CONCLUSION ON PESTICIDES PEER REVIEW

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Peer review of the pesticide risk assessment of the active substance carbon dioxide

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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, France, and co-rapporteur Member State, Austria, for the pesticide active substance carbon dioxide 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 carbon dioxide as an insecticide and acaricide on stored cereal grains, oilseeds, medicinal plants, cereal products, spices, tobacco, tea, dried fruits and other stored plant products (except semolina and oilseed meal) (all indoor uses). The reliable end points, appropriate for use in regulatory risk assessment, are presented.

Keywords: Carbon dioxide, peer review, risk assessment, pesticide, insecticide, acaricide

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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. Carbon dioxide 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), France, and co-rapporteur Member State (co-RMS), Austria, received an application from Carbon Dioxide Renewal Taskforce for the renewal of approval of the active substance carbon dioxide. In addition, the applicant submitted an application for inclusion of the substance in Annex IV of Regulation (EC) No 396/2005.

An initial evaluation of the dossier on carbon dioxide 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 carbon dioxide by fumigation according to the representative uses as an insecticide and acaricide on stored cereal grains, oilseeds, medicinal plants, cereal products, spices, tobacco, tea, dried fruits and other stored plant products (except semolina and oilseed meal) (all indoor uses), as proposed at EU level result in a sufficient insecticidal and acaricidal efficacy against the target organisms.

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 carbon dioxide.

In the area of mammalian toxicology, the assessment of the data package revealed no issues that could not be finalised for the representative uses as an insecticide and acaricide neither areas of concern.

With respect to the residues section, the active substance carbon dioxide is not considered to result in consumers exposure, and it is proposed it be included in Annex IV of Regulation (EC) No 396/2005.

The information available on environmental fate and behaviour was considered sufficient to complete the necessary environmental exposure considerations for the representative uses assessed.

A low risk to all groups of non-target organisms was concluded for the representative uses.

Carbon dioxide 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.

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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 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, France, and co-RMS, Austria, received an application from Carbon Dioxide Renewal Taskforce for the renewal of approval of the active substance carbon dioxide. 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 applicant, the co-RMS (Austria), the European Commission and EFSA about the admissibility.

The RMS provided its initial evaluation of the dossier on carbon dioxide in the RAR, which was received by EFSA on 17 December 2019 (France, 2019). Furthermore, this conclusion also addresses the assessment required from EFSA under Article 12 of Regulation (EC) No 396/2005. On 21 February 2020, EFSA invited the Member States to submit their Good Agricultural Practices (GAPs) that are authorised nationally, in the format of specific GAP forms. All the GAPs were collected by EFSA and they are made publicly available as a background document to this conclusion, in the format of a specific GAP overview file.

In accordance with Article 12 of the Regulation, EFSA distributed the RAR to the Member States and the applicant, Carbon Dioxide Renewal Taskforce, for consultation and comments on 19 February 2020. 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 20 April 2020. 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 applicant was invited to respond to the comments received. The comments and the applicant's response were evaluated by the RMS in column 3.

The need for expert consultation and the necessity for additional information to be submitted by the applicant in accordance with Article 13(3) of the Regulation were considered in a telephone conference between EFSA and the RMS on 25 June 2020. On the basis of the comments received, the applicant's response to the comments and the RMS's evaluation thereof, it was concluded that additional information should be requested from the applicant, and that EFSA should conduct an expert consultation in the areas of mammalian toxicology including a joint expert consultation on ED properties in the areas of mammalian toxicology and ecotoxicology.

[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.

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 and on the proposal for inclusion of the substance in Annex IV of Regulation (EC) No 396/2005 and on the Article 12 MRL review of Regulation (EC) No 396/2005 took place with Member States via a written procedure in March 2021.

This conclusion report summarises the outcome of the peer review of the risk assessment of the active substance and the representative formulation, evaluated on the basis of the representative uses of carbon dioxide as an insecticide and acaricide on stored cereal grains, oilseeds, medicinal plants, cereal products, spices, tobacco, tea, dried fruits and other stored plant products (except semolina and oilseed meal) (all indoor uses), 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. Furthermore, this conclusion also addresses the assessment required from EFSA under Article 12 of Regulation (EC) No 396/2005. On 21 February 2020, EFSA invited the Member States to submit their good agricultural practices (GAPs) that are authorised nationally, in the format of specific GAP forms. All the GAPs were collected by EFSA and they are made publicly available as a background document to this conclusion, in the format of a specific GAP overview file.

