CONCLUSION ON PESTICIDES PEER REVIEW

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Peer review of the pesticide risk assessment of the active substance copper compounds copper(I), copper(II) variants namely copper hydroxide, copper oxychloride, tribasic copper sulfate, copper(I) oxide, Bordeaux mixture

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Abstract

The conclusions of the EFSA following the peer review of the initial risk assessments carried out by the competent authorities of the rapporteur Member State, France, and co-rapporteur Member State, Germany, for the pesticide active substance copper compounds 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 copper compounds as a fungicide on grapes, tomatoes and cucurbits. The reliable end points appropriate for use in regulatory risk assessment are presented. Missing information identified as being required by the regulatory framework is listed. Concerns are identified.

Keywords: copper compounds, peer review, risk assessment, pesticide, fungicide

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Summary

Commission Implementing Regulation (EU) No 844/2012 (hereinafter referred to as 'the Regulation') 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. Copper compounds are one of the active substances listed in Regulation (EU) No 686/2012.

In accordance with Article 1 of the Regulation, the rapporteur Member State (RMS), France, and co-rapporteur Member State (co-RMS), Germany, received an application from European Union (EU) Copper Task Force for the renewal of approval of the active substance copper compounds. Complying with Article 8 of the Regulation, the RMS checked the completeness of the dossier and informed the applicants, the co-RMS (Germany), the European Commission and the European Food Safety Authority (EFSA) about the admissibility.

The RMS provided its initial evaluation of the dossier on copper compounds in the renewal assessment report (RAR), which was received by EFSA on 16 December 2016. In accordance with Article 12 of the Regulation, EFSA distributed the RAR to the Member States and the applicants, EU Copper Task Force, for comments on 3 February 2017. 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 5 April 2017.

Following consideration of the comments received on the RAR, it was concluded that additional information should be requested from the applicants, and that EFSA should conduct an expert consultation in the areas of mammalian toxicology, residues, environmental fate and behaviour and ecotoxicology.

In accordance with Article 13(1) of the Regulation, EFSA should adopt a conclusion on whether copper compounds can be expected to meet the approval criteria provided for in Article 4 of Regulation (EC) No 1107/2009 of the European Parliament and of the Council.

The conclusions laid down in this report were reached on the basis of the evaluation of the representative uses of copper compounds as a fungicide and bactericide on field applications on grapes and field and greenhouse applications on tomatoes and cucurbits as proposed by the applicants. Full details of the representative uses can be found in Appendix A of this report.

Data were submitted to conclude that the representative uses of the copper compounds proposed at central and southern EU level result in a sufficient fungicidal and bactericidal efficacy against the target organisms.

A data gap was identified for a search of the scientific peer-reviewed open literature on the active substance.

Data gaps were identified in the area of identity, technical properties of some formulations and analytical methods.

In the mammalian toxicology area, a data gap was identified for toxicological information on the stabilisers used in the technical concentrates of some manufacturers. Estimated exposure of workers re-entering vineyards treated with copper-based formulations exceed the acceptable operator exposure level (AOEL); considering the results of a repeated-dose toxicity study by inhalation, special care should be given for the protection of operators applying insoluble copper-based formulations.

Regarding the residues in food commodities, data gaps were identified for residue trials compliant with good agricultural practices (GAPs) for all representative uses (grapes, tomatoes, cucurbits with edible peel and cucurbits with inedible peel). Therefore, the consumer risk assessment resulting from the representative uses could not be finalised. It is noted that an indicative consumer exposure calculated on the basis of available data and considering the background levels of copper expected in plant and livestock commodities resulted in a chronic exposure of 72.3% acceptable daily intake (ADI). In addition, the average consumer exposure resulting from copper present in drinking water was estimated at up to 15.1% of the ADI, highlighting that higher chronic exposure may occur due to higher local concentration of copper in tap water.

With respect to the fate and behaviour into the environment, the data presented consist mainly of a review of public scientific literature. Results of a review study of adsorption values for copper in European arable and grazing land soils (Janik et al., 2015) were used in the present assessment; however, a data gap was set because the original paper was not available in the dossier. Data gaps were identified for further information to update the data on speciation of copper in natural waters and to investigate if natural background levels of copper increased in European stream sediment.

In the area of ecotoxicology, data gaps were identified for further information to address the risk to birds and mammals, aquatic organisms, bees and other non-target arthropods and earthworms and other soil macro-organisms. A high risk was concluded for all the representative uses for birds and mammals, aquatic organisms and soil macro-organisms (critical area of concern).

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Background

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

In accordance with Article 13 of the Regulation, unless formally informed by the European Commission that a conclusion is not necessary, EFSA is required to adopt a conclusion on whether the active substance can be expected to meet the approval criteria provided for in Article 4 of Regulation (EC) No 1107/2009 within 5 months from the end of the period provided for the submission of written comments, subject to an extension of an additional 3 months where additional information is required to be submitted by the applicants in accordance with Article 13(3).

In accordance with Article 1 of the Regulation, the RMS, France, and co-RMS, Germany, received an application from European Union (EU) Copper Task Force for the renewal of approval of the active substance copper compounds. Complying with Article 8 of the Regulation, the RMS checked the completeness of the dossier and informed the applicants, the co-RMS, the European Commission and EFSA about the admissibility.

The RMS provided its initial evaluation of the dossier on copper compounds in the RAR, which was received by EFSA on 16 December 2016 (France, 2016).

In accordance with Article 12 of the Regulation, EFSA distributed the RAR to the Member States and the applicants, EU Copper Task Force, for consultation and comments on 3 February 2017. 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 6 April 2017. At the same time, the collated comments were forwarded to the RMS for compilation and evaluation in the format of a reporting table. The applicants were invited to respond to the comments in column 3 of the reporting table. The comments and the applicants' response were evaluated by the RMS in column 3.

The need for expert consultation and the necessity for additional information to be submitted by the applicants in accordance with Article 13(3) of the Regulation were considered in a telephone conference between EFSA, the RMS on 1 June 2017. On the basis of the comments received, the applicants' response to the comments and the RMS's evaluation thereof, it was concluded that additional information should be requested from the applicants, and that EFSA should conduct an expert consultation in the areas of mammalian toxicology, residues, environmental fate and behaviour and ecotoxicology.

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

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

A final consultation on the conclusions arising from the peer review of the risk assessment took place with Member States via a written procedure in November–December 2017.

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 copper compounds as a fungicide and bactericide on grapes, tomatoes and cucurbits, as proposed by the applicants. A list of the relevant end points for the active substance and the formulation is provided in Appendix A.

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

In addition, a key supporting document to this conclusion is the peer review report (EFSA, 2017), 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 (1 June 2017);
- the evaluation table (11 December 2017);
- the reports of the scientific consultation with Member State experts (where relevant);
- the comments received on the assessment of the additional information (where relevant);
- the comments received on the draft EFSA conclusion.

Given the importance of the RAR, including its revisions (France, 2017),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 EU, for which the applicants has not demonstrated that it has regulatory access to the information on which this conclusion report is based.

