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REASONED OPINION

Review of the existing maximum residue levels for zoxamide according to Article 12 of Regulation (EC) No 396/2005 and setting of an import tolerance for onions, garlic and shallots

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Abstract

According to Article 12 of Regulation (EC) No 396/2005, EFSA has reviewed the maximum residue levels (MRLs) currently established at European level for the pesticide active substance zoxamide. To assess the occurrence of zoxamide residues in plants, processed commodities, rotational crops and livestock, EFSA considered the conclusions derived in the framework of Regulation (EC) No 1107/2009, the MRLs established by the Codex Alimentarius Commission and the European authorisations reported by Member States and the UK (including the supporting residues data). Based on the assessment of the available data, MRL proposals were derived, and a consumer risk assessment was carried out. Although no apparent risk to consumers was identified, some information required by the regulatory framework was missing. Hence, the consumer risk assessment is considered indicative only and some MRL proposals derived by EFSA still require further consideration by risk managers. Furthermore, in accordance with Article 6 of Regulation (EC) No 396/2005, the Applicant Gowan Crop Protection Ltd, submitted a request to the competent national authority in Latvia to set an import tolerance for zoxamide in onions (extrapolated to garlic and shallots) based on the use authorised in USA. The data submitted in support of the request were found to be sufficient to derive MRL proposals for all crops under assessment. Based on the risk assessment results, EFSA concluded that the short-term and long-term intake of residues resulting from the use of zoxamide according to the agricultural practices on onions, garlic and shallots is unlikely to present a risk to consumer health.

KEYWORDS

consumer risk assessment, fungicide, MRL review, Regulation (EC) No 396/2005, zoxamide

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SUMMARY

Zoxamide was included in Annex I to Council Directive 91/414/EEC on 1 April 2004 by Commission Directive 2003/119/EC and has been deemed to be approved under Regulation (EC) No 1107/2009, in accordance with Commission Implementing Regulation (EU) No 540/2011, as amended by Commission Implementing Regulation (EU) No 541/2011.

As the active substance was approved before the entry into force of Regulation (EC) No 396/2005 on 2 September 2008, the European Food Safety Authority (EFSA) is required to provide a reasoned opinion on the review of the existing maximum residue levels (MRLs) for that active substance in compliance with Article 12(2) of the aforementioned regulation.

As the basis for the MRL review, on 15 September 2022, EFSA initiated the collection of data for this active substance. In a first step, Member States and the UK were invited to submit by 13 October 2022 their national good agricultural practices (GAPs) that are authorised nationally and the GAPs in non-EU countries for which import tolerances are authorised, in the format of specific GAP forms, allowing the designated rapporteur Member State Latvia (LV) to identify the critical GAPs in the format of a specific GAP overview file. Subsequently, Member States and the UK were requested to provide residue data supporting the critical GAPs, within a period of 1 month, by 25 January 2023. On the basis of all the data submitted by Member States, the UK and the EU Reference Laboratories for Pesticides Residues (EURLs), EFSA asked the rapporteur Member State (RMS) to complete the Pesticide Residues Overview File (PROFile) and to prepare a supporting evaluation report. The PROFile and evaluation report and an updated GAP overview file were provided by the RMS to EFSA on 05 April 2023. Subsequently, EFSA performed the completeness check of these documents with the RMS. The outcome of this exercise including the clarifications provided by the RMS was compiled in the completeness check report.

Furthermore, in accordance with Article 6 of Regulation (EC) No 396/2005, the Applicant Gowan Crop Protection Ltd submitted a request to the national competent authority in Latvia to set an import tolerance for zoxamide in onions (extrapolated to garlic and shallots) based on the use authorised in the United States of America (USA). The Evaluating Member State Latvia (EMS) drafted an evaluation report in accordance with Article 8 of Regulation (EC) No 396/2005, which was submitted to the European Commission and forwarded to EFSA. EFSA assessed the application and the evaluation report as required by Article 10 of the regulation (EC) No 396/2005. EFSA identified data gaps and points which needed further clarification, which were requested from the EMS. On 3 July 2023, the EMS submitted the requested information and a revised evaluation report, which replaced the previously submitted evaluation report.

For reasons of efficiency EFSA also assessed this application in this reasoned opinion.

Based on the information provided by the RMS/EMS, Member States, the UK and the EURLs, and taking into account the conclusions derived by EFSA in the framework of Regulation (EC) No 1107/2009 and the MRLs established by the Codex Alimentarius Commission (CAC), EFSA prepared in August 2023 a draft reasoned opinion, which was circulated to Member States and the EURLs for consultation via a written procedure. Comments received by 1 September 2023 were considered during the finalisation of this reasoned opinion. The following conclusions are derived.

The metabolism of zoxamide in plant was investigated in primary and rotational crops. According to the results of the metabolism and the hydrolysis studies, the residue definition for enforcement in primary, rotational crops, honey and processed commodities can be proposed as zoxamide (sum of constituent isomers) while for risk assessment can be proposed as sum of zoxamide and metabolite RH-141452, expressed as zoxamide. For processed commodities, a separate residue definition for risk assessment for metabolite RH-150721 was also proposed. An analytical method is available for the enforcement of the proposed residue definition in the main four plant matrix groups and in honey at the limit of quantification (LOQ) of 0.01 mg/kg. Independent laboratory validation (ILV) for high acid content commodities and honey were missing (data gaps). According to the EURLs, the LOQ of 0.01 mg/kg is achievable by using the QuEChERS method in routine analyses in the main four plant matrix groups, black tea and honey.

Available residue trials data were considered sufficient to derive MRL proposals as well as risk assessment values for all commodities under evaluation, except for table grapes, wine grapes, aubergines and honey, where tentative MRLs are derived and for spring onions/Welsh onions and chives for which no residue trials were available (data gap).

Zoxamide is authorised for use on potatoes that might be fed to livestock. Livestock dietary burden calculations were therefore performed for different groups of livestock according to OECD guidance. Since the calculated dietary burdens for all groups of livestock were found to be below the trigger value of 0.004 mg/kg bw per day, further investigation of residues as well as the setting of MRLs in commodities of animal origin is unnecessary.

Chronic consumer exposure resulting from the authorised uses reported in the framework of this review and from the new intended import tolerance was calculated using revision 3.1 of the EFSA PRIMo. For those commodities where data were insufficient to derive a MRL, EFSA considered the existing EU MRL for an indicative calculation. The highest chronic exposure represented 0.5% of the acceptable daily intake (ADI) (PT general population). Acute exposure calculations were not carried out for the parent because an acute reference dose (ARfD) was not deemed necessary for this active substance.

Apart from the MRLs evaluated in the framework of this review, internationally recommended CXLs have also been established for zoxamide. Additional calculations of the consumer exposure, considering these CXLs, were therefore carried out and the highest chronic exposure did not change, accounting to 0.5% of the ADI (PT general population).

Since metabolite RH-150721 was proposed for separate residue definition for processing commodities, consumer exposure calculations were performed for the potential exposure to this metabolite in processed commodities. Considering the large margin of safety for the chronic exposure of raw commodities respect to the ADI of 0.5 mg/kg bw per day set for parent (0.5% of the ADI, PT general population), exceedances of the ADI of 0.04 mg/kg bw per day set for metabolite RH-150721 are not expected. Therefore, only acute exposures were calculated for metabolite RH-150721. As a worst-case

scenario, it was assumed a full conversion of the parent to the metabolite. The highest acute exposure was calculated for pumpkin (boiled), representing 49% of the ARfD.

Based on the risk assessment results, EFSA concluded that the short-term and long-term intake of residues resulting from the use of zoxamide according to the existing uses, the new intended agricultural practices on onions, garlic and shallots and the existing CXLs are unlikely to present a risk to consumer health.

BACKGROUND

Regulation (EC) No 396/2005[1] (hereinafter referred to as 'the Regulation') establishes the rules governing the setting and the review of pesticide maximum residue levels (MRLs) at European level. Article 12(2) of that Regulation stipulates that the European Food Safety Authority (EFSA) shall provide, within 12 months from the date of the inclusion or non-inclusion of an active substance in Annex I to Council Directive 91/414/EEC,[2] a reasoned opinion on the review of the existing MRLs for all active substances included in Annex I to Council Directive 91/414/EEC before 2 September 2008.

Zoxamide was included in Annex I to Council Directive 91/414/EEC on 1 April 2004 by means of Commission Directive 2003/119/EC[3] which has been deemed to be approved under Regulation (EC) No 1107/2009,[4] in accordance with Commission Implementing Regulation (EU) No 540/2011,[5] as amended by Commission Implementing Regulation (EU) No 541/2011.[6] Therefore, EFSA initiated the review of all existing MRLs for that active substance.

By way of background information, zoxamide was evaluated by UK, designated originally as rapporteur Member State (RMS) in the framework of Council Directive 91/414/EEC and was included in Annex I to directive 91/414/EEC on 1 April 2004 by Commission Directive 2003/119/EC which has been deemed to be approved under Regulation (EC) No 1107/2009, in accordance with Commission Implementing Regulation (EU) No 540/2011, as amended by Commission Implementing Regulation (EU) No 541/2011. The approval of zoxamide is restricted to uses as fungicide. In 2016, EFSA initiated the peer review process for the renewal of the approval of zoxamide in accordance with Implementing Regulation (EU) No 844/2012.[7] The EFSA conclusion of the pesticide risk assessment of zoxamide has been adopted on 18 August 2017 (EFSA, 2017).

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

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

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

As the basis for the MRL review, on 15 September 2022, EFSA initiated the collection of data for this active substance. In a first step, Member States and UK[8] were invited to submit by 13 October 2022 their good agricultural practices (GAPs) that are authorised nationally and the GAPs in non-EU countries for which import tolerances (IT) are authorised, in the format of specific GAP forms. In the framework of this consultation, 15 Member States and the UK provided feedback on their national authorisations of zoxamide. Based on the GAP data submitted, the designated RMS, Latvia, was asked to identify the critical GAPs to be further considered in the assessment, in the format of a specific GAP overview file. Subsequently, in a second step, Member States and the UK were requested to provide residue data supporting the critical GAPs by 25 January 2023.

On the basis of all the data submitted by Member States, the UK and the EU Reference Laboratories for Pesticides Residues (EURLs), EFSA asked Latvia to complete the PROFile and to prepare a supporting evaluation report. The PROFile and the supporting evaluation report, and an updated GAP overview file, were submitted to EFSA on 05 April 2023. Subsequently,

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

[2]Council Directive 91/414/EEC of 15 July 1991 concerning the placing of plant protection products on the market. OJ L 230, 19.8.1991, p. 1–32. Repealed by Regulation (EC) No 1107/2009.

[3]Commission Directive 2003/119/EC of 5 December 2003 amending Council Directive 91/414/EEC to include mesosulfuron, propoxycarbazone and zoxamide as active substances. OJ L 325, 12.12.2003, p. 41–43.

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

[5]Commission Implementing Regulation (EU) No 540/2011 of 25 May 2011 implementing Regulation (EC) No 1107/2009 of the European Parliament and of the Council as regards the list of approved active substances. OJ L 153, 11.6.2011, p. 1–186.