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 carbon dioxide 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, 2021), 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 (29 June 2020);
- the evaluation table (29 April 2021);
- 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 (France, 2020), 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 formulated product

The International Organization for Standardization does not require a common name for carbon dioxide (IUPAC).

The representative formulated products for the evaluation were 'Aligal-2' and 'Carbo Kohlensäure', both gas formulations (GA), containing 999 g/kg carbon dioxide. The plant protection products are identical with the technical material.

The representative uses evaluated comprise applications by fumigation as insecticide/acaricide for the control of insects and mites in stored plant products and their storage objects (except oilseed meal), in stored cereal grains, oilseeds, medicinal plants, spices, tobacco, tea and dried fruits. Full details of the GAPs can be found in the list of end points in Appendix B.

Data were submitted to conclude that the representative uses of carbon dioxide proposed at EU level result in a sufficient insecticidal and acaricidal effect following the guidance document SANCO/2012/11251-rev. 4 (European Commission, 2014).

Conclusions of the evaluation

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

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

The minimum purity of carbon dioxide technical material is 999 g/kg. The specification of carbon dioxide is in accordance with European Industrial Gases Association (EIGA) specification[5] and the requirements of Commission Regulation No 231/2012[6] laying down specifications for food additives including maximum contents for relevant impurities (i.e. phosphane, benzene, carbon monoxide, methanol, hydrogen cyanide), as given in Appendix A. The specification proposed for the renewal of the active substance is identical with the specification of the first inclusion. The Food and Agriculture Organization (FAO) pesticide specification does not exist for this substance.

The available data regarding the identity of carbon dioxide and its physical and chemical properties are given in Appendix B.

International Society of Beverage Technologists (ISBT) standardised analytical methods exist for all key characteristics of the specification. The method used for the determination of carbon dioxide and relevant impurities is considered as internationally recognised methods.

The need for analytical methods for the determination of residues of carbon dioxide in plant materials, foodstuff of animal origin, in soil and water or body fluids and tissues have been waived due to the use pattern and the nature of the compound.

A gas chromatographic method exists for the determination of carbon dioxide in the air with a limit of quantification (LOQ) of 500 ppm (v/v).

2. Mammalian toxicity

Carbon dioxide was discussed at the Pesticides Peer Review Experts' Meeting TC 38 in December 2020. The following guidance documents were followed in the production of this conclusion: European Commission (2003, 2012a), EFSA (2014) and EFSA PPR Panel (2012).

The data package for carbon dioxide is limited and relied on published data.

Carbon dioxide technical materials comply with the specifications set by the European Industrial Gases Association (EIGA) including maximum contents for relevant impurities (see Section 1). However, as carbon dioxide is applied at high rates up to 88 kg/m^3, and in view of the application pattern, the amount of trace impurities in the technical material could reach significant levels. Hazard and (dietary[7] and non-dietary) exposure[8] were assessed for the relevant impurities identified (phosphane, benzene, carbon monoxide, methanol and hydrogen cyanide). These impurities are substances with well-established toxicological profiles and the proposed toxicological reference values are the ones in force at European level (France, 2020). The majority of the experts, including the RMS, agreed to use these values to estimate the risk to consumers and non-dietary exposure.[8]

Carbon dioxide is transported via blood (as carbonate) or erythrocytes and is eliminated through exhalation or by excretion in urine. Carbon dioxide is the end product of catabolic pathways in mammals.

Carbon dioxide is a gas. The relevant route of exposure is by inhalation.

[5] Carbon dioxide food and beverages grade, source qualification, quality standards and verification; EIGA Doc 70/17 Revision of Doc 70/08 (https://www.eiga.eu/index.php?eID=dumpFile&t=f&f=2872&token=7c1d5f281ad6d876a038a2de4324ea74e9961353)

[6] Commission Regulation (EU) No 231/2012 of 9 March 2012 laying down specifications for food additives listed in Annexes II and III to Regulation (EC) No 1333/2008 of the European Parliament and of the Council (22.3.2012 Official Journal of the European Union L 83/1).

[7] Refer to Section 3 'Residues' for further details.

[8] Refer to experts' consultations 2.3 and 2.5 in the Report of Pesticide Peer Review Meeting TC 38 (15 December 2020). One MS suggested that non-stationary detectors on clothing should be recommended to protect operators and workers from exceeding CO_2 exposure next to the monitoring of treated and surrounding areas (EFSA, 2021).

Based on supportive information from literature, a lethal concentration (LC_{50}) is proposed (LC_{50} 40.8% and 41.3% for male and female rats, respectively).

