

APPROVED: 12 June 2020

doi: 10.2903/j.efsa.2020.5755

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

European Food Safety Authority (EFSA),
Himdata Abdourahime, Maria Anastassiadou, Maria Arena, Domenica Auteri, Stefania Barmaz,
Alba Brancato, Laszlo Bura, Luis Carrasco Cabrera, Eugenia Chaideftou, Arianna Chiusolo,
Daniele Court Marques, Federica Crivellente, Chloe De Lentdecker, Mark Egsmose,
Gabriella Fait, Lucien Ferreira, Valeria Gatto, Luna Greco, Alessio Ippolito, Frederique Istace,
Samira Jarrah, Dimitra Kardassi, Renata Leuschner, Alfonso Lostia, Christopher Lythgo,
Silvia Messinetti, Ileana Miron, Tunde Molnar, Laura Padovani, Juan Manuel Parra Morte,
Ragnor Pedersen, Marianna Raczky, Hermine Reich, Silvia Ruocco, Katri Elina Saari,
Miguel Santos, Rositsa Serafimova, Rachel Sharp, Alois Stanek, Franz Streissl,
Juergen Sturma, Csaba Szentes, Andrea Terron, Manuela Tiramani, Benedicte Vagenende,
Patricija Vainovska and Laura Villamar-Bouza

Abstract

The conclusions of EFSA following the peer review of the initial risk assessments carried out by the competent authorities of the rapporteur Member State the United Kingdom and co-rapporteur Member State Greece for the pesticide active substance mancozeb are reported. The context of the peer review was that required by Commission Implementing Regulation (EU) No 844/2012. The conclusions were reached on the basis of the evaluation of the representative uses of mancozeb as a fungicide on wheat (winter/spring), grapevine, potatoes and tomatoes. The reliable end points, appropriate for use in regulatory risk assessment are presented. Missing information identified as being required by the regulatory framework is listed. Concerns are identified.

© 2020 European Food Safety Authority. *EFSA Journal* published by John Wiley and Sons Ltd on behalf of European Food Safety Authority.

Keywords: mancozeb, peer review, risk assessment, pesticide, fungicide

Requestor: European Commission

Question number: EFSA-Q-2015-00585

Correspondence: pesticides.peerreview@efsa.europa.eu

Note: This document was first published on the EFSA website in November 2019 in a sanitised form, making unavailable information claimed confidential by the applicant. The full version is now available, following the confidentiality decision process.

Suggested citation: EFSA (European Food Safety Authority), Abdourahime H, Anastassiadou M, Arena M, Auteri D, Barmaz S, Brancato A, Bura L, Carrasco Cabrera L, Chaideftou E, Chiusolo A, Court Marques D, Crivellente F, De Lentdecker C, Egsmose M, Fait G, Ferreira L, Gatto V, Greco L, Ippolito A, Istace F, Jarrah S, Kardassi D, Leuschner R, Lostia A, Lythgo C, Messinetti S, Miron I, Molnar T, Padovani L, Parra Morte JM, Pedersen R, Raczky M, Reich H, Ruocco S, Saari KE, Santos M, Serafimova R, Sharp R, Stanek A, Streissl F, Sturma J, Szentes C, Terron A, Tiramani M, Vagenende B, Vainovska P and Villamar-Bouza L, 2019. Conclusion on the peer review of the pesticide risk assessment of the active substance mancozeb. *EFSA Journal* 2020;18(12):5755, 28 pp. <https://doi.org/10.2903/j.efsa.2020.5755>

ISSN: 1831-4732

© 2020 European Food Safety Authority. *EFSA Journal* published by John Wiley and Sons Ltd on behalf of European Food Safety Authority.

This is an open access article under the terms of the [Creative Commons Attribution-NoDerivs](#) License, which permits use and distribution in any medium, provided the original work is properly cited and no modifications or adaptations are made.



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



Summary

Commission Implementing Regulation (EU) No 844/2012, 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. Mancozeb is one of the active substances listed in Regulation (EU) No 686/2012.

In accordance with Article 1 of Regulation (EU) No 844/2012, the rapporteur Member State (RMS), the United Kingdom, and co-rapporteur Member State (co-RMS), Greece, received an application from EU Mancozeb Task Force (EU MTF) (UPL Europe Ltd. and Indofil Industries B.V.) and Agria SA for the renewal of approval of the active substance mancozeb.

An initial evaluation of the dossier on mancozeb 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 mancozeb according to the representative uses as a fungicide on wheat (winter/spring), grapevine, potato and tomato grown in permanent and non-permanent greenhouse, as proposed at the European Union (EU) level, result in a sufficient fungicidal efficacy against the target fungal diseases.

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 mancozeb or the representative formulations.

In the mammalian toxicology assessment, the phototoxicity potential of mancozeb could not be finalised since contradictory results were obtained in two *in vitro* tests. Furthermore, the non-dietary exposure of bystander and resident for the use on tomatoes could not be finalised. Moreover, three critical areas of concern were identified: mancozeb classification as reproductive toxicant category 1B, criteria met for endocrine disruption for humans and non-dietary exposure estimates exceeding the reference values (for uses in potatoes, cereals, grapevine and tomatoes).

The consumer dietary risk assessment cannot be finalised pending the identified data gaps to complete the residue data sets for all the representative uses in compliance with the agreed residue definitions for monitoring and risk assessment in plants which will impact the livestock dietary burden calculation and exposure assessment. As the risk to human or animal health through the consumption of drinking water containing 1,3-dichloro hydantoin was not adequately addressed, this has led to the identification of a data gap and results in the consumer risk assessment being not finalised.

The data available on environmental fate and behaviour are sufficient to carry out the required environmental exposure assessments at EU level for the representative uses. The potential for groundwater exposure above the parametric drinking water limit of 0.1 µg/L by mancozeb and its soil transformation products ethylenebisisothiocyanatesulfide (EBIS), ethylenethiourea (ETU), ethylenurea (EU) and M11 was assessed as low for the representative uses assessed.

In the area of ecotoxicology, four critical areas of concern were identified. Firstly, it was concluded that mancozeb is likely to meet the criteria for endocrine disruption for non-target organisms. Furthermore, a high risk to birds, mammals, non-target arthropods and soil macroorganisms was concluded for all representative uses. It should, however, be noted that a low risk would be concluded for the representative use to tomatoes if the use was restricted to high technology (permanent) greenhouses. A high risk to aquatic organisms was indicated for all representative uses (including the use to tomatoes in high technology (permanent) greenhouses) except for the use to potatoes where a low risk was indicated provided risk mitigation measures are used.

Table of contents

Abstract.....	1
Summary.....	3
Background	5
The active substance and the formulated product.....	6
Conclusions of the evaluation	7
1. Identity, physical/chemical/technical properties and methods of analysis	7
2. Mammalian toxicity.....	7
3. Residues.....	10
4. Environmental fate and behaviour	12
5. Ecotoxicology	13
6. Overview of the risk assessment of compounds listed in residue definitions triggering assessment of effects data for the environmental compartments (Tables 1–6).....	17
7. Data gaps.....	19
8. Particular conditions proposed to be taken into account to manage the risk(s) identified	20
9. Concerns	20
9.1. Issues that could not be finalised	20
9.2. Critical areas of concern.....	21
9.3. Overview of the concerns identified for each representative use considered.....	21
References.....	22
Abbreviations	24
Appendix A – List of end points for the active substance and the representative formulation.....	26
Appendix B – Used compound codes	27

Background

Commission Implementing Regulation (EU) No 844/2012¹, as amended by Commission Implementing Regulation (EU) No 2018/1659², (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 1107/2009³. 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). 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 and maximum 30 months, depending on the type of information requested.

In accordance with Article 1 of the Regulation, the RMS the United Kingdom and co-RMS Greece received an application from EU MTF (UPL Europe Ltd. and Indofil Industries B.V.) and Agria SA for the renewal of approval of the active substance mancozeb. Complying with Article 8 of the Regulation, the RMS checked the completeness of the dossier and informed the applicants, the co-RMS (Greece), the European Commission and EFSA about the admissibility.

The RMS provided its initial evaluation of the dossier on mancozeb in the RAR, which was received by EFSA on 27 September 2017 (United Kingdom, 2017).

In accordance with Article 12 of the Regulation, EFSA distributed the RAR to the Member States and the applicants, EU Mancozeb Task Force (EU MTF; UPL Europe Ltd. and Indofil Industries B.V.) and Agria SA, for consultation and comments on 26 February 2018. EFSA also provided comments. In addition, EFSA conducted a public consultation on the RAR. EFSA collated and forwarded all comments received to the European Commission on 28 April 2018. At the same time, the collated comments were forwarded to the RMS for compilation and evaluation in the format of a reporting table. The applicants were invited to respond to the comments in column 3 of the reporting table. The comments and the applicants' response were evaluated by the RMS in column 3.

The need for expert consultation and the necessity for additional information to be submitted by the applicants in accordance with Article 13(3) of the Regulation were considered in a telephone conference between EFSA, the RMS and ECHA on 28 June 2018. On the basis of the comments received, the applicants' response to the comments and the RMS's evaluation thereof, it was concluded that additional information should be requested from the applicants, and that EFSA should conduct an expert consultation in the areas of mammalian toxicology, residues and ecotoxicology.

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

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

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.

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 April–May 2019.

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 mancozeb as a fungicide on wheat (winter/spring), grapevine, potatoes and tomatoes, as proposed by the applicants. In accordance with Article 12(2) of Regulation (EC) No 1107/2009, risk mitigation options identified in the RAR and considered during the peer review are presented in the conclusion. A list of the relevant end points for the active substance and the formulation is provided in Appendix A.

In addition, a key supporting document to this conclusion is the peer review report (EFSA, 2019), 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 2018);
- the evaluation table (27 May 2019);
- 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 (United Kingdom, 2019), and the peer review report, both documents are considered as background documents to this conclusion and thus are made publicly available.

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

The active substance and the formulated product

Mancozeb is the ISO common name for manganese ethylenebis(dithiocarbamate) (polymeric) complex with zinc salt (IUPAC).

The representative formulated products for the evaluation were 'Penncozeb 80 WP', 'Dithane M-45' and 'Mancozeb 800 WP', all wettable powders (WP) containing 805 g/kg, 800 g/kg and 805 g/kg mancozeb, respectively.

The representative uses evaluated for 'Penncozeb 80 WP' and 'Dithane M-45' as a fungicide were foliar spray applications against various fungal diseases in winter and spring wheat and in potato in the EU and in grapevine in central and southern zone. The representative uses evaluated for 'Mancozeb 800 WP' as a fungicide were foliar spray applications against fungal diseases in tomato in high technology (permanent) and non-high technology (non-permanent) greenhouse in central and southern zone. As it is unclear whether the use is restricted to high technology (permanent) greenhouses, a conclusion, assuming both high technology (permanent) greenhouse and other types of greenhouse structures has been presented. Full details of the Good Agricultural Practice (GAPs) can be found in the list of end points in Appendix A.

