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CONCLUSION ON PESTICIDES PEER REVIEW

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

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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 Czech Republic and co-rapporteur Member State Austria for the pesticide active substance pyrimethanil and of confirmatory data following the maximum residue limit (MRL) review under Article 12 of Regulation (EC) No 396/2005 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 uses of pyrimethanil as a fungicide on grapevine and pome fruit (field uses), strawberry and lettuce (field and greenhouse uses). 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

fungicide, MRL Article 12 confirmatory data, peer review, pesticide, pyrimethanil, 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. Pyrimethanil 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 rapporteur Member State (RMS), Czech Republic and co-rapporteur Member State (co-RMS), Austria, received an application from BASF Agro B.V. Arnhem (NL) Freienbach Branch and Arysta LifeScience for the renewal of approval of the active substance pyrimethanil. In addition, BASF Agro B.V. Arnhem (NL) Freienbach Branch and Arysta LifeScience submitted application for the assessment of confirmatory data following the review of the MRLs according to Article 12 of Regulation (EC) No 396/2005.

An initial evaluation of the dossier on pyrimethanil was provided by the 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 pyrimethanil according to the representative uses as a **fungicide** on grapevine and pome fruit (field uses), strawberry and lettuce (field and greenhouse uses), as proposed at EU level result in a sufficient fungicidal efficacy against the target fungi.

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** issues not finalised were identified with regard to the acceptable levels for acetylacetone in the specifications, and with regard to the toxicity profile of metabolites M605F004 and M605F007.

In the **residue** section, the consumer risk assessment could not be finalised due to lack of data on the toxicity of M605F004 and M605F007, the resulting residue definition being provisional and in view of missing residue field trials with lettuce analysing for M605F004 and its conjugates. The confirmatory data provided in the context of the review of the existing MRLs were partly addressed.

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 exception that information is missing regarding the identity of a soil metabolite U2. Consequently, the soil, groundwater, surface water and sediment exposure assessments for this metabolite was not finalised. In addition, information to address the nature of residues that have the potential to be present in drinking water when raw water is abstracted for the production of drinking water was not available.

In the area of **ecotoxicology**, the risk assessment for aquatic and soil organisms could not be finalised for the unknown metabolite U2. A high long-term risk to mammals for the representative use to lettuce in greenhouses was concluded. Furthermore, for the representative use to lettuce (both field and greenhouses) and to strawberries (three applications in the field), a high chronic risk to fish was concluded in two FOCUS surface water scenarios while for the representative use to strawberries (two applications in greenhouses), a high risk was concluded for a single scenario. For the representative uses to pome fruits, grapevines and strawberries, the current assessments indicate a high chronic risk to bees, while the risk assessment to honey bee larvae could not be finalised for all representative uses.

According to point 3.6.5 and 3.8.2 of Annex II to Regulation (EC) No 1107/2009, as amended by Commission Regulation (EU) 2018/605, it can be concluded that pyrimethanil is **not** an **endocrine disruptor** for human health and non-target organisms.

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 applicants 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 applicants 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 RMS Czech Republic and co-RMS Austria received an application from BASF Agro B.V. Arnhem (NL) Freienbach Branch and Arysta LifeScience for the renewal of approval of the active substance pyrimethanil. In addition, BASF Agro B.V. Arnhem (NL) Freienbach Branch and Arysta LifeScience submitted application for the assessment of confirmatory data following the review of the maximum residue level (MRL) according to Article 12 of Regulation (EC) No 396/2005[4] Complying with Article 8 of the Regulation, the RMS checked the completeness of the dossier and informed the applicants, the co-RMS (Austria), the European Commission and EFSA about the admissibility.

The RMS provided its initial evaluation of the dossier on pyrimethanil in the RAR, which was received by EFSA on 2 November 2018 (Czech Republic, 2018). The RAR included a proposal to set MRLs, submitted under Article 7 of Regulation (EC) No 396/2005.

In accordance with Article 12 of the Regulation, EFSA distributed the RAR to the Member States and the applicants, BASF Agro B.V. Arnhem (NL) Freienbach Branch and Arysta LifeScience, for consultation and comments on 17 January 2019. 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 23 April 2019. At the same time, the collated comments were forwarded to the RMS for compilation and evaluation in the format of a reporting table. The applicants were invited to respond to the comments in column 3 of the reporting table. The comments and the applicants' 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 applicants in accordance with Article 13(3) of the Regulation were considered in a telephone conference between EFSA, the RMS on 04 July 2019. On the basis of the comments received, the applicants' response to the comments and the RMS's evaluation thereof, it was concluded that additional information should be requested from the applicants, and that EFSA should conduct an expert consultation in the areas of mammalian toxicology, residues, environmental fate and behaviour, and ecotoxicology.

In addition, following a consultation with Member States in the Pesticides Peer Review Expert meetings 18 and 21 (November 2019), it was considered necessary to apply an additional clock stop of 30 months in accordance with Commission Implementing Regulation (EU) No 2018/1659, to be able to conclude whether the approval criteria for endocrine disruption in line with the scientific criteria for the determination of endocrine disrupting properties, as laid down in Commission Regulation (EU) 2018/605,[5] are met.

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

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

[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.

[4]Regulation (EC) No 396/2005 of the European Parliament and of the Council of 23 February 2005 on maximum residue levels of pesticides in or on food and feed of plant and animal origin and amending Council Directive 91/414/EEC. OJ L 70, 16.3.2005, p. 1–16.

[5]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.

A final consultation on the conclusions arising from the peer review of the risk assessment, on the proposed MRLs and on the Article 12 MRL review of Regulation (EC) No 396/2005 took place with Member States via a written procedure in June–July 2024.

This conclusion report summarises the outcome of the peer review of the risk assessment of the active substance and the formulation for representative uses, evaluated on the basis of the representative uses of pyrimethanil as a fungicide on grapevine and pome fruit (field uses), strawberry and lettuce (field and greenhouse uses), as proposed by the applicants. 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 are presented in the conclusion. Confirmatory data following the Article 12 MRL review were assessed.

A list of the relevant end points for the active substance and the formulation, the proposed MRLs and the assessment of confirmatory data following the Article 12 MRL review 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:

- the comments received on the RAR;
- the reporting table (05 July 2019 14 August 2023[6]);
- the evaluation table (31 July 2024);
- the reports of the scientific consultation with Member State experts (where relevant);
- the comments received on the assessment of the additional information (where relevant);
- the comments received on the draft EFSA conclusion.

Given the importance of the RAR, including its revisions (Czech Republic, 2023), 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

Pyrimethanil is the ISO common name for *N*-(4,6-dimethylpyrimidin-2-yl)aniline (IUPAC).

The formulation for representative uses for the evaluation was 'SCALA', a suspension concentrate (SC) containing 400 g/L pyrimethanil (BAS 605 04 F).

The information on the active substance and the formulation for representative uses, including the co-formulants in this formulation, was considered in the overall assessment during the peer review. None of the co-formulants is an unacceptable co-formulant listed in Annex III of Regulation (EC) No 1107/2009,[7] however one component of a co-formulant is a not approved active substance under Regulation (EC) No 1107/2009. Details on the composition of the formulation 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 according to Regulation (EC) 1272/2008 was provided by the applicant and assessed by the RMS (please see Volumes 3 CP of the RAR).

The representative uses evaluated were broadcast foliar spray application against *Botrytis cinerea* on grapevine (field uses), strawberry (field, greenhouse permanent and non-permanent structures) and lettuce (field, greenhouse permanent and non-permanent structures), *Venturia inaequalis* on apples and *Venturia pirina* on pears. Full details of the GAPs can be found in the list of end points in Appendix B.

Data were submitted to conclude that the uses of pyrimethanil according to the representative uses proposed at EU level result in a sufficient fungicidal efficacy against the target pathogens, 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 'SCALA' (BAS 605 04 F), studies were performed for acute toxicity endpoints. With regard to the co-formulants contained in 'SCALA' (BAS 605 04 F), sufficient toxicological data were available for all components, but one (present well below 10% in the formulation for representative use). For this co-formulant, insufficient information about its specification/composition was available

[6]Reporting Table following consultation on the revised RAR on the assessment of the endocrine disrupting properties made available after the 30-month clock stop.

[7]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.

and EFSA considered that the available toxicological information for this component did not sufficiently address the repeated dose toxicity potential of 'SCALA' (BAS 605 04 F) over long-term exposure and might be considered for further assessment. It is noted that collected information (not covering all endpoints), including the existing approved uses other than plant protection products, under EU regulated frameworks, did not highlight any additional concern (see Section 10).[8]

Regarding ecotoxicology, the experts at TC 117 agreed that ecotoxicity data with the previous formulation, 'SCALA' (BAS 605 01 F) can be used for the current formulation for representative uses 'SCALA' (BAS 605 04 F). These formulations were tested in an acute test for all groups of non-target organisms except for birds. Based on the available data with the active substance and the formulation for representative uses, the formulation did not show higher toxicity than the active substance. No long-term data with the formulation for representative uses were available for birds, mammals and fish. Therefore, available data for the individual components were retrieved and were discussed at TC 117.[9] No additional chronic data were found, however no concerns were identified. Pending the outcome on the data gap identified in mammalian toxicology for one of the components in the formulation for representative uses, further consideration to non-target organisms may be necessary.

A data gap has been identified for a clear presentation of the inclusion/exclusion criteria for the assessment of the relevance and reliability of the outcomes of the literature data searches, dealing with side effects on health and published within the 10 years before the date of submission of the dossier, to be reported by the RMS in the RAR in accordance with EFSA guidance on the submission of scientific peer-reviewed open literature for the approval of pesticide active substances under Regulation (EC) No 1107/2009 (EFSA, 2011a).

1 | IDENTITY, PHYSICAL/CHEMICAL/TECHNICAL PROPERTIES AND METHODS OF ANALYSIS

The following guidance documents were followed in the production of this conclusion: European Commission (2000, 2010a, 2010b).

The proposed specification for pyrimethanil is based on batch data from industrial production. The proposed minimum purity of the technical material is 975 g/kg. Cyanamide and aniline are considered relevant impurities with a maximum content of 0.5 and 4 g/kg, respectively. Acetylacetone is also considered a relevant impurity, however the maximum acceptable level in the technical material cannot be set (see Section 2 and **data gap** in Section 9.1.1). Based on the data submitted for the renewal, an update of the current reference specification is proposed as new relevant impurities were identified. The batches used in the toxicological assessment do not support the original and newly proposed reference specification (see Section 2) while the batches in the ecotoxicity studies were in compliance with the original and newly proposed specification (see Section 5). There is no FAO specification available for pyrimethanil. Five-batch data were provided for a source of Arysta and concluded by RMS as equivalent to the current and newly proposed reference specification.

