CONCLUSION ON PESTICIDES PEER REVIEW

efsa JOURNAL

APPROVED: 5 July 2023

doi: 10.2903/j.efsa.2023.8112

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

European Food Safety Authority (EFSA),
Fernando Álvarez, Maria Arena, Domenica Auteri, Sofia Batista Leite, Marco Binaglia, Anna Federica Castoldi, Arianna Chiusolo, Ana-Andreea Cioca, Angelo Colagiorgi, Mathilde Colas, Federica Crivellente, Chloe De Lentdecker, Isabella De Magistris, Mark Egsmose, Gabriella Fait, Franco Ferilli, Varvara Gouliarmou, Katrin Halling, Laia Herrero Nogareda, Alessio Ippolito, Frederique Istace, Samira Jarrah, Dimitra Kardassi, Aude Kienzler, Anna Lanzoni, Roberto Lava, Renata Leuschner, Alberto Linguadoca, Jochem Louisse, Christopher Lythgo, Oriol Magrans, Iris Mangas, Ileana Miron, Tunde Molnar, Laura Padovani, Vincenzo Padricello, Martina Panzarea, Juan Manuel Parra Morte, Simone Rizzuto, Anamarija Romac, Agnès Rortais, Rositsa Serafimova, Rachel Sharp, Csaba Szentes, Andrea Terron, Anne Theobald, Manuela Tiramani, Giorgia Vianello and Laura Villamar-Bouza

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 Greece and co-rapporteur Member State Finland for the pesticide active substance urea and the considerations as regards the inclusion of the substance in Annex IV of Regulation (EC) No 396/2005 are reported. The context of the peer review was that required by 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 urea as an attractant of fruit fly *Bactrocera oleae* on olive crops. 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 reported where identified.

Keywords: urea, peer review, risk assessment, pesticide, attractant

Requestor: European Commission

Question number: EFSA-Q-2017-00295

Correspondence: pesticides.peerreview@efsa.europa.eu

Declarations 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.

Acknowledgements: EFSA wishes to thank the rapporteur Member State Greece for the preparatory work on this scientific output.

Suggested citation: EFSA (European Food Safety Authority), Álvarez, F., Arena, M., Auteri, D., Leite, S. B., Binaglia, M., Castoldi, A. F., Chiusolo, A., Cioca, A.-A., Colagiorgi, A., Colas, M., Crivellente, F., De Lentdecker, C., De Magistris, I., Egsmose, M., Fait, G., Ferilli, F., Gouliarmou, V., Halling, K., ... Villamar-Bouza, L. (2023). Peer review of the pesticide risk assessment of the active substance urea. *EFSA Journal*, *21*(8), 1–23. https://doi.org/10.2903/j.efsa.2023.8112

ISSN: 1831-4732

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

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 as amended by Commission Implementing Regulation (EU) No 2016/183. Urea is one of the active substances listed in that Regulation.

In accordance with Article 1 of Regulation (EU) No 844/2012, the rapporteur Member State (RMS), Greece, and co-rapporteur Member State (co-RMS), Finland, received an application from N.G. Stavrakis-Phytophyl and Forestry Research for the renewal of approval of the active substance urea. As of 13 September 2021, the applicant Forestry Research has decided to formally withdraw its application from the European approval process. As a result, the assessments in relation to the representation uses of the plant protection product as a fungicide supported by the applicant Forestry Research have been considered obsolete.

An initial evaluation of the dossier on urea 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 urea according to the representative uses as an attractant of fruit fly *Bactrocera oleae* on olive crops, as proposed at southern Europe (SEU) level result in a sufficient attractant efficacy of the target fruit fly-*B. oleae*.

The assessment of the data package revealed no issues that need to be included as critical areas of concern with respect to the identity, physical, chemical and technical properties of the formulation for representative uses and analytical methods. However, a new reference specification could not be proposed due to the absence of data, leading to an issue that could not be finalised.

In the area of **mammalian toxicology**, urea is of low toxicological concern and no risks to human health could be expected from the use as a plant protection product. However, it cannot be concluded if limit values for toxicological relevant impurities were exceeded in the technical urea as no batch analysis data were provided.

With respect to the section of **residues** in food and feed, when urea is applied under proposed method for the representative uses, insignificant residues of urea (or of its relevant impurities) are expected on olive fruits. Dietary exposure from this pesticidal use is anticipated to be lower than the dietary exposure of the consumer from other sources. Criterion 4 for inclusion into Annex IV of Regulation (EC) No 396/2005 is considered met.

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 as an insect attractant on olive crops.

In the area of **ecotoxicology**, a low risk to all groups of non-target organisms was concluded for the representative uses.

The active substance urea **does not meet the criteria for endocrine disruption** for humans and non-target organisms according to points 3.6.5 and 3.8.2 of Annex II to Regulation (EC) No 1107/2009, as amended by Commission Regulation (EU) 2018/605.

Table of contents

Background

Commission Implementing Regulation (EU) No 844/2012[1], as amended by Commission Implementing Regulation (EU) No 2018/1659[2], (hereinafter referred to as 'the Regulation'), lays down the provisions for the procedure of the renewal of the approval of active substances, submitted under Article 14 of Regulation (EC) No 1107/2009[3]. This regulates for the European Food Safety Authority (EFSA) the procedure for organising the consultation of Member States, the applicant(s) and the public on the initial evaluation provided by the rapporteur Member State (RMS) and/or co-rapporteur Member State (co-RMS) in the renewal assessment report (RAR), and the organisation of an expert consultation where appropriate.

In accordance with Article 13 of the Regulation, unless formally informed by the European Commission that a conclusion is not necessary, EFSA is required to adopt a conclusion on whether the active substance can be expected to meet the approval criteria provided for in Article 4 of Regulation (EC) No 1107/2009 within 5 months from the end of the period provided for the submission of written comments, subject to an extension of an additional 3 months where additional information is required to be submitted by the applicant(s) in accordance with Article 13(3). Furthermore, in accordance with Article 13(3a), where the information available in the dossier is not sufficient to conclude the assessment on whether the approval criteria for endocrine disruption are met, additional information can be requested to be submitted in a period of minimum 3 months, not exceeding 30 months, depending on the type of information requested.

