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REASONED OPINION

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Updated reasoned opinion on the toxicological properties and maximum residue levels (MRLs) for the benzimidazole substances carbendazim and thiophanate-methyl

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Abstract

In compliance with Article 43 of Regulation (EC) No 396/2005, EFSA received from the European Commission in 2020 a mandate to provide its reasoned opinion on the toxicological properties and maximum residue levels (MRLs) for the benzimidazole substances carbendazim and thiophanate-methyl. Specifically, EFSA was asked to assess whether thiophanate-methyl or carbendazim has clastogenic potential and, in case clastogenic potential can be excluded, to derive toxicological reference values necessary for consumer risk assessment and assessment of maximum residue levels (MRLs). Although these active substances are no longer authorised within the European Union, MRLs were established by the Codex Alimentarius Commission (codex maximum residue limits; CXLs), and import tolerances are in place. Based on the assessment of the available data, toxicological reference values and MRL proposals were derived and a consumer risk assessment was carried out. Some information required by the regulatory framework was found to be missing and a possible acute risk to consumers was identified. Hence, the consumer risk assessment was considered indicative only and all MRL proposals derived by EFSA still require further consideration by risk managers. In October 2022, to ensure that MRLs derived by EFSA in its assessment of 2021 are safe for consumers also in view of endocrine-disrupting properties, EFSA was requested to carry out a follow-up assessment taking into account the scientific criteria for identifying endocrine disruptors (ED). Based on the outcome of the assessment, the experts agreed that the reference values are also covering the concern related to the identified hazards indicative of endocrine disruption for thiophanate-methyl. No further considerations on the impact of the ED assessment on the current reference values were needed for carbendazim since the ED criteria are not met for this substance. Therefore, the risk assessment and the MRL recommendations derived in 2021 are confirmed.

KEYWORDS

benzimidazole substances, carbendazim, consumer risk assessment, MRL, Regulation (EC) No 396/2005, thiophanate-methyl

CONTENTS

SUMMARY

Carbendazim was firstly included in Annex I to Directive 91/414/EEC in 2006 by Commission Directive 2006/135/EC. After the first approval, EFSA published in 2009 a reasoned opinion on the refined risk assessment regarding certain MRLs of concern for the active substance. Carbendazim was then evaluated by EFSA during the peer review for renewal of approval in 2010, in the framework of Commission Regulation (EC) No 1107/2009. On 10 May 2011, the approval of carbendazim was renewed by Commission Directive 2011/58/EU. Following the renewal of the approval, EFSA published two reasoned opinions, including the one on the review of all existing MRLs in compliance with Article 12(2) of Regulation (EC) No 396/2005. On 11 March 2015, carbendazim was included in the list of candidates for substitution by Commission Implementing Regulation (EU) 2015/408, due to its classification as toxic for reproduction category 1B, in accordance with the provisions of Regulation (EC) No 1272/2008. Carbendazim is also classified as mutagenic category 1B. In 2019, the European Chemicals Agency (ECHA) published several opinions from the Biocidal Products Committee (BPC) for carbendazim as product types 7 (PT7; film preservatives), 9 (PT9; fibre, leather, rubber and polymerised materials preservatives) and 10 (PT10; construction material preservatives). Carbendazim is currently not approved in the European Union for uses as pesticide.

Thiophanate-methyl was firstly included in Annex I to Directive 91/414/EEC in 2005 by Commission Directive 2005/53/EC. After the first approval, EFSA published several reasoned opinions on the assessment and modification of the existing maximum residue levels (MRLs) for thiophanate-methyl, including the assessment of all the existing MRLs in compliance with Article 12(2) of Regulation (EC) No 396/2005. The active substance was then evaluated by EFSA during the peer review for renewal of approval in 2018, in the framework of Commission Regulation (EC) No 1107/2009 and according to Commission Implementing Regulation (EU) No 844/2012. On 15 October 2020, the approval of the active substance thiophanate-methyl was not renewed by Commission Implementing Regulation (EU) 2020/1498. Thiophanate-methyl is classified as mutagenic category 2 in accordance with the provisions of Regulation (EC) No 1272/2008 and proposed for classification as carcinogen category 2, based on the latest evaluation by ECHA Committee for risk assessment (RAC) under the classification and labelling (CLH) process (ECHA, 2019b).

Through the different assessments, the two active substances presented clear aneugenic properties, while the characterisation of their clastogenic potential remained outstanding. It is noted that during the re-assessment of thiophanate-methyl under the EFSA pesticide peer review, evidence of clastogenicity was found for thiophanate-methyl and carbendazim. On the other hand, during the assessment by ECHA RAC in 2019 under classification and labelling scheme, which also included the assessment of further data that were not available at the time of the EFSA pesticide peer review, it was confirmed the aneugenic potential of thiophanate-methyl but not the clastogenic potential.

Based on the above, on 13 November 2020, EFSA received from the European Commission a mandate to deliver, in accordance with Article 43 of Regulation (EC) No 396/2005, a reasoned opinion on the toxicological properties and maximum residue levels (MRLs) for the benzimidazole substances carbendazim and thiophanate-methyl. EFSA was asked to first assess whether thiophanate-methyl or carbendazim has clastogenic potential. In case clastogenic potential can be excluded, EFSA shall derive toxicological reference values necessary to perform consumer risk assessment and assessment of MRLs.

The European Commission also asked EFSA to involve ECHA and the respective rapporteur Member States (Germany for carbendazim and Sweden for thiophanate-methyl) in the assessment, and to consult with the EU Reference Laboratories for Residues of Pesticides on the achievable limits of analytical determination for benomyl, carbendazim and thiophanate-methyl in different matrices.

Subsequent to the request from the European Commission, EFSA compiled a master list on genotoxicity studies available, based on the data submitted to EFSA during the pesticides peer review; to ECHA in the context of the CLH process (for thiophanate-methyl) and for the application for approval of carbendazim as active substance in biocidal products under Reg. (EU) No 528/2012; also including the pertinent studies suggested in the mandate from European Commission and a screening of the published literature available (PubMed). This master list (Appendix F) was further screened for studies relevant to assess the aneugenic and in particular the clastogenic potential of carbendazim and thiophanate-methyl. The studies identified as relevant to assess these endpoints (Appendices G for carbendazim and H for thiophanate-methyl) were discussed at the related EFSA experts meeting which was held on 15 January 2021.

In the meantime, EFSA initiated the collection of data in order to gather the most up-to-date information to review the MRLs of carbendazim and thiophanate-methyl. Considering that the two active substances are no longer approved for use as pesticides in EU, Member States (including the two RMSs) and the UK[1] were invited to submit by 25 January 2021 good agricultural practices (GAPs) in non-EU countries for which GAPs for import tolerance (IT) are authorised.

On the basis of the feedback received by Member States and the information submitted by the EU Reference Laboratories for Pesticides Residues (EURLs) and the conclusions derived by EFSA in the framework of Regulation (EC) No 1107/2009, EFSA completed the Pesticide Residues Overview File (PROFile) and prepared in May 2021 a draft reasoned opinion, which was circulated to Member States, ECHA and EURLs for consultation via a written procedure. Comments received by 14 June 2021 were considered during the finalisation of this reasoned opinion. The following conclusions were derived.

The experts of the peer review experts meeting (TC 39, January 2021) on mammalian toxicology agreed that, by considering the new data available to the ECHA RAC, in a weight of evidence approach, there is direct evidence in vitro, and indirect evidence in vivo, that thiophanate-methyl is aneugenic but not clastogenic. The majority of experts agreed that the

[1]The United Kingdom withdrew from EU on 1 February 2020. In accordance with the Agreement on the Withdrawal of the United Kingdom from the EU, and with the established transition period, the EU requirements on data reporting also apply to the United Kingdom data collected until 31 December 2020'.

most suitable basis for setting the acceptable daily intake (ADI) and acute reference dose (ARfD) for thiophanate-methyl is the no observed adverse effect level (NOAEL) of 2 mg/kg bw per day for maternal and developmental toxicity in the rabbit and applying an uncertainty factor of 100. The resulting ADI and ARfD is 0.02 mg/kg bw (per day). Regarding carbendazim, the experts agreed that the weight of evidence suggests that there is direct evidence in vitro and in vivo that carbendazim is not clastogenic but aneugenic and agreed to maintain previous ADI and ARfD of carbendazim of 0.02 mg/kg bw (per day).

The metabolism of thiophanate-methyl and carbendazim in plants was investigated in primary crops. According to the results of the metabolism studies and the available toxicological studies, the residue definitions for enforcement and risk assessment can be proposed as 'thiophanate-methyl' and 'carbendazim', separately. A specific residue definition for rotational crops is not deemed necessary considering that only import tolerances were considered in the present assessment. These residue definitions are also applicable to processed commodities. Fully validated analytical methods are available for the separate enforcement of the proposed residue definitions in the main four matrices at the limit of quantification (LOQ) of 0.01 mg/kg. According to the EURLs, this LOQ is achievable by using the QuEChERS method in routine analyses. Nevertheless, the EURLs highlighted that during routine analyses, benomyl degrades rapidly to carbendazim and therefore using routine methods is not possible to analyse separately for benomyl and carbendazim.

Available residue trials data were considered sufficient to derive MRL proposals as well as risk assessment values for all commodities under evaluation. Considering that homogenisation of samples leads to a drastically reduced storage stability, pending additional data to ensure that no degradation of thiophanate-methyl and carbendazim occurred in samples during storage, all the derived MRLs should be considered tentative only.

Thiophanate-methyl and carbendazim are authorised for use on citrus fruits that might be fed to livestock. Livestock dietary burden calculations were therefore performed for different groups of livestock according to OECD guidance. Based on the uses reported in the framework of this assessment, significant exposure to thiophanate-methyl and to carbendazim is expected for cattle and swine only; therefore, the nature and magnitude of residues in animals were investigated only in these groups of livestock.

The metabolism of thiophanate-methyl and carbendazim residues in livestock was investigated in lactating goats and cow at dose rate covering the maximum dietary burdens calculated in this review. For thiophanate-methyl, the residue definition for enforcement and risk assessment was proposed as parent 'thiophanate-methyl' only. For carbendazim, the relevant residue definition for enforcement in all animal matrices was set as the 'sum of carbendazim and 5-hydroxy-carbendazim, expressed as carbendazim'. The same residue definition also applies for risk assessment in muscle, fat, liver and kidney while an additional metabolite (4-hydroxy-carbendazim) is also included for risk assessment in milk. Available feeding studies performed with thiophanate-methyl and carbendazim demonstrated that no residues above the LOQ are expected in cattle milk and in cattle and swine tissues following their exposure to thiophanate-methyl and carbendazim and MRLs for these commodities can be established at the enforcement LOQ.

Fully validated analytical methods using LC-MS/MS (QuEChERS) are available for the separate enforcement of thiophanate-methyl, carbendazim and 5-hydroxy-carbendazim at the LOQ of 0.01 mg/kg for each compound in all animal matrices.

According to the EURLs, it is expected that this LOQ would be achievable for the separate enforcement of thiophanate-methyl and carbendazim during routine analyses. Moreover, the same LOQ is also valid for benomyl (measured as carbendazim). Analytical methods for the enforcement of 5-hydroxy-carbendazim are currently not available to the EURLs but according to the information shared during the MSC on the draft reasoned opinion, they will perform validation experiments in animal matrices to provide LOQs for routine analysis. According to the EURLs, the analytical standards for carbendazim, benomyl, thiophanate-methyl and 5-hydroxy-carbendazim are commercially available.

Chronic and acute consumer exposure resulting from the authorised uses reported in the framework of this assessment was calculated using revision 3.1 of the EFSA PRIMo.

For thiophanate-methyl, the highest chronic exposure was calculated for German child, representing 8% of the ADI. With regard to the acute exposure, however, an exceedance of the ARfD was identified for oranges, grapefruits, mandarins and papaya, representing 314%, 186%, 140% and 106% of the ARfD, respectively.

For carbendazim, the highest chronic exposure was calculated for Dutch toddler, representing 7% of the ADI while the highest acute exposure was calculated for mandarins, representing 84% of the ARfD.

Furthermore, before proposing a refinement of the risk assessment, a combined acute risk assessment was performed summing the results from the acute risk assessment of thiophanate-methyl and carbendazim. According to this calculation, an exceedance of the ARfD was identified for oranges, grapefruits, mandarins, mangoes, papaya and lemons, representing 342%, 203%, 224%, 143%, 133% and 129% of the ARfD. It is, however, noted by EFSA that the approach followed for the combined exposure assessment leads to an overestimation of the exposure in lemons, mandarins and limes, where residues resulting from the use of carbendazim and thiophanate-methyl have been combined while co-occurrence of these residues is not expected to occur in practice for these three crops.

A second (scenario EU2, reflecting option 1 in Table 1) and a third (scenario EU3, reflecting option 2 in Table 1) exposure calculations were therefore performed, considering possible fall-back GAPs and assuming that residues from the uses of carbendazim and thiophanate-methyl are not co-occurring in lemons.

According to the results of the second calculation (scenario EU2), the highest acute exposure for thiophanate-methyl is calculated for limes, representing 48% of the ARfD, the highest acute exposure for carbendazim is calculated for mandarins,

representing 84% of the ARfD and the highest combined acute exposure is calculated for mandarins, representing 84% of the ARfD.

According to the results of the third calculation (scenario EU3), the highest acute exposure for thiophanate-methyl is calculated for lemons, representing 81% of the ARfD, the highest acute exposure for carbendazim is calculated for mandarins, representing 84% of the ARfD and the highest combined acute exposure is calculated for lemons, representing 88% of the ARfD.

These calculations show that no risk for consumers is identified for lemons in case residues from the uses of carbendazim and thiophanate-methyl are not co-occurring.

In order to perform a combined chronic risk assessment, results from the chronic risk assessment of thiophanate-methyl and results from the chronic risk assessment of carbendazim from the refined calculations were summed (scenario EU2 and EU3). This calculation has been done for the Dutch diet (toddler), the British diet (infant) and the French diet (toddler) being the diets with the highest estimated exposure.

The highest chronic exposure for scenario EU2 was calculated for the Dutch diet (toddler), representing 10% of the ADI. The highest chronic exposure for scenario EU3 was calculated for the Dutch diet (toddler), representing 9% of the ADI.

Based on these calculations, an acute risk to consumers was identified for the most critical GAPs for thiophanate-methyl on oranges, grapefruits, mandarins, mangoes and papaya and for lemons, if the residues from the uses of carbendazim and thiophanate-methyl are co-occurring. However, fall-back GAPs were identified for mandarins and lemons, for which a second (scenario EU2) and a third (scenario EU3) risk assessments did not indicate risk to consumers. For the remaining commodities, although some major uncertainties remain due to the data gaps identified, the indicative exposure calculation did not indicate a risk to consumers.

In October 2022, in order to ensure that MRLs derived by EFSA in its assessment of 2021 are safe for consumers also in view of endocrine-disrupting properties, EFSA was requested to carry out a follow-up assessment taking into account the scientific criteria for identifying endocrine disruptors (ED) detailed in Commission Regulation (EU) 2018/605 and the joint guidance document to identify endocrine-disrupting substances as adopted by ECHA and EFSA (2018).

In November 2023, a peer review experts meeting (TC 118-119) on mammalian toxicology was held and, based on the outcome of the meeting, EFSA updated the reasoned opinion, which was circulated to the Commission, Member States and ECHA and for consultation via a written procedure. No comments were received by 21 December 2023. The following additional conclusions are derived.

Based on the outcome of the assessment of the ED potential of thiophanate-methyl for humans, the experts agreed that the ED criteria for thyroid (T)-modality are met. The experts agreed that the current toxicological reference values for thiophanate-methyl are sufficiently protective for consumers, including the identified hazards indicative of endocrine disruption. No further considerations on the impact of the ED assessment on the current reference values were needed for carbendazim, since the ED criteria are not met for this substance. Therefore, the risk assessment and the MRL recommendations derived in 2021 and reported above are confirmed.

BACKGROUND

Carbendazim was firstly included in Annex I to Directive 91/414/EEC[2] in 2006 by Commission Directive 2006/135/EC.[3] After the first approval, EFSA published a reasoned opinion on the refined risk assessment regarding certain MRLs of concern for the active substance (EFSA, 2009). Carbendazim was then evaluated by EFSA during the peer review for renewal of approval in the framework of Commission Regulation (EC) No 1107/2009[4] in 2010 (EFSA, 2010). On 10 May 2011, the approval of carbendazim was renewed by Commission Directive 2011/58/EU.[5] Following the renewal of the approval, EFSA published two reasoned opinions, including the one on the review of all existing MRLs in compliance with Article 12(2) of Regulation (EC) No 396/2005[6] (EFSA, 2012, 2014). On 11 March 2015, carbendazim was included in the list of candidates for substitution Commission Implementing Regulation (EU) 2015/408,[7] due to its classification as toxic for reproduction category 1B, in accordance with the provisions of Regulation (EC) No 1272/2008.[8] Carbendazim is also classified as mutagenic 1B. In 2019, the European Chemicals Agency (ECHA) published several opinions from the Biocidal Products Committee (BPC) for carbendazim as product types 7 (P7; film preservatives), 9 (P9; fibre, leather, rubber and polymerised materials preservatives) and 10 (P10; construction material preservatives) (ECHA, 2019a, 2019c, 2019d). Carbendazim is currently not approved in the European Union for uses as pesticide.

Thiophanate-methyl was firstly included in Annex I to Directive 91/414/EEC in 2005 by Commission Directive 2005/53/EC.[9] After the first approval, EFSA published several reasoned opinions on the assessment and modification of the existing maximum residue levels (MRLs) for thiophanate-methyl, including the assessment of all the existing MRLs in compliance with Article 12(2) of Regulation (EC) No 396/2005 (EFSA, 2009, 2012, 2014). The active substance was then evaluated by EFSA during the peer review for renewal of approval in the framework of Commission Regulation (EC) No 1107/2009 and according to Commission Implementing Regulation (EU) No 844/2012[10] in 2018 (EFSA, 2018a). On 15 October 2020, the approval of the active substance thiophanate-methyl was not renewed by Commission Implementing Regulation (EU) 2020/1498.[11] Thiophanate-methyl is classified as mutagenic category 2 in accordance with the provisions of Regulation (EC) No 1272/2008, and proposed for classification as carcinogen category 2, based on the latest evaluation by ECHA RAC under the classification and labelling (CLH) process (ECHA, 2019b).

Terms of Reference

According to the specific mandate received from the European Commission in 2020 in accordance with Article 43 of Regulation (EC) No 396/2005, EFSA shall provide a reasoned opinion on:

- The toxicological properties of benzimidazole substances carbendazim and thiophanate-methyl, specifically, to check whether thiophanate-methyl or carbendazim have clastogenic potential;
- In case clastogenic potential can be excluded, EFSA will derive toxicological reference values (TRVs) necessary for the consumer risk assessment and the setting of maximum residue levels;
- EFSA should consider the pertinent studies for carbendazim and thiophanate-methyl as available thorough previous assessments (ECHA, 2019a, 2019b, 2019c, 2019d; EFSA, 2010, 2018a) and as referred in the background section of the mandate;
- EFSA will involve the European Chemicals Agency (ECHA) and the respective rapporteur Member States and consult with the EU Reference Laboratories for Residues of Pesticides on the achievable limits of analytical determination for benomyl, carbendazim and thiophanate-methyl in different matrices;
- EFSA will provide its Reasoned Opinion by 13 July 2021.

[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 2006/135/EC of 11 December 2006 amending Council Directive 91/414/EEC to include carbendazim as active substance. OJ L 349, 12.12.2006, p. 37–41.

[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 Directive 2011/58/EU of 10 May 2011 amending Council Directive 91/414/EEC to renew the inclusion of carbendazim as active substance. OJ L 122, 11.5.2011, p. 71–75.

[6]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.

[7]Commission Implementing Regulation (EU) 2015/408 of 11 March 2015 on implementing Article 80(7) of Regulation (EC) No 1107/2009 of the European Parliament and of the Council concerning the placing of plant protection products on the market and establishing a list of candidates for substitution. OJ L 67, 12.3.2015, p. 18–22.

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

[9]Commission Directive 2005/53/EC of 16 September 2005 amending Council Directive 91/414/EEC to include chlorothalonil, chlorotoluron, cypermethrin, daminozide and thiophanate-methyl as active substances. OJ L 241, 17.9.2005, p. 51–56.

[10]Commission Implementing Regulation (EU) No 844/2012 of 18 September 2012 setting out the provisions necessary for the implementation of the renewal procedure for active substances, as provided for in Regulation (EC) No 1107/2009 of the European Parliament and of the Council concerning the placing of plant protection products on the market.OJ L 252, 19.9.2012, p. 26–32.

[11]Commission Implementing Regulation (EU) 2020/1498 of 15 October 2020 concerning the non-renewal of approval of the active substance thiophanate-methyl, in accordance with Regulation (EC) No 1107/2009 of the European Parliament and of the Council concerning the placing of plant protection products on the market, and amending the Annex to Commission Implementing Regulation (EU) No 540/2011.C/2020/7017. OJ L 342, 16.10.2020, p. 5–7.

According to the mandate received from the European Commission in 2022 in accordance with Article 43 of Regulation (EC) No 396/2005, EFSA is requested to:

- using the principles of the joint guidance document to identify endocrine-disrupting substances as adopted by EFSA and ECHA (2018), to assess whether, taking into account all available evidence and as a minimum the pertinent studies referred to in the background section of the mandate, carbendazim and thiophanate-methyl meet the scientific criteria for the determination of endocrine-disrupting properties detailed in Commission Regulation (EU) 2018/605;[12]
- in case carbendazim and/or thiophanate-methyl would be recognised as endocrine disruptor(s):
    - to consider whether the toxicological reference values for consumer risk assessment (acceptable daily intake [ADI], ARfD) derived by EFSA in 2021 for the active substance(s) cover the identified endocrine-disrupting properties of the substance(s) and are still sufficiently protective for consumers;
    - to derive toxicological reference values for consumer risk assessment (ADI, ARfD), should the ones proposed by EFSA in 2021 not be considered protective;
    - to assess the chronic and acute risk to consumers for carbendazim and thiophanate-methyl, taking into account the feasibility to derive toxicological reference values for consumer risk assessment;
    - to recommend MRLs for carbendazim and thiophanate-methyl in accordance with the residue definition and the residue data (GAPs and supporting residue trials) considered by EFSA in 2021, and advise risk managers on alternative options;
- to share its draft Reasoned Opinion for a 2-week consultation with the Commission, ECHA and the Member States before finalising it.

The active substance and its use pattern

Carbendazim is the ISO common name for methyl benzimidazol-2-ylcarbamate (IUPAC). Carbendazim is a metabolite of thiophanate-methyl.

Thiophanate-methyl is the ISO common name for dimethyl (1,2-phenylenedicarbamothioyl)dicarbamate (IUPAC).

The chemical structure of the active substances and the main metabolites are reported in Appendix E.

The EU MRLs for both active substances are established in Annexes II and III of Regulation (EC) No 396/2005. Codex maximum residue limits (CXLs) for thiophanate-methyl and carbendazim were also established by the Codex Alimentarius Commission (CAC).

Assessment

EFSA has based its assessment on the following documents:

- the PROFile as prepared by EFSA;
- the report of the pesticide peer review experts meeting on mammalian toxicology (TC 39) and related background documents (EFSA, 2021a, 2021b, 2021c)
- the renewal assessment report (RAR) and its final addendum on the active substance carbendazim, prepared by the rapporteur Member State, Germany, in accordance with Article 5(5) of Council Directive 91/414/EEC (Germany, 2009, 2010)
- the renewal assessment report (RAR) on the active substance thiophanate-methyl prepared by the rapporteur Member State, Sweden, in the framework of Commission Implementing Regulation (EU) No 844/201 (Sweden, 2016, 2017);
- the conclusion on the peer review of the pesticide risk assessment of the active substance carbendazim (EFSA, 2010);
- the conclusion on the peer review of the pesticide risk assessment of the active substance thiophanate-methyl (EFSA, 2018a);
- the ECHA RAC CLH opinion on thiophanate-methyl (ECHA, 2019b).
- the ECHA BPC opinion for carbendazim as product types PT7, PT9 and PT10 (ECHA, 2019a, 2019c, 2019d) and related Competent Authority assessment Report (CAR) (Germany, 2019).
- the previous reasoned opinions on the assessment, modification and review of the existing MRLs for carbendazim and thiophanate methyl (EFSA, 2009, 2012, 2014).
- the report of the pesticide peer review experts meeting on mammalian toxicology (TC 118–119) and related background documents including the EFSA ED assessment reports and Appendices E Excel files (EFSA, 2023a, 2023b, 2023c, 2023d, 2023e).

[12]Commission Regulation (EU) 2018/605 of 19 April 2018 amending Annex II to Regulation (EC) No 1107/2009 by setting out scientific criteria for the determination of endocrine disrupting properties. OJ L 101, 20.4.2018, p. 33–36.

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 546/2011[13] and the currently applicable guidance documents relevant for the consumer risk assessment of pesticide residues (ECHA and EFSA, 2018; European Commission, 1997a, 1997b, 1997c, 1997d, 1997e, 1997f, 1997g, 2000, 2010a, 2010b, 2017; 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 | MAMMALIAN TOXICOLOGY

Under the remit of the mandate received in 2020 only conclusions regarding clastogenicity and aneugenicity have been considered with the aim to consider the setting of reference values for the active substances thiophanate-methyl and carbendazim. The assessment of ED properties of the two substances was under the remit of another mandate received in 2022, as outlined in the previous terms of reference.