The main data regarding the identity of pyrimethanil and its physical and chemical properties are given in Appendix B. **Data gaps** for spectral data and content of the relevant impurities acetylacetone and aniline in the formulation before and after storage were set (see Section 10). A **data gap** for n-octanol/water partition coefficient of unidentified soil metabolite U2 (once the metabolite is fully identified) was set to support ecotoxicology assessment (see Sections 5 and 10).

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 and the impurities in the technical material and for determination of the active substance and relevant impurity cyanamide in the formulation for representative uses. However, a **data gap** for method(s) for determination of the relevant impurities acetylacetone and aniline in the formulation was set (see Section 10).

Pyrimethanil residue can be monitored in food and feed of plant origin by multi-residue method DFG-S19 using liquid chromatography with tandem mass spectrometry (LC–MS/MS) with limit of quantification (LOQ) of 0.01 mg/kg in all commodity groups. Pyrimethanil residue in commodities with high oil content can be determined also by the quick, easy, cheap, effective and safe method (QuEChERS) using LC–MS/MS with a LOQ of 0.01 mg/kg. It is noted that extraction efficiency of the procedure used in both methods was not verified for dry and high-oil content matrices because of lack of metabolism studies in these commodities (not required for the representative uses evaluated). Pyrimethanil, M605F002 and M605F003 in food of animal origin can be determined by LC–MS/MS with LOQ of 0.01 mg/kg of each analyte in all animal matrices. However, conjugates of the metabolites M605F002 and M605F003 were also included in the residue definition for monitoring in food of animal origin. It is noted that the method was additionally validated for kidney, liver and milk including an enzymatic hydrolysis step.[10] However the efficiency of this step was demonstrated for sulfate conjugates but not for sugar conjugates, therefore additional data to demonstrate efficiency of the hydrolysis step for all type of conjugates of M605F002 and M605F003 in all animal matrices is needed (**data gap**, see Section 10). Extraction efficiency was demonstrated for metabolite M605F002 and/or its conjugates (M605F023 and M605F035) in milk and for metabolite M605F003 and/or its conjugates (M605F020 and M605F021) in liver, kidney and milk. Therefore, extraction efficiency needs to be addressed for all components of the residue definition for all other matrices in which residues above or equal to LOQ

[8]Refer to experts' consultation 2.15 in the Report of Pesticides Peer Review Experts' TC 114 (EFSA, 2024).

[9]Refer to experts' consultation 5.10 in the Report of the Pesticides Peer Review Experts' TC 117 (EFSA, 2024).

[10]Refer to open point 1.5 in the evaluation table (EFSA, 2024).

is expected (**data gap**, see Section 10). In addition, it is noted that the residue definition for monitoring in animal products is provisional (see Section 3) and therefore additional monitoring method might be needed if new components are included in the residue definition.

Pyrimethanil residue in environmental compartments and drinking water can be monitored by LC–MS/MS with LOQs 0.01 mg/kg in soil, 0.05 µg/L in water and 0.00034 µg/L in air.

LC–MS/MS methods can be used for monitoring of pyrimethanil, M605F002 and M605F003 in body fluids (urine and blood) with LOQ of 0.01 mg/L of each analyte. Pyrimethanil residue in body tissues can be determined by using the monitoring methods for residue in food of animal origin.

2 | MAMMALIAN TOXICITY

The toxicological profile of the active substance pyrimethanil and its metabolites was discussed at the Pesticides Peer Review Experts' meeting 18 (4–8 November 2019) and at the Pesticides Peer Review Experts' Teleconference (TC) 114 following ED clock stop (4–8 September 2023). The assessment is based on the following guidance documents: ECHA (2017), ECHA-EFSA Guidance (2018), EFSA (2011a, 2011b, 2014a), EFSA PPR Panel (2017), European Commission (2003, 2012, 2017).

The batches used in toxicity studies are not compliant with the original and newly proposed reference specification for the active substance and associated impurities, leading to a data gap and an issue that could not be finalised (see Sections 1 and 9.1.1). Acceptable levels cannot be proposed for the toxicologically relevant impurity acetylacetone (more acutely toxic than the active substance pyrimethanil and with positive in vitro finding and inconsistent in vivo data to address a possible clastogenic potential), while maximum acceptable levels are proposed at 0.5 g/kg for cyanamide and at 4 g/kg for aniline,[11] respectively (both considered toxicologically relevant impurities).

The analytical methods used in feed, body fluids and tissues, air and any additional matrices used in support of the toxicity studies are overall considered fit-for-purpose and validated.

The oral absorption of pyrimethanil is estimated to account for > 80% of the administered dose. Excretion occurs predominantly via urine. In the rat, pyrimethanil is widely distributed in liver, kidney, thyroid, adrenals, blood, ovaries and renal fat. There was no evidence for bioaccumulation. The main metabolic pathway identified is via aromatic oxidation on one or both rings and/or the methyl group of the molecule, followed by conjugation. Based on comparative in vitro metabolism, no unique human metabolites have been identified.

The residue definition for body fluids and tissues is pyrimethanil in blood and the sum of pyrimethanil, SN 614276 (M605F002) and SN 614277 (M605F003) in urine for the purpose of human biomonitoring.

Pyrimethanil has a low **acute toxicity** after oral, dermal and inhalation exposure. It is neither a skin or eye irritant, nor a skin sensitiser.

Pyrimethanil is not expected to be phototoxic on the basis the results of the in vitro 3T3 study (although borderline results were observed in the first of the two experiments). However, considering that the absorption/extinction coefficient at 290 nM is > 10 L/mol/cm and that the absorption maximum of pyrimethanil is between 205 and 271 nm, a data gap has been concluded (**data gap**, see Section 10).[12]

Short-term oral toxicity studies were provided for rats, mice and dogs. The adverse effects included: reduced body weight and body weight gain, proteinuria and histopathological findings in liver and thyroid in the rat; decreased body weight gain, increased liver weight and histopathological findings in the thyroid, kidneys and urinary bladder in the mouse; decreased body weight gain and water consumption, vomiting and haematological findings in the dog. The dog appeared as the most sensitive species. A no observed adverse effect level (NOAEL) of 6 mg/kg bw per day was identified in a 90-day dog study, due to systemic toxicity effects observed at and above 80 mg/kg bw per day.[13] In a 1-year study in dog a NOAEL of 30 mg/kg bw per day was identified[13] and considered more reliable due to the large dose-spacing applied in the 90-day study.[14]

Based on the available **genotoxicity** data set, the active substance is unlikely to be genotoxic.[15]

After **long-term exposure**, target organs for toxicity included thyroid and liver in the rat and urinary bladder in the mouse. The relevant NOAEL in male rat is 1.3 mg/kg bw per day (from the 2-year rat study), based on increased focal cystic degeneration in the liver, increased relative liver weight and increase in some clinical chemistry parameters (mainly gamma-glutamyl transferase, GGT) observed at 17 mg/kg bw per day in male rat. RMS disagreed[16] with this long-term NOAEL.

Treatment-related increased incidence of tumours in the thyroid was observed in rats and included follicular cell adenoma with a relevant NOAEL for carcinogenicity of 17 mg/kg bw per day; such finding was considered unlikely to be relevant for humans..[17]

[11]Refer to experts' consultation 1.1 in the Report of Pesticides Peer Review Experts' Meeting 18 (EFSA, 2024).
[12]Refer to experts' consultation 2.1 in the Report of Pesticides Peer Review Experts' Meeting 18 (EFSA, 2024).
[13]Refer to experts' consultation 2.2 in the Report of Pesticides Peer Review Experts' Meeting 18 (EFSA, 2024).
[14]Refer to experts' consultation 2.16 in the Report of Pesticides Peer Review Experts' TC 114 (EFSA, 2024).
[15]Refer to experts' consultation 2.3 in the Report of Pesticides Peer Review Experts' Meeting 18 (EFSA, 2024).
[16]Refer to experts' consultation 2.5 in the Report of Pesticides Peer Review Experts' Meeting 18 (EFSA, 2024).
[17]Refer to experts' consultation 2.4 in the Report of Pesticides Peer Review Experts' Meeting 18 (EFSA, 2024).

With regard to **reproductive toxicity** studies in rats, the parental NOAEL from the extended one generation reproductive toxicity (EOGRT) study is 140 mg/kg bw per day, based on statistically significant decrease in body weight, body weight gain and food consumption, increase in absolute and relative liver weight and histopathological findings in liver, thyroid and pituitary gland. The offspring NOAEL is 140 mg/kg bw per day, based on statistically significant decrease in body weight gain. Finally, the reproductive NOAEL is 140 mg/kg bw per day, based on statistically significant decrease in mean number of implantation sites/dam and subsequently decreased number of delivered and live born pups/dam[16].

In the rat **developmental** study, the maternal NOAEL is 85 mg/kg bw per day, based on reduced body weight gain and clinical signs; the developmental NOAEL is 85 mg/kg bw per day, based on reduced litter weight and foetal body weight.[18] In the rabbit teratogenicity study, the maternal NOAEL is 45 mg/kg bw per day, based on reduced body weight gain and clinical signs, and the developmental NOAEL is 45 mg/kg bw per day, based on reduced foetal body weight, retardation of foetal development and increased incidence of skeletal variations related to maternal toxicity.

With respect to **neurotoxicity**, reduced grip strength, motor activity and body temperature were observed in the acute neurotoxicity study in rats, triggering a NOAEL of 100 mg/kg bw for both neurotoxicity and systemic toxicity.[19] No findings indicative of neurotoxic potential were observed in a 13-week repeated neurotoxicity study. The NOAEL for neurotoxic effects was then set at 392 mg/kg bw per day (top dose). The NOAEL for systemic toxicity was set at 38.7 mg/kg bw per day, based on reduced food consumption and body weight gain.

A NOAEL of 139 mg/kg bw per day was set for **developmental neurotoxicity** (**DNT)** effects in the DNT cohort of the EOGRT study, based on decreases in brain weight, in the thickness of hippocampus and corpus callosum, and in startle amplitude.[20]

As regards **immunotoxicity**, pyrimethanil did not show any potential for immunotoxic effects in the standard regulatory toxicity studies.

The **acceptable daily intake** (**ADI**) is established at 0.013 mg/kg bw per day, on the basis of the relevant long-term NOAEL of 1.3 mg/kg bw per day in the 2-year rat study based on liver findings. The standard uncertainty factor (UF) of 100 was applied. The effects in the liver were not considered toxicologically relevant during the previous peer review where the ADI was set at 0.17 mg/kg bw per day, based on the same 2-year study in the rat, applying an UF of 100 (EFSA, 2006; European Commission, 2010a, 2010b).

