Review of the existing maximum residue levels for propineb according to Article 12 of Regulation (EC) No 396/2005

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Abstract

According to Article 12 of Regulation (EC) No 396/2005, EFSA has reviewed the maximum residue levels (MRLs) currently established at European level for the pesticide active substance propineb. Although this active substance is no longer authorised within the EU, due to insufficient information in order to conclude on the consumer risk assessment for the active substance, the toxicity of the metabolite propane-1,2-diamine (PDA) the impact on non-target organisms and the risk to honeybees, MRLs based on the use of propineb were established by the Codex Alimentarius Commission (codex maximum residue limits; CXLs) and are still in place. Additionally, propineb has potential endocrine-disrupting properties related to the hazards of its major metabolite 4-methylimidazolidine-2-thione (PTU). Lacking a full toxicological characterisation for the compound PDA, exposure data for metabolites propineb-DIDT in plants and PDA in processed commodities and considering that propineb-MRLs correlated to CXLs were based on EU uses that were withdrawn following the non-renewal and are no longer in place, it was not possible for EFSA to perform an assessment of these MRLs and their incorporation in European legislation cannot be recommended. Nevertheless, available data allowed EFSA to propose a marker residue and a limit of quantification (LOQ) for enforcement against potential illegal uses.

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Summary

Propineb was initially included in Annex I to Directive 91/414/EEC on 1 April 2004 by Commission Directive 2003/39/EC, and was deemed to be approved under Regulation (EC) No 1107/2009, in accordance with Commission Implementing Regulation (EU) No 540/2011, as amended by Commission Implementing Regulation (EU) No 541/2011. As the active substance was approved before the entry into force of Regulation (EC) No 396/2005 on 2 September 2008, the European Food Safety Authority (EFSA) is required to provide a reasoned opinion on the review of the existing maximum residue levels (MRLs) for that active substance in compliance with Article 12(2) of the aforementioned regulation.

In the meantime, an application for renewal of the approval of propineb in accordance with Article 1 of Regulation (EU) No 844/2012 was submitted by Bayer CropScience AG. The process of renewal of the first approval, with Italy designated as rapporteur Member State (RMS) has been completed by EFSA in 2016. In 2018, a decision of non-renewal of propineb was taken by Commission Implementing Regulation (EU) 2018/309.

As the basis for the MRL review, in order to verify whether import tolerances may still be in place in some Member States, on 17 December 2019 EFSA initiated the collection of data for this active substance. In a first step, Member States were invited to submit by 24 January 2020 their Good Agricultural Practices (GAPs) reflecting import tolerances currently in place in a standardised way, in the format of specific GAP forms, allowing the designated rapporteur Member State Italy to identify the critical GAPs in the format of a specific GAP overview file. However, no further information was provided by Member States during the collection period. Although the use of propineb is no longer authorised within the European Union (EU) and uses authorised in third countries were not reported to EFSA, the Codex Limits (CXLs) based on the use of propineb, which were previously evaluated by the JMPR, are currently still in place.

Taking into account the conclusions derived by EFSA in the framework of Regulation (EC) No 1107/2009 and the MRLs established by the Codex Alimentarius Commission, EFSA prepared in March 2020 a draft reasoned opinion, which was circulated to Member States and EURLs for consultation via a written procedure. Comments received by 8 May 2020 were considered during the finalisation of this reasoned opinion. The following conclusions are derived.

Primary crop metabolisms of propineb were investigated in apples, grapes, tomato and potatoes following foliar application. Based on the available data and given the relevance of unchanged parent compound after foliar treatments, parent compound, determined as propane-1,2-diamine (PDA) and expressed as propineb, is considered to be the most adequate marker for enforcement in plants. For risk assessment, the residue definition was set as (a) Propineb, (determined as PDA and expressed as propineb); (b) 4-methylimidazolidine-2-thione (PTU); (c) Propineb-DIDT (provisional); (d) PTU and PDA (for processed commodities). Nevertheless, due to the lack of full toxicological data package for the compound PDA, exposure data for metabolites propineb-DIDT in plants and PDA in processed commodities and considering that propineb-MRLs correlated to CXLs were based on EU uses for propineb that were withdrawn following the non-renewal and are no longer in place, it was not possible for EFSA to further consider these MRLs. Consequently, incorporation of propineb-MRLs correlated to CXLs in the European legislation is not recommended.

It is expected that enforcement laboratories will be able to enforce propineb with a limit of quantification (LOQ) of 0.05 mg/kg in all plant commodities, when propineb is determined as PDA and expressed as propineb.

Livestock metabolism of propineb was investigated in laying hens and goat. In this case, the parent was not a sufficient marker in contrast with metabolite PTU which was mainly identified in all animal commodities. Therefore, PTU (free and conjugated) was proposed for enforcement. An analytical method was not available for the determination of PTU (free and conjugated) in animal matrices. According to the EURLs, determination of free PTU only is achievable in milk, muscle, liver and kidney at an LOQ of 0.01 mg/kg and in fat at an LOQ of 0.005 mg/kg.