The active substances and the formulated products

The active substances are copper(I) and copper(II) ions. The variants of copper that were considered in this conclusion were copper hydroxide, copper oxychloride, Bordeaux mixture, tribasic copper sulfate and copper(I) oxide.

Copper hydroxide is the common name for copper(II) hydroxide (or copper(2+) hydroxide or cupric hydroxide) (IUPAC).

Copper oxychloride is the common name for dicopper(II) chloride trihydroxide (IUPAC).

Bordeaux mixture is a traditional mixture of copper(II) sulfate (or copper(2+) sulfate or cupric sulfate) (IUPAC) and calcium hydroxide (IUPAC) in variable proportions.

Tribasic copper sulfate or basic copper sulfate is the common name for copper(II) hydroxide sulfate (IUPAC).

Copper(I) oxide or cuprous oxide is the common name for copper(I) oxide (or copper(1+) oxide or cuprous oxide) (IUPAC).

These substances are considered by the International Organization for Standardization not to require a common name. The name used in this conclusion for the active substances was copper.

The representative formulated product for the evaluation of copper hydroxide was 'Funguran-OH 50 WP', a wettable powder (WP) containing 500 g/kg copper and for the evaluation of copper oxychloride, 'Curenox 50 WG', a water dispersible granule (WG) containing 500 g/kg copper, respectively. The representative formulated product for the evaluation of Bordeaux mixture was 'Poltiglia Caffaro 20 DF New', a WG containing 200 g/kg copper, while for the evaluation of tribasic copper sulfate 'Cuproxat SC', a suspension concentrate containing 190 g/L copper. The representative formulated product for the evaluation of copper(I) oxide was 'Nordox 75 WG', a WG containing 750 g/kg copper.

The representative uses evaluated were spray applications for the control of *Plasmopara viticola, Elsinoë ampelina* and bacterial necrosis in grapes, spray applications for the control of various fungal and bacterial diseases in field and protected tomatoes and cucurbits in the central and southern European zones as defined by the Regulation (EC) No 1107/2009. Full details of the good agricultural practices (GAPs) can be found in the list of end points in Appendix A.

Data were submitted to conclude that the representative uses of the copper compounds proposed at central and southern EU level result in a sufficient fungicidal and bactericidal efficacy against the target organisms, following the guidance document SANCO/2012/11251-rev. 4 (European Commission, 2014).

A data gap has been identified for a search of the scientific peer-reviewed open literature on the active substance, dealing with side effects on health, residues 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).

A comprehensive review of data and of knowledge available on various aspects of copper (eco)toxicity and environmental fate and behaviour was provided in the dossier and thoroughly reviewed in the RAR and during the peer review. Various aspects of the environmental risk assessment

of copper compounds were discussed at the Peer Review experts' meetings; however, the available data resulted as not sufficient to fully address the specificity of copper (e.g. adsorption behaviour, bioavailability, essentiality and homeostasis) in the context of the environmental risk assessment. It is noted that the available guidance in the area of pesticide active substance environmental risk assessment do not specifically cover metal compounds. Nonetheless, the available data on copper compounds were assessed and considered for their merits in the light of the currently available methodologies and knowledge taking into considerations the specific characteristics of copper.

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/10597/2003-rev. 10.1 (European Commission, 2012) and SANCO/825/00-rev. 8.1 (European Commission, 2010).

The proposed specifications for the five copper compounds are based on batch data from industrial scale production.

Copper hydroxide technical material is produced by eight manufacturers with different minimum purities. The minimum purities of copper hydroxide technical materials manufactured by Albaugh, Cinkarna, IQV, Isagro, Kocide, Nufarm, Saldeco and Spiess-Urania are 609 g/kg, 616 g/kg, 625 g/kg, 593 g/kg, 618 g/kg, 609 g/kg, 584 g/kg and 583 g/kg, respectively, all expressed as total copper content. All technical materials are meeting the requirements of the FAO specification AGP:CP/362 (1998) developed under the old procedure with minimum purity of 573 g/kg.

Copper oxychloride technical material is produced by nine manufacturers with different minimum purities. The proposed minimum purities of copper oxychloride technical materials manufactured by Albaugh, Cinkarna, IQV, Isagro, Manica, Montanwerke, Prince Erachem and Saldeco Spiess-Urania are 571 g/kg, 577 g/kg, 575 g/kg, 570 g/kg, 577 g/kg, 569 g/kg, 573 g/kg, 581 g/kg and 579 g/kg, respectively, all expressed as total copper content. All technical materials are meeting the requirements of the FAO specification AGP: CP/251 (1991) for copper oxychloride (44.2Oxch/TC/S, 1989) developed under the old procedure with minimum purity of 550 g/kg.

Bordeaux mixture is produced by five manufacturers with different minimum purities. The minimum purities of Bordeaux mixture manufactured by IQV, Isagro, Manica, Saldeco and UPL are 263 g/kg, 263 g/kg, 270 g/kg, 276 g/kg and 257 g/kg, respectively, all expressed as total copper content. All technical materials are meeting the requirements of the FAO specification AGP:CP/251 (1991) for copper sulfate (44.2s/TC/S, 1989) developed under the old procedure with minimum purity of 250 g/kg.

It should be noted that the specification for Bordeaux mixture is based on the formulae without the water contribution.

Tribasic copper sulfate is produced by five manufacturers with different minimum purities. The minimum purities of tribasic copper sulfate technical material manufactured by Albaugh, Cinkarna, Manica, Nufarm and UPL are 518 g/kg, 540 g/kg, 530 g/kg, 543 g/kg (dry weight basis) and 490 g/kg, respectively, all expressed as total copper content. It should be noted that Nufarm is manufacturing a technical concentrate (TK) with minimum purity of 324 g/kg expressed as total copper content. There is no FAO specification for basic copper sulfate.

The minimum purity of copper(I) oxide technical material manufactured by Nordox is 858 g/kg as total copper content. The technical material is meeting the requirements of the FAO specification AGP: CP/251 (1991) for cuprous oxide (44.lox/TC/S, 1989) developed under the old procedure with minimum purity of 820 g/kg.

In all technical materials of copper hydroxide, copper oxychloride, Bordeaux mixture, tribasic copper sulfate and copper(I) oxide the following: cobalt, mercury, chromium, antimony are considered relevant impurities with maximum content of 3 mg/kg, 5 mg/kg, 100 mg/kg and 7 mg/kg, respectively, while arsenic, cadmium, lead and nickel are considered relevant impurities with maximum 0.1 mg/g, 0.1 mg/g, 0.3 mg/g and 1 mg/g of the Cu content, respectively. The specifications for the As, Cd and Pb content are meeting the requirements of the FAO specifications AGP:CP/362 and AGP:CP/251.

As new relevant impurities were defined in comparison to the first approval and, as the original reference specifications are not reflected by manufacturing data and no information on the

toxicological batches are available, it is proposed to update the reference specifications for all five copper compounds.