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

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

Conclusions of the evaluation

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

The following guidance documents were followed in the production of this conclusion: SANCO/3029/99-rev. 4 (European Commission, 2000a), SANCO/3030/99-rev. 4 (European Commission, 2000b), SANCO/825/00-rev. 8.1 (European Commission, 2010) and SANCO/10597/2003-rev. 10.1 (European Commission, 2012).

The reference specification from the original approval of mancozeb states a minimum purity of 800 g/kg, with the manufacturing impurity ethylenethiourea (ETU) being considered of toxicological relevance and specified with a maximum limit of 0.5% of the mancozeb content. The proposed minimum purity of the technical material by the EU MTF composed of UPL and Indofil is 850 g/kg, while the minimum purity proposed by Agria is 915 g/kg. In both cases, the minimum purity is expressed including additives/stabilisers. The proposed specifications were based on batch data from industrial scale production. ETU was considered a relevant impurity with a maximum content of 0.3% (see Section 2). It is proposed to update the reference specification based on the renewal data also supported by the toxicological considerations on the impurities (see also Section 2). A tentative FAO specification exists under the old procedure with a minimum declared content of 85% mancozeb and the ETU content should not exceed 0.5% of the mancozeb content at the time of manufacture (AGP:CP/85 Rome, 1980).

Data gaps were identified for applicant Agria for a suspensibility study at the lowest use concentration and for an analytical method for the determination of one impurity in the technical material. The main data regarding the identity of mancozeb and its physical and chemical properties are given in Appendix A.

Satisfactory methods are available for the generation of pre-approval data required for the risk assessment. Adequate CIPAC methods exist for the determination of the active substance content in the technical material and in the representative formulations. The content of the relevant impurity in the technical material and representative formulations can be determined by high-performance liquid chromatography with ultraviolet detection (HPLC-UV) and by gas chromatography with flame ionisation detection (GC-FID).

The residue definition for monitoring in food and feed of plant and animal origin was defined as dithiocarbamates (mancozeb expressed as CS₂) (see Section 3). Monitoring mancozeb in food and feed of plant origin is done by conversion of mancozeb to CS₂ and detection by gas chromatography with mass spectrometry (GC-MS) with a limit of quantification (LOQ) of 0.03 mg/kg (expressed as CS₂) in high water content, dry and high oil content commodities and a LOQ of 0.05 mg/kg in high acid content commodities. Monitoring of the residues in animal matrices (meat, fat, liver, milk and egg) is done by transformation of mancozeb to CS₂ and quantification by GC-MS with a LOQ of 0.03 mg/kg (expressed as CS₂).

Mancozeb can be monitored in soil by transformation to CS₂ and quantification by GC-MS with a LOQ of 0.05 mg/kg (expressed as mancozeb).

Mancozeb residues in ground water and surface water can be monitored by liquid chromatography with tandem mass spectrometry (LC-MS/MS) using derivatisation with a LOQ of 0.1 µg/L, expressed as mancozeb. Mancozeb can be monitored in air using LC-MS/MS method with derivatisation with a LOQ of 5 µg/m³ expressed as mancozeb.

Residues of ETU in body fluids and tissues can be determined by LC-MS/MS with LOQs of 10 µg/L and 0.01 mg/kg, respectively.

Data gaps were identified for applicant Agria to provide an independent laboratory validation (ILV) for the monitoring method for plant matrices, primary and confirmatory methods for meat, milk and fat and an ILV for all animal matrices, additional validation data to reach the LOQ of 0.1 µg/L for drinking water, new monitoring method for the determination of residues in air and an analytical method for the determination of ETU in body fluids.

2. Mammalian toxicity

The following guidance documents were followed in the production of this conclusion: SANCO/221/2000-rev. 10-final (European Commission, 2003), SANCO/10597/2003-rev. 10.1 (European Commission, 2012), ECHA and EFSA (2018), EFSA PPR Panel (2012), EFSA (2014) and ECHA (2017).

Some aspects of the hazard characterisation and risk assessments have been discussed in the Pesticides Peer Review Meeting 190 session 1 in February 2019.

The major rat metabolite of mancozeb, ETU, is also considered a relevant impurity. ETU showed a more severe toxicity profile (Acute Tox. 4; Repr. 1B⁴) than the parent, therefore only the new proposed technical specifications are considered acceptable from a toxicological point of view. At the level specified in the new proposed technical specifications (0.3%), the toxicological relevant impurity ETU does not pose a concern.

Mancozeb is partially (50%) but rapidly (3–6 h) absorbed after single oral administration at 1.5 mg/kg body weight (bw) in rats. It is widely distributed with the thyroid having the highest levels of radioactivity and rapidly and extensively excreted, mainly via urine and via faeces. Mancozeb is extensively metabolised (> 95%), through two common metabolic pathways (hydrolysis and oxidation) which both lead ultimately to the formation of glycine. ETU, ethyleneurea (EU), ethylenediamine (EDA) and *N*-acetyl EDA are the major metabolites found in rat urine and bile. Other (minor) metabolites are: ethylenebisisothiocyanatesulfide (EBIS), Jaffe's Base (Reg. No. 6002546), glycine and *N*-formyl glycine. An *in vitro* interspecies comparative metabolism study is not technically feasible due to the unstable nature of mancozeb in aqueous solutions. However, available information in different species (e.g. rat, mouse, dog and human) indicates qualitatively similar metabolism of mancozeb.

Being mancozeb rapidly metabolised, the residue definition for body fluids (urine and plasma) should include the major rat metabolite ETU for the purpose of human biomonitoring.

Mancozeb demonstrated low acute toxicity by the oral (LD₅₀ > 5,000 mg/kg bw), dermal (LD₅₀ > 2,000 mg/kg bw) and inhalation (4-hr LC₅₀ > 5 mg/L) route. It is neither a skin irritant nor an eye irritant. Mancozeb is a moderate skin sensitizer and is classified Skin Sens 1 (H317) (ECHA, 2019). Concerning phototoxicity, two valid *in vitro* studies with mancozeb are available revealing contradictory results (one positive and one negative). Furthermore, the UVB wavelength where mancozeb showed significant absorption was not investigated as there is no OECD test for UVB absorber. Based on this, the phototoxicity potential of mancozeb cannot be concluded (data gap and issue not finalised).

In the short-term dietary studies, the thyroid was the target organ in rats, dogs and mice. In addition, neurotoxicity was observed in rats and liver toxicity and anaemia were detected in dogs. The short-term no observed adverse effect level (NOAEL) in mice is 18 mg/kg bw per day, based on decreased body weights, thyroid and liver effects at 180 mg/kg bw per day. The short-term NOAEL in rats is 6.8 mg/kg bw per day, based on effects on body weight gain and changes in thyroid hormone (T4) levels at 27.5 mg/kg bw per day. The short-term NOAEL in dog is 2.3 mg/kg bw per day based on effects on body weight, food consumption and changes in thyroid hormone levels and thyroid weight, from a 1-year study. This NOAEL of 2.3 mg/kg bw per day is concluded to be the overall short-term NOAEL for mancozeb. RMS disagreed with this overall short-term NOAEL.⁵ Based on effects on the thyroid (in 3 species) and on the nervous system (in rat), mancozeb is classified as STOT-RE 2 (ECHA, 2019).

Overall, the genotoxic potential is of low concern. However, further investigations of the gene mutation potential in mammalian cells assay compliant with modern standards and using the representative material should be provided to confirm this conclusion (data gap).

In the long-term dietary studies, the thyroid was still the target organ in rats and mice. In mice, the long-term systemic toxicity NOAEL is 13 mg/kg bw per day based on effects on body weight and thyroid hormone levels observed at 130 mg/kg bw per day. Mancozeb is not carcinogenic in mice up to 180 mg/kg bw per day. The relevant long-term systemic NOAEL is 4.8 mg/kg bw per day from the 2-year study in rats, based on decreased body weight, thyroid toxicity (effects on thyroid hormones, thyroid hypertrophy and hyperplasia) and bilateral retinopathy at 30.9 mg/kg bw per day. The carcinogenicity NOAEL in rat is 4.8 mg/kg bw per day, based on thyroid tumours (follicular carcinomas and adenomas) observed at the highest tested dose (30.9 mg/kg bw per day). Mancozeb is classified as carcinogen category 2, based on these thyroid tumours observed in rats (ECHA, 2019).

Mancozeb has no effects on reproduction/fertility. From the two multigeneration reproduction toxicity studies, the overall NOAEL for reproductive toxicity is 70 mg/kg bw per day (the highest dose tested). The NOAEL for parental toxicity is 7 mg/kg bw per day, based on decreases in body weight and food consumption and thyroid toxicity at 65 mg/kg bw per day. The NOAEL for offspring toxicity is

⁴ Regulation (EC) No 1272/2008 of the European Parliament and of the Council of 16 December 2008 on classification, labelling and packaging of substances and mixtures, amending and repealing Directives 67/548/EEC and 1999/45/EC, and amending Regulation (EC) No 1907/2006. OJ L 353, 31.12.2008, 1–1355.

⁵ Refer to experts' consultation 2.2 in the Report of Pesticides Peer Review experts' meeting 190-session 1 (EFSA, 2019).

7 mg/kg bw per day, based on delayed eye opening, decreased weight and viability at 65 mg/kg bw per day observed in the second study.

Four rat developmental toxicity studies were provided. Maternal toxicity was manifested by decreased body weight and food consumption as well as death and paralysis found in one study. The maternal NOAELs ranged from 32 and 160 mg/kg bw per day (the latter value in the most recent study). An overall maternal NOAEL of 60 mg/kg bw per day was agreed by the experts⁶ considering that the lowest LOAEL was 128 mg/kg bw per day. Developmental toxicity findings included malformations, increased resorptions, delayed development and the developmental NOAELs ranged from 60 to 160 mg/kg bw per day (the latter value in the most recent study). An overall developmental NOAEL of 160 mg/kg bw per day was established by the experts considering that the lowest LOAEL was 225 mg/kg bw per day and malformations were observed at doses greater than 500 mg/kg bw per day. In the two rabbit developmental toxicity studies, maternal toxicity was manifested by deaths, decreases in body weight and food consumption and abortions. The maternal NOAELs ranged from 30 to 55 mg/kg bw per day, while no developmental effects were observed. An overall maternal NOAEL of 55 mg/kg bw per day was established by the experts considering that the lowest LOAEL was 80 mg/kg bw per day. Mancozeb is classified for developmental toxicity as Repr. 1B; H360D (ECHA, 2019), based on malformations observed in the rat developmental toxicity studies leading to a critical area of concern with regard to the approval criteria, Annex II, Part 3.6.4 of Regulation (EC) No 1107/2009. With regard to the assessment of the endocrine disrupting potential of mancozeb according to the ECHA/EFSA guidance (2018), mancozeb is considered to meet the criteria for endocrine disruption for humans through the T-modality based on effects observed in the thyroid (thyroid follicular cell hypertrophy, increased thyroid weight, thyroid follicular cell hyperplasia and tumours of the thyroid gland (adenomas and carcinomas)). Based on the available information, it can be concluded that the approval criteria on the endocrine disrupting potential for mancozeb as set out in point 3.6.5 of Annex II to Regulation (EC) No 1107/2009, as amended by Commission Regulation (EU) 2018/605, are met leading to a critical area of concern.