[6]Commission Implementing Regulation (EU) No 541/2011 of 1 June 2011 amending Implementing Regulation (EU) No 540/2011 implementing Regulation (EC) No 1107/2009 of the European Parliament and of the Council as regards the list of approved active substances. OJ L 153, 11.6.2011, p. 187–188.

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

[8]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 in particular with the Protocol on IE/NI, the EU requirements on data reporting are also applicable to NI.

EFSA performed the completeness check of these documents with the RMS. The outcome of this exercise including the clarifications provided by the RMS was compiled in the completeness check report.

Furthermore, in accordance with Article 6 of Regulation (EC) No 396/2005, the Applicant Gowan Crop Protection Ltd submitted a request to the competent national authority in Latvia to set an import tolerance for zoxamide in onions (extrapolated to garlic and shallots) based on the use authorised in USA. The EMS drafted an evaluation report in accordance with Article 8 of Regulation (EC) No 396/2005, which was submitted to the European Commission and forwarded to the European Food Safety Authority (EFSA). EFSA assessed the application and the evaluation report as required by Article 10 of the MRL regulation. EFSA identified data gaps and points which needed further clarification, which were requested from the EMS. Following the submission of the requested toxicological studies, a pesticide peer review experts' meeting on zoxamide mammalian toxicity took place on 21 April 2023. On 3 July 2023, the EMS submitted the requested information and a revised evaluation report (Latvia, 2019), which replaced the previously submitted evaluation report.

For reasons of efficiency, this application was also assessed in this reasoned opinion.

Considering all the available information, and taking into account the MRLs established by the Codex Alimentarius Commission (CAC) (i.e. codex maximum residue limit; CXLs), EFSA prepared in August 2023 a draft reasoned opinion, which was circulated to Member States and the EURLs for commenting via a written procedure. All comments received by 01 September 2023 were considered by EFSA during the finalisation of the reasoned opinion.

The **evaluation reports** submitted by the RMS/EMS in the framework of the MRL application (Latvia, 2019) and in the framework of the MRL review (Latvia, 2023), taking into account also the information provided by Member States and the UK during the collection of data, and the **EURLs report on analytical methods** (EURLs, 2023) are considered as main supporting documents to this reasoned opinion and, thus, made publicly available.

In addition, further supporting documents to this reasoned opinion are the **completeness check report** (EFSA, 2023a), the report on the pesticide peer review TC 100–zoxamide-mammalian toxicity (EFSA, 2023b) and the **Member States consultation report** (EFSA, 2023c). These reports are developed to address all issues raised in the course of the review, from the initial completeness check to the reasoned opinion. Furthermore, the exposure calculations for all crops considered in the framework of this assessment performed using the EFSA Pesticide Residues Intake Model (**PRIMo**) and the **PROFile** as well as the **GAP overview file** listing all authorised uses are key supporting documents and made publicly available as background documents to this reasoned opinion.[9] A screenshot of the report sheet of the PRIMo is presented in Appendix C.

Terms of reference

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

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

According to Article 10 of Regulation (EC) No 396/2005, EFSA shall provide a reasoned opinion on:

- the risks to the consumer and where relevant to animals associated with the setting, modification or deletion of an MRL

The active substance and its use pattern

Zoxamide is the ISO common name for (RS)-3,5-dichloro-N-(3-chloro-1-ethyl-1-methyl-2-oxopropyl)-p-toluamide (IUPAC).

The chemical structure of the active substance and its main metabolites are reported in Appendix F.

The EU MRLs for zoxamide are established in Annexes II and IIIB of Regulation (EC) No 396/2005.

Codex maximum residue limits (CXLs) for zoxamide were also established by the Codex Alimentarius Commission (CAC). An overview of the MRL changes that occurred since the entry into force of the Regulation mentioned above is provided below (Table 1).

[9]Background documents to this reasoned opinion are published on OpenEFSA portal and are available at the following link: https://open.efsa.europa.eu/study-inventory/EFSA-Q-2008-649.

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

Procedure	Legal implementation	Remarks
MRL application	Regulation (EC) No 171/2017[a]	Lettuces and salad plants, spinaches and similar leaves and herbs and edible flowers (EFSA, 2016)
Implementation of CAC (2010)	Regulation (EC) No 520/2011[b]	Cucurbits with edible and inedible peel, CCPR 42 (EFSA, 2010)

[a]Commission Regulation (EU) 171/2017 of 30 January 2017 amending Annexes II, III and IV to Regulation (EC) No 396/2005 of the European Parliament and of the Council as regards maximum residue levels for aminopyralid, azoxystrobin, cyantraniliprole, cyflufenamid, cyproconazole, diethofencarb, dithiocarbamates, fluazifop-P, fluopyram, haloxyfop, isofetamid, metalaxyl, prohexadione, propaquizafop, pyrimethanil, Trichoderma atroviride strain SC1 and zoxamide in or on certain products. OJ L 30, 3.2.2017, p. 45–111.

[b]Commission Regulation (EU) No 520/2011 of 25 May 2011 amending Annexes II and III to Regulation (EC) No 396/2005 of the European Parliament and of the Council as regards maximum residue levels for benalaxyl, boscalid, buprofezin, carbofuran, carbosulfan, cypermethrin, fluopicolide, hexythiazox, indoxacarb, metaflumizone, methoxyfenozide, paraquat, prochloraz, spirodiclofen, prothioconazole and zoxamide in or on certain products. OJ L 140, 27.5.2011, p. 2–47.

For the purpose of this MRL review, all the uses of zoxamide currently authorised within the EU as submitted by the Member States and the UK during the GAP collection, have been reported by the RMS in the GAP overview file. The critical GAPs identified in the GAP overview file were then summarised in the PROFile and considered in the assessment. The details of the authorised critical GAPs received under the MRL review and the additional GAP for zoxamide provided in the framework of the MRL application are given in Appendix A.

ASSESSMENT

EFSA has based its assessment on the following documents:

- the PROFile submitted by the RMS;
- the evaluation report accompanying the PROFile (Latvia, 2023);
- the renewal assessment report (RAR) and its addenda prepared under Commission Regulation (EC) 1107/2009 (Latvia, 2016, 2017);
- the conclusion on the peer review of the pesticide risk assessment of the active substance zoxamide (EFSA, 2017);
- the Joint Meeting on Pesticide residues (JMPR) Evaluation report (FAO, 2007, 2009b);
- the previous reasoned opinion on zoxamide (EFSA, 2016);
- the evaluation report submitted by the EMS in the framework of the MRL application (Latvia, 2019);
- the report on the pesticide peer review TC 100–zoxamide-mammalian toxicity (EFSA, 2023b).

For this assessment, the data requirements established in Regulation (EU) No 544/2011[10] and the relevant guidance documents are applicable (EFSA, 2019b; European Commission, 1997a, 1997b, 1997c, 1997d, 1997e, 1997f, 1997g, 2020; OECD, 2011, 2013). The assessment is performed in accordance with the legal provisions of the Uniform Principles for the Evaluation and the Authorisation of Plant Protection Products adopted by Commission Regulation (EU) No 546/2011.[11]

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

The toxicological profile of the active substance zoxamide and its metabolites was peer reviewed in 2017 and its outcome reported in an EFSA conclusion (EFSA, 2017); the toxicological reference values were implemented through Regulation (EU) 2018/692[12] and renewal report (European Commission, 2018). Additional toxicological information on metabolites was submitted to the EMS in support to the MRL application (Latvia, 2019). This information was discussed during the Pesticides Peer Review teleconference 100 (EFSA, 2023b).[13]

The data are summarised in Appendix B.1 (list of end-points) and the outcome of the metabolites assessment is presented in Table 2.

Based on a complete and negative genotoxicity data package in vitro for each metabolite, consisting of gene mutation in bacteria and in mammalian cells and in vitro micronucleus test, the six metabolites RH-129151, RH-141288, RH-141452, RH-141455, RH-150721 and RH-24549 are concluded unlikely to be genotoxic. Metabolite **RH-141288** is

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

[11]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.

[12]Commission Implementing Regulation (EU) 2018/692 of 7 May 2018 renewing the approval of the active substance zoxamide 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. OJ L 117, 8.5.2018, p. 9–12.

[13]See experts' consultation point 2.1 at the Pesticide Peer Review Teleconference 100 (EFSA, 2023).

considered a major rat metabolite and the acceptable daily intake (ADI) established for the parent zoxamide is applicable to this metabolite. The ADI of the parent covers also the toxicological profile of RH-141452 and RH-24549. For **RH-141452**, this conclusion is based on short-term toxicity studies in rats presenting a no observed adverse effect level (NOAEL) of 538 mg/kg bw per day to which, applying an uncertainty factor (UF) of 1000, results in a similar ADI as for the parent. Since the ADI for zoxamide is based on a 1-year toxicity study in dogs presenting a significantly lower NOAEL than in rats (50 vs. 1500 mg/kg bw per day, respectively), and since zoxamide metabolites short-term toxicity investigations were performed only in rats (and not in dogs), an additional UF of 10 is considered appropriate to derive ADIs for zoxamide metabolites. However, it was noted that a specific ADI of 0.54 mg/kg bw per day can also be used for RH-141452 metabolite if needed, based on the referred 90-day toxicity study in rats and applying an UF of 1000. Based on its chemical structure similarity with RH-141452, read-across of the toxicological profile of **RH-24549** was considered appropriate.

The metabolites RH-141455, RH-150721 and RH-129151 were found to be potentially more toxic than zoxamide and specific toxicological reference values were set for these metabolites. For **RH-141455**, an ADI of 0.3 mg/kg bw per day was derived, based on the NOAEL of 368 mg/kg bw per day for reduced body weight gain in males in a 14-day toxicity study in rats and applying an UF of 1000. This ADI is supported by the lowest observed adverse effect level (LOAEL) of 924 mg/kg bw per day in the 90-day toxicity study in rats and applying an additional UF of 3 to account for the LOAEL. No ARfD is considered needed as was not defined for the parent and the limited data package does not indicate the occurrence of acute effects.

For **RH-150721**, an ADI of 0.04 mg/kg bw per day was set, based on the NOAEL of 44 mg/kg bw per day for reduced body weight gain in the 90-day toxicity study in female rats and applying an UF of 1000. The ARfD is 0.22 mg/kg bw, based on the LOAEL of 66 mg/kg bw per day for reduced body weight gains in males and females from day 1–2 in the 14-day toxicity study in rats and applying an UF of 300. Read across of the toxicological profile of this metabolite was considered appropriate for metabolite **RH-129151**, based on chemical structure and functional groups comparison. Accordingly, the ADI and ARfD of RH-150721 are applicable to RH-129151.

TABLE 2 Overview of the toxicological profile of zoxamide metabolites.