The toxicological profile of both substances was discussed during the Pesticide Peer Review TC 39 (15 January 2021) and the ED properties were discussed during the Pesticide Peer Review TC 118–TC 119 (17 November 2023).[14]

Regarding thiophanate-methyl, the experts agreed that the data available to ECHA RAC (ECHA, 2019b) suggest that there is direct evidence in vitro that thiophanate-methyl is not clastogenic but aneugenic, and there is indirect evidence in vivo that thiophanate-methyl is not clastogenic but aneugenic. Regarding the assessment of the ED potential of thiophanate-methyl for humans, the experts agreed that Scenario 1b of the EFSA/ECHA ED guidance (ECHA-EFSA, 2018) is applicable and the ED criteria for thyroid (T)-modality, as laid down in point 3.6.5 of Annex II to Regulation (EC) No 1107/2009, as amended by Commission Regulation (EU) 2018/605, are met (more details are given under Appendix B.1.1). The majority of experts agreed that the most suitable basis for setting the ADI and acute reference dose (ARfD) for thiophanate-methyl is the NOAEL of 2 mg/kg bw per day for maternal and developmental toxicity in the rabbit and applying an uncertainty factor (UF) of 100. The resulting ADI and ARfD is 0.02 mg/kg bw (per day). The overall NOAEL for the T-mediated effects is 14.6 mg/kg bw per day based on a two-generation toxicity study in rat. Considering that the effects observed for the T-modality are mainly based on hepatic enzyme induction, and therefore, a thresholder monotonic dose–response relationship is expected, the experts agreed that the current ADI and ARfD are sufficiently protective for consumers, including the identified hazard indicative of endocrine disruption. For the oestrogen, androgen and steroidogenesis (EAS)-modalities, scenario 2a(ii) is applicable for the E-modality (ED criteria not met) while for the A and S modalities, scenario 2a(iii) is applicable (further data to be generated to allow conclusion). Therefore, a residual uncertainty remains for the A and S modalities concerning the ED properties of thiophanate-methyl. However, no additional UF is considered necessary to cover this uncertainty based on lack of adversity in the available data set for the in vivo endpoints that are expected to be sensitive to perturbations on the A and S modalities. In addition, the available information on the endocrine activity for the A and S modalities from the ToxCast database is not showing any concern.

Regarding carbendazim, the experts agreed that there is no additional data that challenge previous conclusion on the genotoxicity profile of carbendazim as assessed by EFSA (2010) and ECHA (2019a, 2019c, 2019d). Therefore, the experts agreed that the weight of evidence suggests that there is direct evidence in vitro and in vivo that carbendazim is not clastogenic but aneugenic and agreed to maintain previous ADI and ARfD of carbendazim of 0.02 mg/kg bw (per day). The available data do not indicate that carbendazim is an endocrine disruptor (see also Appendix B.1.2); therefore, no further consideration on the impact of the ED assessment on the current ADI and ARfD is needed.

As thiophanate-methyl and carbendazim share a similar toxicological effect, i.e. aneugenic potential, these compounds can be considered together in a combined risk assessment. The experts noted that there are differences in potency, where thiophanate-methyl showed a lower potency for aneugenicity compared to carbendazim and that there are also differences in the toxicological profile regarding other toxicity endpoints (e.g. thyroid, as a critical target organ for thiophanate-methyl and for the ED assessment). It is also noted that carbendazim is a metabolite of thiophanate-methyl. The reference values proposed for carbendazim and thiophanate-methyl are protective of the aneugenic potential of both substances and are also covering the concern related to the identified hazards indicative of endocrine disruption for thiophanate-methyl.

2 | RESIDUES IN PLANT: RESIDUE DEFINITIONS, ANALYTICAL METHODS FOR ENFORCEMENT AND MRL PROPOSALS

The **metabolism** of thiophanate-methyl in **primary crops** has been assessed in the framework of the MRL review for carbendazim and thiophanate-methyl (EFSA, 2014). During the peer review for the renewal of thiophanate-methyl, these studies were reassessed vs. the current data requirements and additional metabolism studies were considered (EFSA, 2018a).

The metabolism of carbendazim in primary crops has been assessed in the framework of the peer review for the renewal of carbendazim (EFSA, 2010) and in the MRL review for carbendazim and thiophanate methyl (EFSA, 2014).

[13]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.

[14]For full details on the expert's discussion, please refer to the Report on the pesticide peer review TC 118 –TC 119 Carbendazim and thiophanate-methyl (EFSA, 2023a).

Primary crop metabolism of thiophanate-methyl and carbendazim was investigated separately for foliar application in four different crop groups (fruit crops, root crops, pulses and oilseeds and cereals). Additional studies where carbendazim was applied to strawberry plants via hydroponic solution (considered informative only; EFSA, 2010) or thiophanate-methyl was applied to tomato plants by drip irrigation are also available (EFSA, 2018a). Studies investigating the metabolism of benomyl, another active substance of the group of benzimidazoles, in rice, soyabeans and sugar beets were also taken into account during the MRL review, as this compound shares a similar metabolism with thiophanate-methyl and it is degraded mainly into carbendazim (EFSA, 2014).

For each active substance, metabolic patterns in the different studies were shown to be similar. After foliar treatments, carbendazim was shown to be a main metabolite of thiophanate-methyl. The following additional metabolites were also observed: **2-AB** (both in metabolism studies with thiophanate-methyl and carbendazim) and metabolites **FH-432** and **DX-105** (identified in the metabolism studies with thiophanate-methyl as intermediate compounds before the cyclisation to form carbendazim).

In particular, following foliar applications of thiophanate-methyl on apples (relevant for the uses under assessment), parent and carbendazim were the main compounds identified (accounting for up to 64% and for up to 29% total radioactive residue (TRR), respectively). At PHIs of 1 and 7 days, most of the TRR was found in the rinsate (97%–93% TRR), with limited translocation into the pulp (3%–7% TRR). Metabolites **2-AB**, **FH-432** and **DX-105** were identified in the rinsate but were present at low proportions (accounting for 0.6%–1.2% TRR, for 3%–5% TRR and for 1%–2% TRR, respectively). Following foliar application of thiophanate-methyl on grapes, at harvest (35 DAT) carbendazim was the main compound identified in berries accounting for 53% TRR. Thiophanate-methyl, metabolites **FH-432** and **DX-105** were identified at low proportions (accounting for 4% TRR, for 4% and for 0.5% TRR, respectively) while metabolite **2-AB** was only found in the leaves (1.2% TRR) (Sweden, 2016, 2017).

Following foliar application of carbendazim on peaches, TRR was 1 mg eq/kg and 1.27 mg eq/kg immediately after the first and the second treatment, respectively. The extraction procedure removed over 97% of the TRR in the peaches. The only detectable residue in these extracts was carbendazim, but its levels were not reported. After treatment with NaOH to release unextractable radioactivity, the only residue found was **2-AB**, which is converted from carbendazim. No further metabolites were detected in any sample (Germany, 2009, 2010).

Therefore, the main compounds identified in the available metabolism studies with foliar applications on fruit crops were thiophanate-methyl and carbendazim while metabolites 2-AB, FH-432 and DX-105 were only present at low proportions.

It is noted that thiophanate-methyl is also authorised for post-harvest dip treatment on citrus fruits, for which no representative metabolism study is available. Nevertheless, considering that in the available studies on fruit crops thiophanate-methyl was applied close to the harvest, a different metabolism is not expected following post-harvest treatment according to the authorised use and no additional studies are required.

Since thiophanate-methyl and carbendazim are no longer authorised for uses as plant protection products in EU and only import tolerances were considered in the present assessment, there is no need to investigate the **nature** and **magnitude** of residues in **rotational crops**.

The **nature of residues in processed commodities** was investigated and evaluated in previous EFSA assessments (EFSA, 2010, 2014, 2018a). Thiophanate-methyl was shown to be stable to pasteurisation. Substantial breakdown was observed following conditions simulating boiling/brewing/baking and sterilisation. Carbendazim was the major degradation product in both cases, accounting for maximum amounts of 14.2% (boiling/brewing/baking) and 92.0% (sterilisation) of the applied radioactivity. 2-AB was formed under sterilisation conditions only, accounting for 10.3% of the radioactivity (EFSA, 2014, 2018a). Carbendazim was shown to be stable during pasteurisation, cooking, brewing and sterilisation (EFSA, 2010, 2014). Based on the above data, it is concluded that thiophanate-methyl and carbendazim are the relevant compounds to be included in the residue definition for processed commodities.

In the framework of the peer review for the renewal of thiophanate-methyl, **storage stability** of thiophanate-methyl and carbendazim was demonstrated for a period of 12 months at –18°C in high acid content (grapes), high oil content (rapeseeds), high protein content (dry peas) and high starch content commodities (wheat grain). Nevertheless, this stability was only observed when samples were not homogenised before storage, whereas homogenisation of samples leads to a drastically reduced storage stability (EFSA, 2018a). In the framework of a previous MRL application, storage stability of thiophanate-methyl was demonstrated for 36 months at –18°C in commodities with high water content (apples) (EFSA, 2012). In this study, the apples were cut in half before storage and further homogenised before analysis. In the framework of the peer review for carbendazim, storage stability of carbendazim was demonstrated for 30 months at –18°C in high water content commodities (tomatoes) and for 18 months at –18°C in high oil content commodities (soyabean oil) (EFSA, 2010).

Based on the results from the studies on the nature of residues of thiophanate-methyl in primary, rotational crops and processed commodities, during the peer review for the renewal of this active substance, metabolites **2-AB**, **FH-432**, **DX-105** were tentatively proposed for inclusion in the residue definition for risk assessment, pending confirmation on their toxicological profiles (EFSA, 2018a). Nevertheless, considering that the uses under assessment are for fruit crops only, where the main components of the TRR were identified as thiophanate-methyl and its metabolite carbendazim and considering that the crops under assessment are expected to be consumed as peeled and/or are minor crops, **the residue definition for both enforcement and risk assessment can be limited to parent 'thiophanate-methyl' and its metabolite 'carbendazim'**. It is underlined that this conclusion is limited to the present assessment and might need to be reconsidered for different uses and crops. Considering the different toxicological properties of carbendazim and

thiophanate-methyl (i.e. differences in potency regarding aneugenic potential and differences in the toxicological profile regarding other toxicity endpoints, see Section 1), separate residue definitions are recommended. It is noted that the residue definition for carbendazim currently set in the Regulation also includes the active substance benomyl. Nevertheless, considering that the toxicological assessment of benomyl was never carried out at EU level, it is not considered any longer appropriate to include benomyl in the residue definition.

Analytical methods for the enforcement of thiophanate-methyl and carbendazim were submitted and evaluated in previous EFSA assessments (EFSA, 2014, 2018a). Fully validated analytical methods using LC-MS/MS (QuEChERS) are available for the separate enforcement of thiophanate-methyl and carbendazim at the LOQ of 0.01 mg/kg in high water content, high acid content, high oil content and dry matrices (EFSA, 2018a).

According to the information submitted by the EURLs, this LOQ is achievable for the separate enforcement of thiophanate-methyl and carbendazim during routine analyses. Moreover, the same LOQ is also valid for benomyl (measured as carbendazim) (EURLs, 2021). Furthermore, the EURLs highlighted that during routine analyses, benomyl degrades rapidly to carbendazim, and therefore, using routine methods is not possible to analyse separately for benomyl and carbendazim.

In order to collect the most up-to-date information to review the maximum residue levels (MRLs) for the benzimidazole substances carbendazim and thiophanate-methyl, in December 2020, EFSA launched a data call asking all Member States to submit GAPs in non-EU countries for which import tolerances (IT) are authorised. Based on the feedback received by Germany during the data call, no additional import tolerances are currently in place for carbendazim and thiophanate methyl, apart from the ones already assessed in the framework of the review of the MRLs for carbendazim and thiophanate-methyl. No additional GAPs were submitted by the other Member States.

Therefore, to assess the **magnitude of residues in primary crops**, EFSA considered all the residue trials relevant for the crops under assessment reported in the framework of the review of the existing MRLs for carbendazim and thiophanate-methyl (EFSA, 2014).

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, 2017).

The available data were sufficient to derive MRLs and risk assessment values for all crops under assessment, taking note of the following considerations:

- Mangoes and okra (lady fingers): results from the available trials supporting the authorised use of thiophanate-methyl on these crops are reported as sum of thiophanate-methyl and carbendazim, expressed as carbendazim or as thiophanate-methyl. Although the derived MRLs and risk assessment values are expected to be overestimated, EFSA deemed it acceptable considering that mangoes and okra are only very minor crops. Nevertheless, four residue trials on mangoes and four residue trials on okra (lady fingers) compliant with the import tolerance GAPs for thiophanate-methyl are still desirable (minor deficiency).
- Citrus fruits (post-harvest use for thiophanate-methyl): As the MRL derived by the OECD calculator can be overestimated for these types of treatments, the proposed MRL was based on the mean plus four times the standard deviation in line with the EFSA guidelines on residues trials and MRL calculations (EFSA, 2015).

During the MRL review, no information was given on whether samples were homogenised prior storage or after and this information is still required (data gap). Considering that homogenisation of samples leads to a drastically reduced storage stability, pending additional data to ensure that no degradation of thiophanate-methyl and carbendazim occurred in samples during storage, all the derived MRLs should be considered tentative only.

The **magnitude of residues of thiophanate-methyl and carbendazim in processed commodities** was also investigated. Robust processing factors for enforcement and risk assessment were derived for several processed commodities in the framework of a previous MRL assessment (EFSA, 2009), during the review of the existing MRLs for thiophanate-methyl and carbendazim (EFSA, 2014) and in the framework of the peer review for the renewal for the approval for thiophanate-methyl (EFSA, 2018a). The processing factors relevant for the present assessment are reported in Appendix B.2.2.4.

Considering the outcome of the risk assessment (see Section 4), additional processing studies may be useful to refine the risk assessment, especially for papayas for which no peeling factor could be derived. In addition, if further robust processing factors were to be required by risk managers, in particular for enforcement purposes, additional processing studies would be needed for the other processed commodities where a tentative processing factor is derived.

3 | RESIDUES IN LIVESTOCK: RESIDUE DEFINITIONS, ANALYTICAL METHODS FOR ENFORCEMENT AND MRL PROPOSALS

Thiophanate-methyl and carbendazim are authorised for use on citrus fruits that might be fed to livestock. Livestock dietary burden calculations were, therefore, performed for different groups of livestock according to OECD guidance (OECD, 2013), which has now also been agreed upon at European level. The input values for all relevant commodities are summarised in Appendix D.1.

The **dietary burden calculations** were performed for thiophanate-methyl and for carbendazim, separately, in line with the proposed residue definitions for risk assessment (RD-RA 1 and RD-RA 2). For carbendazim, residues arising from the use of thiophanate-methyl and residues arising from the use of carbendazim were compared and the highest values were

used for the calculation of the dietary burden. This approach is valid only assuming that crops are not treated with both thiophanate-methyl and carbendazim during the same crop cycle. For lemons, lime and mandarin (dry pulp), the residues arising from treatment with carbendazim were higher than the residues arising from treatment with thiophanate-methyl (see footnote (a) in Appendix D.1).

Based on the uses reported in the framework of this assessment, significant exposures to thiophanate-methyl and to carbendazim are expected for cattle and swine only; therefore, the nature and magnitude of residues in animals were investigated only in these groups of livestock.

The **metabolism of thiophanate-methyl in lactating ruminants** (goat) was assessed in the MRL review and during the peer review for the renewal (EFSA, 2018a). According to the available study, the metabolism of thiophanate-methyl is extensive and releases several compounds. During the peer review, it was proposed to include in the residue definition for risk assessment for ruminants thiophanate-methyl, 4-hydroxy-carbendazim (4-OH-MBC), 5-hydroxy-carbendazim (5-OH-MBC) and 5-hydroxy-carbendazim sulfate (5-OH-MBC-S). Furthermore, it was flagged that plant metabolites FH-432 and DX-105 were not recovered in the animal metabolic pathways, and thus, their fate in the animals was considered not addressed by the available studies. Consequently, during the peer review, it was not possible to conclude on the relevant compounds to be monitored in animal matrices (EFSA, 2018a).

In the framework of the present assessment, however, none of the compounds identified in the metabolism study is likely to be present at significant levels considering the calculated exposure of ruminants to thiophanate-methyl. This conclusion is confirmed by the results of the available **feeding studies** performed with **thiophanate-methyl** (see Section B.3.2.1) which were considered in the MRL review and re-assessed during the peer review for the renewal of thiophanate-methyl (EFSA, 2014, 2018a). Therefore, under the framework of this assessment, parent compound only is considered a sufficient marker for enforcement and risk assessment of thiophanate-methyl residues and MRLs for cattle and swine tissues and for cattle milk can be established at the LOQ of 0.01 mg/kg. It is underlined that this conclusion is limited to the present assessment and might need to be reconsidered for different uses and crops. As poultry and sheep are not expected to be exposed to significant levels of thiophanate-methyl residues, residue definition and MRLs for poultry and sheep commodities are not needed.

The **storage stability of thiophanate-methyl** covering the conditions of the samples from the feeding study was investigated during the peer-review for the renewal of thiophanate-methyl where storage stability data for 4-hydroxy-carbendazim residues in animal matrices were identified as a data gap (EFSA, 2018a). Considering that at the calculated dietary burden thiophanate-methyl is expected to be a sufficient marker for enforcement and risk assessment and that livestock feeding studies were only considered to confirm the results of the metabolism study, no additional storage stability study is required in the present assessment. Nevertheless, pending confirmation that samples from trials on plants were not homogenised, the derived MRLs should be considered tentative only.

The **metabolism of carbendazim in lactating ruminants** (cow and goat) was assessed in the framework of the peer review for the renewal of carbendazim and during the MRL review. Based on these studies, EFSA concluded that the residue definition for enforcement in ruminants should be set as the 'sum of carbendazim and 5-hydroxy-carbendazim, expressed as carbendazim'. The same residue definition was proposed for risk assessment in muscle, fat, liver and kidney. For risk assessment in milk, however, the residue definition should also include the metabolite 4-hydroxy-carbendazim (EFSA, 2010, 2014). These residue definitions are still considered valid in the present assessment, noting that residue definitions and MRLs for poultry and sheep commodities are not needed since these livestock are not expected to be exposed to significant levels of carbendazim residues.

Analytical methods for the enforcement of thiophanate-methyl, carbendazim and 5-hydroxy-carbendazim were submitted and evaluated during the peer review for the renewal of thiophanate-methyl (EFSA, 2018a). According to the information available, fully validated analytical methods using LC-MS/MS (QuEChERS) are available for the separate enforcement of these compounds at the LOQ of 0.01 mg/kg in all animal matrices (EFSA, 2018a).

According to the EURLs, screening methods are available for livestock commodities suggesting that this LOQ would be achievable for the separate enforcement of thiophanate-methyl and carbendazim during routine analyses. Moreover, the same LOQ is also valid for benomyl (measured as carbendazim). Analytical methods for the enforcement of 5-hydroxy-carbendazim are currently not available to the EURLs (EURLs, 2021) but, according to the information shared during the MSC on the draft reasoned opinion, validation experiments in animal matrices to provide LOQs for routine analysis (EFSA, 2021d) will be performed.

According to the results of the **livestock feeding studies** performed with **carbendazim** and assessed in the framework of the peer review for the renewal of carbendazim and during the MRL review (EFSA, 2010, 2014), no residues above the combined LOQ of 0.02 mg/kg are expected in cattle tissues and milk and in swine tissues following their exposure to carbendazim. Therefore, MRLs for these commodities can be established at the combined enforcement LOQ of 0.02 and the conversion factor from enforcement to risk assessment in milk can be proposed as 1.

Since the **storage conditions** of the samples from the livestock feeding studies were not reported and storage stability data for metabolite 4-hydroxy-carbendazim (metabolite relevant for the risk assessment of milk) are not available, and pending confirmation that samples from trials on plants were not homogenised, the derived MRLs should be considered tentative only.

4 | CONSUMER RISK ASSESSMENT

In the framework of this assessment, only the uses of thiophanate-methyl reported in Appendix A were considered; however, the uses of thiophanate-methyl and carbendazim were previously also assessed by the JMPR (FAO, 1994, 1998, 2003). The CXLs, resulting from these assessments by JMPR and adopted by the CAC, are now international recommendations that need to be considered by European risk managers when establishing MRLs. It is, however, noted that a different residue definition for enforcement and risk assessment has been derived by the JMPR (FAO, 1998) as the 'sum of thiophanate-methyl, carbendazim and benomyl, expressed as carbendazim'. Based on the incompatibility of the residue definitions and considering as well that benomyl has never been evaluated at EU level, is not approved for use in Europe and that import tolerances were never evaluated at EU level for this active substance, the existing CXLs were not considered further in this assessment and should not be recommended.

Since carbendazim and thiophanate methyl share a similar toxicological effect (see Section 1), EFSA proposes to perform the risk assessment of carbendazim and thiophanate-methyl separately and then to sum the results from the two single assessments to obtain their combined exposures. This approach allows to evaluate the effect of a combined exposure still considering the respective toxicological reference values.

Chronic and acute exposure calculations for all crops reported in the framework of this review were performed using revision 3.1 of the EFSA PRIMo (EFSA, 2018b, 2019). Input values for the exposure calculations were derived in compliance with the decision tree reported in Appendix E. Hence, for those commodities where a tentative MRL could be derived by EFSA in the framework of this review, input values were derived according to the internationally agreed methodologies (FAO, 2009).

For carbendazim, residues arising from the use of thiophanate-methyl and residues arising from the use of carbendazim were compared and the highest values were used for the calculation of the exposure. This approach is valid only assuming that crops are not treated with both thiophanate-methyl and carbendazim during the same crop cycle. Furthermore, considering the effect of processing on the nature of the residue observed in the hydrolysis study on thiophanate-methyl (see Section 2), values from residue trials have been adjusted assuming that, following boiling/brewing/baking, thiophanate-methyl levels would be reduced by 15% and converted to carbendazim. According to the OECD guidelines on the magnitude of pesticide residues in processed commodities (OECD, 2008) and in line with approach followed during the MRL review (EFSA, 2014), the effect of boiling/brewing/baking has been considered relevant for mangoes and papaya (that can be consumed as jam and marmalades) and for okra that is usually consumed cooked. Additionally, thiophanate-methyl residues were expressed as carbendazim considering that the ratio between the two molecular weights is 0.56. It is acknowledged by EFSA that this approach may overestimate the exposure calculations for carbendazim in raw agricultural commodities. However, in the absence of more adequate data for refinement of the exposure calculations, the most conservative approach was applied. For citrus fruit and mangoes, the peeling factors derived in Section 2 have also been considered. For the commodities of animal origin, considering that no residues of carbendazim and thiophanate-methyl are expected in the raw commodities, the effect of processing was not deemed relevant.

All input values included in the exposure calculations are summarised in Appendix D.2.

The calculated exposure values were compared with the toxicological reference values for thiophanate-methyl and for carbendazim (ADI of 0.02 mg/kg bw per day and ARfD of 0.02 mg/kg bw), derived or confirmed in this assessment.

For **thiophanate-methyl**, the highest chronic exposure was calculated for German child, representing 8% of the ADI. With regard to the acute exposure, however, an exceedance of the ARfD was identified for oranges, grapefruits, mandarins and papaya, representing 314%, 186%, 140% and 106% of the ARfD, respectively.

For **carbendazim**, the highest chronic exposure was calculated for Dutch toddler, representing 7% of the ADI while the highest acute exposure was calculated for mandarins, representing 84% of the ARfD.

Furthermore, before proposing a refinement of the risk assessment, a **combined acute risk assessment** was performed summing the results from the acute risk assessment of thiophanate-methyl and carbendazim. This approach is considered valid provided that carbendazim and thiophanate methyl are not used together on the same crop in the same season. According to this calculation, an exceedance of the ARfD was identified for oranges, grapefruits, mandarins, mangoes, papaya and lemons, representing 342%, 203%, 224%, 143%, 133% and 129% of the ARfD. It is, however, noted by EFSA that the approach followed for the combined exposure assessment leads to an overestimation of the exposure in lemons, mandarins and limes, where residues resulting from the use of carbendazim and thiophanate-methyl have been combined while co-occurrence of these residues is not expected to occur in practice for these three crops.

A second (scenario EU2) and a third (scenario EU3) exposure calculation were therefore performed, as described below and assuming that residues from the uses of carbendazim and thiophanate-methyl are not co-occurring in lemons.

Scenario EU2 (reflecting option 1 in Table 1): excluding the uses of thiophanate-methyl on oranges, grapefruits, mandarins, lemons, mangoes and papaya and considering as a fall-back GAPs for mandarins and lemons the uses of carbendazim. No fall-back GAPs could be identified for oranges, grapefruits, papaya and mangoes. According to the results of this second calculation, the highest acute exposure for thiophanate-methyl is calculated for limes, representing 48% of the ARfD, the highest acute exposure for carbendazim is calculated for mandarins, representing 84% of the ARfD and the highest combined acute exposure is calculated for mandarins, representing 84% of the ARfD.