In accordance with Article 1 of the Regulation, the RMS Greece and co-RMS Finland received an application from N.G. Stavrakis-Phytophyl and Forestry Research for the renewal of approval of the active substance urea. In addition, the applicant submitted an application for inclusion of the substance in Annex IV 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 (Finland), the European Commission and EFSA about the admissibility.

The RMS provided its initial evaluation of the dossier on urea in the RAR, which was received by EFSA on 2 July 2020 (Greece, 2021).

In accordance with Article 12 of the Regulation, EFSA distributed the RAR to the Member States and the applicants, N.G. Stavrakis-Phytophyl and Forestry Research, for consultation and comments on 28 April 2021. 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 28 June 2021. At the same time, the collated comments were forwarded to the RMS for compilation and evaluation in the format of reporting table. In addition, the applicants were invited to respond to the comments received. 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 and the RMS on 12 August 2021. 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 and ecotoxicology.

In addition, following a consultation with Member States in the Pesticides Peer Review Expert meeting Teleconference 77 (May 2022), it was considered necessary to apply an additional clock stop of 4 months and half 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

[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, pp. 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, pp. 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, pp. 1–16.

criteria for the determination of endocrine disrupting properties, as laid down in Commission Regulation (EU) 2018/605[5], are met.

On 28 September 2021, the applicant Forestry Research decided to formally withdraw its application from the European approval process. As a result, the assessments in relation to the representative fungicide use of the plant protection product supported by the applicant Forestry Research have been considered obsolete.

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

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

A final consultation on the conclusions arising from the peer review of the risk assessment took place with Member States via a written procedure in June 2023.

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 urea as an attractant of fruit fly *B. oleae* on olive crops, as proposed by the applicant. In accordance with Article 12(2) of Regulation (EC) No 1107/2009, risk mitigation options identified in the RAR and considered during the peer review, if any, are presented in the conclusion.

A list of the relevant end points for the active substance and the formulation is provided in Appendix B. In addition, the considerations as regards the cut-off criteria for urea according to Annex II of Regulation (EC) No 1107/2009 are summarised in Appendix A.

A key supporting document to this conclusion is the peer review report (EFSA, 2023a), 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 (12 August 2021 and 14 April 2023[6]);
- the evaluation table (July 2023);
- the report(s) of the scientific consultation with Member State experts (where relevant);
- the comments received on the assessment of the additional information (where relevant);
- the comments received on the draft EFSA conclusion.

Given the importance of the RAR, including its revisions (Greece, 2021; Greece, 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.

[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, pp. 33–36.

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

The active substance and the formulation for representative use(s)

Urea is the IUPAC name for this active substance, there is no ISO common name.

The formulation for representative uses for the evaluation is 'ENTOMELA 75 SL' a soluble concentrate (SL) containing 255 g/kg urea and hydrolysed proteins, a **data gap** was identified for the applicant to provide a statement on the pure content of hydrolysed proteins in the formulation calculated based on the organic nitrogen, excluding inorganic nitrogen and nitrogen from urea, i.e. according to the conclusions reached following the recent peer-review of the active substance hydrolysed proteins (EFSA, 2023b) (see Section 10).

The representative uses evaluated comprise spot bait spray in southern Europe (SEU) applications to olive trees to attract olive fruit fly *B. oleae*. Full details of the GAP can be found in the list of end points in Appendix B.

Data were submitted to conclude that the use of urea according to the representative uses proposed in southern Europe (SEU) result in a sufficient attractant efficacy of the target organisms, following the guidance document SANCO/2012/11251-rev. 4 (European Commission, 2014b).

Conclusions of the evaluation

1. Identity, physical/chemical/technical properties and methods of analysis

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

A GLP five-batch analysis study of urea was not provided (**data gap**, see Section 10), thus a specification, including the minimum purity, the content of additive(s) and impurities, cannot be proposed. Formaldehyde, biuret, and heavy metals (cadmium, hexavalent chromium, mercury, nickel, lead, inorganic arsenic) were considered relevant impurities with maximum levels of below 1 g/kg (formaldehyde), 12 g/kg (biuret), 3 mg/kg (cadmium), 2 mg/kg (hexavalent chromium), 1 mg/kg (mercury), 50 mg/kg (nickel), 120 mg/kg (lead) and 40 mg/kg (inorganic arsenic) (see Section 2). However, due to the lack of GLP batch analysis, data compliance of the technical urea with these levels cannot be concluded. A data gap was identified due to insufficient information on the method of manufacture of the technical urea, including information on starting materials, origin of impurities in the technical urea, and information on the identity and content of additives and impurities in the technical urea (**data gap**, see Section 10). An update of the current reference specification is required as the current specification does not include relevant impurities, however due to the above-mentioned data gaps an updated reference specification cannot be proposed (issue that could not be finalised, see Section 9.1). A FAO specification does not exist for urea.

The assessment of the data package revealed no issues that need to be included as critical areas of concern with respect to the identity, physical, chemical and technical properties of the formulation for the representative uses. A full physicochemical data package for the active substance was not provided (data gap, see Section 10), in addition data gaps were identified for spectrum data (UV/Vis, IR NMR and MS) for the relevant impurities, biuret and formaldehyde, and for the content of the formaldehyde before and after storage of the formulation for representative uses (see Section 10). The main data regarding the identity of urea and its physical and chemical properties are given in Appendix B.

