in humans according to point 3.6.5 of Annex II to Regulation (EC) No 1107/2009; for non-target organisms, the assessment of the endocrine disruption potential of pirimicarb according to point 3.8.2 of Annex II to Regulation (EC) No 1107/2009, as amended by Commission Regulation (EU) 2018/605,[38] cannot be concluded (**issue not finalised**, see Section 9.1.1).

7 | OVERVIEW OF THE RISK ASSESSMENT OF COMPOUNDS LISTED IN RESIDUE DEFINITIONS TRIGGERING ASSESSMENT OF EFFECTS DATA FOR THE ENVIRONMENTAL COMPARTMENTS (TABLES 2–5)

TABLE 2 Soil.

Compound (name and/or code)	Ecotoxicology
Pirimicarb	Low risk for field uses Data gap for the use to ornamentals in greenhouses[a]
R31805	Low risk for field uses Data gap for the use to ornamentals in greenhouses
R34885	Low risk to soil organisms
R34836	Low risk for field uses Data gap for the use to ornamentals in greenhouses[a]
R34865	Low risk for field uses Data gap for the use to ornamentals in greenhouses[a]
R35140	Low risk to soil organisms

[a]Only relevant for the representative use to ornamentals grown in pots placed on soil inside permanent greenhouses and when the greenhouse is removed and land is returned to open field agricultural / horticultural production.

TABLE 3 Groundwater.[a]

Compound (name and/or code)	>0.1 μg/L at 1 m depth for the representative uses[b] Step 2	Biological (pesticidal) activity/ relevance Step 3a.	Hazard identified Steps 3b. and 3c.	Consumer RA triggered Steps 4 and 5	Human health relevance
Pirimicarb	No	Yes	–	–	Yes
R31805	No	Not triggered	Not triggered Genotoxicity inconclusive General toxicity inconclusive	No for the representative uses assessed	No for the representative uses assessed
R34885	No	Not triggered	Not triggered Genotoxicity inconclusive General toxicity inconclusive	No for the representative uses assessed	No for the representative uses assessed

[35]See experts' consultation 2.13 of the Pesticides Peer Review Experts' TC 131, March 2024 (EFSA, 2024).
[36]See experts' consultation 5.10 of the Pesticides Peer Review Experts' meeting TC 131, March 2024 (EFSA, 2024).
[37]See RAR vol. 3 B.9 CA B.9.2.3.2. for the table reporting the uncertainty analysis (Sweden, 2024).
[38]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.

TABLE 3 (Continued)

Compound (name and/or code)	>0.1 μg/L at 1 m depth for the representative uses[b] Step 2	Biological (pesticidal) activity/ relevance Step 3a.	Hazard identified Steps 3b. and 3c.	Consumer RA triggered Steps 4 and 5	Human health relevance
R34836	No	Not triggered	Not triggered Similar toxicity as pirimicarb, including its carcinogenic potential	No for the representative uses assessed	No for the representative uses assessed
R34865	No	Not triggered	Not triggered Genotoxicity inconclusive General toxicity inconclusive	No for the representative uses assessed	No for the representative uses assessed
R35140	No	Not triggered	Not triggered No toxicological data/ assessment available	No for the representative uses assessed	No for the representative uses assessed

[a]Assessment according to European Commission guidance of the relevance of groundwater metabolites (2003).
[b]FOCUS scenarios or relevant lysimeter.

8 | PARTICULAR CONDITIONS PROPOSED TO BE TAKEN INTO ACCOUNT BY RISK MANAGERS

TABLE 4 Surface water and sediment.

Compound (name and/or code)	Ecotoxicology
Pirimicarb	High risk to aquatic invertebrates in the majority of scenarios[a] Data gap for sediment dwelling organisms
R31805*	Low risk to aquatic organisms
R34885	High risk to aquatic invertebrates in the majority of scenarios[a] Data gap for sediment dwelling organisms
R34836	High risk to aquatic invertebrates in the majority of scenarios[a] Data gap for sediment dwelling organisms
R34865*	Low risk to aquatic organisms
R35140	High risk to aquatic invertebrates in the majority of scenarios[a] Data gap for sediment dwelling organisms
R16210*	Low risk to aquatic organisms

*Metabolite is not a carbamate.
[a]Assessed as 'holistically assessed carbamate moiety' (HAM, see Sections 4 and 5).

TABLE 5 Air.

Compound (name and/or code)	Toxicology
Pirimicarb	> 0.747 mg/L – ≤ 1.065 mg/L air/4 h (nose only), Acute Tox 3 (H331)

Risk mitigation measures (RMMs) identified following consideration of Member State (MS) and/or applicant's proposal(s) during the peer review, if any, are presented in this section. These measures applicable for human health and/or the environment leading to a reduction of exposure levels of operators, workers, bystanders/residents, environmental compartments and/or non-target organisms for the representative uses are listed below. The list may also cover any RMMs as appropriate, leading to an acceptable level of risks for the respective non-target organisms.