Name (code)	% of the applied/absorbed dose in excreta, tissues and downstream metabolic pathway	Genotoxicity conclusion and basis	General toxicity conclusion and basis
RH-141288 identified > 10% in hydrolysis study with zoxamide	4%–6.4% in faeces; 7.8%–8.6% of glucuronic acid conj. in bile (corrected by oral absorption of 60% represents > 10% of absorbed dose)	Ames, in vitro gene mutation and in vitro MN tests: (–) Unlikely to be genotoxic	The metabolite (in its glucuronic acid conjugated form) is considered a major metabolite in rat metabolism studies and its chemical structure similar to the parent The ADI set for the parent, zoxamide, is applicable to RH-141288
RH-141452	n.d. postulated metabolite/ intermediate < 2% amino acid conj. (M20) found in urine	Ames, in vitro gene mutation and in vitro MN tests: (–) Unlikely to be genotoxic	The ADI of the parent covers the toxicity of the metabolite. If needed, an ADI of 0.54 mg/kg bw per day may be used based on the NOAEL of 538 mg/kg bw per day from the 90-day toxicity study in rats, applying an overall UF of 1000 No ARfD is needed as was not defined for the parent, the limited data package available does not indicate acute effects
RH-24549 identified > 10% in hydrolysis study with zoxamide	n.d. postulated intermediate	Ames, in vitro gene mutation and in vitro MN tests: (–) Unlikely to be genotoxic	Functional groups were analysed for the metabolite and the parent. The closest structure similarity was seen with metabolite RH-141452 (which is also its precursor in the hydrolysis) and read-across was considered appropriate. The ADI set for RH-141452 is applicable to RH-24549
RH-141455	n.d. postulated metabolite	Ames, in vitro gene mutation and in vitro MN tests: (–) Unlikely to be genotoxic	The ADI is 0.3 mg/kg bw per day, based on the NOAEL of 368 mg/kg bw per day for reduced body weight gain in males in a 14-day toxicity study in rats and applying an UF of 1000; the ADI is supported by the LOAEL of 924 mg/kg bw per day in the 90-day toxicity study in rats and applying an additional UF of 3 to account for the LOAEL No ARfD is required, as was not defined for the parent
RH-150721 identified > 10% in hydrolysis study with zoxamide	n.d. postulated intermediate	Ames, in vitro gene mutation and in vitro MN tests: (–) Unlikely to be genotoxic	The ADI is 0.04 mg/kg bw per day, based on the NOAEL of 44 mg/kg bw per day for reduced bw gain in the 90-day toxicity study in female rats and applying an UF of 1000. The ARfD is 0.22 mg/kg bw, based on the LOAEL of 66 mg/kg bw per day for reduced body weight gains in males and females from day 1–2 in the 14-day toxicity study in rats and applying an UF of 300.

TABLE 2 (Continued)

Name (code)	% of the applied/absorbed dose in excreta, tissues and downstream metabolic pathway	Genotoxicity conclusion and basis	General toxicity conclusion and basis
RH-129151 identified > 10% in hydrolysis study with zoxamide	n.d. Postulated intermediate	Ames, in vitro gene mutation and in vitro MN tests: (–) Unlikely to be genotoxic	RH-150721 was shown to be the most potent zoxamide metabolite assessed. Although RH-129151 presents an additional functional group (cycloketone) compared to either the parent or other zoxamide metabolites, read-across from RH-150721 is considered to represent a worst case with similar level of uncertainty The ADI and ARfD set for RH-150721 are applicable to RH-129151

Abbreviations: (–), negative; ADI, acceptable daily intake; ARfD, acute reference dose; conj., conjugate; LOAEL, lowest observed adverse effect level; MN, micronucleus; n.d., not detected/not identified; NOAEL, no observed adverse effect level; UF, uncertainty factor.

2 | RESIDUES IN PLANTS

2.1 | Nature of residues and methods of analysis in plants

2.1.1 | Nature of residues in primary crops and in honey

In the framework of the peer review, the metabolism in primary crops was investigated after foliar spray application in fruits (grape, tomato, cucumber), pulses and oilseeds (pea) and root crops (potato) using zoxamide ^{14}C-labelled in the phenyl ring (EFSA, 2017). In fruits, zoxamide was the main component of the total radioactive residue (TRR) in tomato (44%) and in both cucumber (98%) and grape (98%). The remaining TRR was extensively metabolised to a range of metabolites representing less than 10% TRR in these commodities, except for metabolite RH-141452 which was observed only in tomato and constituted with 15% TRR (0.044 mg/kg) and 11% (0.056 mg/kg), being a major metabolite in green and red tomatoes, respectively. While zoxamide remained with more than 90% the predominant compound in peas straw and pods, in fresh and dried peas, the residue of zoxamide decreased to 18% and 12%, respectively, and lead to incorporation of radioactivity in the natural compounds. In potatoes, two major metabolites RH-141452 and RH-141455 were observed at 21% TRR (0.037 mg/kg) and 39% TRR (0.067 mg/kg), respectively. Parent zoxamide was not found in potato tubers.

Regarding honey, honey is a product originated from sugary secretions of plants (floral nectar mainly). Based on the similar results of metabolism studies in the three different primary crop groups, EFSA expects that residues in floral nectar resulting from the use of zoxamide in primary crops would also consist mainly of zoxamide. The nectar is processed by bees following a process of regurgitation and then the honey is stored under specific conditions in the beehives before harvesting. Further information, on whether enzymatic processes occurring in the bee gut involved in the production of honey or the storage in the beehive have an impact on the nature of residues is not available, but in principle would be desirable (European Commission, 2018).

2.1.2 | Nature of residues in rotational crops

Zoxamide is authorised in crops that can be grown in rotation. The geometric mean DT_{50} in soil of zoxamide is 5.5 days, while the DT_{50} of soil metabolites are less than 60 days (EFSA, 2017). Therefore, in principle further investigation on residues in rotational crops are not required.

Nevertheless, a confined rotational crop study, performed with ^{14}C-labelled zoxamide applied directly to bare soil at a rate of 4 × 500 g a.s./ha, was assessed in the framework of the peer review (EFSA, 2017). Leafy vegetables (mustard), root (radish/turnip), small grain (wheat/sorghum) and oilseed (soybean) crops were planted into the soil at 30, 137/145, 210 or 365 days after the last application (DALA). Zoxamide was not detected in any of the analysed plant parts, instead several metabolites were observed among which RH-141452 was identified mainly in the immature parts of the crops [max 23.5% TRR (0.023 mg/kg) in immature soybean forage] and to a lower extent in mature crops [max 7% TRR (0.004 mg/kg) in radish tops]. However, it remains unclear whether degradation of zoxamide occurred in soil with the preferential plant uptake of metabolites or whether the degradation of zoxamide is part of the metabolism in plants (EFSA, 2017). Nevertheless, since no additional metabolites were observed in this study, the metabolism in rotational crops was considered similar to the metabolism in primary crops (EFSA, 2017).

2.1.3 | Nature of residues in processed commodities

In the framework of the peer review, a radiolabelled vinification study analysing for zoxamide, RH-150721 (sum of isomers) and RH-139432 was provided as a surrogate of the standard hydrolysis study. Data from this study give an indication that

a significant degradation will occur to RH-150721 (sum of isomers). However, it was noted that the nature of residue under the standard hydrolysis conditions at processing was not addressed with this study for the whole range of full processes and a new hydrolysis study performed in accordance with the current recommendations was requested (EFSA, 2017).

New hydrolysis studies with zoxamide, RH-141455, RH-141452 and RH-129151 were reported in the framework of current MRL application (Latvia, 2019) and MRL review (Latvia, 2023).

In the studies performed with parent, zoxamide hydrolysed to form RH-150721 (up to a mean maximum of 46.7% TRR upon pasteurisation), RH-141288 (up to a mean maximum of 27.3% TRR upon sterilisation), RH-24549 (up to a mean maximum of 62.7% TRR upon baking/boiling/brewing), RH-129151 (up to a mean maximum of 20.8% TRR upon sterilisation). Thus, zoxamide is not stable under processing conditions leading to the formation of several degradates upon processing.

Studies performed with RH-141455 and RH-141452 showed that these metabolites are stable under all processing conditions.

Studies performed with RH-129151, showed that it degrades into RH-24549 up to 13.6% TRR, upon pasteurisation, up to 73.2% upon baking/boiling/brewing and up to 13.8% TRR upon sterilisation; into RH-150721 up to 70.8%TRR upon pasteurisation; and into RH-141288 up to 26.7% TRR upon sterilisation.

A study investigating the degradates of zoxamide in processed tomatoes (juice, puree and preserves) was also reported for the MRL review (Latvia, 2023). The only treatment which resulted in significant levels of degradates was puree (obtained from whole tomatoes cooked for 20–30 min), where the formation of RH-129151 and RH-150721 was observed. In the puree zoxamide amounted to 3.1% (0.092 mg/kg) of the radioactivity applied, while RH-129151 and RH-150721 reached levels of 10.9% (0.324 mg/kg) of the radioactivity applied and 6.7% (0.199 mg/kg), respectively. These metabolites were not found in tomatoes juice and preserves.

2.1.4 | Analytical methods for enforcement purposes in plant commodities and in honey

During the peer review (EFSA, 2017), a multiresidue QuEChERS method based on LC–MS/MS was validated for the enforcement of zoxamide (sum of constituent isomers) in high water content (potato, lettuce), high acid content (grapes), high oil content (rapeseed), dry commodities (dry bean) and processed commodities (potato chips and flakes, grape juice, wine and raisins) with a LOQ of 0.01 mg/kg. One additional MRM transition was monitored for confirmation purposes. This primary method is supported by an independent laboratory validation (ILV) only in high water content commodities and missing in high acid content (data gap). Extraction efficiency was addressed in high water content commodities (pea whole plant) and dry commodities (dry peas) (Latvia, 2017). In the framework of this review, uses on grapes (high acid content commodity) were reported, but extraction efficiency on this matrix was not demonstrated. For future MRL applications, demonstration of extraction efficiency in high acid content and high oil content matrices might be required.

In case in future there is the need to quantify R and S isomers individually, an enantioselective analytical method was made available for the quantification of R and S isomers with individual LOQ of 0.005 mg/kg in high water, dry and high oil commodities (Latvia, 2023). ILV was not available.

For honey, validation data of a multiresidue method QuEChERS using high-performance liquid chromatography with tandem mass spectrometry (HPLC-MS/MS) were included by the RMS-Latvia in the Evaluation Report (Latvia, 2023), but the method has not been peer reviewed. Despite the minor deviations from SANTE/2020/12830 (European Commission, 2021), i.e. a multi-flower honey was not tested in the validation and the pH was not determined, EFSA considers the primary detection as sufficiently validated with LOQ of 0.01 mg/kg for zoxamide (sum of constituent isomers). The method also allows the quantification of each isomer (R and S) individually. However, an ILV was missing (data gap).

During the completeness check, the EURLs provided a multi-residue analytical method using LC–MS/MS, with a LOQ of 0.01 mg/kg for the routine analysis of zoxamide (sum of constituent isomers) in the four main matrix groups and in black tea. Zoxamide in honey can be monitored by multiresidue QuEChERS LC–MS/MS with LOQ of 0.01 mg/kg, in routine analysis (EURLs, 2023).

2.1.5 | Stability of residues in plants and in honey

The storage stability of zoxamide and metabolites RH-141452 and RH-141455 and RH-150721 in potatoes and grapes (berries, juice, wine and raisins) was investigated in the framework of the peer review (EFSA, 2017). In addition, new studies submitted under this review investigated the stability of zoxamide [R,S, sum], metabolites RH-141452, RH-141455, RH-150721 [R,S, sum], RH-24549, RH-141288 [R,S, sum] and RH-129151 [R, S, sum] in high water content (tomatoes, cucumbers, onions), high starch content (potatoes) and high acid content commodities (grapes), in honey and in processed products (wine, grape juice, potatoes flakes, fried potatoes and canned tomatoes) stored at ≤ –18°C for up to 26 months (Latvia, 2023).