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 copper hydroxide, copper oxychloride, Bordeaux mixture, tribasic copper sulfate and copper(I) oxide or the representative formulations. Data gaps were, however, identified for the MSDS of starting materials, for spectroscopic characterisations by infrared (IR) and X-ray diffraction of the batches of copper hydroxide, copper oxychloride and copper sulfate, and some additional confidential information concerning the batches, including specification, all relevant to Albaugh. Data gaps were also identified for persistent foam at the maximum use concentration after 2 years shelf life for Curenox 50 WG, for suspensibility and wet sieve test during low temperature storage for Cuproxat SC. The main data regarding the identity of copper hydroxide, copper oxychloride, Bordeaux mixture, tribasic copper sulfate and copper(I) oxide and their physical and chemical properties are given in Appendix A.

Adequate methods are available for the generation of preapproval data required for the risk assessment. Methods of analysis are available for the determination of the active substance and relevant impurities in the technical materials and for the determination of the active substance in the representative formulations. The methods are suitable for total copper determination but not specific to each copper variant. It is agreed that the active substance is determined as total copper, while the identity of variant is determined by spectroscopic characterisations. The total amount of the variant is then calculated stoichiometrically. Data gaps were identified for a selective method for the determination of copper in Cuproxat SC and for analytical method(s) for the determination of the relevant impurities in the representative formulations.

Copper residues can be determined in food and feed of plant origin by atomic absorption spectroscopy (AAS) with a limit of quantification (LOQ) of 0.2 mg/kg in commodities of high water and high acid content. Data gaps were identified for additional validation data for oily and dry commodities and for an ILV for plants. It should be noted that an internationally recognised standard method for copper analysis in plant matrices exists (EN 13805); however, no performance characteristics for the method were provided. The EN 14082 method using AAS can be used for the determination of copper in foodstuff of animal origin; however, no performance characteristics for the method were provided. It should be noted that for the representative uses evaluated, there is no need for monitoring methods in animal matrices. Adequate analytical method using ICP-AES exists for the determination of total copper in soil with a LOQ of 5 mg/kg. An analytical method using ICP-MS is available for the determination of dissolved copper in surface water with a LOQ of 0.3 μg/L; however, this LOQ does not comply with the ground water directive which requires a limit of 0.1 μg/L for pesticides. As a consequence additional validation, data are required and a data gap was identified also for an ILV for drinking water. Copper residues in air can be determined by ICP-OES with a LOQ of 0.3 ng/m^3.

An ICP-AES method exists for the determination of copper in body fluids and tissues with a LOQ of 3 mg/kg in plasma and a LOQ of 359 mg/kg in liver, respectively.

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), Guidance on dermal absorption (EFSA PPR Panel, 2012) and Guidance on the Application of the CLP Criteria (ECHA, 2015).

Copper (I) and (II) variants were discussed during the Pesticides Peer Review Meeting 168 in October 2017.

No analysis of the impurity profile of the batches used in the toxicological studies is available; however, apart from heavy metals, which are relevant impurities and for which maximum levels have been established (see Section 1), no concern is identified. Some manufacturers include stabilisers in the technical concentrate material of copper hydroxide, copper oxychloride, tribasic copper sulfate, and copper I oxide and toxicological information has not been provided on these chemicals (data gap).

Copper has been the subject of extensive research. It is widely distributed in biological tissues, where it occurs largely in the form of organic complexes, many of which are metalloproteins and function as enzymes. Copper enzymes are involved in a variety of metabolic reactions, such as the utilisation of oxygen during cell respiration and energy utilisation. They are also involved in the synthesis of essential compounds, such as neurotransmitters and complex protein of connective tissues of the skeleton and blood vessels.

Copper is present in almost all foods, most human diets naturally include between 1 and 2 mg person per day of copper. Copper levels in blood and tissues are generally stable; the body is able to maintain a balance of dietary copper intake and excretion that allows normal physiological processes to take place. Up to 93% of the copper in the blood is bound to the enzyme caeruloplasmin, while the majority of the rest is bound to albumin and amino acids, there is strong evidence that absorbed copper is never released free in the blood or in the cells.

A bioequivalence study was performed to compare the five variants of copper, copper hydroxide, copper oxychloride, Bordeaux mixture, tribasic copper sulfate and copper (I) oxide with copper sulfate pentahydrate on bile-cannulated rats demonstrating that toxicological studies on copper sulfate could be used in the toxicological risk assessment of the five variants. Absorption, distribution and excretion rates were similar between the six variants of copper following oral ingestion of 20 mg Cu/kg body weight (bw); liver is the principal organ of regulation of copper, and main excretion occurs via the bile. Liver copper levels increase significantly following dosing with T_{max} at 12 h; depuration is rapid, with levels returning to control by 48 h after dosing. These findings were consistent with the homeostatic bioregulation of copper found in the open literature.

Oral absorption of copper varies according to the copper content of the diet between 12% and 56%. In rats, 50% oral absorption was established. During the previous assessment, oral absorption of copper was established at 36% for humans with a copper-adequate diet. The EFSA NDA Panel reviewed the data in 2015 and the Panel considered that absorption of copper from a mixed diet is around 50% (EFSA NDA Panel, 2015); the peer review experts agreed with this assessment and this value has been used to derive the acceptable operator exposure level (AOEL). Distribution occurs directly from the intestine to the liver, which controls the distribution of copper to the rest of the body via the bloodstream, bound to caeruloplasmin. Metabolism does not occur. Copper does not accumulate, except in cases of genetic disease or chronic administration of high doses, where copper accumulates in the liver. Excretion is rapid, via the bile, in a trypsin-independent protein fragment; therefore, enterohepatic circulation does not occur. Significant amounts of copper are excreted bound to metallothioneins contained in intestinal brush border cells, sloughed off and lost in faeces; minor amounts are also excreted in urine and from skin and hair.

Acute toxicity studies were conducted on the different copper (I) and (II) variants, leading to different classifications regarding oral or inhalation toxicity, some variants showing potential to cause serious eye damage as reported in Appendix A (harmonised classification according to Reg. (EC) 1272/2008[3]) (ECHA, 2014a–e). Target organs of excess of copper intake are the liver (inflammation), kidneys (histopathological changes) and hyperplasia and hyperkeratosis of the stomach and haematological changes in rats, while mice are less sensitive, showing adverse effects only in the stomach. Dogs accumulate copper more easily than other species and are considered less relevant for the human risk assessment. The relevant short-term no observed adverse effect level (NOAEL) is 16 mg Cu/kg bw per day from the rat 90-day study. A 28-day toxicity study by inhalation in rats performed with cuprous oxide did not evidence systemic toxicity up to the highest dose level of 2 mg Cu/m^3; however, a no observed adverse effect concentration (NOAEC) for local effects was established at 0.2 mg Cu/m^3 based on a pattern of responses observed in the lung and lung-draining lymph nodes typical from inhalation of poorly soluble aerosol particles. These results indicate that special care should be given for the protection of operators applying insoluble copper-based formulations.