It is noted that final decisions on the need of RMMs to ensure the safe use of the plant protection product containing the concerned active substance will be taken by risk managers during the decision-making phase. Consideration of the validity and appropriateness of the RMMs remains the responsibility of MSs at product authorisation, taking into account their specific agricultural, plant health and environmental conditions at national level.

8.1 | Particular conditions proposed for the representative uses evaluated

TABLE 6 Risk mitigation measures proposed for the representative uses assessed.

	Winter wheat	Spring wheat	Sugar beet	Ornamentals in greenhouse
Representative use	**Foliar spray**	**Foliar spray**	**Foliar spray**	**Foliar spray**
Operator exposure	Use of PPE is required[a]	Use of PPE is required[a]	Use of PPE is required[a]	Use of PPE is required[a], as well as downward spraying and drift reduction technology
Worker exposure	Use of PPE is required[b]	Available RMM are not sufficient	Use of PPE is required[b]	Use of PPE is required[c]
Bystander/resident exposure	Available RMM are not sufficient	Available RMM are not sufficient	Available RMM are not sufficient	Downward spraying, 5 m buffer zone and drift reduction technology are required
Risk to aquatic organisms	RMM equivalent to 20 m no-spray buffer zone combined with a 20 m vegetated buffer for 3/9 scenarios.[d] Insufficient RMM for all other scenarios	RMM equivalent to 20 m no-spray buffer zone combined with a 20 m vegetated buffer for 1/5 scenarios[e] Insufficient RMM for all other scenarios	RMM equivalent to 20 m no-spray buffer zone combined with a 20 m vegetated buffer for 1/4 scenarios[e] Insufficient RMM for all other scenarios	–

[a]For tractor-mounted applications: workwear + gloves (during mixing/loading (ML) and application (A)) + drift reduction (EFSA, 2022); coverall and sturdy footwear + gloves (ML & A) + respiratory protective equipment (RPE) (German model). For hand-held or trolley applications in greenhouse: workwear + gloves + RPE (ML & A).

[b]For inspection/irrigation (2 h): use of workwear is required (EFSA, 2022).

[c]Use of workwear and gloves is required and a minimum re-entry interval of 3 days for limited re-entry activities (2 h, after one application) up to 16 days for more extensive re-entry activities (8 h, after three applications) (EFSA, 2022).

[d]D3, D5 and D6.

[e]D3.

9 | CONCERNS AND RELATED DATA GAPS

9.1 | Concerns for the representative uses evaluated

9.1.1 | 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 one or more of 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[39] 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.

The following issues or assessments that could not be finalised have been identified, together with the reasons including the associated data gaps where relevant, which are reported directly under the specific issue to which they are related:

1. A hazard concern for phototoxicity and photomutagenicity of pirimicarb is identified based on positive results in the in vitro phototoxicity test (OECD TG 432).

   a. Further data to address the phototoxic potential of pirimicarb (i.e. OECD TG 498 test and/or agreed methodology to assess the risk to phototoxic and photomutagenic pesticide active substances) are needed to conclude. However, it is noted that validated photomutagenicity test or agreed methodology to assess the risk to phototoxic and photomutagenic pesticide active substances are currently not available (relevant for all representative uses, see Section 2).

2. The developmental neurotoxicity potential of pirimicarb could not be finalised considering existing concern based on the neurotoxic MoA of the active substance and the neurotoxicity findings observed in the dataset available for the peer review.

   a. A developmental neurotoxicity study is not available (relevant for all representative uses; see Section 2).

[39]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.

3. The consumer dietary risk assessment could not be concluded since the risk assessment residue definition for plant and livestock could not be finalised but only provisionally proposed pending the following data gaps to be addressed (see Section 3).

   a. A metabolism study investigating the fate of R34836 in ruminants was not available (relevant for all the representative uses, see Section 3).
   b. Four rotational crops trials (two NEU and two SEU) analysing for all compounds covered by the residue definition for risk assessment (including R31805, R34865, R34836, R34885) on crops representative of the relevant crop groups, supported by storage stability and validated analytical methods (relevant for all representative uses including ornamentals grown in pot where pots are placed on the soil; see Section 3)
   c. Eight GAP compliant residue trials on sugar beet leaves conducted in NEU and analysed according to the risk assessment residue definition (relevant for sugar beet use, see Section 3).
   d. Further assessment of the genotoxicity/toxicological profile of metabolites R31805, R34865, R34885, 406405 and R16210 (only genotoxicity) needs to be provided (relevant for all representative uses; see Sections 2 and 3).

4. The consumer risk assessment is not finalised with regard to the unknown nature of residues that might be present in drinking water, consequent to water treatment following abstraction of surface water that might contain metabolites of the active substance (see Sections 3 and 4).

   a. Information to address the issue of possible chlorinated transformation products of residues of surface water metabolites that might be formed from drinking water treatment processes when surface water is abstracted for the production of drinking water was not available. If an assessment is provided to show that concentrations at the point of abstraction for drinking water purposes will be low, this needs clear calculations and justification for the assumptions used in calculations. Should this consideration indicate that novel compounds might be expected to be formed from water treatment, the risk to human or animal health through the consumption of drinking water containing them needs to be addressed (relevant to comply with the conditions of approval, not dependent of any specific use, see Sections 3 and 4).