Scenario EU3 (reflecting option 2 in Table 1): excluding the uses of thiophanate methyl on oranges, grapefruits, mandarins, mangoes and papaya and the use of carbendazim on lemons and considering as a fall-back GAP for mandarins the use of carbendazim and as fall-back GAP for lemons the use of thiophanate-methyl. As in scenario EU2, no fall-back GAPs could

be identified for oranges, grapefruits, papaya and mangoes. According to the results of this third calculation, the highest acute exposure for thiophanate-methyl is calculated for lemons, representing 81% of the ARfD, the highest acute exposure for carbendazim is calculated for mandarins, representing 84% of the ARfD and the highest combined acute exposure is calculated for lemons, representing 88% of the ARfD.

These calculations show that no risk for consumers is identified for lemons in case residues from the uses of carbendazim and thiophanate-methyl are not co-occurring.

In order to perform a **combined chronic risk assessment**, results from the chronic risk assessment of thiophanate-methyl and results from the chronic risk assessment of carbendazim from the refined calculations were summed (for scenario EU2 and EU3, respectively). This calculation has been done for the Dutch diet (toddler), the British diet (infant) and the French diet (toddler) being the diets with the highest estimated exposure.

The highest chronic exposure for scenario EU2 was calculated for the Dutch diet (toddler), representing 10% of the ADI. The highest chronic exposure for scenario EU3 was calculated for the Dutch diet (toddler), representing 9% of the ADI.

Based on these calculations, an acute risk to consumers was identified for the most critical GAPs for thiophanate-methyl on oranges, grapefruits, mandarins, mangoes and papaya and for lemons, if the residues from the uses of carbendazim and thiophanate-methyl are co-occurring. However, fall-back GAPs were identified for mandarins and lemons, for which a second (scenario EU2) and a third risk (scenario EU3) assessment did not indicate risk to consumers. For the remaining commodities, although some major uncertainties remain due to the data gaps identified in the previous sections, the indicative exposure calculation did not indicate a risk to consumers.

Conclusions

The experts of the peer review experts meeting (TC 39, January 2021) on mammalian toxicology agreed that by considering the new data available to ECHA RAC, the weight of evidence suggests that there is direct evidence in vitro that thiophanate-methyl is not clastogenic but aneugenic whereas there is indirect evidence in vivo that thiophanate-methyl is not clastogenic but aneugenic. The majority of experts agreed that the most suitable basis for setting the ADI and Acute Reference Dose (ARfD) for thiophanate-methyl is the NOAEL of 2 mg/kg bw per day for maternal and developmental toxicity in the rabbit and applying an uncertainty factor of 100. The resulting ADI and ARfD is 0.02 mg/kg bw (per day). Regarding carbendazim, the experts agreed that the weight of evidence suggests that there is direct evidence in vitro and in vivo that carbendazim is not clastogenic but aneugenic and agreed to maintain previous ADI and ARfD of carbendazim of 0.02 mg/kg bw (per day).

The metabolism of thiophanate-methyl and carbendazim in plants was investigated in primary crops. According to the results of the metabolism studies and the available toxicological studies, the residue definitions for enforcement and risk assessment can be proposed as 'thiophanate-methyl' and 'carbendazim', separately. A specific residue definition for rotational crops is not deemed necessary considering that only import tolerances were considered in the present assessment. These residue definitions are also applicable to processed commodities. Fully validated analytical methods are available for the separate enforcement of the proposed residue definitions in the main four matrices at the LOQ of 0.01 mg/kg. According to the EURLs, this LOQ is achievable by using the QuEChERS method in routine analyses. Nevertheless, the EURLs highlighted that during routine analyses, benomyl degrades rapidly to carbendazim and therefore using routine methods is not possible to analyse separately for benomyl and carbendazim.

Available residue trials data were considered sufficient to derive MRL proposals as well as risk assessment values for all commodities under evaluation. Considering that homogenisation of samples leads to a drastically reduced storage stability, pending additional data to ensure that no degradation of thiophanate-methyl and carbendazim occurred in samples during storage, all the derived MRLs should be considered tentative only.

Thiophanate-methyl and carbendazim are authorised for use on citrus fruits that might be fed to livestock. Livestock dietary burden calculations were, therefore, performed for different groups of livestock according to OECD guidance. Based on the uses reported in the framework of this assessment, significant exposure to thiophanate-methyl and to carbendazim is expected for cattle and swine only; therefore, the nature and magnitude of residues in animals were investigated only in these groups of livestock.

The metabolism of thiophanate-methyl and carbendazim residues in livestock was investigated in lactating goats and cow at dose rate covering the maximum dietary burdens calculated in this review. For thiophanate-methyl, the residue definition for enforcement and risk assessment was proposed as parent 'thiophanate-methyl' only. For carbendazim, the relevant residue definition for enforcement was set as the 'sum of carbendazim and 5-hydroxy-carbendazim, expressed as carbendazim'. The same residue definition also applies for risk assessment in muscle, fat, liver and kidney while an additional metabolite (4-hydroxy-carbendazim) is also included for risk assessment in milk. Available feeding studies performed with thiophanate-methyl and carbendazim demonstrated that no residues above the LOQ are expected in cattle milk and in cattle and swine tissues following their exposure to thiophanate-methyl and carbendazim and MRLs for these commodities can be established at the enforcement LOQ.

Fully validated analytical methods using LC-MS/MS (QuEChERS) are available for the separate enforcement of thiophanate-methyl, carbendazim and 5-hydroxy-carbendazim at the LOQ of 0.01 mg/kg for each compound in all animal matrices.

According to the EURLs, it is expected that this LOQ would be achievable for the separate enforcement of thiophanate-methyl and carbendazim during routine analyses. Moreover, the same LOQ is also valid for benomyl (measured as carbendazim). Analytical methods for the enforcement of 5-hydroxy-carbendazim are currently not available to the EURLs but according to the information shared during the MSC on the draft reasoned opinion they will perform validation experiments in animal matrices to provide LOQs for routine analysis. According to the EURLs, the analytical standards for carbendazim, benomyl, thiophanate-methyl and 5-hydroxy-carbendazim are commercially available.

Chronic and acute consumer exposure resulting from the authorised uses reported in the framework of this review was calculated using revision 3.1 of the EFSA PRIMo.

For thiophanate-methyl, the highest chronic exposure was calculated for German child, representing 8% of the ADI. With regard to the acute exposure, however, an exceedance of the ARfD was identified for oranges, grapefruits, mandarins and papaya, representing 314%, 186%, 140% and 106% of the ARfD, respectively.

For carbendazim, the highest chronic exposure was calculated for Dutch toddler, representing 7% of the ADI while the highest acute exposure was calculated for mandarins, representing 84% of the ARfD.

Furthermore, before proposing a refinement of the risk assessment, a combined acute risk assessment was performed summing the results from the acute risk assessment of thiophanate-methyl and carbendazim. According to this calculation, an exceedance of the ARfD was identified for oranges, grapefruits, mandarins, mangoes, papaya and lemons, representing 342%, 203%, 224%, 143%, 133% and 129% of the ARfD. It is, however, noted by EFSA that the approach followed for the combined exposure assessment leads to an overestimation of the exposure in lemons, mandarins and limes, where residues resulting from the use of carbendazim and thiophanate-methyl have been combined while co-occurrence of these residues is not expected to occur in practice for these three crops.

A second (scenario EU2, reflecting option 1 in Table 1) and a third (scenario EU3, reflecting option 2 in table 1) exposure calculations were therefore performed, considering possible fall-back GAPs and assuming that residues from the uses of carbendazim and thiophanate-methyl are not co-occurring in lemons.

According to the results of the second calculation (scenario EU2), the highest acute exposure for thiophanate-methyl is calculated for limes, representing 48% of the ARfD, the highest acute exposure for carbendazim is calculated for mandarins, representing 84% of the ARfD and the highest combined acute exposure is calculated for mandarins, representing 84% of the ARfD.

According to the results of the third calculation (scenario EU3), the highest acute exposure for thiophanate-methyl is calculated for lemons, representing 81% of the ARfD, the highest acute exposure for carbendazim is calculated for mandarins, representing 84% of the ARfD and the highest combined acute exposure is calculated for lemons, representing 88% of the ARfD.

These calculations show that no risk for consumers is identified for lemons in case residues from the uses of carbendazim and thiophanate-methyl are not co-occurring.

In order to perform a combined chronic risk assessment, results from the chronic risk assessment of thiophanate-methyl and results from the chronic risk assessment of carbendazim from the refined calculations were summed (scenario EU2 and EU3). This calculation has been done for the Dutch diet (toddler), the British diet (infant) and the French diet (toddler) being the diets with the highest estimated exposure.

The highest chronic exposure for scenario EU2 was calculated for the Dutch diet (toddler), representing 10% of the ADI. The highest chronic exposure for scenario EU3 was calculated for the Dutch diet (toddler), representing 9% of the ADI.

Based on these calculations, an acute risk to consumers was identified for the most critical GAPs for thiophanate-methyl on oranges, grapefruits, mandarins, mangoes and papaya and for lemons, if the residues from the uses of carbendazim and thiophanate-methyl are co-occurring. However, fall-back GAPs were identified for mandarins and lemons, for which a second (scenario EU2) and a third (scenario EU3) risk assessments did not indicate risk to consumers. For the remaining commodities, although some major uncertainties remain due to the data gaps identified, the indicative exposure calculation did not indicate a risk to consumers.

In October 2022, in order to ensure that MRLs derived by EFSA in its assessment of 2021 are safe for consumers also in view of endocrine-disrupting properties, EFSA was requested to carry out a follow-up assessment taking into account the scientific criteria for identifying endocrine disruptors (ED) detailed in Commission Regulation (EU) 2018/605 and the joint guidance document to identify endocrine-disrupting substances as adopted by EFSA and ECHA (2018). Based on the outcome of the assessment, the experts of the peer review experts meeting (TC 118–119, November 2023) on mammalian toxicology agreed that the reference values are also covering the concern related to the identified hazards indicative of endocrine disruption for thiophanate-methyl. No further considerations on the impact of the ED assessment on the current reference values were needed for carbendazim since the ED criteria are not met for this substance. Therefore, the risk assessment and the MRL recommendations derived in 2021 and reported above and in the next section, are confirmed.

Recommendations

MRL recommendations were derived in compliance with the decision tree reported in Appendix I 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. In particular, all tentative MRLs need to be confirmed by the following data:

1. Information on whether samples from residue trials were homogenised prior or after storage;
2. Information on the storage condition of the samples from the livestock feeding studies performed with carbendazim;
3. Storage stability study for metabolite 4-hydroxy-carbendazim in milk.

Moreover, it is highlighted that an exceedance of the ARfD was observed for oranges, grapefruits, mandarins, lemons, mangoes and papaya. Consequently, risk managers should consider measures for reduction of the consumer exposure. Furthermore, in order to avoid decline of residues during storage of food samples, enforcement laboratories are recommended not to homogenise samples prior to storage.

To inform further risk management discussions, it is noted that carbendazim is classified as toxic for reproduction category 1B in accordance with Regulation (EC) No 1272/2008.

It is noted that the residue definition for carbendazim currently in the Regulation also includes the active substance benomyl. Nevertheless, considering that a toxicological assessment of benomyl was never carried out at EU level, it is not considered any longer appropriate to include benomyl in the residue definition. As the use of benomyl is no longer authorised within the EU, this change of residue definition will only have consequences for food products treated with benomyl that may be imported from third countries. Hence, if no need to establish import tolerances for benomyl is identified by risk managers, MRLs for benomyl may be established at a specific LOQ or at the default MRL of 0.01 mg/kg. It is also underlined for further considerations by risk managers that, according to the EURLs, it is not possible to analyse separately for benomyl and carbendazim using routine methods.

Minor deficiencies were also identified in the assessment, but these deficiencies are not expected to impact either on the validity of the MRLs derived. The following data are therefore considered desirable but not essential:

- Additional residue trials on mangoes and on okra (lady fingers) compliant with the import tolerance GAPs for thiophanate-methyl with samples analysed separately for thiophanate-methyl and carbendazim.

TABLE 1 Summary table.

Code number	Commodity	Existing EU MRL (mg/kg)	Existing CXL (mg/kg)	Outcome of the review	
				MRL (mg/kg)	Comment
Enforcement residue definition: thiophanate-methyl					
110010	Grapefruits	6	–	–	Further consideration needed[a] Data gap #1
110020	Oranges	6	1	–	Further consideration needed[b] Data gap #1
110030	Lemons	6	–	Option 1[c]: –	Further consideration needed[d] Data gap #1
				Option 2[e]: 7	Further consideration needed[d] Data gap #1
110040	Limes	6	–	7	Further consideration needed[d] Data gap #1
110050	Mandarins	6	–	–	Further consideration needed[a] Data gap #1
163030	Mangoes	1	5	–	Further consideration needed[b] Data gap #1
163040	Papayas	1	–	–	Further consideration needed[a] Data gap #1
231040	Okra/lady's fingers	1	–	0.9	Further consideration needed[d] Data gap #1
Enforcement residue definition (existing): thiophanate-methyl and carbendazim, expressed as carbendazim **Enforcement residue definition (proposed):** thiophanate-methyl					
1011010	Swine muscle	0.05*	–	0.01*	Further consideration needed[d] Data gap #1
1011020	Swine fat tissue	0.05*	–	0.01*	Further consideration needed[d] Data gap #1
1011030	Swine liver	0.05*	0.05*	0.01*	Further consideration needed[f] Data gap #1
1011040	Swine kidney	0.05*	0.05*	0.01*	Further consideration needed[f] Data gap #1
1012010	Bovine muscle	0.05*	0.05*	0.01*	Further consideration needed[f] Data gap #1
1012020	Bovine fat tissue	0.05*	–	0.01*	Further consideration needed[d] Data gap #1

(Continues)

TABLE 1 (Continued)

Code number	Commodity	Existing EU MRL (mg/kg)	Existing CXL (mg/kg)	Outcome of the review	
				MRL (mg/kg)	Comment
1012030	Bovine liver	0.05*	0.05*	0.01*	Further consideration needed[f] Data gap #1
1012040	Bovine kidney	0.05*	0.05*	0.01*	Further consideration needed[f] Data gap #1
1015010	Equine muscle	0.05*	–	0.01*	Further consideration needed[d] Data gap #1
1015020	Equine fat tissue	0.05*	–	0.01*	Further consideration needed[d] Data gap #1
1015030	Equine liver	0.05*	0.05*	0.01*	Further consideration needed[f] Data gap #1
1015040	Equine kidney	0.05*	0.05*	0.01*	Further consideration needed[f] Data gap #1
1020010	Cattle milk	0.05*	0.05*	0.01*	Further consideration needed[f] Data gap #1
1020040	Horse milk	0.05*	0.05*	0.01*	Further consideration needed[f] Data gap #1
Enforcement residue definition (existing): sum of benomyl and carbendazim, expressed as carbendazim **Enforcement residue definition (proposed):** carbendazim					
110010	Grapefruits	0.2	–	–	Further consideration needed[a] Data gap #1
110020	Oranges	0.2	1	–	Further consideration needed[b] Data gap #1
110030	Lemons	0.7	–	Option 1[c]: 0.9	Further consideration needed[d] Data gap #1
				Option 2[e]: 0.2	Further consideration needed[d] Data gap #1
110040	Limes	0.7	–	0.9	Further consideration needed[d] Data gap #1
110050	Mandarins	0.7	–	0.9	Further consideration needed[d] Data gap #1
163030	Mangoes	0.5	5	–	Further consideration needed[b] Data gap #1
163040	Papayas	0.2	–	–	Further consideration needed[a] Data gap #1
231040	Okra/lady's fingers	2	–	1.5	Further consideration needed[d] Data gap #1
Enforcement residue definition (existing): carbendazim and thiophanate-methyl, expressed as carbendazim **Enforcement residue definition (proposed):** sum of carbendazim and 5-hydroxy-carbendazim, expressed as carbendazim					
1011010	Swine muscle	0.05*	–	0.02*	Further consideration needed[d] Data gaps #1,2
1011020	Swine fat tissue	0.05*	–	0.02*	Further consideration needed[d] Data gaps #1,2
1011030	Swine liver	0.05*	0.05*	0.02*	Further consideration needed[f] Data gaps #1,2
1011040	Swine kidney	0.05*	0.05*	0.02*	Further consideration needed[f] Data gaps #1,2
1012010	Bovine muscle	0.05*	0.05*	0.02*	Further consideration needed[f] Data gaps #1,2
1012020	Bovine fat tissue	0.05*	–	0.02*	Further consideration needed[d] Data gaps #1,2
1012030	Bovine liver	0.05*	0.05*	0.02*	Further consideration needed[f] Data gaps #1,2
1012040	Bovine kidney	0.05*	0.05*	0.02*	Further consideration needed[f] Data gaps #1,2
1015010	Equine muscle	0.05*	–	0.02*	Further consideration needed[d] Data gaps #1,2

TABLE 1 (Continued)

Code number	Commodity	Existing EU MRL (mg/kg)	Existing CXL (mg/kg)	Outcome of the review	
				MRL (mg/kg)	Comment
1015020	Equine fat tissue	0.05*	–	0.02*	Further consideration needed[d] Data gaps #1,2
1015030	Equine liver	0.05*	0.05*	0.02*	Further consideration needed[f] Data gaps #1,2
1015040	Equine kidney	0.05*	0.05*	0.02*	Further consideration needed[f] Data gaps #1,2
1020010	Cattle milk	0.05*	0.05*	0.02*	Further consideration needed[f] Data gaps #1,2,3
1020040	Horse milk	0.05*	0.05*	0.02*	Further consideration needed[f] Data gaps #1,2,3
–	Other commodities of plant and/or animal origin	See Reg. 559/2011	–	–	Further consideration needed[g]
Enforcement residue definition (proposed): benomyl					
–	Commodities of plant and/or animal origin	–	–	–	Further consideration needed[g]

Abbreviations: CXL, codex maximum residue limit; MRL, maximum residue level.

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

[a]GAP evaluated at EU level is not fully supported by data and a risk to consumers cannot be excluded; no CXL is available. Either a specific LOQ or the default MRL of 0.01 mg/kg may be considered (combination E-I in Appendix I).

[b]GAP evaluated at EU level is not fully supported by data and a risk to consumers cannot be excluded; CXL is not compatible with EU residue definitions. Either a specific LOQ or the default MRL of 0.01 mg/kg may be considered (combination E-II in Appendix I).

[c]Option 1: MRL based on the authorised use for carbendazim, assuming that the authorised use of thiophanate-methyl will be withdrawn.

[d]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; no CXL is available (combination F–I in Appendix I). It is noted that carbendazim is classified as toxic for reproduction category 1B in accordance with Regulation (EC) No 1272/2008.

[e]Option 2: MRL based on the authorised use for thiophanate-methyl, assuming that the authorised use of carbendazim will be withdrawn.

[f]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; CXL is not compatible with EU residue definitions (combination F-II in Appendix I). It is noted that carbendazim is classified as toxic for reproduction category 1B in accordance with Regulation (EC) No 1272/2008.

[g]There are no import tolerances reported at EU level; no CXL is available or CXL is not compatible with EU residue definitions. Either a specific LOQ or the default MRL of 0.01 mg/kg may be considered (combination A-I/II in Appendix I).

ABBREVIATIONS

a.i.	active ingredient
a.s.	active substance
ADI	acceptable daily intake
AR	applied radioactivity
ARfD	acute reference dose
BBCH	growth stages of mono- and dicotyledonous plants
BVL	Bundesamt für Verbraucherschutz und Lebensmittelsicherheit, Germany
bw	body weight
CAC	Codex Alimentarius Commission
CAS	Chemical Abstract Service
CCPR	Codex Committee on Pesticide Residues
CEN	European Committee for Standardization (Comité Européen de Normalisation)
CF	conversion factor for enforcement residue definition to risk assessment residue definition
CIRCA	(EU) Communication & Information Resource Centre Administrator
CS	capsule suspension
CV	coefficient of variation (relative standard deviation)
CXL	codex maximum residue limit
DAT	days after treatment
EC	emulsifiable concentrate
eq	residue expressed as a.s. equivalent
EURLs	European Union Reference Laboratories for Pesticide Residues (former CRLs)
FAO	Food and Agriculture Organization of the United Nations
GAP	Good Agricultural Practice
HPLC-MS/MS	high performance liquid chromatography with tandem mass spectrometry
HR	highest residue

IEDI	international estimated daily intake
IESTI	international estimated short-term intake
ILV	independent laboratory validation
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/MS	liquid chromatography with tandem mass spectrometry
LOQ	limit of quantification
Mo	monitoring
MRL	maximum residue level
MS	Member States
MS	mass spectrometry detector
MS/MS	tandem mass spectrometry detector
NEDI	national estimated daily intake
NESTI	national estimated short-term intake
NOAEL	no observed adverse effect level
NTMDI	national theoretical maximum daily intake
OECD	Organisation for Economic Co-operation and Development
PBI	plant back interval
PF	processing factor
PHI	preharvest interval
ppm	parts per million (10^{-6})
PRIMo	(EFSA) Pesticide Residues Intake Model
PROFile	(EFSA)Pesticide Residues Overview File
QuEChERS	Quick, Easy, Cheap, Effective, Rugged, and Safe (analytical method)
RA	risk assessment
RAC	raw agricultural commodity
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
TMDI	theoretical maximum daily intake
TRR	total radioactive residue
WHO	World Health Organization

UPDATE

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CONFLICT OF INTEREST

If you wish to access the declaration of interests of any expert contributing to an EFSA scientific assessment, please contact interestmanagement@efsa.europa.eu.

REQUESTOR

European Commission

QUESTION NUMBERS

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APPENDIX A

Summary of authorised uses considered for the review of MRLs

A.1 | Import tolerances – thiophanate-methyl

				Preparation		Application				Application rate per treatment				
Crop and/or situation	MS or country	F G or I[a]	Pests or group of pests controlled	Type[b]	Conc. a.s.	Method Kind	Range of growth stages and season[c]	Number min–max	Interval between application (min)	a.s./hL min–max	Water L/ha min–max	Rate and unit	PHI (days)[d]	Remarks
Grapefruits	Non-EU	I	Penicillium	SC	500 g/L	Post-harvest treatment–dipping	n.a.	1–1		–	–	0.18 kg a.i./hL	3	
Oranges	Non-EU	I	Penicillium	SC	500 g/L	Post-harvest treatment–dipping	n.a.	1–1		–	-	0.18 kg a.i./hL	3	
Lemons	Non-EU	I	Penicillium	SC	500 g/L	Post-harvest treatment – dipping	n.a.	1–1		–	–	0.18 kg a.i./hL	3	
Limes	Non-EU	I	Penicillium	SC	500 g/L	Post-harvest treatment – dipping	n.a.	1–1		–	–	0.18 Kg a.i./hL	3	
Mandarins	Non-EU	I	Penicillium	SC	500 g/L	Post-harvest treatment – dipping	n.a.	1–1		–	–	0.18 Kg a.i./hL	3	
Mangoes	Non-EU	F	'Alternaria, Cercospora Dothiorella Collelotrichum gloeosporioies Botryodiplodia theobromae	SC	500 g/L	Foliar treatment – spraying	81–86	1–2	10	–	–	0.075 kg a.i./hL	14	
Papayas	Non-EU	F	Anthracnosis	WP	700 g/kg	Foliar treatment – spraying	n.a.	5–5	14	–	–	0.7 kg a.i./ha	3	
Okra	Non-EU	F	Leaf spot	EC	500 g/L	Foliar treatment – spraying	n.a.	1–2	14	–	–	0.49 kg a.i./ha	2	

Abbreviation: MS, Member State.

[a]Outdoor or field use (F), greenhouse application (G) or indoor application (I). Suspension Concentrate.

[b]CropLife International Technical Monograph no 2, 7th Edition. Revised March 2017. Catalogue of pesticide formulation types and international coding system. Growth stage range from first to last treatment (BBCH Monograph, Growth Stages of Plants, 1997, Blackwell, ISBN 3-8263-3152-4), including, where relevant, information on season at time of application.

[c]PHI – minimum preharvest interval.

A.2 | Import tolerances – carbendazim

				Preparation		Application				Application rate per treatment				
Crop and/or situation	MS or country	F G or I[a]	Pests or group of pests controlled	Type[b]	Conc. a.s.	Method kind	Range of growth stages and season[c]	Number min–max	Interval between application min	a.s./hL min–max	Water L/ha min–max	Rate and unit	PHI (days)[d]	Remarks
Lemons	South Africa	I	Penicillium	SC	500 g/L	Foliar treatment – spraying	n.a.	2		–	–	0.013 kg a.i./hL	60	
Limes	South Africa	I	Penicillium	SC	500 g/L	Foliar treatment – spraying	n.a.	2		–	–	0.013 kg a.i./hL	60	
Mandarins	South Africa	I	Penicillium	SC	500 g/L	Foliar treatment – spraying	n.a.	2		–	–	0.013 kg a.i./hL	60	

Abbreviation: MS, Member State.

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

[b]Suspension Concentrate CropLife International Technical Monograph no 2, 7th Edition. Revised March 2017. Catalogue of pesticide formulation types and international coding system. Growth stage range from first to last treatment (BBCH Monograph, Growth Stages of Plants, 1997, Blackwell, ISBN 3-8263-3152-4), including, where relevant, information on season at time of application.

[c]PHI – minimum pre-harvest interval.

APPENDIX B

List of end points

B.1 | MAMMALIAN TOXICOLOGY

B.1.1 | Thiophanate-methyl

Genotoxicity

There is direct evidence in vitro that thiophanate-methyl is not clastogenic but aneugenic whereas there is indirect evidence in vivo that thiophanate-methyl is not clastogenic but aneugenic.