Equivocal results obtained in chromosome aberration tests *in vivo* with copper compounds may reflect the potential oxidative damage to DNA if the robust homeostatic mechanisms are overwhelmed. Under normal uses, copper is unlikely to be genotoxic; no potential for carcinogenicity was seen in rats. No adverse effects were observed on the reproduction or fertility in rats upon oral administration of copper. Developmental effects were observed in mice (decreased foetal weight, increased foetal mortality and incidence of abnormalities) and to a lower extent in rabbits (increased incidence of supernumerary ribs) at maternal toxic doses in rabbits (inappetence, initial body weight loss and lower mean weight gain, gastrointestinal disturbance).

In case of physiological (genetic) dysfunction in human, two diseases may occur in man, namely Wilson's disease and Menkes' disease which are well documented in the medical literature. For both diseases, the copper accumulation causes different effects including neurological ones (e.g. degeneration basal ganglia, mental retardation, seizures). In genetically normal humans and in normal

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

laboratory animals, the natural homeostatic mechanisms that regulate copper prevent any accumulation in brain and neural tissues so that copper does not show a neurotoxic potential. No evidence of immunotoxicity or endocrine disruptive potential has been observed at realistic levels of copper exposure. In addition, copper variants are not classified or proposed to be classified as toxic for reproduction category 2 or carcinogenic category 2, in accordance with the provisions of Regulation (EC) No 1272/2008, and therefore, the conditions of the interim provisions of Annex II, point 3.6.5 of Regulation (EC) No 1107/2009 concerning human health for the consideration of endocrine disrupting properties are not met. A possible causative link between disturbed copper homeostasis and Alzheimer Disease pathology in humans has been hypothesised but could not be substantiated. The condition known as Vineyard Sprayer's Lung (VSL) is characterised by lung lesions and hepatic changes. Most of the published findings date back to the 1970s and 1980s. This condition was linked mostly to onsite preparation of Bordeaux mixture, as a copper sulfate solution neutralised with hydrated lime, and to application techniques at higher rates than those used in modern agriculture. Some of the papers were compromised because the authors did not adequately describe the smoking habits of the subjects; however, there were indications of adverse effects in users of Bordeaux mixture that were exacerbated by smoking. Data on humans show that repeated long-term intakes greater than 30 mg/day are toxic, intakes between 10 and 30 mg/day are without ill-effect, and that intakes of up to 10 mg/day do not even challenge the homeostatic mechanisms.

The acceptable daily intake (ADI)[4] of copper previously established (EFSA, 2008) has been confirmed at 0.15 mg Cu/kg bw per day, in line with the values established by the WHO for copper upper level intake (WHO, 1996) based on human data for infants (adults: 0.2 mg Cu/kg bw per day and infants: 0.15 mg Cu/kg bw per day). This value is supported by animal data (90-day rat study) with a NOAEL of 16 mg Cu/kg bw per day; applying a standard uncertainty factor (UF) of 100. Copper is an essential trace element, and it was noted that an upper limit for copper as a nutrient had been established in an opinion of the EU Scientific Committee for Food (SCF, 2003), based on a NOAEL of 10 mg Cu/day value but adding an uncertainty factor of 2, resulting in a proposed tolerable upper intake level of 5 mg Cu/day for adults (corresponding to half of the ADI currently set in the pesticides area). This approach was considered by the Peer Review in 2008 as inadequate for setting an ADI in the area of pesticides (France, 2007a,b). It was considered at that moment that there is greater risk of health effects from deficiency of copper intake than from excess of copper intake (WHO, 1998), there is no evidence of significant variability within humans and the additional uncertainty factor does not take into consideration the natural homeostatic mechanisms that regulate copper. During the current Peer Review, the experts have confirmed the previous assessment, and no changes in the ADI are proposed.

An AOEL of 0.072 mg Cu/kg bw per day had previously been established based on the WHO data for adults (adults: 0.2 mg Cu/kg bw per day) without the use of a safety factor, but considering a correction for limited oral absorption of 36%. The upper limit to the safe range of oral intake for infants (0.15 mg Cu/kg bw per day) is considered more appropriate to derive the AOEL and the oral absorption value has been revised according to the EFSA NDA opinion on Dietary Reference Values for copper (EFSA NDA Panel, 2015) at 50% resulting in an AOEL of 0.075 mg Cu/kg bw per day; the value is rounded to 0.08 mg Cu/kg bw per day.

The setting of an acute reference dose (ARfD) – as previously agreed (EFSA, 2008) – or an acute acceptable operator exposure level (AAOEL) was not deemed necessary.

Non-dietary risk assessment has been provided for the five representative formulations separately. Overall, for most representative formulations, personal protective equipment (PPE) has to be worn by operators applying copper-based formulations on grapes and tomatoes (indoor and outdoor) to ensure that the AOEL is not exceeded. Workers re-entering tomatoes fields have also to use PPE (workwear and gloves) to ensure that the AOEL is not exceeded, but worker exposure from re-entering vineyard treated with copper exceeds the AOEL even when PPE is worn. Estimated bystander and residential exposure do not exceed the AOEL according to the models proposed; it is noted that residents (child) exposure may exceed the AOEL already after three applications in grapes and 21 days interval or eight applications in grapes and 7 days interval according to the EFSA calculator.

Regarding the search for published open literature, a more detail assessment is needed, such as the criteria used for assessing the relevance and reliability of the retrieved publications.

[4] It should be noted that it was felt by the experts that the term 'ADI' was not fully adequate to copper as a micronutrient essential for life; the term 'upper limit' used in the nutrient area would be more appropriate; therefore in the specific case of copper, the ADI is considered equivalent to an UL.

3. Residues

The assessment in the residue section is based on the OECD guidance document on overview of residue chemistry studies (OECD, 2009), the OECD publication on maximum residue level (MRL) calculations (OECD, 2011), the European Commission guideline document on MRL setting (European Commission, 2011).

Copper compounds were discussed at the Pesticides Peer Review Meeting 167 in October 2017. Specific studies investigating metabolism and distribution of residues in plants following the foliar application of copper are not available. However, the public scientific literature reported by the RMS provided enough information on the uptake, translocation and effects of copper in plants. In plants, copper is absorbed from soil through the roots. From the roots, copper is transported in the sap to the rest of the plant. Upon foliar application, transportation and distribution of copper in plants are limited. The experts agreed to consider copper as a non-systemic-like compound. Copper is a monoatomic element and therefore is considered inherently stable. As no metabolites are expected, the nature of residues in primary crops, rotational crops and processed commodities as well as its stability during storage are considered addressed and specific studies were not required. The relevant residue for monitoring and risk assessment was defined as total copper, including copper residues arising from all variants of copper. This residue definition is expected to cover copper residues arising from all variants of copper (see Section 1) because the analytical methods for enforcement convert them into mineral copper.

