Modification of the existing maximum residue level for captan in hops

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Abstract

In accordance with Article 6 of Regulation (EC) No 396/2005, the applicant ADAMA Agriculture BV on behalf of ADAMA Makhteshim Ltd. submitted a request to the competent national authority in the Netherlands to modify the existing maximum residue level for the active substance captan in hops. The data submitted in support of the request were found to be insufficient to conclude whether the existing residue definitions are appropriate for hops. Although the number of residue trials is sufficient to derive a tentative maximum residue level (MRL) for hops according to the residue definitions derived for fruits and fruiting vegetables, EFSA did not recommend this MRL for being implemented in the MRL legislation because due to the lack of a reliable residue definition for risk assessment. Adequate analytical methods for enforcement are available to control the residues of captan in hops.

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Summary

In accordance with Article 6 of Regulation (EC) No 396/2005, ADAMA Agriculture BV on behalf of ADAMA Makhteshim Ltd. submitted an application to the competent national authority in the Netherlands (evaluating Member State (EMS)) to modify the existing maximum residue level (MRL) for the active substance captan in hops. The EMS drafted an evaluation report in accordance with Article 8 of Regulation (EC) No 396/2005, which was submitted to the European Commission and forwarded to the European Food Safety Authority (EFSA) on 17 July 2017. To accommodate for the intended use of captan, the EMS proposed to raise the existing MRL in hops from the limit of quantification (LOQ) 0.1 to 200 mg/kg.

EFSA assessed the application and the evaluation report as required by Article 10 of the Regulation and identified points which needed further clarification, which were requested from the EMS. The EMS did not agree with certain points for which EFSA requested further information, and asked EFSA to resume the assessment based on the information provided in the revised evaluation report submitted to EFSA on 23 May 2018. EFSA considered that not all points for which further information was requested were fully addressed and decided to finalise the reasoned opinion taking into account the different view expressed by the EMS.

Based on the conclusions derived by EFSA in the framework of the peer review under Directive 91/414/EEC, the data evaluated under previous MRL assessments, including the review of the existing MRLs for captan according to Article 12 of Regulation (EC) No 396/2005 and the additional data provided by the EMS in the framework of this application, the following conclusions are derived.

The metabolism of captan following foliar application has been investigated in crops belonging to the group of fruit crops; limited information is available for the group of leafy crops. While EFSA is of the opinion that a new metabolism study representative for the intended use in hops needs to be provided, the EMS did not agree with EFSA and requested EFSA to finalise the assessment despite this essential data gap. EFSA highlights that the lack of robust information on the metabolic behaviour in primary crops belonging to the leafy crops group is a source of additional (non-standard) uncertainty in the assessment for the risk managers to consider.

Studies investigating the effect of processing on the nature of captan (hydrolysis studies) demonstrated that the active substance captan is not stable and almost totally degraded to THPI under hydrolytic conditions representative of pasteurisation, boiling/brewing/baking and sterilisation. While THPI was hydrolytically stable under conditions representing pasteurisation, baking, boiling/brewing, it was shown to be slightly unstable under sterilisation conditions, forming low levels of degradation products.

For rotational crops, the soil degradation studies indicate that the DT_{90} value of captan and the relevant soil metabolites (THPI and THPAM) are all expected to be lower than the trigger value of 100 days and relevant residues in rotational crops are not expected.

Based on the metabolic pattern identified in the metabolism studies in fruits and fruiting vegetables, the results of hydrolysis studies, the toxicological significance of metabolites and/or degradation products, and the capabilities of enforcement analytical methods, the residue definitions for plant products for enforcement and risk assessment were proposed by the MRL review as ‘sum of captan and THPI, expressed as captan’, noting that this residue definition is applicable to the group of fruits and fruiting vegetables and is provisional for the group of leafy crops. The limited data available on the nature of residues (metabolism studies) in leafy crops is a source of additional (non-standard) uncertainty in the risk assessment and therefore further risk management considerations are required.

Sufficiently validated analytical methods based on gas chromatography with mass spectrometry (GC-MS) are available to quantify residues in the crops assessed in this application according to the enforcement residue definition established in the MRL legislation. The methods enable quantification of residues at or above 0.05 mg/kg for captan and 0.1 mg/kg for THPI in green hop cones and dried hop cones (LOQ).

The available residue trials are sufficient to calculate a tentative MRL proposal of 200 mg/kg for hops (dried hops cones) based on the provisional residue definition for the group of leafy crops. The OECD MRL calculation is driven by the highest residue value trial which was slightly overdosed and not fully independent. Therefore, based on expert judgement, EFSA proposes as an alternative the MRL of 150 mg/kg.

Tentative processing factors (PF) for dried hop cones to beer were derived from processing studies provided, which demonstrated a reduction of the residues in the processed product.
The occurrence of captan residues in rotational crops was investigated in the framework of the European Union (EU) pesticides peer review under Directive 91/414/EEC. Based on the available information on the nature and magnitude of residues, it cannot be fully excluded that residues in rotational commodities exceed the limit of quantification of 0.01 mg/kg. When Member States grant the authorisation for hops as defined in the Good Agricultural Practice (GAP), further risk management restrictions should be considered to avoid occurrence of residues in rotational crops.

Residues of captan in commodities of animal origin were not assessed since the crop under consideration in this MRL application is normally not fed to livestock.

The toxicological profile of captan was assessed in the framework of the EU pesticides peer review under Directive 91/414/EEC and the data were sufficient to derive an acceptable daily intake (ADI) of 0.1 mg/kg body weight (bw) per day and an acute reference dose (ARfD) of 0.3 mg/kg bw. It is noted that in the framework of the renewal of the approval of captan under Regulation (EC) No 1107/2009, the RMS proposed to revise the toxicological reference values for captan and for the metabolite THPI.

For the metabolite THPI (included in the residue definition), experts agreed during the peer review under Directive 91/414/EEC that the toxicological studies demonstrated the lower toxicity of this metabolite compared with captan. However, the toxicity of the metabolite THPI may need to be reconsidered during the renewal of approval under Regulation (EC) No 1107/2009 because recent studies indicate the acute oral toxicity of THPI may be higher than that of the parent captan. The risk assessment performed in the current reasoned opinion is based on the existing toxicological reference values, assuming that THPI is of similar toxicity as parent captan. The risk assessment may need to be revised, once a decision on the modification of the ADI/ARfD for the parent compound and the metabolite is taken.

For the intended use on hops, the risk assessment is based on a provisional residue definition for the proposed use on hops, taking into account the limited information available regarding the expected metabolic behaviour of captan in primary crops belonging to the group of leafy crops (see Section 1.1.1). The limited data available on the nature of residues (metabolism studies) in leafy crops is a source of additional (non-standard) uncertainty in the risk assessment and further risk management considerations required.

An indicative consumer risk assessment was performed with revision 2 of the EFSA Pesticide Residues Intake Model (PRIMo). The calculated exposure did not exceed the toxicological reference values derived previously in the peer review. The estimated maximum short-term exposure in percentage of the ARfD accounted for 2.0%. The estimated long-term dietary intake was in the range of 2–43% of the ADI. The contribution of residues expected in hops accounted for < 1% of the ADI for all diets.

The peer review of the draft Renewal Assessment Report (dRAR) for the renewal of the active substance in accordance with Regulation (EC) No 1107/2009 is currently ongoing and therefore the conclusions reported in this reasoned opinion might need to be reconsidered in the light of the outcome of the peer review.