Adequate methods are available for the generation of pre-approval data required for the risk assessment. Methods of analysis are available for the determination of the urea, formaldehyde and biuret in the technical material and/or in the formulation for representative uses; however, **data gaps** were identified to demonstrate the applicability of these methods, in terms of specificity, for the determination of urea, formaldehyde and biuret in the formulation for representative uses; and for the determination of urea and biuret in the technical urea (see Section 10). **Data gaps** were set for validated analytical methods for the determination of formaldehyde and additive(s) in the technical urea. In addition, validated analytical methods for the determination of cadmium, hexavalent chromium, mercury, nickel, lead and inorganic arsenic in the technical urea and the formulation 'ENTOMELA 75 SL' were not provided (**data gap**, see Section 10). Analytical methods for the determination of residues in food and feed of plant origin, in food of animal origin, body fluids and tissues and in environmental compartments are not required since no residue definitions are proposed.

2. Mammalian toxicity

The following guidance documents were used in the production of this conclusion: European Commission (2003, 2012), EFSA (2014, 2017), and ECHA (2017).

The active substance urea was discussed at the Pesticide Peer Review Experts' Teleconference 73 in April 2022.

The assessment of urea's toxicological profile relies on literature data and information extracted from EPA reports (US EPA, 2011), the REACH registration Dossier (ECHA, 2011) and the OECD SIDS Report (OECD SIDS, 1994).

Heavy metals (cadmium, hexavalent chromium, mercury, nickel, lead, inorganic arsenic), biuret and formaldehyde have been identified as toxicological relevant impurities in the technical material.

It is noted that according to Regulation (EC) No 1272/2008[7] the generic concentration limit for Carcinogenic 1B is $\geq$ 0.1% w/w. This could in principle be applicable as maximum concentration limit for formaldehyde. Moreover, heavy metals (cadmium, hexavalent chromium, mercury, nickel, lead, inorganic arsenic) and biuret are considered as acceptable contaminants in fertiliser, under Regulation (EU) 2019/1009[8], at limit values of 3 mg/kg, 2 mg/kg, 1 mg/kg, 50 mg/kg, 120 mg/kg, 40 mg/kg and 12 g/kg (or 1.2% w/w), respectively. However, it cannot be concluded whether these values were exceeded in the technical urea as no batch analysis data were provided (see Section 1).

Urea is an endogenous product of protein and amino acid catabolism formed during normal physiological processes in liver for removal of nitrogen from the body. In rats, exogenously administered urea through either intravenous injection or oral administration is well-**absorbed**, widely **distributed** to the kidney, urinary bladder and digestive tract, and rapidly **eliminated** via urine and expired air. Though a comparative *in vitro* metabolism study is not available for urea, a waiver has been accepted based on the nature of the substance and considering that mammals, including humans, are ureotelic organisms and no further **metabolism** of urea is expected.

Urea has low **acute toxicity** when administered via oral, subcutaneous, and intravenous routes to mammals other than ruminants. No evidence was found for urea's skin irritation potential. On the other hand, the peer review considered that the criteria for classification according to Regulation (EC) No 1272/2008 may be met for **Eye Irrit. 2** (H319 – causes serious eye irritation) based on the result of an available study in rabbit (from the REACH Registration dossier). No studies are available to address the skin sensitisation. Overall, although the submitted literature studies provide limited information on the potential toxicity of urea following oral, dermal and subcutaneous exposure, the lack of toxicological concern is supported by the absence of adverse toxicological effects after **sub-chronic** and **chronic** exposure in rats, mice and dogs, and by the historical safe use of urea in cosmetics, personal care products, as a food additive (E927b – carbamide) and fertiliser (European Commission CosIng Database[9]; DG SANTE Food Additives Database[10]). Considering that urea is applied as formulation for representative uses by spraying, that is a condition requiring acute inhalation toxicity assessment according to Regulations (EU) No 283/2013[11] and No 284/2013[12], and in the absence of an appropriate study or a robust justification, further data for supporting the waiving of an inhalation toxicity study are requested (**data gap,** see Section 10).

Urea has been tested for **genotoxic** potential and has shown no mutagenic effects in bacterial systems, whereas chromosomal aberrations have been noted in mammalian test systems at high concentrations (exceeding the limit concentration and limit dose reported in the OECD test guidelines

[7] 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, pp. 1–1355.

[8] Regulation (EU) 2019/1009 of the European Parliament and of the Council of 5 June 2019 laying down rules on the making available on the market of EU fertilising products and amending Regulations (EC) No 1069/2009 and (EC) No 1107/2009 and repealing Regulation (EC) No 2003/2003. PE/76/2018/REV/1. OJ L 170, 25.6.2019, pp. 1–114.

[9] Commission Decision 96/335/EC, repealed with effect from 8 May 2020, https://ec.europa.eu/growth/tools-databases/cosing/index.cfm?fuseaction=search.results.

[10] Commission Regulation (EU) No 1129/2011 of 11 November 2011 amending Annex II to Regulation (EC) No 1333/2008 of the European Parliament and of the Council by establishing a Union list of food additives. *Official Journal of the European Union L*, 295(4), 12–11.

[11] Commission Regulation (EU) No 283/2013 of 1 March 2013 setting out the data requirements for active substances, in accordance with Regulation (EC) No 1107/2009 of the European Parliament and of the Council concerning the placing of plant protection products on the market Text with EEA relevance.

[12] Commission Regulation (EU) No 284/2013 of 1 March 2013 setting out the data requirements for plant protection products, in accordance with Regulation (EC) No 1107/2009 of the European Parliament and of the Council concerning the placing of plant protection products on the market Text with EEA relevance.

473 and 475) at which cytotoxicity is also reported. The substance showed no treatment-related tumours in published studies conducted in mice and rats; these studies were considered of low reliability by the peer review experts. However, considering that the exposure to urea resulting from its use as a plant protection product would be very limited i.e. with minimal impact on the body burden (see semi-quantitative risk assessment below), and despite the uncertainties related to the reliability of the dataset,[13] urea is concluded as unlikely to pose any concern for genotoxicity or carcinogenicity.