Endocrine-disrupting properties.

T-modality

Thiophanate-methyl is an endocrine disruptor (thyroid-modality) of relevance to humans according to the ED scientific criteria in Regulation (EC) 2018/605. **Scenario 1b** of the EFSA/ECHA ED Guidance (ECHA/EFSA, 2018) is applicable.

The overall NOAEL for the T-mediated effects is 14.6 mg/kg bw per day based on a 2-generation toxicity study in rat.

EAS-modalities

A ToxCast estrogen receptor (ER) predictive model is available and negative for thiophanate-methyl; therefore, in line with EFSA/ECHA (2018) ED Guidance, the criteria for the E modality are not met for humans (**Scenario 2a(ii)**).

The Androgen and Steroidogenesis (AS) modalities have not been sufficiently investigated (**Scenario 2a(iii)**).

Summary

	Value (mg/kg bw (per day))	Study	Uncertainty factor
Acceptable Daily Intake (ADI)	0.02	Rabbit, developmental	100
Acute Reference Dose (ARfD)	0.02	Rabbit, developmental	100

B.1.2 | Carbendazim

Genotoxicity

Numerical chromosome aberrations both in vitro and in vivo as a result of the interference with mitotic spindle proteins. Threshold concentration for aneugenic activity in vitro between 0.2-0.6 µg/mL; NOEL for aneuploidy induction in vivo: 50 mg/kg bw	Previous conclusion from EFSA, 2010 supported.

Endocrine-disrupting properties

EATS-modalities

The criteria are not met for the EATS-modalities in a sufficiently investigated dataset. **Scenario 1a** of the EFSA/ECHA ED Guidance (ECHA/EFSA, 2018) is applicable

Summary

	Value (mg/kg bw (per day))	Study	Uncertainty factor
Acceptable Daily Intake (ADI)	0.02 mg/kg bw	Developmental, rat & rabbit	500
Acute Reference Dose (ARfD)	0.02 mg/kg bw	Developmental, rat & rabbit	500

B.2 | RESIDUES IN PLANTS

B.2.1 | Nature of residues and methods of analysis in plants

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

Thiophanate methyl					
Primary crops (available studies)	**Crop groups**	**Crop(s)**	**Application(s)**	**Sampling (DAT)**	**Comment/Source**
	Fruit crops	Apples	Foliar, 3 × 3.9 kg/ha	1, 7	Radiolabelled active substance6 ^{14}C-phenyl -a.s. (EFSA, 2014, 2018)
		Grapes	Foliar, 1 × 1.042 kg a.s./ha	0, 14, 35	^{14}C-phenyl (EFSA, 2018a)
		Tomatoes	Drip irrigation, 1 × 0.702; 1 × 1.386; 1 × 2.314 kg/ha	7	^{14}C-phenyl (Sweden, 2016, 2017)
	Root crops	Sugar beets	Foliar, 3 × 0.39 kg/ha	0, 21	^{14}C-thiocarbonyl (EFSA, 2014, 2018)
	Cereals/grass	Wheat	Foliar, 1 × 0.75 kg/ha	0, 28, 69	^{14}C-thiocarbonyl (EFSA, 2014; Sweden, 2016, 2017)
	Pulses/oilseeds	Lima beans	Foliar, 2 × 1.18 kg/ha	28, 35	^{14}C-thiocarbonyl (EFSA, 2014, 2018) Supportive, not acceptable as a standalone study
		Soyabeans	Run-off, 1 × 700 mg/L	0, 7, 14	^{14}C-thiophanate-methyl (label position not given) mixed with non labelled thiophanate- methyl (EFSA, 2018a)
		Green beans	Run-off (assumed), 1 × 50 mg/L	14	^{14}C-thiophanate-methyl (label position not given) (EFSA, 2018a)
Rotational crops (available studies)	**Crop groups**	**Crop(s)**	**Application(s)**	**PBI (DAT)**	**Comment/Source**
	Root/tuber crops	Carrots	Bare soil, 1 × 1.6 kg/ha	30, 120, 365	(EFSA, 2014, 2018) Studies available but not relevant since only import tolerances under assessment
	Leafy crops	Lettuce	Bare soil, 1 × 1.6 kg/ha	30, 120, 365	(EFSA, 2014, 2018) Same comment as above
	Cereal (small grain)	Wheat	Bare soil, 1 × 1.6 kg/ha	30, 120, 365	(EFSA, 2014, 2018) Same comment as above

(Continued)

Processed commodities (hydrolysis study)	Conditions	Stable?	Comment/Source
	Pasteurisation (20 min, 90°C, pH 4)	Yes	EFSA (2014, 2018)
	Baking, brewing and boiling (60 min, 100°C, pH 5)	No	Thiophanate-methyl degraded to carbendazim that accounted 14.2% (EFSA, 2014, 2018)
	Sterilisation (20 min, 120°C, pH 6)	No	Thiophanate-methyl degraded to carbendazim (92%) and to metabolite 2-AB (10.3%) (EFSA, 2014, 2018)

Carbendazim

Primary crops (available studies)	Crop groups	Crop(s)	Application(s)	Sampling (DAT)	Comment/Source
	Fruit crops	Peaches	Foliar, 2 × 1.12 kg/ha, interval of 14 days between applications	–14, 0	Sampling after each treatment. Study performed with ^{14}C-phenyl carbendazim (EFSA, 2010, 2014)
		Strawberries	Hydroponic, 1 × 0.182 kg as/L	36, 88	Study performed with ^{14}C-imidazole carbendazim Informative only (EFSA, 2010, 2014)
	Root crops	Sugar beet	Foliar, 3 × 0.55 kg/ha Foliar, 5 × 0.55 kg/ha	21 133	Study performed with ^{14}C-phenyl benomyl (FAO, 1998)
	Cereals/grass	Rice	Foliar, 2 × 2.25 kg/ha	–14, 0, 35	Study performed with ^{14}C-phenyl benomyl (EFSA, 2010, 2014)
	Pulses/oilseeds	Beans	Foliar, 2 × 1.12 kg/ha	0, 7, 14, 21, 28	Study performed with ^{14}C-imidazole carbendazim Residues analysed in plants and beans (EFSA, 2010, 2014)
		Soyabeans	Foliar, 2 × 1.1 kg/ha	–14, 0, 35	Study performed with ^{14}C-phenyl benomyl (EFSA, 2014; FAO, 1998)
Rotational crops (available studies)	**Crop groups**	**Crop(s)**	**Application(s)**	**PBI (DAT)**	**Comment/Source**
	Root/tuber crops	Beet	Bare soil, 1.12 kg/ha	30	[2-^{14}C]-carbendazim (EFSA, 2010, 2014) Studies available but not relevant since only import tolerances under assessment
			Bare soil, 3.36 kg/ha	120	
		Radish	3 mg carbendazim/kg soil	224	^{14}C-carbendazim (EFSA, 2010, 2014)
	Leafy crops	Cabbages	Bare soil, 1.12 kg/ha	30	[2-^{14}C]-carbendazim (EFSA, 2010, 2014) Same comment as above
			Bare soil, 3.36 kg/ha	120	
		Lettuce	3 mg carbendazim/kg soil	224	^{14}C-carbendazim (EFSA, 2010, 2014) Same comment as above
	Pulses and oilseeds	Soybean	Bare soil, 2.24 kg/ha	60	80:20 mix of ^{14}C-labelled carbendazim and 2-AB (EFSA, 2010, 2014) Same comment as above
		Alfalfa	Bare soil, 2.24 kg/ha	60	
	Cereal (small grain)	Barley	Bare soil, 1.12 kg/ha	30	[2-^{14}C]-carbendazim (EFSA, 2010, 2014) Same comment as above
			Bare soil, 3.36 kg/ha	145	
		Rye grass	Bare soil, 2.24 kg/ha	60	80:20 mix of ^{14}C-labelled carbendazim and 2-AB (EFSA, 2010, 2014) Same comment as above
Processed commodities (hydrolysis study)	**Conditions**	**Stable?**	**Comment/Source**
	Pasteurisation (20 min, 90°C, pH 4)	Yes	EFSA (2010, 2014)
	Baking, brewing and boiling (60 min, 100°C, pH 5)	Yes	EFSA (2010, 2014)
	Sterilisation (20 min, 120°C, pH 6)	Yes	EFSA (2010, 2014)

Can a general residue definition be proposed for primary crops?	yes	EFSA, 2014, 2018a
Rotational crop and primary crop metabolism similar?	yes	Although rotational crops were not considered in the present assessment, during the peer review for the renewal of thiophanate-methyl it was concluded that the same RD applies for primary and rotational crops (EFSA, 2018a).
Residue pattern in processed commodities similar to residue pattern in raw commodities?	yes	Yes (EFSA, 2014)
Plant residue definition for monitoring (RD-Mo)	RD-Mo 1: thiophanate methyl RD-Mo 2: carbendazim	
Plant residue definition for risk assessment (RD-RA)	RD-RA 1: thiophanate-methyl; RD-RA 2: carbendazim; RD-RA 3 (tentative): 2-AB, FH-432, DX-105, final expression of the RD pending tox assessment of the metabolites RD-RA 3 not relevant for the present assessment since the uses under consideration are for fruit crops only where the main components of the TRR were identified as thiophanate-methyl and its metabolite carbendazim and considering that the commodities assessed are expected to be consumed as peeled and/or are minor crops	
Methods of analysis for monitoring of residues (analytical technique, matrix groups, LOQs)	Matrices with high water content, high oil content, high acid content and dry matrices: LC-MS/MS (QuEChERS), LOQ 0.01 mg/kg for each compound. Confirmatory method and ILV available (EFSA, 2018a)	

a.i.: active ingredient; DAT: days after treatment; PBI: plant-back interval; HPLC–MS/MS: high-performance liquid chromatography with tandem mass spectrometry; LC–MS/MS: liquid chromatography with tandem mass spectrometry; LOQ: limit of quantification; ILV: independent laboratory validation.

B.2.1.2 | Stability of residues in plants

Plant products (available studies)	Category	Commodity	T (°C)	Stability period		Compounds covered	Comment/ source
				Value	Unit		
	High water content	Apples, cut in half	–18	36	Months	Thiophanate-methyl	EFSA (2012)
		Tomatoes	–18	30	Months	Carbendazim	EFSA (2010)
	High oil content	Rapeseeds, intact	–18	12	Months	Thiophanate-methyl Carbendazim	EFSA (2018)
		Rapeseeds, homogenised	–18	1	Month	Thiophanate-methyl	EFSA (2018)
		Rapeseeds, homogenised	–18	3	Months	Carbendazim	EFSA (2018)
	High protein content	Dry peas, intact	–18	12	Months	Thiophanate-methyl Carbendazim	EFSA (2018)
		Dry peas, homogenised	–18	3	Months	Thiophanate-methyl Carbendazim	EFSA (2018)
	High starch content	Wheat, intact	–18	12	Months	Thiophanate-methyl Carbendazim	EFSA (2018)
		Wheat, homogenised	–18	2	Weeks	Thiophanate-methyl	EFSA (2018)
		Wheat, homogenised	–18	3	Months	Carbendazim	EFSA (2018)
	High acid content	Grapes, intact	–18	12	Months	Thiophanate-methyl Carbendazim	EFSA (2018)
		Grapes, homogenised	–18	<10	Days	Thiophanate-methyl	EFSA (2018)
		Grapes, homogenised	–18	1	Month	Carbendazim	EFSA (2018)
		Strawberries, Intact	–18	9	Months	Thiophanate-methyl	EFSA (2018)
		Strawberries, Intact	–18	12	Months	Carbendazim	EFSA (2018)
	Processed commodities	Soyabeans, oil	–18	18	Months	Carbendazim	EFSA (2010)

B.2.2 | Magnitude of residues in plants

B.2.2.1 | Summary of residues data from the supervised residue trials performed with thiophanate methyl – Primary crops

Commodity	Region/indoor[a]	Residue levels observed in the supervised residue trials (mg/kg)	Comments/source	Calculated MRL (mg/kg)	HR[b] (mg/kg)	STMR[c] (mg/kg)
RD-Mo 1: thiophanate methyl **RD-RA 1:** thiophanate methyl						
Citrus fruits	Import	**Oranges:** 1.4; 1.7; 2.6; 2.9 **Mandarins:** 2.0; 2.4; 3.1; 4.3	Combined data set on oranges and mandarins compliant with GAP for post-harvest treatment of citrus fruits (EFSA, 2014) MRL based on mean + 4 SD (6.21)	7 (tentative)[d]	4.3	2.5
Mangoes	Import	< 0.1; 0.2; 0.2; 0.6	Trials on mangoes compliant with GAP. Residues determined as sum of thiophanate-methyl and carbendazim, expressed as thiophanate-methyl, deemed acceptable for a minor crop (EFSA, 2014) MRL_{OECD} = 1.16	1.5 (tentative)[d]	0.6	0.2
Papaya	Import	0.3; 0.39; 0.42; 0.59	Trials on papaya compliant with GAP (EFSA, 2014) MRL_{OECD} = 1.28	1.5 (tentative)[d]	0.59	0.41
Okra, lady's fingers	Import	0.03; 0.07; 0.15; 0.23; 0.26; 0.48	Trials on okra compliant with GAP. Residues determined as sum of thiophanate-methyl and carbendazim, expressed as thiophanate-methyl, deemed acceptable for a minor crop (EFSA, 2014) MRL_{OECD} = 0.85	0.9 (tentative)[d]	0.48	0.19
RD-Mo 2: carbendazim **RD-RA 2:** carbendazim						
Citrus fruits	Import	**Oranges:** 0.06; 0.06; 0.08; 0.09 **Mandarins:** 0.08; 0.08; 0.08; 0.09	Combined data set on oranges and mandarins compliant with GAP for post-harvest treatment of citrus fruits (EFSA, 2014) MRL based on mean + 4 SD (0.124)	0.2 (tentative)[d]	0.09	0.08
Mangoes	Import	< 0.05; 0.12; 0.12; 0.35	Trials on mangoes compliant with GAP. Residues determined as sum of thiophanate-methyl and carbendazim, expressed as carbendazim deemed acceptable for a minor crop (EFSA, 2014) MRL_{OECD} = 0.68	0.7 (tentative)[d]	0.35	0.12
Papaya	Import	0.03; 0.07; 0.08; 0.08	Trials on papaya compliant with GAP (EFSA, 2014) MRL_{OECD} = 0.20	0.2 (tentative)[d]	0.08	0.08
Okra, lady's fingers	Import	0.05; 0.13; 0.27; 0.42; 0.46; 0.87	Trials on okra compliant with GAP. Residues determined as sum of thiophanate-methyl and carbendazim, expressed as carbendazim deemed acceptable for a minor crop (EFSA, 2014) MRL_{OECD} = 1.54	1.5 (tentative)[d]	0.87	0.35

Abbreviations: GAP, Good Agricultural Practice; Mo: residue levels expressed according to the monitoring residue definition; MRL, maximum residue level; OECD, Organisation for Economic Co-operation and Development; RA: residue levels expressed according to risk assessment residue definition.

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

[a]NEU: Outdoor trials conducted in northern Europe, SEU: Outdoor trials conducted in southern Europe, Indoor: indoor EU trials or Country code: if non-EU trials.

[b]Highest residue. The highest residue for risk assessment (RA) refers to the whole commodity and not to the edible portion.

[c]Supervised trials median residue. The median residue for risk assessment (RA) refers to the whole commodity and not to the edible portion.

[d]Although a sufficient number of data is available, MRL proposal is tentative because it was not reported whether or not the analysed samples used to derive MRL and risk assessment values were homogenised prior storage (see also body text).

B.2.2.2 | Summary of residues data from the supervised residue trials performed with carbendazim – Primary crops

Commodity	Region/ indoor[a]	Residue levels observed in the supervised residue trials (mg/kg)	Comments/source	Calculated MRL (mg/kg)	HR[b] (mg/kg)	STMR[c] (mg/kg)
RD-Mo 2: carbendazim **RD-RA 2:** carbendazim						
Lemons Lime Mandarins	Import (SA)	0.05; 0.15; 0.15; 0.20; 0.22; 0.24; 0.24; 0.24; 0.27; 0.27; 0.30; 0.31; 0.34; 0.35; 0.44; 0.60	Combined data set on oranges (8) and lemons (8). Extrapolation to mandarins and limes possible $MRL_{OECD} = 0.82$	0.9 (tentative)[d]	0.60	0.26

Abbreviations: GAP, Good Agricultural Practice; Mo: residue levels expressed according to the monitoring residue definition; MRL, maximum residue level; OECD, Organisation for Economic Co-operation and Development; RA: residue levels expressed according to risk assessment residue definition.

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

[a]NEU: Outdoor trials conducted in northern Europe, SEU: Outdoor trials conducted in southern Europe, Indoor: indoor EU trials or Country code: if non-EU trials.

[b]Highest residue. The highest residue for risk assessment (RA) refers to the whole commodity and not to the edible portion.

[c]Supervised trials median residue. The median residue for risk assessment (RA) refers to the whole commodity and not to the edible portion.

[d]Although a sufficient number of data is available, MRL proposal is tentative because it was not reported whether or not the analysed samples used to derive MRL and risk assessment values were homogenised prior storage (see also body text).

B.2.2.3 | Residues in rotational crops

Residues in rotational and succeeding crops expected based on confined rotational crop study?	not triggered	Only import tolerances were considered in the present assessment.
Residues in rotational and succeeding crops expected based on field rotational crop study?	not triggered	Only import tolerances were considered in the present assessment.

B.2.2.4 | Processing factors

Processed commodity	Number of valid studies[a]	Processing factor (PF)		Comment/source
		Individual values	Median PF	
RD Mo 1: thiophanate-methyl **RD RA 1:** thiophanate-methyl				
Mangoes, peeled	4	0.17; 0.29; 0.5; 0.6	0.40	Processing factors based on the sum of thiophanate-methyl and carbendazim (EFSA, 2009, 2014)
Citrus fruits, peeled	10	Not available	0.11	EFSA (2009, 2014)
Orange, juice	4	4 × 0.03	0.03	1 balance study and 3 follow-up studies (EFSA, 2014)
Citrus fruits, dry pomace	4	0.75; 1.49; 1.53; 1.66	1.51	1 balance study and 3 follow up studies (EFSA, 2014)
Orange, marmalade	4	0.23; 0.26; 0.74; 0.93	0.50	1 balance study and 3 follow up studies (EFSA, 2014)
Citrus fruits, wet pomace	1	1.23	1.23	Tentative[b] 1 balance study (EFSA, 2014)
RD Mo 2: carbendazim **RD RA 2:** carbendazim				
Mangoes, peeled	4	0.17; 0.29; 0.5; 0.6	0.40	Processing factors based on the sum of thiophanate-methyl and carbendazim, expressed as thiophanate-methyl (EFSA, 2009, 2014)
Citrus fruits, peeled	16	0.53; 0.50; 0.35; 0.43; 0.50; 0.30; 2 × 0.40; 0.80; 0.33; 0.63; 0.60; 0.45; 0.46; 0.47; 0.63	0.47	EFSA (2009, 2014)
Orange, juice	4	3 × < 0.04; < 0.05	< 0.04	1 balance study and 3 follow-up studies (EFSA, 2014)
Citrus fruits, dry pomace	4	24.6; 25.2; 26.3; 43.3	25.7	1 balance study and 3 follow-up studies (EFSA, 2014)
Orange, marmalade	4	0.4; 0.41; 0.62; 0.63	0.51	1 balance study and 3 follow-up studies (EFSA, 2014)
Citrus fruits, wet pomace	1	1.28	1.28	Tentative[b] 1 balance study (EFSA, 2014)

Abbreviations: PF, Processing factor (=Residue level in processed commodity expressed according to RD-Mo/Residue level in raw commodity expressed according to RD-Mo).

[a]Studies with residues in the RAC at or close to the LOQ were disregarded (unless concentration may occur)

[b]A tentative PF is derived based on a limited data set.

B.3 | RESIDUES IN LIVESTOCK

Relevant groups (subgroups)	Dietary burden expressed in				Most critical subgroup[a]	Most critical commodity[b]	Trigger exceeded (Y/N)	Comments
	mg/kg bw per day		mg/kg DM					
	Median	Maximum	Median	Maximum				
Thiophanate-methyl								
Cattle (all)	0.032	0.032	0.83	0.83	Dairy cattle	Grapefruits, dried pulp	Y	–
Cattle (dairy only)	0.032	0.032	0.83	0.83	Dairy cattle	Grapefruits, dried pulp	Y	–
Sheep (all & ewe only)	–	–	–	–	–	–	N	–
Swine (all)	0.014	0.014	0.62	0.62	Swine (breeding)	Grapefruits, dried pulp	Y	–
Poultry (all & layer only)	–	–	–	–	–	–	N	–

Relevant groups (subgroups)	Dietary burden expressed in mg/kg bw per day Median	Maximum	mg/kg DM Median	Maximum	Most critical subgroup[a]	Most critical commodity[b]	Trigger exceeded (Y/N)	Comments
Carbendazim								
Cattle (all)	0.055	0.055	1.44	1.44	Dairy cattle	Lemons, dried pulp	Y	Based on the uses of both thiophanate-methyl and carbendazim
Cattle (dairy only)	0.055	0.055	1.44	1.44	Dairy cattle	Lemons, dried pulp	Y	Based on the uses of both thiophanate-methyl and carbendazim
Sheep (all & ewe only)	–	–	–	–	–	–	N	–
Swine (all)	0.025	0.025	1.08	1.08	Swine (breeding)	Lemons, dried pulp	Y	Based on the uses of both thiophanate-methyl and carbendazim
Poultry (all & layer only)	–	–	–	–	–	–	N	–

[a]When one group of livestock includes several subgroups (e.g. poultry 'all' including broiler, layer and turkey), the result of the most critical subgroup is identified from the maximum dietary burdens expressed as 'mg/kg bw per day'.

[b]The most critical commodity is the major contributor identified from the maximum dietary burden expressed as 'mg/kg bw per day'.

B.3.1 | Nature of residues and methods of analysis in livestock

B.3.1.1 | Metabolism studies, methods of analysis and residue definitions in livestock

Livestock (available studies)	Animal	Dose (mg/kg bw/d)	Duration (days)	Comment/source
	Thiophanate-methyl			
	Laying hen	2.9–3.5	10	^{14}C-phenyl ring label, hens (EFSA, 2014, 2018)
	Lactating ruminants	1.15–1.19	5	^{14}C-phenyl ring, goat (EFSA, 2014, 2018)
	Pig	–	–	Not available and not required since the metabolism in ruminants and rat is similar (EFSA, 2014)
	Carbendazim			
	Laying hen	0.37 8.8[a]	6	[2-^{14}C]-carbendazim, hens (EFSA, 2010, 2014)
	Lactating ruminants	2.1[b] 1.8[c]	5 30	[2-^{14}C]-carbendazim, cow (EFSA, 2010, 2014) ^{14}C-phenyl, goat (EFSA, 2010, 2014)
	Pig	–	–	Not available and not required since the metabolism in ruminants and rat is similar (EFSA, 2014)

[a]In the study summary, the administrated dose was only expressed in mg/kg feed as received (5 and 120 mg/ kg feed as received). Based on this information, EFSA derived theoretical administrated doses, assuming a body weight of 1.9 kg, a daily intake of 0.12 kg of feed (dry matter basis) and feed composed of maize grain and pulses.

[b]In the study summary, the administrated dose was only expressed in mg/kg feed as received (50 mg/ kg feed as received). Based on this information, EFSA derived a theoretical administrated dose, assuming a body weight of 550 kg, a daily intake of 20 kg of feed (dry matter basis) and feed only composed of hay.

[c]In the study summary, the administrated dose was only expressed in mg/animal per day (73 mg/animal/day). Based on this information, EFSA derived a theoretical administrated dose, assuming a body weight of 40 kg.