5. The risk to honeybees could not be finalised with the available information (relevant for winter and spring wheats and sugar beet representative uses, see Section 5).

   a. Suitable acute oral toxicity studies with honeybees are needed.
   b. Risk assessment for honeybees, in accordance with both European Commission (2002a) and the EFSA (2013) guidance document, are needed.
   c. Further consideration of the uncertainty related to the risk to honeybees via consumption of contaminated insect honeydew is needed.
   d. The risk assessment for honeybees from plant metabolites, provided by the applicant, should be evaluated.
   e. Information to address the risk to honey bees from sublethal effects.

6. The risk to soil dwelling organisms could not be finalised for the representative uses on pot grown ornamentals cultivated in greenhouses (permanent) when pots are placed on soil whilst PEC soil were not available for these uses (see Sections 4 and 5)

   a. To cover the situation where pot plants are placed on soil in greenhouses rather than on a concrete floor, tables or benches, PEC soil for pirimicarb and metabolites R31805, R34836, R34865 were not available and would be needed, as would the consequent risk assessment to soil dwelling organisms in the situation that greenhouses are removed and land is returned to open field agricultural/horticultural production (relevant for the pot grown ornamentals in greenhouses (permanent) representative uses evaluated, see Sections 4 and 5).

7. A conclusion on the endocrine disrupting properties of pirimicarb for non-target organisms through the EAS-modalities could not be drawn (see Section 6)

   a. Further data would be needed, i.e. a Mode of action analysis followed by further data to investigate adversity (e.g. level 5 study according to OECD TG 240 Medaka extended one generation).

9.1.2 | 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 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 Regulation (EC) No 1107/2009.

The following critical areas of concern are identified, together with any associated data gaps, where relevant, which are reported directly under the specific critical area of concern to which they are related:

8. High risk to aquatic organisms, in the majority of the assessed scenarios with maximum risk mitigation measures in line with FOCUS (2007) guidance as set out in Section 4, for all representative uses (see Section 5).

9.1.3 | Overview of the concerns identified for each representative use considered (Table 7)

In addition to the issues indicated below, the assessment of the endocrine disrupting properties of pirimicarb for non-target organisms other than wild mammals according to the scientific criteria for the determination of endocrine disrupting properties as set out in point 3.8.2 of Annex II to Regulation (EC) No 1107/2009, as amended by Commission Regulation (EU) 2018/605, could not be finalised.

TABLE 7 Overview of concerns reflecting the issues not finalised, critical areas of concerns and the risks identified that may be applicable for some but not for all uses or risk assessment scenarios.

Representative use		Winter wheat Foliar spray, one application	Spring wheat Foliar spray, two applications	Sugar beet Foliar spray, one application	Ornamentals pot plants Foliar Spray in greenhouses (permanent), three applications
Operator risk	Risk identified				X[c]
	Assessment not finalised				
Worker risk	Risk identified		X		
	Assessment not finalised				
Resident/bystander risk	Risk identified	X	X	X	X[c]
	Assessment not finalised				
Consumer risk	Risk identified				
	Assessment not finalised	X[3]	X[3]	X[3]	X[3,d]
Risk to wild non-target terrestrial vertebrates	Risk identified	X[e]	X[e]	X[e,f]	X
	Assessment not finalised				
Risk to wild non-target terrestrial organisms other than vertebrates	Risk identified	X[g]	X[g]	X[g]	
	Assessment not finalised	X[5]	X[5]	X[5]	X[6,h]
Risk to aquatic organisms	Risk identified	6/9 FOCUS scenarios[8]	4/5 FOCUS scenarios[8,i]	3/4 FOCUS scenarios[8]	X[8]
	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				

Notes: The superscript numbers relate to the numbered points indicated in Sections 9.1.1 and 9.1.2. Where there is no superscript number, see Sections 2–7 for further information.

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

[b]Value for non-relevant metabolites prescribed in SANCO/221/2000-rev. 10 final, European Commission (2003).

[c]Only for high ornamentals (upward spraying), see Section 2.

TABLE 7 (Continued)

[d]Only for pot grown ornamentals in greenhouses where pots are placed on soil, see Section 3.

[e]High acute risk to birds, see Section 5.

[f]High acute risk to large herbivorous mammals was concluded for the representative use to sugar beet. It should be noted that this assessment was performed using the endpoint from the study with a comparable formulation to the one for representative uses. A risk assessment using the endpoint for pirimicarb indicated a low acute risk to mammals, see Section 5.

[g]High in-field risk to non-target arthropods, see Section 5.

[h]The assessment for soil dwelling organisms is of low risk when the plant pots are not placed on soil. E.g. in greenhouses where pots sit on concrete, tables or benches, see Section 4 and 5.