Residue trials investigating the magnitude of residues in primary crops were reported for grapes, tomatoes, cucurbits with edible peel and cucurbits with inedible peel. However, GAP compliant trials were only identified for the indoor GAP on cucurbits with inedible peel. Furthermore, as only six residue trials were available to support this GAP, two additional trials supporting the indoor GAP on cucurbits with inedible peel were identified as a data gap. Full data packages supporting the critical GAPs for grapes (northern Europe (NEU) and southern Europe (SEU)), tomatoes (NEU, SEU and indoor), cucurbits with edible peel (NEU, SEU and indoor) and cucurbits with inedible peel (NEU and SEU) were also identified as data gaps. In addition, although no residues higher than the copper background levels are expected in grapes for the less critical GAP with application before flowering, this assumption should be confirmed by residue trials. Therefore, residue trials supporting the GAP on grapes with preflowering applications were also identified as a data gap.

A data gap has been identified for further information on residue levels in pollen and in bee products for human consumption resulting from residues taken up by honeybees from crops at blossom.

Studies investigating the magnitude of residues in processed commodities allowed deriving robust processing factors for peeled melons as well as for processed commodities of tomatoes (washed and canned), wine grapes (must, juice, wine, wet pomace), table grapes (raisins) and cucumber (washed).

Copper is a natural element and is also present in soil. It is an essential nutrient for plant growth development, and therefore, all soil-grown crops may contain copper, including the crops that are not supposed to undergo pesticide treatments with copper (off-label crops). Based on the scientific literature, the experts agreed that plant would not absorb more than the essential nutritional amount. Therefore, field trials on rotational crops were not deemed necessary and a comprehensive survey on the copper background levels in plant commodities was used as a surrogate to assess the residue levels in all off-label crops (including rotational crops).

As none of the crops of the representative use is expected to be fed to livestock, further investigation on the nature and magnitude of residues in animal commodities was not triggered in this assessment.

Considering the major data gaps identified for grapes, tomatoes, cucurbits with edible peel and cucurbits with inedible peel, the consumer risk assessment resulting from the representative uses could not be finalised. An indicative calculation considering the median background levels for grapes and the supervised trials median residue (STMR) for cucurbits with inedible peel was performed by the RMS. This calculation was updated by EFSA considering the robust peeling factor derived for all cucurbits with inedible peel and resulted in a chronic exposure of 3.5% of the ADI (FR all population). It is noted that acute exposure calculations were not carried out because an ARfD was not deemed necessary for copper.

The RMS performed a second exposure calculation to consider the endogenous levels of copper present in all other plant commodities (including rotational crops) as well as in animal commodities. It is noted that although not triggered under this review, the assessment of residues in animal

commodities based on the background levels was performed in the framework of the MRL review under article 12 of Regulation 396/2005. The calculation of the RMS was slightly amended by EFSA considering a consolidation of the calculation for the medians derived from the background levels in plants and the assessment of residue levels in livestock performed in the MRL review. In this scenario, the highest chronic exposure was calculated for the WHO Cluster diet B representing 72.3% of the ADI. This result was approved by the experts and was found consistent with the outcome of a previous EFSA opinion on dietary reference values for copper (EFSA NDA Panel, 2015). In this opinion, the highest average dietary intake of copper was estimated at 0.099 mg/kg bw per day (i.e. 0.50 mg/kg bw per day for infants of 5 kg), equivalent to 66% of the ADI.

In addition to food of plant and animal origin, the consumer exposure that would result from copper present in drinking water was also estimated. The calculated exposures range between 0.62% and 15.1% of the ADI when considering median and average concentrations of copper in tap water and the water consumption data recommended by the WHO. Reference was also made to EFSA NDA Panel opinion (2015) where the average copper intake associated to water and water-based beverages was estimated up to 0.008 mg/kg bw per day (equivalent to 5.4% of the ADI). However, it was stressed by the experts that the above figures do not consider possible higher chronic exposures which may be due to higher local concentration of copper in tap water.

4. Environmental fate and behaviour

Copper compounds were discussed at the Pesticides Peer Review TC 152 in October 2017.

The data presented in the dossier and summarised in the RAR on the fate and behaviour of copper in soil consist mainly of a review of public scientific literature.

Copper is an element and therefore cannot be degraded. In soil, copper is present in a number of forms partitioned between soil and solution. The mobile substance is primarily Cu^{2+} ion present in the soil solution. The amount of Cu^{2+} ion in the soil solution is controlled primarily by pH and the amount of dissolved organic carbon in the soil.

According to Commission Regulation 2015/232/EC, a review of European monitoring programmes was provided and used to identify 'background levels' of copper present in soil from natural or anthropogenic sources other than the regulated use for the soil exposure assessments. Considering the representative uses 'background levels' used in the present assessment were 160 mg Cu/kg soil (90^{th} percentile) for grape and 26 mg Cu/kg soil (90^{th} percentile) for tomatoes and cucurbits.

From the results of a study of adsorption in European arable and grazing land soils (Janik et al., 2015), that were presented in the RAR, it was indicated that copper exhibited medium mobility to immobility in soil. It was concluded that the adsorption of copper was pH dependent. However, the original paper by Janik et al. (2015) and the clarification on the results of individual soils were not available in the dossier; therefore, a data gap was set (see Section 7).

New Predicted environmental concentration (PEC) in soil (PEC_{soil}) calculations were provided respect to the ones presented in the confirmatory data (EFSA, 2013a). Calculations were based on the assumption of no degradation, no crop interception, even distribution of copper in upper 5 cm soil layer for the uses in grapes and 20 cm for the uses in tomatoes and cucurbits, and following a single seasonal application. The flexible dosing regimen proposed for grapes, for which the amount of copper applied must not exceed 30 kg/ha in total in any rolling year was also taken into account. In order to reflect the influence of the long-term use of copper, different 'background levels' derived for European arable and vineyard soils were considered in the calculation of accumulation of total copper based on 10-year application. More detail on the different 'background levels' can be found in Appendix A.

Although unable to degrade, in aquatic systems, copper is able to react with a wide range of materials, and then, it is rapidly bound to minerals, precipitated as insoluble inorganic salts, or bound to organic matter. Dissipation in aqueous phase based on total copper concentrations in a microcosm study ranged from 4 to 30.5 days. At the highest concentrations in the microcosm study, DT_{50} values were around 1 day, while at lower concentrations, no changes in free cupric ion concentrations were observed, indicating $DT_{50} << 1$ day. Due to this very rapid dissipation of copper (Cu^{2+} ions) from surface waters, it was considered that the single application scenario represents the worst-case for the exposure assessment. The majority of copper in the sediment was found to be bound to solid matter. Additionally, some scientific literature studies were presented, in which both speciation of copper and solubility of copper in water were investigated. However, no further information was provided to update information describing the speciation of copper in natural waters; therefore, a data gap was set.

The necessary surface water and sediment exposure assessments (PEC calculations) were carried out for copper using the FOCUS (FOCUS, 2001) Step 1 and Step 2 approach (version 3.1 of the Steps 1–2 in FOCUS calculator). It was agreed to use the geomean K_{doc} value (Janik et al., 2015) derived for soil pH range 5.5–6.5 (in $CaCl_2$ solution). Furthermore, a $DegT_{50}$ for the water/sediment of 1000 days was used to reflect the non-transformation of an inorganic compound.