Considering that the enforcement of potential illegal uses falls under the remit of risk managers, EFSA is not in a position to recommend whether the default MRL of 0.01 mg/kg, as defined by regulation (EC) No 396/2005, should apply or whether the setting of specific LOQs for plant and animal commodities is necessary. EFSA notes, however, that parent propineb (determined as PDA and expressed as propineb) and metabolites PTU and PDA are considered as good indicators for enforcement of potential illegal uses originating from the use of propineb, in plant, animal and processed commodities, respectively. LOQs of 0.05 mg/kg for propineb (determined as PDA and expressed as propineb) in plant commodities and 0.01 mg/kg for PTU (free and conjugated) in animal commodities would provide a satisfactory level of protection for European consumers.
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Background

Regulation (EC) No 396/2005\(^1\) (hereinafter referred to as ‘the Regulation’) establishes the rules governing the setting and the review of pesticide maximum residue levels (MRLs) at European level. Article 12(2) of that Regulation stipulates that the European Food Safety Authority (EFSA) shall provide by 1 September 2009 a reasoned opinion on the review of the existing MRLs for all active substances included in Annex I to Directive 91/414/EEC\(^2\) before 2 September 2008.

Propineb was initially included in Annex I to Council Directive 91/414/EEC on 1 April 2004 by means of Commission Directive 2003/39/EC\(^3\) which has been deemed to be approved under Regulation (EC) No 1107/2009\(^4\), in accordance with Commission Implementing Regulation (EU) No 540/2011\(^5\), as amended by Commission Implementing Regulation (EU) No 541/2011\(^6\). Therefore, EFSA initiated the review of all existing MRLs for that active substance. In the meantime, an application for renewal of the approval of propineb in accordance with Article 1 of Regulation (EU) No 844/2012\(^7\) was submitted by Bayer CropScience AG. Subsequently, in the framework of Regulation (EC) No 1107/2009 propineb was evaluated by Italy, designated as rapporteur Member State (RMS). A peer review on the initial evaluation of the RMS was conducted by EFSA, leading to the conclusions as set out in the EFSA conclusion (EFSA, 2016). Consequently, the approval of propineb was not renewed by Commission Implementing Regulation (EU) 2018/309\(^8\).

According to the legal provisions, EFSA shall base its reasoned opinion in particular on the relevant assessment report prepared under Directive 91/414/EEC repealed by Regulation (EC) No 1107/2009. It should be noted, however, that, in the framework of Regulation (EC) No 1107/2009, only a few representative uses are evaluated, whereas MRLs set out in Regulation (EC) No 396/2005 should accommodate all uses authorised within the European Union (EU) and uses authorised in third countries that have a significant impact on international trade. The information included in the assessment report prepared under Regulation (EC) No 1107/2009 is therefore insufficient for the assessment of all existing MRLs for a given active substance.

As the basis for the MRL review, on 17 December 2019 EFSA initiated the collection of data for this active substance. In a first step, Member States were invited to submit by 24 January 2020 their Good Agricultural Practices (GAPs) reflecting import tolerances currently in place, in a standardised way, in the format of specific GAP forms. In the framework of this consultation no Member States provided feedback on import tolerances in place for propineb. Although the use of propineb is no longer authorised within the European Union (EU) and uses authorised in third countries were not reported to EFSA, Codex Limits (CXLs) based on the use of propineb, which were previously evaluated by the JMPR, are currently still in place.

Considering all the available information, and taking into account the MRLs established by the Codex Alimentarius Commission (CAC) (i.e. codex maximum residue limit; CXLs), EFSA prepared in March 2020 a draft reasoned opinion, which was circulated to Member States and EURLs for commenting via a written procedure. All comments received by 8 May 2020 were considered by EFSA during the finalisation of the reasoned opinion.

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1. Regulation (EC) No 396/2005 of the European Parliament and of the Council of 23 February 2005 on maximum residue levels of pesticides in or on food and feed of plant and animal origin and amending Council Directive 91/414/EEC. OJ L 70, 16.3.2005, p. 1–16.
2. 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. Repealed by Regulation (EC) No 1107/2009.
3. Commission Directive 2003/39/EC of 15 May 2003 amending Council Directive 91/414/EEC to include propineb and propyzamide as active substances. OJ L 124, 20.5.2003, p. 30–32.
4. Regulation (EC) No 1107/2009 of the European Parliament and of the Council of 21 October 2009 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.
5. Commission Implementing Regulation (EU) No 540/2011 of 25 May 2011 implementing Regulation (EC) No 1107/2009 of the European Parliament and of the Council as regards the list of approved active substances. OJ L 153, 11.6.2011, p. 1–186.
6. Commission Implementing Regulation (EU) No 541/2011 of 1 June 2011 amending Implementing Regulation (EU) No 540/2011 implementing Regulation (EC) No 1107/2009 of the European Parliament and of the Council as regards the list of approved active substances. OJ L 153, 11.6.2011, p. 187–188.
7. 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.
8. Commission Implementing Regulation (EU) 2018/309 of 1 March 2018 concerning the non-renewal of approval of the active substance propineb, in accordance with Regulation (EC) No 1107/2009 of the European Parliament and of the Council concerning the placing of plant protection products on the market, and amending the Annex to Commission Implementing Regulation (EU) No 540/2011. C/2018/1108.OJ L 60, 2.3.2018, p. 16–18.
Supporting document to this reasoned is the Member States consultation report (EFSA, 2020). Furthermore, the exposure calculations for all crops considered in the framework of this review performed using the EFSA Pesticide Residues Intake Model (PRIMo) is a key supporting document and thus made publicly available as background document to this reasoned opinion. A screenshot of the report sheet of the PRIMo is presented in Appendix A.