As regards **human data**, no concern or incident has been reported with urea during any phase of development, production or use of the active substance. Only one urea-poisoning incidence has been described in workers (n = 80) assumed to have consumed accidentally a urea fertiliser; the symptoms included loss of appetite, nausea, vomiting, extreme excitement, severe general convulsions and recovered within a few days. However, the description of the study is limited and lacks to demonstrate a direct evidence of urea consumption.

No reference values, i.e. acceptable daily intake (**ADI**), (acute) acceptable operator exposure level (**A-AOEL**) or acute reference dose (**ARfD**), are considered needed for urea due to the lack of toxicological concern, supported by the absence of adverse toxicological effects after **sub-chronic** and **chronic** exposure in rats, mice, and dogs, and its historical safe use. The setting of the toxicological reference values was considered not necessary in the previous evaluation (EFSA, 2012). However, to better address potential uncertainties about urea's genotoxicity and carcinogenicity potential[14] and about the limited toxicological data package, a semi-quantitative risk assessment has been proposed to demonstrate the limited exposure to urea from its use in the formulation for representative uses.[15] The **dermal absorption** values for the formulation for representative uses are 10% and 50% (default values) for the undiluted and diluted product, respectively. For the semi-quantitative risk assessment, the non-dietary exposure for operators, workers, bystanders and residents has been compared to the estimated dose of low concern of 20 mg/kg body weight (bw) per day indicated in the OECD SIDS report and extrapolated from the available carcinogenicity study in rat and the physiological range of urea excreted in urine (20–35 g per day). The results confirmed the limited exposure to urea from its use in the formulation for representative uses.

The formulation for representative use contains two active substances, hydrolysed proteins, and urea. Hydrolysed proteins is an active substance included in Annex I to Directive 91/414/EEC[16] and deemed to be approved under Regulation (EC) No 1107/2009; as such it was discussed at the Pesticide Peer Review Experts' TC 73 in April 2022. It was concluded that, being a low-risk substance, no reference values are needed for hydrolysed proteins.

3. Residues

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

Urea representative use is as an insect attractant, for the control and the suppression of the olive fruit fly and the Mediterranean fruit fly in olive trees as a spot bait spray treatment in combination with an insecticide. When applied under proposed method, insignificant residues of urea (or of its relevant impurities: biuret and formaldehyde) are expected on olive fruits. Therefore, a quantitative consumer dietary risk assessment is not necessarily due to the specific kinds of application. It may be necessary to reassess this conclusion and the consumer risk assessment pending the outcome of the outstanding data on the specification of technical material.

At least one of the five criteria for inclusion into Annex IV of Regulation (EC) No 396/2005[17] can be considered met for urea used as an insect attractant for the control and the suppression of the olive fruit fly (European Commission, 2015). In particular, the dietary exposure from the pesticidal use is anticipated to be lower than the dietary exposure of the consumer from other sources (Criterion 4 met).

[13] Refer to experts' consultation 2.1 in the Report of Pesticides Peer Review Experts' TC 73 (EFSA, 2023a).
[14] Refer to experts' consultation 2.1 in the Report of Pesticides Peer Review Experts' TC 73 (EFSA, 2023a).
[15] Refer to experts' consultation 2.3 in the Report of Pesticides Peer Review Experts' TC 73 (EFSA, 2023a).
[16] Council Directive 91/414/EEC of 15 July 1991 concerning the placing of plant protection products on the market. OJ L 230, 19.8.1991, pp. 1–32.
[17] 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, pp. 1–16.

4. Environmental fate and behaviour

No specific studies on the fate and behaviour of urea in the environment were submitted. However, several open literature papers and technical reports from different organisations (US EPA, OECD and ECHA) were considered to address active substance data points, and the necessary exposure assessment was conducted based on default worst-case endpoints.

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

In soils urea is expected to be rapidly transformed via enzymatic hydrolysis to ammonia and carbamic acid, which is spontaneously converted to carbonic acid. Following the oxidation of carbonic acid and ammonia, the final products of urea dissipation in soil are carbon dioxide, nitrite and nitrate, respectively. Anaerobic metabolism is not expected to be a significant route of degradation in soil. Reliable studies on mobility of urea in soil were not submitted, therefore for the purpose of exposure assessment a default conservative soil adsorption coefficient (Koc) of 10 mL/g was used.

Based on the available information, urea is considered stable against hydrolysis in aquatic systems without urease. On the other hand, when urease is involved, a reaction rapidly takes place, in which one molecule of urea is hydrolysed to form ammonia and carbonic acid. Although no reliable endpoints from water/sediment system studies were available for urea, biodegradation is expected to be the major fate process in the aquatic environment.

Based on the information available, the application of urea as an insecticide attractant to olive trees will produce significantly less nitrogen than the amounts expected from the use of fertilisers, and it is not expected to significantly contribute to eutrophication of the surface water bodies.

The necessary surface water and sediment exposure assessments (predicted environmental concentrations (PEC) calculations) were carried out for urea using the FOCUS (FOCUS, 2001) step 1 and step 2 approach (version 3.2 of the Steps 1–2 in FOCUS calculator). Step 2 PEC surface water (PECsw) for ammonia, nitrites and nitrates were calculated by multiplying urea's moles (derived from the maximum FOCUS Step 2 PECsw value) by 2 (assuming that two molecules of transformation product are produced by one molecule of urea) and by the molecular weight of the respective product (ammonia, nitrite and nitrate). Further, using the same approach, Step 3 PECsw calculations for nitrites and nitrates were derived from FOCUS Step 3 PECsw values calculated for urea for the FOCUS scenarios D6 and R4.