The **acute reference dose** (**ARfD**) is 1 mg/kg bw based on the acute neurotoxicity study in the rat in which a NOAEL of 100 mg/kg bw was set. The standard UF of 100 was applied. No ARfD was set during the previous peer review (EFSA, 2006; European Commission, 2010a, 2010b).

The **acceptable operator exposure level** (**AOEL**) is 0.3 mg/kg bw per day based on the 1-year dog study in which a NOAEL of 30 mg/kg bw per day was set. The standard UF of 100 was applied with no correction for oral absorption. This value differs from the previous peer review where the AOEL of 0.12 mg/kg bw per day was set based on the 90-day and 2-year studies in the rat, applying an UF of 100 and a correction for absorption of 72% (EFSA, 2006; European Commission, 2010a, 2010b).

The **acute AOEL (AAOEL)** is 1 mg/kg bw based on the same point of departure as for setting the ARfD. The standard UF of 100 was applied. During previous the peer review, an AAOEL was not set (EFSA, 2006; European Commission, 2010a, 2010b).

The dermal absorption values of pyrimethanil in 'SCALA' (BAS 605 04 F) are 2.1% for the concentrate, and 44% for the 0.2 g/L spray dilution, applicable to the supported uses of the product on grapevine, pome fruit, strawberry and lettuce.

For the outdoor uses (grapevine, pome fruit and strawberry/lettuce), the non-dietary exposure estimates were provided with the EFSA model (EFSA, 2014a) while refined DFR and DT_{50} values were based on experimental data. For the use on **grapevine**, the predicted estimates are below the (A)AOEL for operators wearing gloves, as well as for workers during pruning/tying (based on 2 field studies) and for residents/bystanders when drift reduction is applied. For the use on **pome fruit**, the predicted estimates are below the (A)AOEL for operators except for manual handheld application in late season (with dense foliage), as well as for workers when applying refined DFR and DT_{50} values, and for residents/bystanders (without mitigation measures). For the use on **strawberry/lettuce outdoor**, the predicted estimates are below the (A)AOEL for operators, as well as for workers with use of gloves, and for residents/bystanders (without mitigation measures).

For the indoor use on **strawberry/lettuce**, the non-dietary exposure estimates were provided with the Dutch Greenhouse model (not validated at EU level). The predicted estimates are below the (A)AOEL for operators when using gloves, coverall and respiratory protective equipment, as well as for workers when applying refined DFR and DT_{50} values (based on field studies), while residents/bystanders are considered covered by the outdoor use on the same crop.

The grouping approach of metabolites based on the Tanimoto index was considered appropriate.[21] The three groups identified were: (1) hydroxylation/oxidation products and their conjugates; (2) pyrimidin-moiety cleavage products and their derivatives and conjugates; (3) phenyl-moiety cleavage products. Genotoxicity assessment (based on QSAR prediction, weight of evidence analysis and experimental data) was considered negative for all the metabolites in the different 3 groups.

[18]Refer to experts' consultation 2.7 in the Report of Pesticides Peer Review Experts' Meeting 18 (EFSA, 2024).

[19]Refer to experts' consultation 2.8 in the Report of Pesticides Peer Review Experts' Meeting 18 (EFSA, 2024).

[20]Refer to experts' consultation 2.16 in the Report of Pesticides Peer Review Experts' TC 114 (EFSA, 2024).

[21]Refer to experts' consultation 2.10 in the Report of Pesticides Peer Review Experts' Meeting 18 (EFSA, 2024).

Amongst the different metabolites, **M605F004**, belonging to **group 1**, was identified as a rat metabolite present also in plants, rotational crops and livestock (see Section 3). While it displayed no genotoxicity potential (based on QSAR prediction, experimental data and weight of evidence analysis), no conclusion could be drawn on its general toxicity profile and applicable toxicological reference values (**data gap** leading to **an issue that could not be finalised**, see Section 9.1.1). The data gap applies also to sugar conjugates of M605F004 (i.e. M605F027 and M605F041) and might be considered applicable also to the malonyl-β-O glucoside of M605F004, M605F028. **M605F007**, belonging to **group 2**, was identified as a rat metabolite present also in soil, water (sediment) and rotational crops (see Sections 3 and 4): being acutely toxic (LD_{50} of 735 mg/kg bw), the criteria for classification[22] as Acute Tox. 4, H302 might be met for this metabolite; the in vitro bacterial mutagenicity (Ames test) and in vitro micronucleus tests were negative. The genotoxicity assessment was therefore considered negative, but no conclusion could be drawn on the general toxicity and toxicological reference values (**data gap** leading to **an issue that could not be finalised**, see Section 9.1.1). Pending confirmation of groundwater exposure from the unidentified soil metabolite U2 (see Section 4), an assessment of its toxicological profile might be warranted (see Sections 4, 7 and 9.1.1).

3 | RESIDUES

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

Pyrimethanil was discussed at the Pesticides Peer Review Meeting 20 (18–21 November 2019).

3.1 | Representative use residues

Metabolism studies were submitted on lettuce, apples, grapes, tomatoes (foliar spray application), on carrots (soil and foliar treatments) and on wheat (seed treatment). The studies on lettuce and fruit crops are acceptable and compliant with the representative uses. The carrot study is acceptable but its compliance with any future GAP on root crops should be further assessed. Overall, the studies were considered sufficient to elucidate the metabolism of pyrimethanil which was qualitatively similar in the various crops. Pyrimethanil was the major residue and recovered in all plant parts. Various conjugates of M605F004 were found in all crops but summed up to levels above 10% TRR only in lettuce. Hence the **risk assessment residue definition for leafy crops** upon foliar treatment is set as pyrimethanil and M605F004 and its conjugates, which is however provisional pending upon the toxicity of M605F004 and its conjugates (for data gap see Section 2). The **residue definitions** for **risk assessment for root and fruit crops (foliar treatment**) and for **enforcement** (all crops) are set as pyrimethanil. The new metabolism study on wheat with seed treatment covering the cereal/grass crop category aimed to address the request for confirmatory data originated from MRL review (EFSA, 2011a) (see Section 3.2). The available study in wheat grain was considered acceptable according to guidelines. However, as no identification was performed due to very low levels of identified residue, it cannot be used for extrapolation to other crops following seed treatment. Therefore, the **residue definition** for **risk assessment** and **enforcement** is set as pyrimethanil for **cereals** upon seed treatment. Pyrimethanil is stable under standard hydrolysis conditions and for **processed commodities** of all crops, except leafy crops, the residue definition is pyrimethanil. For processed commodities of leafy crops, the residue definition is pyrimethanil and M605F004 and its conjugates. Valid residue field trials were provided for grapes and apple. No residues field trials for lettuce analysing for the metabolite M605F004 and its conjugates were provided (**data gap**, see Section 9.1.1) and information on the application rate in the residue field trials with strawberries is requested to conclude on their validity (**data gap**). Processing factors for grapes were derived from open literature studies. As the reported residues were not in line with the residues from the supervised field trials, a data gap is set for studies establishing processing factors for grapes juice, pomace, must and raisin (see evaluation table open point 3.13 in EFSA, 2024). The studies for derivation of processing factors for apple and strawberry are adequate. Sufficient frozen storage stability data were provided for pyrimethanil, M605F005, M605F007 and M605F025 in different crops commodities. Storage stability of M605F004 and its conjugates should be addressed in the context of the residue field trials with lettuce (see data gap above). Two rotational crops metabolism studies covering the maximum seasonal annual rate for strawberries and three plant back intervals (PBI) were provided. The metabolic picture was similar as in primary crops with pyrimethanil detected in all plant parts in two PBIs. Other metabolites were M605F004 and its conjugates (major in cereal based feed but occurring also in leafy and root crops), M605F007 (all plant parts but major only in leafy crops), M605F025 (major in tuber and cereal based feed at PBI 2 and 3) and M605F005 (major in lettuce and cereal based feed) were reported. A sufficient number of rotational crop field trials in NEU and SEU zone with application rate which is covering the PECsoil for the soil metabolite M605F007 was provided. The trials demonstrated that for the analysed compounds, a significant uptake of residues of pyrimethanil and M605F007 occurs mainly at 30 days PBI. M605F025 was only recovered in wheat straw and M605F005 was never detected in any crop part at any PBI. Based on these studies the **rotational crop residue definition for enforcement** is set as pyrimethanil and for **risk assessment it is provisional** set as pyrimethanil, M605F004, its conjugates and M605F007. Data gaps are set to

[22]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.

address the toxicity of M605F007 and M605F004 and its conjugates (see Section 2) and the residue definition is considered provisional pending upon the toxicity of these two metabolites. Shortcomings in the trials are noted and pending the information on the toxicity of M605F004 and its conjugates, field trials analysing for M605F004 and its conjugates might become necessary.

As the representative uses are during flowering on the melliferous crops strawberry and pome fruit one underdosed field residue trial with apples to investigate the residue of pyrimethanil in pollen and honey was provided. Whereas not fully reliable, results of this single trial indicate that residues of pyrimethanil in honey and pollen might occur. This is confirmed by the residue trials submitted in the context of the application to set MRLs which was not available during the peer-review (EFSA, 2023). However, it is also noted that these trials analysed only for pyrimethanil in honey and did not consider the contribution of the two metabolites M605F004 and its conjugates and M605F007 which are proposed to be included in the risk assessment residue definition for rotated crops. Therefore, a data gap is set to address the residues of M605F004 and its conjugates and M605F007 in honey (**data gap**).

Regarding the animal dietary burden, residues from the use on apple triggers a metabolism study with pyrimethanil for ruminants. New guideline and GLP compliant metabolism studies with pyrimethanil fed to hens (pyrimidine label only) and goat (both pyrimidinyl and phenyl label) were provided in addition to a former study with goat. M605F002 and its conjugates were major in cow, goat and poultry tissues, whereas the major residue in milk accounting for 27% TRR was M605F021, a conjugate of M605F003. As residues of free M605F003 are not expected, a conversion factor for milk cannot be derived from the study. Hence, the **residue definition for enforcement and risk assessment for milk** are set as 'sum of pyrimethanil and M605F003 including conjugates, expressed as pyrimethanil'; whereas for **ruminant** and **poultry tissues (including egg),** the **residue definition for enforcement and risk assessment** are set as 'sum of pyrimethanil and M605F002 including conjugates, expressed as pyrimethanil'. It should be noted that pyrimethanil was not recovered in any of the tissues analysed. However, the inclusion of parent pyrimethanil in the **enforcement** residue definition by default is proposed for alignment with international standards. Pending the relevant assessment of the metabolites M605F004 and its conjugates and M605F007 in plant commodities, their potential transfer to animal matrices should be further investigated. The proposed RDs for ruminant and poultry matrices have therefore to be regarded as **provisional**. A guideline and GLP compliant feeding study with lactating cows was available analysing for pyrimethanil and M605F002 in tissues and M605F003 and its conjugates in milk. It should be noted that the residue values consider only carry over of pyrimethanil (both from primary and rotational crop) but not of the metabolites M605F004 and its conjugates (PC and RC) and M605F007 which have to be considered once toxicological data are available (data gap see Section 2) and the residue definitions for primary and rotational crops are finalised.