In humans, inhalation of carbon dioxide at levels of approximately 10% in air is accompanied by loss of consciousness; lower air concentrations can lead to increased blood pressure, heart rate and respiratory minute volume. Short-term increased concentrations of carbon dioxide in office buildings, school buildings or industrial workplaces at up to 4000 ppm are common exposure levels and the observed symptoms (i.e. typical of sick building syndrome) are reversible.

Carbon dioxide is considered to be devoid of genotoxic and carcinogenic potentials, based on the use as food additive, literature data and history of safe uses (e.g. occupationally exposed people). Regarding the reproductive and developmental toxicity, it was agreed that the effects observed in rodents and rabbits[9] are likely to be secondary to low level and/or lack of oxygen and to general toxicity.[10] Furthermore, carbon dioxide can cause adverse effects such as headache, reduced hearing ability, loss of judgement and ultimately loss of consciousness that may be interpreted as signs of neurotoxicity. However, these symptoms are rather part of systemic toxicity than indicative of a specific neurotoxic potential.

The acceptable operator exposure concentrations (**AOECs**) for carbon dioxide are 5000 ppm for adults and 1000 ppm for children (bystander and resident); the acute acceptable operator exposure levels (**AAOELs**) are 15,000 ppm for adults and 3,000 ppm for children (bystander and resident). These values were based on human observational studies used to derive the long term (8 h) and short term (15 min) occupational exposure limits (OELs). Considering the different inhalation rate compared to adult, an additional uncertainty factor[11] of 5 was agreed for children and is applicable also for the general population, bystanders and residents including vulnerable population. These values are in line with the biocide's assessment (ECHA, 2020).[12] As for consumer exposure, the acceptable daily intake (**ADI**) and acute reference dose (**ARfD**) could not be set because of the lack of toxicological data; however, due to the unlikelihood of significant residues of carbon dioxide, ADI and ARfD are not needed (see Section 3). Reference values were not set in the previous conclusion (EFSA, 2013).

Carbon dioxide in Aligal-2 and Carbo Kohlensäure is intended to be applied by fumigation for post-harvest storage in gas-tight silos, bulk storage (Aligal-2) and pressured chambers (Aligal-2 and Carbo Kohlensäure). Operators are not exposed to carbon dioxide; the processes for mixing, loading and application are automated. To ensure that workers are not exposed to levels exceeding acceptable thresholds (5,000 ppm) monitoring of the treated and surrounding areas was recommended by experts.[8] For bystanders and residents, the exposure is below the reference values when considering a resident buffer zone of 30 metres and a wind speed of 2–5 m/s. However, the buffer zone could be subjected to revision considering the wind speed reached in the different member states.[8] With regard to the relevant impurities (phosphane, benzene, carbon monoxide, methanol and hydrogen cyanide), no undue risk for operators, workers, residents and bystanders was predicted.

3. Residues

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

Since carbon dioxide is a major compound involved in all the biological systems and the metabolic processes of living organisms, no MRLs were proposed to support the uses of carbon dioxide as a plant protection product on stored food commodities and a consumer dietary risk assessment was considered unnecessary. However, due to the high application rates of carbon dioxide and in view of the application pattern, the amount of trace relevant impurities in the technical material (Sections 1 and 2) could reach significant levels and the potential concern for the consumer was considered. The relevance of the impurities from a consumer perspective was assessed by the RMS considering worst-case assumptions. According to this assessment, acute and chronic risk for the consumer remains acceptable for the representative uses for all relevant impurities considered (see Appendix B).

Considering that carbon dioxide is naturally occurring and being a gas, no residues are expected in the treated commodities, it can be included in Annex IV of Regulation (EC) No 396/2005. Therefore, the MRL review under Article 12 is considered addressed.

[9] Refer to list of endpoints (Appendix B) for further details about the effects observed.
[10] Refer to experts' consultation 2.1 in the Report of Pesticide Peer Review Meeting TC 38 (15 December 2020) (EFSA, 2021).
[11] Refer to experts' consultation 2.4 in the Report of Pesticide Peer Review Meeting TC 38 (15 December 2020) (EFSA, 2021).
[12] Final CAR assessment report for carbon dioxide generated from propane, butane or a mixture of both by combustion (August 2020). Available at: ECHA website.