The necessary groundwater exposure assessments were appropriately carried out using FOCUS (European Commission, 2014a) scenarios and the models PEARL 4.4.4 and PELMO 5.5.3. Attractants and repellents are not defined as pesticides in Council Directive 98/83/EC, therefore the parametric drinking water limit of 0.1 μg/L for pesticides and their relevant metabolites as defined by the drinking water directive 98/83/EC is not applicable for urea. PEC groundwater for the transformation products nitrites and nitrates were calculated by multiplying urea's moles, derived from the worst case PECgw for urea, by 2 (assuming that two molecules of transformation product are produced by one molecule of urea) and by the molecular weight of the respective product (ammonia, nitrite, nitrate). It can be concluded that no exceedance is expected for nitrate and nitrite when PECgw values are compared against the parametric drinking water limits set (Council Directive 98/83/EC on the quality of water intended for human consumption) for these inorganic compounds (50 mg/L and 0.5 mg/L, respectively).

The applicant provided appropriate information to address the effect of water treatments processes on the nature of the residues that might be present in surface water and groundwater when surface water or groundwater are abstracted for drinking water. The conclusion of this consideration was that neither urea nor any of its transformation products that trigger assessment (ammonia, nitrate and nitrite) would be expected to undergo any substantial transformation due to oxidation at the disinfection stage of usual water treatment processes.

The atmospheric half-life estimated with the Atkinson model (EPIWEB 4.1, AOPWIN v. 1.92) for urea (5.3 days) gives an indication that when applied as a spray, aerosols formed at the time of spraying may have the potential to be subject to long range transport to areas where it has not been used, via the atmosphere (FOCUS, 2008). However, as urea is not persistent in soil and in the water sediment system, it does not fulfil the POP (Persistent Organic Pollutant) criteria laid out in Regulation (EC) No 1107/2009. Hydrolytic degradation of urea produces gaseous ammonia (NH_3) emissions to air.

Ammonia is considered stable in air by readily absorbed and dissolved in atmospheric humidity, later ammonia is reintroduced to the soil via wet deposition.

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

5. Ecotoxicology

The risk assessment was based on the following documents: EFSA (2013).

For **birds and terrestrial vertebrates**, no studies have been performed on the active or formulation for representative use and no risk assessment could be performed for birds and terrestrial vertebrates.

No additional information for data waiving has been submitted for birds, therefore a conclusion cannot be drawn for birds. However, considering the available evidence from the literature, the acute and long-term risks for birds from the representative use of urea are expected to be low. Regarding terrestrial vertebrate other than birds, due to the low toxicity of urea reported in the literature, its ubiquitous presence in ecosystem and the fact that the release for the proposed uses will be much lower than the release of urea as a fertiliser, the acute and long-term risk to terrestrial vertebrate other than birds from the representative use of urea are expected to be low. No additional data are needed concerning the potential bioaccumulation of urea due to low log Pow value (< -1.73). No metabolite has been identified for which a risk assessment was required, given the properties of the active substance.

For **aquatic organisms**, during the current review of the approval for the active substance, acute toxicity studies were requested, in agreement with the current data requirement (Regulation (EU) 283/2013 and 284/2013). Acute toxicity studies on fish (*Oncorhynchus mykiss*), aquatic invertebrates (*Daphnia magnia*) and algae (*Pseudokirchneriella subcapitata*) were available (limit tests) with a formulation ('ENTOMELA 50 SL') which have a lower content of urea than the formulation for representative use ('ENTOMELA 75 SL'). The reliability and usability of these studies for the risk assessment of urea and its formulation for representative use[18] was discussed and agreed at the expert meeting. No chronic toxicity studies were available. A quantitative acute risk assessment has been performed for aquatic organisms and overall, a low risk was identified at FOCUS step 2 when uses are made according to the intended GAP. The metabolites ammonia, nitrite and nitrate were also considered with regards to surface water; relevant endpoints are not available for these metabolites. However, it is considered that the risk is covered by the parent (urea). Nevertheless, a risk assessment was presented for transformation products and a low risk was identified for ammonia and nitrite at FOCUS step 2 for all aquatic organisms. For nitrate, a low risk was identified at FOCUS step 3 for all aquatic organisms.

No data with the active substance or the formulation for representative use was available to address the risk for **honeybees** and **non-target arthropods other than bees.** Since the absence of attractivity to bees and other non-target arthropods could not be demonstrated, the RMS concluded that the risk to bees and other non-target arthropods could not be assessed. However, the application pattern and the environmental profile of urea suggests a low concern, and the risk assessment for bees and non-target arthropods is low for the representative uses.

No data with the active substance or the formulation for representative use was available to address the risk for **earthworms**, **soil meso and macrofauna, sol nitrogen transformation and biological methods for sewage treatment**. However, a low risk was concluded for all representative uses with a weight of evidence (WoE) approach that considered the following lines of evidence: (i) urea is a naturally occurring compounds which biodegrades rapidly in soil to ammonia and bicarbonate and is not expected to bioaccumulate; (ii) urea degrades rapidly in most soils to be assimilated into the nitrogen cycle and the high water solubility and low adsorption of urea indicate very low exposure to sediment organisms; (iii) the levels of nitrogen released to the environment by using urea as plant protection product at the highest application rate are far below the levels of urea applied as fertiliser; (iv) exposure to the active substances is low when it is used according to the proposed GAP; (v) there is no available literature data suggesting negative effects of the active substance in earthworm, soil macro and micro-organisms at these level of exposure.

No data with the active substance or the formulation for representative uses was available to address the risk for **non-target terrestrial plants.** In the submitted open literature studies some negative effects were found at concentration of exposure slightly below the proposed application rate.

[18] Refer to the experts' consultation point 5.2 discussed during the Pesticide Peer Review TC 77 on 5–6 May 2022 (EFSA, 2023a).

Therefore, the RMS concluded that the risk could not be assessed. However, based on the same WoE as above, the risk to non-target terrestrial plants is low.