An indicative and provisional consumer risk assessment using PRIMo vs 3.1 and considering only the residues from pyrimethanil in primary crops indicates that the estimated chronic consumer exposure corresponds to 28% of the ADI at the maximum (NL, toddler). An acute intake accounted at the highest for 47% of the ARfD (lettuce). Pending the outstanding data (toxicity of the metabolites M605F004 and its conjugate and of M605F007 and complete data on magnitude of residues) and upon finalisation of the residue definitions for risk assessment, the consumer risk assessment will need to be recalculated taking also into account an updated dietary burden calculation.

The consumer risk assessment from the consumption of drinking water is also not finalised as appropriate information to address the effect of water treatment processes on the nature of the residues that might be present in surface water, when surface water is abstracted for drinking water were not provided. It is unclear if there might be groundwater exposure from the unidentified soil metabolite U2. Should this be the case, information to address the effect of water treatment processes on the nature of the U2 residue that might be present in groundwater when groundwater is abstracted for drinking water would also be required (see Sections 4 and 9.1.1).

3.2 | Maximum residue levels and confirmatory data MRL review

A MRL application was received to address the confirmatory data set in the context of the review of existing maximum residue level for pyrimethanil according to Article 12 of Regulation (EC) No 396/2005 (EFSA, 2011b) for a metabolism study with seed treatment on cereals and a completely validated analytical method and its interlaboratory validation for enforcement of pyrimethanil residues in liver, kidney, eggs, muscle, milk and fat.

A new metabolism study on wheat with seed treatment was submitted and addressed the above request. The findings are discussed in Section 3.1. A validated analytical method and its ILV for enforcement of pyrimethanil residues in liver, kidney, eggs, muscle, milk and fat was also submitted but had shortcomings leading to a data gap (see Section 1). The additional data provided only partly addressed the confirmatory data in the context of the Article 12 MRL review.

It should be noted that in the framework of the MRL review for pyrimethanil according to Article 12 of Regulation (EC) No 396/2005 (EFSA, 2011a), post-harvest treatments on fruit crops were also included. Given the late application times in the metabolism studies with fruit, the residue definitions from the foliar treatment on fruit crops can be extended to the post-harvest treatment.

An update of the consumer risk assessment that was conducted in the review of MRLs according to Article 12 of Regulation (EC) No 396/2005 (EFSA, 2011a), has been performed using PRIMo vs 3.1. When considering the ADI of 0.013 mg/kg bw per day and residues from all existing uses reported in the review of existing MRLs according to Article 12 (EFSA, 2011a), in the subsequent MRL assessments and Codex MRLs taken over in the EU legislation (EFSA, 2015, 2016, 2018; FAO, 2013) and the

proposed MRLs in EFSA, 2023, which are under implementation in the EU MRL regulation, the ADI was exceeded (342% ADI, DE child) The highest acute intake represented 98% of the ARfD (pears). The impact of residues of M605F004 and its metabolites from use on lettuce or other leafy crops and residues in rotated crops was not included in this calculation.

4 | ENVIRONMENTAL FATE AND BEHAVIOUR

Pyrimethanil was discussed at the Pesticides Peer Review Meeting 19 (11–14 November 2019).

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, pyrimethanil exhibited moderate to high persistence, forming the major (> 10% applied radioactivity (AR)) metabolite M605F007 (max. 11.5% AR), which also exhibited moderate to high persistence. The unidentified minor non transient metabolite U2 reached levels (5.9% at 245 days, max. 6.6% AR at 364 days, in one soil experiment) that triggers identification and further assessment. Identification of U2 and information to complete environmental exposure assessments for it have been identified as a data gap and assessment not finalised (see Section 9.1.1). Mineralisation of the phenyl and pyrimidine ring ^{14}C radiolabels to carbon dioxide accounted for 4%–7% AR after 90–91 days. The formation of unextractable residues (not extracted by acetonitrile followed by Soxhlet-extraction with acetonitrile/water) for these radiolabels accounted for 42%–62% AR after 90–105 days. In an anaerobic soil incubation pyrimethanil was essentially stable. Pyrimethanil exhibited high to low mobility in soil. Metabolite M605F007 exhibited high to medium soil mobility. It was concluded that the adsorption of pyrimethanil and M605F007 was not pH dependent. In satisfactory field dissipation studies carried out at six sites in Germany, two in France and one each in Italy and Spain (spray application to the soil surface on bare soil plots or this application regime with subsequent sand covering) pyrimethanil exhibited moderate to high persistence and Metabolite M605F007 also exhibited moderate to high persistence. Field study DegT50 values were derived following normalisation to FOCUS reference conditions (20°C and PF2 soil moisture) following the EFSA (2014b) DegT50 guidance. In accordance with this EFSA (2014b) DegT50 guidance the field data endpoints for pyrimethanil were combined with lab values to derive modelling endpoints but for Metabolite M605F007 only the field data endpoints were used to derive modelling endpoints.

In a lysimeter study of 2 years duration all chromatographically resolved components in leachate accounted for < 0.07 µg/L, as annual average concentrations. Pyrimethanil was not detected in any individual leachate sample above the limit of analytical detection, which was 0.01 µg/L.

In laboratory incubations in dark aerobic natural sediment water systems, pyrimethanil exhibited moderate to high persistence, partitioning to sediment (max 47%–68% AR after 14–30 days), forming the metabolite M605F007 at levels triggering assessment (max. 6% AR in water and 4.4% AR in sediment at study end, 100 days). The unextractable sediment fraction (not extracted by methanol/water then methanol or acetonitrile/water then acetonitrile including a final acetonitrile Soxhlet) was a sink for the phenyl and pyrimidine ring ^{14}C radiolabels, accounting for 16%–48% AR at study end. Mineralisation of these radiolabels accounted for 2%–9% AR at the end of the study. Pyrimethanil was stable in a laboratory sterile aqueous photolysis experiment. The necessary surface water and sediment exposure assessments (predicted environmental concentrations (PEC) calculations) were carried out for the metabolite M605F007, 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 pyrimethanil, appropriate step 3 (FOCUS, 2001) and step 4 calculations were available.[23] The step 4 calculations appropriately followed the FOCUS (FOCUS, 2007) guidance, with no-spray drift buffer zones of up to 20 m being implemented for the drainage scenarios (representing a 59%–93% spray drift reduction), and combined no-spray buffer zones with vegetative buffer strips of up to 20 m (reducing solute flux in run-off by 80% and erosion runoff of mass adsorbed to soil by 95%) being implemented for the run-off scenarios. The EVA 2.1 model was used to estimate atmospheric deposition rates for pyrimethanil to surface water in line with FOCUS (2008) air guidance. The SWAN tool (version 4.0.1) was appropriately used to implement these mitigation measures/add the necessary atmospheric deposition 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. pyrimethanil), 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.

The applicant and RMS correctly indicated that the surface water exposure assessment provided for the field uses on lettuce and strawberry would cover the representative greenhouse uses on lettuce and strawberry.

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.[24] The potential for groundwater exposure from the representative uses by pyrimethanil and its soil metabolite M605F007 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 applicant did not provide appropriate information to address the effect of water treatment processes on the nature of the residues that might be present in surface water, when surface water is abstracted for drinking water. This has led to the identification of a data gap and results in the consumer risk assessment not being finalised. It is unclear if there might

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

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

be groundwater exposure from the unidentified soil metabolite U2. Should this be the case information to address the effect of water treatment processes on the nature of the U2 residue that might be present in groundwater when groundwater is abstracted for drinking water would also be required (see Sections 3 and 9.1.1).

The PEC in soil, surface water, sediment and groundwater covering the representative uses assessed can be found in Appendix B. A key to the persistence and mobility class wording used, relating these words to numerical DT and Koc endpoint values can be found in Appendix C.

5 | ECOTOXICOLOGY

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

Aspects of the ecotoxicology assessment were discussed during the Pesticides Peer Review Experts' Meeting 21 (18–22 November 2019) and at Pesticides Peer Review Experts' teleconference (TC) 117 (18–20 September 2023).

The batches used in the ecotoxicity studies were sufficiently compliant with the original and newly proposed reference specification.

The applicant confirmed that the representative uses in greenhouses is for both permanent greenhouses and for other types of structure such as walk-in tunnels.[25] Exposure to non-target organisms from uses in other types of structure such as walk-in tunnels is considered to be comparable to field uses (see below). However, it is noted that exposure to birds, mammals, bees, non-target arthropods other than bees, soil organisms and non-target terrestrial plants from uses in permanent greenhouses is minimal and low risk can be concluded for those groups of taxa. No separate surface water exposure assessment is available for permanent greenhouses (see Section 4) and, therefore, the conclusion on the risk assessment for aquatic organisms is based on the field uses (see below).

Suitable acute and reproductive toxicity data with the active substance were available for **birds** and **mammals**. An acute toxicity study for mammals with the formulation 'BAS 605 01 F' was available. The long-term endpoint for the assessment of wild mammals was discussed at the experts' meeting.[26] The experts at TC117 agreed to revise the previously agreed endpoint considering the new extended one generation reproductive toxicity study.[27]

A low acute dietary risk to birds and mammals was concluded for all representative uses based on a screening risk assessment. Likewise, a low long-term dietary risk to birds was concluded for all representative uses based on a screening or tier 1 assessment. A high long-term risk to mammals was indicated at the tier 1 for all representative uses. Several refinement options were discussed at the experts meeting.[28] Overall, the experts agreed that the following refinements were reliable (i) DT_{50} value for plant material for the central and southern zone, (ii) refined residue value for large fruit, (iii) a refined deposition value for the use in strawberries and (iv) refined focal species and proportion of dietary items (PD) in the northern zone for pome fruit and strawberries. As a result of the refined assessment, a low long-term risk to wild mammals was concluded for the representative uses to pome fruit, grapevines and strawberries. Even considering the available refinements, a high long-term risk to mammals was concluded for the representative uses to lettuce (field and greenhouse[29]).