**Terms of Reference**

According to Article 12 of Regulation (EC) No 396/2005, EFSA shall provide a reasoned opinion on:

- the inclusion of the active substance in Annex IV to the Regulation, when appropriate;
- the necessity of setting new MRLs for the active substance or deleting/modifying existing MRLs set out in Annex II or III of the Regulation;
- the inclusion of the recommended MRLs in Annex II or III to the Regulation;
- the setting of specific processing factors as referred to in Article 20(2) of the Regulation.

**The active substance and its use pattern**

Propineb is the ISO common name for polymeric zinc propylenebis(dithiocarbamate) (IUPAC). The chemical structure of the active substance and its main metabolites are reported in Appendix B.

The EU MRLs for propineb are established in Annexes II and III of Regulation (EC) No 396/2005. CXLs based on the use of propineb were also established by the CAC. According to non-approval under Regulation (EC) No 1107/2009, plant protection products containing propineb are no longer authorised in EU Member States (authorisations for emergency situations in plant protection granted in application of Article 53 of Regulation (EC) No 1107/2009 are not considered in the context of this reasoned opinion). For the purpose of this MRL review, Member States did not report any use authorised in third countries that might have a significant impact on international trade.

It is underlined that, although two lists of MRLs are currently set for propineb (one as propineb and specific for this active substance, and one as CS₂, covering all dithiocarbamates), the present review is focussing only on the MRLs currently set as propineb (expressed as propylenediamine).

**Assessment**

Although the use of propineb is no longer authorised within the EU and uses authorised in third countries were not reported to EFSA, the uses of propineb were previously evaluated by the JMPR and CXLs were established (FAO, 1993, 2004). The CXLs resulting from this assessment by JMPR and adopted by the CAC, are now international recommendations that need to be considered by European risk managers when establishing MRLs. To facilitate consideration of propineb-MRLs correlated to CXLs by risk managers, EFSA assessed the available data with particular attention to the analytical methods and the nature of residues in plants and livestock. EFSA mainly bases its assessment on the renewal assessment report (RAR) prepared under Regulation (EU) No 1107/2009 (Italy, 2015, 2016) and the conclusion on the peer review of the pesticide risk assessment of the active substance propineb (EFSA, 2016).

1. **Residues in plants**

The metabolism of propineb was investigated after foliar treatment in fruits (apple, grapes, tomato) and root crops (potatoes) (Italy, 2015, 2016) in the framework of the peer review (EFSA, 2016) and JMPR (FAO, 2004). In all studies [propane-1-¹⁴C], propineb was used.

Parent propineb was recovered at a high proportion in apple (15–31% total radioactive residue (TRR)), grapes (11–41% TRR), tomato (11% TRR) and potato vines (28.6% TRR). The predominant metabolite of the total residues in apple and tomato was identified as the metabolite 4-methylimidazolidine-2-thione (PTU) (15% and 30% TRR, respectively). Several minor metabolites that accounted for < 10% TRR were identified as PU and propineb-DIDT in the fruit crops. In potato tuber, propineb was extensively degraded and was not detected while the metabolite PU was the predominant compound of the total residues (21% TRR). The metabolic pathway of propineb was similar in fruits and root crops.

Studies investigating the nature of residues in processed commodities were assessed (Italy, 2015, 2016) in the framework of the peer review (EFSA, 2016) and JMPR (FAO, 2004). Studies were conducted with radiolabelled [propane-1-¹⁴C] propineb simulating representative hydrolytic conditions.
for 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). The studies demonstrated that propineb is totally degraded when subject to hydrolytic conditions. The main degradation products are PTU (36% to 98% of the applied radioactivity (AR)) and propane-1,2-diamine (PDA) (2-62% of the applied radioactivity (AR)). PDA was mainly formed under the conditions simulating pasteurisation, and PTU under conditions simulating sterilisation. Therefore, metabolites PTU and PDA of propineb need to be considered in processed commodities.

The storage stability of propineb and its metabolites PTU was investigated in the framework of the peer review (EFSA, 2016) and JMPR (FAO, 2004). The storage stability of both compounds was investigated in high water (tomato, apple), high starch (potato) and high acid (orange, grapes) matrices (Italy, 2015, 2016; EFSA, 2016). In high water, high starch and high acid content commodities, the available studies demonstrated storage stability for propineb for a period of 24 months when stored at or lower than –18°C. PTU, was unstable in all commodity groups investigated with storage period of 2 days in tomatoes and oranges, 2–3 days in grapes, 15 days in potatoes and 34 days in apples. Storage stability data for metabolites propineb-DIDT, PU and PDA were not available.