[i]For a single application to spring cereals, 3/5 FOCUS scenarios indicated a high risk for early and late applications, see Section 5.

10 | LIST OF OTHER OUTSTANDING ISSUES

Remaining data gaps not leading to critical areas of concern or issues not finalised but considered necessary to comply with the data requirements, and which are relevant for some or all of the representative uses assessed at EU level. Although not critical, these data gaps may lead to uncertainties in the assessment and are considered relevant.

These data gaps refer only to the representative uses assessed and are listed in the order of the sections:

- For two of the components of the formulation for representative uses 'Pirimor', genotoxicity, long-term toxicity/carcinogenicity data were not available; therefore, in order to allow a final conclusion on the safety assessment of 'Pirimor', genotoxicity, repeated dose toxicity (short- and long-term) data for these component might be considered for further assessment (to be confirmed by Member States when assessing applications for PPP authorisation; relevant for all representative uses evaluated; see Section 'the active substance and the formulation for representative uses').
- An ILV of the monitoring method for feed/food of plant origin (relevant for all representative uses evaluated; see Section 1).
- Extraction efficiency for high-water content and dry plant commodities (relevant for all representative uses evaluated; see Section 1).
- A validated monitoring method for metabolite R34865 in animal products. This request may become obsolete or extended to other metabolites if the additional data needed for finalising the residue definition for monitoring in ruminants are provided, and R34865 is excluded and/or other metabolites are included in the residue definition (relevant for all representative uses evaluated; see Section 1 and data requirement 1.5 in evaluation table Section 1).
- Final report of the validation study for the monitoring method in soil (relevant for all representative uses evaluated; see Section 1).
- Selectivity of the monitoring method for surface water (relevant for all representative uses evaluated; see Section 1).
- Additional validation data to demonstrate efficiency of the step aiming to convert metabolite R34885 to R34836 or a new validated monitoring method for metabolite R34885 in surface water (relevant for all representative uses evaluated; see Section 1).
- An ILV of the monitoring method for determination of pirimicarb in drinking water (relevant for all representative uses evaluated; see Section 1).
- Retention capacity of the sorbent used in the monitoring method in air (relevant for all representative uses evaluated; see Section 1).
- A validated method for monitoring the metabolite R34865 in body fluids (blood) and tissues (relevant for all representative uses evaluated; see Section 1).
- Data for further assessment of the toxicological relevance of the impurities are needed (relevant for all representative uses evaluated; see Sections 1 and 2).
- Storage stability data for metabolite R34885 in case the compound would be included in the risk assessment residue definition for plants (relevant for all representative uses evaluated; see Section 3).
- Storage stability data for metabolite R34836 covering sugar beet leaves (relevant for sugar beet use, see Section 3).
- Additional two GAP compliant residue trials on wheat straw conducted in NEU and analysed according to the risk assessment residue definition (relevant for the representative use in wheat: see Section 3).
- Fish metabolism studies covering all the compounds relevant for risk assessment residue definition (relevant for wheat use, see Section 3).
- Residue trials for pollen and bee products analysing for all compounds covered by the residue definition for the plant risk assessment (relevant for all representative uses; see Section 3).
- Reliable field dissipation trial endpoints were not available for pirimicarb (four geographical locations needed) nor its soil metabolites R31805, R34885 and R34865 (three geographical locations needed) that based on their laboratory DT endpoints, trigger their investigation under field conditions (relevant for all representative uses evaluated; see Section 4).
- Surface water exposure assessments (PEC) were not available for uses on pot plants in greenhouses (permanent) where pots stand on soil (relevant for representative uses evaluated for protected pot grown ornamentals, when pots stand on soil in greenhouses (permanent); see Section 4).
- Further information is needed to address the risk to birds from metabolite R34836 (relevant for all representative field uses, see Section 5).
- Further information is needed to address the risk to sediment dwelling organisms from pirimicarb and sediment

metabolites (R34885, R34836, R35140) (relevant for all representative uses assessed, see Section 5).