Overall, parent zoxamide (racemate) and the investigated metabolites were stable for at least 18 months in all matrices except for metabolite RH-129151 which was stable only for 6 months in tomato (raw and processed) and degraded significantly after 3 months in cucumbers, grape berries/bunches, grape juice and wine; and for metabolite RH-150721 that was stable for less than 3 months in cucumbers (see Appendix B.2.1.2).

Zoxamide (racemate) has been demonstrated as stable in frozen honey (high sugar content) samples for at least 85 days.

The RMS also reported a study on the stability of RH-129151 (R, S and sum) in final sample extracts of raw agricultural and processed commodities of grapes (fruits, juice, wine and raisins), potatoes (potato tubers, fried potatoes and potato flakes),

tomatoes (tomato fruits and peeled tomatoes) and cucumber fruits when stored for 8 and 24 h under dark and refrigerated conditions at 4°C (± 2°C). As a result of the spiking experiments, the racemate RH-129151 was considered stable for 24 h in the final sample extracts of all the tested commodities when stored at 4°C (± 2°C) in dark.

2.1.6 | Proposed residue definitions

The metabolism of zoxamide in all primary crops was similar in the three crop groups whereas additional metabolites were identified in potatoes. The metabolism in rotational crops is similar to the metabolism observed in primary crops and the processing of zoxamide leads to the generation of several degradates.

As the parent compound was found to be a sufficient marker in fruits, roots and pulses and oilseeds, rotational crops and processed commodities, the residue definition for enforcement is proposed as zoxamide only (sum of constituent isomers) (for primary, rotational crops, honey and processed commodities).

An analytical method for the enforcement of the proposed residue definition at the LOQ of 0.01 mg/kg in the four main plant matrices and in honey is available (EFSA, 2017). However, ILV for high acid content commodities and honey were missing (data gaps). According to the EURLs, the LOQ of 0.01 is achievable by using multiresidue methods in routine analyses (EURLs, 2023) in the four plant matrix groups, black tea and honey. The analytical standard for zoxamide is commercially available (EURLs, 2023).

In available trials supporting the existing uses and the MRL application, residues of metabolite RH-141452 in fruits occurred at levels above the LOQ in grapes, cucumbers and onions, while metabolite RH-141455 was observed always below the LOQ in all plant commodities. Furthermore, an extensive data set of more than 20 overdosed trials on potatoes reported in the RAR and its addenda (Latvia, 2016, 2017) demonstrate that metabolites RH-141452 and RH-141455 are not expected to occur at levels above the LOQ in potatoes (see also Section 2.2.1). Metabolite RH-150721 was never found at levels above the LOQ in the raw commodities.

For risk assessment, parent and metabolite RH-141452 are toxicologically relevant and thus should be considered in the consumer exposure. Metabolite RH-141452 encountered in the rat metabolism and was considered covered by the toxicological profile of the parent compound (see Section 1). Therefore, the residue for risk assessment in raw commodities from primary and rotational crops and for honey is proposed as the sum of zoxamide and RH-141452, expressed as zoxamide.

The only metabolite consistently found at levels above the LOQ in processed commodities was RH-150721 (e.g. grape juice, must, wine, raisins, and tomato juice, puree, canned). For metabolite RH-150721 an ADI lower than the parent was set; also, an ARfD was derived for this metabolite while for parent was considered not necessary (see Section 1). Therefore, for processed commodities, two separated residue definitions for risk assessment are proposed: sum of zoxamide and RH-141452, expressed as zoxamide; metabolite RH-150721.

2.2 | Magnitude of residues in plants

2.2.1 | Magnitude of residues in primary crops and in honey

To assess the magnitude of zoxamide residues resulting from the reported GAPs, EFSA considered all residue trials reported by the RMS in its evaluation report supporting the MRL review (Latvia, 2023). All residue trial samples considered in this framework were stored in compliance with the conditions for which storage stability of residues was demonstrated. Decline of residues during storage of the trial samples is therefore not expected.

The number of residue trials and extrapolations were evaluated in accordance with the European guidelines on comparability, extrapolation, group tolerances and data requirements for setting MRLs (European Commission, 2020).

Residue trials are not available to support the authorisations on Spring onions/Welsh onions and chives. Therefore, MRL and risk assessment values could not be derived for these crops and the following data gaps were identified:

- Spring onions/Welsh onions: Four trials on Spring onions/Welsh onions compliant with the southern outdoor GAP are required.
- Chives: Four trials on chives compliant with the southern outdoor GAP are required.

For all other crops, available residue trials are sufficient to derive (tentative) MRL and risk assessment values, taking note of the following considerations:

- Table and wine grapes: The number of residue trials analysing for metabolites RH-141452 and supporting the northern and southern GAPs is not compliant with the data requirements for these crops. Nevertheless, considering that in the available trials, this metabolite was always measured at low levels, further trials are not required.
- Aubergines: Although a tentative MRL can be derived from an extrapolation from trials performed on tomatoes with five instead of three applications, four residue trials compliant with the southern GAP and analysing for parent and metabolite RH-141452 are still required (data gap).

- Potatoes: The number of residue trials supporting the southern outdoor/indoor GAP is not compliant with the data requirements for this crop. However, it is noted that an extensive data set of more than 20 overdosed trials performed with 10–7 applications reported in the RAR and its addenda (Latvia, 2016, 2017) demonstrate that residues of parent and metabolites RH-141452 are not expected to occur at levels above the LOQ when zoxamide is applied according to the authorised uses. Therefore, the reduced number of residue trials is considered acceptable in this case because all results were below the LOQ and residues above the LOQ are not expected to occur. Further residue trials are therefore not required.
- Onions: The number of residue trials supporting the southern outdoor GAP is not compliant with the data requirements for this crop. Moreover, metabolite RH-141452 was only analysed in two trials. However, since all results were below the LOQ and the import tolerance GAP is clearly more critical, the reduced number of residue trials is considered acceptable in this case. Further residue trials on onions are therefore not required.
- Cucurbits with inedible peel: The number of residue trials analysing for metabolites RH-141452 and supporting the southern GAP is not compliant with the data requirements for these crops. Nevertheless, considering that the indoor GAP, which is fully supported by data, is clearly more critical, further trials are not required.

Residue trials were analysed separately for parent zoxamide and several metabolites, including RH-141452 which is proposed to be included in the residue definition for risk assessment. To express the residues levels according to the residue definition for risk assessment proposed, the levels of metabolite RH-141452 found in the trials were recalculated as parent equivalents using a correction factor of 1.52 based on the molecular weight (MW) of parent 336.6 g/mol and a MW of RH-141452 of 221.03 g/mol (336.6/221.03 = 1.52). Conversion factors from enforcement to risk assessment were derived for all crops under consideration.

In the framework of the current MRL review, four semi-field (tunnel) trials were performed with honeybees with a use pattern of 3 × 180 g a.s./ha with a minimum interval of 7(+1) days during full flowering phase of *Phacelia tanacetifolia* (Latvia, 2023). This application pattern (3 applications during full flowering) can be considered a worst-case scenario of exposure from the application of zoxamide to the melliferous crops reported in this assessment (e.g. aubergines, cucurbits). Pollen analysis confirmed that the bees gathered nectar mainly from the treated Phacelia (Latvia, 2023). Based on the available residue data, residues up to 0.0784 mg/kg can be found in honey samples, when zoxamide is applied at a rate of 3 × 180 g a.s./ha with a minimum interval of 7(+1) days, resulting in an MRL proposal of 0.2 mg/kg. Residue trials were analysed for parent only, however, since there is a wide margin of safety and the contribution of honey to the overall exposure is minimal (see Section 4), additional trials analysing for metabolite RH-141452 are not required.

Additionally, in order to derive MRLs accommodating the import tolerance for onions (extrapolated to garlic and shallots), EFSA considered all residue trials reported by the EMS (Latvia, 2019). The detailed description of the existing use of zoxamide authorised in the United States in onions, which is the basis for the current MRL application, is reported in Appendix A.4.

In support of the import tolerance MRL application, the applicant provided 12 GAP compliant residue trials performed in different regions of United States and Canada during the 2011 and 2012 growing seasons. All samples taken were analysed for the parent zoxamide compound as well as the metabolites RH-141452 and RH-141455. In all these residue trials, parent zoxamide and the metabolite RH141452 were measured at levels above the LOQ while the metabolite RH141455 was always below the LOQ. Residue of parent zoxamide was within a range of 0.05–0.44 mg/kg resulting in an MRL proposal of 0.7 mg/kg. This MRL proposal is extrapolated to garlic and shallots (European Commission, 2020).

According to the assessments of the EMS, the analytical methods used to analyse the residue trials were sufficiently validated and fit for purpose and the samples of these residue trials were stored under conditions for which integrity of the samples has been demonstrated (Latvia, 2019).

2.2.2 | Magnitude of residues in rotational crops

There were no studies investigating the magnitude of residues in rotational crops available for this review. The rotational confined crop study (Section 2.1.2) was performed with an application rate equivalent to 2.2N rate for the most critical GAP that can be rotated (potatoes). This same GAP on potatoes was assessed in the peer review, where it was concluded that significant individual residue compounds are unlikely to be present in rotational crops (EFSA, 2017). Therefore, it can be concluded that residues of zoxamide and its relevant metabolite RH-141452 in rotational commodities are not expected to exceed 0.01 mg/kg, provided that zoxamide is applied in compliance with the GAPs reported in Appendix A.

2.2.3 | Magnitude of residues in processed commodities

The effect of industrial processing and/or household preparation was assessed on studies conducted on grapes and tomato (Latvia, 2019). An overview of all available processing studies is available in Appendix B.2.2.3. Robust processing factors for zoxamide (fully supported by data) could be derived for all processed commodities: table grapes raisins, wine grapes (pre- and post-pasteurisation) juice, must, wine and tomato juice, puree and canned.

Further processing studies are not required as they are not expected to affect the outcome of the risk assessment. However, if more robust processing factors were to be required by risk managers, in particular for enforcement purposes, additional processing studies would be needed.

2.2.4 | Proposed MRLs

The available data are considered sufficient to derive MRL proposals as well as risk assessment values for all commodities under evaluation, except for table grapes, wine grapes, aubergines and honey where tentative MRLs are derived and for spring onions and chives for which no residue trials were available.

3 | RESIDUES IN LIVESTOCK

Zoxamide is authorised for use on potatoes 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. Since the calculated dietary burdens for all groups of livestock were found to be below the trigger value of 0.004 mg/kg bw per day further investigation of residues as well as the setting of MRLs in commodities of animal origin is unnecessary.

Although not needed for the current MRL review, the metabolism of zoxamide residues in livestock was investigated in lactating goats (Latvia, 2017) and assessed in the framework of the peer review (EFSA, 2017). In this study, zoxamide radiolabelled in the phenyl ring of the molecule was administered orally to a lactating goat once a day for 7 consecutive days. The test material was dosed at levels equivalent to a dietary concentration of 60.7 mg/kg (equivalent to 2.82 mg/kg bw per day). Zoxamide was not detected in the goat study and the metabolites RH-141452 and RH-141455 were observed as terminal compounds of a minor metabolic pathway (EFSA, 2017). It was also noted in the peer review that from the potato metabolism study it was evident that animals will be mainly exposed to RH-141452 and RH-141455, and therefore, the metabolic picture depicted with zoxamide cannot be quantitatively representative for the fate of RH-141452 and RH-141455 in ruminants (EFSA, 2017).