A low risk to birds and mammals from pyrimethanil via secondary poisoning and from consumption of contaminated water was concluded for all representative uses. A consideration of the need for a secondary poisoning assessment for the unknown soil metabolite U2 should be done once the metabolite is fully characterised (see Section 4). Furthermore, the plant metabolite M605F028 was detected at more than 10% TRR in plant metabolism studies but no risk assessment was available (**data gap**, needed for all representative uses, see Section 10).

Suitable **aquatic** acute and chronic toxicity data (fish, aquatic invertebrates, algae, aquatic plants and sediment-dwelling organisms) were available with the active substance, pyrimethanil. Furthermore, data demonstrating the acute toxicity of metabolite M605F007[30] to fish, aquatic invertebrates and algae were available. Acute toxicity data with 'BAS 605 01 F' were available for fish and aquatic invertebrates. Toxicity data with the representative product ('SCALA' (BAS 605 04 F)) were available for algae.

The acute aquatic risk assessment for pyrimethanil was performed using a regulatory acceptable concentration (RAC) value calculated for fish. The chronic risk assessment was also driven by the RAC for fish. When considering risk mitigation measures (see Section 8.1), a low risk to aquatic organisms was concluded in the majority of the FOCUS surface water (sw) scenarios for all representative uses. Details of the outcome of the aquatic risk assessment are summarised in the following table (Table 1).

[25]Refer to reply to comment number 5(123) in the reporting table.

[26]Refer to experts' consultation 5.2 in the Report of the Pesticides Peer Review Meeting 21 (EFSA, 2024).

[27]Refer to experts' consultation 5.8 in the Report of the Pesticides Peer Review TC 117 (EFSA, 2024).

[28]Refer to experts' consultation 5.1 and 5.3 in the Report of Pesticides Peer Review Meeting 21 (EFSA, 2024).

[29]A high long-term risk to mammals was concluded for the representative use to lettuce in the field and in greenhouses, with the exception of applications made in permanent greenhouses for which limited exposure to wild mammals is expected.

[30]Metabolites M605F007 and U2 trigger the need for a risk assessment for aquatic organisms in surface water.

TABLE 1 Outcome of the aquatic risk assessment for the representative uses.

		Grapevines	Pome fruit	Strawberry (field uses)	Strawberry (greenhouse uses[a])	Lettuce (field uses)	Lettuce (greenhouse uses[a])
Acute risk assessment	**Step 3**	Low risk for all scenarios (5/5)	High risk for all scenarios (7/7)	High risk for 3/7 scenarios	Low risk for all scenarios (7/7)	Low risk for all scenarios (7/7)	Refer to field uses
	Step 4	–	Covered by chronic risk assessment	Covered by chronic risk assessment	–	–	–
Chronic risk assessment	**Step 3**	High risk for all scenarios (5/5)	High risk for all scenarios (7/7)	High risk for 4/7 scenarios	High risk for 4/7 scenarios	High risk for 4/7 scenarios	Refer to field uses
	Step 4	With risk mitigation[b], low risk for all scenarios (5/5)	With risk mitigation[b], low risk for all scenarios (7/7)	With risk mitigation[b], low risk for 5/7 scenarios High risk for 2/7 scenarios[c]	With risk mitigation[b], low risk for 6/7 scenarios High risk for 1/7 scenarios[d]	With risk mitigation[b], low risk for 6/7 scenarios High risk for 1/7 scenarios[d]	With risk mitigation[b], low risk for 6/7 scenarios High risk for 1/7 scenarios[d]
Chronic risk to sediment dwelling organisms	**Step 1 and 2**	Low risk at step 1	Low risk at step 2	Low risk at step 2	Low risk at step 2	Low risk at step 2	Refer to field uses

[a]Greenhouse refers to all types of structure. No separate assessment was provided for permanent structures.

[b]For details of the required mitigation measures see Section 8.1.

[c]High chronic risk to fish for D6 and R3 scenarios even when considering the proposed risk mitigation.

[d]High chronic risk to fish for D6 scenario even when considering the proposed risk mitigation.

A low risk to aquatic organisms from metabolite M605F007 was demonstrated at $FOCUS_{sw}$ Step 1 for all representative uses. Since the soil metabolite U2 is not characterised and no exposure assessment is available (see Section 4), no risk assessment for this metabolite to aquatic organisms could be performed (**data gap** leading to an issue not finalised, see Section 9).

Suitable acute (contact and oral) toxicity data with **honey bees** were available for pyrimethanil and BAS 605 01 F. Furthermore, chronic oral toxicity data with 'BAS 605 01 F' were available for honey bees. An acute (single dose) toxicity study with 'SCALA' (BAS 605 04 F) was available for honey bee larvae; however, a repeated dose study was not available. No data investigating accumulative effects or sub-lethal effects to honey bees were available (**data gap**, see Section 10). Acute (contact and oral) toxicity data with **bumble bees** were available for the product 'BAS 605 01 F'. In addition, two semi-field studies and a field study investigating effects of applications of 'BAS 605 01 F' to honey bees were available.

An acute risk assessment for honey bees, covering both pyrimethanil and 'BAS 605 01 F' was performed according to EFSA (2013). Low risk was concluded at the screening step. A risk assessment for honey bees in accordance with the European Commission (2002) guidance document was not presented, but a low acute risk to honey bees, for all representative uses, would be indicated using that guidance. A low acute risk to bumble bees was also indicated with the available assessment.

The chronic risk to adult honey bees was assessed using EFSA (2013). For the representative uses to grapevine, pome fruit and strawberries, a high chronic risk was indicated at tier 1 for the 'treated crop' scenario when applications are made before, or during, flowering. For applications made after flowering and for all other scenarios, a low chronic risk was indicated to honey bee adults. Furthermore, a low risk for the representative uses to lettuce was indicated for all scenarios for the growth stages assessed. Owing to a lack of a suitable endpoint from a repeated dose study, a tier 1 chronic risk to honey bee larvae was not available.

The results of the available higher tier studies were discussed at the experts' meeting.[31] The experts noted that the semi-field studies and the field study indicated a potential effect on honey bee brood. However, since the observed differences between the treatment and the control were not observed in a consistent manner, it was agreed that the studies should not be regarded an indicating a clear effect to honey bee brood. Nevertheless, since data and a suitable risk assessment to exclude an effect to honey bee brood were not available, a low risk could not be concluded (**data gap**, leading to an issue not finalised, see Section 9.1.1). No risk assessment for metabolites occurring in nectar and pollen was available (**data gap**, see Section 10).

Tier 1 toxicity studies, performed with 'BAS 605 01 F' or the formulation for representative uses and the two indicator species (*Aphidius rhopalosiphi* and *Typhlodromus pyri*) for **non-target arthropods other than bees** were available. In

[31]Refer to experts' consultation 5.5 in the Report of Pesticides Peer Review Experts' Meeting 21 (EFSA, 2024).

addition, glass-plate Tier 2 studies were available for eight species and extended laboratory Tier 2 studies were available for four species. Several semi-field and field studies were also available. Based on the available tier 1 risk assessments, a low risk to non-target arthropods in the off-field area was indicated for all representative uses. However, for one Tier 1 species (*A. rhopalosiphi)*, a high in-field risk was indicated for all representative uses. Based on the available Tier 2 risk assessment, and with consideration of the higher tier studies, a low in-field risk to non-target arthropods was concluded for all representative uses.

Chronic toxicity data with 'SCALA' (BAS 605 04 F), 'BAS 605 01' F and metabolite M605F007 were available for **earthworms**. Chronic toxicity data with 'SCALA' (BAS 605 04 F) was also available for two additional species of **soil macroorganisms**. An earthworm field study investigating effects of applications of 'SCALA' (BAS 605 04 F) on the earthworm community was also available.

The Tier 1 risk assessment for 'SCALA' (BAS 605 04 F) indicated a high chronic risk to earthworms for the representative uses to pome fruit, lettuce and strawberries, whilst a low risk was indicated for the uses to grapevines. The risk to earthworms was refined using the available earthworm field study and a low risk to earthworms was concluded for all representative uses. A low risk to soil macroorganisms other than earthworms was concluded for all representative uses based on the available Tier 1 risk assessment. For the metabolite M605F007, low risk was concluded for earthworms (at Tier 1) and for other soil macroorganims (at screening level). Suitable toxicity studies were available which demonstrated a low risk to **soil microorganisms**, for all representative uses from the formulation for representative uses, 'SCALA' (BAS 605 04 F) and metabolite M605F007. However, as the soil metabolite U2 is not characterised and no exposure assessment is available (see Section 4), no risk assessment for this metabolite to soil organisms could be performed **(data gap** leading to an issue not finalised, see Section 9.1.1).

Based on the available data and risk assessment, a low risk to **non-target terrestrial plants** was demonstrated for all representative uses. A low risk to **organisms involved in biological methods for sewage treatment** was also concluded.

6 | ENDOCRINE DISRUPTION PROPERTIES

The endocrine disruption potential of pyrimethanil was discussed at the Pesticide Peer Review Experts' Meeting 18 (in November 2019) and at the Pesticide Peer Review Experts' Meeting TC 114 (Mammalian toxicology–Ecotoxicology joint session on ED in September 2023).

With regard to the assessment of the endocrine disruption potential of pyrimethanil **for humans and non-target organisms** according to the ECHA/EFSA guidance (2018), in determining whether pyrimethanil 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 pyrimethanil with the EAS and T signalling pathways using the available evidence in the data set.

For humans, for the EAS-modalities, the dataset was considered complete and a pattern of EAS-mediated adversities was not observed. Regarding the T-modality, the dataset was also considered complete, and a clear pattern indicative of perturbation of hypothalamic–pituitary-thyroid (HPT) axis was not identified. Therefore, in line with ECHA/EFSA guidance (2018), **scenario 1a** is applicable and pyrimethanil is not considered to meet the ED criteria for EATS modalities for humans as laid down in point 3.6.5 of Annex II to Regulation (EC) No1107/2009.

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), a 21-day Fish screening Assay, an EASZY Assay,[32] and a number of relevant literature papers were available.

Regarding the T-modality, the AMA[33] was valid and reliable and did not show any positive evidence for endocrine activity.

For EAS-modalities,[34] although some uncertainties were identified with regards to the testing strategy followed and the findings[35] in the available studies, it can be concluded that the available dataset and weight of evidence do not suggest a pattern of EAS-mediated endocrine activity.