6. Endocrine disruption properties

With regard to the assessment of the endocrine disruption potential of urea **for humans and non-target organisms** according to the ECHA/EFSA guidance (2018), although no (eco) toxicological data are available to assess the endocrine disrupting properties of urea, this does not appear scientifically necessary for the following reasons:

- No concern of adversity in the assessed ED mediated endpoints in the literature studies;
- Known biological and toxicological properties of urea;
- Exposure consideration (the impact of the urea use as plant protection product on the level of the physiological endogenous level is considered unlikely to be relevant);
- Urea is naturally occurring and used as a nutrient source by plants and animals, and part of the N-cycle in fish (Lauff and Wood, 1996);
- Urea is widely used for several purposes and approved in different regulatory processes i.e. as cosmetic ingredients,[19] feed additives[20] for cattle, fertilisers (ECHA, 2011);
- Available evidence in fish and amphibians (Stay et al., 1978; Kaushik et al., 1983; Schuytema and Nebeker, 1999; Zhao et al., 2018) from the literature review indicates no concern for endocrine disruptive properties for urea.

Based on the available information, it can be concluded that it is unlikely that urea meets the criteria for endocrine disruption for humans and non-target organisms according to points 3.6.5 and 3.8.2 of Annex II to Regulation (EC) No 1107/2009, as amended by Commission Regulation (EU) 2018/605.

[19] Regulation (EC) No 1223/2009 of the European Parliament and of the Council of 30 November 2009 on cosmetic products.
[20] Commission Implementing Regulation (EU) No 839/2012 of 18 September 2012 concerning the authorisation of urea as a feed additive for ruminants. OJ L 252, 19.9.2012, pp. 11–13.

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

Table 1: Soil

Compound (name and/or code)	Ecotoxicology
Urea	Low risk

Table 2: 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
Urea	Not relevant[(c)]	Yes	–	–	Yes
Nitrate	0.533 mg/L	Not triggered	Not triggered	No	No
Nitrite	0.395 mg/L	Not triggered	Not triggered	No	No

(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.
(c): Attractants are not defined as pesticides in Council Directive 98/83/EC,[21] therefore the parametric drinking water limit of 0.1 µg/L for pesticides and their relevant metabolites as defined by the drinking water directive 98/83/EC is not applicable for urea. The drinking water standards applicable from Council Directive 98/83/EC are: **nitrate 50 mg/L and nitrite 0.5 mg/L**.

Table 3: Surface water and sediment

Compound (name and/or code)	Ecotoxicology
Urea	Low risk
Ammonia	Low risk
Nitrate	Low risk
Nitrite	Low risk

Table 4: Air

Compound (name and/or code)	Toxicology
Urea	Not available (data gap)
Ammonia	Acute Tox. 3 (H331, toxic if inhaled)

[21] Council Directive 98/83/EC of 3 November 1998 on the quality of water intended for human consumption. OJ L 330, 5.12.1988, p. 32–54.

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.

No particular conditions are proposed for the representative use evaluated.

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[22] and if the issue is of such importance that it could, when finalised, become a concern (which would also be listed as a critical area of concern if it is of relevance to all representative uses).

An issue is also listed as 'could not be finalised' if the available information is considered insufficient to conclude on whether the active substance can be expected to meet the approval criteria provided for in Article 4 of Regulation (EC) No 1107/2009.

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

1) An update of the current reference specification is required as the specification for the first approval did not consider formaldehyde, biuret heavy metals (cadmium, hexavalent chromium, mercury, nickel, lead, inorganic arsenic) as relevant impurities. However, due to the lack of five batch analysis GLP data, a new reference specification cannot be proposed (see Section 1).
    a) it cannot be concluded if limit values for toxicological relevant impurities were exceeded in the technical urea as no batch analysis data were provided (see Section 2).

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.

[22] 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, pp. 127–175.

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 5)

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

To be noted that the technical urea specification cannot be concluded for N.G. Stavrakis-Phytophyl.

Table 5: 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		Olive crops Spot bait spray
Operator risk	Risk identified	
	Assessment not finalised	
Worker risk	Risk identified	
	Assessment not finalised	
Resident/bystander risk	Risk identified	
	Assessment not finalised	
Consumer risk	Risk identified	
	Assessment not finalised	
Risk to wild non-target terrestrial vertebrates	Risk identified	
	Assessment not finalised	
Risk to wild non-target terrestrial organisms other than vertebrates	Risk identified	
	Assessment not finalised	
Risk to aquatic organisms	Risk identified	
	Assessment not finalised	
Groundwater exposure to active substance	Legal parametric value breached	
	Assessment not finalised	
Groundwater exposure to metabolites	Legal parametric value breached[(a)]	
	Parametric value of 10 μg/L[(b)] breached	
	Assessment not finalised	

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

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

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

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:

- Sufficient information on the method of manufacture of the active substance, including information on starting materials and detailed information of the origin of impurities and information on the identity and content of additives and impurities in the technical urea (relevant for all the representative uses, see Section 1).
- A GLP five batch analysis study of urea as manufactured was not provided (relevant for all the representative uses, see Section 1).
- A validated analytical method for the determination of additive(s) in the technical material was not provided (relevant for all the representative uses, see Section 1).
- A statement on the pure content of hydrolysed proteins in the formulation 'ENTOMELA 75 SL' calculated based on the organic nitrogen, excluding inorganic nitrogen and nitrogen from urea, was not provided (relevant for all the representative uses, see Section 1).
- A full physicochemical data package for the active substance was not provided (relevant for all the representative uses, see Section 1).
- Spectrum data (UV/Vis, IR, NMR, MS) for the relevant impurities biuret and formaldehyde were not provided (relevant for all the representative uses, see Section 1).
- Data on the content of the relevant impurity formaldehyde before and after storage of the formulation 'ENTOMELA 75 SL' were not provided (relevant for all the representative uses, see Section 1).
- Data to demonstrate the applicability of the method ISO 18643:2016, in terms of specificity, for determination of biuret in the technical urea and in the formulation 'ENTOMELA 75 SL' were not provided (relevant for all the representative uses, see Section 1).
- Data to demonstrate the applicability of the method ISO 19746:2017, in terms of specificity, for determination of urea in the technical material and in the formulation 'ENTOMELA 75 SL' were not provided (relevant for all the representative uses, see Section 1).
- A validated analytical method for the determination of the relevant impurity formaldehyde in the technical urea was not provided (relevant for all the representative uses, see Section 1).
- Data to demonstrate the applicability of the method 82/434/EEC, in terms of specificity, for determination of formaldehyde in the formulation for representative uses 'ENTOMELA 75 SL' were not provided (relevant for all the representative uses, see Section 1).
- Validated analytical methods for the determination of cadmium, hexavalent chromium, mercury, nickel, lead and inorganic arsenic in the technical urea and the formulation 'ENTOMELA 75 SL' were not provided (relevant for all the representative uses, see Section 1).
- Acute inhalation toxicity assessment was not available for urea, further data for supporting the waiving of an inhalation toxicity study for inhalation toxicity are requested (relevant for all the representative uses evaluated; see Section 2).
- An evaluation of the scientific papers on 'ready biodegradability' that the OECD and EPA reports have been based on against the OECD 301 protocol was not available (relevant for all the representative uses, see Section 4).
- Comprehensive justifications for considering each scientific paper used in the scientific peer-reviewed open literature search as non-relevant for the environmental exposure assessment of the active substance and its relevant metabolites, were not available (relevant for all the representative uses evaluated, see Section 4).