During the peer review, two hyphenated analytical methods based on liquid chromatography (LC) or gas chromatography (GC) coupled to tandem mass spectrometry (MS/MS) detection were validated. Analytical methods for the determination of residue as propineb were not available; however, residues were measured by hot acid hydrolysis trapping of CS₂ in isooctane followed by GC–MS/MS or LC–MS/MS analysis of the propylenediamine derivative (PDA). Both methods are considered suitable for enforcing propineb in dry matrices, high water, high acid and high oil content commodities with a limit of quantification (LOQ) of 0.05 mg/kg (determined and expressed as CS₂) or with an LOQ of 0.01 mg/kg in high acid, high oil matrices and 0.05 mg/kg in high water, high starch and dry matrices (determined as PDA and expressed as propineb). Both methods were validated by an independent laboratory (ILV) in orange, grape, apple, dry beans, sunflower seed (determined and expressed as CS₂) and avocado (determined as PDA and expressed as propineb) (EFSA, 2016). During the Members State consultation, information from preliminary experiments, on the availability of analytical methods for the enforcement of propineb (determined and expressed as PDA), as well as for the determination of PTU and the determination of free PDA, were received by the EURs (EURs, 2020). Propineb, determined and expressed as PDA (therefore not in line with the proposed residue definition), can be monitored by applying a single residue method involving reductive cleavage with HCl/SnCl₂ and followed by QuEChERS extraction of the aqueous phase at high pH, with an LOQ of 0.05 mg/kg in high water and high acid commodities, 0.1 mg/kg in dry commodities and 0.2 mg/kg in high oil commodities. For PTU, an LOQ of 0.01 mg/kg is achievable using the QuPPe method in high water, high acid and dry commodities. Validation data were not available for high oil commodities. For free PDA, an LOQ of 0.05 mg/kg is achievable using the QuPPe method in high water and high acid commodities. For high oil and dry commodities validation data were not available.

The metabolism of propineb was similar in all crops assessed. In processed commodities, a different pattern was observed; therefore a separate residue definition for processed commodities was needed.

For raw commodities, propineb was found to be a sufficient marker in fruits and root crops; however, due to analytical limitations in the determination of residue as propineb, two different residue definitions for enforcement are applicable. In contrast for processed commodities, metabolite PDA was found to be the most appropriate marker since parent was degraded. Therefore, based on the above, the following residue definitions for enforcement were agreed for raw and processed plant commodities during the peer review:

1) Dithiocarbamates determined and expressed as CS₂, including maneb, mancozeb, metiram, propineb, thiram and ziram.
2) Propineb, determined as PDA and expressed as propineb – the way the residue definition will be expressed is pending upon the requested toxicity profile of PDA.
3) PDA for processed commodities.

For risk assessment, the peer review concluded that metabolites PTU, propineb-DIDT, PU and PDA are toxicologically relevant and thus should be considered in the consumer exposure. Therefore, separate residue definitions were agreed for plants on the basis of specific toxicological reference values proposed, respectively, for PTU and propineb-DIDT:
1) Propineb, determined as PDA and expressed as propineb – the way the residue definition will be expressed is pending upon the requested toxicity profile of PDA

2) PTU

3) Propineb-DIDT (provisional)

4) PTU and PDA for processed commodities.

The residue definition for risk assessment set by JMPR for both plant and animal commodities, was set as ‘propineb and PTU’.

EFSA notes that the residue definitions for enforcement and risk assessment proposed in the peer review (EFSA 2016) are still considered applicable; however, since the scope of the current review is focused on propineb uses only, recommendations under this review apply only for the propineb specific MRLs, and not to the MRL that are set for all dithiocarbamates.

2. Residues in livestock

Livestock metabolism of propineb was investigated in the framework of Directive 91/414/EEC (Italy, 2015, 2016, EFSA, 2016) and by the JMPR (FAO, 2004). The metabolism of propineb with radiolabelled [propane-1-14C] propineb was investigated in laying hens and goat.

The parent compound was extensively degraded and was not recovered in any animal matrix. The main compounds identified were PTU, both free and conjugated, (12% TRR in eggs, 18.5% TRR in milk, and 23–59% TRR in poultry and ruminants’ tissues.), PU (18%–50% TRR in poultry tissues and eggs, < 10% TRR in goat matrices), 2-methylthio-4-methylimidazoline (25% TRR kidney, 17% TRR muscle and 48% TRR milk).

As the metabolite PTU was found to be a sufficient marker in livestock commodities, the residue definition for enforcement is proposed as PTU, free and conjugated. This proposal is inconsistent with the proposal derived from JMPR in which the residue definition for enforcement was set as total dithiocarbamates, determined as CS₂, evolved during acid digestion and expressed as mg CS₂/kg.

Analytical methods using hot acid hydrolysis trapping of CS₂ in isooctane followed by GC–MS/MS or LC–MS/MS analysis of the PDA (free) were fully validated for the determination of propineb in all animal tissues, milk and eggs, with LOQs of 0.05 mg/kg (determined as CS₂) and 0.01 mg/kg (determined as PDA) (EFSA, 2016). However, an analytical method is not available for the determination of PTU (free and conjugated) in animal matrices. According to the EURels (EURels, 2020), for free PTU only, an LOQ of 0.01 mg/kg is achievable using the QuPPe method in milk, muscle, liver and kidney and 0.005 mg/kg in fat. Moreover, the EURels emphasised that only free PTU was validated. Conjugated PTU components were not studied as they were not available nor the analytical method employed includes any specific de-conjugation step.