According to point 3.6.5 and 3.8.2 of Annex II to Regulation (EC) No 1107/2009, as amended by Commission Regulation (EU) 2018/605, it can be concluded that pyrimethanil is not an endocrine disruptor.

[32]The study was performed in line with OECD TG 250: EASZY assay – Detection of Endocrine Active Substances, acting through oestrogen receptors, using transgenic tg(cyp19a1b:GFP) Zebrafish embrYos.

[33]Refer to experts' consultation 5.9 in the Report of the Peer Review Experts' meeting report TC 114 (EFSA, 2024).

[34]Refer to experts' consultation 5.7 in the Report of the Peer Review Experts' meeting report TC 114 (EFSA, 2024).

[35]See uncertainty analysis in Section 2.10 of Volume 1 of the RAR.

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
Pyrimethanil	Low risk to soil dwelling organisms
M605F007	Low risk to soil dwelling organisms
Unidentified U2	Data gap

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
Pyrimethanil	No	Yes	–	–	Yes
M605F007	No	No data Assessment not triggered	Acutely toxic in the rat; Ames test and in vitro micronucleus negative; no data/open for general toxicity	No	Not triggered for the representative uses assessed
Unidentified U2	Data gap	Open	Open	Open	Open

[a]Assessment according to European Commission guidance of the relevance of groundwater metabolites (2003).

[b]FOCUS scenarios or relevant lysimeter. Ranges indicated for FOCUS scenarios include the result from the model giving the highest concentration at each scenario, as needed to comply with European Commission (2014a) guidance.

TABLE 4 Surface water and sediment.

Compound (name and/or code)	Ecotoxicology
Pyrimethanil	Considering risk mitigation, low risk to aquatic organisms in the majority of FOCUS surface water scenarios
M605F007	Low risk to aquatic organisms
Unidentified U2	Data gap

TABLE 5 Air.

Compound (name and/or code)	Toxicology
Pyrimethanil	Rat LD_{50} inhalation 1.98 mg/L air for 4 h nose-only

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

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)

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

Representative use	Strawberries		Pome fruit	Grapevine	Lettuce	
	F	G			F	G
	Foliar spray	Foliar spray	Foliar spray	Foliar spray	Foliar spray	Foliar spray
Operator risk	–	Use of gloves, coverall and RPE is required	Available RMM insufficient for manual handheld application in late season	Use of gloves is required	–	Use of gloves, coverall and RPE is required
Worker exposure		Use of gloves is required	–	–		Use of gloves is required
Bystander/ resident exposure	–	–	–	Drift reduction is required	–	–
Risk to aquatic organisms	RMM equivalent to 20 m no-spray buffer zone combined with a 20 m vegetated runoff buffer for 2 scenarios[a] + RMM equivalent to 10 m no-spray buffer zone combined with a 10 m vegetated runoff buffer for 1 scenario[b]	RMM equivalent to 20 m no-spray buffer zone combined with a 20 m vegetated runoff buffer for 2 scenarios[c] + RMM equivalent to 10 m no-spray buffer zone combined with a 10 m vegetated runoff buffer for 1 scenario[d]	RMM equivalent to 20 m no-spray buffer zone combined with a 20 m vegetated runoff buffer for 3 scenarios[e] + 20 m no-spray buffer zone, 4 scenarios[f]	RMM equivalent to 10 m no-spray buffer zone combined with a 10 m vegetated runoff buffer for 1 scenario[g] + 10 m no-spray buffer zone, 4 scenarios[h]	RMM equivalent to 20 m no-spray buffer zone combined with a 20 m vegetated runoff buffer for 3 scenarios[i]	RMM equivalent to 20 m no-spray buffer zone combined with a 20 m vegetated runoff buffer for 3 scenarios[i]

[a]R1 and R4. Insufficient risk mitigation for D6 and R3 scenario.
[b]R2.
[c]R3, R4. Insufficient risk mitigation for D6 scenario.
[d]R1.
[e]R1, R3, R4.
[f]R2, D3, D4, D5.
[g]R1.
[h]D6, R2, R3, R4.
[i]R1, R3, R4. Insufficient risk mitigation for D6 scenario.

8.2 | Particular conditions proposed for the maximum residue level applications

No particular conditions are proposed for the MRL application.

9 | CONCERNS AND RELATED DATA GAPS

9.1 | Concerns and related data gaps 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[36] 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.

[36]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.

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. The batches used in toxicity studies are not representative of the original and new reference specifications for the active substance pyrimethanil and associated impurities, since for an impurity the applicant did not provide enough information to exclude their relevance from the toxicological point of view (see Section 2):

    a. Further information or experimental data to clarify possible clastogenic potential (i.e. an in vitro mammalian cells micronucleus test) for acetylacetone in order to set the acceptable levels in the reference specification (relevant for all the representative uses evaluated; see Section 2).

2. The consumer risk assessment could not be finalised due to missing residue data for the representative use on lettuce and due to lack of toxicological information on the metabolites M605F007 and M605F004 (and its sugar conjugates M605F027 and M605F041) and might be considered applicable also to malonyl-β-O glucoside M605F028 (see Sections 2 and 3).

    a. The general toxicity of M605F004 and its conjugates, and of M605F007 should be addressed (relevant for all representative uses, see Section 2).
    b. Eight residue field trials for each zone (indoor, NEU and SEU) with lettuce performed according to cGAP, covered by storage stability data and using a validated analytical method analysing for metabolite M605F004 and its conjugates (relevant for the representative use on lettuce, see Section 3).
    c. Data and information were not available to demonstrate that residues of pyrimethanil will have no immediate or delayed harmful effects on human health, including that of vulnerable groups or animal health, …through drinking water (taking into account substances resulting from water treatment) (relevant to comply with the conditions of approval, not dependent of any specific use, see Section 4).

3. The groundwater exposure assessment and soil dwelling organism and aquatic organism risk assessments for unidentified soil metabolite U2 could not be finalised whilst the environmental exposure assessments needed were not available (see Section 4).

    a. Satisfactory information to identify the soil metabolite U2 was not available. Substance property information (degradation rate and adsorption) was not available. Consequently, the soil, surface water, sediment and groundwater exposure assessments for unidentified U2 were not available (relevant for all the representative uses assessed, see Sections 3 and 4).
    b. Suitable risk assessments for soil and aquatic organisms were not available for the unidentified metabolite U2 (see Section 5).

4. The risk assessment for honey bee larvae could not be finalised (relevant for all representative uses, see Section 5).

    a. Suitable toxicity data and risk assessment for the assessment of honey bee larvae were not available.

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:

- Critical areas of concern were not identified.

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

(If a particular condition proposed to be taken into account to manage an identified risk, as listed in Section 8, has been evaluated as being effective, then 'risk identified' is not indicated in Table 7.)

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		Grape vines Foliar spray	Pome fruits Foliar spray	Lettuce (field) Foliar spray	Lettuce (greenhouse) Foliar spray	Strawberries (field) Foliar spray	Strawberries (greenhouse) Foliar spray
Operator risk	Risk identified		X[h]				
	Assessment not finalised						
Worker risk	Risk identified						
	Assessment not finalised						
Resident/bystander risk	Risk identified						
	Assessment not finalised						
Consumer risk	Risk identified						
	Assessment not finalised	X[2]	X[2]	X[2]	X[2]	X[2]	X[2]
Risk to wild non-target terrestrial vertebrates	Risk identified			X	X[c]		
	Assessment not finalised						
Risk to wild non-target terrestrial organisms other than vertebrates	Risk identified	X[f]	X[f]			X[f]	X[g]
	Assessment not finalised	X[3,4]	X[3,4]	X[3,4]	X[3,4]	X[3,4]	X[3,4]
Risk to aquatic organisms	Risk identified			1/7[e]	1/7[e]	2/7[d]	1/7[e]
	Assessment not finalised	X[3]	X[3]	X[3]	X[3]	X[3]	X[3]
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	X[3]	X[3]	X[3]	X[3]	X[3]	X[3]

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 to 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]High long-term risk to mammals for the representative use to lettuce in greenhouses with the exception of uses in permanent greenhouses.

[d]High chronic risk to fish for D6 and R3 scenario even when considering the proposed risk mitigation.

[e]High chronic risk to fish for D6 scenario even when considering the proposed risk mitigation.

[f]High chronic risk to adult honey bees based on a tier 1 assessment according to EFSA (2013).

[g]High chronic risk to adult honey bees based on a tier 1 assessment according to EFSA (2013) with the exception of uses in permanent greenhouses.

[h]It refers to manual handheld application in late season (with dense foliage).

9.2 | Issues related to the maximum residue level applications

9.2.1 | Issues not finalised under the maximum residue level applications

None identified.

9.2.2 | Consumer risk identified under the maximum residue level applications

None identified.

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 one of the components of the formulation for representative uses 'SCALA' (BAS 605 04 F), in order to allow a final conclusion on the safety assessment of 'SCALA' (BAS 605 04 F), further information on this component in relation to its specification/composition and repeated-dose toxicity information over the long-term 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 'General aspects').
- Clear presentation of the inclusion/exclusion criteria for the assessment of the relevance and reliability of the outcomes of the searches, dealing with side effects on health and published within the 10 years before the date of submission of the dossier, to be reported by the RMS in the RAR in accordance with EFSA guidance on the submission of scientific peer-reviewed open literature for the approval of pesticide active substances under Regulation (EC) No 1107/2009 (EFSA, 2011a, 2011b) (relevant for all the representative uses evaluated; see Section 'General aspects').
- Spectral data and content of the relevant impurities acetylacetone and aniline in the formulation before and after storage (relevant for all the representative uses evaluated; see Section 1).
- N-octanol/water partition coefficient of unidentified soil metabolite U2 (relevant for all the representative uses evaluated; see Sections 1 and 5).
- Method(s) for determination of the relevant impurities acetylacetone and aniline in the formulation (relevant for all the representative uses evaluated; see Section 1).
- For the monitoring method for animal products additional data on the efficiency of the hydrolysis step for all type of conjugates of M605F002 and M605F003 in all animal matrices (relevant for all the representative uses evaluated; see Section 1).
- Extraction efficiency of the procedure used in the monitoring method for animal products for all components of the residue definition and in all matrices in which residues above or equal to LOQ is expected (relevant for all the representative uses evaluated; see Section 1).
- Phototoxicity study considering that absorption maximum of pyrimethanil is between 205 and 271 nm and the molar extinction/absorption coefficient at 290 nm is > 10 L/mol/cm (relevant for the representative use evaluated; see Section 2).
- Upon presentation of the actual application rates in strawberry residue trials in NEU and in SEU it should be considered whether a scaling of the residue results is required and the impact of the MRL proposal, HR and STMR derived from these residue field trials should be reconsidered. Otherwise, additional GAP compliant residue field trials with strawberry in both zones are required (relevant for the representative use on strawberries, see Section 3).
- Studies establishing processing factors for grapes juice, grape pomace, grape must and raisins are required (relevant for the representative use on grapevines, see Section 3).
- Study investigating the residue in pollen and bee products for human consumption resulting from residues taken up by honeybees from crops at blossom (relevant for the representative uses on strawberry and pome fruit, see Sections 3).
- A risk assessment for birds and mammals for the metabolite M605F028 formed in food items was not available (relevant for all representative uses, see Section 5).
- A risk assessment for bees from the metabolites occurring in pollen and nectar was not available (relevant for all representative uses, see Section 5).
- Suitable toxicity data to cover sub-lethal effects in honey bees was not available (relevant for all representative uses, see Section 5).