First, partial PEC in surface water (PEC_{sw}) were calculated considering all entry routes to water bodies and no crop interception. In order to consider mitigation measures, PEC_{sw} were calculated considering:

- only run-off and drainage (using no spray drift option) and applying 90% mitigation measures (20 m vegetative buffer zone).
- only spray drift and applying spray drift mitigations up to 95% (20 m no-spray buffer zone).

These PEC_{sw} obtained applying mitigation measures were summed in order to derive the final PEC results from all entry routes to water bodies that introduced the maximum mitigation agreed in FOCUS Landscape and mitigation (FOCUS, 2007) guidance.

For indoor uses in tomatoes and cucurbits, PEC_{sw} via spray drift were calculated using a drift percentage of 0.1%.

The PEC in sediment (PEC_{sed}) accumulation for total copper over a period of 10 years via spray drift and run-off/drainage were calculated following the representative uses with a K_{doc} worst-case default value of 10,000 mL/g and adding a value of 17 mg/kg (median) as background level of copper in sediment coming from the available monitoring data. In addition, no-spray drift buffer zones of up to 20 m were used to cover drainage situations (representing a 90% spray drift reduction) and combined no-spray buffer zones with vegetative buffer strips of up to 20 m (reducing solute flux in run-off by 80% erosion runoff by 95%) being used for calculations to cover run-off situations. However, no further information was provided in order to investigate if natural background levels of copper increased and consequently to assess the relevance of the median concentrations of copper in European stream sediment; therefore, a data gap was set.

The necessary groundwater exposure assessments were carried out using FOCUS (FOCUS, 2009) scenarios and the models PEARL 4.4.4 and PELMO 5.5.3 for total copper. 'Background levels' of copper were added to the top soil for all representative uses in the first year. A DT_{50} value of 1,000,000 days was used in order to reflect the persistence of copper in soil. Simulations were carried out using the standard approach for implementing adsorption reduction with depth based on organic carbon as defined for the FOCUS scenarios. As there were indications that adsorption might be pH dependent, it was agreed to use a geometric mean K_{doc} value calculated from soils in the $pH_{(CaCl2)}$ range 4–5. Considering the flexible dosing regimen proposed for grapes for which the amount of copper applied must not exceed 30 kg/ha in total in any rolling year, the maximum annual cumulative applied rate of 6,000 g copper/ha/year was used for the present assessment. The potential for groundwater exposure from the representative uses by the copper compounds above the parametric drinking water limit of 0.1 μg/L for pesticides was concluded to be low in geoclimatic situations that are represented by all nine FOCUS groundwater scenarios.

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

A case was made to address the effect of water treatments processes on the nature of the residues that might be present in surface water and groundwater, when surface water or groundwater is abstracted for drinking water, and it was concluded that drinking water treatments have no significant effects on copper speciation, and therefore, the consumer risk from the consumption of drinking water is low.

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 (2013b).

Several aspects of the risk assessment were discussed at Pesticides Peer Review Meeting 169 (9–10 October 2017).

It is noted that the representative uses on tomatoes and cucurbits included greenhouse uses. It cannot be excluded that these representative uses included uses in non-permanent greenhouse; the risk assessment was performed accordingly.

The Tier I acute and long-term risk assessment to **birds and mammals** was indicated as high for all the representative uses. As risk refinement, position papers were provided where a Weight of

Evidence (WoE) approach was presented to support a homeostatic mechanism in birds and mammals. The WoE was discussed at the Pesticides Peer Review Meeting 169; the experts considered the evidence provided as not satisfactory to exclude the acute risk to birds and mammals. Furthermore, the experts concluded that the data from the wildlife reports which were part of the evidence provided along with information of bird population (e.g. abundance and density), may be indicative of the absence of incidents but not sufficient to address the acute risk identified. The experts concluded that the WoE could be considered acceptable for addressing the long-term risk to birds and mammals for application rate up to 5 kg a.s./ha; however, further data were considered necessary to draw a conclusion covering all the feeding guild categories, i.e. omnivorous and frugivorous birds and large herbivorous and frugivorous mammals (data gap). By generating further data, the experts considered it useful to focus on, e.g. further investigation of the avoidance and further data on residue in food items.

A low risk was concluded for secondary poisoning and from consumption of contaminated water.

The end points to be used in the risk assessment for **aquatic organisms** (including sediment dwellers) were discussed at the Pesticide Peer Review meeting 169. The experts agreed that the Tier 1 risk assessment for aquatic organisms should be performed using the end point expressed as dissolved copper. During the experts' meeting, the use of the Biotic Ligand Model for the normalisation of the end points to be used in the risk assessment was discussed. Overall, the experts recognised the relevance of this model; however, uncertainties were raised (i.e. parametrisation of the model, lack of validation at EU level), and therefore, the model was not further considered in the assessment. At Tier 1 level, a high risk to aquatic organisms was concluded for all the representative uses. Refined end points based on species sensitivity distribution were available for both the acute and chronic risk assessment for fish and were discussed and agreed in the Pesticide Peer Review meeting 169. It is noted that during the Pesticides Peer Review TC 152 (Environmental fate and behaviour), it was agreed that total or dissolved copper might be considered as equivalent; the species sensitivity distribution (SSD) were built using data expressed both as total and dissolved copper pending on how the studies had been designed and reported. Using these refinements in the risk assessment, a high acute and chronic risk to fish was still concluded for all the representative uses (data gap). With respect to algae and aquatic invertebrates, a microcosm study was available. The experts at the Pesticide Peer Review meeting 169 agreed to use the end point derived from this study (ETO-RAC) together with an assessment factor of 2. Using this refinement, a high risk to algae and aquatic invertebrates was concluded for the uses on grapes (data gap) whilst a low risk was concluded for the uses on tomatoes and cucurbits in field (provided that mitigation measures are considered) and greenhouse. The risk assessment for sediment dwellers was discussed at the Pesticide Peer Review meeting 169, considering that end points were available for six different species, in line with EFSA PPR Panel (2015), the experts agreed to lower the assessment factor for the sediment to 5. Considering the agreed assessment factor in the risk assessment, a high risk to sediment dwellers (exposure via sediment) was still concluded for all the representative uses (data gap).

Acute oral and contact toxicity tests on **honeybees** were performed with the representative formulations and only hazard quotient (HQ) values according to the European Commission (2002a) were calculated (data gap). The HQ value calculated for the worst-case scenarios (1.25 kg a.s./ha) indicated a high oral and contact risk for some formulations. The values were not calculated for each single representative use. Chronic and larvae end points were not available (data gap). A tunnel test already considered with the confirmatory data (European Food Safety Authority, 2013a) was available where a statistically significant reduction is observed for flight intensity at the highest dose tested (2500 g Cu/ha). Data from literature provided by the applicants indicated that, chronic exposure of copper via feeding of copper solutions as an anti-varroa treatment in hives did not show adverse effects on bees at dose similar to the current apiculture practices (1–2 g Cu/L preparation). Overall, with the available data, it was not possible to draw a conclusion on various aspects of the risk assessment to bees.

