Review of the existing maximum residue levels for bromuconazole 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 bromuconazole. To assess the occurrence of bromuconazole residues in plants, processed commodities, rotational crops and livestock, EFSA considered the conclusions derived in the framework of Directive 91/414/EEC as well as the authorisations reported by Member States (including the supporting residues data). Based on the assessment of the available data, MRL proposals were derived and a consumer risk assessment was carried out. Although no apparent risk to consumers was identified, some information required by the regulatory framework was missing. Hence, the consumer risk assessment is considered indicative only and all MRL proposals derived by EFSA still require further consideration by risk managers.

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Keywords: bromuconazole, MRL review, Regulation (EC) No 396/2005, consumer risk assessment, triazole, fungicide, triazole derivative metabolites (TDMs)

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Summary

Bromuconazole was included in Annex I to Directive 91/414/EEC on 1 February 2011 by Commission Directive 2010/92/EU, and has been 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 after 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(1) of the aforementioned regulation. To collect the relevant pesticide residues data, EFSA asked Belgium, as the designated rapporteur Member State (RMS), to complete the Pesticide Residues Overview File (PROFile) and to prepare a supporting evaluation report. The PROFile and evaluation report provided by the RMS were made available to the Member States. A request for additional information was addressed to the Member States in the framework of a completeness check period, which was initiated by EFSA on 8 August 2016 and finalised on 8 October 2016. After having considered all the information provided, EFSA prepared a completeness check report which was made available to Member States on 18 November 2016.

Based on the conclusions derived by EFSA in the framework of Directive 91/414/EEC and the additional information provided by the RMS and Member States, EFSA prepared in June 2017 a draft reasoned opinion, which was circulated to Member States for consultation via a written procedure. Comments received by 26 July were considered during the finalisation of this reasoned opinion. The following conclusions are derived.

The metabolism of bromuconazole was investigated in cereals and in fruits crops. For cereals, studies performed with phenyl-labelled and triazole-labelled bromuconazole were available. A significant part of the identified residues was bromuconazole (all isomers) but cleavage of the molecule was demonstrated in the study performed with triazole labelled. A confined rotational crop study performed with phenyl-labelled bromuconazole showed a similar metabolism in cereals as for primary crops. However, rotational crops study performed with triazole-labelled bromuconazole is still required to fully address the nature of residues in rotational crops. Based on the available studies, bromuconazole (any ratios of constituent isomers) was considered as the relevant residue for enforcement in cereals. Bromuconazole can be enforced in dry commodities and cereal straw with a limit of quantification (LOQ) of 0.01 mg/kg. For risk assessment, bromuconazole and two triazole derivative metabolites (TDMs – triazole alanine and triazole acetic acid) were considered relevant. However, since there are indications that bromuconazole and TDMs may have different toxicities, those compounds need to be considered in two separate risk assessments. Thus, bromuconazole (any ratio of constituent isomer) was also proposed as a residue definition for risk assessment. It is noted that a residue definition including TDMs will be assessed in the framework of an overall assessment of the confirmatory data on the TDMs. The proposed residue definitions are limited to cereal crops.

The available residue trials performed on wheat were sufficient to derive MRL and risk assessment values for bromuconazole in wheat and rye (grain and straw). The MRLs proposed in this review do not take into account the residues corresponding to the TDMs.

Based on the results of the confined rotational crop study performed with cereals, root crops, leafy crops and oilseeds and on the rotational crop residue trials investigating the level of bromuconazole residues in cereals grown in rotation, it was not possible to conclude whether bromuconazole residues in succeeding crops would remain below the enforcement LOQ of 0.01 mg/kg in all commodities. Additional information on the test conditions of the rotational crop field studies and/or new rotational crop field studies covering the plateau concentration in soil were required. Furthermore, EFSA was not able to conclude on potential TDMs residues levels in rotational crops.

The effect of processing on the nature and magnitude of bromuconazole residues was not investigated but this is currently not considered necessary. With regard to residues of TDMs, EFSA was not able to address the need for processing studies since no information on residues of TDMs in wheat and rye grains is available.

The dietary burdens calculated for all diets of cattle, sheep and poultry were found to exceed the trigger value of 0.1 mg/kg dry matter (DM). The metabolism of bromuconazole was assessed in ruminants and poultry. These studies indicate that bromuconazole is extensively degraded since found at very low levels in tissues. However, as the remaining radioactivity was not identified, the nature of residues in edible tissues was not fully elucidated. A livestock metabolism studies performed with triazole-labelled bromuconazole is still required to address this point. Furthermore, a final conclusion...
on the residue definition of bromuconazole in animal origin commodities also needs to take into consideration the potential intake of TDMs by livestock, which could not be assessed in this review. Therefore, the residue definition for enforcement and risk assessment proposed as bromuconazole (any ratio of constituent isomers) is considered on a tentative basis. Bromuconazole was classified as fat-soluble. There are no livestock feeding studies available but, at the calculated dietary burdens, levels of bromuconazole are not expected to exceed the LOQ in commodities of animal origin. Further studies may be needed in the future to assess the occurrence of potential remaining residues.

Chronic and acute consumer exposure to bromuconazole resulting from the authorised uses reported in the framework of this review was calculated using revision 2 of the EFSA Pesticide Residues Intake Model (PRIMo). The highest chronic exposure represented 4.9% of the acceptable daily intake (ADI) (FR toddler) and the highest acute exposure amounted to 2.5% of the acute reference dose (ARfD) (wheat grain).

It is highlighted that the above assessment did not take into consideration the triazole derivatives metabolites. Since these metabolites may be generated by several pesticides belonging to the group of triazole fungicides, a comprehensive dietary risk assessment for TDMs considering data for several triazole fungicides is being currently carried out by EFSA in the framework of the confirmatory data assessment. This work will involve a re-assessment of the toxicological end points for the TDMs as well as an overall consumer exposure assessment to relevant TDMs arising from all triazole fungicides.
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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(1) of that Regulation stipulates that the European Food Safety Authority (EFSA) shall provide, within 12 months from the date of the inclusion or non-inclusion of an active substance in Annex I to Directive 91/414/EEC\(^2\) a reasoned opinion on the review of the existing MRLs for bromuconazole. As bromuconazole was included in Annex I to Council Directive 91/414/EEC on 1 February 2011 by means of Commission Directive 2010/92/EU\(^3\), and 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\(^6\), EFSA initiated the review of all existing MRLs for that active substance.

According to the legal provisions, EFSA shall base its reasoned opinion in particular on the relevant assessment report prepared under Directive 91/414/EEC. It should be noted, however, that, in the framework of Directive 91/414/EEC, 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 Directive 91/414/EEC is therefore insufficient for the assessment of all existing MRLs for a given active substance.

To gain an overview of the pesticide residues data that have been considered for the setting of the existing MRLs, EFSA developed the Pesticide Residues Overview File (PROFile). The PROFile is an inventory of all pesticide residues data relevant to the risk assessment and MRL setting for a given active substance. This includes data on:

- the nature and magnitude of residues in primary crops;
- the nature and magnitude of residues in processed commodities;
- the nature and magnitude of residues in rotational crops;
- the nature and magnitude of residues in livestock commodities;
- the analytical methods for enforcement of the proposed MRLs.

Belgium, the designated rapporteur Member State (RMS) in the framework of Directive 91/414/EEC, was asked to complete the PROFile for bromuconazole and to prepare a supporting evaluation report (Belgium, 2012). The PROFile and the supporting evaluation report were submitted to EFSA on 22 May 2012 and made available to the Member States. A request for additional information was addressed to the Member States in the framework of a completeness check period which was initiated by EFSA on 8 August 2016 and finalised on 8 October 2016. Additional evaluation reports were submitted by European Union Reference Laboratories for Pesticide Residues and France (EURLs, 2016; France, 2016) and, after having considered all the information provided by RMS and Member States, EFSA prepared a completeness check report which was made available to all Member States on 18 November 2016. No further clarifications were sought from Member States.

Based on the conclusions derived by EFSA in the framework of Directive 91/414/EEC and the additional information provided by the Member States, EFSA prepared in June 2017 a draft reasoned opinion, which was submitted to Member States for commenting via a written procedure. All comments received by 26 July 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 2010/92/EU of 21 December 2010 amending Council Directive 91/414/EEC to include bromuconazole as active substance. OJ L 338, 22.12.2010, p. 44–46.

\(^4\) 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.
The evaluation report submitted by the RMS (Belgium, 2012) and the evaluation reports submitted by EURIs and France (EURIs, 2016; France, 2016) are considered as supporting documents to this reasoned opinion and, thus, are made publicly available.

In addition, key supporting documents to this reasoned opinion are the completeness check report (EFSA, 2017a) and the Member States consultation report (EFSA, 2017b). These reports are developed to address all issues raised in the course of the review, from the initial completeness check to the reasoned opinion. Also, the chronic and acute exposure calculations for all crops reported in the framework of this review performed using the EFSA Pesticide Residues Intake Model (PRIMO) (excel file) and the PROFile are key supporting documents and made publicly available as background documents to this reasoned opinion. Furthermore, a screenshot of the Report sheet of the PRimo(EU) is presented in Appendix C.

Considering the importance of the completeness check and consultation report, all documents are considered as background documents to this reasoned opinion and, thus, are made publicly available.

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

Bromuconazole is the ISO common name for 1-[(2RS,4RS:2RS,4SR)-4-bromo-2-(2,4-dichlorophenyl)tetrahydrofurfuryl]-1H-1,2,4-triazole (IUPAC). Bromuconazole is a mixture of two diastereomeric pairs of enantiomers. The ratio of the diastereomers (2R,4S:2S,4R) to (2R,4R:2S,4S) of the substance used in the submitted tests and studies was ranging between 1.04:1 and 1.33:1. The ratio of the enantiomers in each diastereomer was not reported but is assumed to be 1:1.

Bromuconazole belongs to the group of triazole compounds which are used as fungicides; it causes inhibition of C-14-demethylase in sterol biosynthesis. It is used as a broad-spectrum fungicide, with preventative and curative action, for control of diseases caused by ascomycetes, basidiomycetes and deuteromycetes.