The MRL recommendations proposed by EFSA are reported in the summary table below. Full details of all endpoints and the consumer risk assessment can be found in Appendices B–D.
| Code<sup>(a)</sup> | Commodity | Existing EU MRL (mg/kg) | Proposed EU MRL (mg/kg) | Comment/justification |
|-----------------|------------|------------------------|-------------------------|-----------------------|
| 0700000         | Hops       | 0.1*                   |                         | Lacking a metabolism study in leafy crops which is representative for the intended use in hops, a final conclusion on the appropriate residue definition for risk assessment and enforcement cannot be derived. The submitted residue trials are sufficient to calculate a tentative MRL proposal of 200 mg/kg for hops (dried hop cones) based on the provisional residue definition for the group of leafy crops. The OECD MRL calculation is driven by the highest residue value observed in a trial which was slightly overdosed and not fully independent. Therefore based on expert judgement EFSA proposes as an alternative the MRL of 150 mg/kg. The limited data available on the nature of residues in leafy crops is a source of additional (non-standard) uncertainty in the risk assessment. The indicative exposure assessment did not lead to exposure exceeding the toxicological reference values |

MRL: maximum residue level; OECD: Organisation for Economic Co-operation and Development.

*: Indicates that the MRL is set at the limit of analytical quantification (LOQ).

<sup>(a)</sup>: Commodity code number according to Annex I of Regulation (EC) No 396/2005.
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Assessment

The applicant requested the modification of the existing maximum residue level (MRL) for captan in hops. The detailed description of the intended use of captan which is the basis for the MRL application is reported in Appendix A.

Captan is the ISO common name for \(N\)-(trichloromethylthio)cyclohex-4-ene-1,2-dicarboximide (IUPAC). The chemical structures of the active substance and its main metabolites are reported in Appendix E.

Captan was evaluated in the framework of Directive 91/414/EEC\(^1\) with Italy designated as rapporteur Member State (RMS) for the representative uses assessed were foliar treatments on pome fruits, peaches/nectarines and tomatoes. The draft assessment report (DAR) prepared by the RMS has been peer reviewed by the European Food Safety Authority (EFSA, 2009). Captan has been approved\(^2\) for use as a fungicide on 1 October 2007. The process for renewal of the approval of the active substance captan under Regulation (EC) No 1107/2009 is currently ongoing, with Austria designated as RMS and Italy designated as co-rapporteur Member State (co-RMS).

The European Union (EU) MRLs for captan are established in Annex II of Regulation (EC) No 396/2005\(^3\). The review of existing MRLs according to Article 12 of Regulation (EC) No 396/2005 (MRL review) has been performed (EFSA, 2014). For a number of crops, EFSA identified some information on analytical methods as unavailable and therefore proposed tentative MRLs. The proposed MRLs, including the tentative MRLs have been implemented in the MRL legislation by Commission Regulation (EU) 2016/452\(^4\).

In accordance with Article 6 of Regulation (EC) No 396/2005, ADAMA Agriculture BV on behalf of ADAMA Makhteshim Ltd. submitted an application to the competent national authority in the Netherlands (EMS) to modify the existing MRL for the active substance captan in hops. The EMS drafted an evaluation report in accordance with Article 8 of the Regulation, which was submitted to the European Commission and forwarded to EFSA on 17 July 2017. To accommodate for the intended use of captan, the EMS proposed to raise the existing MRL from the limit of quantification (LOQ) 0.1 to 200 mg/kg. EFSA assessed the application and the evaluation report as required by Article 10 of the Regulation and identified points which needed further clarification, which were requested from the EMS. The EMS did not agree with certain points for which EFSA requested further information, and asked EFSA to resume the assessment based on the information provided in the revised evaluation report submitted to EFSA on 23 May 2018 (Netherlands, 2017).

EFSA based its assessment on the evaluation report submitted by the EMS (Netherlands, 2017), the DAR (and its addendum) prepared under Council Directive 91/414/EEC (Italy, 2003, 2009), the Commission review report on captan (European Commission, 2008), the EFSA conclusion on the peer review of the pesticide risk assessment of the active substance captan (EFSA, 2009), the EFSA reasoned opinion the review of the existing MRLs for captan according to Article 12 of Regulation (EC) No 396/2005 (EFSA, 2014), and the draft Renewal Assessment Report (dRAR) prepared in the framework of the renewal of the active substance under Regulation (EC) No 1107/2009 (Austria, 2017), as well as the conclusions from previous EFSA reasoned opinions on captan (EFSA, 2018).

For this application, the data requirements established in Regulation (EU) No 544/2011\(^5\) and the guidance documents applicable at the date of submission of the application to the EMS are applicable (European Commission, 1997a–g, 2000, 2010a,b, 2017; OECD, 2011, 2013). The assessment is performed in accordance with the legal provisions of the Uniform Principles for the Evaluation and the Authorisation of Plant Protection Products adopted by Commission Regulation (EU) No 546/2011\(^6\).

\(^1\) Council Directive 91/414/EEC of 15 July 1991 concerning the placing of plant protection products on the market. OJ L 230, 19.8.1991, p. 1–32.

\(^2\) Commission Directive 2007/5/EC of 7 February 2007 amending Council Directive 91/414/EEC to include captan, folpet, formetanate and methiocarb as active substances. OJ L 35, 8.2.2007, p. 11–17.

\(^3\) Regulation (EC) No 396/2005 of the Parliament and of the Council of 23 February 2005 on maximum residue levels of pesticides in or on food and feed of plant and animal origin and amending Council Directive 91/414/EEC. OJ L 70, 16.3.2005, p. 1–16.

\(^4\) Commission Regulation (EU) 2016/452 of 29 March 2016 amending Annexes II and III to Regulation (EC) No 396/2005 of the European Parliament and of the Council as regards maximum residue levels for captan, propiconazole and spiroxamine in or on certain products. OJ L 79, 30.3.2016, p. 10–27.

\(^5\) Commission Regulation (EU) No 544/2011 of 10 June 2011 implementing Regulation (EC) No 1107/2009 of the European Parliament and of the Council as regards the data requirements for active substances. OJ L 155, 11.6.2011, p. 1–66.

\(^6\) 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.
As the EU pesticides peer review of the active substance captan in accordance with Regulation (EC) No 1107/2009 is not yet finalised, the conclusions reported in this reasoned opinion might need to be reconsidered in the light of the outcome of the peer review.

A selected list of end points of the studies assessed by EFSA in the framework of the this MRL application, review, including the end points of relevant studies assessed previously, submitted in support of the current MRL application, are presented in Appendix B.

The evaluation report submitted by the EMS (Netherlands, 2017) and the exposure calculations using the EFSA Pesticide Residues Intake Model (PRIMo) are considered as supporting documents to this reasoned opinion and, thus, are made publicly available as background documents.

1. **Residues in plants**

1.1. **Nature of residues and methods of analysis in plants**

1.1.1. **Nature of residues in primary crops**

The metabolism of captan in primary crops has been investigated in the framework of the EU pesticides peer review under Directive 91/414/EEC and in the framework of the MRL review (Italy 2003, 2009; EFSA, 2009, 2014).

The MRL review assessed metabolism studies representative for the group of fruits and fruiting vegetable. In addition, a metabolism study in lettuce was provided (foliar treatment 4 \* 4.48 kg a.s./ha, 7 days interval, sampling on the day of the last treatment); however, the study was found to be not representative for the authorised Good Agricultural Practices (GAPs), because the use conditions did not sufficiently reflect the GAP. The MRL review concluded that in order to extend the proposed residue definition to leafy crops (foliar treatment) and cereals (seed treatment), additional metabolism studies representative of the GAPs are required (EFSA, 2014).

The data gap related to metabolism studies in leafy crops was not implemented in the MRL regulation implementing the MRLs recommended in the framework of the MRL review, since the existing use on crops belonging to the group of leafy crops (i.e. scarole and leek) were not supported by any residue trials and therefore no MRL proposal for the residue definition tentatively proposed for leafy crops could be derived.