Tier 1 data and extended laboratory studies with the standard species and additional species of **non-target arthropods** were available for all the representative formulations. The use of Multiple Application Factor (MAF_{soil}) for BBCH <20 was discussed at the Peer Review experts' meeting 169. Considering the available evidence showing that copper accumulates in soil, the experts did not consider the use of the MAF as appropriate. In light of this, low risk for non-target arthropods was concluded for Bordeaux mixture (Poltiglia Caffaro 20 DF New) and Copper (I) oxide (Nordox 75) for all the representative uses. High risk was concluded for all the representative uses of copper hydroxide (Funguran-OH), copper oxychloride (Curenox 50) and tribasic copper sulfate (Cuproxat SC) (data gap).

Several chronic laboratory studies were available on **earthworms** and **other soil macro-organisms**. High risk was concluded for soil organisms at Tier 1 level. Approaches for refining the risk such as the geometric mean calculated when more than one study was available on the same species and the SSD were discussed at the Peer Review experts' meeting 169. Overall, the experts did not support the geometric mean considering the variability in the different study designs (e.g. duration of the exposure, type of end point). The SSD, although could be, in general, a powerful tool for soil organisms, was not agreed upon because of the lack of a suitable guidance recommending this type of refinements in combination with a proper assessment factor.

A multiyear field study was available to further refine the risk to earthworms. The study was performed in two sites in Germany, on grassland with three different application rates (4, 8, 40 kg a.s./ha). A NOAEC at 4 kg a.s./ha was derived from this study considering the transient effects on abundance and biomass of earthworms. Consequently, low risk was only concluded for the use on grapes up to an application rate of 3.75 kg/ha/year for all the assessed copper compounds (data gap).

No suitable refinements of the Tier 1 risk were available for soil macro-organisms. The proposal for extrapolating the results of the multiyear field study with earthworms to other soil macro-organisms was not supported by the experts at the Peer Review experts' meeting 169, although the available laboratory data seem to show that earthworms are more sensitive than other soil macro-organisms (data gap).

A data gaps were identified for the extended summary of the study Menezes Oliveiras et al., 2013 and for a certified translation of Strumpf et al., 2015, both studies may include relevant information pertaining soil organisms.

Low risk to **soil microorganisms** and **biological methods of sewage treatment** were concluded.

For **non-target terrestrial plants**, a low risk at Tier 1 level was concluded for all the representative uses without mitigation measures.

With regard to the endocrine disruption potential, as discussed in Section 2, it is unlikely that copper compounds are an endocrine disruptor in mammals. The same conclusion could be drawn for other non-target organisms though specific data were not available.

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
Total copper	No degradation and limited dissipation.	High risk

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
Total copper	Medium mobility to immobile K_{doc} 350–1062833 mL/g	No	Yes	Yes

(a): FOCUS scenarios or relevant lysimeter.

Table 3: Surface water and sediment

Compound (name and/or code)	Ecotoxicology
Total copper, dissolved copper	High risk to surface water and sediment organisms

Table 4: Air

Compound (name and/or code)	Toxicology
Total copper as copper hydroxide	Rat LC_{50} inhalation = 0.45 mg/L air (whole body); H330, 'Fatal if inhaled'
Total copper as copper oxychloride	Rat LC_{50} inhalation = 2.83 mg/L air (nose only); H332, 'harmful if inhaled'
Total copper as Bordeaux mixture	Rat LC_{50} inhalation = 1.97 mg/L air (whole body); H332, 'harmful if inhaled'
Total copper as tribasic copper sulfate	Not feasible
Total copper as copper (I) oxide	Rat LC_{50} inhalation = 2.92 mg/L air (nose-only); H332, 'harmful if inhaled'

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).

7.1. Data gaps identified for the representative uses evaluated

- A search of the scientific peer-reviewed open literature on the active substance dealing with side effects on health, residues 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 all representative uses evaluated; submission date proposed by the applicants: unknown).
- MSDS of starting materials (relevant for the representative uses evaluated for Albaugh, submission date proposed by the applicants: unknown; see Section 1).
- Spectroscopic characterisations by IR and X-ray diffraction of the batches of copper hydroxide, copper oxychloride and copper sulfate (relevant for the representative uses evaluated for Albaugh, submission date proposed by the applicants: unknown; see Section 1).
- Five-batch data of copper hydroxide for two relevant impurities and two compounds used as starting materials (relevant for the representative uses evaluated for Albaugh, submission date proposed by the applicants: unknown; see Section 1).
- Five-batch data of copper oxychloride and tribasic copper sulfate for two relevant impurities and the number of expected crystallisation water for tribasic copper sulfate, analytical closure of batches of copper oxychloride (relevant for the representative uses evaluated for Albaugh, submission date proposed by the applicants: unknown; see Section 1).
- A selective method for the determination of copper in Cuproxat SC (relevant for the representative uses evaluated for Cuproxat SC, submission date proposed by the applicants: unknown; see Section 1).
- Persistent foam at the maximum use concentration after 2 years shelf life for Curenox 50 WG (relevant for the representative uses evaluated for Curenox 50 WG, submission date proposed by the applicants: unknown; see Section 1).
- Suspensibility and wet sieve test during low temperature storage for Cuproxat SC (relevant for the representative uses evaluated for Cuproxat SC, submission date proposed by the applicants: unknown; see Section 1).
- Analytical method(s) for the determination of the relevant impurities in the representative formulations (relevant for all the representative uses evaluated, submission date proposed by the applicants: unknown; see Section 1).
- Additional validation data for the plant residue method for oily and dry commodities (relevant for all the representative uses evaluated, submission date proposed by the applicants: unknown; see Section 1).
- ILV for the plant residue method (relevant for all the representative uses evaluated, submission date proposed by the applicants: unknown; see Section 1).
- Additional validation data for the residue method for ground water to show compliance with a LOQ of 0.1 μg/L. (relevant for all the representative uses evaluated, submission date proposed by the applicants: unknown; see Section 1).
- ILV for the residue method for drinking water (relevant for all the representative uses evaluated, submission date proposed by the applicants: unknown; see Section 1).
- Toxicological information on the stabilisers used in the technical concentrates by some manufacturers of copper hydroxide, copper oxychloride, tribasic copper sulfate and copper I oxide, relevant for all representative uses evaluated; submission date proposed by the applicants: unknown; see Section 2).
- Full residue data sets supporting the northern and southern outdoor GAPs with post-flowering applications on grapes (relevant for the representative uses on grapes; submission date proposed by the applicants: unknown; see Section 3).