The chemical structure of the active substance and its main metabolites are reported in Appendix F. Bromuconazole was evaluated in the framework of Directive 91/414/EEC with Belgium designated as RMS. Following the peer review, which was carried out by EFSA (2008), a decision on non-inclusion of the active substance in Annex I to Directive 91/414/EEC was published by means of Commission Directive 2008/832/EC.7 The applicant made a resubmission of the application under an accelerated procedure (Regulation (EC) No 33/20088), the RMS evaluation of the additional data in the format of an Additional Report of bromuconazole (Belgium, 2009) has been peer reviewed by EFSA (2010). Bromuconazole was approved on 1 February 2011 under Commission Directive 2010/92/EU of 21 December 2010. The representative use supported for the peer review process was a foliar application on wheat (two spraying application from BBCH 29-31 to 49-65). According to Regulation (EU) No 540/2011, as amended by Commission Implementing Regulation (EU) No 541/2011, bromuconazole has been approved under Regulation (EC) No 1107/2009. This approval is restricted to fungicide uses only. According to the Annex of the approval Directive, a specific provision of the approval that the applicant was required to submit to the European Commission further studies in the areas of residues and ecotoxicology by 31 January 2013 (‘further information on residues of triazole derivative metabolites (TDMs) in primary crops, rotational crops and products of animalorigin’). The confirmatory data was addressed and reported in the revised Review Report of March 2016 (European Commission, 2016a).

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7 2008/832/EC: Commission Decision of 3 November 2008 concerning the non-inclusion of bromuconazole in Annex I to Council Directive 91/414/EEC and the withdrawal of authorisations for plant protection products containing that substance. OJ L 295, 4.11.2008, p. 53–54.
8 Commission Regulation (EC) No 33/2008 of 17 January 2008 laying down detailed rules for the application of Council Directive 91/414/EEC as regards a regular and an accelerated procedure for the assessment of active substances which were part of the programme of work referred to in Article 8(2) of that Directive but have not been included into its Annex I. OJ L 15, 18.1.2008, p. 5–12.
The EU MRLs for bromuconazole are established in Annexes IIIA of Regulation (EC) No 396/2005 and CXLs for active substance are not available. An overview of the MRL changes that occurred since the entry into force of the Regulation mentioned above is provided below (Table 1).

Table 1: Overview of the MRL changes since the entry into force of Regulation (EC) No 396/2005

| Procedure | Legal implementation | Remarks |
|-----------|----------------------|---------|
| Art. 10 (EFSA, 2015) | Not legally implemented | The application intended to modify the existing MRLs on wheat and rye. However, based on the submitted information, EFSA concluded that no change of the existing MRLs were required |

For the purpose of this MRL review, the critical uses of bromuconazole currently authorised within the EU have been collected by the RMS and reported in the PROFile. The additional good agricultural practices (GAPs) reported by Member States during the completeness check were also considered. The details of the authorised GAPs for bromuconazole are given in Appendix A. The RMS did not report any use authorised in third countries that might have a significant impact on international trade.

Assessment

EFSA has based its assessment on the PROFile submitted by the RMS, the evaluation report accompanying the PROFile (Belgium, 2012), the draft assessment report (DAR), the Additional Report and its Addendum (evaluating the confirmatory data) prepared under Council Directive 91/414/EEC (Belgium, 2005, 2009, 2013), the review report on bromuconazole (European Commission, 2016a), the conclusion on the peer review of the pesticide risk assessment of the active substance bromuconazole (EFSA, 2010), the previous reasoned opinion on bromuconazole (EFSA, 2015) as well as the evaluation reports submitted during the completeness check (EURLs, 2016; France, 2016). The assessment is performed in accordance with the legal provisions of the uniform principles for evaluation and authorisation of plant protection products as set out in Commission Regulation (EU) No 546/20119 and the currently applicable guidance documents relevant for the consumer risk assessment of pesticide residues (European Commission, 1997a,b, 2000, 2010a, 2016b; OECD, 2011, 2013). More detailed information on the available data and on the conclusions derived by EFSA can be retrieved from the list of end points reported in Appendix B.

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 bromuconazole was investigated in cereals (wheat) and in fruits crops (apples and bananas). The studies reported during the peer review were performed using phenyl-labelled bromuconazole only (Belgium, 2005, 2009). One additional study performed on wheat with triazole-labelled bromuconazole was submitted after the peer review and evaluated in the framework of the confirmatory data process (Belgium, 2013).

Based on the phenyl-labelled studies, a similar metabolic pathway was depicted in wheat, bananas and apples. In these studies, the major part of the identified residues was bromuconazole (all isomers), ranging from 12% of the total radioactive residue (TRR) (0.02 mg eq./kg) in wheat grain to 81% of the TRR (7 mg eq./kg) in bananas. However, these findings have to be balanced, especially in wheat, because of the low identification rates (total identified TRR was only 17–40% TRR in wheat fractions). These low identification rates suggest a potential cleavage of the molecule. Some of the studies performed on wheat indicate a stereoselective metabolism with diastereomer LS85064610 being the predominant compound. However, the available studies did not investigate the ratios of enantiomers in each diastereomer.

The metabolism study performed with triazole-labelled bromuconazole in wheat confirmed the assumption on the cleavage of the molecule. The study indicates an extensive degradation of the

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9 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.

10 Diastereoisomer LS850646 of bromuconazole; see Appendix F.
parent compound in wheat grain. The cleavage of the molecule results in significant levels of TDMs in wheat grain: triazole alanine (66% TRR; 0.33 mg eq./kg) and triazole acetic acid (23% TRR; 0.12 mg eq./kg). In straw, hay and forage, the TDMs were not identified and the degradation of the parent compound was less extensive; bromuconazole accounts for 17–97% of the TRR and the remaining radioactivity consisted of unidentified multicomponent fraction of rather polar nature, minor (conjugated) metabolites. The main identified degradation compound was the 4-hydroxy metabolite\textsuperscript{11} (7.2% TRR; 0.15 mg eq./kg).

1.1.2. Nature of residues in rotational crops

Cereals can be grown in rotation with other plants. Furthermore, the soil studies demonstrate that the degradation rate of bromuconazole is slow; the DT\textsubscript{50} in soil is 657 days (EFSA, 2010), which means that the DT\textsubscript{90} is above the trigger value of 100 days. Thus, further investigation on the nature and magnitude of bromuconazole in rotational crops is necessary.

The metabolism of bromuconazole in rotational crops was assessed in the framework of the peer review. A confined rotational crop study with phenyl-labelled bromuconazole was conducted using radish, lettuce, mustard and wheat planted after aging of the treated soil (620 kg a.s./ha) for 1 month, 3 months and 1 year (Belgium, 2009). Significant residue levels were found in wheat straw (up to 0.62 mg eq./kg) and forage (up to 0.13 mg eq./kg). The levels of radioactivity found in radish, wheat grain, lettuce and mustard ranged between 0.01 and 0.04 mg eq./kg, depending on the plant back interval.

Unchanged parent compound and some other metabolites of minor importance were identified in wheat straw, wheat forage, radish root and radish leaf, but only the parent compound was present at significant levels. As for the primary crops, a large portion of the residue remains unidentified, but it was composed of a wide range of polar fractions. Therefore, the metabolic pattern investigated with phenyl-labelled bromuconazole in rotational crops was concluded to be similar to the metabolism in cereals as primary crops (EFSA, 2010). As in primary crops, the ratio of enantiomers in each bromuconazole diastereomer was not investigated.

As only a study performed with phenyl-labelled bromuconazole was available, a data requirement for a confined rotational crops study performed with triazole-labelled bromuconazole was identified during the peer review (EFSA, 2010); this data gap has not been addressed by confirmatory data and thus, such a study is still required (see also European Commission, 2016a). In the meanwhile, it is noted that soil uptake of TDMs residues has been observed for other triazole fungicides. Therefore, pending the assessment of a rotational crop study with triazole-labelled compound, the above conclusion is regarded as tentative only.

1.1.3. Nature of residues in processed commodities

The effect of processing on the nature of bromuconazole residues was not investigated. It is acknowledged that residues above the trigger value of 0.1 mg/kg (European Commission, 1997c) were observed in only one sample of wheat grain. Also, noting that the chronic exposure does not exceed 10% of the ADI (see also Section 3), studies on the nature and magnitude of bromuconazole residues in processed wheat or rye products are currently not considered necessary.

Since no information on residues of TDMs in the wheat and rye grains is available (see also Section 1.2.1), EFSA is not in position to address the need for studies investigating TDMs residues in processed products.

1.1.4. Methods of analysis in plants

During the peer review, an analytical method using gas chromatography with electron capture detector (GC-ECD) was validated for enforcement of bromuconazole in dry commodities (wheat grain) and cereal straw with a limit of quantification (LOQ) of 0.05 mg/kg (EFSA, 2010). During the completeness check, EURLs informed EFSA that another method using gas chromatography with tandem mass spectrometry (GC–MS/MS) was validated for enforcement of bromuconazole in dry commodities (wheat grain) with a LOQ of 0.01 mg/kg (EURLs, 2016).

Hence, it is concluded that bromuconazole can be enforced in dry commodities with a LOQ of 0.01 mg/kg and in cereals straw with an LOQ of 0.05 mg/kg.

\textsuperscript{11} 4-Hydroxy bromuconazole (diastereoisomers LS860550 and LS860551); see Appendix F for details.
In addition, EURLs informed EFSA that bromuconazole could also be enforced with a LOQ of 0.01 mg/kg in high water content, high acid content and high oil content commodities (EURL, 2016).

1.1.5. Stability of residues in plants

Storage stability of each individual diastereomers constituent of bromuconazole (LS850646 and LS850647) was demonstrated in dry commodities (wheat grain) and cereal straw for a period of 20 months at –18°C (EFSA, 2010).

1.1.6. Proposed residue definitions

The available studies indicate that the parent compound (including different ratios of isomers) is a relevant residue for enforcement and risk assessment in cereals. However, the parent compound does not represent the major part of the residues in these crops since the cleavage of triazole linkage was found to release significant levels of TDMs, in particular triazole alanine and triazole acetic acid, in cereal grains.