In support of the current MRL application, the previously assessed lettuce metabolism study was submitted. EFSA is of the opinion that the design of the metabolism study in lettuce is not reflecting the intended use in hops: the GAP for the intended use on hops foresees an interval between the first application and the harvest of at least 42 days (minimum 7 days interval and minimum 28 days preharvest interval (PHI)) and up to 56 days or more (maximum 14 days interval and minimum 28 days PHI). Furthermore, in the intended use GAP for hops, application is at growth stage BBCH 55–85, whereas in the metabolism study on lettuce the first spray application was at BBCH 22–26. The metabolism study should reflect the proposed use pattern and the PHI. The growth stage of the crops at application and sampling should be similar to that of the anticipated field use of the pesticide. Although the study gives a qualitative picture of the metabolic pattern, the results are of limited value to elucidate the amount of different metabolites to occur in harvested crops and to decide for which metabolites further toxicological data are required. Considering the late application of captan on the day of the sampling (3 hours after the treatment), the metabolic pattern is likely to be shifted towards parent captan, while the total radioactive residue (TRR%) for metabolites are expected to be underestimated. Thus, EFSA concludes that the available metabolism study in lettuce does not fully support the intended use on hops.

The EMS also suggested considering the results of the metabolism studies with folpet which is a molecule with structural similarities with captan (Netherlands, 2017). However, the cyclohexene ring structure of captan is subject to different metabolic pathways than the aromatic benzene ring structure of folpet with formation of captan epoxide and THPI epoxide. Thus, EFSA considered the bridging of metabolism data from folpet to captan as not appropriate to address the data requirements.

The need to provide a sufficiently representative metabolism study in leafy crops was discussed with the EMS, who provided reasoning that the metabolism study in lettuce is acceptable because a total of 21 days elapsed between the first application and the harvest (Netherlands, 2017). The EMS stated that the conclusion reached by EFSA, regarding the need for an additional metabolism study in leafy crop, does not reflect the view of the EMS and requested EFSA to finalise the assessment and to include the opinion of the EMS in the reasoned opinion.
Considering the different view expressed by the EMS on the need for additional data to elucidate the metabolic behaviour in hops, EFSA decided to finalise the reasoned opinion despite the lack of robust information on the metabolic behaviour in primary crops belonging to the leafy crops group, highlighting the additional (non-standard) uncertainty in the assessment to provide risk managers the necessary information to take an informed decision.

1.1.2. Nature of residues in rotational crops

Captan is proposed to be used on hops, which can be grown in rotation with other crops. According to the soil degradation studies evaluated in the framework of the peer review under Directive 91/414/EEC, the DT90 value of captan and the relevant soil metabolites (THPI and THPAM) are all expected to be lower than the trigger value of 100 days (EFSA, 2009). According to the European guidelines on rotational crops (European Commission, 1997b), further investigation of residues in rotational crops is not required and relevant residues in rotational crops are not expected.

1.1.3. Nature of residues in processed commodities

The effect of processing on the nature of captan was investigated in the framework of previous MRL applications (Austria, 2010; France, 2010; EFSA, 2011). These studies showed that the captan is not stable and almost totally degraded to THPI under hydrolytic conditions representative of pasteurisation (20 min at 90°C, pH 4), boiling/brewing/baking (60 min at 100°C pH 5) and sterilisation (20 min at 120°C, pH 6) (EFSA, 2011). While THPI was hydrolytically stable under conditions representing pasteurisation, backing, boiling/brewing, it was shown to be slightly unstable under sterilisation conditions, forming low levels of degradation products at individual amounts up to 11.4% applied radioactivity (AR). Consequently, as for primary crops, EFSA proposed to set the residue definition for enforcement and risk assessment in processed commodities as the ‘sum of captan and THPI, expressed as captan’ (EFSA, 2014).

For hops being used as an ingredient in beer production, the relevant process is boiling. Thus, in beer, captan residues are expected to degrade to a large extent to THPI. Considering that lacking a robust metabolism study in leafy crops, the occurrence of other relevant metabolites in hops and the formation of additional degradation products related to these metabolites in processed products cannot be excluded.

1.1.4. Methods of analysis in plants

Analytical methods for the determination of captan and the metabolite THPI were assessed during the EU pesticides peer review under Directive 91/414/EEC and during the MRL review (EFSA, 2009, 2014). The methods were sufficiently validated for residues of captan in food of plant origin with an LOQ of 0.05 mg/kg in acidic and in high water content commodities. The metabolite THPI can be enforced in food of plant origin with an LOQ of 0.01 mg/kg in high water content commodities. However, the MRL review identified that an independent laboratory validation (ILV) and a confirmatory method for the determination of THPI in high water commodities and a fully validated method with its ILV and with a confirmatory method for the determination of THPI in acidic commodities were missing (EFSA, 2014).

New methods of analysis for the determination of captan residues and residues of THPI have been submitted in the dossier for the renewal of the approval under Regulation (EC) No 1107/2009 for which the peer review is currently ongoing (Austria, 2017; Netherlands, 2017). The methods allow quantifying residues at or above the LOQ of 0.01 mg/kg for each analyte in crops belonging to the groups of high water content, high oil content, high acid content and dry matrices, with confirmatory method and ILV available (Austria, 2017; Netherlands, 2017).

In the present MRL application, validation data were submitted for the determination of captan and the metabolite THPI in hops and beer (Netherlands, 2017). The method is sufficiently validated for hops (green hop cones and dried hop cones) and allows for quantifying residues at or above the LOQ of 0.05 mg/kg for captan and the LOQ of 0.1 mg/kg for THPI; and a confirmatory method and ILV are available (Netherlands, 2017). For beer, the method allows for quantifying residues at or above the LOQ 0.01 mg/kg for each analyte (captan and THPI) (Netherlands, 2017).
1.1.5. Stability of residues in plants

In support of the present application, information was submitted on the stability of residues in dried hop cones and it was demonstrated that residues of captan and the metabolite THPI were stable for at least 12 months when stored at −18°C (Netherlands, 2017).

Storage stability of captan and the metabolite THPI in plants stored under frozen conditions was also investigated in the framework of the EU pesticides peer review under Directive 91/414/EEC (EFSA, 2014). The frozen storage stability of total residues of captan and THPI (expressed as captan equivalents) was demonstrated for 20 months in high water content commodities (tomatoes) and for 14 months in high acid content commodities (strawberries), when stored at −20°C (Italy, 2003).

1.1.6. Proposed residue definitions

Based on the metabolic pattern identified in the metabolism studies in fruits and fruiting vegetables, the results of hydrolysis studies, the toxicological significance of metabolites and/or degradation products, and the capabilities of enforcement analytical methods, the following residue definition was proposed by the MRL review for plant products noting that the residue is applicable only to the group of fruits and fruiting vegetables and is provisional for the group of leafy crops (EFSA, 2014):

- Residue definition for risk assessment and enforcement for plant products: sum of captan and THPI, expressed as captan.

In order to extend the proposed residue definitions to the group of leafy crops (foliar application), the MRL review considered that additional metabolism studies representative of the proposed GAPs are required (EFSA, 2014).

In the present application, the applicant submitted argumentation regarding the expected metabolic behaviour of captan in primary crops belonging to the group of leafy crops (see Section 1.1.1, above). Taking into account the limited information available and the argumentation provided, EFSA used this residue definition for the proposed use on hops assessed in this application to perform an indicative risk assessment.

1.2. Magnitude of residues in plants

1.2.1. Magnitude of residues in primary crops

In support of the MRL application, the applicant submitted five residue trials performed in hops. The samples were analysed for the parent compound and the metabolite THPI included in the residue definitions for enforcement and risk assessment. According to the assessment of the EMS, the methods used were sufficiently validated and fit for purpose. The samples of these residue trials were stored under conditions for which integrity of the samples has been demonstrated (Netherlands, 2017).

The trials were conducted in Germany (two locations) and Poland (two locations) during the 2014 and 2015 growing seasons. Two trials were conducted at the same geographical location in Germany during the same growing season with different crop varieties and different application rates. EFSA considered that trials conducted at the same geographical location during the same growing season are different experimental conditions within the same trial (within the same experimental site) and are not fully independent. The experimental conditions for one of the residue trials with the highest residue measured deviated from the GAP (slightly overdosed) but were considered to be still within the acceptable deviation of the nominal seasonal application rate. Therefore, EFSA included both residue trial values (considered as being from the same trial location and growing season but with different experimental conditions), noting, however, that the higher residue value was slightly overdosed.