4. Environmental fate and behaviour

Carbon dioxide represents the end point in mineralisation of organic substances. Therefore, it is not subject to biological degradation. Since it is a gas, carbon dioxide used as a fumigant will rapidly enter the atmosphere when vented. Overall, the route of dissipation is mainly by volatilisation. The contribution of these uses being assessed compared to carbon dioxide in air coming from other anthropogenic activity and the naturally occurring carbon dioxide concentration in air, might be considered negligible. Testing for the biodegradability of carbon dioxide and testing for route and rate of degradation in soil or water is scientifically unjustified and therefore not relevant. Because of the rapid dilution of carbon dioxide in air adjacent to storage facilities, it is not reasonable to calculate predicted environmental concentration (PEC) values for environmental compartments from the use of carbon dioxide in storage protection.

5. Ecotoxicology

Toxicity data with the carbon dioxide were not available for any group of non-target organisms other than aquatic organisms for which there were only some supportive toxicity studies obtained from the literature. The representative uses of carbon dioxide are considered to result in a negligible additional exposure to non-target organisms compared to the carbon dioxide usually present in air (see Section 4). Consequently, a low risk to birds, mammals, aquatic organisms, bees, non-target arthropods other than bees, soil organisms, non-target terrestrial plants and sewage treatment organisms was concluded.

6. Endocrine disruption properties

With regard to the assessment of the endocrine-disrupting potential of carbon dioxide **for humans** according to the ECHA/EFSA guidance (2018), oestrogen, androgen and steroidogenesis modalities (EAS) modality is considered sufficiently investigated and no effects were observed. Although insufficient toxicological data were available to assess T-modality, it does not appear scientifically necessary, considering the technical difficulties in the administration of the active substance, the limitations due to the intrinsic toxicological characteristics of the active substance, i.e. dose limiting systemic toxicity, and the ubiquitously presence of carbon dioxide in the atmosphere. Therefore, the waiver for the T-modality is considered justified.

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, ecotoxicological data were not available to assess the endocrine-disrupting properties according to the ECHA/EFSA Guidance. However, the need for such data did not appear to be scientifically justifiable by mainly considering the ubiquitous presence of carbon dioxide in the atmosphere and the inherent properties of the substance which may compromise the feasibility of testing. Additionally, it has to be considered that, as indicated in Section 4, exposure to non-target organisms for the representative uses can be considered comparable to carbon dioxide in air coming from other anthropogenic activity and naturally occurring carbon dioxide. Considering the above, it can be concluded that carbon dioxide does not to 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.

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
Not applicable	No data available

Table 2: Groundwater

Compound (name and/ or code)	> 0.1 µg/L at 1 m depth for the representative uses[(a)] Step 2	Biological (pesticidal) activity/relevance Step 3a	Hazard identified Steps 3b and 3c	Consumer RA triggered Steps 4 and 5	Human health relevance
Not applicable	Not applicable	–	–	–	–

(a): As carbon dioxide is an inorganic insecticide and acaricide, the parametric drinking water limit of 0.1 µ/L for pesticides and their relevant metabolites as defined by the drinking water directive 98/83/EEC is not applicable.

Table 3: Surface water and sediment

Compound (name and/or code)	Ecotoxicology
Not applicable	No reliable data available

Table 4: Air

Compound (name and/or code)	Toxicology
Carbon dioxide	LC_{50}: 40.8% and 41.3% for male and female (limited information since the relation is not linear)

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.

- Adequate ventilation (e.g. with a 'certificate of gas clearance') before humans can re-enter treated and/or surrounding areas (i.e. chambers, buildings and silos) is recommended for all representative uses (please, refer to Section 2).
- A 30-m buffer zone for resident (subjected to revision considering the wind-speeds in the different member states) is recommended for all representative uses (please, refer to Section 2).

9. Concerns and related data gaps

9.1. Issues that could not be finalised

An issue is listed as 'could not be finalised' if there is not enough information available to perform an assessment, even at the lowest tier level, for 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[13] 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.

[13] 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:

- **None**

9.2. Critical areas of concern

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

An issue is also listed as a critical area of concern if the assessment at 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:

- **None**

9.3. 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.)