4 | CONSUMER RISK ASSESSMENT

In the framework of this review, only the uses of zoxamide reported by the RMS in Appendix A were considered; however, the use of zoxamide was previously also assessed by the JMPR (FAO, 2007, 2009b). 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. To facilitate consideration of these CXLs by risk managers, the consumer exposure was calculated both with and without consideration of the existing CXLs.

4.1 | Consumer risk assessment without consideration of the existing CXLs

Chronic exposure calculations for all crops reported in the framework of this review were performed using revision 3.1 of the EFSA PRIMo (EFSA, 2018, 2019a). 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, 2009a). For those commodities where data were insufficient to derive an MRL in Section 1, EFSA considered the existing EU MRL for an indicative calculation. All input values included in the exposure calculations are summarised in Appendix D. Acute exposure calculations were not carried out because an acute reference dose (ARfD) was not deemed necessary for this active substance.

The exposure values calculated were compared with the toxicological reference value for zoxamide, derived by EFSA (EFSA, 2017). The highest chronic exposure was calculated for PT general representing 0.5% of the acceptable daily intake (ADI). These calculations indicate that the uses assessed under this review result in a consumer exposure lower than the toxicological reference values. For honey residue trials were analysed for parent only, however, since there is a wide margin of safety and the contribution of honey to the overall exposure is minimal (0.0002%), this is not deemed to have an impact on the consumer risk assessment. These calculations indicate that the uses assessed under this review result in a consumer exposure lower than the toxicological reference values.

4.2 | Consumer risk assessment with consideration of the existing CXLs

To include the CXLs in the calculations of the consumer exposure, CXLs were compared with the EU MRL proposals in compliance with Appendix E and all data relevant to the consumer exposure assessment have been collected from JMPR

evaluations. The residue definition for enforcement in the in the Codex is the same as the one currently in the EU legislation (zoxamide) and consistent with the residue definition proposed in the current review. The residue definition for risk assessment in Codex includes parent only, while for this current review, the inclusion of metabolite RH-141452 was considered necessary. Therefore, the conversion factors derived from the residue trials assessed in this review were also applied to the CXLs.

An overview of the input values used for this exposure calculation is also provided in Appendix D. The exposure values calculated were compared with the toxicological reference value for zoxamide, derived by EFSA (EFSA, 2017). The highest chronic exposure did not change and was calculated for PT general representing 0.5% of the acceptable daily intake (ADI). These calculations indicate that the existing CXLs result in a consumer exposure lower than the toxicological reference values.

4.3 | Consumer risk assessment of metabolite RH-150721 in processed commodities with consideration of the existing CXLs

Since metabolite RH-150721 was proposed for separate residue definition for processing commodities, a consumer risk assessment was performed for the potential exposure to this metabolite in processed commodities.

Considering the large margin of safety for the chronic exposure of raw commodities respect to the ADI of 0.5 mg/kg bw per day set for parent, exceedances of the ADI of 0.04 mg/kg bw per day set for metabolite RH-150721, are not expected. Therefore, only acute exposures were calculated for metabolite RH-150721. As a worst-case scenario, it was assumed a full conversion of the parent to the metabolite considering a correction factor based on the MW of metabolite RH-150721 and the MW of parent (318.19/336.6 = 0.95). The exposure values calculated were compared with the toxicological reference value for RH-150721, derived in Section 1. The highest acute exposure was calculated for pumpkin (boiled), representing 49% of the ARfD. These calculations indicate that, even in the unlikely event that all commodities are consumed processed, the uses assessed under this review and the existing CXLs result in a consumer exposure lower than the toxicological reference values for metabolite RH-150721.

5 | CONCLUSIONS

The metabolism of zoxamide in plant was investigated in primary and rotational crops. According to the results of the metabolism and the hydrolysis studies, the residue definition for enforcement in primary, rotational crops, honey and processed commodities can be proposed as zoxamide (sum of constituent isomers) while for risk assessment can be proposed as sum of zoxamide and metabolite RH-141452, expressed as zoxamide. For processed commodities, a separate residue definition for risk assessment for metabolite RH-150721 was also proposed. An analytical method is available for the enforcement of the proposed residue definition in the main four plant matrix groups and in honey at the LOQ of 0.01 mg/kg. ILV for high acid content commodities and honey were missing (data gaps). According to the EURLs, the LOQ of 0.01 mg/kg is achievable by using the QuEChERS method in routine analyses in the main four plant matrix groups, black tea and honey.

Available residue trials data were considered sufficient to derive MRL proposals as well as risk assessment values for all commodities under evaluation, except for table grapes, wine grapes, aubergines and honey, where tentative MRLs are derived and for spring onions/Welsh onions and chives for which no residue trials were available.

Zoxamide is authorised for use on potatoes that might be fed to livestock. Livestock dietary burden calculations were therefore performed for different groups of livestock according to OECD guidance. Since the calculated dietary burdens for all groups of livestock were found to be below the trigger value of 0.004 mg/kg bw per d, further investigation of residues as well as the setting of MRLs in commodities of animal origin is unnecessary.

Chronic consumer exposure resulting from the authorised uses reported in the framework of this review and from the new intended import tolerance was calculated using revision 3.1 of the EFSA PRIMo. For those commodities where data were insufficient to derive a MRL, EFSA considered the existing EU MRL for an indicative calculation. The highest chronic exposure represented 0.5% of the ADI (PT general population). Acute exposure calculations were not carried out for the parent because an ARfD was not deemed necessary for this active substance.

Apart from the MRLs evaluated in the framework of this review, internationally recommended CXLs have also been established for zoxamide. Additional calculations of the consumer exposure, considering these CXLs, were therefore carried out and the highest chronic exposure did not change, accounting to 0.5% of the ADI (PT general population).

Since metabolite RH-150721 was proposed for separate residue definition for processing commodities, consumer exposure calculations were performed for the potential exposure to this metabolite in processed commodities. Considering the large margin of safety for the chronic exposure of raw commodities respect to the ADI of 0.5 mg/kg bw per day set for parent (0.5% of the ADI, PT general population), exceedances of the ADI of 0.04 mg/kg bw per day set for metabolite RH-150721, are not expected. Therefore, only acute exposures were calculated for metabolite RH-150721. As a worst-case scenario, it was assumed a full conversion of the parent to the metabolite. The highest acute exposure was calculated for pumpkin (boiled), representing 49% of the ARfD.

Based on the risk assessment results, EFSA concluded that the short-term and long-term intake of residues resulting from the use of zoxamide according to the existing uses, the new intended agricultural practices on onions, garlic and shallots and the existing CXLs are unlikely to present a risk to consumer health.

RECOMMENDATIONS

MRL recommendations were derived in compliance with the decision tree reported in Appendix E of the reasoned opinion (see Table 3). All MRL values listed as 'Recommended' in the table are sufficiently supported by data and are therefore proposed for inclusion in Annex II to the Regulation. The remaining MRL values listed in the table are not recommended for inclusion in Annex II because they require further consideration by risk managers (see Table 2 footnotes for details). In particular, some tentative MRLs and existing EU MRLs need to be confirmed by the following data:

1. ILV in one additional matrix besides high water content matrices. Considering the uses reported in this review, the most relevant are high acid content matrices (relevant for table and wine grapes).
2. Residue trials supporting the southern outdoor GAP on Spring onions/Welsh onions and chives.
3. Additional residue trials supporting the southern outdoor GAP on aubergines.
4. ILV for honey.

EFSA also underlines that, according to the information provided by the EURLs, the analytical standard for zoxamide, RH-141455 (2,6-dichloroterephthalic acid) and RH-141452 (3,5-dichloro-4-(hydroxymethyl)benzoic acid) are commercially available (EURLs, 2023).

TABLE 3 Summary table.

Code number	Commodity	Existing EU MRL (mg/kg)	Existing CXL (mg/kg)	Outcome of the review/MRL application	
				MRL (mg/kg)	Comment
Enforcement residue definition: zoxamide (sum of constituent isomers)					
151010	Table grapes	5	5	5	Further consideration needed[a] Data gap # 1
151020	Wine grapes	5	5	5	Further consideration needed[a] Data gap # 1
211000	Potatoes	0.02*	0.02	0.02	Recommended[b]
220010	Garlic	0.02*	–	0.7	Recommended[c]
220020	Onions	0.02*	–	0.7	Recommended[c]
220030	Shallots	0.02*	–	0.7	Recommended[c]
220040	Spring onions/green onions and Welsh onions	0.02*	–	0.02	Further consideration needed[d] Data gap # 2
231010	Tomatoes	0.5	2	2	Recommended[b]
231030	Aubergines/eggplants	0.02*	–	0.5	Further consideration needed[e] Data gap # 3
232010	Cucumbers	2	2	2	Recommended[b]
232020	Gherkins	2	2	2	Recommended[b]
232030	Courgettes	2	2	2	Recommended[b]
233010	Melons	2	2	2	Recommended[f]
233020	Pumpkins	2	2	2	Recommended[f]
233030	Watermelons	2	2	2	Recommended[f]
256020	Chives	30	–	30	Further consideration needed[d] Data gap # 2
1040000	Honey and other apiculture products	0.05*	–	0.2	Further consideration needed[e] Data gap #4
–	Other commodities of plant and/or animal origin	See Reg. 2017/171	–	–	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]MRL is derived from the existing CXL, which is not sufficiently supported by data but for which no risk to consumers is identified; GAP evaluated at EU level, which is also not fully supported by data, would lead to a lower tentative MRL (combination F-V in Appendix E).

[b]MRL is derived from the existing CXL, which is supported by data and for which no risk to consumers is identified; GAP evaluated at EU level, which is also fully supported by data, leads to a lower MRL (combination H-VII in Appendix E).

[c]New MRL derived based on a GAP authorised in USA and Canada fully supported by data. No risk to consumers is identified.

[d]GAP evaluated at EU level is not supported by data but no risk to consumers was identified for the existing EU MRL; no CXL is available (combination D-I in Appendix E).

[e]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 E).

[f]MRL is derived from a GAP evaluated at EU level, which is fully supported by data and for which no risk to consumers is identified; existing CXL is covered by the recommended MRL (combination H-III in Appendix E).

[g]There are no relevant authorisations or import tolerances reported at EU level; no CXL is available. Either a specific LOQ or the default MRL of 0.01 mg/kg may be considered (combination A-I in Appendix E).