The range of growth stages in the residues trials (BBCH 65–79 and BBCH 71–82, at first and last treatments, respectively) is narrower than the overall range of growth stages foreseen in the intended use GAP (BBCH 55–85), which was considered a minor deviation.

Overall, five trials were considered to be sufficiently GAP-compliant and the residue levels (reported as sum of captan and THPI, expressed as captan) ranged from 4.2 to 102.4 mg/kg in dried hop cones and from 1.9 to 78.4 mg/kg in green hop cones. The high variability of residues in hops cones observed in the field trials is expected to be representative of the variability of residues that may occur in hops as a result of commercial agricultural practices. Hops are considered a minor crop in Europe and a minimum of four GAP-compliant trials is considered sufficient. The number and the quality of the trials are sufficient to calculate an MRL of 200 mg/kg for hops (dried hops cones). The OECD MRL...
calculation is driven by the highest residue value trial which was slightly overdosed and not fully independent. Therefore, based on expert judgement, EFSA proposes as an alternative the MRL of 150 mg/kg.

### 1.2.2. Magnitude of residues in rotational crops

The possible transfer of captan residues to crops that are grown in crop rotation has been assessed in EU pesticides peer review (Italy, 2003). The available studies demonstrated that no significant residues (residues below 0.01 mg/kg) are expected in succeeding crops (beets (root and tuber vegetables), lettuce (leafy vegetables) and wheat (cereals)) planted in soil treated using 14C-trichloromethyl- or 1,2-14C-cyclohexene-labelled captan at a rate of 4.48 kg a.s./ha for each labelled form. Identification of the metabolic pattern in immature crops indicated that captan was not present and only very low amounts of THPI were detected (EFSA, 2014). Since the maximum annual application rate for the crops under consideration (i.e. 7.2 kg a.s./ha) is higher than the total application rate tested in the rotational crop study, it cannot be fully excluded that residues in rotational commodities exceed 0.01 mg/kg. When Member States grant the authorisation for hops as defined in the GAP, risk management restrictions should be considered to avoid occurrence of residues in rotational crops.

### 1.2.3. Magnitude of residues in processed commodities

In the present application, two processing studies were submitted for dried hop cones to beer, end of process. The number and quality of the processing studies are sufficient to derive a tentative processing factor for the current residue definition based on a limited data set, which demonstrated a reduction of the residues in the processed product (Netherlands, 2017). However, the tentative processing factors need to be reconsidered, if the residue definition for leafy crops is revised and/or if additional standard hydrolysis studies for metabolites relevant for leafy crops are reconsidered necessary.

### 1.2.4. Proposed MRLs

The available data are considered sufficient to derive a tentative MRL as well as indicative risk assessment values for hops (see Appendix B.1.2.1). The part of the product to which the EU MRLs for hops apply is the dried hops cones, and is also applicable to hops in the form of pellets and un-concentrated powder. In Section 3, EFSA assessed whether residues on these crops resulting from the intended uses are likely to pose a consumer health risk.

### 2. Residues in livestock

An assessment of residues in livestock is not required because the commodities under consideration are not used for feed purposes.

### 3. Consumer risk assessment

EFSA performed an indicative dietary risk assessment using revision 2 of the EFSA PRIMo (EFSA, 2007). This exposure assessment model contains food consumption data for different subgroups of the EU population and allows the acute and chronic exposure assessment to be performed in accordance with the internationally agreed methodology for pesticide residues (FAO, 2016). The risk assessment is indicative, since a final conclusion on the appropriate residue definition for leafy crops could not be derived (see Section 1.1.6).

The existing toxicological reference values for captan used in the risk assessment (i.e. acceptable daily intake (ADI) of 0.1 mg/kg body weight (bw) per day and acute reference dose (ARfD) of 0.3 mg/kg bw) were derived in the EU pesticides peer review in the framework of the EU pesticides peer review under Directive 91/414/EEC (EFSA, 2009). It is noted that in the framework of the renewal of the approval under Regulation (EC) No 1107/2009 (AIR III), the RMS also proposed new toxicological reference values for captan (Austria, 2017) for which the peer review is currently ongoing.7

For the metabolites THPI, 3-OH THPI and 5-OH THPI, it was agreed during the peer review in the framework of the approval under Directive 91/414/EEC that the toxicological studies demonstrated the

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7 The RMS proposed in the draft Renewal Assessment Report a new ADI (0.25 mg/kg bw per day) and a new ARfD (0.9 mg/kg bw) for captan (Austria, 2017).
lower toxicity of these metabolites compared with captan (EFSA, 2009). Mechanistic data indicated also that THPI, 3-OH-THPI and 5-OH-THPI do not have the potential to induce critical effects (carcinogenic, reproductive toxicity effects). Nevertheless, as it was not possible to set specific reference values for these metabolites, the peer review concluded that the reference values for captan would also apply for these three metabolites (EFSA, 2009). The toxicity of the metabolite THPI may need to be reconsidered during the renewal of approval under Regulation (EC) No 1107/2009 (AIR III) as proposed by the RMS Austria, because recent studies indicate the acute oral toxicity of THPI may be higher than that of the parent captan, and significantly higher than reported in the original DAR of 2003 (Austria, 2017).

The indicative risk assessment performed in the current reasoned opinion is based on the existing toxicological reference values derived by the pesticides peer review in 2009 (EFSA, 2009), assuming that THPI is of similar toxicity as parent captan. It is however noted that the peer review of the risk assessment of captan for renewal of the approval under Regulation (EC) No 1107/2009 (AIR III) is currently on going; and the risk assessment may need to be revised if the toxicological reference values for the compounds included in the residue definition for risk assessment are revised.

For further details on the exposure calculations, a screenshot of the Report sheet of the PRiMo is presented in Appendix C.

3.1. Short-term (acute) dietary risk assessment

The acute exposure assessment was performed only with regard to the commodities under consideration assuming the consumption of a large portion of the food items as reported in the national food surveys (EFSA, 2007). As hops are usually bulked before processing, the risk assessment was performed with the supervised trials median residue (STMR) value (case 3 of the international estimated short-term intake (IESTI) equation) (see Appendix D.2).

The indicative risk assessment performed under the assumption that THPI is of similar toxicity as captan did not indicate a risk to consumer health; for hops, the estimated maximum exposure in percentage of the ARfD accounted for 2.0% (see Appendix B.3). The calculation is affected by additional (non-standard) uncertainty, related to the lack of reliable residue definition for leafy crops.

3.2. Long-term (chronic) dietary risk assessment

In the framework of the MRL review, a comprehensive long-term exposure assessment was performed, taking into account the existing uses at EU level (EFSA, 2014). EFSA updated the calculation with the relevant STMR value for hops derived from the residue trials submitted in support of this MRL application and the STMR derived in a contemporaneous assessment for cranberries (EFSA, 2018). The input values used in the exposure calculations are summarised in Appendix D.2.

Although uncertainty remains regarding the residue definition for leafy crops and the appropriateness of the toxicological reference values used in the risk assessment, the indicative risk assessment did not indicate a risk to consumer health. The estimated long-term dietary intake was in the range of 2–43% of the ADI. The contribution of residues expected in hops accounted for < 1% of the ADI for all diets. The contribution of residues expected in the commodities assessed in this application to the overall long-term exposure is presented in more detail in Appendix B.3.

EFSA concluded that, the indicative exposure calculation, based on the estimated the long-term intake of residues of captan resulting from the intended use on hops and the existing uses, did not indicate a risk to consumer health.

4. Conclusion and Recommendations

The data submitted in support of this MRL application were found to be sufficient to derive a tentative MRL proposal for hops.