3. Consumer risk assessment

The toxicological assessment of propineb was peer reviewed under Directive 91/414/EEC which resulted in an acceptable daily intake (ADI) and an acute reference dose (ARfD) being established at 0.007 mg/kg body weight (bw) per and 0.1 mg/kg bw, respectively. It is noted that:

a) a lack of toxicological data for the compound PDA, found in the metabolism studies was previously identified by EFSA (2016);

b) the potential exposure to metabolites propineb-DIDT in plants and PDA in processed commodities was not sufficiently investigated by the JMPR;

c) the propineb-MRLs correlated to CXLs were based on EU GAPs that are no longer in place.

Consequently, for risk assessment purposes further investigation of the metabolite propineb-DIDT for plants and PDA for processed commodities is required in order to be consistent with the residue definition proposed by EFSA.

Due to the above uncertainties, an assessment of the propineb-MRLs correlated to CXLs that are currently in place is not possible.

Nevertheless, in order to assess whether the reported LOQ (expressed as propineb), is sufficiently protective for European consumers, chronic and acute intake calculations assuming a LOQ of 0.05 mg/kg

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9 The above are restricted to fruit crops with possible extension to root crops pending upon clarification on whether the analytical method for the determination of propineb residues as PDA is also able to analyse all the metabolites containing the ‘propineb methyl diamine moiety’ as PTU and PU compounds (EFSA, 2016).

10 The way the residue definition will be expressed is pending upon the requested toxicity profile of PDA.
The calculated exposures were compared with the toxicological reference values derived for propineb; detailed results of the calculations are presented in Appendix A. The highest chronic exposure was calculated for Dutch toddler, representing 43% of the ADI, and the highest acute exposure was calculated for potatoes, representing 8% of the ARfD. EFSA highlights that this calculation does not reflect real exposure of consumers to propineb residues. This theoretical calculation only indicates that the LOQ value of 0.05 mg/kg would provide a satisfactory level of protection for the European consumers.

Although an analytical method is not available for enforcement for the proposed residue definition in livestock, in order to assess whether the default LOQ of 0.01 mg/kg for PTU (free and conjugated) is sufficiently protective for European consumers, chronic and acute intake calculations were performed using revision 3.1 of the EFSA PRIMo (EFSA, 2018, 2019). For PTU, an ADI and an ARfD are established at 0.002 mg/kg bw per and 0.012 mg/kg bw, respectively (EFSA 2016).

The calculated exposures were compared with the toxicological reference values derived for PTU; detailed results of the calculations are presented in Appendix A. The highest chronic exposure was calculated for Dutch toddler, representing 31% of the ADI and the highest acute exposure was calculated for cow milk, representing 10% of the ARfD.

EFSA highlights that this calculation does not reflect real exposure of consumers to PTU residues. This theoretical calculation only indicates that the LOQ value of 0.01 mg/kg would provide a satisfactory level of protection for the European consumers.

Conclusions and recommendations

Although the use of propineb is no longer authorised within the EU and uses authorised in third countries were not reported to EFSA, the CXLs based on the use of propineb, which were previously evaluated by the JMPR, are currently still in place.

Primary crop metabolisms of propineb were investigated in apples, grapes, tomato and potatoes following foliar application. Based on the available data and given the relevance of unchanged parent compound after foliar treatments, parent compound, determined as PDA and expressed as propineb, is considered to be the most adequate marker for enforcement in plants. For risk assessment, the residue definition was set as (a) Propineb, (determined as PDA and expressed as propineb); (b) PTU; (c) Propineb-DIDT (provisional); (d) PTU and PDA (for processed commodities). Nevertheless, due to the lack of full toxicological data package for the compound PDA, exposure data for metabolites propineb-DIDT in plants and PDA in processed commodities and considering that the propineb-MRLs correlated to CXLs were based on EU uses that were withdrawn following the non-renewal and are no longer in place, it was not possible for EFSA to perform an assessment of these MRLs. Consequently, incorporation of propineb-MRLs correlated to CXLs in the European legislation is not recommended.

It is expected that enforcement laboratories will be able to enforce propineb with a LOQ of 0.05 mg/kg in all plant commodities, when propineb is determined as PDA and expressed as propineb.

Livestock metabolism of propineb was investigated in laying hens and goat. In this case, the parent was not a sufficient marker in contrast with metabolite PTU which was mainly identified in all animal commodities. Therefore PTU (free and conjugated) was proposed for enforcement. An analytical method was not available for the determination of PTU (free and conjugated) in animal matrices. According to the EURLs, determination of free PTU only is achievable in milk, muscle, liver and kidney at an LOQ of 0.01 mg/kg and in fat at an LOQ of 0.005 mg/kg.