Mancozeb has no immunotoxic potential based on the available toxicity data package. Neurotoxicity NOAEL is 8.2 mg/kg bw per day, based on myelin damage with Schwann cells proliferation of nerve tissue observed at 49 mg/kg bw per day in a 90-day study in rats. In a developmental neurotoxicity (DNT) study, no effects are observed in the weanlings, while the maternal toxicity NOAEL is 15 mg/kg bw per day, based on decreased bw and thyroid pathology at 30 mg/kg bw per day.

The acceptable daily intake (**ADI**) for mancozeb is 0.023 mg/kg bw per day, based on the 1-year study in dogs (NOAEL 2.3 mg/kg bw per day), and applying an uncertainty factor (UF) of 100. The RMS disagreed with the value of the ADI.⁷ The current ADI is 0.05 mg/kg bw per day (European Commission, 2009).

The acute reference dose (**ARfD**) is 0.15 mg/kg bw based on maternal toxicity (NOAEL 15 mg/kg bw per day) observed in the DNT study in rats, applying an UF of 100. The current ARfD is 0.6 mg/kg bw (European Commission, 2009).

The acceptable operator exposure level (**AOEL**) is 0.011 mg/kg bw per day based on the same basis as the ADI and taking into consideration an oral absorption value of 50%. The RMS disagreed with the value of the ADI.⁷ The current AOEL is 0.035 mg/kg bw per day (European Commission, 2009).

The acute acceptable operator exposure level (**AAOEL**) is 0.075 mg/kg bw based on the same basis as the ARfD and corrected by oral absorption of 50%.

An extensive set of toxicity studies were provided for **ETU**, a major urinary rat metabolite of mancozeb. The metabolite is unlikely to be genotoxic and it is classified for acute toxicity (Acute Tox. 4; H302) and developmental toxicity (Repr. 1B; H360).⁴ The ADI and the AOEL are 0.002 mg/kg bw per day, based on a NOAEL of 0.2 mg/kg bw per day set in the 1-year study in dog, also supported by parental NOAEL of 0.2 mg/kg bw per day set in the extended one-generation reproductive toxicity study (EOGRTS) in rat, and an UF of 100. The ARfD and the AAOEL are 0.01 mg/kg bw, based on a NOAEL of 5 mg/kg bw per day set in the developmental toxicity study in rat, applying an UF of 100 and an additional UF of 5 (providing a sufficient margin of safety regarding developmental effects observed at 10 mg/kg bw per day and hence close to the NOAEL). Other metabolites were discussed during the experts' meeting but they were not further considered for the consumer risk assessment (see Section 3).

⁶ Refer to experts' consultation 2.5 in the Report of Pesticides Peer Review experts' meeting 190-session 1 (EFSA, 2019).

⁷ Refer to experts' consultation 2.10 in the Report of Pesticides Peer Review experts' meeting 190-session 1 (EFSA, 2019).

Dermal absorption values for representative formulations of mancozeb (Penncozeb 80 WP, Dithane M-45, Agria Mancozeb 800 WP) are 0.7% and 1% for the concentrate products and for the spray dilutions, respectively.

For Penncozeb 80 WP and Dithane M-45, the operator exposure estimates exceed the AOEL even considering the highest level of personal protective equipment (PPE) for the use on potatoes, cereals and grapevine. The exposure of residential children is also above the AOEL for these uses, while the worker exposure is above the AOEL only for the use in grapevine. For Mancozeb 800 WP, the representative use is for tomatoes in greenhouse, and currently no harmonised model is available for protected situations. However, based on EUROPOEM, the operator exposure estimates are below the AOEL with use of PPE while the worker exposure estimates are above the AOEL. For the use in permanent greenhouse, the exposure of bystanders and residents to vapour from ventilation systems should have been further considered (data gap and issue not finalised). The RMS was of the opinion that bystander and resident exposure for the permanent greenhouse use should be considered negligible.

Considering the combined exposure to ETU and mancozeb for Penncozeb 80 WP and Dithane M-45, only the predicted exposure for bystanders (adult + child) and residents (adult) were below the AOEL for the use on potatoes and cereals, while only the predicted exposure for bystanders (adult + child) were below the AOEL for the use on grapevines. For Mancozeb 800 WP, no exposure estimates for ETU could be performed and no combined exposure estimates could be performed (data gap and issue not finalised). Overall, no representative products have demonstrated exposure estimates below the AOEL/AAOEL for operator, worker, bystander and/or resident (critical area of concern).

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).

Mancozeb was discussed at the Pesticides Peer Review Meeting 191 in January 2019.

Metabolism of mancozeb in primary crops was investigated upon foliar treatment in pulses/oilseeds (soya bean), root crops (sugar beet, potatoes), fruit crops (tomatoes) and cereals (wheat) using ^{14}C labelling on one or two methanediyl carbons of mancozeb. The metabolic patterns in the different crops were considered similar. Mancozeb was detected in low proportions (< 10% total radioactive residues (TRR)) in all edible crop parts and was shown to be extensively degraded with the major part of the radioactive residues being incorporated into natural constituents of the plant (amino acids, proteins, sugars) (50% TRR in wheat grain to 78% TRR in soya bean seeds). In all crops, numerous minor metabolites were identified and accounted for < 10% of the TRR. The experts were of the opinion that sufficient data are available to depict the metabolic pathway of mancozeb for all crop groups. The residue definition for **monitoring** is proposed as 'Dithiocarbamates (mancozeb) determined and expressed as CS_2 '. For **risk assessment**, given that quantifiable residue levels of ETU were recovered in grapes and wheat grain and straw from the GAP-compliant residue trials and ETU is considered as toxicologically more potent compared to mancozeb (see Section 2), the experts agreed to set the residue definition for all crop categories as 'mancozeb and ETU'. Although mancozeb and its major soil metabolites showed very low to moderate persistence in soil (DT_{90} < 100 days), available confined rotational crop metabolism studies in cereal small grains (wheat), leafy crops (lettuce) and root crops (radish) showed that neither the parent mancozeb nor the metabolites identified in primary crops were detected in any plant part and only glycine was found in significant proportions in wheat forage and straw (up to 35% TRR), in lettuce (up to 50% TRR) and in radish root (52% TRR) at 7- and 123-day plant-back intervals (PBIs). Besides a major fraction of the radioactive residues was characterised as polar components with further incorporation into natural constituents of the plants. Specific residue definitions are not deemed necessary for rotational crops.

In a hydrolysis study conducted with metiram and simulating standard food processing conditions the parent compound was shown to degrade mainly into ETU that accounted for up to 52% of the applied radioactivity (AR) at pasteurisation, 88.4% AR at baking/brewing and boiling and was almost completely degraded into ETU (98.6% AR) at sterilisation. In view of the similar structures of metiram and mancozeb, similar behaviour of both compounds under hydrolysis conditions is expected and no further hydrolysis study with mancozeb is required. The risk assessment residue definition set for primary crops also applies to processed commodities.

A sufficient number of acceptable residue field trials on grapes conducted according to the northern Europe (NEU) GAP is available whilst a complete residue data set on grapes compliant with the southern Europe (SEU) GAP that determine mancozeb (CS_2) and ETU and supported by acceptable storage

stability data is required (data gap). Most of the residue trials in potatoes that were submitted are not compliant with the representative use. Moreover, in view of the limited stability of mancozeb residues (1 month) and the rapid degradation of ETU residues in potatoes (within 2 weeks) observed when samples are not homogenised with dry ice, the results cannot be relied on as in all the residue trials analysis of mancozeb and ETU had not been done immediately after sampling. Therefore, complete NEU and SEU residue data packages are required on potatoes with immediate residue analysis after sampling and covering the residue definitions for monitoring and risk assessment (data gap). Sufficient and valid residue trials on wheat compliant, respectively, with the NEU and SEU GAPs are available for the determination of mancozeb (CS₂) in grain and straw. For the determination of ETU residues in wheat grain, a complete and valid residue data set compliant with the NEU GAP has been provided while three additional residue trials compliant with the SEU GAP are still required (data gap). The frozen storage stability studies for ETU residues in cereal and wheat grain showed equivocal results indicating acceptable stability over 12 months in wheat grain and instability in cereal grain whilst mancozeb residues were shown to be stable for up to 24.5 months in wheat grain. A clarification is therefore needed on the discrepancies in these frozen storage stability results and the validity of the field residue trials analysing ETU residues in wheat grain should be demonstrated in regard to the work-up and the maximum storage time interval of the residue samples (data gap). A data gap is also set for storage stability data on ETU in cereal straw and covering the maximum storage time interval of the wheat residue trials (data gap). A complete GAP-compliant residue data set on indoor tomatoes and covering the residue definitions for monitoring and risk assessment is required (data gap).

The metabolism of mancozeb in livestock was investigated in laying hens and in lactating goats. In poultry, the parent compound was extensively degraded in all matrices except in muscle and fat where it accounted for up to 23.4% TRR and 55% TRR, respectively. Metabolite EU was predominant in eggs (29.5% TRR) and muscle (36.5% TRR) whilst combined EDA/glycine compounds accounted for ca. 11% TRR in eggs and muscle, 13% TRR in liver and 28% TRR in kidney. Besides other identified minor metabolites (< 10% TRR), a significant fraction of the radioactive residues consisted of unidentified polar compounds with levels ranging between 14% TRR in eggs and kidney to 37% TRR in liver. In goat matrices, parent mancozeb was never detected and all the identified metabolites accounted for a level < 10% TRR except ETU that was found at 10.5% TRR in muscle only. The major part of the radioactivity was shown to be incorporated mainly into amino acids in muscle, liver and kidney (27–52% TRR). No metabolites' identification was carried out in milk and fat. Although these studies were not fully guideline compliant, the experts were of the opinion that the metabolism of mancozeb in animal matrices has been sufficiently investigated and agreed to set the **monitoring** residue definition for animals as 'Dithiocarbamates (mancozeb) determined and expressed as CS₂'. For **risk assessment**, the potential inclusion of EU compound predominant in eggs and poultry muscle was excluded in view of its lower toxicity compared to the parent compound and the residue definition is proposed as 'mancozeb and ETU'.