ABBREVIATIONS

AAOEL	acute acceptable operator exposure level
AChE	acetylcholinesterase
ADE	actual dermal exposure
ADI	acceptable daily intake
AF	assessment factor
AMA	amphibian metamorphosis assay
AOEL	acceptable operator exposure level
AR	applied radioactivity
ARfD	acute reference dose
a.s.	active substance
bw	body weight
CI	confidence interval
CIPAC	Collaborative International Pesticides Analytical Council Limited
C&L	classification and labelling
CL	confidence limits
DM	dry matter
DT_{50}	period required for 50% dissipation (define method of estimation)
DT_{90}	period required for 90% dissipation (define method of estimation)
dw	dry weight
EAS	oestrogen, androgen and steroidogenesis modalities
ECHA	European Chemicals Agency
EEC	European Economic Community
FAO	Food and Agriculture Organization of the United Nations
FSTRA	fish short-term reproduction assay
GAP	Good Agricultural Practice
GC–MS	gas chromatography–mass spectrometry
IEDI	international estimated daily intake
IESTI	international estimated short-term intake
ISO	International Organization for Standardization
IUPAC	International Union of Pure and Applied Chemistry
JMPR	Joint Meeting of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Expert Group on Pesticide Residues (Joint Meeting on Pesticide Residues)
K_{doc}	organic carbon linear adsorption coefficient
K_{Foc}	Freundlich organic carbon adsorption coefficient
LC	liquid chromatography
LC–MS	liquid chromatography–mass spectrometry
LC–MS-MS	liquid chromatography with tandem mass spectrometry
LD_{50}	lethal dose, median; dosis letalis media
LOQ	limit of quantification
MOA	mode of action
MRL	maximum residue level
MS	mass spectrometry
NOAEL	no observed adverse effect level
OECD	Organisation for Economic Co-operation and Development
PEC	predicted environmental concentration
PEC_{soil}	predicted environmental concentration in soil
QSAR	quantitative structure–activity relationship
RAC	regulatory acceptable concentration
RAR	Renewal Assessment Report
SMILES	simplified molecular-input line-entry system
TMDI	theoretical maximum daily intake
TRR	total radioactive residue
TSH	thyroid-stimulating hormone (thyrotropin)
UF	uncertainty factor
UV	ultraviolet
WG	water-dispersible granule
WHO	World Health Organization

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CONFLICT OF INTEREST

If you wish to access the declaration of interests of any expert contributing to an EFSA scientific assessment, please contact interestmanagement@efsa.europa.eu.

REQUESTOR

European Commission

QUESTION NUMBER

EFSA-Q-2015-00625

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REFERENCES

ECHA (European Chemicals Agency). (2014). Committee for Risk Assessment (RAC) Opinion proposing harmonised classification and labelling at EU level of pirimicarb (ISO). CLH-O-0000001412-86-39/F. Adopted 4 December 2014. https://echa.europa.eu/documents/10162/8678ab3a-3323-4eca-b81a-9659a7a9f5cf

ECHA (European Chemicals Agency). (2017). Guidance on the Application of the CLP Criteria; Guidance to Regulation (EC) No 1272/2008 on classification, labelling and packaging (CLP) of substances and mixtures. Version 5.0, July 2017. Reference: ECHA-17-G-21-EN; ISBN: 978–92–9020-050-5. https://echa.europa.eu/guidance-documents/guidance-on-clp

ECHA and EFSA and JRC (European Chemicals Agency and European Food Safety Authority with the technical support of the Joint Research Centre), Andersson, N., Arena, M., Auteri, D., Barmaz, S., Grignard, E., Kienzler, A., Lepper, P., Lostia, A. M., Munn, S., Parra Morte, J. M., Pellizzato, F., Tarazona, J., Terron, A., & Van der Linden, S. (2018). Guidance for the identification of endocrine disruptors in the context of regulations (EU) No 528/2012 and (EC) No 1107/2009. *EFSA Journal*, *16*(6), 5311. https://doi.org/10.2903/j.efsa.2018.5311

EFSA (European Food Safety Authority). (2005). Conclusion regarding the peer review of the pesticide risk assessment of the active substance pirimicarb, finalised: 10 August 2005. *EFSA Scientific Report*, *43*, 1–76. https://www.efsa.europa.eu/en/efsajournal/pub/rn-43

EFSA (European Food Safety Authority). (2008). Opinion on a request from EFSA related to the default Q10 value used to describe the temperature effect on transformation rates of pesticides in soil. *EFSA Journal*, *6*(1), 622. https://doi.org/10.2903/j.efsa.2008.622

EFSA (European Food Safety Authority). (2009). Guidance on risk assessment for birds and mammals on request from EFSA. *EFSA Journal*, *7*(12), 1438. https://doi.org/10.2903/j.efsa.2009.1438

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

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*, *11*(7), 3295. https://doi.org/10.2903/j.efsa.2013.3295

EFSA (European Food Safety Authority). (2014). Reasoned opinion on the review of the existing maximum residue levels(MRLs) for pirimicarb according to article 12 of regulation (EC)No 396/20051. *EFSA Journal*, *12*(5), 3688. https://doi.org/10.2903/j.efsa.2014.3688

EFSA (European Food Safety Authority). (2015). Last version of calculator from EFSA 2014b: Guidance on the assessment of exposure of operators, workers, residents and bystanders in risk assessment for plant protection products. *EFSA Journal*, *12*(10), 3874. https://doi.org/10.2903/j.efsa.2014.3874

EFSA (European Food Safety Authority), Charistou, A., Coja, T., Craig, P., Hamey, P., Martin, S., Sanvido, O., Chiusolo, A., Colas, M., & Istace, F. (2022). Guidance on the assessment of exposure of operators, workers, residents and bystanders in risk assessment of plant protection products. *EFSA Journal*, *20*(1), 7032. https://doi.org/10.2903/j.efsa.2022.7032