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		Stored cereal grains	Oilseeds	Stored plant products except semolina and oilseed meal	Medicinal plants	Cereal products	Spices	Tobacco	Tea	Dried fruits
			Fumigation							
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									
	Parametric value of 10 µg/L[(a)] breached									
	Assessment not finalised									

(a): 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:

- **None**

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Abbreviations

1/*n*	slope of Freundlich isotherm
λ	wavelength

ADE	actual dermal exposure
ADI	acceptable daily intake
AF	assessment factor
AP	alkaline phosphatase
ARfD	acute reference dose
AV	avoidance factor
BUN	blood urea nitrogen
CAS	Chemical Abstracts Service
CHO	Chinese hamster ovary cells
CI	confidence interval
CL	confidence limits
DAR	draft assessment report
DAT	days after treatment
DM	dry matter
EAS	oestrogen, androgen and steroidogenesis modalities
ECHA	European Chemicals Agency
EEC	European Economic Community
FAO	Food and Agriculture Organization of the United Nations
FID	flame ionisation detector
FIR	food intake rate
FOB	functional observation battery
FOCUS	Forum for the Co-ordination of Pesticide Fate Models and their Use
GAP	Good Agricultural Practice
GC	gas chromatography
GM	geometric mean
GS	growth stage
HQ	hazard quotient
HR	hazard rate
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)
LC	liquid chromatography
LC_{50}	lethal concentration, median
LC-MS	liquid chromatography–mass spectrometry
LC-MS-MS	liquid chromatography with tandem mass spectrometry
LOQ	limit of quantification
M/L	mixing and loading
mm	millimetre (also used for mean measured concentrations)
MOA	mode of action
MRL	maximum residue level
MS	mass spectrometry
NOEL	no observed effect level
OECD	Organisation for Economic Co-operation and Development
OM	organic matter content
Pa	pascal
PD	proportion of different food types
PEC	predicted environmental concentration
PHI	preharvest interval
PIE	potential inhalation exposure
PPE	personal protective equipment
ppm	parts per million (10^{-6})
PT	proportion of diet obtained in the treated area
PTT	partial thromboplastin time
RAC	regulatory acceptable concentration

RAR	Renewal Assessment Report
RBC	red blood cells
REACH	Registration, Evaluation, Authorisation of Chemicals Regulation
SC	suspension concentrate
SMILES	simplified molecular-input line-entry system
TK	technical concentrate
TWA	time-weighted average
UV	ultraviolet
W/S	water/sediment
WHO	World Health Organization

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

Properties		Conclusion[(a)]
CMR	Carcinogenicity (C)	Carbon dioxide is not considered carcinogenic according to point 3.6.3 of Annex II of Regulation (EC) 1107/2009.
	Mutagenicity (M)	Carbon dioxide is not considered mutagenic according to point 3.6.2 of Annex II of Regulation (EC) 1107/2009.
	Toxic for Reproduction (R)	Carbon dioxide is not considered toxic for reproduction according to point 3.6.4 of Annex II of Regulation (EC) 1107/2009.
Endocrine-disrupting properties		Carbon dioxide 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**	Carbon dioxide is not considered to be a persistent organic pollutant (POP) according to point 3.7.1 of Annex II of Regulation (EC) 1107/2009 as it does not bioaccumulate.
	Bioaccumulation	
	Long-range transport	
PBT	**Persistence**	Carbon dioxide is not considered to be a persistent, bioaccumulative and toxic (PBT) substance according to point 3.7.2 of Annex II of Regulation (EC) 1107/2009 as it does not bioaccumulate.
	Bioaccumulation	
	Toxicity	
vPvB	**Persistence**	Carbon dioxide is not considered to be a very persistent, very bioaccumulative substance according to point 3.7.3 of Annex II of Regulation (EC) 1107/2009 as it does not bioaccumulate.
	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 representative formulation

Appendix B can be found in the online version of this output ('Supporting information' section): https://doi.org/10.2903/j.efsa.2021.6605

Appendix C – Used compound codes Used compound codes

Code/trivial name[a]	IUPAC name/SMILES notation/InChiKey[b]	Structural formula[c]
phosphane **phosphine**	phosphane P XYFCBTPGUUZFHI-UHFFFAOYSA-N	PH_3
hydrogen cyanide	hydrocyanic acid C#N LELOWRISYMNNSU-UHFFFAOYSA-N	HC≡N
benzene	Benzene c1ccccc1 UHOVQNZJYSORNB-UHFFFAOYSA-N	
carbon monoxide	carbon monoxide [O+]#[C-] UGFAIRIUMAVXCW-UHFFFAOYSA-N	
methanol	methanol CO OKKJLVBELUTLKV-UHFFFAOYSA-N	CH_3-OH

(a): The metabolite name in bold is the name used in the conclusion.
(b): ACD/Name 2018.2.2 ACD/Labs 2018 Release (File version N50E41, Build 103230, 21 July 2018).
(c): ACD/ChemSketch 2018.2.2 ACD/Labs 2018 Release (File version C60H41, Build 106041, 7 December 2018).