References

ECHA (European Chemicals Agency), 2011. REACH registration dossier – Urea (EC number: 200-315-5; CAS number: 57-13-6). First published: 2 March 2011.

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

ECHA (European Chemicals Agency) and EFSA (European Food Safety Authority) with the technical support of the Joint Research Centre (JRC), Andersson N, Arena M, Auteri D, Barmaz S, Grignard E, Kienzler A, Lepper P, Lostia AM, Munn S, Parra Morte JM, Pellizzato F, Tarazona J, Terron A and Van der Linden S, 2018. Guidance for the identification of endocrine disruptors in the context of Regulations (EU) No 528/2012 and (EC) No 1107/2009. EFSA Journal 2018;16(6):5311,135 pp. https://doi.org/10.2903/j.efsa.2018.5311

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

EFSA (European Food Safety Authority), 2012. Peer review report to the conclusion regarding the peer review of the pesticide risk assessment of the active substance urea. Available online: www.efsa.europa.eu

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

EFSA (European Food Safety Authority), 2014. Guidance on the assessment of exposure of operators, workers, residents and bystanders in risk assessment for plant protection products. EFSA Journal 2014;12(10):3874, 55 pp. https://doi.org/10.2903/j.efsa.2014.3874

EFSA (European Food Safety Authority), 2017. Guidance on dermal absorption. EFSA Journal 2017; 15(6):4873, 60 pp. https://doi.org/10.2903/j.efsa.2017.4873

EFSA (European Food Safety Authority), 2023a. Peer review report to the conclusion regarding the peer review of the pesticide risk assessment of the active substance urea. Available online: www.efsa.europa.eu

EFSA (European Food Safety Authority), 2023b. Conclusion on the peer review of the pesticide risk assessment of the active substance hydrolysed proteins. EFSA Journal 2023;21(6):8079, 20 pp. https://doi.org/10.2903/j.efsa.2023.8079

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

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

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

European Commission, 2011. Commission Regulation (EU) No 1129/2011 of 11 November 2011 amending Annex II to Regulation (EC) No 1333/2008 of the European Parliament and of the Council by establishing a Union list of food additives. Official Journal of the European Union L, 295(4), 12–11.

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

European Commission, 2014a. Assessing potential for movement of active substances and their metabolites to ground water in the EU. Report of the FOCUS Workgroup. EC Document Reference SANCO/13144/2010-v. 3,613 pp., as outlined in Generic guidance for tier 1 FOCUS groundwater assessment, v. 2.2 May 2014.

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

European Commission, 2015. Guidance document on criteria for the inclusion of active substances into Annex IV of Regulation (EC) N° 396/2005. SANCO/11188/2013 rev. 2, 14 September 2015.

FOCUS (Forum for the Co-ordination of Pesticide Fate Models and their Use), 2001. FOCUS surface water scenarios in the EU evaluation process under 91/414/EEC. Report of the FOCUS Working Group on Surface Water Scenarios. EC Document Reference SANCO/4802/2001-rev. 2, 245 pp., as updated by Generic guidance for FOCUS surface water scenarios, v. 1.4 May 2015.

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

Greece, 2021. Renewal Assessment Report (RAR) on the active substance urea prepared by the rapporteur Member State Greece, in the framework of Commission Implementing Regulation (EU) No 844/2012, February 2021. Available online: www.efsa.europa.eu

Greece, 2023. Revised Renewal Assessment Report (RAR) on urea prepared by the rapporteur Member State Greece in the framework of Commission Implementing Regulation (EU) No 844/2012, May 2023. Available online: www.efsa.europa.eu

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

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

Kaushik SJ, Dabrowski KR, Dabrowska H, Olah E and Luquet P, 1983. Utilization of dietary urea in rainbow trout. Annals of Nutrition and Metabolism, 27(2), 94–106. https://doi.org/10.1159/000176628

Lauff and Wood, 1996. Respiratory gas exchange, nitrogenous waste excretion, and fuel usage during starvation in juvenile rainbow trout, *Oncorhynchus mykiss*. Journal of Comparative Physiology B, 165, 542–551.

McCall PJ, Laskowski DA, Swann RL and Dishburger HJ, 1980. Measurements of sorption coefficients of organic chemicals and their use in environmental fate analysis. Test protocols for environmental fate and movement of toxicants. In: Proceedings of the 94th Annual Meeting of the American Association of Official Analytical Chemists (AOAC), Oct 21–22, Washington, D.C., pp. 89–109.

OECD SIDS, 1994. Screening information data set (SIDS) of OECD high production volume chemicals programme.

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

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

Schuytema GS and Nebeker AV, 1999. Effects of ammonium nitrate, sodium nitrate, and urea on red-legged frogs, pacific treefrogs, and African clawed frogs. Bulletin of Environmental Contamination and Toxicology, 63, 357–364.