ABBREVIATIONS

a.i.	active ingredient
ADI	acceptable daily intake
ARfD	acute reference dose
bw	body weight
CAC	Codex Alimentarius Commission
CF	conversion factor for enforcement residue definition to risk assessment residue definition
DM	dry matter
eq	residue expressed as a.s. equivalent
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–MS/MS	liquid chromatography with tandem mass spectrometry
LOAEL	lowest observed adverse effect level
LOQ	limit of quantification
Mo	monitoring
MRL	maximum residue level
MS	Member States
MS	mass spectrometry detector
MS/MS	tandem mass spectrometry detector
MW	molecular weight
NEDI	national estimated daily intake
NEU	Northern Europe
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
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
SEU	southern European
STMR	supervised trials median residue
TMDI	theoretical maximum daily intake
TRR	total radioactive residue
UF	uncertainty factor
WG	water dispersible granule
WHO	World Health Organization

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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 under this assessment

A.1 | AUTHORISED OUTDOOR USES IN NORTHERN EU

				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 & 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
Table grapes	SI	F	Plasmopara viticola	WG	330 g/kg	Foliar treament – spraying	14–89	4	7	–	–	132 g a.s./ha	28	
Wine grapes	AT, SI	F	Plasmopara viticola	WG	330 g/kg	Foliar treament – spraying	15–89	4	7	–	–	132 g a.s./ha	28	
Potatoes	NL, PL, AT, CZ, DE	F	Late blight (P. infestans)	SC	180 g/L	Foliar treament – spraying	31–93	5	7	–	–	180 g a.s./ha	7	

Abbreviation: MS, Member State.

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

[b]CropLife International Technical Monograph no 2, 7th Edition. Revised March 2017. Catalogue of pesticide formulation types and international coding system.

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

[d]PHI – minimum pre-harvest interval.

A.2 | AUTHORISED OUTDOOR USES IN SOUTHERN EU

				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 & 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
Table grapes	EL, IT	F	Plasmopara viticola	WG	24% (w/w)	Foliar treament – spraying	15–79	5	8	–	–	180 g a.s./ha	28	
Wine grapes	EL, IT	F	Plasmopara viticola	WG	24% (w/w)	Foliar treament – spraying	15–79	5	8	–	–	180 g a.s./ha	28	
Potatoes	IT, EL	F	Late blight (P. infestans)	SC	240 g/L	Foliar treament – spraying	20–80	5	8	–	–	180 g a.s./ha	7	
Garlic	IT, EL	F	Peronospora destructor	SC	240 g/L	Foliar treament – spraying	13–89	4	8	–	–	180 g a.s./ha	14	
Onions	IT, EL	F	Peronospora destructor	SC	240 g/L	Foliar treament – spraying	13–89	4	8	–	–	180 g a.s./ha	14	
Shallots	IT, EL	F	Peronospora destructor	SC	240 g/L	Foliar treament – spraying	13–89	4	8	–	–	180 g a.s./ha	14	

(Continues)

(Continued)

				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 & 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
Spring onions	EL	F	Peronospora destructor	SC	240 g/L	Foliar treament – spraying	13–89	4	8	–	–	180 g a.s./ha	14	
Tomatoes	IT, EL	F	Phytophtora infestans; Alternaria solani	SC	240 g/L	Foliar treament – spraying	20–89	5	8	–	–	180 g a.s./ha	3	
Aubergines	ES, HR, EL	F	Phytophthora infestans	SC	240 g/L	Foliar treament – spraying	13–89	3	7	–	–	148.5 g a.s./ha	3	ES: min. BBCH 13 HR: min. BBCH 51; min. application rate 120 g a.i./ha EL: min BBCH 13, max. BBCH 89; interval 10 days
Cucumbers	IT, EL	F	Pseudoperonospora cubensis	WG	330 g/kg	Foliar treament – spraying	11–89	4	8	–	–	180 g a.s./ha	3	
Gherkins	IT, EL	F	Pseudoperonospora cubensis	SC	240 g/L	Foliar treament – spraying	11–89	4	8	–	–	180 g a.s./ha	3	
Courgettes	IT, EL	F	Pseudoperonospora cubensis	SC	240 g/L	Foliar treament – spraying	11–89	4	8	–	–	180 g a.s./ha	3	
Melons	IT, EL	F	Pseudoperonospora cubensis	SC	240 g/L	Foliar treament – spraying	11–89	4	8	–	–	180 g a.s./ha	3	
Pumpkins	IT, EL	F	Pseudoperonospora cubensis	SC	240 g/L	Foliar treament – spraying	11–89	4	8	–	–	180 g a.s./ha	3	
Watermelons	IT, EL	F	Pseudoperonospora cubensis	SC	240 g/L	Foliar treament – spraying	11–89	4	8	–	–	180 g a.s./ha	3	
Chives	EL	F	Peronospora destructor	SC	240 g/L	Foliar treament – spraying	13–89	3	8	–	–	180 g a.s./ha	14	

Abbreviation: MS, Member State.

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

[b]CropLife International Technical Monograph no 2, 7th Edition. Revised March 2017. Catalogue of pesticide formulation types and international coding system.

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

[d]PHI – minimum pre-harvest interval.

A.3 | AUTHORISED INDOOR USES IN EU

				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 & 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
Tomatoes	IT, EL	I	Phytophtora infestans; Alternaria solani	SC	240 g/L	Foliar treament – spraying	20–85	5	8	–	–	180 g a.s./ha	3	
Cucumbers	IT, EL	I	Pseudoperonospora cubensis	SC	240 g/L	Foliar treament – spraying	11–89	4	8	–	–	180 g a.s./ha	3	
Gherkins	IT, EL	I	Pseudoperonospora cubensis	SC	240 g/L	Foliar treament – spraying	11–89	4	8	–	–	180 g a.s./ha	3	
Courgettes	IT, EL	I	Pseudoperonospora cubensis	SC	240 g/L	Foliar treament – spraying	11–89	4	8	–	–	180 g a.s./ha	3	
Melons	IT, EL	I	Pseudoperonospora cubensis	SC	240 g/L	Foliar treament – spraying	11–89	4	8	–	–	180 g a.s./ha	3	
Pumpkins	IT, EL	I	Pseudoperonospora cubensis	SC	240 g/L	Foliar treament – spraying	11–89	4	8	–	–	180 g a.s./ha	3	
Watermelons	IT, EL	I	Pseudoperonospora cubensis	SC	240 g/L	Foliar treament – spraying	11–89	4	8	–	–	180 g a.s./ha	3	

Abbreviation: MS, Member State.

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

[b]CropLife International Technical Monograph no 2, 7th Edition. Revised March 2017. Catalogue of pesticide formulation types and international coding system.

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

[d]PHI – minimum pre-harvest interval.

A.4 | AUTHORISED USE CONSIDERED UNDER MRL APPLICATION FOR IMPORT TOLERANCE

				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 & 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
Onions, Garlic, Shallots	USA & Canada	F	Bortrytis leaf blight, downy mildew, neck rot, purple blotch, Rust	DF	83 g/kg	Foliar Spray	Protective spray when disease is reported.	1–8	7	Dilute sprays: 144–407 Conc sprays: 96.4–204.3	Conc. sprays: 93.5–140.3 Dilute sprays: 187–1403	135–191 g a.s./ha	7	This is a combination product of zoxamide 8.3% and mancozeb 66.7%

Abbreviation: MS, Member State.

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

[b]CropLife International Technical Monograph no 2, 7th Edition. Revised March 2017. Catalogue of pesticide formulation types and international coding system.

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

[d]PHI – minimum pre-harvest interval.

APPENDIX B

List of end points

B.1 | MAMMALIAN TOXICOLOGY

Other toxicological studies (Regulation (EU) N° 283/2013, Annex Part A, point 5.8)

Studies performed on metabolites or impurities	Genotoxicity:
RH-141288	Ames test: negative *In vitro* gene mutation in Chinese hamster V79 cells: negative *In vitro* micronucleus test in human lymphocytes: negative The metabolite is considered a major metabolite in rat metabolism studies and its chemical structure considered similar to the parent; accordingly, the ADI set for the parent, zoxamide, is applicable to RH-141288.
RH-141452	Rat metabolism study: majority was eliminated unchanged trough urine. Mice acute oral LD_{50} > 5,000 mg/kg bw Genotoxicity: Ames test: negative *In vitro* gene mutation (HPRT-locus) in Chinese hamster V79 cells: negative *In vitro* micronucleus test in Chinese hamster: negative 14-day, rat: NOAEL 416 mg/kg bw per day, based on decreased body weight, food consumption and associated microscopic changes of vacuolation in zona glomerulosa of adrenal cortex, decreased cellularity (thymus, spleen) and decreased secretion (accessory sex glands) at 1,268 mg/kg bw per day 90-day, rat: NOAEL >538 mg/kg bw per day (highest dose tested) **The ADI** of the parent (0.5 mg/kg bw per day) covers the toxicity profile of the metabolite RH-141452, taking into consideration the similarity in the toxicity profile of the metabolite and the parent. If needed, an ADI of 0.54 mg/kg bw per day may be used, based on the NOAEL of 538 mg/kg bw per day from the 90-day toxicity study in rats, applying an overall UF of 1000. **No ARfD** is required, as was not defined for the parent.
RH-24549	Genotoxicity: Ames test: negative *In vitro* gene mutation (HPRT-locus) in Chinese hamster V79 cells: negative *In vitro* micronucleus test in Chinese hamster V79 cells: negative Based on the comparison of chemical structure and functional groups, the ADI set for RH-141452 is applicable to RH-24549.

RH-141455	Rat metabolism study: greater than 96 % radioactivity excreted from faeces and urine was identified to be unchanged RH-141455. Mice acute oral LD_{50}: > 5,000 mg/kg bw Genotoxicity: Ames test: negative *In vitro* mutation test in mouse lymphoma L5178Y cells: negative *In vitro* micronucleus test in human lymphocytes: negative 14-day, rat: NOAEL 368 mg/kg bw per day, based on reduced body weight gain in males at the top dose level of 1,123 mg/kg bw per day. 90-day rat (limit test) LOAEL 924 mg/kg bw per day, based on dehydration, soft stool, caecal enlargement, reduced body weight gain in males. **The ADI is 0.3 mg/kg bw per day**, based on the NOAEL of 368 mg/kg bw per day for reduced body weight gain in males in the 14-day study and applying an UF of 1,000; the ADI is supported by the LOAEL of 924 mg/kg bw per day in the 90-day study and applying an additional UF of 3 to account for the LOAEL. **No ARfD** is required, as was not defined for the parent.
RH-150721	Genotoxicity: Ames test: negative *In vitro* gene mutation in mouse lymphoma L5178Y cells: negative *In vitro* micronucleus test in Chinese hamster V79 cells: negative 14-day, rat: LOAEL 66 mg/kg bw per day, based on reduced body weight gain (at all dose levels tested). 90-day, rat: NOAEL 44 mg/kg bw per day, based on reduced body weight gain in females treated with 134 mg/kg bw per day. **The ADI is 0.04 mg/kg bw per day**, based on the NOAEL of 44 mg/kg bw per day for reduced bw gain in the 90-day study in female rats and applying an UF of 1000. **The ARfD is 0.22 mg/kg bw**, based on the LOAEL of 66 mg/kg bw per day for reduced body weight gains in males and females from day 1-2 in the 14-day toxicity study and applying an UF of 300.
RH-129151	Genotoxicity: Ames test: negative In vitro gene mutation (HPRT-locus) in Chinese hamster V79 cells: negative In vitro micronucleus test in Chinese hamster V79 cells: negative Based on the comparison of chemical structure and functional groups, the ADI and ARfD set for RH-150721 are applicable to RH-129151.