Time needed to reach a plateau concentration in milk and eggs (days)	Milk: 4 days (study with thiophanate-methyl); 1 day (study with carbendazim)	EFSA, 2010, 2014, 2018a
	Eggs: 4 days (eggs white); 8 days (eggs yolk) (study with thiophanate methyl); 14 days (study with carbendazim)	EFSA, 2010, 2014, 2018a
Metabolism in rat and ruminant similar	Yes	EFSA, 2014
Can a general residue definition be proposed for animals?	No	EFSA, 2014, 2018a
Animal residue definition for monitoring (RD-Mo)	RD-Mo 1 (cattle and swine tissues, milk): thiophanate-methyl RD-Mo 2 (cattle and swine tissues, milk): sum of carbendazim and 5-hydroxy-carbendazim, expressed as carbendazim (EFSA 2010, 2014)	
Animal residue definition for risk assessment (RD-RA)	RD-RA 1 (cattle and swine tissues, milk): thiophanate-methyl RD-RA 2 (cattle and swine tissues): sum of carbendazim and 5-hydroxy-carbendazim, expressed as carbendazim (EFSA, 2014) RD-RA 3 (milk): sum of carbendazim, 5-hydroxy-carbendazim and 4-hydroxy-carbendazim, expressed as carbendazim (EFSA, 2014)	
Fat soluble residues	No	EFSA, 2014
Methods of analysis for monitoring of residues (analytical technique, matrix groups, LOQs)	Milk, muscle, fat, liver, kidney: LC-MS/MS (QuEChERS) 0.01 mg/kg thiophanate-methyl 0.01 mg/kg carbendazim 0.01 mg/kg 5-hydroxy-carbendazim 0.01 mg/kg 5-hydroxy-carbendazim-S Confirmatory method and ILV available (EFSA, 2018)	

B.3.1.2 | Stability of residues in livestock

Animal products (available studies)	Animal	Commodity	T (°C)	Stability period Value	Unit	Compounds covered	Comment/Source
	Bovine	Muscle	–20 ± 10	8	Months	Thiophanate-methyl Carbendazim	No info on the storage stability of metabolites 5-OH-MBC and 5-OH-MBC-S (EFSA, 2018a)
	Bovine	Liver	–20 ± 10	7	Months	Carbendazim 5-OH-MBC	No info on the storage stability of thiophanate-methyl and 5-OH-MBC-S (EFSA, 2018a)
	Bovine	Milk	–20 ± 10	8	Months	Carbendazim 5-OH-MBC-S	No info on the storage stability of thiophanate-methyl, 4-OH-MBC and 5-OH-MBC (EFSA, 2018a)
	Poultry	Muscle	–25 ca.	8	Months	Carbendazim 5-OH-MBC	No info on the storage stability of thiophanate-methyl and 5-OH-MBC-S (EFSA, 2018a)
	Poultry	Liver	–25 ca.	8	Months	Thiophanate-methyl 5-OH-MBC	No information on the storage stability of carbendazim and 5-OH-MBC-S (EFSA, 2018a)
	Poultry	Eggs	–25 ca.	10	Months	Carbendazim 5-OH-MBC	No info on the storage stability of 5-OH-MBC-S (EFSA, 2018a)
	Poultry	Eggs	–25 ca.	9	Months	Thiophanate-methyl	

B.3.2 | Magnitude of residues in livestock

B.3.2.1 | Summary of the residue data from livestock feeding studies

Animal commodity	Residues at the closest feeding level (mg/kg) Mean	Highest	Estimated value at 1N $STMR_{Mo}$[a] (mg/kg)	HR_{Mo}[b] (mg/kg)	MRL proposal (mg/kg)	CF[c]
Thiophanate-methyl						
Cattle (all) – Closest feeding level (2.6 mg/kg bw; 81.25N rate)[d]						
Muscle	n.r.	< 0.05	< 0.01	< 0.01	0.01* (tentative)[e]	1
Fat	n.r.	< 0.05	< 0.01	< 0.01	0.01* (tentative)[e]	1
Liver	n.r.	0.20	< 0.01	< 0.01	0.01* (tentative)[e]	1
Kidney	n.r.	0.38	< 0.01	< 0.01	0.01* (tentative)[e]	1
Cattle (dairy only) – Closest feeding level (2.6 mg/kg bw; 81.25N rate)[d]						
Milk[f]	n.r.	0.23	< 0.01	< 0.01	0.01* (tentative)[e]	1
Sheep (all)/Sheep (ewe only) – No need to set MRLs since sheep are not expected to be exposed to significant levels of thiophanate residues						
Swine (all)[g] – Closest feeding level (2.6 mg/kg bw; 186N rate)[d]						
Muscle	n.r.	< 0.05	< 0.01	< 0.01	0.01* (tentative)[e]	1
Fat	n.r.	< 0.05	< 0.01	< 0.01	0.01* (tentative)[e]	1
Liver	n.r.	0.20	< 0.01	< 0.01	0.01* (tentative)[e]	1
Kidney	n.r.	0.38	< 0.01	< 0.01	0.01* (tentative)[e]	1
Poultry (all)/Poultry (layer only) – No need to set MRLs since poultry are not expected to be exposed to significant levels of thiophanate residues						
Carbendazim						
Cattle (all) – Closest feeding level (0.09 mg/kg bw; 1.64N rate)[d]						
Muscle	< 0.02	< 0.02	< 0.02	< 0.02	0.02* (tentative)[i]	1
Fat	0.03[h]	0.03[h]	< 0.02	<0.02	0.02* (tentative)[i]	1
Liver	< 0.02	< 0.02	< 0.02	< 0.02	0.02* (tentative)[i]	1
Kidney	< 0.02	< 0.02	< 0.02	< 0.02	0.02* (tentative)[i]	1
Cattle (dairy only) – Closest feeding level (0.09 mg/kg bw; 1.64N rate)[d]						
Milk[f]	< 0.02	n.a.	< 0.02	< 0.02	0.02* (tentative)[i]	1
Sheep (all)/Sheep (ewe only) – No need to set MRLs since sheep are not expected to be exposed to significant levels of carbendazim residues						

(Continues)

(Continued)

Animal commodity	Residues at the closest feeding level (mg/kg)		Estimated value at 1N		MRL proposal (mg/kg)	CF[c]
	Mean	Highest	$STMR_{Mo}$[a] (mg/kg)	HR_{Mo}[b] (mg/kg)		
Swine (all)[g] – Closest feeding level (0.09 mg/kg bw; 3.6N rate)[d]						
Muscle	< 0.02	< 0.02	< 0.02	< 0.02	0.02* (tentative)[i]	1
Fat	0.03	0.03	< 0.02	< 0.02	0.02* (tentative)[i]	1
Liver	< 0.02	< 0.02	< 0.02	< 0.02	0.02* (tentative)[i]	1
Kidney	< 0.02	< 0.02	< 0.02	< 0.02	0.02* (tentative)[i]	1
Poultry (all)/Poultry (layer only) – No need to set MRLs since poultry are not expected to be exposed to significant levels of carbendazim residues						

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

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

[a]Median residues expressed according to the residue definition for monitoring (sum of carbendazim and 5-hydroxy-carbendazim, expressed as carbendazim), recalculated at the 1N rate for the median dietary burden.

[b]Highest residues covering the sum of all relevant compounds and expressed as parent (thiophanate-methyl) or highest residues expressed according to the residue definition for monitoring (sum of carbendazim and 5-hydroxy-carbendazim, expressed as carbendazim) recalculated at the 1N rate for the maximum dietary burden.

[c]Conversion factor to recalculate residues according to the residue definition for monitoring to the residue definition for risk assessment.

[d]Closest feeding level and N dose rate related to the maximum dietary burden.

[e]Pending confirmation that samples from trials on plants were not homogenised, the derived MRLs should be considered tentative only.

[f]For milk, mean was derived from samplings performed from day 1 to day 28 (daily mean of 3 cows).

[g]Since extrapolation from cattle to other ruminants and swine is acceptable, results of the livestock feeding study on ruminants were relied upon to derive the MRL and risk assessment values in swine.

[h]5-hydroxy-carbendazim was quantified in the renal fat of one animal at 0.02 mg/kg. Nevertheless, considering that no residues of this compound were detected in renal fat from the two higher dose groups, this value is considered to be an outlier and is reported only for completeness.

[i]Pending confirmation that samples from trials on plants were not homogenised, information on the storage conditions of the samples from the livestock feeding studies and storage stability data for 4-hydroxy-carbendazim (metabolite relevant for the risk assessment of carbendazim in milk), the derived MRLs should be considered tentative only.

B.4 | Consumer risk assessment

ARfD	**Thiophanate-methyl:** 0.02 mg/kg bw **Carbendazim:** 0.02 mg/kg bw
Highest IESTI, according to EFSA PRIMo (rev.3.1)	**Scenario EU1 (without considering risk mitigation measures)** **Thiophanate-methyl:** Oranges: 314 % of ARfD Grapefruits: 186 % of ARfD Mandarins: 140 % of ARfD Papaya: 106 % of ARfD Lemons: 81 % of ARfD Mangoes: 80 % of ARfD Limes: 48 % of ARfD Milk, cattle: 6 % of the ARfD Other products of animal origin from cattle and swine: <1 % of the ARfD **Carbendazim:** Mandarins: 84 % of ARfD Mangoes: 63 % of ARfD Lemons: 48 % of ARfD Limes: 28 % of ARfD Oranges: 28 % of ARfD Papaya: 27 % of ARfD Grapefruits: 17 % of ARfD Milk, cattle: 12 % of the ARfD Other products of animal origin from cattle and swine: <1 % of the ARfD **Combined:** Oranges: 342 % of ARfD Grapefruits: 203 % of ARfD Mandarins: 224 % of ARfD Mangoes: 143 % of ARfD Papaya: 133 % of ARfD Lemons: 129 % of ARfD Limes: 76 % of ARfD Milk, cattle: 18 % of the ARfD Other products of animal origin from cattle and swine: <2 % of the ARfD **Scenario EU2 (with risk mitigation measures)** **Thiophanate-methyl:** Limes: 48 % of the ARfD Milk, cattle: 6 % of the ARfD Other products of animal origin from cattle and swine: <1 % of the ARfD **Carbendazim:** Mandarins: 84 % of ARfD Lemons: 48 % of ARfD Limes: 28 % of ARfD Milk, cattle: 12 % of the ARfD Other products of animal origin from cattle and swine: <1 % of the ARfD **Combined:** Mandarins: 84 % of ARfD Limes: 76 % of ARfD Lemons: 48 % of ARfD

	Milk, cattle: 18 % of the ARfD Other products of animal origin from cattle and swine: <2 % of the ARfD **Scenario EU3 (with risk mitigation measures)** **Thiophanate-methyl:** Lemons: 81 % of ARfD Limes: 48 % of the ARfD Milk, cattle: 6 % of the ARfD Other products of animal origin from cattle and swine: <1 % of the ARfD **Carbendazim:** Mandarins: 84 % of ARfD Limes: 28 % of the ARfD Milk, cattle: 12 % of the ARfD Lemons: 7 % of the ARfD Other products of animal origin from cattle and swine: <1 % of the ARfD **Combined:** Lemons: 88 % of ARfD Mandarins: 84 % of ARfD Limes: 76 % of ARfD Milk, cattle: 18 % of the ARfD Other products of animal origin from cattle and swine: <2 % of the ARfD
NESTI (% ARfD)	Not assessed in this review.
Assumptions made for the calculations	**Scenario EU1 (without considering risk mitigation measures)** The calculation is based on the highest residue levels expected in raw agricultural commodities, except for citrus fruits and mango where the peeling factors were also applied. Considering the effect of processing on the nature of the residue observed in the hydrolysis study on thiophanate-methyl, values derived from residue trials have been adjusted assuming that, following boiling/brewing/baking, thiophanate-methyl levels would be reduced by 15 % and converted into carbendazim. Additionally, thiophanate-methyl residues were expressed as carbendazim considering that the ratio between the two molecular weights is 0.56. The effect of boiling/brewing/baking has been considered relevant for mangoes and papaya (that can be consumed as jam and marmalades) and for okra that are usually consumed cooked. For the commodities of animal origin, considering that no residues of thiophanate-methyl and carbendazim are expected in the raw commodities, the effect of processing has not been deemed relevant. **Scenario EU2 (with risk mitigation measures)** The highest residue levels from the uses of thiophanate-methyl on oranges, grapefruits, mandarins, lemons, mangoes and papaya were disregarded (assuming that these GAPs will be withdrawn) and the highest residue levels from the uses of carbendazim on mandarins and lemons were considered to derive a fall-back MRL for these crops.

	Scenario EU3 (with risk mitigation measures) The highest residue levels from the uses of thiophanate-methyl on oranges, grapefruits, mandarins, mangoes and papaya and from the use of carbendazim on lemons were disregarded (assuming that these GAPs will be withdrawn) and the highest residue levels from the use of carbendazim on mandarins and from the use of thiophanate-methyl on lemons were considered to derive fall-back MRLs for these crops. **In all scenario, CXLs could not be assessed since the residue definitions proposed by the JMPR are different.**

ARfD: acute reference dose; bw: body weight; NESTI: national estimated short-term intake; PRIMo: (EFSA) Pesticide Residues Intake Model; WHO: World Health Organization; IESTI: international estimated short-term intake.

ADI	**Thiophanate-methyl:** 0.02 mg/kg bw per day **Carbendazim:** 0.02 mg/kg bw per day
TMDI according to EFSA PRIMo	Not assessed in this review.
NTMDI, according to (to be specified)	Not assessed in this review.
Highest IEDI, according to EFSA PRIMo (rev.3.1)	**Scenario EU1 (without considering risk mitigation measures)** **Thiophanate-methyl:** 8 % ADI (DE child) **Carbendazim:** 7 % ADI (NL toddler) **Scenario EU2 (with risk mitigation measures)** **Thiophanate-methyl:** 3 % ADI (NL toddler) 2 % ADI (UK infant) 2 % ADI (FR toddler) **Carbendazim:** 7 % ADI (NL toddler) 4 % ADI (UK infant) 4 % ADI (FR toddler) **Combined:** 10 % ADI (NL toddler) 6 % ADI (UK infant) 6 % ADI (FR toddler) **Scenario EU3 (with risk mitigation measures)** **Thiophanate-methyl:** 3 % ADI (NL toddler) 2 % ADI (UK infant) 2 % ADI (FR toddler) **Carbendazim:** 6 % ADI (NL toddler) 4 % ADI (UK infant) 4 % ADI (FR toddler)

	Combined: 9 % ADI (NL toddler) 6 % ADI (UK infant) 6 % ADI (FR toddler)
NEDI (% ADI)	Not assessed in this review.
Assumptions made for the calculations	**Scenario EU1 (without considering risk mitigation measures)** The calculation is based on the median residue levels derived for raw agricultural commodities, except for citrus fruits and mango where the peeling factors were also applied. Considering the effect of processing on the nature of the residue observed in the hydrolysis study on thiophanate-methyl, values derived from residue trials have been adjusted assuming that, following boiling/brewing/baking, thiophanate-methyl levels would be reduced by 15 % and converted into carbendazim. Additionally, thiophanate-methyl residues were expressed as carbendazim considering that the ratio between the two molecular weights is 0.56. The effect of boiling/brewing/baking has been considered relevant for mangoes and papaya (that can be consumed as jam and marmalades) and for okra that are usually consumed cooked. For the commodities of animal origin, considering that no residues of thiophanate-methyl and carbendazim are expected in the raw commodities, the effect of processing has not been deemed relevant. The contributions of commodities where no GAP was reported were not included in the calculation. **Scenario EU2 (with risk mitigation measures):** The median residue levels from the uses of thiophanate-methyl on oranges, grapefruits, mandarins, lemons, mangoes and papaya were disregarded (assuming that these GAPs will be withdrawn) and the median residue levels from the uses of carbendazim on mandarins and lemons were considered to derive a fall-back MRL for these crops. **Scenario EU3 (with risk mitigation measures)** The median residue levels from the uses of thiophanate-methyl on oranges, grapefruits, mandarins, mangoes and papaya and from the use of carbendazim on lemons were disregarded (assuming that these GAPs will be withdrawn) and the median residue levels from the use of carbendazim on mandarins and from the use of thiophanate-methyl on lemons were considered to derive fall-back MRLs for these crops. **In all scenario, CXLs could not be assessed since the residue definitions proposed by the JMPR are different.**

ADI: acceptable daily intake; bw: body weight; NEDI: national estimated daily intake; PRIMo: (EFSA) Pesticide Residues Intake Model; WHO: World Health Organization; TMDI: theoretical maximum daily intake; NTMDI: national theoretical maximum daily intake.

cConsumer exposure assessment through drinking water resulting from groundwater metabolite(s) according to SANCO/221/2000 rev.10 Final (25/2/2003)

Metabolite(s)	Not assessed in this review.
ADI (mg/kg bw per day)	Not assessed in this review.
Intake of groundwater metabolites (% ADI)	Not assessed in this review.

B.5 | PROPOSED MRLS

Code number	Commodity	Existing EU MRL (mg/kg)	Existing CXL (mg/kg)	Outcome of the review	
				MRL (mg/kg)	Comment
Enforcement residue definition: thiophanate-methyl					
110010	Grapefruits	6	–	–	Further consideration needed[a] Data gap #1
110020	Oranges	6	1	–	Further consideration needed[b] Data gap #1
110030	Lemons	6	–	Option 1[c]: –	Further consideration needed[d] Data gap #1
				Option 2[e]: 7	Further consideration needed[d] Data gap #1
110040	Limes	6	–	7	Further consideration needed[d] Data gap #1
110050	Mandarins	6	–	–	Further consideration needed[a] Data gap #1
163030	Mangoes	1	5	–	Further consideration needed[b] Data gap #1
163040	Papayas	1	–	–	Further consideration needed[a] Data gap #1
231040	Okra/lady's fingers	1	–	0.9	Further consideration needed[d] Data gap #1
Enforcement residue definition (existing): thiophanate-methyl and carbendazim, expressed as carbendazim **Enforcement residue definition (proposed):** thiophanate-methyl					
1011010	Swine muscle	0.05*	–	0.01*	Further consideration needed[d] Data gaps #1
1011020	Swine fat tissue	0.05*	–	0.01*	Further consideration needed[d] Data gaps #1
1011030	Swine liver	0.05*	0.05*	0.01*	Further consideration needed[f] Data gaps #1
1011040	Swine kidney	0.05*	0.05*	0.01*	Further consideration needed[f] Data gaps #1
1012010	Bovine muscle	0.05*	0.05*	0.01*	Further consideration needed[f] Data gaps #1
1012020	Bovine fat tissue	0.05*	–	0.01*	Further consideration needed[d] Data gaps #1
1012030	Bovine liver	0.05*	0.05*	0.01*	Further consideration needed[f] Data gaps #1
1012040	Bovine kidney	0.05*	0.05*	0.01*	Further consideration needed[f] Data gaps #1
1015010	Equine muscle	0.05*	–	0.01*	Further consideration needed[d] Data gaps #1
1015020	Equine fat tissue	0.05*	–	0.01*	Further consideration needed[d] Data gaps #1
1015030	Equine liver	0.05*	0.05*	0.01*	Further consideration needed[f] Data gaps #1
1015040	Equine kidney	0.05*	0.05*	0.01*	Further consideration needed[f] Data gaps #1
1020010	Cattle milk	0.05*	0.05*	0.01*	Further consideration needed[f] Data gaps #1

(Continues)

(Continued)

Code number	Commodity	Existing EU MRL (mg/kg)	Existing CXL (mg/kg)	Outcome of the review	
				MRL (mg/kg)	Comment
1020040	Horse milk	0.05*	0.05*	0.01*	Further consideration needed[f] Data gaps #1
Enforcement residue definition (existing): sum of benomyl and carbendazim, expressed as carbendazim **Enforcement residue definition (proposed):** carbendazim					
110010	Grapefruits	0.2	–	–	Further consideration needed[a] Data gap #1
110020	Oranges	0.2	1	–	Further consideration needed[b] Data gap #1
110030	Lemons	0.7	–	Option 1[(c)]: 0.9	Further consideration needed[d] Data gap #1
				Option 2[(e)]: 0.2	Further consideration needed[d] Data gap #1
110040	Limes	0.7	–	0.9	Further consideration needed[d] Data gap #1
110050	Mandarins	0.7	–	0.9	Further consideration needed[d] Data gap #1
163030	Mangoes	0.5	5	–	Further consideration needed[b] Data gap #1
163040	Papayas	0.2	–	–	Further consideration needed[a] Data gap #1
231040	Okra/lady's fingers	2	–	1.5	Further consideration needed[d] Data gap #1
Enforcement residue definition (existing): carbendazim and thiophanate-methyl, expressed as carbendazim **Enforcement residue definition (proposed):** sum of carbendazim and 5-hydroxy-carbendazim, expressed as carbendazim					
1011010	Swine muscle	0.05*	–	0.02*	Further consideration needed[d] Data gaps #1,2
1011020	Swine fat tissue	0.05*	–	0.02*	Further consideration needed[d] Data gaps #1,2
1011030	Swine liver	0.05*	0.05*	0.02*	Further consideration needed[f] Data gaps #1,2
1011040	Swine kidney	0.05*	0.05*	0.02*	Further consideration needed[f] Data gaps #1,2
1012010	Bovine muscle	0.05*	0.05*	0.02*	Further consideration needed[f] Data gaps #1,2
1012020	Bovine fat tissue	0.05*	–	0.02*	Further consideration needed[d] Data gaps #1,2
1012030	Bovine liver	0.05*	0.05*	0.02*	Further consideration needed[f] Data gaps #1,2
1012040	Bovine kidney	0.05*	0.05*	0.02*	Further consideration needed[f] Data gaps #1,2
1015010	Equine muscle	0.05*	–	0.02*	Further consideration needed[d] Data gaps #1,2
1015020	Equine fat tissue	0.05*	–	0.02*	Further consideration needed[d] Data gaps #1,2
1015030	Equine liver	0.05*	0.05*	0.02*	Further consideration needed[f] Data gaps #1,2
1015040	Equine kidney	0.05*	0.05*	0.02*	Further consideration needed[f] Data gaps #1,2
1020010	Cattle milk	0.05*	0.05*	0.02*	Further consideration needed[f] Data gaps #1,2,3
1020040	Horse milk	0.05*	0.05*	0.02*	Further consideration needed[f] Data gaps #1,2,3
–	Other commodities of plant and/or animal origin	See Reg. 559/2011	–	–	Further consideration needed[g]

(Continued)

Code number	Commodity	Existing EU MRL (mg/kg)	Existing CXL (mg/kg)	Outcome of the review	
				MRL (mg/kg)	Comment
Enforcement residue definition (proposed): benomyl					
–	Commodities of plant and/or animal origin	–	–	–	Further consideration needed[g]

Abbreviations: CXL, codex maximum residue limit; MRL, maximum residue level.

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

[F]The residue definition is fat soluble.

[a]GAP evaluated at EU level is not fully supported by data and a risk to consumers cannot be excluded; no CXL is available. Either a specific LOQ or the default MRL of 0.01 mg/kg may be considered (combination E-I in Appendix I).

[b]GAP evaluated at EU level is not fully supported by data and a risk to consumers cannot be excluded; CXL is not compatible with EU residue definitions. Either a specific LOQ or the default MRL of 0.01 mg/kg may be considered (combination E-II in Appendix I).

[c]Option 1: MRL based on the authorised use for carbendazim, assuming that the authorised use of thiophanate-methyl will be withdrawn.

[d]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; no CXL is available (combination F-I in Appendix I). It is noted that carbendazim is classified as toxic for reproduction category 1B in accordance with Regulation (EC) No 1272/2008.

[f]Option 2: MRL based on the authorised use for thiophanate-methyl, assuming that the authorised use of carbendazim will be withdrawn.

[g]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; CXL is not compatible with EU residue definitions (combination F-II in Appendix I). It is noted that carbendazim is classified as toxic for reproduction category 1B in accordance with Regulation (EC) No 1272/2008.

[h]There are no relevant authorisations or import tolerances reported at EU level; no CXL is available or CXL is not compatible with EU residue definitions. Either a specific LOQ or the default MRL of 0.01 mg/kg may be considered (combination A-I/II in Appendix I).