The livestock dietary burden calculation was carried out for both mancozeb and ETU and was considered as provisional in regard to the outstanding residue field trials on potatoes and the acceptability of the trials on wheat (see data gaps). Robust processing factors (PF), respectively, for mancozeb and ETU could also not be derived for potato and wheat processed matrices that may be fed to livestock. Sufficient processing residue trials analysing for mancozeb and ETU in those commodities and within a time interval for which acceptable storage stability is demonstrated for both compounds should be provided (data gap). Meanwhile and as a very conservative approach, the default PFs for the relevant potatoes and wheat feed items have been considered in the intake calculation. Poultry and ruminant feeding studies were conducted with mancozeb and ETU simultaneously fed to the animals. These studies were not considered guideline compliant in view of the identified deficiencies to reliably estimate the residue levels of mancozeb and ETU in products of animal origin. Pending the finalisation of the dietary burden calculation and whether feeding studies are triggered, new poultry and ruminant feeding studies covering the residue definitions for monitoring and risk assessment will have to be provided. Overall, the livestock exposure assessment cannot currently be finalised. Although wheat and potatoes by-products are feed items, fish metabolism data are not required as mancozeb and ETU are considered as not fat soluble ($\log P_{ow} < 3$).

Field residue trials on apples were submitted to analyse the residues of mancozeb (as CS₂) and ETU in nectar and were proposed to be extrapolated to grapevines. Besides the deficiencies identified in these residue trials on apples, i.e. underdosed studies compared to the representative use on grapes, whether the maximum storage time interval of the residue samples is supported by acceptable storage stability data for mancozeb and ETU in apples is unknown, an extrapolation to grapevines is

not possible considering the structures of the flowers for apples and grapevines that are different. As grapevines show melliferous capacity and treatment takes place at flowering, the data requirement to determine the residues of mancozeb (CS₂) and ETU in pollen and bee products for human consumption resulting from residues taken up by honeybees from grapes at blossom needs to be addressed (data gap). Wheat, tomatoes and potatoes do not have any melliferous capacity (European Commission, 2018).

For the time being, the consumer chronic dietary risk assessment cannot be performed pending the identified data gaps to complete the residue data sets for all the representative uses in compliance with the agreed residue definitions for monitoring and risk assessment in plants which will impact the livestock dietary burden calculation and exposure assessment. A provisional acute dietary intake was conducted for mancozeb and ETU residues in grapevines and wheat grain. An acute intake concern was identified for table grapes only when mancozeb residues from NEU residue trials are considered (IESTI: 179% ARfD; DE infant). No acute intake concern was noted for table grapes, wine grapes and wheat (39% ARfD, 4.7% ARfD and 7% ARfD, respectively) when ETU residues are considered. This indicative calculation will be reconsidered pending upon the assessment of the outstanding data. Additionally, the consumer risk assessment through drinking water containing 1,3-dichloro hydantoin that might be produced following the drinking water treatment process of chlorination is not finalised (see Section 4).

4. Environmental fate and behaviour

The rates of dissipation and degradation in the environmental matrices investigated were estimated using FOCUS (2006) kinetics guidance. In soil laboratory incubations under aerobic conditions in the dark, mancozeb exhibited very low to low persistence, forming the major (> 10% AR) EBIS (max. 29% AR, which exhibited very low persistence), M11 (max. 20% AR postulated to be a dimer of ethylenebisdithiocarbamate, very low persistence), ETU (max. 25% AR, very low to moderate persistence) and EU (max. 18.5% AR, very low to low persistence). Mineralisation of the ethylene ¹⁴C radiolabels to carbon dioxide accounted for 41–52% AR after 93–120 days. The formation of unextractable residues (not extracted by acetonitrile/EDTA, acetonitrile/water and EDTA in water or buffered acetonitrile/water) for these radiolabels accounted for 48–59% AR after 93–120 days. Mancozeb exhibited medium to slight mobility in soil. EBIS exhibited medium to low soil mobility and ETU and EU exhibited very high soil mobility. It was concluded that the adsorption of these compounds was not pH dependent. Though soil mobility information was not available for M11 its groundwater leaching potential was considered to be covered by the available assessments for ETU, which is more persistent in soil and was formed at slightly higher levels.

In laboratory incubations in dark aerobic natural sediment water systems, mancozeb exhibited very low persistence, forming the major metabolites EBIS (max. 31% AR primarily in water, exhibiting very low to low persistence), ETU (max. 52% AR primarily in water, exhibiting low persistence) and EU (max. 43% AR primarily in water, exhibiting low persistence). The identified metabolite hydantoin reached levels triggering assessment (max. 12% AR primarily in water, this max. occurring 14 days after dosing). Four unidentified metabolites (ascribed as unknowns 1, 2a, 2b and 3) also reached levels triggering assessment at 6, 13, 15 and 8.4% AR, respectively. The unextractable sediment fraction (not extracted by acetonitrile/water) was a sink for the ethylene ¹⁴C radiolabels, accounting for 35–44% AR at study end (105–106 days). Mineralisation of these radiolabels accounted for 18–58% AR at the end of the study. In a sterile aqueous photolysis study, the metabolite EDA reached levels that triggered assessment (max. 19% AR). The necessary surface water and sediment exposure assessments (predicted environmental concentrations (PEC) calculations) were carried out for the metabolites EBIS, ETU, EU, M11, unknown 1, unknown 2b, unknown 3, EDA and hydantoin using the FOCUS (2001) step 1 and step 2 approach (version 3.2 of the Steps 1-2 in FOCUS calculator). The PEC calculated for unknown 2b was accepted as covering the PEC for unknown 2a. For the active substance mancozeb, appropriate step 3 (FOCUS, 2001) and step 4 calculations were available.⁸ The step 4 calculations appropriately followed the FOCUS (2007) guidance, with no-spray drift buffer zones of up to 20 m (cereals and potato) and 30 m (vines) being implemented for all the FOCUS scenarios (representing a 79–95% spray drift reduction). The SWAN tool (version 4.0.1) was appropriately used to implement these spray drift mitigation measures in the simulations.

For the representative protected use on tomatoes, in relation to just the situation of cultivation in high technology (permanent) greenhouse, the necessary surface water and sediment PEC were

⁸ Simulations utilised the agreed Q10 of 2.58 (following EFSA, 2008) and Walker equation coefficient of 0.7.

appropriately calculated assuming a 0.2% emission of mancozeb from greenhouses being redeposited on an adjacent surface water body. This approach is referred to in FOCUS (2008) guidance as being appropriate. For other greenhouse structures that are situated at distances from adjacent water bodies, the PEC for vines (open field) can be used as a surrogate for the use on tomatoes as the single application dose rates are the same and spray drift is the exposure route that drove the maximum PEC needed for the risk assessment and the vines spray drift values are those appropriate to taller fruiting vegetables, i.e. trained vining tomatoes typically cultivated under protection.

The necessary groundwater exposure assessments were appropriately carried out using FOCUS (European Commission, 2014a) scenarios and the models PEARL 4.4.4, PELMO 5.5.3 and MACRO 5.5.4.⁹ The potential for groundwater exposure from the representative uses by mancozeb and its soil metabolites EBIS, ETU and EU above the parametric drinking water limit of 0.1 µg/L was concluded to be low in geoclimatic situations that are represented by all 9 FOCUS groundwater scenarios. For the metabolite M11, the same conclusion was reached considering its properties (as already discussed above) and the simulation results for ETU.

The applicant provided appropriate information to address the effect of the water treatments processes of ozonation and chlorination on the nature of the hydantoin residues that might be present in surface water, when surface water is abstracted for drinking water. The conclusion of this consideration was that *N*-chloro derivatives of hydantoin (e.g. 1,3-dichloro hydantoin) would be expected to be formed. However, the risk to human or animal health through the consumption of drinking water containing 1,3-dichloro hydantoin was not adequately addressed. This has led to the identification of a data gap (see Section 7) and results in the consumer risk assessment not being finalised (see Section 9).

The PEC in soil, surface water, sediment and groundwater covering the representative uses assessed can be found in Appendix A of this conclusion, including PEC of manganese and zinc ions. The applicant presented peer reviewed literature on the levels of manganese and zinc ions present in soils. The PEC values were lower than the levels that were available from the literature presented.

5. Ecotoxicology

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

Some aspects of the hazard characterisation and risk assessments were discussed in the Pesticides Peer Review meeting 192 session 1 in February 2019.

The test material of used in the ecotoxicity studies was concluded to be sufficiently representative of the technical specification.

Although the applicant was requested⁹ to clarify the type of structure the representative use to tomatoes will be used in, it is still not clear whether the use is restricted to high technology (permanent) greenhouses. As such, a conclusion, assuming both high technology (permanent) greenhouse and other types of greenhouse structures, has been reached. For the uses in high technology (permanent) greenhouse, with the exception of aquatic organisms (see paragraph below), a low risk to all groups of non-target organisms is concluded on the basis of minimal exposure. For applications to tomatoes in greenhouses which are not high technology, this is considered to lead to exposure equivalent to applications made in the field. Therefore, a conclusion of the risk to non-target organisms for this use is given in the following paragraphs.

Sufficient toxicity data were available to perform a risk assessment for **birds and mammals** from mancozeb and its metabolite ETU. For the representative uses to wheat, grapevines and potatoes, a low acute risk to birds was concluded based on the tier 1 risk assessment for both mancozeb and metabolite ETU. A low acute risk to mammals was also concluded at tier 1 for the majority of the tier 1 generic focal species for both mancozeb and ETU. The exception was for the small herbivorous

⁹ Refer to data requirement 5.16 in the Evaluation table (EFSA, 2019).

mammal (for details refer to Appendix A). A refined risk assessment using a refined geometric mean endpoint for mancozeb and measured residue data for ETU was available and was sufficient to conclude a low acute risk to mammals.

The tier 1 long-term risk assessment for wheat, grapevines and potatoes indicated a high risk to birds and mammals from both mancozeb and ETU for several of the tier 1 generic focal species (for details refer to Appendix A). A comprehensive refined risk assessment considering specific focal species relevant for the representative uses was discussed at the experts' meeting. Furthermore, sufficient data were available to refine the residue per unit dose (RUD) value for grapes, the residue decline (DT₅₀) in foliage and deposition values. Where suitable data were available, and agreed by the experts at the meeting, the ecological parameters PT and PD were also refined. When considering all of the refinements, a high long-term risk was concluded for the majority of the specific focal species for birds and mammals for the representative uses to wheat, grapevines and potatoes. This conclusion is applicable to both mancozeb and metabolite ETU.