The TDMs (including triazole alanine and triazole acetic acid) may be generated by several pesticides belonging to the group of triazole fungicides. In a previous assessment, specific toxicological reference values were agreed by the experts for triazole alanine and triazole acetic acid (EFSA, 2011). However, it is noted that a comprehensive dietary risk assessment for TDMs considering data for several triazole fungicides is being currently carried out by EFSA in the framework of the confirmatory data assessment. This work will involve a re-assessment of the toxicological end points for the TDMs as well as an overall consumer exposure assessment to relevant TDMs arising from all triazole fungicides. Therefore, the risk assessment to TDMs cannot be addressed in the present opinion. In the meanwhile, since there are indications that bromuconazole and its two main TDMs (triazole alanine and triazole acetic acid) may have different toxicities, a separate risk assessment can be performed for the parent compound only.

For enforcement, the parent compound is considered as a relevant marker because it is the only specific compound to be present in crops at harvest; indeed, TDMs are not specific to bromuconazole. Therefore, the residue definition for enforcement can be set as bromuconazole (any ratio of constituent isomer). This is consistent with the proposal derived during the peer review (EFSA, 2010). As discussed in the previous paragraph, a risk assessment for the parent compound can be performed independently from the TDMs, thus the residue definition for risk assessment is also proposed as bromuconazole (any ratio of constituent isomer). For the future, a second residue definition for risk assessment including triazole alanine and triazole acetic acid should be considered. This will be assessed pending upon the overall assessment of the confirmatory data on the TDMs. No conclusion is proposed for fruit crops because metabolism studies performed with the triazole label were not available. Therefore, the proposed residue definition is limited to cereal crops.

In addition, EFSA emphasises that the available studies did not investigate into details the possible impact of plant metabolism on the isomer ratio of bromuconazole: some of the studies indicate a stereoselective metabolism with diastereomer LS850646 being the predominant compound, but the available studies did not investigate the ratios of enantiomers in each diastereomer. Further investigation on this matter would in principle be required. Since guidance on the consideration of isomer ratios in the consumer risk assessment is not yet available, EFSA recommends that this issue is reconsidered when such guidance is available.

1.2. Magnitude of residues in plants

1.2.1. Magnitude of residues in primary crops

To assess the magnitude of bromuconazole residues resulting from the reported GAPs, EFSA considered all residue trials reported by the RMS in its evaluation report (Belgium, 2012), including residue trials evaluated in the framework of the peer review (Belgium, 2005, 2009) and in the framework of a previous MRL application (EFSA, 2015). All residue trial samples considered in this framework were stored in compliance with the storage conditions for which stability of the residues has been demonstrated. Decline of residues during storage of the trial samples is therefore not expected.

The number of residue trials and extrapolations were evaluated in accordance with the European guidelines on comparability, extrapolation, group tolerances and data requirements for setting MRLs (European Commission, 2016b).
The available residue trials performed on wheat were sufficient to derive MRL and risk assessment values for bromuconazole in wheat and rye (grain and straw). It is noted that, in line with the findings of the metabolism studies, a shift in the diastereomer ratio of bromuconazole was observed in harvested samples, especially in the wheat straw.

It is highlighted that in the available residue trials, analysis were only carried out for bromuconazole, in accordance with the residue definition proposed in Section 1.1.6. However, as the TDMs should also be considered in a separate risk assessment, further residue trials performed with bromuconazole and analysing for TDMs residue levels (in particular triazole alanine and triazole acetic acid) should still be required.

1.2.2. Magnitude of residues in rotational crops

The results of the confined rotational crop study indicate a potential residue uptake, mainly in cereals straw and forage (see also Section 1.1.2). Bromuconazole levels up to 0.08 mg/kg were found in straw, 0.05 mg/kg in forage and 0.02 mg/kg in radish roots.

Considering the critical GAPs (cGAPs) reported in this review (1 application at BBCH 30-69 at the rate of 200 g a.s./ha), assuming a soil density of 1.5 kg/L, soil depth of 20 cm, crop interception of 50% and considering the DT50 in soil of 657 days (pattern of decline described by single first order kinetics), the plateau concentration in soil, taking into account accumulation over the years, is 0.104 mg/kg soil.

Rotational crop residue trials investigating the level of bromuconazole residues in cereals grown in rotation were assessed during the peer review (Belgium, 2009). In these studies, wheat and barley were sown between 30 and 300 days after one application of bromuconazole to the preceding wheat plants. These studies were performed with one application at 250 g a.s./ha. However, information on the soil used and soil cultivation practice in the rotational crop field studies (soil density, soil ploughing (mixing) depth, bromuconazole soil concentration in the root zone, etc.) was not available. Therefore, it is not possible to know if the plateau concentration expected in soil after use of bromuconazole at the cGAP (0.104 mg/kg soil) is covered by these studies. At harvest of the rotational wheat, bromuconazole levels were below the LOQ in all parts of the crops: < 0.02 mg/kg in grain and forage and < 0.05 mg/kg in straw.

During the peer review, based on the representative uses (two applications at the rate of 200 g a.s./ha), the above studies allowed to conclude that the bromuconazole level per se in succeeding crops was not expected to exceed 0.05 mg/kg (EFSA, 2010). Nevertheless, considering the above-mentioned deficiencies of the available rotational field studies, it is not possible to conclude whether residues in rotational crops would remain below 0.01 mg/kg, which is the enforcement LOQ proposed in all plant matrices (see Section 1.1.4). Therefore, further information on the test conditions of the rotational crop field studies (soil density, soil cultivation (mixing) depth, bromuconazole soil concentration in the root zone, etc.) are required. Alternatively, new rotational crop field studies covering the calculated plateau concentration in soil as outlined above should be provided. In the meantime, appropriate restrictions could be considered with the aim of avoiding residues exceeding the LOQ of 0.01 mg/kg in rotational crops.

Furthermore, no information on TDMs levels in succeeding crops is available (see also Section 1.1.2). Therefore, EFSA is not in position to conclude on the TDMs residues levels in rotational crops. However, it is noted that soil uptake of TDMs residues has been observed for other triazole fungicides. Further data on the residue levels of TDMs in rotational crops may be needed in the future.

1.2.3. Magnitude of residues in processed commodities

There is currently no need to investigate the effect of industrial and/or household processing (see also Section 1.1.3).

1.2.4. Proposed MRLs

MRL proposals and risk assessment values were derived for bromuconazole. The available data on primary crops are considered sufficient to derive MRL proposals as well as risk assessment values for wheat and rye grain. Tentative MRLs were also derived for wheat and rye straw in view of the future need to set MRLs in feed items.
2. Residues in livestock

Bromuconazole is authorised for use on wheat and rye that might be fed to livestock. Livestock dietary burdens were therefore calculated for different groups of livestock according to OECD guidance (OECD, 2013), which has now also been agreed upon at European level. It is noted that only the dietary burdens for bromuconazole were calculated. The input values for all relevant commodities are summarised in Appendix D. The dietary burdens calculated for all diets of cattle, sheep and poultry were found to exceed the trigger value of 0.1 mg/kg DM. Behaviour of residues was therefore assessed in these groups of livestock.

Since no information on TDMs levels in the wheat and rye (grains and straw) is available (see also Section 1.2.1), EFSA was not able to assess the intake of TDMs by livestock. However, considering the relevant amounts of TDMs found in wheat metabolism study (particularly in straw), the potential intake of TDMs residues into commodities of animal origin may be significant. Therefore, studies investigating the metabolism of TDMs in products of animal origin should be required.

2.1. Nature of residues and methods of analysis in livestock

The metabolism of bromuconazole was assessed during the peer review in ruminants (goats and cows) and poultry (two studies on laying hens) (Belgium, 2009). Only studies performed with phenyl-labelled bromuconazole are available; study details are reported in Appendix B.2.1.

These studies indicate that bromuconazole is extensively degraded and rapidly eliminated via urine and faeces (up to 90% TRR). In ruminants, significant levels of radioactive residues were only found in cow and goat liver (0.51–0.60 mg eq./kg) and kidney (0.05–0.24 mg eq./kg) at 7N rate.12 Similar results were observed in poultry where the highest levels of radioactive residues were found in liver (1.36 mg eq./kg), kidney (1.41 mg eq./kg) and eggs (0.13 mg eq./kg) at 30N rate.13

In all of these studies, only the parent compound was recovered, but at very low levels: 0.02 mg/kg in goat liver (7N rate), 0.02 mg/kg in hen liver and fat (60N14 rate). Nevertheless, the rest of the radioactivity remained unidentified in all of these metabolism studies. Therefore, it is considered that the nature of residues in edible tissues is still not elucidated. During the peer review, a data requirement for livestock metabolism studies performed with triazole-labelled bromuconazole was set. Indeed, those studies could provide further information on the unidentified radioactivity. Since this data gap has not been addressed by the confirmatory data, such studies are still required (see also European Commission, 2016a). Furthermore, a final conclusion on the residue definition in commodities of animal origin also needs to take into consideration the potential intake of TDMs by livestock, which could not be assessed in this review (see above). Therefore, the nature of bromuconazole residues in livestock commodities is still open, and thus, only a tentative residue definition could be proposed. Considering the above, the residue definition for enforcement and risk assessment proposed during the peer review, bromuconazole (any ratio of constituent isomers), is still considered on a tentative basis. Bromuconazole was classified as fat-soluble (EFSA, 2010).

During the peer review, an analytical method using GC-ECD, with confirmation by gas chromatography with mass spectrometry (GC-MS), was validated for enforcement of bromuconazole in all commodities of animal origin with a LOQ of 0.01 mg/kg for milk and 0.02 mg/kg for all other matrices (EFSA, 2010). EURLs informed EFSA that bromuconazole could be enforced with a LOQ of 0.01 mg/kg in livestock commodities by means of liquid chromatography-mass spectrometry quadrupole time-of-flight (LC-MS-q-ToF). However, the validation data provided in the evaluation report of EURLs were too limited (EURLs, 2016). Therefore, the enforcement LOQ of 0.02 mg/kg is retained for the assessment for all animal commodities other than milk.

The storage stability of bromuconazole residues in commodities of animal origin was not assessed and may need to be addressed in future, only if livestock feeding studies would be provided (see also Section 2.2).