APPENDIX C

Pesticide Residue Intake Model (PRIMo)

- PRIMo (Scenario EU1) thiophanate-methyl – without risk mitigation measures

European Food Safety Authority

EFSA PRIMo revision 3.1; 2021/01/06

Thiophanate-methyl

LOQs (mg/kg) range from: 0.01 to: 0.01

Toxicological reference values

ADI (mg/kg bw per day):	0.02	ARfD (mg/kg bw):	0.02
Source of ADI:		Source of ARfD:	
Year of evaluation:		Year of evaluation:	

Input values | Details - chronic risk assessment | Supplementary results - chronic risk assessment | Details - acute risk assessment/children | Details - acute risk assessment/adults

Comments:

Normal mode

Chronic risk assessment: JMPR methodology (IEDI/TMDI)

No of diets exceeding the ADI : ---

	Calculated exposure (% of ADI)	MS Diet	Exposure (µg/kg bw per day)	Highest contributor to MS diet (in % of ADI)	Commodity/ group of commodities	2nd contributor to MS diet (in % of ADI)	Commodity/ group of commodities	3rd contributor to MS diet (in % of ADI)	Commodity/ group of commodities	Exposure resulting from: MRLs set at the LOQ (in % of ADI)	Exposure resulting from: commodities not under assessment (in % of ADI)
TMDI/NEDI/IEDI calculation (based on average food consumption)	8%	DE child	1.54	6%	Oranges	1.0%	Milk: Cattle	0.6%	Mandarins		8%
	7%	NL toddler	1.42	3%	Oranges	3%	Milk: Cattle	0.6%	Mandarins		7%
	6%	FR child 3 15 yr	1.26	5%	Oranges	1%	Milk: Cattle	0.2%	Mandarins		6%
	5%	FR toddler 2 3 yr	0.96	2%	Oranges	1%	Milk: Cattle	1%	Mandarins		5%
	5%	NL child	0.92	2%	Oranges	1%	Milk: Cattle	0.9%	Mandarins		5%
	4%	UK toddler	0.86	3%	Oranges	1%	Milk: Cattle	0.4%	Mandarins		4%
	4%	ES child	0.80	3%	Oranges	0.6%	Milk: Cattle	0.2%	Mandarins		4%
	4%	DE women 14-50 yr	0.78	3%	Oranges	0.6%	Milk: Cattle	0.3%	Lemons		4%
	4%	UK infant	0.77	2%	Milk: Cattle	2%	Oranges	0.1%	Bovine: Muscle/meat		4%
	4%	IE adult	0.71	1%	Oranges	1.0%	Grapefruits	0.7%	Mandarins		4%
	3%	DE general	0.68	2%	Oranges	0.6%	Milk: Cattle	0.3%	Lemons		3%
	3%	GEMS/Food G07	0.62	2%	Oranges	0.3%	Milk: Cattle	0.3%	Mandarins		3%
	3%	SE general	0.56	1%	Oranges	0.6%	Milk: Cattle	0.6%	Mandarins		3%
	3%	GEMS/Food G11	0.55	1%	Oranges	0.5%	Lemons	0.5%	Grapefruits		3%
	3%	GEMS/Food G10	0.52	2%	Oranges	0.3%	Lemons	0.3%	Milk: Cattle		3%
	2%	GEMS/Food G06	0.50	1%	Oranges	0.4%	Mandarins	0.4%	Lemons		2%
	2%	ES adult	0.46	2%	Oranges	0.2%	Milk: Cattle	0.2%	Mandarins		2%
	2%	NL general	0.45	1%	Oranges	0.4%	Milk: Cattle	0.2%	Mandarins		2%
	2%	GEMS/Food G08	0.37	0.6%	Oranges	0.4%	Lemons	0.3%	Mandarins		2%
	2%	GEMS/Food G15	0.36	0.9%	Oranges	0.4%	Milk: Cattle	0.2%	Mandarins		2%
	2%	UK vegetarian	0.32	1%	Oranges	0.2%	Milk: Cattle	0.2%	Grapefruits		2%
	1%	FR infant	0.29	0.8%	Milk: Cattle	0.3%	Oranges	0.2%	Mandarins		1%
	1%	FR adult	0.26	0.8%	Oranges	0.2%	Milk: Cattle	0.1%	Mandarins		1%
	1%	DK child	0.25	0.6%	Milk: Cattle	0.3%	Oranges	0.1%	Mandarins		1%
	1%	RO general	0.25	0.6%	Milk: Cattle	0.4%	Oranges	0.1%	Grapefruits		1%
	1%	UK adult	0.23	0.8%	Oranges	0.1%	Milk: Cattle	0.1%	Grapefruits		1%
	1%	PT general	0.21	0.8%	Oranges	0.1%	Mandarins	0.1%	Lemons		1%
	1%	IT toddler	0.20	0.7%	Oranges	0.3%	Mandarins	0.0%	Lemons		1%
	0.8%	IT adult	0.16	0.5%	Oranges	0.2%	Mandarins	0.0%	Lemons		0.8%
	0.8%	FI adult	0.15	0.6%	Oranges	0.2%	Mandarins	0.0%	Grapefruits		0.8%
	0.8%	FI 3 yr	0.15	0.5%	Mandarins	0.2%	Oranges	0.0%	Grapefruits		0.8%
	0.7%	DK adult	0.15	0.3%	Milk: Cattle	0.2%	Oranges	0.1%	Mandarins		0.7%
	0.7%	FI 6 yr	0.14	0.4%	Mandarins	0.2%	Oranges	0.0%	Grapefruits		0.7%
	0.4%	LT adult	0.08	0.2%	Milk: Cattle	0.1%	Oranges	0.0%	Swine: Muscle/meat		0.4%
	0.3%	IE child	0.07	0.2%	Milk: Cattle	0.1%	Oranges	0.0%	Swine: Muscle/meat		0.3%
	0.2%	PL general	0.03	0.1%	Lemons	0.0%	Mandarins	0.0%	Oranges		0.2%

Conclusion:

The estimated long-term dietary intake (TMDI/NEDI/IEDI) was below the ADI.

The long-term intake of residues of thiophanate-methyl is unlikely to present a public health concern.

DISCLAIMER: Dietary data from the UK were included in PRIMO when the UK was a member of the European Union.

Acute risk assessment /children	Acute risk assessment/adults/general population
Details - acute risk assessment/children	Details - acute risk assessment/adults

The acute risk assessment is based on the ARfD. DISCLAIMER: Dietary data from the UK were included in PRIMO when the UK was a member of the European Union.

The calculation is based on the large portion of the most critical consumer group.

Show results for all crops

Unprocessed commodities

Results for children
No. of commodities for which ARfD/ADI is exceeded (IESTI): 4

IESTI

Highest % of ARfD/ADI	Commodities	MRL/input for RA (mg/kg)	Exposure (µg/kg bw)
314%	Oranges	7/0.47	63
186%	Grapefruits	7/0.47	37
140%	Mandarins	7/0.47	28
106%	Papayas	1.5/0.5	21
81%	Lemons	7/0.47	16
80%	Mangoes	1.5/0.2	16
48%	Limes	7/0.47	9.5
6%	Milk: Cattle	0.01/0.01	1.2
0.6%	Swine: Muscle/meat	0.01/0.01	0.12
0.4%	Bovine: Liver	0.01/0.01	0.08
0.4%	Bovine: Muscle/meat	0.01/0.01	0.07
0.3%	Equine: Muscle/meat	0.01/0.01	0.06
0.2%	Bovine: Kidney	0.01/0.01	0.04
0.1%	Bovine: Fat tissue	0.01/0.01	0.02
0.09%	Swine: Fat tissue	0.01/0.01	0.02

Expand/collapse list

Results for adults
No. of commodities for which ARfD/ADI is exceeded (IESTI): ---

IESTI

Highest % of ARfD/ADI	Commodities	MRL/input for RA (mg/kg)	Exposure (µg/kg bw)
73%	Oranges	7/0.47	15
42%	Mandarins	7/0.47	8.5
42%	Grapefruits	7/0.47	8.5
35%	Papayas	1.5/0.5	7.0
26%	Mangoes	1.5/0.2	5.3
21%	Lemons	7/0.47	4.2
17%	Limes	7/0.47	3.3
2%	Milk: Cattle	0.01/0.01	0.39
0.3%	Bovine: Muscle	0.01/0.01	0.06
0.2%	Swine: Muscle/meat	0.01/0.01	0.05
0.2%	Equine: Muscle/meat	0.01/0.01	0.05
0.2%	Bovine: Liver	0.01/0.01	0.04
0.1%	Swine: Kidney	0.01/0.01	0.02
0.1%	Bovine: Kidney	0.01/0.01	0.02
0.1%	Swine: Fat tissue	0.01/0.01	0.02

Total number of commodities exceeding the ARfD/ADI in children and adult diets (IESTI calculation) 4

Processed commodities

Results for children
No of processed commodities for which ARfD/ADI is exceeded (IESTI): ---

IESTI

Highest % of ARfD/ADI	Processed commodities	MRL/input for RA (mg/kg)	Exposure (µg/kg bw)
38%	Lemons/jam	7/2.5	7.6
20%	Oranges/juice	7/0.08	4.0
1%	Limes/juice	7/2.5	0.23

Expand/collapse list

Results for adults
No of processed commodities for which ARfD/ADI is exceeded (IESTI): 1

IESTI

Highest % of ARfD/ADI	Processed commodities	MRL/input for RA (mg/kg)	Exposure (µg/kg bw)
136%	Grapefruits/juice	7/2.5	27
24%	Lemons/juice	7/2.5	4.7
6%	Oranges/juice	7/0.08	1.1
3%	Okra, lady's fingers/boiled	0.9/0.41	0.66

Conclusion:
The estimated short-term intake (IESTI) exceeded the toxicological reference value for 4 commodities.

For processed commodities, the toxicological reference value was exceeded in one or several cases.

- PRIMo (Scenario EU1) carbendazim – without risk mitigation measures

European Food Safety Authority

EFSA PRIMo revision 3.1; 2021/01/06

Carbendazim

LOQs (mg/kg) range from: 0.02 to: 0.02

Toxicological reference values

ADI (mg/kg bw per day):	0.02	ARfD (mg/kg bw):	0.02
Source of ADI:		Source of ARfD:	
Year of evaluation:		Year of evaluation:	

Input values

Details - chronic risk assessment | Supplementary results - chronic risk assessment

Details - acute risk assessment/children | Details - acute risk assessment/adults

Comments:

Refined calculation mode

Chronic risk assessment: JMPR methodology (IEDI/TMDI)

No of diets exceeding the ADI : ---

TMDI/NEDI/IEDI calculation (based on average food consumption)	Calculated exposure (% of ADI)	MS Diet	Expsoure (µg/kg bw per day)	Highest contributor to MS diet (in % of ADI)	Commodity/ group of commodities	2nd contributor to MS diet (in % of ADI)	Commodity/ group of commodities	3rd contributor to MS diet (in % of ADI)	Commodity/ group of commodities	Exposure resulting from: MRLs set at the LOQ (in % of ADI)	Exposure resulting from: commodities not under assessment (in % of ADI)
	7%	NL toddler	1.40	6%	Milk: Cattle	0.4%	Oranges	0.3%	Mandarins		7%
	4%	UK infant	0.85	4%	Milk: Cattle	0.2%	Oranges	0.1%	Bovine: Muscle/meat		4%
	4%	FR toddler 2 3 yr	0.79	3%	Milk: Cattle	0.5%	Mandarins	0.3%	Oranges		4%
	3%	NL child	0.70	2%	Milk: Cattle	0.4%	Mandarins	0.3%	Oranges		3%
	3%	FR child 3 15 yr	0.67	2%	Milk: Cattle	0.6%	Oranges	0.1%	Bovine: Muscle/meat		3%
	3%	DE child	0.64	2%	Milk: Cattle	0.8%	Oranges	0.2%	Mandarins		3%
	3%	UK toddler	0.55	2%	Milk: Cattle	0.4%	Oranges	0.2%	Mandarins		3%
	2%	SE general	0.43	1%	Milk: Cattle	0.4%	Bovine: Muscle/meat	0.3%	Mandarins		2%
	2%	ES child	0.41	1%	Milk: Cattle	0.4%	Oranges	0.1%	Bovine: Muscle/meat		2%
	2%	DE women 14-50 yr	0.39	1%	Milk: Cattle	0.4%	Oranges	0.1%	Lemons		2%
	2%	FR infant	0.38	2%	Milk: Cattle	0.1%	Mandarins	0.0%	Oranges		2%
	2%	DE general	0.38	1%	Milk: Cattle	0.3%	Oranges	0.1%	Lemons		2%
	2%	DK child	0.35	1%	Milk: Cattle	0.2%	Swine: Muscle/meat	0.1%	Bovine: Muscle/meat		2%
	2%	GEMS/Food G11	0.31	0.8%	Milk: Cattle	0.2%	Lemons	0.1%	Oranges		2%
	1%	RO general	0.29	1%	Milk: Cattle	0.1%	Swine: Muscle/meat	0.1%	Oranges		1%
	1%	GEMS/Food G07	0.28	0.6%	Milk: Cattle	0.3%	Oranges	0.1%	Mandarins		1%
	1%	NL general	0.27	0.8%	Milk: Cattle	0.2%	Oranges	0.1%	Mandarins		1%
	1%	IE adult	0.25	0.4%	Milk: Cattle	0.3%	Mandarins	0.2%	Oranges		1%
	1%	GEMS/Food G08	0.25	0.6%	Milk: Cattle	0.2%	Swine: Muscle/meat	0.2%	Lemons		1%
	1%	GEMS/Food G15	0.25	0.7%	Milk: Cattle	0.1%	Swine: Muscle/meat	0.1%	Oranges		1%
	1%	GEMS/Food G10	0.25	0.5%	Milk: Cattle	0.2%	Oranges	0.1%	Lemons		1%
	1.0%	ES adult	0.20	0.5%	Milk: Cattle	0.2%	Oranges	0.1%	Mandarins		1.0%
	0.9%	GEMS/Food G06	0.19	0.2%	Milk: Cattle	0.2%	Mandarins	0.2%	Oranges		0.9%
	0.8%	DK adult	0.16	0.5%	Milk: Cattle	0.1%	Swine: Muscle/meat	0.1%	Mandarins		0.8%
	0.8%	FR adult	0.15	0.4%	Milk: Cattle	0.1%	Oranges	0.1%	Swine: Muscle/meat		0.8%
	0.6%	LT adult	0.11	0.4%	Milk: Cattle	0.1%	Swine: Muscle/meat	0.0%	Bovine: Muscle/meat		0.6%
	0.6%	UK vegetarian	0.11	0.3%	Milk: Cattle	0.2%	Oranges	0.0%	Mandarins		0.6%
	0.5%	UK adult	0.11	0.3%	Milk: Cattle	0.1%	Oranges	0.1%	Bovine: Muscle/meat		0.5%
	0.4%	IE child	0.08	0.4%	Milk: Cattle	0.0%	Swine: Muscle/meat	0.0%	Oranges		0.4%
	0.3%	FI 3 yr	0.05	0.2%	Mandarins	0.0%	Oranges	0.0%	Grapefruits		0.3%
	0.2%	IT toddler	0.05	0.1%	Mandarins	0.1%	Oranges	0.0%	Lemons		0.2%
	0.2%	FI 6 yr	0.05	0.2%	Mandarins	0.0%	Oranges	0.0%	Lemons		0.2%
	0.2%	PT general	0.04	0.1%	Oranges	0.0%	Mandarins	0.0%	Lemons		0.2%
	0.2%	IT adult	0.04	0.1%	Mandarins	0.1%	Oranges	0.0%	Lemons		0.2%
	0.2%	FI adult	0.03	0.1%	Mandarins	0.1%	Oranges	0.0%	Lemons		0.2%
	0.1%	PL general	0.01	0.0%	Lemons	0.0%	Mandarins	0.0%	Oranges		0.1%

Conclusion:
The estimated long-term dietary intake (TMDI/NEDI/IEDI) was below the ADI.
The long-term intake of residues of Carbendazim is unlikely to present a public health concern.
DISCLAIMER: Dietary data from the UK were included in PRIMO when the UK was a member of the European Union.

Acute risk assessment /children	Acute risk assessment/adults/general population
Details - acute risk assessment/children	Details - acute risk assessment/adults

The acute risk assessment is based on the ARfD. DISCLAIMER: Dietary data from the UK were included in PRIMO when the UK was a member of the European Union.

The calculation is based on the large portion of the most critical consumer group.

Show results for all crops

Unprocessed commodities

Results for children
No. of commodities for which ARfD/ADI is exceeded (IESTI): ---

IESTI

Highest % of ARfD/ADI	Commodities	MRL/input for RA (mg/kg)	Exposure (µg/kg bw)
84%	Mandarins	0.9/0.28	17
63%	Mangoes	0.7/0.16	13
48%	Lemons	0.9/0.28	9.7
28%	Limes	0.9/0.28	5.7
28%	Oranges	0.2/0.04	5.6
27%	Papayas	0.2/0.13	5.5
17%	Grapefruits	0.2/0.04	3.3
12%	Milk: Cattle	0.02/0.02	2.5
1%	Swine: Muscle/meat	0.02/0.02	0.24
0.8%	Bovine: Liver	0.02/0.02	0.16
0.7%	Bovine: Muscle/meat	0.02/0.02	0.14
0.6%	Equine: Muscle/meat	0.02/0.02	0.12
0.4%	Bovine: Kidney	0.02/0.02	0.08
0.2%	Bovine: Fat tissue	0.02/0.02	0.04
0.2%	Swine: Fat tissue	0.02/0.02	0.03

Expand/collapse list

Results for adults
No. of commodities for which ARfD/ADI is exceeded (IESTI): ---

IESTI

Highest % of ARfD/ADI	Commodities	MRL/input for RA (mg/kg)	Exposure (µg/kg bw)
25%	Mandarins	0.9/0.28	5.1
21%	Mangoes	0.7/0.16	4.1
13%	Lemons	0.9/0.28	2.5
10%	Limes	0.9/0.28	2.0
9%	Papayas	0.2/0.13	1.8
6%	Oranges	0.2/0.04	1.3
4%	Milk: Cattle	0.02/0.02	0.77
4%	Grapefruits	0.2/0.04	0.76
0.6%	Bovine: Muscle	0.02/0.02	0.11
0.5%	Swine: Muscle/meat	0.02/0.02	0.10
0.5%	Equine: Muscle/meat	0.02/0.02	0.10
0.4%	Bovine: Liver	0.02/0.02	0.08
0.2%	Swine: Kidney	0.02/0.02	0.04
0.2%	Bovine: Kidney	0.02/0.02	0.04
0.2%	Swine: Fat tissue	0.02/0.02	0.04

Total number of commodities exceeding the ARfD/ADI in children and adult diets (IESTI calculation)

Processed commodities

Results for children
No of processed commodities for which ARfD/ADI is exceeded (IESTI): ---

IESTI

Highest % of ARfD/ADI	Processed commodities	MRL/input for RA (mg/kg)	Exposure (µg/kg bw)
4%	Lemons/jam	0.9/0.26	0.77
0.8%	Oranges/juice	0.2/0	0.17
0.1%	Limes/juice	0.9/0.26	0.02

Expand/collapse list

Results for adults
No of processed commodities for which ARfD/ADI is exceeded (IESTI): ---

IESTI

Highest % of ARfD/ADI	Processed commodities	MRL/input for RA (mg/kg)	Exposure (µg/kg bw)
7%	Okra, lady's fingers/boiled	1.5/0.91	1.5
4%	Grapefruits/juice	0.2/0.08	0.87
2%	Lemons/juice	0.9/0.26	0.48

Conclusion:
No exceedance of the toxicological reference value was identified for any unprocessed commodity.
A short-term intake of residues of Carbendazim is unlikely to present a public health risk.
For processed commodities, no exceedance of the ARfD/ADI was identified.

- PRIMo (Scenario EU2) thiophanate-methyl – with risk mitigation measures

European Food Safety Authority

EFSA PRIMo revision 3.1; 2021/01/06

Thiophanate-methyl

LOQs (mg/kg) range from:	0.01	to:	0.01
Toxicological reference values			
ADI (mg/kg bw per day):	0.02	ARfD (mg/kg bw):	0.02
Source of ADI:		Source of ARfD:	
Year of evaluation:		Year of evaluation:	

Input values | Details - chronic risk assessment | Supplementary results - chronic risk assessment | Details - acute risk assessment/children | Details - acute risk assessment/adults

Comments:

Normal mode

Chronic risk assessment: JMPR methodology (IEDI/TMDI)

No of diets exceeding the ADI : ---

TMDI/NEDI/IEDI calculation (based on average food consumption)

Calculated exposure (% of ADI)	MS Diet	Expsoure (µg/kg bw per day)	Highest contributor to MS diet (in % of ADI)	Commodity/ group of commodities	2nd contributor to MS diet (in % of ADI)	Commodity/ group of commodities	3rd contributor to MS diet (in % of ADI)	Commodity/ group of commodities	Exposure resulting from MRLs set at the LOQ (in % of ADI)	Exposure resulting from commodities not under assessment (in % of ADI)
3%	NL toddler	0.62	3%	Milk: Cattle	0.1%	Bovine: Muscle/meat	0.0%	Swine: Muscle/meat	3%	3%
2%	UK infant	0.40	2%	Milk: Cattle	0.1%	Bovine: Muscle/meat	0.0%	Bovine: Liver	2%	2%
2%	FR toddler 2 3 yr	0.32	1%	Milk: Cattle	0.1%	Bovine: Muscle/meat	0.1%	Swine: Muscle/meat	1%	2%
1%	NL child	0.27	1%	Milk: Cattle	0.1%	Swine: Muscle/meat	0.0%	Bovine: Muscle/meat	1%	1%
1%	FR child 3 15 yr	0.26	1%	Milk: Cattle	0.1%	Bovine: Muscle/meat	0.1%	Swine: Muscle/meat	1%	1%
1%	UK toddler	0.22	1%	Milk: Cattle	0.1%	Bovine: Muscle/meat	0.0%	Limes	1%	1%
1%	DE child	0.21	1.0%	Milk: Cattle	0.0%	Swine: Muscle/meat	0.0%	Bovine: Muscle/meat	1.0%	1%
0.878%	FR infant	0.18	0.8%	Milk: Cattle	0.0%	Swine: Muscle/meat	0.0%	Bovine: Muscle/meat	0.8%	0.9%
0.862%	SE general	0.17	0.6%	Milk: Cattle	0.2%	Bovine: Muscle/meat	0.0%	Limes	0.6%	0.9%
0.815%	DK child	0.16	0.6%	Milk: Cattle	0.1%	Swine: Muscle/meat	0.1%	Bovine: Muscle/meat	0.6%	0.8%
0.766%	ES child	0.15	0.6%	Milk: Cattle	0.1%	Bovine: Muscle/meat	0.1%	Swine: Muscle/meat	0.6%	0.8%
0.708%	DE general	0.14	0.6%	Milk: Cattle	0.1%	Swine: Muscle/meat	0.0%	Bovine: Muscle/meat	0.6%	0.7%
0.698%	DE women 14-50 yr	0.14	0.6%	Milk: Cattle	0.0%	Swine: Muscle/meat	0.0%	Bovine: Muscle/meat	0.6%	0.7%
0.7%	RO general	0.13	0.6%	Milk: Cattle	0.1%	Swine: Muscle/meat	0.0%	Bovine: Muscle/meat	0.6%	0.7%
0.5%	NL general	0.10	0.4%	Milk: Cattle	0.0%	Swine: Muscle/meat	0.0%	Bovine: Muscle/meat	0.4%	0.5%
0.5%	GEMS/Food G11	0.10	0.4%	Milk: Cattle	0.1%	Swine: Muscle/meat	0.0%	Bovine: Muscle/meat	0.4%	0.5%
0.5%	GEMS/Food G15	0.09	0.4%	Milk: Cattle	0.1%	Swine: Muscle/meat	0.0%	Bovine: Muscle/meat	0.4%	0.5%
0.4%	GEMS/Food G07	0.09	0.3%	Milk: Cattle	0.1%	Swine: Muscle/meat	0.0%	Bovine: Muscle/meat	0.3%	0.4%
0.4%	GEMS/Food G08	0.08	0.3%	Milk: Cattle	0.1%	Swine: Muscle/meat	0.0%	Bovine: Muscle/meat	0.3%	0.4%
0.4%	GEMS/Food G10	0.08	0.3%	Milk: Cattle	0.0%	Bovine: Muscle/meat	0.0%	Swine: Muscle/meat	0.3%	0.4%
0.4%	DK adult	0.07	0.3%	Milk: Cattle	0.0%	Swine: Muscle/meat	0.0%	Bovine: Muscle/meat	0.3%	0.4%
0.3%	ES adult	0.06	0.2%	Milk: Cattle	0.0%	Bovine: Muscle/meat	0.0%	Swine: Muscle/meat	0.2%	0.3%
0.3%	IE adult	0.06	0.2%	Milk: Cattle	0.1%	Limes	0.0%	Bovine: Muscle/meat	0.2%	0.3%
0.3%	FR adult	0.06	0.2%	Milk: Cattle	0.0%	Swine: Muscle/meat	0.0%	Bovine: Muscle/meat	0.2%	0.3%
0.3%	LT adult	0.05	0.2%	Milk: Cattle	0.0%	Swine: Muscle/meat	0.0%	Bovine: Muscle/meat	0.2%	0.3%
0.2%	IE child	0.04	0.2%	Milk: Cattle	0.0%	Swine: Muscle/meat	0.0%	Swine: Fat tissue	0.2%	0.2%
0.2%	UK adult	0.04	0.1%	Milk: Cattle	0.0%	Bovine: Muscle/meat	0.0%	Limes	0.1%	0.2%
0.2%	UK vegetarian	0.03	0.2%	Milk: Cattle	0.0%	Limes	0.0%	Bovine: Fat tissue	0.2%	0.2%
0.2%	GEMS/Food G06	0.03	0.1%	Milk: Cattle	0.0%	Okra/lady's fingers	0.0%	Bovine: Muscle/meat	0.1%	0.2%
	IT toddler			FRUIT AND TREE NUTS		FRUIT AND TREE NUTS				
	IT toddler			FRUIT AND TREE NUTS		FRUIT AND TREE NUTS				
	IT toddler			FRUIT AND TREE NUTS		FRUIT AND TREE NUTS				
	IT toddler			FRUIT AND TREE NUTS		FRUIT AND TREE NUTS				
	IT toddler			FRUIT AND TREE NUTS		FRUIT AND TREE NUTS				
	IT toddler			FRUIT AND TREE NUTS		FRUIT AND TREE NUTS				
	IT toddler			FRUIT AND TREE NUTS		FRUIT AND TREE NUTS				

Conclusion:
The estimated long-term dietary intake (TMDI/NEDI/IEDI) was below the ADI.
The long-term intake of residues of thiophanate-methyl is unlikely to present a public health concern.
DISCLAIMER: Dietary data from the UK were included in PRIMO when the UK was a member of the European Union.

Acute risk assessment/children	Acute risk assessment/adults/general population
Details - acute risk assessment/children	Details - acute risk assessment/adults

The acute risk assessment is based on the ARfD. DISCLAIMER: Dietary data from the UK were included in PRIMO when the UK was a member of the European Union.

The calculation is based on the large portion of the most critical consumer group.