EFSA (European Food Safety Authority). (2023a). Statement concerning the review of the approval of the active substance pirimicarb. *EFSA Journal*, *21*(2), 7807. https://doi.org/10.2903/j.efsa.2023.7807

EFSA (European Food Safety Authority), Adriaanse, P., Arce, A., Focks, A., Ingels, B., Jolli, D., Lambin, S., Rundlof, M., Sußenbach, D., Del Aguila, M., Ercolano, V., Ferilli, F., Ippolito, A., Cs, S., Neri, F. M., Padovani, L., Rortais, A., Wassenberg, J., & Auteri, D. (2023b). Revised guidance on the risk assessment of plant protection products on bees (Apis mellifera, Bombus spp. and solitary bees). *EFSA Journal*, *21*(5), 7989. https://doi.org/10.2903/j.efsa.2023.7989

EFSA (European Food Safety Authority). (2024). Peer review report to the conclusion regarding the peer review of the pesticide risk assessment of the active substance pirimicarb. https://open.efsa.europa.eu/questions/EFSA-Q-2015-00625

EFSA PPR Panel (EFSA Panel on Plant Protection Products and their Residues). (2012). Guidance on dermal absorption. *EFSA Journal*, *10*(4), 2665. https://doi.org/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*, *11*(7), 3290. https://doi.org/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 Risk Assessment for Birds and Mammals Under Council Directive 91/414/EEC. SANCO/4145/2000.

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. (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. pp. 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. (2014a). 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. 3, 613 pp., as outlined in Generic guidance for tier 1 FOCUS groundwater assessment, v. 2.2, May 2014.

European Commission. (2014b). Guidance document on the renewal of approval of active substances to be assessed in compliance with Regulation (EU) No 844/2012. SANCO/2012/11251-rev. 4, 12 December 2014.

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. 1.4, May 2015.

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 updated by the Generic guidance for Estimating Persistence and Degradation Kinetics from Environmental Fate Studies on Pesticides in EU Registration, v. 1.1, December 2014.

FOCUS (Forum for the Co-ordination of Pesticide Fate Models and their Use). (2007). Landscape and mitigation factors in aquatic risk assessment. Volume 1. Extended summary and recommendations. Report of the FOCUS Working Group on Landscape and Mitigation Factors in Ecological Risk Assessment. EC Document Reference SANCO/10422/2005 v.2.0, 169 pp.

FOCUS (Forum for the Co-ordination of Pesticide Fate Models and their Use). (2008). Pesticides in air: considerations for exposure assessment. Report of the FOCUS Working Group on Pesticides in Air. EC Document Reference SANCO/10553/2006-Rev. 2, June 2008.

JMPR (Joint Meeting on Pesticide Residues). (2004). Report of the Joint Meeting of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Core Assessment Group on Pesticide Residues, Rome, Italy, 20–29 September 2004, 383 pp.

JMPR (Joint Meeting on Pesticide Residues). (2007). Report of the Joint Meeting of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Core Assessment Group on Pesticide Residues, Geneva, Switzerland, 18–27 September 2007, 164 pp.

McCall, P. J., Laskowski, D. A., Swann, R. L., & Dishburger, H. J. (1980). Measurements of sorption coefficients of organic chemicals and their use in environmental fate analysis. In: Test protocols for environmental fate and movement of toxicants. In: Proceedings of the 94th annual meeting of the American Association of Official Analytical Chemists (AOAC). Oct 21–22, Washington, DC. pp. 89–109.

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. www.oecd.org

SETAC (Society of Environmental Toxicology and Chemistry). (2001). In M. P. Candolfi, K. L. Barrett, P. J. Campbell, R. Forster, N. Grandy, M. C. Huet, G. Lewis, P. A. Oomen, R. Schmuck, & H. Vogt (Eds.), *Guidance document on regulatory testing and risk assessment procedures for plant protection products with non-target arthropods. ESCORT 2 workshop*.

Sweden. (2022). Addendum Article 21 of Regulation (EC) No 1107/2009 on pirimicarb (genotoxicity of metabolites, residue definition, and acceptability of the acute risk to birds); June 2022, updated in September and December 2022. https://open.efsa.europa.eu/questions/EFSA-Q-2022-00584?search=pirimicarb

Sweden. (2024). Revised renewal assessment report (RAR) on pirimicarb prepared by the rapporteur member state Sweden in the framework of commission implementing regulation (EU) No 844/2012, august 2024. https://open.efsa.europa.eu/questions/EFSA-Q-2015-00625

The United Kingdom. (2017). Renewal Assessment Report (RAR) on the active substance pirimicarb prepared by the rapporteur Member State The United Kingdom, in the framework of Commission Implementing Regulation (EU) No 844/2012, December 2017. https://www.efsa.europa.eu/en/consultations/call/180323, www.efsa.europa.eu

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APPENDIX A

Consideration of cut-off criteria for pirimicarb according to Annex II of Regulation (EC) No 1107/2009 of the European Parliament and of the Council