12 7N comparing the highest nominal dose rates of the studies 0.40–0.43 mg/kg bw per day to the highest dietary burden calculated for sheep (lamb): 0.058 mg/kg bw per day.
13 30N comparing the highest nominal dose rate of the study 0.75 mg/kg bw per day to the highest dietary burden calculated for poultry: 0.024 mg/kg bw per day.
14 60N comparing the highest nominal dose rate of the study 20 ppm to the highest dietary burden calculated for poultry: 0.35 mg/kg DM.
2.2. Magnitude of residues in livestock

There are no livestock feeding studies available for bromuconazole. However, such studies should be provided only after having addressed the nature of residues in animal tissues (see Section 2.1).

In the meanwhile, it is noted that the highest level of bromuconazole observed in ruminant tissues was 0.02 mg eq./kg (goat liver at 7N rate). Similarly, the highest level of bromuconazole observed in poultry tissues was 0.02 mg eq./kg (liver and fat at 60N rate). Therefore, EFSA concludes that levels of bromuconazole above the LOQ are not expected in commodities of ruminants and poultry and thus, MRLs can be set at the enforcement LOQ for bromuconazole. However, it is highlighted that this conclusion is only valid for the tentative residue definition (parent compound only) while additional metabolism studies are still required to fully address the nature of residues in livestock (see also Section 2.1). Consequently, the MRLs derived for livestock commodities are only proposed on a tentative basis.

3. Consumer risk assessment

Chronic and acute exposure calculations for all crops reported in the framework of this review were performed using revision 2 of the EFSA PRIMo (EFSA, 2007). Input values for the exposure calculations were derived in compliance with the decision tree reported in Appendix E. Hence, for wheat and rye grains as well as for livestock commodities where tentative MRLs could be derived by EFSA in the framework of this review, input values were derived according to the internationally agreed methodologies (FAO, 2009). All input values included in the exposure calculations are summarised in Appendix D.

The exposures calculated were compared with the toxicological reference values for bromuconazole, derived by EFSA (2010) under Directive 91/414/EEC. The highest chronic exposure was calculated for French toddler, representing 4.9% of the acceptable daily intake (ADI), and the highest acute exposure was calculated for wheat grain, representing 2.5% of the acute reference dose (ARfD). Although major uncertainties remain due to the data gaps identified in the previous sections (especially with regard to residue levels in rotational crops and on the nature and magnitude of residue in livestock), this indicative exposure calculation did not indicate a risk to consumers.

EFSA emphasises that the above assessment does not consider the possible impact of plant and livestock metabolism on the isomer ratio of bromuconazole and further investigation on this matter would in principle be required. Since guidance on the consideration of isomer ratios in the consumer risk assessment is not yet available, EFSA recommends that this issue is reconsidered when such guidance is available.

It is also highlighted that the above assessment does not yet take into consideration the TDMS. Since these metabolites may be generated by several pesticides belonging to the group of triazole fungicides, EFSA recommends that a separate risk assessment should be performed for TDMS as soon as the confirmatory data requested for triazole compounds in the framework of Directive 91/414/EEC have been evaluated and a general methodology on the risk assessment of triazole compounds and their TDMS is available.

Conclusions

The metabolism of bromuconazole was investigated in cereals and in fruits crops. For cereals, studies performed with phenyl-labelled and triazole-labelled bromuconazole were available. A significant part of the identified residues was bromuconazole (all isomers) but cleavage of the molecule was demonstrated in the study performed with triazole labelled. A confined rotational crop study performed with phenyl-labelled bromuconazole showed a similar metabolism in cereals as for primary crops. However, rotational crops study performed with triazole-labelled bromuconazole is still required to fully address the nature of residues in rotational crops. Based on the available studies, bromuconazole (any ratios of constituent isomers) was considered as the relevant residue for enforcement in cereals. Bromuconazole can be enforced in dry commodities and cereal straw with a LOQ of 0.01 mg/kg. For risk assessment, bromuconazole and two TDMS (triazole alanine and triazole acetic acid) were considered relevant. However, since there are indications that bromuconazole and TDMS may have different toxicities, those compounds need to be considered in two separate risk assessments. Thus, bromuconazole (any ratio of constituent isomer) was also proposed as a residue definition for risk assessment. It is noted that a residue definition including TDMS will be assessed in the framework of an overall assessment of the confirmatory data on the TDMS. The proposed residue definitions are limited to cereal crops.
The available residue trials performed on wheat were sufficient to derive MRL and risk assessment values for bromuconazole in wheat and rye (grain and straw). The MRLs proposed in this review do not take into account the residues corresponding to the TDMs.

Based on the results of the confined rotational crop study performed with cereals, root crops, leafy crops and oilseeds and on the rotational crop residue trials investigating the level of bromuconazole residues in cereals grown in rotation, it was not possible to conclude whether bromuconazole residues in succeeding crops would remain below the enforcement LOQ of 0.01 mg/kg in all commodities. Additional information on the test conditions of the rotational crop field studies and/or new rotational crop field studies covering the plateau concentration in soil were required. Furthermore, EFSA was not able to conclude on potential TDMs residues levels in rotational crops.

The effect of processing on the nature and magnitude of bromuconazole residues was not investigated but this is currently not considered necessary. With regard to residues of TDMs, EFSA was not able to address the need for processing studies since no information on residues of TDMs in wheat and rye grains is available.

The dietary burdens calculated for all diets of cattle, sheep and poultry were found to exceed the trigger value of 0.1 mg/kg DM. The metabolism of bromuconazole was assessed in ruminants and poultry. These studies indicate that bromuconazole is extensively degraded since found at very low levels in tissues. However, as the remaining radioactivity was not identified, the nature of residues in edible tissues was not fully elucidated. A livestock metabolism studies performed with triazole-labelled bromuconazole is still required to address this point. Furthermore, a final conclusion on the residue definition of bromuconazole in animal origin commodities also needs to take into consideration the potential intake of TDMs by livestock, which could not be assessed in this review. Therefore, the residue definition for enforcement and risk assessment proposed as bromuconazole (any ratio of constituent isomers) is considered on a tentative basis. Bromuconazole was classified as fat-soluble. There are no livestock feeding studies available but, at the calculated dietary burdens, levels of bromuconazole are not expected to exceed the LOQ in commodities of animal origin. Further studies may be needed in the future to assess the occurrence of potential remaining residues.

Chronic and acute consumer exposure to bromuconazole resulting from the authorised uses reported in the framework of this review was calculated using revision 2 of the EFSA PRIMo. The highest chronic exposure represented 4.9% of the ADI (FR toddler) and the highest acute exposure amounted to 2.5% of the ARfD (wheat grain).

It is highlighted that the above assessment did not take into consideration the TDMs. Since these metabolites may be generated by several pesticides belonging to the group of triazole fungicides, a comprehensive dietary risk assessment for TDMs considering data for several triazole fungicides is being currently carried out by EFSA in the framework of the confirmatory data assessment. This work will involve a re-assessment of the toxicological end points for the TDMs as well as an overall consumer exposure assessment to relevant TDMs arising from all triazole fungicides.

**Recommendations**

MRL recommendations were derived in compliance with the decision tree reported in Appendix E of the reasoned opinion (see Table 2). None of the MRL values listed in the table are recommended for inclusion in Annex II to the Regulation as they are not sufficiently supported by data. Tentative MRLs for wheat and barley grains as well as for livestock commodities need to be confirmed by the following data:

- A confined rotational crops study performed with triazole-labelled bromuconazole (data gap relevant for the authorised uses on wheat and rye);
- Detailed information on the test conditions used in the rotational crop field studies (soil density, soil ploughing (mixing) depth, bromuconazole soil concentration in the root zone, etc.) or a new rotational crop field studies covering the plateau concentration in soil (data gap relevant for the authorised uses on wheat and rye);
- Livestock metabolism studies (ruminant and poultry) performed with triazole-labelled bromuconazole (data gap also relevant for the authorised uses on wheat and rye).

It is noted that the need for further studies regarding residues in rotational crops and the need to investigate the nature of residues in livestock commodities and are both triggered by the authorised uses on wheat and rye. Therefore, the above data gaps are relevant for the authorised uses on wheat and rye. Consequently, the MRLs derived on wheat and rye grain are considered tentative.
If the above-reported data gaps are not addressed in the future, Member States are recommended to withdraw or modify the relevant authorisations at national level. In particular, appropriate restrictions could be considered with the aim of avoiding residues exceeding the LOQ of 0.01 mg/kg in rotational crops.

It is highlighted that the consumer risk assessment for TDMs was not addressed in this review. However, several data gaps which were identified during the peer review (EFSA, 2010 see also European Commission, 2016a) were not addressed so far. In the view of a comprehensive dietary risk assessment for TDMs considering data for several triazole fungicides, the following data are still missing:

- residue trials on wheat and/or rye compliant with the northern and southern GAPs performed with bromuconazole and analysing for TDMs residue levels (in particular triazole alanine and triazole acetic acid);
- studies investigating the metabolism of TDMs in livestock (goat and poultry).