For the intended use on hops, data gaps were identified and the MRL proposal for hops is affected by a degree of additional (non-standard) uncertainty. The risk assessment is based on a provisional residue definitions for the proposed use on hops, taking into account the limited information available regarding the expected metabolic behaviour of captan in primary crops belonging to the group of leafy crops (see Section 1.1.1, above). The limited data available on the nature of residues (metabolism studies) in leafy crops is a source of additional (non-standard) uncertainty in the risk assessment and further risk management considerations required.
Based on the provisional residue definition, the indicative exposure calculation for residues of captan and its metabolite THPI did not exceed the existing toxicological reference values.

The peer review of the dRAR for the renewal of the active substance in accordance with Regulation (EC) No 1107/2009 is not yet finalised and therefore the conclusions reported in this reasoned opinion might need to be reconsidered in the light of the outcome of the peer review.

The MRL recommendations are summarised in Appendix B.4.

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Abbreviations

a.s. active substance
ADI acceptable daily intake
AR applied radioactivity
ARfD acute reference dose
BBCH growth stages of mono- and dicotyledonous plants
bw body weight
CF conversion factor for enforcement to risk assessment residue definition
DAR draft assessment report
DAT days after treatment
dRAR draft Renewal Assessment Report
DT$_{90}$ period required for 90% dissipation (define method of estimation)
EMS evaluating Member State
FAO Food and Agriculture Organization of the United Nations
GAP Good Agricultural Practice
GC–MS gas chromatography with mass spectrometry
HR highest residue
IEDI international estimated daily intake
IESTI international estimated short-term intake
ILV independent laboratory validation
InChIKey International Chemical Identifier Key
ISO International Organisation for Standardisation
IUPAC International Union of Pure and Applied Chemistry
LOQ limit of quantification
MRL maximum residue level
NEU northern Europe
OECD Organisation for Economic Co-operation and Development
PBI plant-back interval
PF processing factor
PHI pre-harvest interval
PRIMO (EFSA) Pesticide Residues Intake Model
RA risk assessment
RAC raw agricultural commodity
RD residue definition
RMS rapporteur Member State
SANCO Directorate-General for Health and Consumers
SC suspension concentrate
SEU southern Europe
STMR supervised trials median residue
TRR total radioactive residue
WHO World Health Organization
### Appendix A – Summary of intended GAP triggering the amendment of existing EU MRLs

| Crop and/or situation | NEU, SEU, MS or country | Pests or group of pests controlled | Preparation | Application | Application rate per treatment | Remarks |
|-----------------------|-------------------------|-----------------------------------|-------------|-------------|---------------------------------|---------|
|                       | F                       | N./G.                             | Type(b)     | Conc. a.s.  | Method kind | Range of growth stages & season(c) | Number min–max | Interval between application (min) | g a.s./hl min–max | Water L/ha min–max | Rate | Unit | PHI (days)(d) |          |
| Hops                  | NEU (DE, CZ)            | Pseudo-peronospora humuli         | SC          | a) Captan: 360 g a.s./L | Foliar spray | BBCH 55–85 | 3 | 7 days | a) Captan: 86–133 | 1,800–2,800 | a) Captan: 2.4 | kg a.s./ha | 28 | Interval between applications is 7–14 days |
|                       |                         |                                   | b) Potassium phosphonate: 660 g a.s./L (equivalent to 440 g/L phosphonic acid equivalents) |             |           |                        |                  |                      | a) PP*: 105–164 | b) PP*: 2.95 | |
|                       |                         |                                   |             |             |           |                        |                  |                      |                          |                      |            |          |              |          |

GAP: Good Agricultural Practice; MRL: maximum residue level; NEU: northern European Union; SEU: southern European Union; MS: Member State; a.s.: active substance; SC: suspension concentrate.

(a): Outdoor or field use (F), greenhouse application (G) or indoor application (I).

(b): CropLife International Technical Monograph no 2, 6th Edition. Revised May 2008. Catalogue of pesticide formulation types and international coding system.

(c): Growth stage range from first to last treatment (BBCH Monograph, Growth Stages of Plants, 1997, Blackwell, ISBN 3-8263-3152-4), including, where relevant, information on season at time of application.

(d): PHI: minimum preharvest interval.
## Appendix B – List of end points

### B.1. Residues in plants

#### B.1.1. Nature of residues and methods of analysis in plants

#### B.1.1.1. Metabolism studies, methods of analysis and residue definitions in plants

| Primary crops (available studies) | Crop groups | Crop(s) | Application(s) | Sampling (DAT) | Comment/source |
|----------------------------------|-------------|---------|----------------|----------------|----------------|
| Fruit crops                      | Tomatoes    | Foliar, G | 4 × 4.48 kg a.s./ha, 7 day interval | 0 | $^{13}$C-trichloromethyl EFSA (2014) |
|                                  | Tomatoes    | Foliar, G | 4 × 4.48 kg a.s./ha, 7 day interval | 0 | 1,2-$^{14}$C-cyclohexene EFSA (2014) |
|                                  | Apples      | Foliar, F | 1 × 0.12 kg as/L | 0, 20 | $^{14}$C-carbonyl EFSA (2014) |
|                                  | Apples      | Foliar, F | 2 × 0.12 kg as/L, 30 day interval | 20 | $^{14}$C-carbonyl EFSA (2014) |
|                                  | Apples      | Foliar, F | 3 × 0.12 kg as/L, 30 day interval | 20 | $^{14}$C-carbonyl EFSA (2014) |
| Leafy crops                      | Lettuce     | Foliar, G | 4 × 4.48 kg a.s./ha, 7 day interval | 0 | $^{13}$C-trichloromethyl EFSA (2014) |
|                                  | Lettuce     | Foliar, G | 4 × 4.48 kg a.s./ha, 7 day interval | 0 | 1,2-$^{14}$C-cyclohexene EFSA (2014) |
| Rotational crops (available studies) | Crop groups | Crop(s) | Application(s) | PBI (DAT) | Comment/source |
| Root/tuber crops                 | Beet        | Bare soil, G | 4.48 kg a.s./ha (for each labelled form) | | $^{13}$C-trichloromethyl and 1,2-$^{14}$C-cyclohexene EFSA (2014) |
|                                  | Beet        | Bare soil, G | 4.48 kg a.s./ha (for each labelled form) | Sowing: 34 DAT Harvest: 43, 54, 61, 126, 131 DAT | $^{13}$C-trichloromethyl and 1,2-$^{14}$C-cyclohexene EFSA (2014) |
|                                  | Lettuce     | Bare soil, G | 4.48 kg a.s./ha (for each labelled form) | Sowing: 34 DAT Harvest: 43, 54, 61, 75 DAT | $^{13}$C-trichloromethyl and 1,2-$^{14}$C-cyclohexene EFSA (2014) |
|                                  | Lettuce     | Bare soil, G | 4.48 kg a.s./ha (for each labelled form) | Sowing: 34 DAT Harvest: 43, 54, 61, 126, 131 DAT | $^{13}$C-trichloromethyl and 1,2-$^{14}$C-cyclohexene EFSA (2014) |
|                                  | Lettuce     | Bare soil, G | 4.48 kg a.s./ha (for each labelled form) | Sowing: 34 DAT Harvest: 43, 54, 61, 75, 131 DAT | $^{13}$C-trichloromethyl and 1,2-$^{14}$C-cyclohexene EFSA (2014) |
|                                  | Lettuce     | Bare soil, G | 4.48 kg a.s./ha (for each labelled form) | Sowing: 34 DAT Harvest: 43, 54, 61, 75, 131 DAT | $^{13}$C-trichloromethyl and 1,2-$^{14}$C-cyclohexene EFSA (2014) |
|                                  | Lettuce     | Bare soil, G | 4.48 kg a.s./ha (for each labelled form) | Sowing: 34 DAT Harvest: 43, 54, 61, 75, 131 DAT | $^{13}$C-trichloromethyl and 1,2-$^{14}$C-cyclohexene EFSA (2014) |
|                                  | Lettuce     | Bare soil, G | 4.48 kg a.s./ha (for each labelled form) | Sowing: 34 DAT Harvest: 43, 54, 61, 75, 131 DAT | $^{13}$C-trichloromethyl and 1,2-$^{14}$C-cyclohexene EFSA (2014) |
| Cereal (small grain)             | Wheat       | Bare soil, G | 4.48 kg a.s./ha (for each labelled form) | Sowing: 88 DAT Harvest: 105, 116, 138, 158 DAT | $^{13}$C-trichloromethyl and 1,2-$^{14}$C-cyclohexene EFSA (2014) |
|                                  | Wheat       | Bare soil, G | 4.48 kg a.s./ha (for each labelled form) | Sowing: 88 DAT Harvest: 105, 116, 224 DAT | $^{13}$C-trichloromethyl and 1,2-$^{14}$C-cyclohexene EFSA (2014) |
## Processed Commodities (hydrolysis study)