No acute or long-term risk assessment for birds and mammals was available for the representative use to tomatoes made in greenhouses which are not high technology. EFSA added a tier 1 risk assessment for mancozeb to Appendix A which showed a low acute risk to birds and mammals (using the geometric mean endpoint). However, a high long-term risk was indicated to all tier 1 generic focal species for birds and mammals. As a high long-term risk to birds and mammals has been indicated for all representative uses this leads to a critical area of concern.

A risk assessment was not available to identify and assess the risk to birds and mammals from metabolites other than ETU. As such a data gap for further assessment is identified. Furthermore, no risk assessment for metabolite ETU was available for the use to tomatoes made in greenhouses which are not high technology (permanent) (data gap). A low risk to birds and mammals via secondary poisoning and via the consumption of contaminated water was concluded.

Toxicity data were available to characterise the hazard of mancozeb to **aquatic organisms**. A low risk to aquatic plants was concluded on the basis of the tier 1 risk assessment using FOCUS step 2 PEC values (for all representative uses). All other groups of aquatic organisms needed higher tier refinement together with FOCUS steps 3 and 4 PEC values. The following points summarise the key outcome of the higher tier hazard characterisation and aquatic risk assessments:

- i) A tier 2a acute RAC for fish was determined by calculating the geometric mean of the available data. This RAC was discussed and agreed at the experts meeting.¹⁰ Using the tier 2a RAC, a low acute risk to fish was concluded for all FOCUS surface water scenarios for the representative uses to cereals, grapevines, tomatoes greenhouses which are not high technology and potatoes provided that risk mitigation measures were used (refer to Appendix A for details). A low acute risk to fish was also concluded for the use to tomatoes in high technology (permanent) greenhouses.
- ii) A pulsed exposure fish early-life stage study was available and discussed at the experts meeting. The majority of the experts agreed that the study met the requirements of EFSA PPR Panel (2013). Consequently, it was agreed that results of this study could be used for the refined risk assessment (tier 2c) as long as it was demonstrated that the exposure in the study sufficiently replicated the exposure profile predicted for the representative uses. A detailed consideration of the exposure profile in the study (corrected for the assessment factor) was available and indicated that it was sufficiently representative for all FOCUS surface water scenarios for the representative use on potatoes provided risk mitigation measures are used. Consequently, a low chronic risk to fish was concluded for the representative use to potatoes. It was concluded that the exposure profile in the study did not cover the predicted exposure profile for the representative use to cereals (accounting for the suggested level of mitigation). However, it should be acknowledged that the comparison was done using a slightly conservative method and further assessment may in fact demonstrate that the exposure is covered. The predicted exposure profile for the representative use grapevines was not covered by the exposure in the refined pulsed exposure study; therefore, a high chronic risk to fish was concluded for all focus surface water scenarios for grapevines. No consideration of the predicted exposure profile for the use to tomatoes in greenhouses (both high technology and not high technology greenhouses) was available; therefore, a high chronic risk to fish was concluded for these uses.

¹⁰ Refer to experts' consultation 5.9 in the Report of Pesticides Peer Review experts' meeting 192-session 1 (EFSA, 2019).

- iii) Several mesocosm studies were available and used to derive an ETO-RAC for aquatic invertebrates (addressing both the acute and chronic toxicity). The ETO-RAC was discussed and agreed at the experts meeting.¹¹ Using the ETO-RAC, a low acute and chronic risk to aquatic invertebrates was concluded for all FOCUS surface water scenarios for the representative uses to cereals, vines, tomatoes greenhouses which are not high technology and potatoes provided that risk mitigation measures were used (refer to Appendix A for details). A low acute and chronic risk to aquatic invertebrates was also concluded for the representative use to tomatoes in high technology (permanent) greenhouses.
- iv) Using the tier 1 endpoints together with FOCUS step 4 surface water modelling a low risk to sediment dwelling organisms and algae was concluded for all FOCUS surface water scenarios for the representative uses to cereals, vines, tomatoes in greenhouses which are not high technology and potatoes provided that risk mitigation measures were used. A low risk to sediment dwelling organisms and algae was also concluded for the representative use to tomatoes in high technology (permanent) greenhouses.

In summary, the outcome of the aquatic risk assessment for mancozeb is driven by the chronic risk to fish for which a high risk is concluded for all representative uses with the exception of the use on potatoes. For the use on potatoes, a low chronic risk to fish was concluded, for all FOCUS surface water scenarios, provided risk mitigation measures equivalent to a 20 m buffer zone are used (see Section 8).

There are ten surface water metabolites which triggered the need for an aquatic risk assessment (EBIS, ETU, EU, M11, EDA, unknown 1, unknown 2a, unknown 2b, unknown 3 and hydantoin). A low risk to aquatic organisms was concluded for ETU, EU, EBIS (with risk mitigation), M11, unknown 1, unknown 2a and unknown 3. A data gap was concluded for further information to address the risk to aquatic organisms from metabolites unknown 2b and EDA. The RMS did not consider that hydantoin triggered the need for an aquatic risk assessment and therefore did not evaluate the argumentation provided by the applicant and therefore a further data gap was concluded.

Toxicity data for **honey bees** were available demonstrating the acute oral, acute contact, chronic oral and sublethal toxicity (hypopharyngeal glands (HPG)) to adult bees and toxicity to honey bee larvae. Furthermore, acute oral and acute contact toxicity data were available for bumblebees and acute contact toxicity solitary bees. The RMS only utilised the acute oral and contact toxicity endpoint for honey bees in a risk assessment according to European Commission (2002a). This assessment indicated a low acute risk to honey bees. The applicant provided a risk assessment, addressing all relevant exposure routes, for honey bees, bumble bees and solitary bees according to EFSA (2013). Although requested,¹² the RMS did not evaluate the applicant's risk assessment but included it in the RAR as an appendix. It is noted that the available tier 1 risk assessment indicated a high chronic risk to adult honey bees and a high risk to honey bee larvae. A tier 2 risk assessment using refined residue values was also presented and indicated a low risk. The acute risk assessment for bumble bees, solitary bees and for honey bees via consumption of contaminated water also indicated a low risk. However, as these assessments have not been peer reviewed, a data gap is concluded (relevant for all outdoor uses). A colony feeding field study with honey bees was available and indicated a potential concern for colony strength. It was suggested that the observed differences were within natural variability and should not be considered as treatment related. Owing to the few replicates used in the study, it is agreed that the results of the study should not be considered to confirm a high risk to honey bees; but equally, it cannot be used to exclude a risk to honey bees. Therefore, the risk assessment for honey bees remains open pending the evaluation of the available tier 2 refinements discussed above.

On the basis of the available risk assessment, a low acute risk assessment for honey bees from metabolite ETU was concluded. No risk assessment addressing the chronic risk or the risk to honey bee larvae, from metabolite ETU, was available. Furthermore, other relevant metabolites in pollen and nectar were not identified. Consequently, a data gap to address the risk to bees from metabolites (other than the acute risk from metabolite ETU) in pollen and nectar was concluded.

No specific assessment was performed for pollinators which may be introduced to greenhouses for pollination services; however, it is noted that the acute contact and oral toxicity to bumble bees is low.

The tier 1 risk assessment for the standard indicator species indicated a high risk to **non-target arthropods** for the representative uses to wheat, vines and potatoes. Refined multiple application factor (MAF) values were used for the tier 2 in-field risk assessment. The resulting tier 2 risk

¹¹ Refer to experts' consultation 5.11 in the Report of Pesticides Peer Review experts' meeting 192-session 1 (EFSA, 2019).

¹² Refer to open point 5.60 in the Evaluation table (EFSA, 2019).

assessment indicated a high in-field risk. A low off-field risk to non-target arthropods was indicated provided that risk mitigation measures are used. Several higher tier field studies were available and discussed at the experts meeting. The experts agreed with the assessment of the RMS who had concluded numerous reliability issues with the studies. It was agreed that the available data were not sufficient to demonstrate the potential for recovery and consequently a high in-field risk to non-target arthropods was concluded for the representative uses in cereals, grapevines and potatoes. No specific risk assessment for non-target arthropods was performed for the representative use to tomatoes in greenhouses which are not high technology. However, EFSA added a tier 1 and tier 2 risk assessment in Appendix A which indicated a high risk. As a high risk to in-field populations of non-target arthropods has been indicated for all representative uses this leads to a critical area of concern.

Chronic toxicity data for **earthworms** and other **soil macroorganisms** was available and discussed at the experts' meeting. On the basis of the available tier 1 risk assessment a low chronic risk to earthworms was concluded. However, a high chronic risk to other soil macroorganisms was indicated for all representative outdoor uses. An interim report for an ongoing field study investigating the effects on collembolans and soil mites was available. The available results indicated an effect on several taxa with no clear recovery by the final available sampling date (167 days after treatment). The results of the final assessment were not yet available and therefore it is unknown whether recovery will occur within 1 year. Consequently, a high risk to soil macroorganisms was concluded for the representative uses to wheat, grapevines, potatoes and tomatoes in open protected greenhouse structures. As a high risk to soil macroorganisms has been indicated for all representative uses this leads to a critical area of concern.

There are four soil metabolites which triggered the need for an assessment to soil dwelling organisms (EBIS, ETU, EU, M11). On the basis of the available risk assessment, a low risk to earthworms and other soil macroorganisms was concluded for ETU. It was also concluded that the EBIS, EU and M11 would have also been covered in the available toxicity studies performed with the parent substance mancozeb. Therefore, a low chronic risk to earthworms for these metabolites could also be concluded. However, as a high chronic risk to other soil macroorganisms from mancozeb has been concluded, the risk posed from these metabolites remains unresolved.

A low risk to **soil microorganisms** from mancozeb and metabolites was concluded for all representative uses. A low risk to non-target terrestrial plants and sewage treatment organisms was also concluded for all representative uses.

An assessment of the **endocrine disrupting properties** of mancozeb in line with ECHA and EFSA (2018) was presented.

As discussed in Section 2, mancozeb is considered to meet the criteria for endocrine disruption for humans through the T-modality. Adversity in mammals was based on thyroid follicular cell hypertrophy, increased thyroid weight, thyroid follicular cell hyperplasia, tumours of the thyroid gland (adenomas and carcinomas).

According to the assessment strategy in ECHA and EFSA Guidance (2018), the relevance of the observed effects in the mammalian toxicology data set at population level for wild mammals was discussed. Considering that no other apical effects for example on growth and development were observed in the available data package for mammals, including a development neurotoxicity study, the experts agreed that the observed effects cannot be considered relevant at population level.