### Table 2: Summary table

| Code number | Commodity       | Existing EU MRL (mg/kg) | Outcome of the review MRL (mg/kg) | Comment |
|-------------|-----------------|-------------------------|-------------------------------|---------|
| 500070      | Rye grain       | 0.2                     | 0.03                          | Further consideration needed (a) |
| 500090      | Wheat grain     | 0.2                     | 0.2                           | Further consideration needed (a) |
| 1012010     | Bovine muscle   | 0.05*                   | 0.02*                         | Further consideration needed (a) |
| 1012020     | Bovine fat tissue | 0.05*                  | 0.02*                         | Further consideration needed (a) |
| 1012030     | Bovine liver    | 0.05*                   | 0.02*                         | Further consideration needed (a) |
| 1012040     | Bovine kidney   | 0.05*                   | 0.02*                         | Further consideration needed (a) |
| 1013010     | Sheep muscle    | 0.05*                   | 0.02*                         | Further consideration needed (a) |
| 1013020     | Sheep fat tissue | 0.05*                  | 0.02*                         | Further consideration needed (a) |
| 1013030     | Sheep liver     | 0.05*                   | 0.02*                         | Further consideration needed (a) |
| 1013040     | Sheep kidney    | 0.05*                   | 0.02*                         | Further consideration needed (a) |
| 1014010     | Goat muscle     | 0.05*                   | 0.02*                         | Further consideration needed (a) |
| 1014020     | Goat fat tissue | 0.05*                   | 0.02*                         | Further consideration needed (a) |
| 1014030     | Goat liver      | 0.05*                   | 0.02*                         | Further consideration needed (a) |
| 1014040     | Goat kidney     | 0.05*                   | 0.02*                         | Further consideration needed (a) |
| 1015010     | Equine muscle   | 0.05*                   | 0.02*                         | Further consideration needed (a) |
| 1015020     | Equine fat tissue | 0.05*                  | 0.02*                         | Further consideration needed (a) |
| 1015030     | Equine liver    | 0.05*                   | 0.02*                         | Further consideration needed (a) |
| 1015040     | Equine kidney   | 0.05*                   | 0.02*                         | Further consideration needed (a) |
| 1016010     | Poultry muscle  | 0.05*                   | 0.02*                         | Further consideration needed (a) |
| 1016020     | Poultry fat tissue | 0.05*                  | 0.02*                         | Further consideration needed (a) |
| 1016030     | Poultry liver   | 0.05*                   | 0.02*                         | Further consideration needed (a) |
| 1020010     | Cattle milk     | 0.05*                   | 0.01*                         | Further consideration needed (a) |
| 1020020     | Sheep milk      | 0.05*                   | 0.01*                         | Further consideration needed (a) |
| 1020030     | Goat milk       | 0.05*                   | 0.01*                         | Further consideration needed (a) |
| 1020040     | Horse milk      | 0.05*                   | 0.01*                         | Further consideration needed (a) |
| 1030000     | Birds eggs      | 0.05*                   | 0.02*                         | Further consideration needed (a) |
|             | Other commodities of plant and/or animal origin | See Regulation 149/2008 | – | Further consideration needed (b) |

MRL: maximum residue level.

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

(F): Residue is fat soluble.

(a): Tentative MRL is derived from a GAP evaluated at EU level, which is not fully supported by data but for which no risk to consumers was identified (assuming the existing residue definition); no CXL is available (combination E–I in Appendix E).

(b): There are no relevant authorisations or import tolerances reported at EU level; no CXL is available. Either a specific LOQ or the default MRL of 0.01 mg/kg may be considered (combination A–I in Appendix E).
Review of the existing MRLs for bromuconazole

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Abbreviations

a.i. active ingredient

a.s. active substance
| Abbreviation | Definition |
|--------------|------------|
| ADI          | acceptable daily intake |
| ARfD         | acute reference dose |
| BBCH         | growth stages of mono- and dicotyledonous plants |
| bw           | body weight |
| cGAP         | critical GAP |
| CXL          | codex maximum residue limit |
| DAR          | draft assessment report |
| DAT          | days after treatment |
| DB           | dietary burden |
| DM           | dry matter |
| DS           | powder for dry seed treatment |
| DT₅₀         | period required for 50% dissipation (define method of estimation) |
| DT₉₀         | period required for 90% dissipation (define method of estimation) |
| EC           | emulsifiable concentrate |
| ECD          | electron capture detector |
| EMS          | evaluating Member State |
| EUR Luxembourg for Pesticide Residues (former CRLsF) |
| FAO          | Food and Agriculture Organization of the United Nations |
| GAP          | Good Agricultural Practice |
| GC           | gas chromatography |
| GC-ECD       | gas chromatography with electron capture detector |
| GC-MS        | gas chromatography with mass spectrometry |
| GC-MS/MS     | gas chromatography with tandem mass spectrometry |
| HR           | highest residue |
| IEDI         | international estimated daily intake |
| IESTI        | international estimated short-term intake |
| 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           | liquid chromatography |
| LC-MS-q-ToF  | liquid chromatography–mass spectrometry quadrupole time-of-flight |
| LOQ          | limit of quantification |
| Mo           | monitoring |
| MRL          | maximum residue level |
| NEU          | northern European Union |
| PBI          | plant-back interval |
| PHI          | preharvest interval |
| PRIMo        | (EFSA) Pesticide Residues Intake Model |
| PROFile      | (EFSA) Pesticide Residues Overview File |
| RA           | risk assessment |
| RD           | residue definition |
| RMS          | rapporteur Member State |
| SANCO        | Directorate-General for Health and Consumers |
| SEU          | southern European Union |
| SMILES       | simplified molecular-input line-entry system |
| STMR         | supervised trials median residue |
| TDM          | triazole derivative metabolites |
| TRR          | total radioactive residue |
## Appendix A – Summary of authorised uses considered for the review of MRLs

| Crop Common name | Scientific name | Region | Outdoor/ indoor | Member state or country | Pest controlled | Formulation Type | Content Conc. Unit | Application Method | Growth stage From BBCH | Until BBCH | Number Min. Max. | Interval (days) Min. Max. | Rate Min. Max. Unit | PHI or waiting period (days) | Comments |
|------------------|-----------------|--------|-----------------|-------------------------|-----------------|------------------|------------------|-------------------|----------------------|-------------|----------------|---------------------------|----------------|--------------------------|----------|
| **Critical outdoor GAPs for Northern Europe** | | | | | | | | | | | | | | | |
| Rye | Secale cereale | NEU | Outdoor | HU, AT, BE | Erysiphe graminis, Septoria modorum, Septoria tritici, Puccinia recondita, Fusarium sp. | EC | 167 | g/L | Foliar treatment – spraying | 30 | 69 | – | 1 | – | – | 200 | g a.i./ ha | n.a. | – |
| Wheat | Triticum aestivum | NEU | Outdoor | HU, AT, BE, CZ | Erysiphe graminis, Septoria modorum, Septoria tritici, Puccinia recondita, Fusarium sp. | EC | 167 | g/L | Foliar treatment – spraying | 30 | 69 | – | 1 | – | – | 200 | g a.i./ ha | n.a. | – |
| **Critical outdoor GAPs for Southern Europe** | | | | | | | | | | | | | | | |
| Wheat | Triticum aestivum | SEU | Outdoor | IT | Erysiphe graminis, Septoria modorum, Septoria tritici, Puccinia recondita, Fusarium sp. | EC | 167.0 | g/L | Foliar treatment – spraying | 30 | 69 | – | 1 | – | – | 200 | g a.i./ ha | n.a. | – |

GAP: Good Agricultural Practice; BBCH: growth stages of mono- and dicotyledonous plants; PHI: preharvest interval; NEU: northern European Union; SEU: southern European Union; EC: emulsifiable concentrate; a.i.: active ingredient.
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

| Crop group | Crop(s) | Application(s) | Sampling (DAT) |
|------------|---------|----------------|----------------|
| Fruit crops | Apples | Ph-L: Spray onto fruit surface, 0.02 mg/apple | 78 |
| | Bananas | Ph-L: Spray onto the tree/leaves, 375 mg/tree | 0, 15, 30 |
| Cereals/grass crops | Wheat | Ph-L: Foliar, 300 g/ha at BBCH 31-32 + 200 g/ha at BBCH 65 | 29, 315 |
| | Wheat | Ph-L: Foliar, 220 g/ha at BBCH 37 + 230 g/ha at BBCH 51 | 147 after seeding |
| | Wheat | T-L: Foliar, 2 × 200 g/ha at BBCH 29-31 & 51 | 85 |
| | Wheat | Ph-L: Soil, 300 g/ha | 28, 240, 690 |
| | Wheat | Ph-L: Spray onto leaves surface, 100 μg/leaf | 0, 7, 21, 42 |

Ph-L: Study performed with phenyl-labelled bromuconazole (Belgium, 2005, 2009)
T-L: Study performed with triazole-labelled bromuconazole (Belgium, 2013)

| Crop group | Crop(s) | Application(s) | PBI (DAT) |
|------------|---------|----------------|-----------|
| Root/tuber crops | Radishes | Ph-L: Bare soil, 620 g a.s./ha | 30, 90, 365 |
| Leafy crops | Lettuce | Ph-L: Bare soil, 620 g a.s./ha | 30, 90, 365 |
| Oliseeds | Mustards | Ph-L: Bare soil, 620 g a.s./ha | 30, 90, 365 |
| Cereal (small grain) | Wheat | Ph-L: Bare soil, 620 g a.s./ha | 30, 90, 365 |

Source: Belgium (2009)
Ph-L: Study performed with phenyl-labelled bromuconazole
A study performed with triazole-labelled bromuconazole (T-L) is required. Meanwhile, the conclusion on the nature of residues in rotational crops remains tentative

| Processed commodities (hydrolysis study) | Conditions | Investigated? |
|----------------------------------------|------------|---------------|
| Pasteurisation (20 min, 90°C, pH 4)     | No         |
| Baking, brewing and boiling (60 min, 100°C, pH 5) | No |
| Sterilisation (20 min, 120°C, pH 6)     | No         |
| Not available and not required          |            |
Can a general residue definition be proposed for primary crops? No

Rotational crop and primary crop metabolism similar? Yes (tentative)

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

Plant residue definition for monitoring (RD-Mo) • Cereals only: bromuconazole (any ratio of constituent isomers)

Plant residue definition for risk assessment (RD-RA) RD-risk assessment 1: • Cereals only: bromuconazole (any ratio of constituent isomers)

RD-risk assessment 2 (provisional): • a separate risk assessment needs to be carried out for the triazole derivative metabolites (TDMs). This is foreseen in the framework of the ongoing assessment of the confirmatory data for triazole compounds and TDMs

Conversion factor (monitoring to risk assessment) Not relevant

Methods of analysis for monitoring of residues (analytical technique, crop groups, LOQs) GC-MS/MS (EURL, 2016):
• Validated on dry commodities
• LOQ: 0.01 mg/kg
GC-ECD (EFSA, 2010):
• Validated on dry commodities and cereal straw
• LOQ: 0.05 mg/kg
LC-MS/MS (EURL, 2016):
• Validated in high water content, high acid content and high oil content commodities
• LOQ: 0.01 mg/kg

a.s.: active substance; DAT: days after treatment; BBCH: growth stages of mono- and dicotyledonous plants; PBI: plant-back interval; GC-MS/MS: gas chromatography with tandem mass spectrometry; GC-ECD: gas chromatography with electron capture detector; LC-MS/MS: liquid chromatography with tandem 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 (months) |
|-----------------------------------|---------------|-----------------|--------|-------------------|
|                                   | Dry/high starch | Wheat grain     | –18    | 20                |
|                                   | Specific matrices | Wheat straw    | –18    | 20                |
| Source: Belgium (2009)            |               |                 |        |                   |
### B.1.2. Magnitude of residues in plants