| Conditions                                    | Stable? | Comment/source |
|-----------------------------------------------|---------|----------------|
| Pasteurisation (20 min, 90°C, pH 4)           | No      | EFSA (2014)    |
| Baking, brewing and boiling (60 min, 100°C, pH 5) | No      | EFSA (2014)    |
| Sterilisation (20 min, 120°C, pH 6)           | No      | EFSA (2014)    |
| Other processing conditions                   | –       | –              |

Can a general residue definition be proposed for primary crops?

| Conditions                                    | Stable? | Comment/source |
|-----------------------------------------------|---------|----------------|
| Yes                                           |         | EFSA (2014)    |

Rotational crop and primary crop metabolism similar?

| Conditions                                    | Stable? | Comment/source |
|-----------------------------------------------|---------|----------------|
| Not triggered                                 |         | EFSA (2014)    |

Residue pattern in processed commodities similar to residue pattern in raw commodities?

| Conditions                                    | Stable? | Comment/source |
|-----------------------------------------------|---------|----------------|
| Yes                                           |         | EFSA (2014)    |

Plant residue definition for monitoring (RD-Mo)

**Sum of captan and THPI, expressed as captan**

Provisional residue definition for the proposed use on hops.

Plant residue definition for risk assessment (RD-RA)

**Sum of captan and THPI, expressed as captan**

Provisional residue definition for the proposed use on hops.

Methods of analysis for monitoring of residues (analytical technique, crop groups, LOQs)

- **Methods of analysis submitted in the framework of the approval under Directive 91/414/EEC**
  - Matrices with high water content and high acid content matrices: GC–MS, LOQ 0.05 mg/kg for captan
  - Matrices with high water content: GC–MS, LOQ 0.01 mg/kg for THPI
  - Confirmatory method and ILV missing for determination of THPI in high water content matrices
  - Validated method with its ILV and confirmatory method missing for determination of THPI in high acid content matrices (EFSA, 2014)

- **New methods of analysis submitted in the framework of the Annex I renewal under Regulation (EC) No 1107/2009 and assessed in the Draft Renewal Assessment Report (peer-review ongoing)**
  - Matrices with high water content, high oil content, high acid content and dry matrices: GC–MS, LOQ 0.01 mg/kg for captan and THPI
  - Confirmatory method available. ILV available (Austria, 2017; Netherlands, 2017)

- Validation data and ILV available for hops, green hop cones and dried hop cones: GC–MS, LOQ 0.05 mg/kg for Captan and 0.1 mg/kg for THPI
  - Validation data available for beer: GC–MS, LOQ 0.01 mg/kg for Captan and THPI (Netherlands, 2017)

DAT: days after treatment; a.s.: active substance; PBI: plant-back interval; GC–MS: gas chromatography with mass spectrometry; LOQ: limit of quantification; ILV: independent laboratory validation.
### B.1.1.2. Stability of residues in plants

| Plant products (available studies) | Category          | Commodity         | T (°C) | Stability period | Compounds covered                                                                 | Comment/source                                      |
|-----------------------------------|-------------------|-------------------|--------|-----------------|-----------------------------------------------------------------------------------|-----------------------------------------------------|
|                                   | High water content| Tomatoes          | –20°C  | 20 Months       | Total captan and THPI residues, expressed as captan equivalents                    | Italy (2003), EFSA (2014)                           |
|                                   | High oil content  | –                  | –      | –               | –                                                                                  | –                                                   |
|                                   | High protein content| –                | –      | –               | –                                                                                  | –                                                   |
|                                   | Dry/High starch   | –                  | –      | –               | –                                                                                  | –                                                   |
|                                   | High acid content | Strawberries       | –20°C  | 14 Months       | Total captan and THPI residues, expressed as captan equivalents                    | Italy (2003), EFSA (2014)                           |
|                                   | Processed products| Hop cones, dried  | –18°C  | 12 Months       | Captan, THPI                                                                       | Netherlands (2017)                                  |
|                                   | Others            | –                  | –      | –               | –                                                                                  | –                                                   |
### B.1.2. Magnitude of residues in plants

#### B.1.2.1. Summary of residues data from the supervised residue trials

| Commodity          | Region/indoor\(^{(a)}\) | Residue levels observed in the supervised residue trials (mg/kg) | Comments/Source                                                                 | Calculated MRL (mg/kg) | HR\(^{(b)}\) (mg/kg) | STMR\(^{(c)}\) (mg/kg) | CF\(^{(d)}\) |
|--------------------|--------------------------|---------------------------------------------------------------|--------------------------------------------------------------------------------|------------------------|----------------------|------------------------|--------------|
| Green hop cones    | NEU                      | 1.9, 4.6, 22.0, 33.5, 78.4\(^{(e)}\)                          | Residue trials on hops compliant with GAP                                       | –                      | 78.4                 | 22                     | n.a.         |
| Dried hop cones    | NEU                      | 4.2, 16.0, 33.1, 50.9, 102.4\(^{(e)}\)                        | Residue trials on hops compliant with GAP. The OECD MRL calculation of 200 mg/kg is driven by the highest residue value trial which was slightly overdosed and not fully independent. Therefore based on expert judgement EFSA proposes as an alternative the MRL of 150 mg/kg | 200 or 150             | 102.4                | 33.1                   | n.a.         |

MRL: maximum residue level; GAP: Good Agricultural Practice; OECD: Organisation for Economic Co-operation and Development.

*: Indicates that the MRL is proposed at the limit of quantification.

\(^{(a)}\): NEU: Outdoor trials conducted in northern Europe, SEU: Outdoor trials conducted in southern Europe, Indoor: indoor EU trials or Country code: if non-EU trials.

\(^{(b)}\): Highest residue. The highest residue for risk assessment refers to the whole commodity and not to the edible portion.

\(^{(c)}\): Supervised trials median residue. The median residue for risk assessment refers to the whole commodity and not to the edible portion.

\(^{(d)}\): Conversion factor to recalculate residues according to the residue definition for monitoring to the residue definition for risk assessment.

\(^{(e)}\): Residue trial overdosed at the first application (3.268 kg a.s./ha; 136%) however the total trial application rate was slightly overdosed (9.009 kg a.s./ha; 125.1% with regard to the 3 x 2.4 kg a.s./ha GAP stated in the application form) and was considered to be within the acceptable tolerance.
B.1.2.2. Residues in rotational crops

| Residues in rotational and succeeding crops expected based on confined rotational crop study? | Not triggered | EFSA (2014) |
| Residues in rotational and succeeding crops expected based on field rotational crop study? | Not triggered. | EFSA (2014) |

B.1.2.3. Processing factors

| Processed commodity | Number of valid studies(a) | Processing factor (PF) | CF_P(b) | Comment/source |
|---------------------|---------------------------|------------------------|---------|----------------|
| Dried hop cones/Beer, end of process | 2 | 0.00047; 0.00089 | 0.00068 | n.a. Tentative(c) (Netherlands, 2017) |

(a): Studies with residues in the RAC at or close to the LOQ were disregarded (unless concentration may occur).
(b): Conversion factor for risk assessment in the processed commodity; median of the individual conversion factors for each processing residues trial.
(c): A tentative PF is derived based on a limited dataset and because a final decision on the appropriate residue definition for leafy crops could not yet be taken.