For non-target organisms other than mammals, data on amphibians were assessed. No data on amphibians with mancozeb were available. A number of amphibian metamorphosis studies were available with the ETU metabolite, showing clear effects on thyroid histopathology coupled with delay in development. These effects were considered to be consistent with the effects and the mode of action identified in mammals i.e. inhibition of the peroxidase activity of thyroperoxidase (TPO) probably via ETU metabolite leading in the case of amphibians to delayed development.

Although data on amphibians were only available for ETU, considering the available evidence from metabolism studies showing that ETU is formed in animal body (rat and hen), similar metabolism can be expected in amphibians. Consequently, adverse effects comparable to the ones observed for ETU can be expected after exposure to mancozeb. Therefore, it was concluded that mancozeb is likely to meet the ED criteria for non-target organisms through the T-modality.¹³

For the E, A and S modalities, a Fish Full Life Cycle Test (FFLCT) and a partial life cycle test were available. However, the FFLCT did not include any ED relevant parameters. In the partial life cycle effects on female and male gonads were observed. However, no mechanistic information was available. No further data are however requested, considering the conclusion on the T-modality.

¹³ Refer to experts' consultation 5.16 in the Report of Pesticides Peer Review experts' meeting 192-session 1 (EFSA, 2019).

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

Table 1: Soil

Compound (name and/or code)	Persistence	Ecotoxicology
Mancozeb	Very low to low persistence Single first-order and biphasic kinetics DT ₅₀ 0.017–0.159 days (DT ₉₀ 0.35–33.3 days, 20–23°C 22.5–40% MWHC)	High risk to soil macroorganisms for all outdoor uses. Low risk to earthworms and soil microorganisms
EBIS	very low persistence Single first-order kinetics DT ₅₀ 0.1–0.42 days (20°C 40% MWHC)	Low risk to earthworms and soil microorganisms. Risk assessment for soil macroorganisms is open
ETU	Very low to moderate persistence Single first-order and biphasic kinetics DT ₅₀ 0.1–15.3 days (DT ₉₀ 0.3–50.4 days, 20–25°C 40–70% MWHC)	Low risk to soil organisms
EU	Very low to low persistence Single first-order and biphasic kinetics DT ₅₀ 0.5–8 days (DT ₉₀ 1.6–26.5 days, 20°C 40–45% MWHC)	Low risk to earthworms and soil microorganisms. Risk assessment for soil macroorganisms is open
M11	Very low persistence Single first-order kinetics DT ₅₀ 0.042–0.076 days (20°C 40% MWHC)	Low risk to earthworms and soil microorganisms. Risk assessment for soil macroorganisms is open

DT₅₀: period required for 50% dissipation; DT₉₀: period required for 90% dissipation; MWHC: maximum water-holding capacity.

Table 2: Groundwater

Compound (name and/or code)	Mobility in soil	> 0.1 µg/L at 1 m depth for the representative uses ^(a)	Pesticidal activity	Toxicological relevance
Mancozeb	Medium to slight mobility K _{Foc} 363–2,334 mL/g	No	Yes	Yes
EBIS	Medium to low mobility K _{doc} 279–1,140 mL/g	No	Assessment not triggered	Assessment not triggered ADI = 0.023 mg/kg bw per day ARfD = 0.15 mg/kg bw
ETU	Very high mobility K _{Foc} 3.4–4.6 mL/g	No	Assessment not triggered	Assessment not triggered ADI = 0.002 mg/kg bw per day ARfD = 0.01 mg/kg bw

Compound (name and/or code)	Mobility in soil	> 0.1 µg/L at 1 m depth for the representative uses ^(a)	Pesticidal activity	Toxicological relevance
EU	Very high mobility K _{Foc} 4–19 mL/g	No	Assessment not triggered	Assessment not triggered ADI = 0.06 mg/kg bw per day ARfD = 0.37 mg/kg bw
M11	Information unavailable due to its very transient nature in soil	No	Assessment not triggered	Assessment not triggered

K_{Foc}: Freundlich organic carbon adsorption coefficient; K_{doc}: organic carbon linear adsorption coefficient; ADI: acceptable daily intake; bw: body weight; ARfD: acute reference dose.
(a): FOCUS scenarios or a relevant lysimeter.

Table 3: Surface water and sediment

Compound (name and/or code)	Ecotoxicology
Mancozeb	Low risk to aquatic organisms for representative use to potatoes provided risk mitigation measures are used. High risk to aquatic organisms for all other representative uses
EBIS	Low risk to aquatic organisms
ETU	Low risk to aquatic organisms
EU	Low risk to aquatic organisms
M11	Low risk to aquatic organisms
Unknown 1	Low risk to aquatic organisms
Unknown 2a	Low risk to aquatic organisms
Unknown 2b	Data gap
Unknown 3	Low risk to aquatic organisms
EDA	Data gap
Hydantoin	Data gap

Table 4: Air

Compound (name and/or code)	Toxicology
Mancozeb	Rat LC ₅₀ inhalation > 5 mg/L

LC₅₀: lethal concentration, median.

7. Data gaps

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

- A search of the scientific peer-reviewed open literature on the active substance and its relevant metabolites, dealing with side effects on health and non-target species and published within the 10 years before the date of submission of the dossier, to be conducted and reported in accordance with EFSA guidance on the submission of scientific peer-reviewed open literature for the approval of pesticide active substances under Regulation (EC) No 1107/2009 (EFSA, 2011; relevant for Agria SA for Sections 3 and 5).
- A suspensibility study at the lowest use concentration for Mancozeb 800 WP (relevant for applicant Agria SA; see Section 1).
- Analytical method for the determination of one impurity in the technical material (relevant for applicant Agria SA; see Section 1).
- Additional data concerning methods: ILV for the monitoring method for plant matrices; primary and confirmatory methods for meat, milk and fat and an ILV for all animal matrices; additional validation data to reach the LOQ of 0.1 µg/L for drinking water, new monitoring method for the determination of residues in air and an analytical method for the determination of ETU in body fluids (relevant for applicant Agria SA; see Section 1)
- More investigations of the phototoxicity potential of mancozeb should be provided, considering the contradictory results in two valid *in vitro* studies and the absence of test at wavelengths (UVB) where mancozeb showed significant absorption (since there is no OECD test for UVB absorber) (relevant for all representative uses; see Section 2).
- Further investigations of the gene mutation potential in mammalian cells assay compliant with modern standards and using the representative material should be provided (relevant for all representative uses; see Section 2).
- For the use in permanent greenhouse, the exposure of bystanders and residents to vapour from ventilation systems should be further considered (relevant for representative use in tomatoes; see Section 2).
- Exposure estimates for ETU as well as the combined exposure estimates for ETU and mancozeb should be provided for the tomato uses (relevant for the representative use in tomatoes; see Section 2).
- A complete residue data set on grapes compliant with the SEU GAP that determine mancozeb (CS₂) and ETU and supported by acceptable storage stability data (relevant for the representative use in grapes; see Section 3).
- Complete NEU and SEU residue data packages on potatoes with immediate residue analysis after sampling and covering the residue definitions for monitoring and risk assessment (relevant for the representative use in potatoes; see Section 3).
- Three additional residue trials compliant with the SEU GAP on wheat for the determination of ETU residues in wheat grain (relevant for the representative use in wheat; see Section 3).
- Clarification on the discrepancies in regard to the frozen storage stability results for ETU observed in wheat and cereal grain and the validity of the field residue trials analysing ETU residues in wheat grain should be demonstrated in regard to the work-up and the maximum storage time interval of the residue samples (relevant for the representative use in wheat; see Section 3).
- Storage stability data on ETU in cereal straw and covering the maximum storage time interval of the wheat residue trials (relevant for the representative use in wheat; see Section 3).
- A complete GAP-compliant residue data set on indoor tomatoes and covering the residue definitions for monitoring and risk assessment (relevant for the representative use in tomatoes; see Section 3).
- Sufficient processing residue trials analysing for mancozeb and ETU in potato and wheat processed matrices that may be fed to livestock and within a time interval for which acceptable storage stability is demonstrated for both compounds (relevant for the representative uses in potatoes and wheat; see Section 3).

- Determination of the residues of mancozeb (CS₂) and ETU in pollen and bee products for human consumption resulting from residues taken up by honeybees from grapes at blossom (relevant for the representative use in grapevines; see Section 3).
- Information to address the identity of hydrolysis transformation product of mancozeb ascribed as CPIII was not available (not needed to complete environmental exposure assessments for the representative uses evaluated, but is a requirement of prescribed by the regulation; see evaluation table section 4 contained in the peer review report, EFSA, 2019).
- Information on the risk to human or animal health through the consumption of drinking water containing *N*-chloro derivatives of hydantoin (e.g. 1,3-dichloro hydantoin) that the applicant has indicated have the potential to be formed from the chlorination of surface water that might contain hydantoin was not available (relevant for all representative uses evaluated; see Sections 3 and 4).
- Acute and long-term risk assessments for birds and mammals from ETU and other relevant metabolites (relevant for the representative use in tomatoes in greenhouses which are not high technology; see Section 5).
- Information to identify and assess the risk to birds and mammals from metabolites other than ETU (relevant for the representative use in wheat, grapevines and potatoes; see Section 5).
- Information to address the risk to aquatic organisms from metabolites unknown 2b, EDA and hydantoin (relevant for all representative uses; see Section 5).
- An evaluation and peer review of the available tier 1 and tier 2 bee risk assessments performed according to the EFSA (2013) guidance document (relevant for all representative uses evaluated except tomatoes in high technology (permanent) greenhouses; see Section 5).
- Information to address the risk to bees from metabolites (other than the acute risk from metabolite ETU) in pollen and nectar (relevant for all representative uses evaluated except tomatoes in high technology (permanent) greenhouses; see Section 5).

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

- Risk mitigation measures, equivalent to a 20 m no spray buffer zone, are needed to protect aquatic organisms for the representative use to potatoes (see Section 5).

9. Concerns

9.1. Issues that could not be finalised

An issue is listed as 'could not be finalised' if there is not enough information available to perform an assessment, even at the lowest tier level, for the representative uses in line with the uniform principles in accordance with Article 29(6) of Regulation (EC) No 1107/2009 and as set out in Commission Regulation (EU) No 546/2011¹⁴ and if the issue is of such importance that it could, when finalised, become a concern (which would also be listed as a critical area of concern if it is of relevance to all representative uses).