ABBREVIATIONS

a.s.	active substance
AChE	acetylcholinesterase
ADE	actual dermal exposure
ADI	acceptable daily intake
AF	assessment factor
AAOEL	acute acceptable operator exposure level
AhR	aryl hydrocarbon receptor
AMA	amphibian metamorphosis assay
AOEL	acceptable operator exposure level
AR	applied radioactivity
ARfD	acute reference dose
AST	aspartate aminotransferase (SGOT)
AUC	area under the blood concentration/time curve
AV	avoidance factor

bw	body weight
CFU	colony forming units
CI	confidence interval
CL	confidence limits
DAR	draft assessment report
DAT	days after treatment
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
EINECS	European Inventory of Existing Commercial Chemical Substances
ELINCS	European List of New Chemical Substances
EMDI	estimated maximum daily intake
ERO	ecological recovery option
ETR	exposure toxicity ratio
f(twa)	Time-weighted average factor
FAO	Food and Agriculture Organization of the United Nations
GAP	Good Agricultural Practice
GGT	gamma glutamyl transferase
GM	geometric mean
GS	growth stage
GSH	glutathione
Hb	haemoglobin
Hct	haematocrit
HGPRT	hypoxanthine-guanine phosphoribosyl transferase
HR	highest residue
IEDI	international estimated daily intake
IESTI	international estimated short-term intake
ISO	International Organization for Standardization
IUPAC	International Union of Pure and Applied Chemistry
iv	intravenous
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–MS-MS	liquid chromatography with tandem mass spectrometry
LD_{50}	lethal dose, median; dosis letalis media
LDD_{50}	lethal dietary dose; median
LDH	lactate dehydrogenase
LH	luteinizing hormone
LOAEL	lowest observable adverse effect level
LOD	limit of detection
LOQ	limit of quantification
MAF	multiple application factor
MOA	mode of action
MRL	maximum residue level
MS	mass spectrometry
MSDS	material safety data sheet
MTD	maximum tolerated dose
NOAEC	no observed adverse effect concentration
NOAEL	no observed adverse effect level
OECD	Organisation for Economic Co-operation and Development
OM	organic matter content
PD	proportion of different food types
PEC	predicted environmental concentration
PHED	pesticide handler's exposure data
PHI	pre-harvest interval
PIE	potential inhalation exposure
pK_a	negative logarithm (to the base 10) of the dissociation constant

PPE	personal protective equipment
QSAR	quantitative structure–activity relationship
r^2	coefficient of determination
RAC	regulatory acceptable concentration
RAR	renewal assessment report
REACH	Registration, Evaluation, Authorisation of Chemicals Regulation
RPE	respiratory protective equipment
RUD	residue per unit dose
SC	suspension concentrate
SD	standard deviation
SFO	single first-order
SMILES	simplified molecular-input line-entry system
SPG	specific protection goal
SSD	species sensitivity distribution
STMR	supervised trials median residue
$t_{1/2}$	half-life (define method of estimation)
TK	technical concentrate
TLV	threshold limit value
T_{max}	time until peak blood levels achieved
TMDI	theoretical maximum daily intake
ToxCAST	(US EPA) Toxicity Forecaster
TRR	total radioactive residue
TSH	thyroid-stimulating hormone (thyrotropin)
TWA	time-weighted average
UDS	unscheduled DNA synthesis
UF	uncertainty factor
UV	ultraviolet
W/S	water/sediment
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

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APPENDIX A

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

Properties		Conclusion[a]
CMR	Carcinogenicity (C)	Pyrimethanil is not classified as carcinogen from Harmonised classification according to Annex VI of Regulation (EC) No 1272/2008
	Mutagenicity (M)	Pyrimethanil is not classified as mutagen from Harmonised classification according to Annex VI of Regulation (EC) No 1272/2008
	Toxic for Reproduction (R)	Pyrimethanil is not classified as toxic for the reproduction from Harmonised classification according to Annex VI of Regulation (EC) No 1272/2008
Endocrine disrupting properties		Pyrimethanil is not considered to meet the criteria for endocrine disruption for human health and non-target organisms according to points 3.6.5 and 3.8.2 of Annex II of Regulation No 1107/2009, as amended by Commission Regulation (EU) 2018/605
POP	**Persistence** **Bioaccumulation** **Long-range transport**	Pyrimethanil 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**	Pyrimethanil 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**	Pyrimethanil not considered to be a very persistent, very bioaccumulative substance according to point 3.7.3 of Annex II of Regulation (EC) 1107/2009

[a]Origin of data to be included where applicable (e.g. EFSA, ECHA RAC, Regulation).

APPENDIX B

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

Appendix B can be found in the online version of this output ('Supporting information' section): https://doi.org/10.2903/j.efsa.2024.8998.

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[37] 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 to < 10 days
Moderate persistence	10 to < 60 days
Medium persistence	60 to < 100 days
High persistence	100 days to < 1 year
Very high persistence	A year or more

Notes: 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.

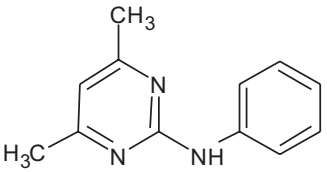
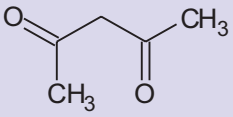
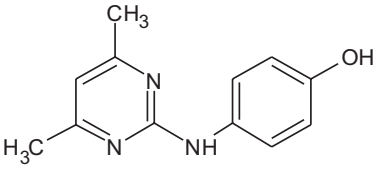
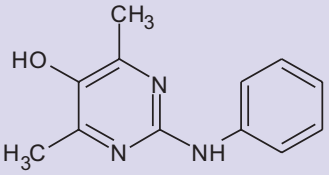
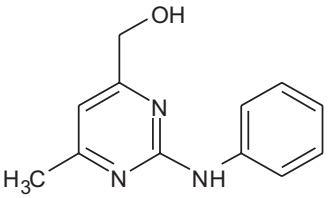
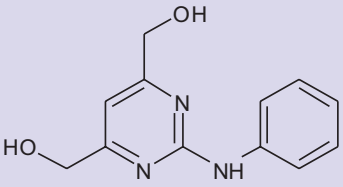
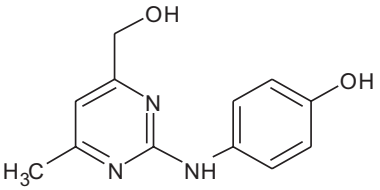
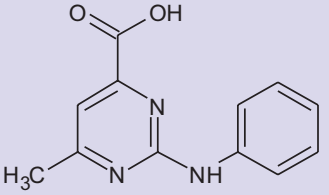
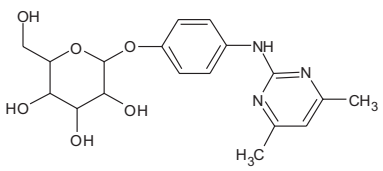
Wording	K_{oc} (either K_{Foc} or K_{doc}) mL/g
Very high mobility	0–50
High mobility	51–150
Medium mobility	151–500
Low mobility	501–2000
Slight mobility	2001–5000
Immobile	> 5000

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

[37] 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]
pyrimethanil	N-(4,6-dimethylpyrimidin-2-yl)aniline Cc1cc(C)nc(Nc2ccccc2)n1 ZLIBICFPKPWGIZ-UHFFFAOYSA-N	
acetylacetone	pentane-2,4-dione CC(=O)CC(C) = O YRKCREAYFQTBPV-UHFFFAOYSA-N	
SN 614276 (M605F002, AN2)	4-[(4,6-dimethylpyrimidin-2-yl)amino]phenol Oc1ccc(cc1)Nc1nc(C)cc(C)n1 NUWWAHKTVOVTNC-UHFFFAOYSA-N	
SN 614277 (M605F003, AN3)	2-anilino-4,6-dimethylpyrimidin-5-ol Cc1nc(Nc2ccccc2)nc(C)c1O YZWHZRWOWLGVQA-UHFFFAOYSA-N	
M605F004 (AN4)	(2-anilino-6-methylpyrimidin-4-yl)methanol OCc1cc(C)nc(Nc2ccccc2)n1 ICVNJIFYUVQAIA-UHFFFAOYSA-N	
M605F005 (AN5)	(2-anilinopyrimidine-4,6-diyl)dimethanol OCc1cc(nc(Nc2ccccc2)n1)CO ZKEBQPCQWMBCSM-UHFFFAOYSA-N	
M605F006 (AN6)	4-{[4-(hydroxymethyl)-6-methylpyrimidin-2-yl]amino}phenol Oc1ccc(cc1)Nc1nc(C)cc(CO)n1 RKIIMHOKNXLKOI-UHFFFAOYSA-N	
M605F034 (pyrimethanil-COOH)	2-anilino-6-methylpyrimidine-4-carboxylic acid O=C(O)c1cc(C)nc(Nc2ccccc2)n1 JMMAPDDAMYEJJN-UHFFFAOYSA-N	
M605F001	4-[(4,6-dimethylpyrimidin-2-yl)amino]phenyl hexopyranoside Cc1nc(nc(C)c1)Nc1ccc(cc1)OC1OC(CO)C(O)C(O)C1O FAAFQZTYXLCXSZ-UHFFFAOYSA-N	