Show results for all crops

Unprocessed commodities

Results for children
No. of commodities for which ARfD/ADI is exceeded (IESTI): ---

IESTI

Highest % of ARfD/ADI	Commodities	MRL/input for RA (mg/kg)	Exposure (µg/kg bw)
48%	Limes	7/0.47	9.5
6%	Milk: Cattle	0.01/0.01	1.2
0.6%	Swine: Muscle/meat	0.01/0.01	0.12
0.4%	Bovine: Liver	0.01/0.01	0.08
0.4%	Bovine: Muscle/meat	0.01/0.01	0.07
0.3%	Equine: Muscle/meat	0.01/0.01	0.06
0.2%	Bovine: Kidney	0.01/0.01	0.04
0.1%	Bovine: Fat tissue	0.01/0.01	0.02
0.09%	Swine: Fat tissue	0.01/0.01	0.02
0.06%	Swine: Kidney	0.01/0.01	0.01
0.06%	Swine: Liver	0.01/0.01	0.01

Expand/collapse list

Results for adults
No. of commodities for which ARfD/ADI is exceeded (IESTI): ---

IESTI

Highest % of ARfD/ADI	Commodities	MRL/input for RA (mg/kg)	Exposure (µg/kg bw)
17%	Limes	7/0.47	3.3
2%	Milk: Cattle	0.01/0.01	0.39
0.3%	Bovine: Muscle	0.01/0.01	0.06
0.2%	Swine: Muscle/meat	0.01/0.01	0.05
0.2%	Equine: Muscle/meat	0.01/0.01	0.05
0.2%	Bovine: Liver	0.01/0.01	0.04
0.1%	Swine: Kidney	0.01/0.01	0.02
0.1%	Bovine: Kidney	0.01/0.01	0.02
0.1%	Swine: Fat tissue	0.01/0.01	0.02
0.07%	Swine: Liver	0.01/0.01	0.01
0.05%	Bovine: Fat tissue	0.01/0.01	0.01

Total number of commodities exceeding the ARfD/ADI in children and adult diets (IESTI calculation)

Processed commodities

Results for children
No of processed commodities for which ARfD/ADI is exceeded (IESTI): ---

IESTI

Highest % of ARfD/ADI	Processed commodities	MRL/input for RA (mg/kg)	Exposure (µg/kg bw)
1%	Limes/juice	7/2.5	0.23

Expand/collapse list

Results for adults
No of processed commodities for which ARfD/ADI is exceeded (IESTI): ---

IESTI

Highest % of ARfD/ADI	Processed commodities	MRL/input for RA (mg/kg)	Exposure (µg/kg bw)
3%	Okra, lady's fingers/boiled	0.9/0.41	0.66

Conclusion:
No exceedance of the toxicological reference value was identified for any unprocessed commodity.
A short-term intake of residues of thiophanate-methyl is unlikely to present a public health risk.
For processed commodities, no exceedance of the ARfD/ADI was identified.

- PRIMo (Scenario EU2) carbendazim – with risk mitigation measures

European Food Safety Authority

EFSA PRIMo revision 3.1; 2021/01/06

Carbendazim

LOQs (mg/kg) range from: 0.02 to: 0.02

Toxicological reference values

ADI (mg/kg bw per day):	0.02	ARfD (mg/kg bw):	0.02
Source of ADI:		Source of ARfD:	
Year of evaluation:		Year of evaluation:	

Input values

Details - chronic risk assessment

Supplementary results - chronic risk assessment

Details - acute risk assessment/children

Details - acute risk assessment/adults

Comments:

Refined calculation mode

Chronic risk assessment: JMPR methodology (IEDI/TMDI)

No of diets exceeding the ADI : ---

	Calculated exposure (% of ADI)	MS Diet	Exposure (µg/kg bw per day)	Highest contributor to MS diet (in % of ADI)	Commodity/ group of commodities	2nd contributor to MS diet (in % of ADI)	Commodity/ group of commodities	3rd contributor to MS diet (in % of ADI)	Commodity/ group of commodities	Exposure resulting from: MRLs set at the LOQ (in % of ADI)	Exposure resulting from: commodities not under assessment (in % of ADI)
TMDI/NEDI/IEDI calculation (based on average food consumption)	7%	NL toddler	1.31	6%	Milk: Cattle	0.3%	Mandarins	0.1%	Bovine: Muscle/meat	6%	7%
	4%	UK infant	0.80	4%	Milk: Cattle	0.1%	Bovine: Muscle/meat	0.0%	Lemons	4%	4%
	4%	FR toddler 2 3 yr	0.73	3%	Milk: Cattle	0.5%	Mandarins	0.1%	Bovine: Muscle/meat	3%	4%
	3%	NL child	0.63	2%	Milk: Cattle	0.4%	Mandarins	0.1%	Swine: Muscle/meat	2%	3%
	3%	FR child 3 15 yr	0.54	2%	Milk: Cattle	0.1%	Bovine: Muscle/meat	0.1%	Swine: Muscle/meat	2%	3%
	2%	DE child	0.48	2%	Milk: Cattle	0.2%	Mandarins	0.1%	Lemons	2%	2%
	2%	UK toddler	0.48	2%	Milk: Cattle	0.2%	Mandarins	0.1%	Bovine: Muscle/meat	2%	2%
	2%	SE general	0.40	1%	Milk: Cattle	0.4%	Bovine: Muscle/meat	0.3%	Mandarins	1%	2%
	2%	FR infant	0.37	2%	Milk: Cattle	0.1%	Mandarins	0.0%	Swine: Muscle/meat	2%	2%
	2%	DK child	0.34	1%	Milk: Cattle	0.2%	Swine: Muscle/meat	0.1%	Bovine: Muscle/meat	1%	2%
	2%	ES child	0.33	1%	Milk: Cattle	0.1%	Bovine: Muscle/meat	0.1%	Swine: Muscle/meat	1%	2%
	2%	DE general	0.31	1%	Milk: Cattle	0.1%	Lemons	0.1%	Swine: Muscle/meat	1%	2%
	2%	DE women 14-50 yr	0.31	1%	Milk: Cattle	0.1%	Lemons	0.1%	Swine: Muscle/meat	1%	2%
	1%	RO general	0.27	1%	Milk: Cattle	0.1%	Swine: Muscle/meat	0.0%	Bovine: Muscle/meat	1%	1%
	1%	GEMS/Food G11	0.27	0.8%	Milk: Cattle	0.2%	Lemons	0.1%	Swine: Muscle/meat	0.8%	1%
	1%	NL general	0.23	0.8%	Milk: Cattle	0.1%	Mandarins	0.1%	Swine: Muscle/meat	0.8%	1%
	1%	GEMS/Food G08	0.23	0.6%	Milk: Cattle	0.2%	Swine: Muscle/meat	0.2%	Lemons	0.6%	1%
	1%	GEMS/Food G07	0.22	0.6%	Milk: Cattle	0.1%	Mandarins	0.1%	Swine: Muscle/meat	0.6%	1%
	1%	GEMS/Food G15	0.22	0.7%	Milk: Cattle	0.1%	Swine: Muscle/meat	0.1%	Mandarins	0.7%	1%
	1.0%	GEMS/Food G10	0.20	0.5%	Milk: Cattle	0.1%	Lemons	0.1%	Mandarins	0.5%	1.0%
	0.9%	IE adult	0.17	0.4%	Milk: Cattle	0.3%	Mandarins	0.0%	Bovine: Muscle/meat	0.4%	0.9%
	0.8%	DK adult	0.15	0.5%	Milk: Cattle	0.1%	Swine: Muscle/meat	0.1%	Mandarins	0.5%	0.8%
	0.7%	ES adult	0.15	0.5%	Milk: Cattle	0.1%	Mandarins	0.1%	Bovine: Muscle/meat	0.5%	0.7%
	0.7%	GEMS/Food G06	0.14	0.2%	Milk: Cattle	0.2%	Mandarins	0.2%	Lemons	0.2%	0.7%
	0.6%	FR adult	0.13	0.4%	Milk: Cattle	0.1%	Swine: Muscle/meat	0.1%	Bovine: Muscle/meat	0.4%	0.6%
	0.5%	LT adult	0.11	0.4%	Milk: Cattle	0.1%	Swine: Muscle/meat	0.0%	Bovine: Muscle/meat	0.4%	0.5%
	0.4%	UK adult	0.08	0.3%	Milk: Cattle	0.1%	Bovine: Muscle/meat	0.0%	Mandarins	0.3%	0.4%
	0.4%	IE child	0.08	0.4%	Milk: Cattle	0.0%	Swine: Muscle/meat	0.0%	Swine: Fat tissue	0.4%	0.4%
	0.4%	UK vegetarian	0.07	0.3%	Milk: Cattle	0.0%	Mandarins	0.0%	Lemons	0.3%	0.4%
	0.2%	FI 3 yr	0.05	0.2%	Mandarins	0.0%	Lemons				0.2%
	0.2%	FI 6 yr	0.04	0.2%	Mandarins	0.0%	Lemons				0.2%
	0.1%	IT toddler	0.03	0.1%	Mandarins	0.0%	Lemons				0.1%
	0.1%	IT adult	0.02	0.1%	Mandarins	0.0%	Lemons				0.1%
	0.1%	FI adult	0.02	0.1%	Mandarins	0.0%	Lemons				0.1%
	0.1%	PT general	0.02	0.0%	Mandarins	0.0%	Lemons				0.1%
	0.1%	PL general	0.01	0.0%	Lemons	0.0%	Mandarins				0.1%

Conclusion:
The estimated long-term dietary intake (TMDI/NEDI/IEDI) was below the ADI.
The long-term intake of residues of Carbendazim is unlikely to present a public health concern.
DISCLAIMER: Dietary data from the UK were included in PRIMO when the UK was a member of the European Union.

Acute risk assessment/children	Acute risk assessment/adults/general population
Details - acute risk assessment/children	Details - acute risk assessment/adults

The acute risk assessment is based on the ARfD. DISCLAIMER: Dietary data from the UK were included in PRIMO when the UK was a member of the European Union.

The calculation is based on the large portion of the most critical consumer group.

Show results for all crops

Unprocessed commodities

Results for children
No. of commodities for which ARfD/ADI is exceeded (IESTI): ---

IESTI

Highest % of ARfD/ADI	Commodities	MRL/input for RA (mg/kg)	Exposure (µg/kg bw)
84%	Mandarins	0.9/0.28	17
48%	Lemons	0.9/0.28	9.7
28%	Limes	0.9/0.28	5.7
12%	Milk: Cattle	0.02/0.02	2.5
1%	Swine: Muscle/meat	0.02/0.02	0.24
0.8%	Bovine: Liver	0.02/0.02	0.16
0.7%	Bovine: Muscle/meat	0.02/0.02	0.14
0.6%	Equine: Muscle/meat	0.02/0.02	0.12
0.4%	Bovine: Kidney	0.02/0.02	0.08
0.2%	Bovine: Fat tissue	0.02/0.02	0.04
0.2%	Swine: Fat tissue	0.02/0.02	0.03
0.1%	Swine: Kidney	0.02/0.02	0.03
0.1%	Swine: Liver	0.02/0.02	0.02

Expand/collapse list

Results for adults
No. of commodities for which ARfD/ADI is exceeded (IESTI): ---

IESTI

Highest % of ARfD/ADI	Commodities	MRL/input for RA (mg/kg)	Exposure (µg/kg bw)
25%	Mandarins	0.9/0.28	5.1
13%	Lemons	0.9/0.28	2.5
10%	Limes	0.9/0.28	2.0
4%	Milk: Cattle	0.02/0.02	0.77
0.6%	Bovine: Muscle	0.02/0.02	0.11
0.5%	Swine: Muscle/meat	0.02/0.02	0.10
0.5%	Equine: Muscle/meat	0.02/0.02	0.10
0.4%	Bovine: Liver	0.02/0.02	0.08
0.2%	Swine: Kidney	0.02/0.02	0.04
0.2%	Bovine: Kidney	0.02/0.02	0.04
0.2%	Swine: Fat tissue	0.02/0.02	0.04
0.1%	Swine: Liver	0.02/0.02	0.03
0.10%	Bovine: Fat tissue	0.02/0.02	0.02

Total number of commodities exceeding the ARfD/ADI in children and adult diets (IESTI calculation)

Processed commodities

Results for children
No of processed commodities for which ARfD/ADI is exceeded (IESTI): ---

IESTI

Highest % of ARfD/ADI	Processed commodities	MRL/input for RA (mg/kg)	Exposure (µg/kg bw)
4%	Lemons/jam	0.9/0.26	0.77
0.1%	Limes/juice	0.9/0.26	0.02

Expand/collapse list

Results for adults
No of processed commodities for which ARfD/ADI is exceeded (IESTI): ---

IESTI

Highest % of ARfD/ADI	Processed commodities	MRL/input for RA (mg/kg)	Exposure (µg/kg bw)
7%	Okra, lady's fingers/boiled	1.5/0.91	1.5
2%	Lemons/juice	0.9/0.26	0.48

Conclusion:
No exceedance of the toxicological reference value was identified for any unprocessed commodity.
A short-term intake of residues of Carbendazim is unlikely to present a public health risk.
For processed commodities, no exceedance of the ARfD/ADI was identified.

- PRIMo (Scenario EU3) thiophanate-methyl – with risk mitigation measures

European Food Safety Authority

EFSA PRIMo revision 3.1; 2021/01/06

Thiophanate-methyl

LOQs (mg/kg) range from: 0.01 to: 0.01

Toxicological reference values

ADI (mg/kg bw per day):	0.02	ARfD (mg/kg bw):	0.02
Source of ADI:		Source of ARfD:	
Year of evaluation:		Year of evaluation:	

Input values

Details - chronic risk assessment | Supplementary results - chronic risk assessment

Details - acute risk assessment/children | Details - acute risk assessment/adults

Comments:

Refined calculation mode

Chronic risk assessment: JMPR methodology (IEDI/TMDI)

No of diets exceeding the ADI : ---

TMDI/NEDI/IEDI calculation (based on average food consumption)	Calculated exposure (% of ADI)	MS Diet	Exposure (µg/kg bw per day)	Highest contributor to MS diet (in % of ADI)	Commodity/ group of commodities	2nd contributor to MS diet (in % of ADI)	Commodity/ group of commodities	3rd contributor to MS diet (in % of ADI)	Commodity/ group of commodities	Exposure resulting from: MRLs set at the LOQ (in % of ADI)	Exposure resulting from: commodities not under assessment (in % of ADI)
	3%	NL toddler	0.66	3%	Milk: Cattle	0.2%	Lemons	0.1%	Bovine: Muscle/meat		3%
	2%	UK infant	0.41	2%	Milk: Cattle	0.1%	Bovine: Muscle/meat	0.0%	Lemons		2%
	2%	FR toddler 2 3 yr	0.32	1%	Milk: Cattle	0.1%	Bovine: Muscle/meat	0.1%	Swine: Muscle/meat		2%
	2%	NL child	0.32	1%	Milk: Cattle	0.2%	Lemons	0.1%	Swine: Muscle/meat		2%
	1%	FR child 3 15 yr	0.26	1%	Milk: Cattle	0.1%	Bovine: Muscle/meat	0.1%	Swine: Muscle/meat		1%
	1%	DE child	0.25	1.0%	Milk: Cattle	0.2%	Lemons	0.0%	Swine: Muscle/meat		1%
	1%	UK toddler	0.23	1%	Milk: Cattle	0.1%	Bovine: Muscle/meat	0.0%	Limes		1%
	1%	GEMS/Food G11	0.20	0.5%	Lemons	0.4%	Milk: Cattle	0.1%	Swine: Muscle/meat		1%
	1%	DE women 14-50 yr	0.20	0.6%	Milk: Cattle	0.3%	Lemons	0.0%	Swine: Muscle/meat		1%
	1.0%	DE general	0.20	0.6%	Milk: Cattle	0.3%	Lemons	0.1%	Swine: Muscle/meat		1.0%
	1.0%	SE general	0.20	0.6%	Milk: Cattle	0.2%	Bovine: Muscle/meat	0.1%	Lemons		1.0%
	0.9%	FR infant	0.18	0.8%	Milk: Cattle	0.0%	Swine: Muscle/meat	0.0%	Bovine: Muscle/meat		0.9%
	0.8%	DK child	0.17	0.6%	Milk: Cattle	0.1%	Swine: Muscle/meat	0.1%	Bovine: Muscle/meat		0.8%
	0.8%	ES child	0.15	0.6%	Milk: Cattle	0.1%	Bovine: Muscle/meat	0.1%	Swine: Muscle/meat		0.8%
	0.8%	GEMS/Food G08	0.15	0.4%	Lemons	0.3%	Milk: Cattle	0.1%	Swine: Muscle/meat		0.8%
	0.7%	RO general	0.14	0.6%	Milk: Cattle	0.1%	Lemons	0.1%	Swine: Muscle/meat		0.7%
	0.7%	GEMS/Food G07	0.13	0.3%	Milk: Cattle	0.2%	Lemons	0.1%	Swine: Muscle/meat		0.7%
	0.7%	GEMS/Food G10	0.13	0.3%	Lemons	0.3%	Milk: Cattle	0.0%	Bovine: Muscle/meat		0.7%
	0.6%	GEMS/Food G15	0.12	0.4%	Milk: Cattle	0.1%	Lemons	0.1%	Swine: Muscle/meat		0.6%
	0.5%	NL general	0.11	0.4%	Milk: Cattle	0.0%	Swine: Muscle/meat	0.0%	Bovine: Muscle/meat		0.5%
	0.5%	GEMS/Food G06	0.11	0.4%	Lemons	0.1%	Milk: Cattle	0.0%	Okra/lady's fingers		0.5%
	0.4%	IE adult	0.07	0.2%	Milk: Cattle	0.1%	Lemons	0.1%	Limes		0.4%
	0.4%	DK adult	0.07	0.3%	Milk: Cattle	0.0%	Swine: Muscle/meat	0.0%	Bovine: Muscle/meat		0.4%
	0.3%	ES adult	0.07	0.2%	Milk: Cattle	0.0%	Bovine: Muscle/meat	0.0%	Swine: Muscle/meat		0.3%
	0.3%	FR adult	0.06	0.2%	Milk: Cattle	0.0%	Swine: Muscle/meat	0.0%	Bovine: Muscle/meat		0.3%
	0.3%	LT adult	0.06	0.2%	Milk: Cattle	0.0%	Swine: Muscle/meat	0.0%	Bovine: Muscle/meat		0.3%
	0.2%	IE child	0.04	0.2%	Milk: Cattle	0.0%	Swine: Muscle/meat	0.0%	Swine: Fat tissue		0.2%
	0.2%	UK adult	0.04	0.1%	Milk: Cattle	0.0%	Bovine: Muscle/meat	0.0%	Lemons		0.2%
	0.2%	UK vegetarian	0.04	0.2%	Milk: Cattle	0.0%	Lemons	0.0%	Limes		0.2%
	0.1%	PL general	0.02	0.1%	Lemons		FRUIT AND TREE NUTS				0.1%
	0.1%	PT general	0.01	0.1%	Lemons		FRUIT AND TREE NUTS				0.1%
	0.0%	IT toddler	0.01	0.0%	Lemons		FRUIT AND TREE NUTS				0.0%
	0.0%	IT adult	0.01	0.0%	Lemons		FRUIT AND TREE NUTS				0.0%
	0.0%	FI adult	0.00	0.0%	Lemons		FRUIT AND TREE NUTS				0.0%
	0.0%	FI 3 yr	0.00	0.0%	Lemons		FRUIT AND TREE NUTS				0.0%
	0.0%	FI 6 yr	0.00	0.0%	Lemons		FRUIT AND TREE NUTS				0.0%

Conclusion:
The estimated long-term dietary intake (TMDI/NEDI/IEDI) was below the ADI.
The long-term intake of residues of thiophanate-methyl is unlikely to present a public health concern.
DISCLAIMER: Dietary data from the UK were included in PRIMO when the UK was a member of the European Union.

Acute risk assessment/children	Acute risk assessment/adults/general population
Details - acute risk assessment/children	Details - acute risk assessment/adults

The acute risk assessment is based on the ARfD. DISCLAIMER: Dietary data from the UK were included in PRIMO when the UK was a member of the European Union.

The calculation is based on the large portion of the most critical consumer group.

Show results for all crops

Unprocessed commodities

Results for children No. of commodities for which ARfD/ADI is exceeded (IESTI):	---	**Results for adults** No. of commodities for which ARfD/ADI is exceeded (IESTI):	---

IESTI

Highest % of ARfD/ADI	Commodities	MRL/input for RA (mg/kg)	Exposure (µg/kg bw)
81%	Lemons	7/0.47	16
48%	Limes	7/0.47	9.5
6%	Milk: Cattle	0.01/0.01	1.2
0.6%	Swine: Muscle/meat	0.01/0.01	0.12
0.4%	Bovine: Liver	0.01/0.01	0.08
0.4%	Bovine: Muscle/meat	0.01/0.01	0.07
0.3%	Equine: Muscle/meat	0.01/0.01	0.06
0.2%	Bovine: Kidney	0.01/0.01	0.04
0.1%	Bovine: Fat tissue	0.01/0.01	0.02
0.09%	Swine: Fat tissue	0.01/0.01	0.02
0.06%	Swine: Kidney	0.01/0.01	0.01
0.06%	Swine: Liver	0.01/0.01	0.01

IESTI

Highest % of ARfD/ADI	Commodities	MRL/input for RA (mg/kg)	Exposure (µg/kg bw)
21%	Lemons	7/0.47	4.2
17%	Limes	7/0.47	3.3
2%	Milk: Cattle	0.01/0.01	0.39
0.3%	Bovine: Muscle	0.01/0.01	0.06
0.2%	Swine: Muscle/meat	0.01/0.01	0.05
0.2%	Equine: Muscle/meat	0.01/0.01	0.05
0.2%	Bovine: Liver	0.01/0.01	0.04
0.1%	Swine: Kidney	0.01/0.01	0.02
0.1%	Bovine: Kidney	0.01/0.01	0.02
0.1%	Swine: Fat tissue	0.01/0.01	0.02
0.07%	Swine: Liver	0.01/0.01	0.01
0.05%	Bovine: Fat tissue	0.01/0.01	0.01

Expand/collapse list

Total number of commodities exceeding the ARfD/ADI in children and adult diets (IESTI calculation)

Processed commodities

Results for children No of processed commodities for which ARfD/ADI is exceeded (IESTI):	---	**Results for adults** No of processed commodities for which ARfD/ADI is exceeded (IESTI):	---

IESTI

Highest % of ARfD/ADI	Processed commodities	MRL/input for RA (mg/kg)	Exposure (µg/kg bw)
38%	Lemons / jam	7/2.5	7.6
1%	Limes / juice	7/2.5	0.23

IESTI

Highest % of ARfD/ADI	Processed commodities	MRL/input for RA (mg/kg)	Exposure (µg/kg bw)
24%	Lemons / juice	7/2.5	4.7
3%	Okra, lady's fingers / boiled	0.9/0.41	0.66

Expand/collapse list

Conclusion:

No exceedance of the toxicological reference value was identified for any unprocessed commodity.
A short-term intake of residues of thiophanate-methyl is unlikely to present a public health risk.
For processed commodities, no exceedance of the ARfD/ADI was identified.