- Residue data sets supporting the GAPs with preflowering applications on grapes (relevant for the representative uses on grapes; submission date proposed by the applicants: unknown; see Section 3).
- Full residue data sets supporting the outdoor (NEU and SEU) and indoor GAPs on tomatoes (relevant for the representative uses on tomatoes); submission date proposed by the applicants: unknown; see Section 3).
- Full residue data sets supporting the outdoor (NEU and SEU) and indoor GAPs on cucurbits with edible peel (relevant for the representative uses on cucumber, gherkins and courgettes); submission date proposed by the applicants: unknown; see Section 3).
- Full residue data sets supporting the northern and southern outdoor GAPs on cucurbits with inedible peel (relevant for the representative uses on melons, pumpkins and watermelons; submission date proposed by the applicants: unknown; see Section 3).
- Two additional residue trials supporting the indoor GAP on cucurbits with inedible peel (relevant for the representative uses on melons, pumpkins and watermelons; submission date proposed by the applicants: unknown; see Section 3).
- Applicants to submit information against the data requirement on residue levels in pollen and in bee products for human consumption resulting from residues taken up by honeybees from crops at blossom (submission date proposed by the applicants: unknown; see Section 3).
- The original paper by Janik et al. (2015) and the clarification on the results of individual soils were not available in the dossier (relevant for all the representative uses evaluated, submission date proposed by the applicants: unknown; see Section 4).
- Further information was not provided to update information describing the speciation of copper in natural water (relevant for all the representative uses evaluated, submission date proposed by the applicants: unknown; see Section 4).
- Further information was not provided in order to investigate if natural background levels of copper increased and consequently to assess the relevance of the median concentrations of copper in European stream sediment (relevant for all the representative uses evaluated, submission date proposed by the applicants: unknown; see Section 4).
- Further information to address the acute and long-term risk to birds and mammals (relevant for all the representative uses evaluated, submission date proposed by applicants: unknown; see Section 5).
- Further information to address the risk to aquatic invertebrates and algae (relevant for the uses on grapes), fish and sediment dwellers (relevant for all the representative uses evaluated, submission date proposed by the applicants: unknown; see Section 5).
- Further data to address the chronic toxicity to honeybees (adult and larvae) (relevant for all the representative uses evaluated, submission date proposed by the applicants: unknown; see Section 5).
- A risk assessment for honeybees in line with EFSA (2013) (relevant for all the representative uses evaluated, submission date proposed by the applicants: unknown; see Section 5).
- Further information to address the risk to non-target arthropods (relevant for the representative uses of Copper hydroxide (Funguran-OH), copper oxychloride (Curenox 50) and tribasic copper sulfate (Cuproxat SC), submission date proposed by the applicants: unknown; see Section 5).
- Further data to refine the risk to earthworms (relevant for all the representative uses except the use on grapes up to an application of 3.75 kg/ha, submission date proposed by the applicants: unknown; see Section 5)
- An extended summary of the study Menezes Oliveiras et al., 2013 and a certified translation of Strumpf et al., 2015 both studies may include relevant information pertaining soil organisms (relevant for all the representative uses evaluated, submission date proposed by the applicants: unknown; see Section 5).
- Further data to refine the risk to soil macro-organisms (relevant for all the representative uses evaluated, submission date proposed by the applicants: unknown; see Section 5). Data gaps identified for the MRL applications.

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

8.1. Particular conditions proposed for the representative uses evaluated

- For most representative formulations, PPE has to be worn by operators applying copper-based formulations on grapes and tomatoes (indoor and outdoor) to ensure that the AOEL is not exceeded (see Section 2).
- Considering the results of a repeated-dose toxicity study by inhalation, special care should be given for the protection of operators applying insoluble copper-based formulations.
- Workers re-entering tomatoes fields have to use PPE (workwear and gloves) to ensure that the AOEL is not exceeded (see Section 2).

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 546/2011[5] 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 consumer risk assessment could not be finalised considering that residue trials supporting the GAPs on grapes, tomatoes, cucurbits with edible peel and cucurbits with inedible peel were missing (see Section 3).

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.

2) A high risk to birds and mammals was identified for all the representative uses (see Section 5).
3) A high risk to aquatic organisms including sediment dwellers was identified for all the representative uses (see Section 5).
4) A high risk to soil macro-organisms was identified for all the representative uses (see Section 5).

[5] 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.

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	
		Grapes all uses	**Tomatoes Cucurbits**
Operator risk	Risk identified		
	Assessment not finalised		
Worker risk	Risk identified	X	
	Assessment not finalised		
Resident/bystander risk	Risk identified		
	Assessment not finalised		
Consumer risk	Risk identified		
	Assessment not finalised	X[1]	X[1]
Risk to wild non-target terrestrial vertebrates	Risk identified	X[2]	X[2]
	Assessment not finalised		
Risk to wild non-target terrestrial organisms other than vertebrates	Risk identified	X[4]	X[4]
	Assessment not finalised		
Risk to aquatic organisms	Risk identified	X[3]	X[3]
	Assessment not finalised		
Groundwater exposure to active substance	Legal parametric value breached		
	Assessment not finalised		
Groundwater exposure to metabolites	Legal parametric value breached[(a)]		
	Parametric value of 10 µg/L[(b)] breached		

Columns are grey if no safe use can be identified. 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): When the consideration for classification made in the context of this evaluation under Regulation (EC) No 1107/2009 is confirmed under Regulation (EC) No 1272/2008 of the European Parliament and of the Council of 16 December 2008.

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

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Abbreviations

a.s.	active substance
AAOEL	acute acceptable operator exposure level
AAS	Atomic absorption spectroscopy
ADI	acceptable daily intake
AOEL	acceptable operator exposure level
ARfD	acute reference dose
bw	body weight
CLP	classification, labelling and packaging
DAR	draft assessment report
DNA	deoxyribonucleic acid
DT_{50}	period required for 50% dissipation (define method of estimation)
ECHA	European Chemicals Agency
FOCUS	Forum for the Co-ordination of Pesticide Fate Models and their Use
GAP	Good Agricultural Practice
HQ	hazard quotient
ICP AES/OES	inductively coupled plasma optical emission spectrometer
ICP-MS	inductively coupled plasma mass spectrometer
IUPAC	International Union of Pure and Applied Chemistry
K_{doc}	organic carbon linear adsorption coefficient
LC_{50}	lethal concentration, median
LOQ	limit of quantification
MAF	multiple application factor
mm	millimetre (also used for mean measured concentrations)

MRL	maximum residue level
MSDS	material safety data sheet
NOAEC	no observed adverse effect concentration
NOAEL	no observed adverse effect level
OECD	Organisation for Economic Co-operation and Development
PEC	predicted environmental concentration
PEC_{sed}	predicted environmental concentration in sediment
PEC_{soil}	predicted environmental concentration in soil
PEC_{sw}	predicted environmental concentration in surface water
PPE	personal protective equipment
ppm	parts per million (10^{-6})
RAR	Renewal Assessment Report
SANCO	Directorate-General for Health and Consumers
SC	suspension concentrate
SD	standard deviation
SSD	species sensitivity distribution
STMR	supervised trials median residue
TK	technical concentrate
T_{max}	time until peak blood levels achieved
UF	uncertainty factor
UV	ultraviolet
VSL	Vineyard Sprayer's Lung
WBC	white blood cell
WG	water-dispersible granule
WHO	World Health Organization
WoE	Weight of Evidence

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.2018.5152