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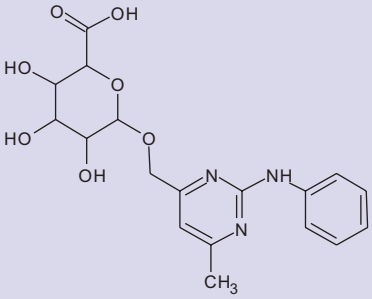
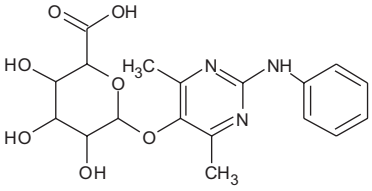
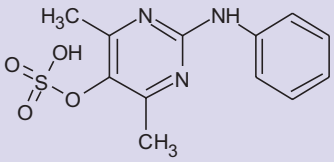
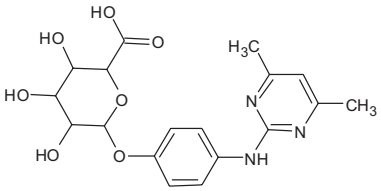
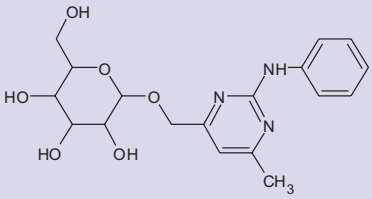
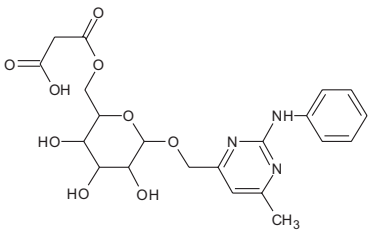
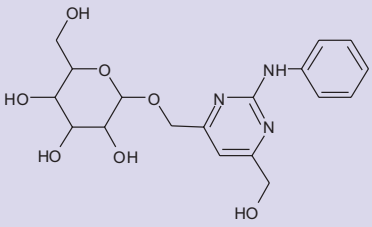
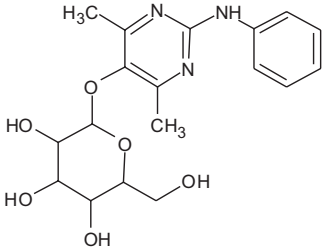
Code/trivial name[a]	IUPAC name/SMILES notation/InChiKey[b]	Structural formula[c]
M605F014	(2-anilino-6-methylpyrimidin-4-yl)methyl hexopyranosiduronic acid O=C(O)C1OC(OCc2cc(C)nc(Nc3ccccc3)n2)C(O)C(O)C1O YSOLUYWUYRYPQF-UHFFFAOYSA-N	
M605F020	2-anilino-4,6-dimethylpyrimidin-5-yl hexopyranosiduronic acid O=C(O)C1OC(Oc2c(C)nc(Nc3ccccc3)nc2C)C(O)C(O)C1O PRAOMVUFOWEIQS-UHFFFAOYSA-N	
M605F021	2-anilino-4,6-dimethylpyrimidin-5-yl hydrogen sulfate O=S(=O)(O)Oc1c(C)nc(Nc2ccccc2)nc1C BHMQYIJWUADZHC-UHFFFAOYSA-N	
M605F023	4-[(4,6-dimethylpyrimidin-2-yl)amino]phenyl hexopyranosiduronic acid Cc1nc(nc(C)c1)Nc1ccc(cc1)OC1OC(C(O)C(O)C1O)C(=O)O LWSYRWGIXHGPNV-UHFFFAOYSA-N	
M605F027	(2-anilino-6-methylpyrimidin-4-yl)methyl hexopyranoside Cc1cc(COC2OC(CO)C(O)C(O)C2O)nc(Nc2ccccc2)n1 BKNJZTUTKHXJLC-UHFFFAOYSA-N	
M605F028	(2-anilino-6-methylpyrimidin-4-yl)methyl 6-*O*-(carboxyacetyl) hexopyranoside O=C(O)CC(=O)OCC1OC(OCc2cc(C)nc(Nc3ccccc3)n2)C(O)C(O)C1O DNQUEEWVJGUUSA-UHFFFAOYSA-N	
M605F029	[2-anilino-6-(hydroxymethyl)pyrimidin-4-yl]methyl hexopyranoside OCc1cc(COC2OC(CO)C(O)C(O)C2O)nc(Nc2ccccc2)n1 RTIOXFPKDWFKRE-UHFFFAOYSA-N	
M605F030	2-anilino-4,6-dimethylpyrimidin-5-yl hexopyranoside Cc1nc(Nc2ccccc2)nc(C)c1OC1OC(CO)C(O)C(O)C1O BHVMXTIFLGDEOZ-UHFFFAOYSA-N	

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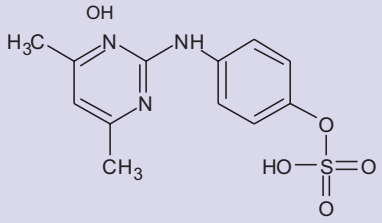
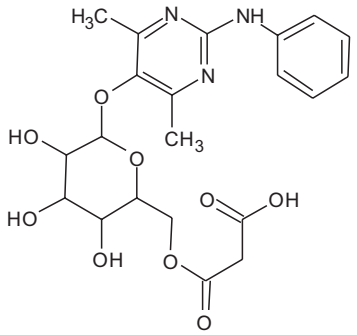
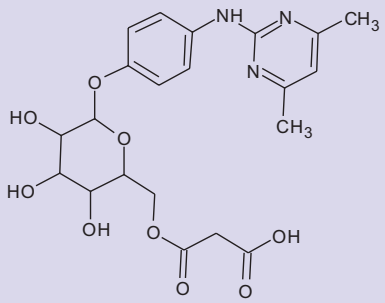
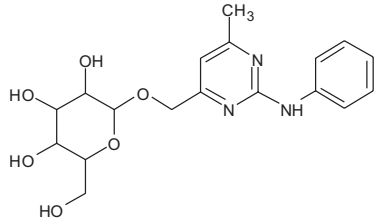
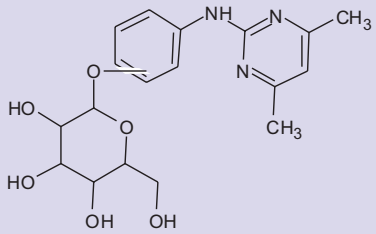
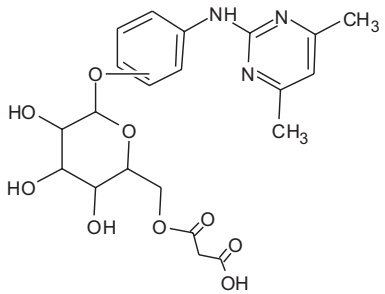
Code/trivial name[a]	IUPAC name/SMILES notation/InChiKey[b]	Structural formula[c]
M605F035	4-[(4,6-dimethylpyrimidin-2-yl)amino]phenyl hydrogen sulfate O=S(=O)(O)Oc1ccc(cc1)Nc1nc(C)cc(C)n1 DWOYONGRJIXXOJ-UHFFFAOYSA-N	
M605F036	2-anilino-4,6-dimethylpyrimidin-5-yl 6-*O*-(carboxyacetyl) hexopyranoside O=C(O)CC(=O)OCC1OC(Oc2c(C)nc(Nc3ccccc3)nc2C)C(O)C(O)C1O XJZMEUUBTKCAJF-UHFFFAOYSA-N	
M605F037	4-[(4,6-dimethylpyrimidin-2-yl)amino]phenyl 6-*O*-(carboxyacetyl) hexopyranoside O=C(O)CC(=O)OCC1OC(Oc2ccc(Nc3nc(C)cc(C)n3)cc2)C(O)C(O)C1O FLFMGHCGNKNIKT-UHFFFAOYSA-N	
M605F038	(2-anilino-6-methylpyrimidin-4-yl)methyl hexopyranoside Cc1cc(COC2OC(CO)C(O)C(O)C2O)nc(Nc2ccccc2)n1 BKNJZTUTKHXJLC-UHFFFAOYSA-N	
M605F039	Structure undefined, a unique name/SMILES/InChiKey cannot be allocated	
M605F040	Structure undefined, a unique name/SMILES/InChiKey cannot be allocated	

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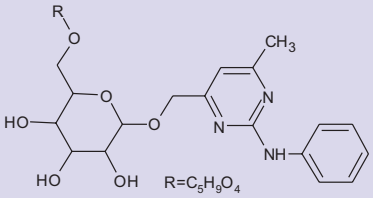
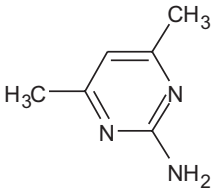
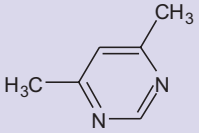
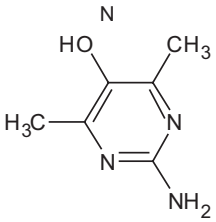
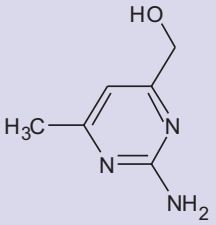
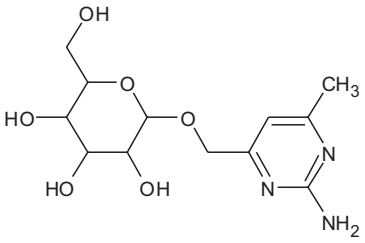
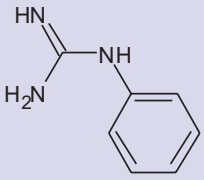
Code/trivial name[a]	IUPAC name/SMILES notation/InChiKey[b]	Structural formula[c]
M605F041	Structure undefined, a unique name/SMILES/InChiKey cannot be allocated	
M605F007 (AN7) **ADMP**	4,6-dimethylpyrimidin-2-amine Cc1cc(C)nc(N)n1 IDQNBVFPZMCDDN-UHFFFAOYSA-N	
M605F008 (AN8)	4,6-dimethylpyrimidine Cc1cc(C)ncn1 LSBIUXKNVUBKRI-UHFFFAOYSA-N	
M605F016 (Py-HO of AN7)	2-amino-4,6-dimethylpyrimidin-5-ol Oc1c(C)nc(N)nc1C BATVWQIPSVQPEI-UHFFFAOYSA-N	
M605F032 (Me-HO of AN7)	(2-amino-6-methylpyrimidin-4-yl)methanol Cc1cc(CO)nc(N)n1 BHTFHKKIXHZCKS-UHFFFAOYSA-N	
M605F033 (Glucoside of M605F032)	(2-amino-6-methylpyrimidin-4-yl)methyl hexopyranoside Cc1cc(COC2OC(CO)C(O)C(O)C2O)nc(N)n1 NANSRIWYFZFDJG-UHFFFAOYSA-N	
M605F025 (Phenylguanidine)	*N*-phenylguanidine NC(=N)Nc1ccccc1 QRJZGVVKGFIGLI-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).