Considering that the enforcement of potential illegal uses falls under the remit of risk managers, EFSA is not in a position to recommend whether the default MRL of 0.01 mg/kg, as defined by regulation (EC) No 396/2005, should apply or whether the setting of specific LOQs for plant and animal commodities is necessary. EFSA notes, however, that parent propineb (determined as PDA and expressed as propineb) and metabolites PTU and PDA are considered as good indicators for enforcement of potential illegal uses originating from the use of propineb, in plant, animal and processed commodities, respectively. LOQs of 0.05 mg/kg for propineb (determined as PDA and expressed as propineb) in plant commodities and 0.01 mg/kg for PTU (free and conjugated) in animal commodities would provide a satisfactory level of protection for European consumers.
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Abbreviations

| Abbreviation | Description |
|--------------|-------------|
| ADI          | acceptable daily intake |
| AR           | applied radioactivity |
| ARfD         | acute reference dose |
| bw           | body weight |
| CAC          | Codex Alimentarius Commission |
| CXL          | codex maximum residue limit |
| EURLs        | European Union Reference Laboratories for Pesticide Residues (former CRLs) |
| FAO          | Food and Agriculture Organization of the United Nations |
| GAP          | Good Agricultural Practice |
| GC–MS/MS     | gas chromatography with tandem mass spectrometry |
| ILV          | independent laboratory validation |
| InChIKey     | International Chemical Identifier Key. |
| ISO          | International Organisation for Standardization |
| IUPAC        | International Union of Pure and Applied Chemistry |
| JMPR         | Joint Meeting of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Expert Group on Pesticide Residues (Joint Meeting on Pesticide Residues) |
| LC–MS/MS     | liquid chromatography with tandem mass spectrometry |
| LOQ          | limit of quantification |
| MRL          | maximum residue level |
| OECD         | Organisation for Economic Co-operation and Development |
| PDA          | propane-1,2-diamine |
| PRImo        | (EFSA) Pesticide Residues Intake Model |
| PTU          | 4-methylimidazolidine-2-thione |
| QuEChERS     | Quick, Easy, Cheap, Effective, Rugged, and Safe (analytical method) |
| Abbreviation | Full Form |
|--------------|-----------|
| RAR          | renewal assessment report |
| RMS          | rapporteur Member State |
| SMILES       | simplified molecular-input line-entry system |
| TRR          | total radioactive residue |
| WHO          | World Health Organization |
**Appendix A – Pesticide Residue Intake Model (PRIMO)**

### PRIMO_Propineb

| LOQs (mg/kg) | ADI (mg/kg bw per day) | ARfD (mg/kg bw) | Source of ADI | Source of ARfD |
|-------------|------------------------|----------------|--------------|---------------|
| 0.05 - 0.05 | 0.007                  | 0.1            | EFSA         | EFSA          |

**Source of ADI and ARfD:**

EFSA PRIMO revision 3.1; 2019/03/19

**Year of evaluation:**

2016

**No of diets exceeding the ADI:**

---

**Exposure (% of ADI)**

| Commodity/group of commodities | Exposure resulting from |
|--------------------------------|-------------------------|
| Bananas                        | 43% 3.03                |
| Oranges                        | 27% 1.91                |
| Wheat                          | 27% 1.86                |
| Potatoes                       | 24% 1.68                |
| Wheat                          | 20% 1.42                |
| Soyabeans                      | 19% 1.36                |
| Potatoes                       | 19% 1.33                |
| Potatoes                       | 19% 1.30                |
| Tomatoes                       | 18% 1.28                |
| Rye                            | 13% 0.94                |
| Potatoes                       | 12% 0.87                |
| Wheat                          | 12% 0.84                |
| Tomatoes                       | 12% 0.82                |
| Bananas                        | 9% 0.65                 |
| Oranges                        | 9% 0.63                 |
| Potatoes                       | 9% 0.62                 |
| Potatoes                       | 8% 0.55                 |
| Potatoes                       | 7% 0.45                 |
| Potatoes                       | 3% 0.18                 |

**Chronic risk assessment:**

JMPR methodology (IEDI/TMDI)

**Conclusion:**

The estimated long-term dietary intake (TMDI/NEDI/IEDI) was below the ADI. The long-term intake of residues of propineb is unlikely to present a public health concern.
The acute risk assessment is based on the ARfD. The calculation is based on the large portion of the most critical consumer group.

### Unprocessed commodities

| ARfD/ADI | Commodity | MRL/input for RA (mg/kg) | Exposure (µg/kg bw) |
|----------|-----------|--------------------------|---------------------|
| 8%       | Potatoes  | 0.05/0.05               | 7.7                 |
| 8%       | Melons    | 0.05/0.05               | 7.6                 |
| 10%      | Oranges   | 0.05/0.05               | 6.6                 |
| 10%      | Watermelons | 0.05/0.05   | 6.1                 |
| 10%      | Pineapples| 0.05/0.05               | 5.1                 |
| 10%      | Bananas   | 0.05/0.05               | 4.9                 |
| 10%      | Mangoes   | 0.05/0.05               | 4.4                 |
| 10%      | Cucumbers | 0.05/0.05               | 3.3                 |
| 10%      | Carrots   | 0.05/0.05               | 3.2                 |
| 10%      | Kiwi fruits | 0.05/0.05   | 3.1                 |