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

| Crop       | Region/indoor\(^{(a)}\) | Residue levels observed in the supervised residue trials relevant to the supported GAPs (mg/kg) | Recommendations/comments (OECD calculations) | MRL proposals (mg/kg) | HR (mg/kg)\(^{(b)}\) | STMR (mg/kg)\(^{(c)}\) |
|------------|--------------------------|-----------------------------------------------------------------------------------------------|---------------------------------------------|----------------------|-------------------|-------------------|
| Wheat grain| NEU                      | < 0.01; < 0.01; < 0.01; < 0.01; < 0.01; < 0.01; < 0.01; < 0.01; < 0.01; 0.01; 0.02                | Trials on wheat compliant with GAP (EFSA, 2015). Northern and southern data were combined to derive MRL and risk assessment values MRL\(_{OECD} = 0.19\) | 0.2 (tentative)\(^{(d)}\) | 0.17             | 0.01             |
|            | SEU                      | < 0.01; < 0.01; < 0.01; 0.01; 0.01; 0.01; 0.03; 0.06; 0.17                                         |                                             |                      |                   |                   |
| Rye grain  | NEU                      | < 0.01; < 0.01; < 0.01; < 0.01; < 0.01; < 0.01; 0.01; 0.01; 0.02                            | Trials on wheat compliant with GAP on rye (EFSA, 2015). Extrapolation to rye is applicable MRL\(_{OECD} = 0.03\) | 0.03 (tentative)\(^{(d)}\) | 0.02             | 0.01             |
|            | SEU                      | 0.19; 0.26; 0.33; 0.44; 0.6; 1.8; 2.3; 2.6                                               |                                             |                      |                   |                   |
| Wheat straw| NEU                      | 0.19; 0.26; 0.33; 0.44; 0.6; 1.8; 2.3; 2.6                                               | Trials on wheat compliant with GAP (EFSA, 2015). Northern and southern data were combined to derive MRL and risk assessment values MRL\(_{OECD} = 5.6\) | 6 (tentative)\(^{(e)}\) | 2.9               | 1.27             |
|            | SEU                      | 0.14; 0.67; 0.74; 2.0; 2.2; 2.5; 2.7; 2.9                                               |                                             |                      |                   |                   |
| Rye straw  | NEU                      | 0.19; 0.26; 0.33; 0.44; 0.6; 1.8; 2.3; 2.6                                               | Trials on wheat compliant with GAP on rye (EFSA, 2015). Extrapolation to rye is applicable MRL\(_{OECD} = 5.06\) | 5 (tentative)\(^{(e)}\) | 2.6               | 0.52             |

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

*: 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.

(c): Supervised trials median residue.

(d): MRL on wheat and rye grain is tentative because of the data gap on the nature of residue in livestock commodities.

(e): Tentative MRL are derived for wheat and rye straw in the view of future need to set MRLs in feed items.
B.1.2.2. Residues in succeeding crops

Confined rotational crop study (quantitative aspect)

Confined rotational crop studies indicate levels of bromuconazole up to 0.08 mg/kg in straw, 0.05 mg/kg in forage and 0.02 mg/kg in radish roots. TRR in all other matrices (radish, wheat grain, lettuce and mustard) ranged between 0.01 and 0.04 mg eq./kg. No information available with regard to TDMs; however, soil uptake of TDMs has been observed for other triazole fungicides.

Field rotational crop study

Rotational crop residue trials performed with 30 and 300 DAT demonstrate bromuconazole levels to remain below the LOQ of 0.02 mg/kg for grain and forage and 0.05 mg/kg for straw. However, no conclusion could be derived on residue levels in rotational crops compared to the LOQ of 0.01 mg/kg. Additional data are required and appropriate restrictions could be considered with the aim of avoiding residues exceeding the LOQ of 0.01 mg/kg in rotational crops.

TRR: total radioactive residue; TDM: triazole derivative metabolites; DAT: days after treatment; LOQ: limit of quantification.

B.1.2.3. Processing factors

| Processed commodity | Number of studies | Processing factor (PF) |
|---------------------|------------------|-----------------------|
|                     |                  | Individual values     | Median PF |
| No studies available but not required |

B.2. Residues in livestock

| Relevant groups | Dietary burden expressed in mg/kg bw per day | mg/kg DM | Most critical diet(a) | Most critical commodity(a) | Trigger exceeded (Y/N) |
|-----------------|---------------------------------------------|---------|----------------------|--------------------------|------------------------|
| Cattle (all diets) | 0.0122                                      | 0.0264  | 0.32(b)              | Cattle (dairy)           | Wheat, straw           | Y                      |
| Cattle (dairy only) | 0.0122                                      | 0.0264  | 0.32                | Cattle (dairy)           | Wheat, straw           | Y                      |
| Sheep (all diets)   | 0.0263                                      | 0.0578  | 0.62                | Sheep (lamb)             | Wheat, straw           | Y                      |
| Sheep (ewe only)    | 0.0204                                      | 0.0451  | 0.61                | Sheep (ram/ewe)          | Wheat, straw           | Y                      |
| Swine (all diets)   | 0.0014                                      | 0.0014  | 0.05                | Swine (finishing)        | Wheat, milled by products | N                     |
| Poultry (all diets) | 0.0115                                      | 0.0242  | 0.17                | Poultry (layer)          | Wheat, straw           | Y                      |
| Poultry (layer only) | 0.0115                                     | 0.0242  | 0.17                | Poultry (layer)          | Wheat, straw           | Y                      |

bw: body weight; DM: dry matter.
(a): Calculated for the maximum dietary burden.
(b): The highest dietary burdens expressed in mg/kg DM result from dairy cattle.
B.2.1. Nature of residues and methods of analysis in livestock

B.2.1.1. Metabolism studies, methods of analysis and residue definitions in livestock

### Livestock (available studies)

| Animal             | Dose (mg/kg bw per day) | Duration (days) | N rate/comment                                                                 |
|--------------------|-------------------------|-----------------|---------------------------------------------------------------------------------|
| Laying hens        | Ph-L: 0.75              | 7               | 30N/compared to poultry layer                                                   |
|                    | Ph-L: 1.4(a)            | 14              | 60N/compared to poultry layer                                                   |
| Lactating cows     | Ph-L: 0.04 and 0.40     | 7               | 0.7 and 7N rate/compared to sheep (lamb)                                        |
| Lactating goat     | Ph-L: 0.02 and 0.43     | 7               | 0.35 and 7N/compared to sheep (lamb)                                            |

Source: Belgium (2009)

Ph-L: Study performed with phenyl-labelled bromuconazole

Studies performed with triazole-labelled bromuconazole (T-L) are required. Meanwhile, only a tentative residue definition can be proposed for livestock commodities

bw: body weight.

(a): Reported as 20 ppm (mg/kg diet) in the summary of the study and recalculated as mg/kg bw per day considering poultry layer standard weight of 1.9 kg and standard diet of 0.13 kg per day.

### Time needed to reach a plateau concentration in milk and eggs (days)

| Metabolism in rat and ruminant similar (Yes/No) | Milk: 2 days | Eggs (yolk): 4 days |
|-----------------------------------------------|--------------|-------------------|
|                                                  | Yes          |                   |

### Animal residue definition for monitoring (RD-Mo)

| Animal residue definition for monitoring (RD-Mo) | Bromuconazole (any ratio of constituent isomers) | (tentative) |
|--------------------------------------------------|--------------------------------------------------|-------------|

### Animal residue definition for risk assessment (RD-RA)

| Animal residue definition for risk assessment (RD-RA) | Bromuconazole (any ratio of constituent isomers) | (tentative) |
|--------------------------------------------------------|--------------------------------------------------|-------------|

### Conversion factor (monitoring to risk assessment)

| Conversion factor (monitoring to risk assessment) | Not relevant |
|---------------------------------------------------|--------------|

### Fat soluble residues (Yes/No)

| Fat soluble residues (Yes/No) | Yes |
|-------------------------------|-----|

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

| Methods of analysis for monitoring of residues (analytical technique, crop groups, LOQs) | GC-ECD (EFSA, 2010): |
|-----------------------------------------------------------------------------------------|-------------------|
|                                                                                         | • Validated in meat, fat, liver kidney milk and eggs |
|                                                                                         | • LOQ: 0.01 mg/kg (milk) |
|                                                                                         | • LOQ: 0.02 mg/kg (for all other commodities) |

GC-ECD: gas chromatography with electron capture detector; LOQ: limit of quantification.