B.2 | RESIDUES IN PLANTS

B.2.1 | Nature of residues and analytical methods for enforcement purposes in plant commodities

B.2.1.1 | Metabolism studies, analytical methods and residue definitions in plants and in honey

Primary crops (available studies)	Crop groups	Crop(s)	Application(s)	Sampling (DAT)	Comment/source
	Fruit crops	Grapes	Foliar application, outdoor, 3 × 1867 g a.s./ha	1	Radiolabelled zoxamide: Phenyl-UL-^{14}C ring (EFSA, 2017)
			Foliar application, outdoor, 3 × 500 g a.s./ha	28	Radiolabelled zoxamide: Phenyl-UL-^{14}C ring (EFSA, 2017)
		Tomato	Foliar application, greenhouse 3 × 860 g a.s./ha	1	Radiolabelled zoxamide: Phenyl-UL-^{14}C ring (EFSA, 2017)
		Cucumber	Foliar application, greenhouse 3 × 1344 g a.s./ha	1	Radiolabelled zoxamide: Phenyl-UL-^{14}C ring (EFSA, 2017)
	Root crops	Potato	Foliar application, outdoor, 3 × 900 g a.s./ha	14	Radiolabelled zoxamide: Phenyl-UL-^{14}C ring (EFSA, 2017)
	Pulses/oilseeds	Peas	Foliar application, outdoor, 2 × 145 g a.s./ha	7, 13, 30	Radiolabelled zoxamide: Phenyl-UL-^{14}C ring (EFSA, 2017)
			Foliar application, outdoor, 2 × 725 g a.s./ha	7, 13, 30	Radiolabelled zoxamide: Phenyl-UL-^{14}C ring (EFSA, 2017)

Rotational crops (available studies)	Crop groups	Crop(s)	Application(s)	PBI (DAT)	Comment/Source
	Root/tuber crops	Radish	Bare soil application, 4 × 500 g a.s./ha	30; 137; 210; 365	Radiolabelled zoxamide: phenyl-UL-^{14}C ring (EFSA, 2017). Zoxamide was not detected in any of the analysed plant parts, instead several metabolites were observed among which RH-141452 was identified mainly in the immature parts of the crops (max 23.5% TRR (0.023 mg/kg) in immature soybean forage) and to a lower extent in mature crops (max 7% TRR (0.004 mg/kg) in radish tops).
		Turnip	Bare soil application, 4 × 500 g a.s./ha	30; 145; 210; 365	
	Leafy crops	Mustard	Bare soil application, 4 × 500 g a.s./ha	30; 137; 210; 365	
	Cereal (small grain)	Sorghum	Bare soil application, 4 × 500 g a.s./ha	30; 137; 210; 365	
	Oilseed	Soybean	Bare soil application, 4 × 500 g a.s./ha	30; 137; 210; 365	

(Continued)

Processed commodities (hydrolysis study)	Conditions	Stable?	Comment/Source
	Zoxamide		
	Pasteurisation (20 min, 90°C, pH 4)	No	Zoxamide (35.3 %); RH-24549 (9.7 %); RH-150721 (46.7 %) (Latvia, 2019, 2023)
	Baking, brewing and boiling (60 min, 100°C, pH 5)	No	Zoxamide (1.2 %); RH-24549 (62.7 %); RH-150721 (11.0 %); RH-129151 (13.1 %) (Latvia, 2019, 2023)
	Sterilisation (20 min, 120°C, pH 6)	No	Zoxamide (0.8 %); RH-24549 (43.0 %); RH-129151 (20.8 %); RH-141288 (27.3 %) (Latvia, 2019, 2023)
	Other processing conditions	No	Radiolabelled vinification study showed that the major residue in wine is metabolite RH-150721. EFSA, 2017
		No	Radiolabelled processing study showed that the major residue in cooked tomatoes (e.g., tomato puree) was mainly RH-129151 and RH-150721. The parent compound amounted to 3.1% TRR (0.092 mg/kg). The main degradation products reached levels of 10.9% TRR (0.324 mg/kg) and 6.7% (0.199 mg/kg), respectively (Latvia, 2023).
	RH-141455		
	Pasteurisation (20 min, 90°C, pH 4)	Yes	99.39 % (Latvia, 2019, 2023)
	Baking, brewing and boiling (60 min, 100°C, pH 5)	Yes	98.95 % (Latvia, 2023)
	Sterilisation (20 min, 120°C, pH 6)	Yes	99.75 % (Latvia, 2023)
	RH-141452		
	Pasteurisation (20 min, 90°C, pH 4)	Yes	99.22 % (Latvia, 2023)
	Baking, brewing and boiling (60 min, 100°C, pH 5)	Yes	100.8 % (Latvia, 2023)
	Sterilisation (20 min, 120°C, pH 6)	Yes	99.29 % (Latvia, 2023)
	RH-129151		
	Pasteurisation (20 min, 90°C, pH 4)	No	RH-129151 (3.4 %); RH-24549 (13.6 %) RH-150721 (70.8 %) (Latvia, 2023)
	Baking, brewing and boiling (60 min, 100°C, pH 5)	No	RH-129151 (26.8 %); RH-24549 (73.2 %) (Latvia, 2023)
	Sterilisation (20 min, 120°C, pH 6)	No	RH-129151 (53.9 %); RH-24549 (13.8 %); RH-141288 (26.7 %) (Latvia, 2023)

Can a general residue definition be proposed for primary crops?	Yes	
Rotational crop and primary crop metabolism similar?	Yes	EFSA (2017)
Residue pattern in processed commodities similar to residue pattern in raw commodities?	No	
Plant residue definition for monitoring (RD-Mo)	Zoxamide (sum of constituent isomers)	
Plant residue definition for risk assessment (RD-RA)	Raw commodities: sum of zoxamide and RH-141452, expressed as zoxamide Processed commodities: RD-1: sum of zoxamide and RH-141452, expressed as zoxamide; RD-2 metabolite RH-150721	
Methods of analysis for monitoring of residues (analytical technique, matrix groups, LOQs)	Zoxamide (sum of constituent isomers) in high water content, high acid content, high oil content and dry commodities (EFSA, 2017): • Multiresidue QuEChERS (LC-MS/MS) • LOQ: 0.01 mg/kg • Confirmation by monitoring 1 additional MRM transition • ILV available for high water content only, missing for high acid content commodities (data gap) • Multiresidue QuEChERS and QuOil methods (LC-MS/MS) for enforcement of zoxamide (sum of constituent isomers) with LOQ = 0.01 mg/kg in four main plant matrices and black tea in routine analysis (EURLs, 2023). honey • Multiresidue QuEChERS (LC-MS/MS) • LOQ: 0.01 mg/kg • Confirmation by monitoring 1 additional MRM transition • ILV missing (data gap) • Multiresidue QuEChERS (LC-MS/MS) with LOQ = 0.01 mg/kg in routine analysis (EURLs, 2023).	

a.s.: active substance; DAT: days after treatment; PBI: plant-back interval; 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 and in honey

Plant products (available studies)	Category	Commodity	T (°C)	Stability period		Compounds covered	Comment/source
				Value	Unit		
	High water content	Tomato	–18	24	Months	Zoxamide [R, S, sum]; RH-141452; RH-150721 [R, S, sum]; RH-24549; RH-141288 [R, S, sum]	Latvia, 2023
			–18	≤ 6	Months	RH-129151 [R, S, sum]	Latvia (2023)
			4	24	Hours	RH-129151 [R, S, sum]	Whole and peeled tomato fruits (Latvia, 2023)
		Cucumber	–18	24	Months	Zoxamide [R, S, sum]; RH-141452, RH-24549; RH-141288 [R, S, sum]	Latvia, 2023
			–18	< 3	Months	RH-129151 [R, S, sum]; RH-150721 [R, S, sum]	Significant degradation after 3 months (Latvia, 2023)
			4	24	Hours	RH-129151 [R, S, sum]	Latvia, 2023
		Onions	–18	24	Months	Zoxamide [R, S, sum]; RH-141452; RH-141455	Latvia, 2023
	High starch content	Potato tubers	–20	24	Months	Zoxamide; RH-141452; RH-141455	Latvia, 2017; EFSA, 2017
			–18	24	Months	Zoxamide [R, S, sum]; RH-141452; RH-141455	Latvia, 2023
			4	24	Hours	RH-129151 [R, S, sum]	Latvia, 2023
	High acid content	Grapes	–20	20	Months	Zoxamide; RH-150721	Latvia, 2017; EFSA, 2017
			–18	26	Months	Zoxamide [R, S, sum]; RH-141452; RH-24549; RH-150721 [R, S, sum]	Latvia, 2023
			–18	≤ 18	Months	RH-141288 [R, S, sum]	Latvia, 2023
			–18	< 3	Months	RH-129151 [R, S, sum]	Significant degradation after 3 months (Latvia, 2023)
			4	24	Hours	RH-129151 [R, S, sum]	Latvia, 2023
	Processed products	Grape, wine	–20	24	Months	Zoxamide; RH-150721	Latvia, 2017; EFSA, 2017
			–18	26	Months	Zoxamide [R, S, sum]	Latvia, 2023
			–18	24	Months	RH-141452; RH-150721 [R, S, sum]; RH-24549; RH-141288 [R, S, sum]	Latvia, 2023
			–18	< 3	Months	RH-129151 [R, S, sum]	Significant degradation after 3 months (Latvia, 2023)
			4	24	Hours	RH-129151 [R, S, sum]	Latvia, 2023
		Grape, juice	–20	24	Months	Zoxamide	Latvia, 2017; EFSA, 2017
			–18	26	Months	Zoxamide [R, S, sum]; RH-141452; RH-24549; RH-141288 [R, S, sum]; RH-150721 [R, S, sum]	Latvia, 2023
			–18	< 3	Months	RH-129151 [R, S, sum]	Significant degradation after 3 months (Latvia, 2023)
			4	24	Hours	RH-129151 [R, S, sum]	Latvia, 2023
		Grape, raisin	–20	24	Months	Zoxamide	Latvia, 2017; EFSA, 2017
			4	24	Hours	RH-129151 [R, S, sum]	Latvia, 2023
		Potato, flakes	–18	24	Months	Zoxamide [R, S, sum]; RH-141452; RH-141455; RH-150721 [R, S, sum]	Latvia, 2023
			4	24	Hours	RH-129151 [R, S, sum]	Latvia, 2023
		Potato, fries	–18	24	Months	Zoxamide [R, S, sum]; RH-141452; RH-141455; RH-150721 [R, S, sum]	Latvia, 2023
			4	24	Hours	RH-129151 [R, S, sum]	Latvia, 2023
		Tomato, canned	–18	24	Months	Zoxamide [R, S, sum]; RH-141452; RH-150721 [R, S, sum]; RH-24549, RH-141288 [R, S, sum]	Latvia, 2023
			–18	≤6	Months	RH-129151 [R, S, sum]	Latvia, 2023
	Others	Honey	–18	85	Days	Zoxamide [R, S, sum]	Latvia, 2023

B.2.2 | Magnitude of residues in plants

B.2.2.1 | Summary of residues data from the supervised residue trials – Primary crops and honey