B.2. Residues in livestock

Not relevant for the commodities under consideration.

B.3. Consumer risk assessment

| ARfD | 0.3 mg/kg bw (EFSA, 2009) |
| Highest IESTI, according to EFSA PRIMo | Hops: 2.0% of ARfD |
| Assumptions made for the calculations | Dried hops are expected to be bulked; therefore the calculation is based on the supervised trial median residues (STMR) The indicative risk assessment is based on a provisional residue definition for the proposed use on hops. The limited data available on the nature of residues (metabolism studies) in leafy crops is a source of additional (non-standard) uncertainty in the risk assessment The indicative risk assessment is based on the toxicological reference values derived in 2009 (EFSA, 2009), assuming that THPI is of similar toxicity as parent captan. The risk assessment may need to be revised if the toxicological reference values for the compounds included in the residue definition for risk assessment are revised |
| ADI | 0.1 mg/kg bw per day (EFSA, 2009) |
| Highest IEDI, according to EFSA PRIMo | 42.9% ADI (DE child) Contribution of crops assessed: Hops: < 1% of ADI (all diets) |
Assumptions made for the calculations

The calculation is based on the median residue levels derived for raw agricultural commodities. The contributions of commodities where no GAP was reported in the framework of the MRL review were not included in the calculation. The indicative risk assessment is based on a provisional residue definition for the proposed use on hops. The limited data available on the nature of residues (metabolism studies) in leafy crops is a source of additional (non-standard) uncertainty in the risk assessment. The indicative risk assessment is based on the toxicological reference values derived in 2009 (EFSA, 2009), assuming that THPI is of similar toxicity as parent captan. The risk assessment may need to be revised if the toxicological reference values for the compounds included in the residue definition for risk assessment are revised.

B.4. Recommended MRLs

| Code (a) | Commodity | Existing EU MRL (mg/kg) | Proposed EU MRL (mg/kg) | Comment/justification |
|---------|-----------|------------------------|-------------------------|-----------------------|
| 0700000 | Hops      | 0.1*                   |                         | Further risk management considerations required |

Enforcement residue definition: Sum of captan and THPI, expressed as captan

Lacking a metabolism study in leafy crops which is representative for the intended use in hops, a final conclusion on the appropriate residue definition for risk assessment and enforcement cannot be derived. The submitted residue trials are sufficient to calculate a tentative MRL proposal of 200 mg/kg for hops (dried hop cones) based on the provisional residue definition for the group of leafy crops. The OECD MRL calculation is driven by the highest residue value observed in a trial which was slightly overdosed and not fully independent. Therefore, based on expert judgement, EFSA proposes as an alternative the MRL of 150 mg/kg.

The limited data available on the nature of residues in leafy crops is a source of additional (non-standard) uncertainty in the risk assessment. The indicative exposure assessment did not lead to exposure exceeding the toxicological reference values.

MRL: maximum residue level; OECD: Organisation for Economic Co-operation and Development.

*: Indicates that the MRL is set at the limit of analytical quantification (LOQ).

(a): Commodity code number according to Annex I of Regulation (EC) No 396/2005.
Appendix C – Pesticide Residue Intake Model (PRIMo)

**Capitan**

| Status of the active substance: | Approved |
| Code no.: | Proposed LOQ |
| LOQ (mg/kg bw): | Proposed LOQ |

### Toxicological end points

| ADI (mg/kg bw per day): | 0.1 |
| ARfD (mg/kg bw): | 0.3 |
| Source of ADI: | EFSA |
| Source of ARfD: | EFSA |
| Year of evaluation: | 2009 |

### Chronic risk assessment–refined calculations

| Commodity/group of commodities | pTMRLs at LOQ (in % of ADI) |
|---------------------------------|-----------------------------|
| **Apples**                      |                             |
| **Pears**                       |                             |
| **Cherries**                    |                             |
| **Crushed olives**              |                             |
| **Tomatoes**                    |                             |
| **Blueberries**                 |                             |
| **Peaches**                     |                             |
| **Strawberries**                |                             |
| **Gooseberries**                |                             |
| **Mixed berries**               |                             |
| **Currants (red, black and white)** |                             |
| **Mixed fruits**                |                             |
| **Figs**                        |                             |
| **HOPS (dried)**                |                             |

#### TMDI (range) in % of ADI

| Commodity/group of commodities | Minimum–Maximum |
|---------------------------------|-----------------|
| **Apples**                      |                 |
| **Pears**                       |                 |
| **Cherries**                    |                 |
| **Crushed olives**              |                 |
| **Tomatoes**                    |                 |
| **Blueberries**                 |                 |
| **Peaches**                     |                 |
| **Strawberries**                |                 |
| **Gooseberries**                |                 |
| **Mixed berries**               |                 |
| **Currants (red, black and white)** |                 |
| **Mixed fruits**                |                 |
| **Figs**                        |                 |
| **HOPS (dried)**                |                 |

#### Highest calculated TMDI values in % of ADI

| Commodity/group of commodities | MS Diet |
|---------------------------------|---------|
| **Apples**                      |         |
| **Pears**                       |         |
| **Cherries**                    |         |
| **Crushed olives**              |         |
| **Tomatoes**                    |         |
| **Blueberries**                 |         |
| **Peaches**                     |         |
| **Strawberries**                |         |
| **Gooseberries**                |         |
| **Mixed berries**               |         |
| **Currants (red, black and white)** |         |
| **Mixed fruits**                |         |
| **Figs**                        |         |
| **HOPS (dried)**                |         |

#### Highest contributor to MS diet in % of ADI

| Commodity/group of commodities | MS Diet |
|---------------------------------|---------|
| **Apples**                      |         |
| **Pears**                       |         |
| **Cherries**                    |         |
| **Crushed olives**              |         |
| **Tomatoes**                    |         |
| **Blueberries**                 |         |
| **Peaches**                     |         |
| **Strawberries**                |         |
| **Gooseberries**                |         |
| **Mixed berries**               |         |
| **Currants (red, black and white)** |         |
| **Mixed fruits**                |         |
| **Figs**                        |         |
| **HOPS (dried)**                |         |

#### 2nd contributor to MS diet in % of ADI

| Commodity/group of commodities | MS Diet |
|---------------------------------|---------|
| **Apples**                      |         |
| **Pears**                       |         |
| **Cherries**                    |         |
| **Crushed olives**              |         |
| **Tomatoes**                    |         |
| **Blueberries**                 |         |
| **Peaches**                     |         |
| **Strawberries**                |         |
| **Gooseberries**                |         |
| **Mixed berries**               |         |
| **Currants (red, black and white)** |         |
| **Mixed fruits**                |         |
| **Figs**                        |         |
| **HOPS (dried)**                |         |

#### 3rd contributor to MS diet in % of ADI

| Commodity/group of commodities | MS Diet |
|---------------------------------|---------|
| **Apples**                      |         |
| **Pears**                       |         |
| **Cherries**                    |         |
| **Crushed olives**              |         |
| **Tomatoes**                    |         |
| **Blueberries**                 |         |
| **Peaches**                     |         |
| **Strawberries**                |         |
| **Gooseberries**                |         |
| **Mixed berries**               |         |
| **Currants (red, black and white)** |         |
| **Mixed fruits**                |         |
| **Figs**                        |         |
| **HOPS (dried)**                |         |

### Conclusion:

The estimated Theoretical Maximum Daily Intakes (TMDI), based on pTMRLs were below the ADI. A long-term intake of residues of Capitan is unlikely to present a public health concern.
## Acute risk assessment/children–refined calculations

The acute risk assessment is based on the ARfD. For each commodity, the calculation is based on the highest reported MS consumption per kg bw and the corresponding unit weight from the MS with the critical consumption. If no data on the unit weight was available from that MS, an average European unit weight was used for the IESTI calculation.