- PRIMo (Scenario EU3) carbendazim – with risk mitigation measures

European Food Safety Authority

EFSA PRIMo revision 3.1; 2021/01/06

Carbendazim

LOQs (mg/kg) range from: 0.02 to: 0.02

Toxicological reference values

ADI (mg/kg bw per day):	0.02	ARfD (mg/kg bw):	0.02
Source of ADI:		Source of ARfD:	
Year of evaluation:		Year of evaluation:	

Input values

Details - chronic risk assessment

Supplementary results - chronic risk assessment

Details - acute risk assessment/children

Details - acute risk assessment/adults

Comments:

Refined calculation mode

Chronic risk assessment: JMPR methodology (IEDI/TMDI)

No of diets exceeding the ADI : ---

	Calculated exposure (% of ADI)	MS Diet	Exposure (µg/kg bw per day)	Highest contributor to MS diet (in % of ADI)	Commodity/ group of commodities	2nd contributor to MS diet (in % of ADI)	Commodity/ group of commodities	3rd contributor to MS diet (in % of ADI)	Commodity/ group of commodities	Exposure resulting from: MRLs set at the LOQ (in % of ADI)	Exposure resulting from: commodities not under assessment (in % of ADI)
TMDI/NEDI/IEDI calculation (based on average food consumption)	6%	NL toddler	1.30	6%	Milk: Cattle	0.3%	Mandarins	0.1%	Bovine: Muscle/meat		6%
	4%	UK infant	0.80	4%	Milk: Cattle	0.1%	Bovine: Muscle/meat	0.0%	Bovine: Liver		4%
	4%	FR toddler 2 3 yr	0.73	3%	Milk: Cattle	0.5%	Mandarins	0.1%	Bovine: Muscle/meat		4%
	3%	NL child	0.62	2%	Milk: Cattle	0.4%	Mandarins	0.1%	Swine: Muscle/meat		3%
	3%	FR child 3 15 yr	0.54	2%	Milk: Cattle	0.1%	Bovine: Muscle/meat	0.1%	Swine: Muscle/meat		3%
	2%	UK toddler	0.48	2%	Milk: Cattle	0.2%	Mandarins	0.1%	Bovine: Muscle/meat		2%
	2%	DE child	0.47	2%	Milk: Cattle	0.2%	Mandarins	0.1%	Swine: Muscle/meat		2%
	2%	SE general	0.39	1%	Milk: Cattle	0.4%	Bovine: Muscle/meat	0.3%	Mandarins		2%
	2%	FR infant	0.37	2%	Milk: Cattle	0.1%	Mandarins	0.0%	Swine: Muscle/meat		2%
	2%	DK child	0.34	1%	Milk: Cattle	0.2%	Swine: Muscle/meat	0.1%	Bovine: Muscle/meat		2%
	2%	ES child	0.33	1%	Milk: Cattle	0.1%	Bovine: Muscle/meat	0.1%	Swine: Muscle/meat		2%
	1%	DE general	0.30	1%	Milk: Cattle	0.1%	Swine: Muscle/meat	0.0%	Mandarins		1%
	1%	DE women 14-50 yr	0.30	1%	Milk: Cattle	0.1%	Swine: Muscle/meat	0.1%	Mandarins		1%
	1%	RO general	0.27	1%	Milk: Cattle	0.1%	Swine: Muscle/meat	0.0%	Bovine: Muscle/meat		1%
	1%	GEMS/Food G11	0.24	0.8%	Milk: Cattle	0.1%	Swine: Muscle/meat	0.1%	Mandarins		1%
	1%	NL general	0.23	0.8%	Milk: Cattle	0.1%	Mandarins	0.1%	Swine: Muscle/meat		1%
	1%	GEMS/Food G15	0.21	0.7%	Milk: Cattle	0.1%	Swine: Muscle/meat	0.1%	Mandarins		1%
	1%	GEMS/Food G07	0.21	0.6%	Milk: Cattle	0.1%	Mandarins	0.1%	Swine: Muscle/meat		1%
	1%	GEMS/Food G08	0.21	0.6%	Milk: Cattle	0.2%	Swine: Muscle/meat	0.1%	Mandarins		1%
	0.9%	GEMS/Food G10	0.18	0.5%	Milk: Cattle	0.1%	Mandarins	0.1%	Bovine: Muscle/meat		0.9%
	0.9%	IE adult	0.17	0.4%	Milk: Cattle	0.3%	Mandarins	0.0%	Bovine: Muscle/meat		0.9%
	0.8%	DK adult	0.15	0.5%	Milk: Cattle	0.1%	Swine: Muscle/meat	0.1%	Mandarins		0.8%
	0.7%	ES adult	0.15	0.5%	Milk: Cattle	0.1%	Mandarins	0.1%	Bovine: Muscle/meat		0.7%
	0.6%	FR adult	0.13	0.4%	Milk: Cattle	0.1%	Swine: Muscle/meat	0.1%	Bovine: Muscle/meat		0.6%
	0.6%	GEMS/Food G06	0.12	0.2%	Milk: Cattle	0.2%	Mandarins	0.1%	Lemons		0.6%
	0.5%	LT adult	0.11	0.4%	Milk: Cattle	0.1%	Swine: Muscle/meat	0.0%	Bovine: Muscle/meat		0.5%
	0.4%	UK adult	0.08	0.3%	Milk: Cattle	0.1%	Bovine: Muscle/meat	0.0%	Mandarins		0.4%
	0.4%	IE child	0.08	0.4%	Milk: Cattle	0.0%	Swine: Muscle/meat	0.0%	Swine: Fat tissue		0.4%
	0.4%	UK vegetarian	0.07	0.3%	Milk: Cattle	0.0%	Mandarins	0.0%	Lemons		0.4%
	0.2%	FI 3 yr	0.05	0.2%	Mandarins	0.0%	Lemons				0.2%
	0.2%	FI 6 yr	0.04	0.2%	Mandarins	0.0%	Lemons				0.2%
	0.1%	IT toddler	0.03	0.1%	Mandarins	0.0%	Lemons				0.1%
	0.1%	IT adult	0.02	0.1%	Mandarins	0.0%	Lemons				0.1%
	0.1%	FI adult	0.02	0.1%	Mandarins	0.0%	Lemons				0.1%
	0.1%	PT general	0.01	0.0%	Mandarins	0.0%	Lemons				0.1%
	0.0%	PL general	0.01	0.0%	Mandarins	0.0%	Lemons				0.0%

Conclusion:
The estimated long-term dietary intake (TMDI/NEDI/IEDI) was below the ADI.
The long-term intake of residues of Carbendazim is unlikely to present a public health concern.
DISCLAIMER: Dietary data from the UK were included in PRIMO when the UK was a member of the European Union.

Acute risk assessment/children	Acute risk assessment/adults/general population
Details - acute risk assessment/children	Details - acute risk assessment/adults

The acute risk assessment is based on the ARfD. DISCLAIMER: Dietary data from the UK were included in PRIMO when the UK was a member of the European Union.

The calculation is based on the large portion of the most critical consumer group.

Show results for all crops

Unprocessed commodities

Results for children
No. of commodities for which ARfD/ADI is exceeded (IESTI): ---

IESTI

Highest % of ARfD/ADI	Commodities	MRL/input for RA (mg/kg)	Exposure (µg/kg bw)
84%	Mandarins	0.9/0.28	17
28%	Limes	0.9/0.28	5.7
12%	Milk: Cattle	0.02/0.02	2.5
7%	Lemons	0.2/0.04	1.4
1%	Swine: Muscle/meat	0.02/0.02	0.24
0.8%	Bovine: Liver	0.02/0.02	0.16
0.7%	Bovine: Muscle/meat	0.02/0.02	0.14
0.6%	Equine: Muscle/meat	0.02/0.02	0.12
0.4%	Bovine: Kidney	0.02/0.02	0.08
0.2%	Bovine: Fat tissue	0.02/0.02	0.04
0.2%	Swine: Fat tissue	0.02/0.02	0.03
0.1%	Swine: Kidney	0.02/0.02	0.03
0.1%	Swine: Liver	0.02/0.02	0.02

Expand/collapse list

Total number of commodities exceeding the ARfD/ADI in children and adult diets (IESTI calculation)

Results for adults
No. of commodities for which ARfD/ADI is exceeded (IESTI): ---

IESTI

Highest % of ARfD/ADI	Commodities	MRL/input for RA (mg/kg)	Exposure (µg/kg bw)
25%	Mandarins	0.9/0.28	5.1
10%	Limes	0.9/0.28	2.0
4%	Milk: Cattle	0.02/0.02	0.77
2%	Lemons	0.2/0.04	0.38
0.6%	Bovine: Muscle	0.02/0.02	0.11
0.5%	Swine: Muscle/meat	0.02/0.02	0.10
0.5%	Equine: Muscle/meat	0.02/0.02	0.10
0.4%	Bovine: Liver	0.02/0.02	0.08
0.2%	Swine: Kidney	0.02/0.02	0.04
0.2%	Bovine: Kidney	0.02/0.02	0.04
0.2%	Swine: Fat tissue	0.02/0.02	0.04
0.1%	Swine: Liver	0.02/0.02	0.03
0.10%	Bovine: Fat tissue	0.02/0.02	0.02

Processed commodities

Results for children
No of processed commodities for which ARfD/ADI is exceeded (IESTI): ---

IESTI

Highest % of ARfD/ADI	Processed commodities	MRL/input for RA (mg/kg)	Exposure (µg/kg bw)
1%	Lemons/jam	0.2/0.08	0.24
0.1%	Limes/juice	0.9/0.26	0.02

Expand/collapse list

Results for adults
No of processed commodities for which ARfD/ADI is exceeded (IESTI): ---

IESTI

Highest % of ARfD/ADI	Processed commodities	MRL/input for RA (mg/kg)	Exposure (µg/kg bw)
7%	Okra, lady's fingers/boiled	1.5/0.91	1.5
0.8%	Lemons/juice	0.2/0.08	0.15

Conclusion:

No exceedance of the toxicological reference value was identified for any unprocessed commodity.
A short-term intake of residues of Carbendazim is unlikely to present a public health risk.
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

	Median dietary burden		Maximum dietary burden	
Feed commodity	**Input value (mg/kg)**	**Comment**	**Input value (mg/kg)**	**Comment**
RD-RA 1: thiophanate-methyl				
Citrus, dry pulp	3.8	STMR × PF (1.51)	3.8	STMR × PF (1.51)
RD-RA 2: carbendazim				
Grapefruit, orange, dry pulp	2.06	STMR × PF (25.7)	2.06	STMR × PF (25.7)
Lemon, lime and mandarin, dry pulp	6.55[a]	STMR × PF (25.7)	6.55[a]	STMR × PF (25.7)

Abbreviations: STMR, supervised trials median residue; PF, processing factor.
[a]Residues arising from the use of carbendazim.

D.2 | CONSUMER RISK ASSESSMENT

	Chronic risk assessment		Acute risk assessment	
Commodity	**Input value (mg/kg)**	**Comment**	**Input value (mg/kg)**	**Comment**
RD-RA 1: thiophanate-methyl				
Grapefruits	0.28	STMR × PF (0.11) (tentative) (scenario EU1)	0.47	HR × PF (0.11) (tentative) (scenario EU1)
Oranges Mandarins	–	No fall-back GAP available (scenario EU2/EU3)	–	No fall-back GAP available (scenario EU2/EU3)
Lemons	0.28	STMR × PF (0.11) (tentative) (scenario EU1)	0.47	HR × PF (0.11) (tentative) (scenario EU1)
	–	No fall-back GAP available (Scenario EU2)	–	No fall-back GAP available (Scenario EU2)
	0.28	STMR × PF (0.11) (tentative) (Scenario EU3)	0.47	HR × PF (0.11) (tentative) (Scenario EU3)
Limes	0.28	STMR × PF (0.11) (tentative)	0.47	HR × PF (0.11) (tentative)
Mangoes	0.07	0.85[a] × STMR × PF (0.4) (tentative) (scenario EU1)	0.20	0.85[a] × HR × PF (0.4) (tentative) (scenario EU1)
	–	No fall-back GAP available (scenario EU2/EU3)	–	No fall-back GAP available (scenario EU2/EU3)
Papaya	0.34	0.85[a] × STMR (tentative) (scenario EU1)	0.50	0.85[a] × HR (tentative) (scenario EU1)
	–	No fall-back GAP available (scenario EU2/EU3)	–	No fall-back GAP available (scenario EU2/EU3)
Okra, lady's fingers	0.16	0.85[a] × STMR (tentative)	0.41	0.85[a] × HR (tentative)
Swine, bovine and equine meat	0.01*	STMR muscle (tentative)	0.01*	HR muscle (tentative)
Swine, bovine and equine fat	0.01*	STMR (tentative)	0.01*	STMR (tentative)
Swine, bovine and equine liver	0.01*	STMR (tentative)	0.01*	STMR (tentative)
Swine, bovine and equine kidney	0.01*	STMR (tentative)	0.01*	STMR (tentative)
Cattle and horse milk	0.01*	STMR (tentative)	0.01*	STMR (tentative)
RD-RA 2: carbendazim				
Grapefruit, Oranges	0.04	STMR CBZ × PF (0.47) (tentative) (scenario EU1)	0.04	HR CBZ × PF (0.47) (tentative) (scenario EU1)
	–	No fall-back GAP available (scenario EU2/EU3)	–	No fall-back GAP Available (scenario EU2/EU3)
Lemons	0.12[b]	STMR CBZ × PF (0.47) (tentative) (scenario EU1/EU2)	0.28[b]	HR CBZ × PF (0.47) (tentative) (scenario EU1/EU2)
	0.04	STMR CBZ × PF (0.47) (tentative) (scenario EU3)	0.04	HR CBZ × PF (0.47) (tentative) (scenario EU3)
Limes, Mandarins	0.12[b]	STMR CBZ × PF (0.47) (tentative)	0.28[b]	HR CBZ × PF (0.47) (tentative)

(Continued)

Commodity	Chronic risk assessment		Acute risk assessment	
	Input value (mg/kg)	Comment	Input value (mg/kg)	Comment
Mangoes	0.06	STMR TM × PF (0.4) × 0.15 × 0.56[(a)] + STMR CBZ × PF (0.4) (tentative) (scenario EU1)	0.16	HR TM × PF (0.4) × 0.15 × 0.56[a] + HR CBZ × PF (0.4) (tentative) (scenario EU1)
	–	No fall-back GAP available (scenario EU2/EU3)	–	No fall-back GAP available (scenario EU2/EU3)
Papaya	0.11	STMR TM × 0.15 × 0.56[a] + STMR CBZ (tentative) (scenario EU1)	0.13	HR TM × PF × 0.15 × 0.56[a] + HR CBZ (tentative) (scenario EU1)
	–	No fall-back GAP available (scenario EU2/EU3)	–	No fall-back GAP available (scenario EU2/EU3)
Okra, lady's fingers	0.36	STMR TM × 0.15 × 0.56[a] + STMR CBZ (tentative)	0.91	HR TM × 0.15 × 0.56[a] + HR CBZ (tentative)
RD-RA 3: sum of carbendazim and 5-hydroxy-carbendazim, expressed as carbendazim				
Swine, bovine and equine meat	0.02*	STMR muscle (tentative)	0.02*	HR muscle (tentative)
Swine, bovine and equine fat	0.02*	STMR (tentative)	0.02*	STMR (tentative)
Swine, bovine and equine liver	0.02*	STMR (tentative)	0.02*	STMR (tentative)
Swine, bovine and equine kidney	0.02*	STMR (tentative)	0.02*	STMR (tentative)
RD-RA 4: sum of carbendazim, 5-hydroxy-carbendazim and 4-hydroxy-carbendazim, expressed as carbendazim				
Cattle and horse milk	0.02*	STMR (tentative)	0.02*	STMR (tentative)

Abbreviations: CBZ, carbendazim; TM, thiophanate-methyl.

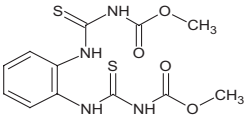
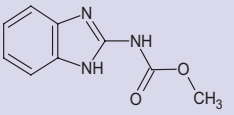
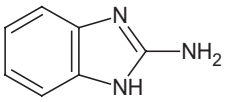
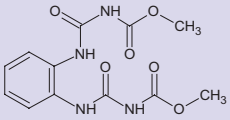
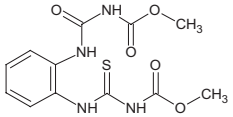
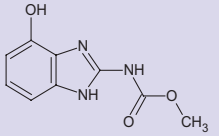
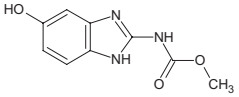
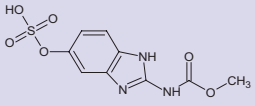
*Indicates that the input value is proposed at the limit of quantification.

[a]Values derived from residue trials have been adjusted assuming that, following boiling/brewing/baking, thiophanate-methyl would be reduced by 15% and converted into carbendazim. Additionally, thiophanate-methyl residues were expressed as carbendazim considering that the ratio between the two molecular weights is 0.56.

[b]Residues arising from the use of carbendazim.

APPENDIX E

Used compound codes

Code/trivial name[a]	IUPAC name/SMILES notation/InChiKey[b]	Structural formula[c]
Thiophanate-methyl	dimethyl (1,2-phenylenedicarbamothioyl)dicarbamate S=C(Nc1ccccc1NC(=S)NC(=O)OC)NC(=O)OC QGHREAKMXXNCOA-UHFFFAOYSA-N	
Carbendazim MBC, CF-27	methyl 1*H*-benzimidazol-2-ylcarbamate O=C(OC)Nc1nc2ccccc2[NH]1 TWFZGCMQGLPBSX-UHFFFAOYSA-N	
2-AB	1*H*-benzimidazol-2-amine Nc1nc2ccccc2[NH]1 JWYUFVNJZUSCSM-UHFFFAOYSA-N	
FH-432	dimethyl (1,2-phenylenedicarbamoyl)biscarbamate O=C(Nc1ccccc1NC(=O)NC(=O)OC)NC(=O)OC ASZYYQWGTGVAMG-UHFFFAOYSA-N	
DX-105	methyl [(2-{[(methoxycarbonyl)carbamothioyl]amino}phenyl) carbamoyl]carbamate S=C(Nc1ccccc1NC(=O)NC(=O)OC)NC(=O)OC NPQZXKVOYZCOW-UHFFFAOYSA-N	
4-hydroxy-carbendazim 4-OH-MBC	methyl (4-hydroxy-1*H*-benzimidazol-2-yl)carbamate O=C(OC)Nc1nc2c(cccc2O)[NH]1 GQINHLNACVSEKE-UHFFFAOYSA-N	
5-hydroxy-carbendazim 5-OH-MBC FH 622	methyl (5-hydroxy-1*H*-benzimidazol-2-yl)carbamate O=C(OC)Nc1nc2cc(O)ccc2[NH]1 UINGPWWYGSJYAY-UHFFFAOYSA-N	
5-hydroxy-carbendazim sulphate 5-hydroxy-carbendazim-S **5-OH-MBC-S**	methyl [5-(sulfooxy)-1*H*-benzimidazol-2-yl]carbamate O=S(=O)(O)Oc1cc2nc(NC(=O)OC)[NH]c2cc1 ZRHUZHWZOGOGOT-UHFFFAOYSA-N	

[a]The metabolite name in bold is the name used in the conclusion.

[b]ACD/Name 2019.1.3 ACD/Labs 2019 Release (File version N05E41, Build 111418, 3 September 2019).

[c]ACD/ChemSketch 2019.1.3 ACD/Labs 2019 Release (File version C05H41, Build 111302, 27 August 2019).

APPENDIX F

Reference list of genotoxicity studies for Thiophanate-methyl and Carbendazim

The reference list in full is provided as background document to the output.

APPENDIX G

Carbendazim (MBC) reference list of studies relevant to assess clastogenicity

The reference list in full is provided as background document to the output.

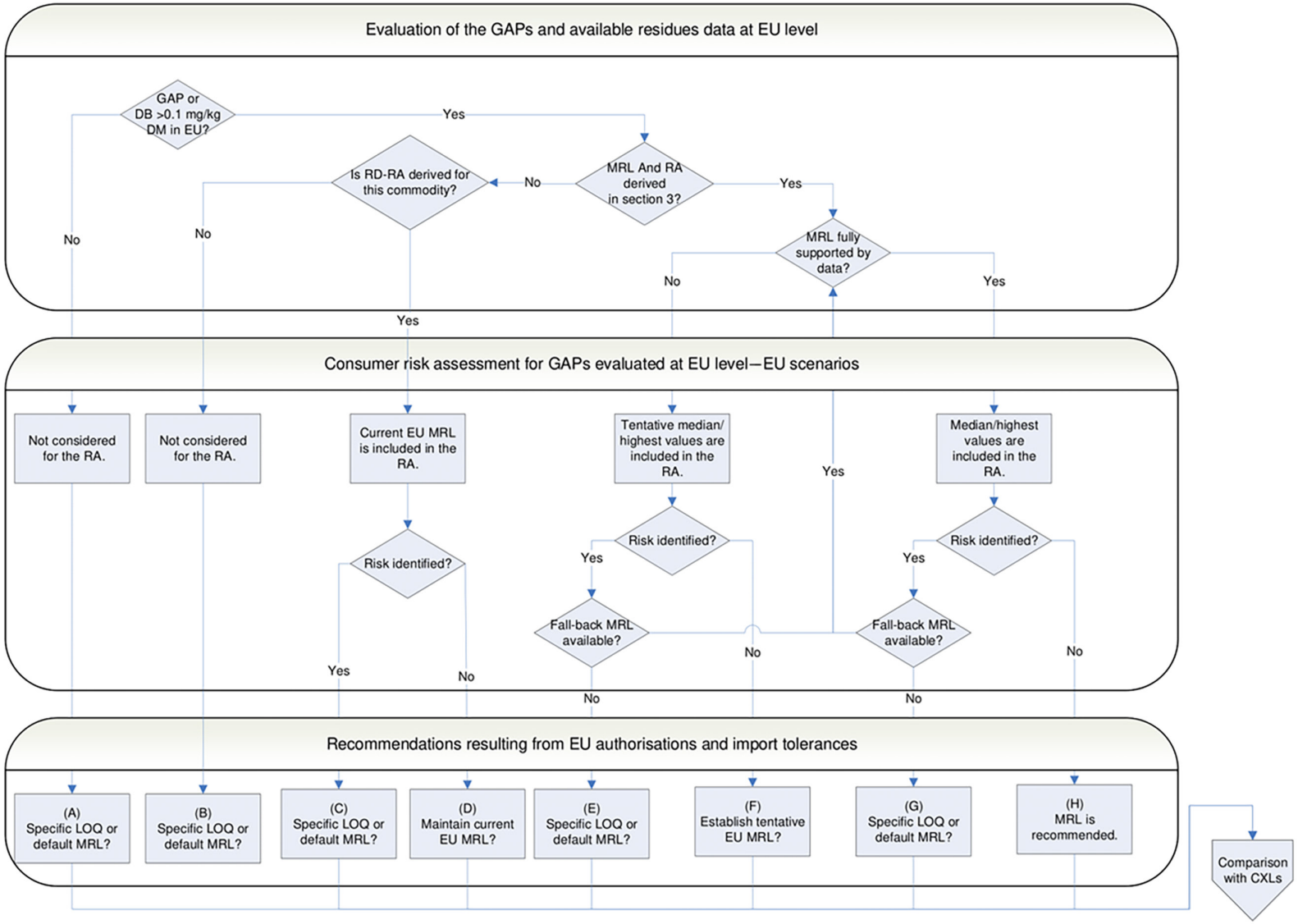
APPENDIX H

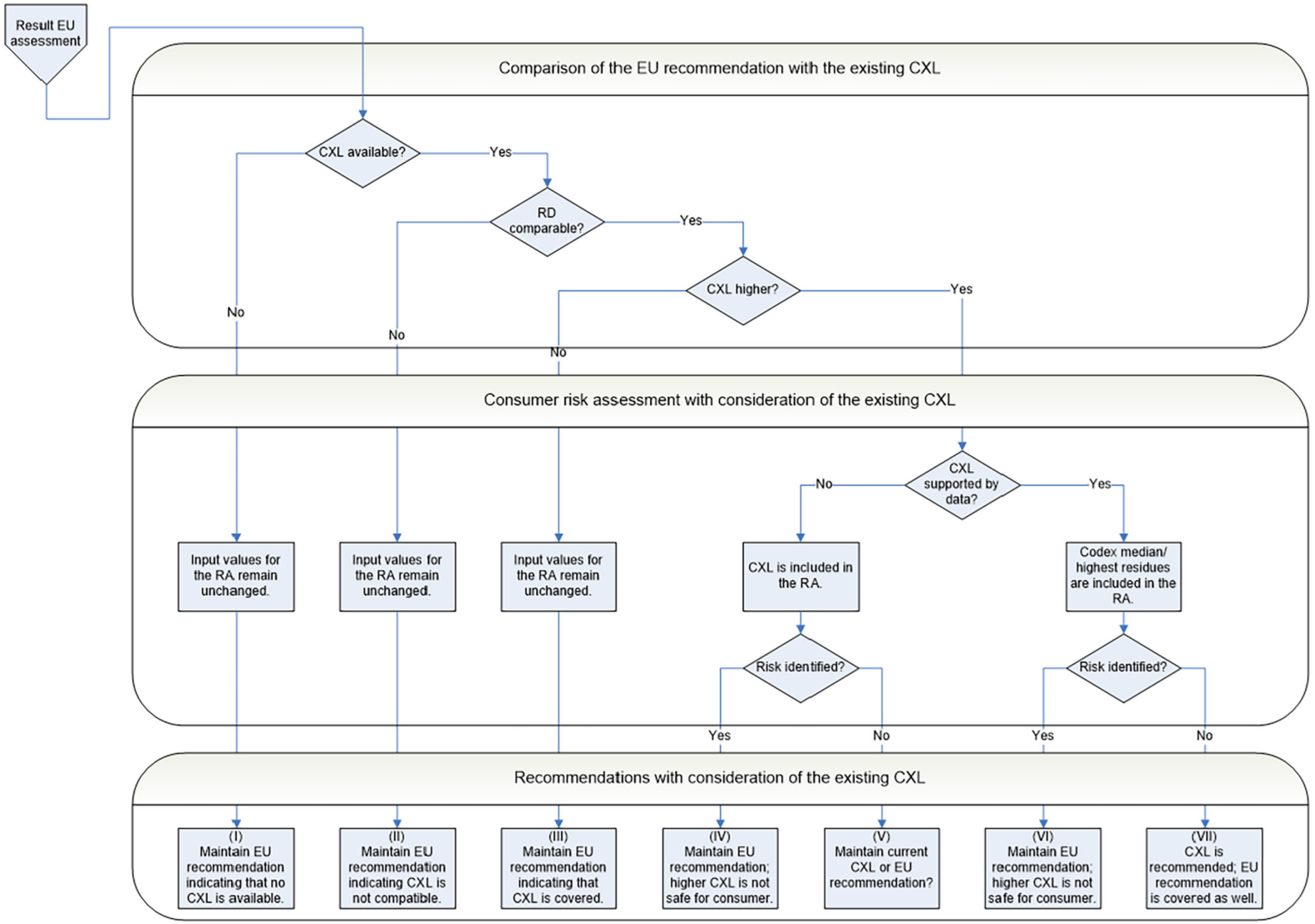
Thiophanate-methyl reference list of studies relevant to assess clastogenicity

The reference list in full is provided as background document to the output.

APPENDIX I

Decision tree for deriving MRL recommendations




Result EU assessment
Comparison of the EU recommendation with the existing CXL
CXL available?
Yes
No
RD comparable?
Yes
No
CXL higher?
Yes
No
Consumer risk assessment with consideration of the existing CXL
Input values for the RA remain unchanged.
Input values for the RA remain unchanged.
Input values for the RA remain unchanged.
CXL supported by data?
No
Yes
CXL is included in the RA.
Codex median/ highest residues are included in the RA.
Risk identified?
Risk identified?
Yes
No
Yes
No
Recommendations with consideration of the existing CXL
(I) Maintain EU recommendation indicating that no CXL is available.
(II) Maintain EU recommendation indicating CXL is not compatible.
(III) Maintain EU recommendation indicating that CXL is covered.
(IV) Maintain EU recommendation; higher CXL is not safe for consumer.
(V) Maintain current CXL or EU recommendation?
(VI) Maintain EU recommendation; higher CXL is not safe for consumer.
(VII) CXL is recommended; EU recommendation is covered as well.