B.2.1.2. Stability of residues in livestock

| Animal products (available studies) | Animal | Commodity | T (°C) | Stability (months/years) |
|-------------------------------------|--------|-----------|--------|-------------------------|
|                                     |        |           |        |                         |

No studies available but not required as no livestock feeding studies were assessed.
### B.2.2. Magnitude of residues in livestock

| Animal commodity | Residues at the closest feeding level (mg/kg) | Estimated value at 1N | MRL proposal (mg/kg) |
|------------------|-----------------------------------------------|-----------------------|----------------------|
|                  | Mean (mg/kg) | Highest (mg/kg) | STMR<sup>(a)</sup> (mg/kg) | HR<sup>(b)</sup> (mg/kg) |
| **Cattle (all diets)** – No studies available but MRL can be set at the LOQ based on the metabolism studies |
| Muscle           | –             | –             | < 0.02          | < 0.02               | 0.02* (tentative)<sup>(c)</sup> |
| Fat              | –             | –             | < 0.02          | < 0.02               | 0.02* (tentative)<sup>(c)</sup> |
| Liver            | –             | –             | < 0.02          | < 0.02               | 0.02* (tentative)<sup>(c)</sup> |
| Kidney           | –             | –             | < 0.02          | < 0.02               | 0.02* (tentative)<sup>(c)</sup> |
| **Cattle (dairy only)** – No studies available but MRL can be set at the LOQ based on the metabolism studies |
| Milk             | –             | –             | < 0.01          | < 0.01               | 0.01* (tentative)<sup>(c)</sup> |
| **Sheep (all diets)** – No studies available but MRL can be set at the LOQ based on the metabolism studies |
| Muscle           | –             | –             | < 0.02          | < 0.02               | 0.02* (tentative)<sup>(c)</sup> |
| Fat              | –             | –             | < 0.02          | < 0.02               | 0.02* (tentative)<sup>(c)</sup> |
| Liver            | –             | –             | < 0.02          | < 0.02               | 0.02* (tentative)<sup>(c)</sup> |
| Kidney           | –             | –             | < 0.02          | < 0.02               | 0.02* (tentative)<sup>(c)</sup> |
| **Sheep (dairy only)** – No studies available but MRL can be set at the LOQ based on the metabolism studies |
| Milk             | –             | –             | < 0.01          | < 0.01               | 0.01* (tentative)<sup>(c)</sup> |
| **Swine** – No studies available but not required |
| Muscle           | –             | –             | –               | –                    | – |
| Fat              | –             | –             | –               | –                    | – |
| Liver            | –             | –             | –               | –                    | – |
| Kidney           | –             | –             | –               | –                    | – |
| **Poultry (all diets)** – No studies available but MRL can be set at the LOQ based on the metabolism studies |
| Muscle           | –             | –             | < 0.02          | < 0.02               | 0.02* (tentative)<sup>(c)</sup> |
| Fat              | –             | –             | < 0.02          | < 0.02               | 0.02* (tentative)<sup>(c)</sup> |
| Liver            | –             | –             | < 0.02          | < 0.02               | 0.02* (tentative)<sup>(c)</sup> |
| **Poultry (layer only)** – No studies available but MRL can be set at the LOQ based on the metabolism studies |
| Egg              | –             | –             | < 0.02          | < 0.02               | 0.02* (tentative)<sup>(c)</sup> |

MRL: maximum residue level; LOQ: limit of quantification.

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

n.a.: not applicable; n.r.: not reported.

(a): Supervised trials median residue recalculated at the 1N rate for the median dietary burden.

(b): Highest residue recalculated at the 1N rate for the maximum dietary burden.

(c): MRL is tentative because the nature of residues in livestock commodities is not fully addressed.

MRL: maximum residue level; LOQ: limit of quantification.

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

n.a.: not applicable; n.r.: not reported.

(a): Supervised trials median residue recalculated at the 1N rate for the median dietary burden.

(b): Highest residue recalculated at the 1N rate for the maximum dietary burden.

(c): MRL is tentative because the nature of residues in livestock commodities is not fully addressed.
### Consumer risk assessment

| ADI     | 0.01 mg/kg bw per day (EFSA, 2010) |
|---------|-----------------------------------|
| Highest IEDI, according to EFSA PRIMo | 4.9% ADI (FR, toddler) |
| Assumptions made for the calculations | The calculation is based on the median residue levels in the raw agricultural commodities and in livestock commodities derived for bromuconazole only. This risk assessment does not take into consideration the triazole derivatives metabolites (TDMs). For livestock commodities, the tentative residue definition considering bromuconazole only was considered. The contributions of commodities where no GAP was reported in the framework of this review were not included in the calculation. |

| ARfD    | 0.1 mg/kg bw (EFSA, 2010) |
|---------|--------------------------|
| Highest IESTI, according to EFSA PRIMo | 2.5% ARfD (wheat) |
| Assumptions made for the calculations | The calculation is based on the highest residue levels in the raw agricultural commodities and in livestock commodities derived for bromuconazole only. This risk assessment does not take into consideration the triazole derivatives metabolites (TDMs). For livestock commodities, only the tentative residue definition considering bromuconazole was considered. |

ADI: acceptable daily intake; bw: body weight; IEDI: international estimated daily intake; PRIMo: (EFSA) Pesticide Residues Intake Model; ARfD: acute reference dose; IESTI: international estimated short-term intake.
### B.4. Proposed MRLs

| Code number (a) | Commodity | Existing EU MRL (mg/kg) | Outcome of the review | Comment |
|-----------------|-----------|-------------------------|-----------------------|---------|
|                 |           | **Existing EU MRL (mg/kg)** | **Outcome of the review** | **Comment** |
|                 |           | **MRL (mg/kg)** | **Comment** |
|                 |           |                     |                     |         |
| 500070          | Rye grain | 0.2                   | 0.03                 | Further consideration needed (a) |
| 500090          | Wheat grain | 0.2                   | 0.2                  | Further consideration needed (a) |
| 1012010         | Bovine muscle | 0.05*                  | 0.02*                | Further consideration needed (a) |
| 1012020         | Bovine fat tissue | 0.05*                  | 0.02*                | Further consideration needed (a) |
| 1012030         | Bovine liver | 0.05*                  | 0.02*                | Further consideration needed (a) |
| 1012040         | Bovine kidney | 0.05*                  | 0.02*                | Further consideration needed (a) |
| 1013010         | Sheep muscle | 0.05*                  | 0.02*                | Further consideration needed (a) |
| 1013020         | Sheep fat tissue | 0.05*                  | 0.02*                | Further consideration needed (a) |
| 1013030         | Sheep liver | 0.05*                  | 0.02*                | Further consideration needed (a) |
| 1013040         | Sheep kidney | 0.05*                  | 0.02*                | Further consideration needed (a) |
| 1014010         | Goat muscle | 0.05*                  | 0.02*                | Further consideration needed (a) |
| 1014020         | Goat fat tissue | 0.05*                  | 0.02*                | Further consideration needed (a) |
| 1014030         | Goat liver | 0.05*                  | 0.02*                | Further consideration needed (a) |
| 1014040         | Goat kidney | 0.05*                  | 0.02*                | Further consideration needed (a) |
| 1015010         | Equine muscle | 0.05*                  | 0.02*                | Further consideration needed (a) |
| 1015020         | Equine fat tissue | 0.05*                  | 0.02*                | Further consideration needed (a) |
| 1015030         | Equine liver | 0.05*                  | 0.02*                | Further consideration needed (a) |
| 1015040         | Equine kidney | 0.05*                  | 0.02*                | Further consideration needed (a) |
| 1016010         | Poultry muscle | 0.05*                  | 0.02*                | Further consideration needed (a) |
| 1016020         | Poultry fat tissue | 0.05*                  | 0.02*                | Further consideration needed (a) |
| 1016030         | Poultry liver | 0.05*                  | 0.02*                | Further consideration needed (a) |
| 1020010         | Cattle milk | 0.05*                  | 0.01*                | Further consideration needed (a) |
| 1020020         | Sheep milk | 0.05*                  | 0.01*                | Further consideration needed (a) |
| 1020030         | Goat milk | 0.05*                  | 0.01*                | Further consideration needed (a) |
| 1020040         | Horse milk | 0.05*                  | 0.01*                | Further consideration needed (a) |
| 1030000         | Birds eggs | 0.05*                  | 0.02*                | Further consideration needed (a) |
|                 | Other commodities of plant and/or animal origin | See Regulation 149/2008 | – | Further consideration needed (a) |

**MRL**: maximum residue level.

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

(F): Residue is fat soluble.

(a): Tentative MRL is derived from a GAP evaluated at EU level, which is not fully supported by data but for which no risk to consumers was identified (assuming the existing residue definition); no CXL is available (combination E-I in Appendix E).

(b): There are no relevant authorisations or import tolerances reported at EU level; no CXL is available. Either a specific LOQ or the default MRL of 0.01 mg/kg may be considered (combination A-I in Appendix E).
Appendix C – Pesticide Residue Intake Model (PRIMo)

- PRIMo(EU)

Bromuconazole

| Status of the active substance | Code no |
|-------------------------------|---------|
| Toxicological end points |
| ADI (mg/kg bw per day) | 0.01 |
| ARfD (mg/kg bw) | 0.1 |

| Source of ADI: | EFSA |
| Source of ARfD: | EFSA |
| Year of evaluation | 2010 |

No of diets exceeding ADI: ---

Highest calculated TMDI values in % of ADI

| MS Diet | Commodity/ group of commodities |
|---------|---------------------------------|
| 4.9 FR toddler | Milk and cream |
| 4.4 UK infant | Milk and cream |
| 4.0 NL child | Milk and cream |
| 3.0 FR infant | Milk and cream |
| 2.6 UK Toddler | Milk and cream |
| 2.5 DK child | Milk and cream |
| 2.4 ES child | Milk and cream |
| 2.3 DE child | Milk and cream |
| 1.8 SE general population 90th percentile | Milk and cream |
| 1.7 WHO Cluster diet B | Milk and cream |
| 1.5 WHO cluster diet D | Milk and cream |
| 1.4 WHO regional European diet | Milk and cream |
| 1.2 WHO Cluster diet E | Milk and cream |
| 1.2 WHO Cluster diet F | Milk and cream |
| 1.1 NL general | Milk and cream |
| 1.0 DK adult | Milk and cream |
| 0.9 FR all population | Milk and cream |
| 0.8 IE adult | Milk and cream |
| 0.8 IT adult | Milk and cream |
| 0.8 FI adult | Milk and cream |
| 0.7 IT kids/babysitter | Wheat |
| 0.6 UK vegetarian | Milk and cream |
| 0.5 UK adult | Milk and cream |
| 0.5 IT adult | Milk and cream |
| 0.4 PT general population | Milk and cream |

3rd contributor to MS diet (in % of ADI)

| Commodity/ group of commodities |
|---------------------------------|
| 0.3 Milk and cream |
| 0.3 Milk and cream |
| 0.3 Milk and cream |
| 0.3 Milk and cream |
| 0.3 Milk and cream |
| 0.3 Milk and cream |
| 0.3 Milk and cream |
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| 0.3 Milk and cream |
| 0.3 Milk and cream |
| 0.3 Milk and cream |

| Commodity/ group of commodities |
|---------------------------------|
| Bovine: meat |
| Bovine: meat |
| Bovine: meat |
| Bovine: meat |
| Bovine: meat |
| Bovine: meat |
| Bovine: meat |
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| Bovine: meat |

Conclusion:
The estimated Theoretical Maximum Daily Intakes (TMDI), based on pTMRLs were below the ADI.
A long-term intake of residues of bromuconazole is unlikely to present a public health concern.
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 lead to an exposure equivalent to 100% of the ARfD.