Properties		Conclusion
CMR	Carcinogenicity (C)	Pirimicarb is not considered to be a carcinogen (category 1A or 1B) according to point 3.6.3 of Annex II of Regulation (EC) No 1107/2009, based on: Harmonised classification according to Regulation (EC) No 1272/2008 and its Adaptations to Technical Process [Table 3.1 of Annex VI of Regulation (EC) No 1272/2008 as amended]: CLP00/ATP09, Carcinogen category 2
	Mutagenicity (M)	Pirimicarb is not considered to be a mutagen according to point 3.6.2 of Annex II of Regulation (EC) No 1107/2009, based on: Harmonised classification according to Regulation (EC) No 1272/2008 and its Adaptations to Technical Process [Table 3.1 of Annex VI of Regulation (EC) No 1272/2008 as amended]: CLP00/ATP09, no classification for mutagenicity
	Toxic for Reproduction (R)	Pirimicarb is not considered to be toxic for reproduction according to point 3.6.4 of Annex II of Regulation (EC) No 1107/2009, based on: Harmonised classification according to Regulation (EC) No 1272/2008 and its Adaptations to Technical Process [Table 3.1 of Annex VI of Regulation (EC) No 1272/2008 as amended]: CLP00/ATP09 no classification for reproductive toxicity
Endocrine disrupting properties		Pirimicarb is not considered to meet the criteria for endocrine disruption for **humans** according to point 3.6.5 of Annex II to Regulation (EC) No 1107/2009; for **non-target organisms**, the assessment of the endocrine disruption potential of pirimicarb according to point 3.8.2 of Annex II to Regulation (EC) No 1107/2009, as amended by Commission Regulation (EU) 2018/605, cannot be concluded
POP	**Persistence** **Bioaccumulation** **Long-range transport**	Pirimicarb is not considered to be a persistent organic pollutant (POP) according to point 3.7.1 of Annex II of Regulation (EC) 1107/2009
PBT	**Persistence** **Bioaccumulation** **Toxicity**	Pirimicarb is not considered to be a persistent, bioaccumulative and toxic (PBT) substance according to point 3.7.2 of Annex II of Regulation (EC) 1107/2009
vPvB	**Persistence** **Bioaccumulation**	Pirimicarb is not considered to be a very persistent, very bioaccumulative substance according to point 3.7.3 of Annex II of Regulation (EC) 1107/2009

APPENDIX B

List of end points for the active substance and the formulation for representative uses

Appendix B can be found in the online version of this output ('Supporting information' section): https://doi.org/10.2903/j.efsa.2024.9046

APPENDIX C

Wording EFSA used in Section 4 of this conclusion, in relation to DT and Koc 'classes' exhibited by each compound assessed

Wording	DT_{50} normalised to 20°C for laboratory incubations[40] or not normalised DT_{50} for field studies (SFO equivalent, when biphasic, the DT_{90} was divided by 3.32 to estimate the DT50 when deciding on the wording to use)
Very low persistence	< 1 day
Low persistence	1–< 10 days
Moderate persistence	10–< 60 days
Medium persistence	60–< 100 days
High persistence	100 days to < 1 year
Very high persistence	A year or more

Note: These classes and descriptions are unrelated to any persistence class associated with the active substance cut-off criteria in Annex II of Regulation (EC) No 1107/2009. For consideration made in relation to Annex II, see Appendix A.

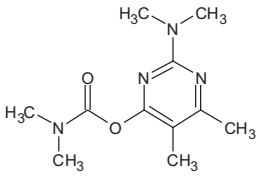
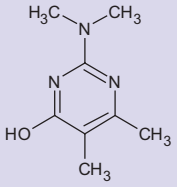
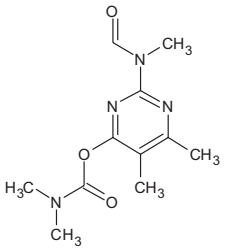
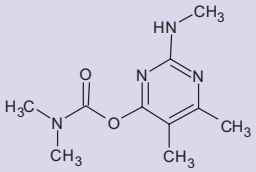
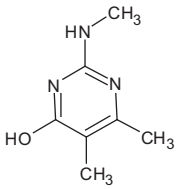
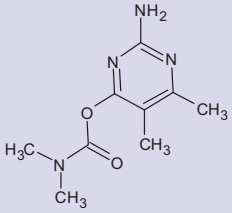
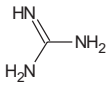
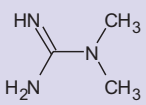
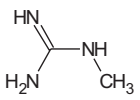
Wording	K_{oc} (either K_{Foc} or K_{doc}) mL/g
Very high mobility	0–50
High mobility	51–150
Medium mobility	151–500
Low mobility	501–2000
Slight mobility	2001–5000
Immobile	> 5000

Note: Based on McCall et al. (1980).