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

- 1) The phototoxicity potential of mancozeb to mammals could not be finalised since contradictory results were obtained in two *in vitro* tests and no OECD test is available for UVB absorbers (see Section 2).
- 2) For the greenhouse use on tomatoes, non-dietary exposure assessment of bystanders and residents to mancozeb could not be finalised, as well as combined non-dietary exposure assessment to mancozeb and ETU for operators, workers, residents and bystanders (see Section 2).
- 3) The consumer dietary risk assessment cannot be finalised pending the identified data gaps to complete the residue data sets for all the representative uses in compliance with the

¹⁴ 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.

agreed residue definitions for monitoring and risk assessment in plants which will impact the livestock dietary burden calculation and exposure assessment (see Section 3).

- 4) It was identified that the drinking water treatment process of chlorination might produce 1,3-dichloro hydantoin when surface water is abstracted to produce drinking water. As the risk to human or animal health through the consumption of drinking water containing 1,3-dichloro hydantoin was not adequately addressed, this has led to the consumer risk assessment being not finalised (see Sections 3 and 4).

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.

- 5) Mancozeb is classified for developmental toxicity as Repr. 1B; H360D (ECHA, 2019) leading to a critical area of concern with regard to the approval criteria, Annex II, Part 3.6.4 of Regulation (EC) No 1107/2009 (see Section 2).
- 6) The approval criteria on the endocrine disrupting potential for mancozeb as set out in point 3.6.5 of Annex II to Regulation (EC) No 1107/2009, as amended by Commission Regulation (EU) 2018/605, are met. Furthermore, it was concluded that mancozeb is likely to meet the approval criteria for endocrine disrupting potential as set out in point 3.8.2 of Annex II to Regulation (EC) No 1107/2009, as amended by Commission Regulation (EU) 2018/605 for non-target organisms (see Sections 2 and 5).
- 7) Operators' exposure estimates are above the AOEL/AAOEL for the uses on potatoes, cereals and grapevine; workers' exposure estimates are above the AOEL for the use on tomatoes and on grapevine; bystanders and residents (children) exposure estimates are above the AOEL/AAOEL for the uses on potatoes, cereals and grapevine. For the combined exposure, operators and workers exposure estimates are above the AOEL/AAOEL for the uses on potatoes, cereals and grapevines, while bystanders' and residents' exposures are above the AOEL/AAOEL for the uses on grapevines (child and adult) and for potatoes and cereals (child) (see Section 2).
- 8) A high long-term risk to birds and mammals is concluded for all representative uses, although it should be noted that, if the representative use to tomatoes is restricted to high technology (permanent) greenhouse, a low risk would be concluded (see Section 5).
- 9) A high risk to non-target arthropods is concluded for all representative uses, although it should be noted that, if the representative use to tomatoes is restricted to high technology (permanent) greenhouse, a low risk would be concluded (see Section 5).
- 10) A high risk to soil macroorganisms is concluded for all representative uses, although it should be noted that, if the representative use to tomatoes is restricted to high technology (permanent) greenhouse, a low risk would be concluded (see Section 5).

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

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

Table 5: Overview of concerns

Representative use		wheat	grape vines	potato	tomato greenhouse
Operator risk	Risk identified	X ⁷	X ⁷	X ⁷	
	Assessment not finalised				X ²
Worker risk	Risk identified	X ⁷	X ⁷	X ⁷	X ⁷
	Assessment not finalised				
Resident/bystander risk	Risk identified	X ⁷	X ⁷	X ⁷	
	Assessment not finalised				X ²
Consumer risk	Risk identified				
	Assessment not finalised	X ^{3,4}	X ^{3,4}	X ^{3,4}	X ^{3,4}
Risk to wild non-target terrestrial vertebrates	Risk identified	X ⁸	X ⁸	X ⁸	X ^{8,(b)}
	Assessment not finalised				
Risk to wild non-target terrestrial organisms other than vertebrates	Risk identified	X ^{9,10}	X ^{9,10}	X ^{9,10}	X ^{9,10,(b)}
	Assessment not finalised				
Risk to aquatic organisms	Risk identified	X	X		X
	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				

The superscript numbers relate to the numbered points indicated in Sections 9.1 and 9.2. Where there is no superscript number, see Sections 2–6 for further information.

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

(b): A high risk was indicated for the use to tomatoes in greenhouses which are not high technology. However, it should be noted that, if the representative use to tomatoes is restricted to high technology (permanent) greenhouses, a low risk would be concluded.

References

- 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), 2019. Committee for Risk Assessment (RAC) Opinion proposing harmonised classification and labelling at EU level of mancozeb. CLH-O-0000001412-86-263/F. Available online: www.echa.europa.eu
- ECHA and EFSA (European Chemicals Agency and 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>. ECHA-18-G-01-EN.
- EFSA (European Food Safety Authority), 2008. Opinion on a request from EFSA related to the default Q10 value used to describe the temperature effect on transformation rates of pesticides in soil. EFSA Journal 2008;6(1):622, 32 pp. <https://doi.org/10.2903/j.efsa.2008.622>
- EFSA (European Food Safety Authority), 2009. Guidance on Risk Assessment for Birds and Mammals on request from EFSA. EFSA Journal 2009;7(12):1438, 358 pp. <https://doi.org/10.2903/j.efsa.2009.1438>
- EFSA (European Food Safety Authority), 2011. Submission of scientific peer-reviewed open literature for the approval of pesticide active substances under Regulation (EC) No 1107/2009. EFSA Journal 2011;9(2):2092, 49 pp. <https://doi.org/10.2903/j.efsa.2011.2092>

- EFSA (European Food Safety Authority), 2013. EFSA Guidance Document on the risk assessment of plant protection products on bees (*Apis mellifera*, *Bombus* spp. and solitary bees). EFSA Journal 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> Available online: www.efsa.europa.eu/efsajournal
- EFSA (European Food Safety Authority), 2019. Peer review report to the conclusion regarding the peer review of the pesticide risk assessment of the active substance mancozeb. Available online: www.efsa.europa.eu
- EFSA PPR Panel (EFSA Panel on Plant Protection Products and their Residues), 2012. Guidance on dermal absorption. EFSA Journal 2012;10(4):2665, 30 pp. <https://doi.org/10.2903/j.efsa.2012.2665>
- EFSA PPR Panel (EFSA Panel on Plant Protection Products and their Residues), 2013. Guidance on tiered risk assessment for plant protection products for aquatic organisms in edge-of-field surface waters. EFSA Journal 2013;11(7):3290, 186 pp. <https://doi.org/10.2903/j.efsa.2013.3290>
- European Commission, 2000a. Residues: guidance for generating and reporting methods of analysis in support of pre-registration data requirements for Annex II (Part A, Section 4) and Annex III (Part A, Section 5) of Directive 91/414. SANCO/3029/99-rev. 4, 11 July 2000.
- European Commission, 2000b. Technical material and preparations: guidance for generating and reporting methods of analysis in support of pre- and post-registration data requirements for Annex II (Part A, Section 4) and Annex III (Part A, Section 5) of Directive 91/414. SANCO/3030/99-rev. 4, 11 July 2000.
- European Commission, 2002a. Guidance Document on Terrestrial Ecotoxicology Under Council Directive 91/414/EEC. SANCO/10329/2002-rev. 2 final, 17 October 2002.
- European Commission, 2002b. Guidance Document on Aquatic Ecotoxicology Under Council Directive 91/414/EEC. SANCO/3268/2001-rev. 4 final, 17 October 2002.
- European Commission, 2003. Guidance Document on Assessment of the Relevance of Metabolites in Groundwater of Substances Regulated under Council Directive 91/414/EEC. SANCO/221/2000-rev. 10 final, 25 February 2003
- European Commission, 2009. Review report for the active substance mancozeb. Finalised in the Standing Committee on the Food Chain and Animal Health at its meeting on 3 June 2005 in view of the inclusion of mancozeb in Annex I of Council Directive 91/414/EEC. SANCO/4058/2001 - rev. 4.4, July 2009, 63 pp.
- European Commission, 2010. Guidance Document on residue analytical methods. SANCO/825/00-rev. 8.1, 16 November 2010
- European Commission, 2011. Guidelines on comparability, extrapolation, group tolerances and data requirements for setting MRLs. SANCO 7525/VI/95-rev. 9. March 2011. p.1–46.
- European Commission, 2012. Guidance document on the assessment of the equivalence of technical materials of substances regulated under Regulation (EC) No 1107/2009. SANCO/10597/2003-rev. 10.1, 13 July 2012.
- European Commission, 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, 2017. Appendix D. Guidelines on comparability, extrapolation, group tolerances and data requirements for setting MRLs. 7525/VI/95-rev. 10.3, June 2017.
- European Commission, 2018. Technical guidelines for determining the magnitude of pesticide residues in honey and setting Maximum Residue Levels in honey. SANTE/11956/2016 rev. 9. 14 September 2018, 41 pp.
- FOCUS (Forum for the Co-ordination of Pesticide Fate Models and their Use), 2001. FOCUS surface water scenarios in the EU evaluation process under 91/414/EEC. Report of the FOCUS Working Group on Surface Water Scenarios. EC Document Reference SANCO/4802/2001-rev. 2, 245 pp., as updated by Generic guidance for FOCUS surface water scenarios, v. 1.4, May 2015.
- FOCUS (Forum for the Co-ordination of Pesticide Fate Models and their Use), 2006. Guidance document on estimating persistence and degradation kinetics from environmental fate studies on pesticides in EU Registration Report of the FOCUS Work Group on Degradation Kinetics. EC Document Reference SANCO/10058/2005-v. 2.0, 434 pp., as updated by the Generic guidance for Estimating Persistence and Degradation Kinetics from Environmental Fate Studies on Pesticides in EU Registration, v. 1.1, December 2014.
- FOCUS (Forum for the Co-ordination of Pesticide Fate Models and their Use), 2007. Landscape and mitigation factors in aquatic risk assessment. Volume 1. Extended summary and recommendations. Report of the FOCUS Working Group on Landscape and Mitigation Factors in Ecological Risk Assessment. EC Document Reference SANCO/10422/2005 v. 2.0, 169 pp.
- FOCUS (Forum for the Co-ordination of Pesticide Fate Models and their Use), 2008. Pesticides in air: considerations for exposure assessment. Report of the FOCUS Working Group on Pesticides in Air. EC Document Reference SANCO/10553/2006-rev. 2, June 2008.
- JMPR (Joint Meeting on Pesticide Residues), 2004. Report of the Joint Meeting of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Core Assessment Group on Pesticide Residues, Rome, Italy, 20–29 September 2004, 383 pp.