### Processed commodities

| ARfD/ADI | Processed commodity | MRL/input for RA (mg/kg) | Exposure (µg/kg bw) |
|----------|---------------------|--------------------------|---------------------|
| 6%       | Sugar beets (root)/sugar | 0.05/0.6       | 5.5                 |
| 6%       | Potatoes/fried      | 0.05/0.05               | 4.7                 |
| 6%       | Broccoli/boiled     | 0.05/0.05               | 3.9                 |
| 6%       | Cauliflowers/boiled | 0.05/0.05               | 3.5                 |
| 6%       | Escaroles/broad-leaved endive | 0.05/0.05 | 3.3                 |
| 6%       | Potatoes/dried (flakas) | 0.05/0.23     | 3.0                 |
| 6%       | Leeks/boiled        | 0.05/0.05               | 2.9                 |
| 6%       | Apples/juice        | 0.05/0.05               | 2.7                 |
| 6%       | Oranges/juice       | 0.05/0.05               | 2.6                 |
| 6%       | Turnips/boiled      | 0.05/0.05               | 2.5                 |
| 6%       | Parsnips/boiled     | 0.05/0.05               | 2.5                 |
| 6%       | Sweet potatoes/boiled | 0.05/0.05   | 2.5                 |
| 6%       | Florence fennels/boiled | 0.05/0.05 | 2.3                 |

### Conclusion:

No exceedance of the toxicological reference value was identified for any unprocessed commodity. A short-term intake of residues of propineb is unlikely to present a public health risk. For processed commodities, no exceedance of the ARfD/ADI was identified.
| Commodity/group of commodities | Exposure exceeding the ADI | No of diets exceeding the ADI | % of ADI exceeding the ADI |
|--------------------------------|---------------------------|-------------------------------|---------------------------|
| Milk: Cattle                    | 0.12                       | 2                              | 92%                       |
| Bovine: Muscle/meat             | 0.08                       | 2                              | 75%                       |
| Poultry: Muscle/meat            | 0.02                       | 2                              | 14%                       |
| Swine: Muscle/meat              | 0.02                       | 2                              | 14%                       |

Conclusion: The estimated long-term dietary intake (TMDI/NEDI/IEDI) was below the ADI.
The acute risk assessment is based on the ARfD. The calculation is based on the large portion of the most critical consumer group.

### Acute risk assessment/children

| Commodity | MRL/Input for RA (mg/kg) | Exposure (µg/kg bw) | % of ARfD/ADI | Commodity | MRL/Input for RA (mg/kg) | Exposure (µg/kg bw) |
|-----------|--------------------------|---------------------|---------------|-----------|--------------------------|---------------------|
| Milk: Cattle | 0.01/0.01 | 1.2 | 3% | Milk: Cattle | 0.01/0.01 | 0.01/0.01 | 0.39 |
| Milk: Goat | 0.01/0.01 | 0.24 | 2% | Milk: Goat | 0.01/0.01 | 0.01/0.01 | 0.18 |
| Poultry: Muscle/meat | 0.01/0.01 | 0.17 | 1% | Milk: Sheep | 0.01/0.01 | 0.01/0.01 | 0.15 |
| Eggs: Chicken | 0.01/0.01 | 0.12 | 1.0% | Poultry: Muscle | 0.01/0.01 | 0.01/0.01 | 0.12 |
| Swine: Muscle/meat | 0.01/0.01 | 0.12 | 0.5% | Bovine: Muscle | 0.01/0.01 | 0.01/0.01 | 0.06 |
| Bovine: Liver | 0.01/0.01 | 0.08 | 0.5% | Other farmed animals: | 0.01/0.01 | 0.01/0.01 | 0.06 |
| Bovine: Edible offals (other) | 0.01/0.01 | 0.07 | 0.4% | Swine: Muscle/meat | 0.01/0.01 | 0.01/0.01 | 0.05 |
| Bovine: Muscle/meat | 0.01/0.01 | 0.07 | 0.4% | Equine: Muscle/meat | 0.01/0.01 | 0.01/0.01 | 0.05 |
| Other farmed animals: | 0.01/0.01 | 0.07 | 0.4% | Sheep: Muscle/meat | 0.01/0.01 | 0.01/0.01 | 0.05 |
| Equine: Muscle/meat | 0.01/0.01 | 0.06 | 0.4% | Poultry: Liver | 0.01/0.01 | 0.01/0.01 | 0.05 |
| Sheep: Muscle/meat | 0.01/0.01 | 0.05 | 0.4% | Eggs: Chicken | 0.01/0.01 | 0.01/0.01 | 0.04 |
| Bovine: Kidney | 0.01/0.01 | 0.04 | 0.3% | Bovine: Liver | 0.01/0.01 | 0.01/0.01 | 0.04 |
| Milk: Sheep | 0.01/0.01 | 0.04 | 0.3% | Bovine: Edible offals (other) | 0.01/0.01 | 0.01/0.01 | 0.03 |
| Swine: Edible offals (other) | 0.01/0.01 | 0.03 | 0.3% | Swine: Other products | 0.01/0.01 | 0.01/0.01 | 0.03 |
| Bovine: Fat tissue | 0.01/0.01 | 0.02 | 0.2% | Sheep: Liver | 0.01/0.01 | 0.01/0.01 | 0.03 |