In the IESTI 1 calculation, the variability factors were 10, 7 or 5 (according to JMPR manual 2002); for lettuce, a variability factor of 5 was used.

In the IESTI 2 calculations, the variability factors of 10 and 7 were replaced by 5. For lettuce, the calculation was performed with a variability factor of 3.

Threshold MRL is the calculated residue level which would result in an exposure equivalent to 100% of the ARfD.

### No of commodities for which ARfD/ADI is exceeded (IESTI 1):

| Highest % of ARfD/ADI | Commodity   | pTMRL/threshold MRL (mg/kg) |
|-----------------------|-------------|-----------------------------|
| 0.2                   | HOPS (dried)| 33.1/-                      |

### No of critical MRLs (IESTI 1):

### No of commodities for which ARfD/ADI is exceeded (IESTI 2):

| Highest % of ARfD/ADI | Commodity   | pTMRL/threshold MRL (mg/kg) |
|-----------------------|-------------|-----------------------------|
| 0.2                   | HOPS (dried)| 33.1/-                      |

### Conclusion:

For processed commodities, no exceedance of the ARfD/ADI was identified.

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## Acute risk assessment/adults/general population–refined calculations

The results of the IESTI calculations are reported for at least 5 commodities. If the ARfD is exceeded for more than 5 commodities, all IESTI values > 90% of ARfD are reported.

**pTMRL**: provisional temporary MRL.

### No of commodities for which ARfD/ADI is exceeded (IESTI 1):

| Highest % of ARfD/ADI | Processed commodities | pTMRL/threshold MRL (mg/kg) |
|-----------------------|-----------------------|-----------------------------|
| 2.0                   | HOPS (dried)          | 33.1/-                      |

### No of critical MRLs (IESTI 1):

### No of commodities for which ARfD/ADI is exceeded (IESTI 2):

| Highest % of ARfD/ADI | Processed commodities | pTMRL/threshold MRL (mg/kg) |
|-----------------------|-----------------------|-----------------------------|
| 2.0                   | HOPS (dried)          | 33.1/-                      |

### Conclusion:

For Captan, IESTI 1 and IESTI 2 were calculated for food commodities for which pTMRLs were submitted and for which consumption data are available.

No exceedance of the ARfD/ADI was identified for any unprocessed commodity.

For processed commodities, no exceedance of the ARfD/ADI was identified.

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Appendix D – Input values for the exposure calculations

D.1. Livestock dietary burden calculations

| Feed commodity | Median dietary burden | Maximum dietary burden |
|----------------|-----------------------|------------------------|
|                | Input value (mg/kg)   | Comment                |
|                |                      |                        |
| Commodities under assessment are not fed to livestock |

D.2. Consumer risk assessment

| Commodity                      | Chronic risk assessment | Acute risk assessment |
|--------------------------------|-------------------------|-----------------------|
|                                | Input value (mg/kg)     | Comment               |
|                                |                         | Input value (mg/kg)   |
|                                |                         | Comment               |

**Risk assessment residue definition:** Sum of captan and THPI, expressed as captan. Provisional residue definition for the proposed use on hops

| Commodity                      | Input value (mg/kg) | Comment               |
|--------------------------------|---------------------|-----------------------|
| Hops                           | 33.1 STMR           | 33.1 STMR             |
| Pome fruits                    | 3.11 STMR (EFSA, 2014) |                      |
| Apricots                       | 1.34 STMR (EFSA, 2014) |                      |
| Cherries                       | 1.00 STMR (EFSA, 2014) |                      |
| Peaches                        | 1.34 STMR (EFSA, 2014) |                      |
| Plums                          | 1.20 STMR (EFSA, 2014) |                      |
| Strawberries                   | 0.47 STMR (EFSA, 2014) |                      |
| Blackberries                   | 5.32 STMR (EFSA, 2014) |                      |
| Raspberries                    | 5.32 STMR (EFSA, 2014) |                      |
| Blueberries                    | 7.86 STMR (EFSA, 2014) |                      |
| Cranberries                    | 7.86 STMR (EFSA, 2018) |                      |
| Currants (black, red and white)| 7.86 STMR (EFSA, 2014) |                      |
| Gooseberries                   | 7.86 STMR (EFSA, 2014) |                      |
| Tomatoes                       | 0.34 STMR (EFSA, 2014) |                      |

**Risk assessment residue definition:** Sum of THPI, 3-OH THPI and 5-OH THPI, expressed as captan

| Commodity                      | Input value (mg/kg) | Comment               |
|--------------------------------|---------------------|-----------------------|
| Ruminant muscle                | 0.08 STMR (EFSA, 2014) |                      |
| Ruminant fat                   | 0.05 STMR (EFSA, 2014) |                      |
| Ruminant liver                 | 0.08 STMR (EFSA, 2014) |                      |
| Ruminant kidney                | 0.08 STMR (EFSA, 2014) |                      |
| Milk: cattle, sheep, goat      | 0.03* STMR (EFSA, 2014) |                      |

STMR: supervised trials median residue.

* Indicates that the MRL is proposed at the limit of quantification.
## Appendix E – Used compound codes

| Code/trivial name | Chemical name /SMILES notation/InChiKey(a) | Structural formula(b) |
|-------------------|--------------------------------------------|-----------------------|
| Captan            | N-(trichloromethylthio)cyclohex-4-ene-1,2-dicarboximide ClC(Cl)(Cl)SN1C(-O)C2CC-CC2C1=O LDVVMCZRFWMZSG-UHFFFAOYSA-N | ![Structural formula](image) |
| THPI              | 3a,4,7,7a-tetrahydro-1H-isooindole-1,3(2H)-dione O=C1NC(-O)C2CC-CC12 CIFFBTOJCKSRJY-UHFFFAOYSA-N | ![Structural formula](image) |
| 3-OH THPI         | (4RS)-4-hydroxy-3a,4,7,7a-tetrahydro-1H-isooindole-1,3(2H)-dione O=C1NC(-O)C2C1CC-CC2O MLJWDNXRMBJJU-UHFFFAOYSA-N | ![Structural formula](image) |
| 5-OH THPI         | (5RS)-5-hydroxy-3a,4,5,7a-tetrahydro-1H-isooindole-1,3(2H)-dione OC1C-CC2C(-O)NC(-O)C2C1 GNUNAYOODXBP-UHFFFAOYSA-N | ![Structural formula](image) |
| THPAM             | 6-carbamoyl-3-cyclohexene-1-carboxylic acid (1RS,6RS;1RS,6SR)-6-carbamoyl-3-cyclohexene-1-carboxylic acid OC(-O)C1CC-CC1C(N)=O AZDKWAOUSBOZMHG-UHFFFAOYSA-N | ![Structural formula](image) |
| Captan epoxide    | 4-[[trichloromethyl]sulfanyl][tetrahydro-1aH-oxireno[7]isooindole-3,5(2H,4H)-dione ClC(Cl)(Cl)SN1C(-O)C2CC3OC3CC2C1=O MAJYQZYGRHDX-UHFFFAOYSA-N | ![Structural formula](image) |
| THPI epoxide      | tetrahydro-1aH-oxireno[7]isooindole-3,5(2H,4H)-dione O=C1NC(-O)C2CC3OC3CC21 ZNMAOBICKRSNB-UHFFFAOYSA-N | ![Structural formula](image) |
| Folpet            | N-(trichloromethylthio)phthalimide ClC(Cl)(Cl)SN1C(-O)c2cccccc2C1=O HKIOYBGHSTUDB-UHFFFAOYSA-N | ![Structural formula](image) |

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

(a): ACD/Name 2015 ACD/Labs 2015 Release (File version N20E41, Build 75170, 19 December 2014).

(b): ACD/ChemSketch 2015 ACD/Labs 2015 Release (File version C10H41, Build 75059, 17 December 2014).