### Table: No of commodities for which ARfD/ADI is exceeded

| Commodity                      | IESTI 1 | IESTI 2 |
|-------------------------------|---------|---------|
| **% of ARfD/ADI Commodities** | | |
| Wheat                         | 2.5     | 2.5     |
| Milk and milk products        | 0.001%  | 0.001%  |
| Bovine: Meat                  | 0.02%   | 0.02%   |
| Birds' eggs                   | 0.00%   | 0.00%   |
| Milk and milk products        | 0.01%   | 0.01%   |

### Table: No of commodities for which ARfD/ADI is exceeded

| Commodity                      | IESTI 1 | IESTI 2 |
|-------------------------------|---------|---------|
| **Threshold MRL**             |         |         |
| Processed commodities         |         |         |
| Bread/pizza                   | 0.17/-  | 0.17/-  |
| Milk and milk products        | 0.01/-  | 0.01/-  |
| Processed commodities         |         |         |
| Processed commodities         |         |         |

### Conclusion:
For bromuconazole, 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.
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                | Input value (mg/kg) | Comment                |
| Rye, grain                      | 0.01* STMR            | 0.01* STMR             |
| Wheat, grain                    | 0.01* STMR            | 0.01* STMR             |
| Wheat, distiller’s grain (dry)  | 0.03 STMR 3.3^(a)     | 0.03 STMR 3.3^(a)      |
| Wheat gluten, meal              | 0.02 STMR 1.8^(a)     | 0.02 STMR 1.8^(a)      |
| Wheat, milled by-pdts           | 0.07 STMR 7^(a)       | 0.07 STMR 7^(a)        |
| Rye, straw                      | 0.52 STMR             | 2.60 HR                |
| Wheat, straw                    | 1.27 STMR             | 2.90 HR                |

STMR: supervised trials median residue; HR: highest residue.

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

(a): For processed commodities of wheat, in the absence of processing factors supported by data, default processing factors of 3.3, 1.8 and 7 were included in the calculation to consider the potential concentration of residues in these commodities.

D.2. Consumer risk assessment

| Commodity                   | Chronic risk assessment | Acute risk assessment |
|-----------------------------|-------------------------|-----------------------|
|                             | Input value (mg/kg)     | Comment               | Input value (mg/kg) | Comment               |
| Rye grain                   | 0.01* STMR (tentative)  | 0.02 HR (tentative)   |
| Wheat grain                 | 0.01* STMR (tentative)  | 0.17 HR (tentative)   |
| Bovine meat                 | 0.02* 0.8 × STMR muscle | 0.02* 0.8 × HR muscle |
|                            | + 0.2 × STMR fat (tentative) | + 0.2 × HR fat (tentative) |
| Bovine fat tissue           | 0.02* STMR (tentative)  | 0.02* HR (tentative)  |
| Bovine liver                | 0.02* STMR (tentative)  | 0.02* HR (tentative)  |
| Bovine kidney               | 0.02* STMR (tentative)  | 0.02* HR (tentative)  |
| Sheep meat                  | 0.02* 0.8 × STMR muscle | 0.02* 0.8 × HR muscle |
|                            | + 0.2 × STMR fat (tentative) | + 0.2 × HR fat (tentative) |
| Sheep fat tissue            | 0.02* STMR (tentative)  | 0.02* HR (tentative)  |
| Sheep liver                 | 0.02* STMR (tentative)  | 0.02* HR (tentative)  |
| Sheep kidney                | 0.02* STMR (tentative)  | 0.02* HR (tentative)  |
| Goat meat                   | 0.02* 0.8 × STMR muscle | 0.02* 0.8 × HR muscle |
|                            | + 0.2 × STMR fat (tentative) | + 0.2 × HR fat (tentative) |
| Goat fat tissue             | 0.02* STMR (tentative)  | 0.02* HR (tentative)  |
| Goat liver                  | 0.02* STMR (tentative)  | 0.02* HR (tentative)  |
| Goat kidney                 | 0.02* STMR (tentative)  | 0.02* HR (tentative)  |
| Equine meat                 | 0.02* 0.8 × STMR muscle | 0.02* 0.8 × HR muscle |
|                            | + 0.2 × STMR fat (tentative) | + 0.2 × HR fat (tentative) |
| Equine fat tissue           | 0.02* STMR (tentative)  | 0.02* HR (tentative)  |
| Equine liver                | 0.02* STMR (tentative)  | 0.02* HR (tentative)  |
| Equine kidney               | 0.02* STMR (tentative)  | 0.02* HR (tentative)  |
| Poultry meat                | 0.02* 0.8 × STMR muscle | 0.02* 0.8 × HR muscle |
|                            | + 0.2 × STMR fat (tentative) | + 0.2 × HR fat (tentative) |
| Poultry fat tissue          | 0.02* STMR (tentative)  | 0.02* HR (tentative)  |
| Poultry liver               | 0.02* STMR (tentative)  | 0.02* HR (tentative)  |
| Cattle milk                 | 0.01* STMR (tentative)  | 0.01* HR (tentative)  |
| Sheep milk                  | 0.01* STMR (tentative)  | 0.01* HR (tentative)  |
| Goat milk                   | 0.01* STMR (tentative)  | 0.01* HR (tentative)  |
### Commodity

| Commodity   | Chronic risk assessment | Acute risk assessment |
|-------------|-------------------------|-----------------------|
|             | Input value (mg/kg)     | Comment               | Input value (mg/kg) | Comment               |
| Horse milk  | 0.01*                   | STMR (tentative)      | 0.01*               | HR (tentative)        |
| Birds eggs  | 0.02*                   | STMR (tentative)      | 0.02*               | HR (tentative)        |

**STMR**: supervised trials median residue; **HR**: highest residue.

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


Appendix E – Decision tree for deriving MRL recommendations

Evaluation of the GAPs and available residues data at EU level

- GAP or DB > 0.1 mg/kg DM in EU?
  - Yes → MRL derived in Section 3?
    - Yes → MRL fully supported by data?
      - Yes → MRL is recommended.
      - No → Not considered for the RA.
    - No → Risk identified?
      - Yes → Fall-back MRL available?
        - Yes → Recommendations resulting from EU authorisations and import tolerances
        - No → Not considered for the RA.
      - No → Not considered for the RA.
  - No → Maintain current EU MRL?
    - Yes → Tentative median/highest values are included in the RA.
    - No → Median/highest values are included in the RA.

Consumer risk assessment for GAPs evaluated at EU level – EU scenarios

- Risk identified?
  - Yes → GAP or DB > 0.1 mg/kg DM in EU?
    - Yes → MRL derived in Section 3?
      - Yes → MRL fully supported by data?
        - Yes → MRL is recommended.
        - No → Not considered for the RA.
      - No → No
    - No → Maintain current EU MRL?
      - Yes → Tentative median/highest values are included in the RA.
      - No → Median/highest values are included in the RA.
  - No → Not considered for the RA.

Recommendations resulting from EU authorisations and import tolerances

- (A) Specific LOQ or default MRL?
- (B) Specific LOQ or default MRL?
- (C) Maintain current EU MRL?
- (D) Specific LOQ or default MRL?
- (E) Establish tentative EU MRL?
- (F) Specific LOQ or default MRL?
- (G) MRL is recommended.

Comparison with CXLs
## Appendix F – Used compound codes

| Code/trivial name | Chemical name/SMILES notation | Structural formula |
|-------------------|--------------------------------|--------------------|
| Bromuconazole     | 1-[(2RS,4RS;2RS,4SR)-4-bromo-2-(2,4-dichlorophenyl) tetrahydrofurfuryl]-1H-1,2,4-triazole BrC2CC(Cn1cncn1)(OC2)c3ccc(Cl)cc3Cl | ![Structural formula](image1) |
| Bromuconazole (diastereomer LS850646) | 1-[(2S,4R)-4-bromo-2-(2,4-dichlorophenyl) tetrahydrofurfuryl]-1H-1,2,4-triazole 1-[(2R,4S)-4-bromo-2-(2,4-dichlorophenyl) tetrahydrofurfuryl]-1H-1,2,4-triazole | ![Structural formula](image2) |
| Bromuconazole (diastereomer LS850647) | 1-[(2S,4S)-4-bromo-2-(2,4-dichlorophenyl) tetrahydrofurfuryl]-1H-1,2,4-triazole 1-[(2R,4R)-4-bromo-2-(2,4-dichlorophenyl) tetrahydrofurfuryl]-1H-1,2,4-triazole | ![Structural formula](image3) |
| 4-Hydroxy metabolite LS860550/LS860551 | 1-[(2RS,4RS;2RS,4SR)-4-hydroxy-2-(2,4-dichlorophenyl) tetrahydrofurfuryl]-1H-1,2,4-triazole OC2CC(Cn1cncn1)(OC2)c3ccc(Cl)cc3Cl | ![Structural formula](image4) |
| Code/trivial name                          | Chemical name/SMILES notation                                      | Structural formula |
|-------------------------------------------|---------------------------------------------------------------------|--------------------|
| **Triazole derivative metabolites**       |                                                                     |                    |
| 1,2,4-Triazole                            | 1H-1,2,4-triazole c1ncnn1                                           | ![Structure](attachment.png) |
| Triazole alanine                          | 3-(1H-1,2,4-triazol-1-yl)-D,L-alanine NC(Cn1cncn1)C(=O)O             | ![Structure](attachment.png) |
| Triazole acetic acid                      | 1H-1,2,4-triazol-1-ylacetic acid O=C(O)Ch1cncn1                      | ![Structure](attachment.png) |
| Triazole lactic acid or Triazolehydroxy propionic acid | (2RS)-2-hydroxy-3-(1H-1,2,4-triazol-1-yl)propanoic acid OC(Cn1cncn1)C(=O)O | ![Structure](attachment.png) |

SMILES: simplified molecular-input line-entry system.