### Acute risk assessment/adults/general population

| Commodity | MRL/Input for RA (mg/kg) | Exposure (µg/kg bw) | % of ARfD/ADI | Commodity | MRL/Input for RA (mg/kg) | Exposure (µg/kg bw) |
|-----------|--------------------------|---------------------|---------------|-----------|--------------------------|---------------------|
| Milk: Cattle | 0.01/0.01 | 1.2 | 3% | Milk: Cattle | 0.01/0.01 | 0.01/0.01 | 0.39 |
| Milk: Goat | 0.01/0.01 | 0.24 | 2% | Milk: Goat | 0.01/0.01 | 0.01/0.01 | 0.18 |
| Poultry: Muscle/meat | 0.01/0.01 | 0.17 | 1% | Milk: Sheep | 0.01/0.01 | 0.01/0.01 | 0.15 |
| Eggs: Chicken | 0.01/0.01 | 0.12 | 1.0% | Poultry: Muscle | 0.01/0.01 | 0.01/0.01 | 0.12 |
| Swine: Muscle/meat | 0.01/0.01 | 0.12 | 0.5% | Bovine: Muscle | 0.01/0.01 | 0.01/0.01 | 0.06 |
| Bovine: Liver | 0.01/0.01 | 0.08 | 0.5% | Other farmed animals: | 0.01/0.01 | 0.01/0.01 | 0.06 |
| Bovine: Edible offals (other) | 0.01/0.01 | 0.07 | 0.4% | Swine: Muscle/meat | 0.01/0.01 | 0.01/0.01 | 0.05 |
| Bovine: Muscle/meat | 0.01/0.01 | 0.07 | 0.4% | Equine: Muscle/meat | 0.01/0.01 | 0.01/0.01 | 0.05 |
| Other farmed animals: | 0.01/0.01 | 0.07 | 0.4% | Sheep: Muscle/meat | 0.01/0.01 | 0.01/0.01 | 0.05 |
| Equine: Muscle/meat | 0.01/0.01 | 0.06 | 0.4% | Poultry: Liver | 0.01/0.01 | 0.01/0.01 | 0.05 |
| Sheep: Muscle/meat | 0.01/0.01 | 0.05 | 0.4% | Eggs: Chicken | 0.01/0.01 | 0.01/0.01 | 0.04 |
| Bovine: Kidney | 0.01/0.01 | 0.04 | 0.3% | Bovine: Liver | 0.01/0.01 | 0.01/0.01 | 0.04 |
| Milk: Sheep | 0.01/0.01 | 0.04 | 0.3% | Bovine: Edible offals (other) | 0.01/0.01 | 0.01/0.01 | 0.03 |
| Swine: Edible offals (other) | 0.01/0.01 | 0.03 | 0.3% | Swine: Other products | 0.01/0.01 | 0.01/0.01 | 0.03 |
| Bovine: Fat tissue | 0.01/0.01 | 0.02 | 0.2% | Sheep: Liver | 0.01/0.01 | 0.01/0.01 | 0.03 |

### Conclusion:

No exceedance of the toxicological reference value was identified for any unprocessed commodity. A short term intake of residues of PTU is unlikely to present a public health risk. For processed commodities, no exceedance of the ARfD/ADI was identified.
### Appendix B – Used compound codes

| Code/trivial name<sup>(a)</sup> | IUPAC name/SMILES notation/InChiKey<sup>(b)</sup>                                                                 | Structural formula<sup>(c)</sup> |
|--------------------------------|---------------------------------------------------------------------------------------------------------------|---------------------------------|
| **propineb**                  | polymeric zinc propylenebis(dithiocarbamate)<br>CC(CNC(=S)[S-][NC(=S)[S-]].[Zn+2]<br>KKMLIVYBGSAJPM-UHFFFAOYSA-L | ![Structural formula](Zn.png)    |
| **CS₂**                       | carbon disulphide <br>S=C=S <br>QGJOPFRUJISHPQ-UHFFFAOYSA-N                                                | S=C=S                           |
| **PDA M04**                   | propane-1,2-diamine <br>CC(N)CN <br>AOHJOMMDDJHIJH-UHFFFAOYSA-N                                               | ![Structural formula](PDA.png)   |
| **PTU M01**                   | 4-methylimidazolidine-2-thione <br>S=C1NCC(C)N1 <br>NGZJXCFNBVJLQN-UHFFFAOYSA-N                              | ![Structural formula](PTU.png)   |
| **PU BCS-AA-17927 M02**       | 4-methylimidazolidin-2-one <br>O=C1NCC(C)N1 <br>DWEQVNFWAKICEY-UHFFFAOYSA-N                                 | ![Structural formula](PU.png)    |
| **Propineb-DIDT BCS-CU99534 M05** | 6-methyl-5,6-dihydroimidazo[2,1-c][1,2,4]dithiazole-3-thione <br>CC1N=C2SS(=S)N2C1 <br>HBPWLKZHSGCXBC-UHFFFAOYSA-N | ![Structural formula](Propineb.png) |

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

<sup>(a):</sup> The metabolite name in bold is the name used in the conclusion.

<sup>(b):</sup> ACD/Name 2019.1.1 ACD/Labs 2019 Release (File version N05E41, Build 110555, 18 July 2019).

<sup>(c):</sup> ACD/ChemSketch 2019.1.1 ACD/Labs 2019 Release (File version C05H41, Build 110712, 24 July 2019).