Stay FS, Malueg KW, Austin RE, Crouse MR, Katko A and Dominguez SE, 1978. Ecological effects of forest fertilization with urea on small Western Cascade streams of Oregon, U. S. A. SIL Proceedings, 1922–2010, 20, 1347–1358. https://doi.org/10.1080/03680770.1977.11896697

US EPA (U.S. Environmental Protection Agency), 2011. Toxicological review of Urea, In Support of Summary Information on the Integrated Risk Information System (IRIS). Available online: https://iris.epa.gov/static/pdfs/1022tr.pdf

Zhao T, Wang X, Wang X, Wang S, Chen Y and Jiang J, 2018. Effects of urea on behavior and functional traits of Asiatictoad (*Bufo gargarizans*) tadpole. Aquatic Ecology, 53, 9–19.

Abbreviations

a.s.	active substance
AAOEL	acute acceptable operator exposure level
ADI	acceptable daily intake
AF	assessment factor
AhR	aryl hydrocarbon receptor
AOEL	acceptable operator exposure level
AOP	adverse outcome pathway
ARfD	acute reference dose
bw	body weight
CAS	Chemical Abstracts Service
DAT	days after treatment
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
EbC_{50}	effective concentration (biomass)
EC_{50}	effective concentration
ECHA	European Chemicals Agency
EEC	European Economic Community
EINECS	European Inventory of Existing Commercial Chemical Substances
ELINCS	European List of New Chemical Substances
EPA	Environmental Protection Agency
FAO	Food and Agriculture Organization of the United Nations
FOCUS	Forum for the Co-ordination of Pesticide Fate Models and their Use
GAP	Good Agricultural Practice
ISO	International Organization for Standardization
IUPAC	International Union of Pure and Applied Chemistry
JMPR	Joint Meeting of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Expert Group on Pesticide Residues (Joint Meeting on Pesticide Residues)
K_{doc}	organic carbon linear adsorption coefficient
K_{Foc}	Freundlich organic carbon adsorption coefficient
MOA	mode of action
MRL	maximum residue level
OECD	Organisation for Economic Co-operation and Development
pK_a	negative logarithm (to the base 10) of the dissociation constant
P_{ow}	partition coefficient between *n*-octanol and water
PPE	personal protective equipment
QSAR	quantitative structure–activity relationship
RAC	regulatory acceptable concentration
RAR	Renewal Assessment Report
REACH	Registration, Evaluation, Authorisation of Chemicals Regulation
RUD	residue per unit dose
SFO	single first-order
SIDS	Screening Information Dataset
SMILES	simplified molecular-input line-entry system
SPG	specific protection goal
SSD	species sensitivity distribution
STMR	supervised trials median residue
TMDI	theoretical maximum daily intake
TRR	total radioactive residue
WHO	World Health Organization

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

Properties		Conclusion[(a)]
CMR	**Carcinogenicity (C)**	Urea is not considered to be mutagenic, carcinogenic or toxic for reproduction according to points 3.6.2, 3.6.3 and 3.6.4 of Annex II of Regulation (EC) No 1107/2009.
	Mutagenicity (M)	
	Toxic for Reproduction (R)	
Endocrine disrupting properties		Urea 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 (EC) No 1107/2009, as amended by Commission Regulation (EU) 2018/605.
POP	**Persistence**	Urea is not considered to be a persistent organic pollutant (POP) according to point 3.7.1 of Annex II of Regulation (EC) No 1107/2009.
	Bioaccumulation	
	Long-range transport	
PBT	**Persistence**	Urea is not considered to be a persistent, bioaccumulative and toxic (PBT) substance according to point 3.7.2 of Annex II of Regulation (EC) No 1107/2009.
	Bioaccumulation	
	Toxicity	
vPvB	**Persistence**	Urea is not considered to be a very persistent, very bioaccumulative substance according to point 3.7.3 of Annex II of Regulation (EC) No 1107/2009.
	Bioaccumulation	

(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 formulation(s) for representative use(s)

Appendix B can be found in the online version of this output ('Supporting information' section): https://doi.org/10.2903/j.efsa.2023.8112.

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[23] or not normalised DT_{50} for field studies (SFO equivalent, when biphasic, the DT_{90} was divided by 3.32 to estimate the DT_{50} 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

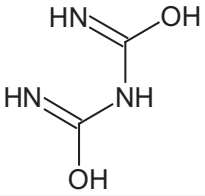
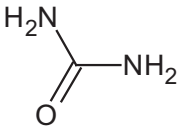
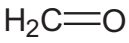
Note these classes and descriptions are unrelated to any persistence class associated with the active substance cut-off criteria in Annex II of Regulation (EC) No 1107/2009. For consideration made in relation to Annex II, see Appendix A.

Wording	K_{oc} (either K_{Foc} or K_{doc}) mL/g
Very high mobility	0 to 50
High mobility	51 to 150
Medium mobility	151 to 500
Low mobility	501 to 2,000
Slight mobility	2,001 to 5,000
Immobile	> 5,000

Based on McCall et al. (1980).

[23] For laboratory soil incubations normalisation was also to field capacity soil moisture (pF2/10kPa). 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]
Biuret	triimidodicarbonic acid N=C(O)NC(=N)O OHJMTUPIZMNBFR-UHFFFAOYSA-N	
Urea	Urea NC(N)=O XSQUKJJJFZCRTK-UHFFFAOYSA-N	
Formaldehyde	Formaldehyde C=O WSFSSNUMVMOOMR-UHFFFAOYSA-N	

(a): The compound name in bold is the name used in the conclusion.
(b): ACD/Name 2021.1.3 ACD/Labs 2021 Release (File version N15E41, Build 123232, 7 July 2021).
(c): ACD/ChemSketch 2021.1.3 ACD/Labs 2021 Release (File version C25H41, Build 123835, 29 August 2021).