- JMPR (Joint Meeting on Pesticide Residues), 2007. Report of the Joint Meeting of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Core Assessment Group on Pesticide Residues, Geneva, Switzerland, 18–27 September 2007, 164 pp.
- OECD (Organisation for Economic Co-operation and Development), 2009. Guidance document on overview of residue chemistry studies. ENV/JM/MONO(2009)31, 28 July 2009.
- OECD (Organisation for Economic Co-operation and Development), 2011. OECD MRL calculator: spreadsheet for single data set and spreadsheet for multiple data set, 2 March 2011. In: Pesticide Publications/Publications on Pesticide Residues. Available online: www.oecd.org
- SETAC (Society of Environmental Toxicology and Chemistry), 2001. Guidance document on regulatory testing and risk assessment procedures for plant protection products with non-target arthropods. ESCORT 2.
- United Kingdom, 2017. Renewal Assessment Report (RAR) on the active substance mancozeb prepared by the rapporteur Member State the United Kingdom, in the framework of Commission Implementing Regulation (EU) No 844/2012, September 2017. Available Online: www.efsa.europa.eu
- United Kingdom, 2019. Revised Renewal Assessment Report (RAR) on the active substance mancozeb prepared by the rapporteur Member State the United Kingdom in the framework of Commission Implementing Regulation (EU) No 844/2012, March 2019. Available Online: www.efsa.europa.eu

Abbreviations

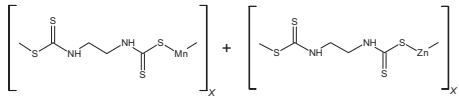
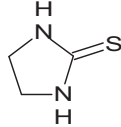
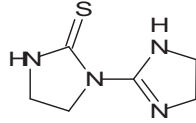
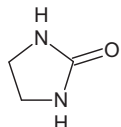
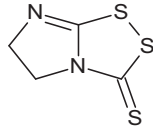
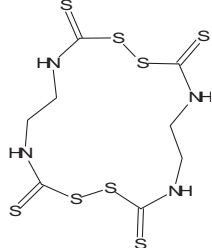
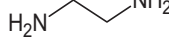
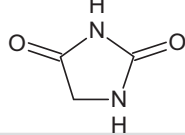
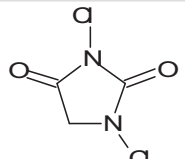
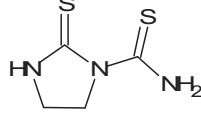
AAOEL	acute acceptable operator exposure level
ADI	acceptable daily intake
AOEL	acceptable operator exposure level
AR	applied radioactivity
ARfD	acute reference dose
bw	body weight
CIPAC	Collaborative International Pesticides Analytical Council Limited
DAR	draft assessment report
DAT	days after treatment
DNT	developmental neurotoxicity
DT ₅₀	period required for 50% dissipation (define method of estimation)
DT ₉₀	period required for 90% dissipation (define method of estimation)
EBIS	ethylenebisisothiocyanatesulfide
ECHA	European Chemicals Agency
EDA	ethylenediamine
EEC	European Economic Community
EOGRS	Extended One Generation Repro-Toxicity Study
ETO	ecological threshold option
ETU	ethylenethiourea
EU	ethylenurea
EUROPOEM	European Predictive Operator Exposure Model
FAO	Food and Agriculture Organization of the United Nations
FFLCT	Fish Full Life Cycle Test
FID	flame ionisation detector
FOCUS	Forum for the Co-ordination of Pesticide Fate Models and their Use
GAP	Good Agricultural Practice
GC	gas chromatography
HPLC	high-pressure liquid chromatography or high-performance liquid chromatography
HPG	hypopharyngeal glands
IESTI	international estimated short-term intake
ILV	independent laboratory validation
InChiKey	International Chemical Identifier Key
ISO	International Organization for Standardization
IUPAC	International Union of Pure and Applied Chemistry
JMPR	Joint Meeting of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Expert Group on Pesticide Residues (Joint Meeting on Pesticide Residues)
K _{doc}	organic carbon linear adsorption coefficient
K _{Foc}	Freundlich organic carbon adsorption coefficient

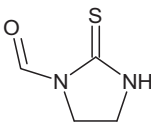
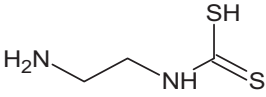
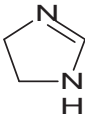
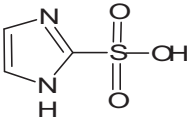
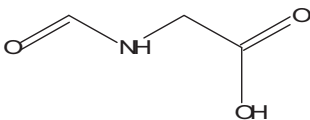
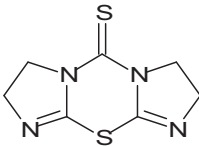
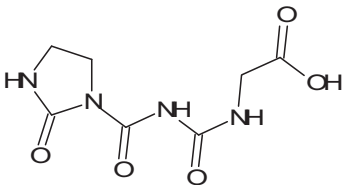
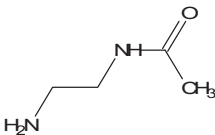
LC ₅₀	lethal concentration, median
LC-MS/MS	liquid chromatography with tandem mass spectrometry
LOAEL	lowest observable adverse effect level
LOQ	limit of quantification
MAF	multiple application factor
MTF	Mancozeb Task Force
MWHC	maximum water-holding capacity
NEU	northern Europe
NOAEL	no observed adverse effect level
OECD	Organisation for Economic Co-operation and Development
PD	proportion of different food types
PEC	predicted environmental concentration
PEC _{air}	predicted environmental concentration in air
PEC _{gw}	predicted environmental concentration in groundwater
PEC _{sed}	predicted environmental concentration in sediment
PEC _{soil}	predicted environmental concentration in soil
PEC _{sw}	predicted environmental concentration in surface water
P _{ow}	partition coefficient between <i>n</i> -octanol and water
PPE	personal protective equipment
PT	proportion of diet obtained in the treated area
RAC	regulatory acceptable concentration
RAR	Renewal Assessment Report
RMS	rappporteur Member State
RUD	residue per unit dose
SEU	southern Europe
SMILES	simplified molecular-input line-entry system
TPO	thyperoxidase
TRR	total radioactive residue
UF	uncertainty factor
UV	ultraviolet
WP	wettable powder
WHO	World Health Organization

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

Appendix A can be found in the online version of this output ('Supporting information' section):
<https://doi.org/10.2903/j.efsa.2020.5755>

Appendix B – Used compound codes

Code/trivial name ^(a)	IUPAC name/SMILES notation/InChiKey ^(b)	Structural formula ^(c)
mancozeb	manganese ethylenebis(dithiocarbamate) (polymeric) complex with zinc salt	
ETU	2-imidazolidinethione <chem>S=C1NCCN1</chem> PDQAZBWRQCGBEV-UHFFFAOYSA-N	
Jaffé's base	1-(4,5-dihydro-1 <i>H</i> -imidazol-2-yl)-2-imidazolidinethione <chem>S=C1NCCN1C=1NCCN=1</chem> LEOYJTSFZDZJNM-UHFFFAOYSA-N	
EU	imidazolidin-2-one <chem>O=C1NCCN1</chem> YAMHXTCMCPHKLN-UHFFFAOYSA-N	
EBIS	5,6-dihydroimidazo[2,1- <i>c</i>][1,2,4]dithiazole-3-thione <chem>S=C1SSC2 = NCCN12</chem> BFTGQIQVUVTBJU-UHFFFAOYSA-N	
M11	1,2,9,10-tetrathia-4,7,12,15-tetraazacyclohexadecane-3,8,11,16-tetrathione <chem>S=C1NCCNC(=S)SSC(=S)NCCNC(=S)SS1</chem> AQQZIFNZOKDYQC-UHFFFAOYSA-N	
EDA	ethane-1,2-diamine <chem>NCCN</chem> PIICEJLVQHRZGT-UHFFFAOYSA-N	
Hydantoin	imidazolidine-2,4-dione <chem>O=C1NC(=O)CN1</chem> WJRBRSFLGUECM-UHFFFAOYSA-N	
1,3-dichloro hydantoin	1,3-dichloro-2,4-imidazolidinedione <chem>O=C1N(Cl)C(=O)CN1Cl</chem> YKZAEXPHYBFRHB-UHFFFAOYSA-N	
TCIT	2-thioxo-1-imidazolidinecarbothioamide <chem>NC(=S)N1CCNC1 = S</chem> CBROQIPVRZGUBN-UHFFFAOYSA-N	

Code/trivial name ^(a)	IUPAC name/SMILES notation/ InChiKey ^(b)	Structural formula ^(c)
<i>N</i>-formyl ETU CPII	2-sulfanylideneimidazolidine-1-carbaldehyde <chem>S=C1NCCN1C=O</chem> SEZXDIZHRQESIV-UHFFFAOYSA-N	
2-(aminoethyl) carbamodithioic acid	(2-aminoethyl)carbamodithioic acid <chem>NCCNC(=S)S</chem> NJGRNRAXMBFJJY-UHFFFAOYSA-N	
2-imidazoline	4,5-dihydro-1 <i>H</i> -imidazole <chem>C1 = NCCN1</chem> MTNDZQHUA FNZQY-UHFFFAOYSA-N	
2-imidazoline sulfonic acid	1 <i>H</i> -imidazole-2-sulfonic acid <chem>O=S(=O)(O)c1ncc[nH]1</chem> LYLDIIUFTYRPPK-UHFFFAOYSA-N	
<i>N</i>-formylglycine	<i>N</i> -formylglycine <chem>O=CNCC(=O)O</chem> UGJBHEZMOKVTIM-UHFFFAOYSA-N	
TDIT	2,3,7,8-tetrahydrodiimidazo[2,1- <i>b</i> :1',2'- <i>e</i>] [1,3,5]thiadiazine-5-thione <chem>S=C1N2CCN=C2SC1 = NCCN21</chem> SJPJEYGYJYODMC-UHFFFAOYSA-N	
M222F001	<i>N</i> -{[(2-oxo-1-imidazolidinyl)carbonyl] carbamoyl} glycine <chem>O=C1NCCN1C(=O)NC(=O)NCC(=O)O</chem> GBFUMICFBCUDRN-UHFFFAOYSA-N	
<i>N</i>-acetyl EDA	<i>N</i> -(2-aminoethyl)acetamide <chem>CC(=O)NCCN</chem> DAKZISABEDGGSV-UHFFFAOYSA-N	

IUPAC: International Union of Pure and Applied Chemistry; SMILES: simplified molecular-input line-entry system; InChiKey: International Chemical Identifier Key.

(a): The metabolite name in bold is the name used in the conclusion.

(b): ACD/Name 2017.2.1 ACD/Labs 2017 Release (File version N40E41, Build 96719, 6 September 2017).

(c): ACD/ChemSketch 2017.2.1 ACD/Labs 2017 Release (File version C40H41, Build 99535, 14 February 2018).