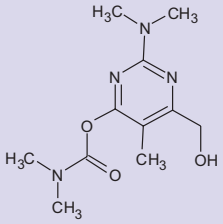
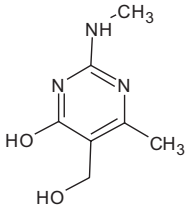
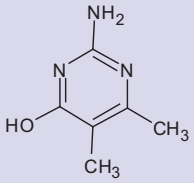
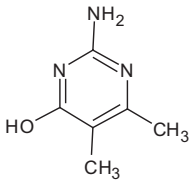
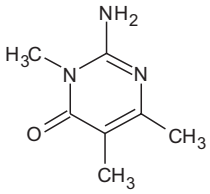
[40] For laboratory soil incubations normalisation was also to field capacity soil moisture (pF2/10 kPa). For laboratory sediment water system incubations, the whole system DT values were used.

APPENDIX D

Used compound codes

Code/trivial name[a]	IUPAC name/SMILES notation/InChiKey[b]	Structural formula[c]
pirimicarb	2-(dimethylamino)-5,6-dimethylpyrimidin-4-yl dimethylcarbamate Cc1nc(nc(OC(=O)N(C)C)c1C)N(C)C YFGYUFNIOHWBOB-UHFFFAOYSA-N	
R31805	2-(dimethylamino)-5,6-dimethylpyrimidin-4-ol Cc1nc(nc(O)c1C)N(C)C MUEHLDAHWSCFAG-UHFFFAOYSA-N	
R34885	5,6-dimethyl-2-(N-methylformamido)pyrimidin-4-yl dimethylcarbamate Cc1nc(nc(OC(=O)N(C)C)c1C)N(C)C=O GDEAMEURJBBCOQ-UHFFFAOYSA-N	
R34836	5,6-dimethyl-2-(methylamino)pyrimidin-4-yl dimethylcarbamate Cc1nc(NC)nc(OC(=O)N(C)C)c1C GTKRZJVAXAQBMB-UHFFFAOYSA-N	
R34865	5,6-dimethyl-2-(methylamino)pyrimidin-4-ol Cc1nc(NC)nc(O)c1C IFOLNWVBRSCJOJ-UHFFFAOYSA-N	
R35140	2-amino-5,6-dimethylpyrimidin-4-yl dimethylcarbamate Cc1c(OC(=O)N(C)C)nc(N)nc1C DIWQKLUHIVULSN-UHFFFAOYSA-N	
R12378	guanidine NC(N)=N ZRALSGWEFCBTJO-UHFFFAOYSA-N	
R16210	*N,N*-dimethylguanidine N=C(N)N(C)C SWSQBOPZIKWTGO-UHFFFAOYSA-N	
R16192	*N*-methylguanidine NC(=N)NC CHJJGSNFBQVOTG-UHFFFAOYSA-N	

(Continued)

Code/trivial name[a]	IUPAC name/SMILES notation/InChiKey[b]	Structural formula[c]
R238177	2-(dimethylamino)-6-(hydroxymethyl)-5-methylpyrimidin-4-yl dimethylcarbamate CN(C)c1nc(CO)c(C)c(OC(=O)N(C)C)n1 YLZGFEXCEZDUAQ-UHFFFAOYSA-N	
R406405	5-(hydroxymethyl)-6-methyl-2-(methylamino)pyrimidin-4-ol Cc1nc(NC)nc(O)c1CO NTGVGPFDHAOUOY-UHFFFAOYSA-N	
R407135	2-amino-5-(hydroxymethyl)-6-methylpyrimidin-4-ol Nc1nc(O)c(CO)c(C)n1 MEIMWQUIKCWVHH-UHFFFAOYSA-N	
R31680	2-amino-5,6-dimethylpyrimidin-4-ol Cc1c(O)nc(N)nc1C APWRLAZEMYLHKZ-UHFFFAOYSA-N	
SYN548582	*N*,*N*,4,5-tetramethyl-2-(methylamino)-6-oxopyrimidine-1(6*H*)-carboxamide O=C1C(C)=C(C)N=C(NC)N1C(=O)N(C)C IPLMSODCSJKGBQ-UHFFFAOYSA-N	
SYN 549580	2-amino-3,5,6-trimethylpyrimidin-4(3*H*)-one NC1=NC(C)=C(C)C(=O)N1C LFEKYWCIYUZCHO-UHFFFAOYSA-N	

[a]The name in bold is the name used in the conclusion.

[b]ACD/Name 2021.1.3 ACD/Labs 2021.1.3 (File Version N15E41, Build 123232, 7 July 2021.

[c]ACD/ChemSketch 2021.1.3 ACD/Labs 2021.1.3 (File Version C25H41, Build 123835, 28 August 2021.

APPENDIX E

Evaluation of data concerning the necessity of pirimicarb as insecticide to control a serious danger to plant health which cannot be contained by other available means, including non-chemical methods

Appendix E can be found in the online version of this output ('Supporting information' section): https://doi.org/10.2903/j.efsa.2024.9046

APPENDIX F

Data collection set

Validated Excel files submitted by MSs and evaluated by EFSA.

Appendix F can be found in the online version of this output ('Supporting information' section): https://doi.org/10.2903/j.efsa.2024.9046