Commodity	Region[a]	Residue levels observed in the supervised residue trials (mg/kg)	Comments/source	Calculated MRL (mg/kg)	HR[b] (mg/kg)	STMR[c] (mg/kg)	CF[d]
Table/wine grapes	NEU	**Mo**: 0.94; 0.231; 0.2656; 0.298; 0.4586; 0.541; 0.768; 0.8598; 1.19; 1.22; 1.508 1.508 **RA**: 0.956; 0.241; –; –; –; 0.551; 0.778; –; 0.551; 0.778; 1.2083; 1.241; 1.519	Trials on table/wine grapes performed with 5 applications of 180 g a.s./ha (first 7 trials) and 5 applications of 150 g a.s/ha (last 4 trials) instead of 4 applications acceptable since first application is not expected to have a significant impact on the final residue levels (Latvia, 2023). MRL_{OECD} = 2.48	3 (tentative)[e]	1.51	0.77	1.0
	SEU	**Mo**: 0.0733; 0.0883; 0.2594; 0.2748; 0.452; 0.52; 0.537; 1.406 **RA**: -; –; –; –; 0.4708; 0.531; 0.5503; 1.416	Trials performed on table/wine grapes compliant with the GAP (Latvia, 2023). MRL_{OECD} = 2.15	3 (tentative)[e]	1.41	0.36	1.0
Potatoes	NEU	**Mo**: < 0.01; < 0.01; < 0.01; < 0.01 **RA:** < 0.02; < 0.02; –; –	Trials on potatoes performed with 6 × 150 g a.s./ha and 5 × 180 g a.s./ha (Latvia, 2023) acceptable since first application is not expected to have a significant impact on the final residue levels. Reduced number of trials acceptable since parent and metabolite RH-141452 are not expected to occur in potatoes. MRL_{OECD} = 0.01	0.01*	0.01	0.01	1.0
	SEU	**Mo**: < 0.01; < 0.01; < 0.01; < 0.01 **RA**: -; –; < 0.02; < 0.02	Trials on potatoes compliant with the GAP (Latvia, 2023). MRL_{OECD} = 0.01	0.01*	0.01	0.01	1.0
Onions, garlic, shallots	SEU	**Mo**: < 0.01; < 0.01; < 0.01; < 0.01 **RA**: 0.039; 0.028; –; –	Trials on onions performed with 5 × 180 g a.s./ha instead of 4 applications acceptable since first application is not expected to have a significant impact on the final residue levels (Latvia, 2023). Extrapolation to garlic, shallots is applicable. Number of trials analysing for parent and metabolite not sufficient to derive a CF. No additional trials required since the USA GAP is clearly more critical. MRL_{OECD} = 0.01	0.01*	0.01	0.01	–
	Import (USA)	**Mo**: 0.02, 0.03, 0.07, 0.10, 0.12, 0.17, 0.20, 0.21, 0.24, 0.26, 0.28, 0.44 **RA**: 0.04, 0.05, 0.12, 0.13, 0.15, 0.20, 0.21, 0.23, 0.28, 0.29, 0.31, 0.44	Trials on dry bulb onions compliant with GAP (**MRL application**, Latvia, 2019). Extrapolation to garlic and shallots is applicable. MRL_{OECD} = 0.7	0.7	0.44	0.18	1.2
Spring onions	SEU	–	No residue trials available.	–	–	–	–
Tomatoes	SEU	**Mo**: 0.04; 0.04; 0.054; 0.0825; 0.094; 0.1 0.113; 0.128; 0.14; 0.158; 0.163; 0.18; 0.197; 0.198; 0.203; 0.215; 0.239 0.302 **RA**: -; –; –; 0.10; –; 0.12; 0.13; 0.14; –; 0.18; –; 0.21; 0.22; 0.23	Trials on tomatoes compliant with GAP (Latvia, 2023). MRL_{OECD} = 0.44	0.5	0.31	0.15	1.1
	EU (indoor)	**Mo**: 0.074; 0.11; 0.147; 0.21; 0.307; 0.313 0.314; 0.377; 0.498; 0.62 **RA**: -; 0.125; 0.162; 0.225; 0.322; 0.328; 0.329; 0.392; 0.513; –;	Trials on tomatoes compliant with GAP (Latvia, 2023). MRL_{OECD} = 0.98	1	0.62	0.31	1.1

Commodity	Region[a]	Residue levels observed in the supervised residue trials (mg/kg)	Comments/source	Calculated MRL (mg/kg)	HR[b] (mg/kg)	STMR[c] (mg/kg)	CF[d]
Aubergines	SEU	**Mo**: 0.04; 0.04; 0.054; 0.0825; 0.094; 0.1; 0.11; 0.113; 0.128; 0.14; 0.158; 0.163; 0.18; 0.197; 0.198; 0.203; 0.215; 0.239 0.302 **RA**: -; –; –; 0.10; –; 0.12; –; 0.13; 0.14; –; 0.18; –; –; 0.21; 0.22; 0.23; –; –	Extrapolation from trials on tomatoes performed with 5 applications instead of 3 applications (except last value of 0.11 mg/kg) are used on tentative basis (Latvia, 2023). MRL_{OECD} = 0.44	0.5 (tentative)[f]	0.30	0.14	1.1
Cucumbers, Gherkins, Courgettes	SEU	**Mo**: 0.0176; 0.02; 0.036; 0.043; 0.0476; 0.054; 0.0585; 0.06; 0.093; 0.117; 0.17; 0.49 **RA**: 0.033; –; 0.053; 0.087; 0.083; 0.069; 0.08; –; 0.161; 0.146; –; –	Trials on cucumbers and courgettes (0.02; 0.06; 0.17; 0.49) compliant with GAP (Latvia, 2023). MRL_{OECD} = 0.62	0.7	0.49	0.06	1.6
	EU (indoor)	**Mo**: 0.0167; 0.028; 0.03; 0.046; 0.055; 0.0569; 0.073; 0.0982; 0.209; 0.49 **RA**: 0.032; 0.043; 0.061; 0.070; 0.072; 0.088; 0.113; 0.224; –	Trials on cucumbers and courgettes (0.03; 0.49) compliant with GAP (Latvia, 2023). MRL_{OECD} = 0.69	0.7	0.49	0.06	1.3
Melons, pumpkins, watermelons	SEU	**Mo**: < 0.01; 0.01; 0.0209; 0.0351; 0.04; 0.0658; 0.0764; 0.0829 **RA**: 0.025; –; 0.036; 0.050; –; 0.081; 0.092; 0.0.098	Trials on melons compliant with GAP (Latvia, 2023). Extrapolation to pumpkins and watermelons is applicable. MRL_{OECD} = 0.16	0.2	0.08	0.04	1.3
	EU (indoor)	**Mo**: < 0.01; 0.0207; 0.021; 0.0403; 0.0986; 0.19; 0.122; 0.241;1.27 **RA**: 0.025; 0.036; 0.036; 0.056; 0.114; –; 0.137; 0.256; 1.285	Trials on melons compliant with GAP (Latvia, 2023). Extrapolation to pumpkins and watermelons is applicable. MRL_{OECD} = 1.83	2	1.27	0.10	1.2
Chives	—	—	No residue trials available.	—	—	—	—
Honey	NEU/SEU	**Mo**: 3x < 0.01, 0.078 **RA**: -	Tunnel test trials performed with 3 × 180 g a.s./ha and 7(±1) days interval on *Phacelia tanacetifolia* (Latvia, 2023). Residue trials were analysed for parent only, however, since there is a wide margin of safety and the contribution of honey to the overall exposure is minimal (see Section 4), additional trials analysing for metabolite RH-141452 are not required.	0.2 (tentative)[g]	0.08	0.01	—

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

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

Mo, residue levels expressed according to the monitoring residue definition; RA, residue levels expressed according to risk assessment residue definition.

[a]NEU: Outdoor trials conducted in northern Europe, SEU: Outdoor trials conducted in southern Europe, EU: indoor EU trials, 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]Conversion factor to recalculate residues according to the residue definition for monitoring to the residue definition for risk assessment. To express the residues levels according to the residue definition for risk assessment proposed, the levels of metabolite RH-141452 found in the trials were recalculated as parent equivalents using a correction factor of 1.52 based on the Molecular Weight (MW) of parent 336.6 and a MW of RH-141452 of 221.03 (336.6/221.03 = 1.52).

[e]MRL is tentative because an ILV in high acid commodities is missing.

[f]MRL is tentative because derived mainly from trials performed with 5 instead of 3 applications.

[g]MRL is tentative because an ILV is missing.

B.2.2.2 | Residues in rotational crops

B.2.2.2.1 | Overall summary

Residues in rotational and succeeding crops expected based on confined rotational crop study?	No	Low residue levels were found in the rotational crop metabolism study using an exaggerated application rate (2.2 N). Residues in crops grown in rotation are not expected if zoxamide is applied according to the GAPs reported in Appendix A.
Residues in rotational and succeeding crops expected based on field rotational crop study?	Not triggered	Not triggered

B.2.2.3 | Processing factors

Processed commodity	Number of valid studies[a]	Processing factor (PF)		Comment/source
		Individual values	Median PF[b]	
Table grapes, raisins	4	1.11; 1.73; 2.2; 3.5	1.97	Latvia, 2017 (2.2; 3.5); Latvia, 2023 (1.11;1.73)
Wine grapes, limpid juice (pre-pasteurisation)	2	0.032; 0.042	0.037	Latvia, 2023
Wine grapes, limpid juice (post-pasteurisation)	6	< 0.01; < 0.01; 0.10[c]/0.012[d] 0.019[c]/0.018[d]; 0.083; 0.405	0.2	Latvia, 2023
Wine grapes, must	4	0.385; 0.846; 1.06; 1.09	0.95	Latvia, 2023
Wine grapes, young wine	8	< 0.01; < 0.02; 0.016[c]/0.02[d]; 0.031[c]/0.032[d]; 0.069; 0.074; 0.077; 0.148	0.05	Latvia, 2023
Wine grapes, bottled wine	10	< 0.01; 0.01/< 0.01[c]; < 0.02; < 0.03; 0.033[c]/0.032[d]; < 0.040; 0.048; 0.05; 0.068; 0.123	0.05	Latvia, 2023
Tomatoes, juice (pre-pasteurisation)	2	0.211; 0.363	0.287	Latvia, 2023
Tomatoes, juice (post-pasteurisation)	3	< 0.08; 0.155; 0.19	0.155	Latvia, 2023
Tomatoes, puree (pre-pasteurisation)	2	< 0.05; < 0.08	< 0.07	Latvia, 2023
Tomatoes, puree (post-pasteurisation)	3	< 0.05; < 0.08; < 0.09	< 0.08	Latvia, 2023
Tomato, canned (peeled) pre-pasteurisation	2	0.129; 0.160	0.145	Latvia, 2023
Tomato, canned (peeled) post-pasteurisation	3	< 0.05; < 0.08; < 0.09	< 0.08	Latvia, 2023
Melon, peeled	11	n.r.	0.17	Latvia, 2023

Abbreviation: 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]Median of the individual processing factors for each processing residues trial.

[c]Mean of 3 analytical determinations were calculated: 2 grape samples analysed just before processing phase start and 1 grape sample from the field was analysed.

[d]Mean of 2 grape samples analysed just before processing phase start was calculated.

B.3 | RESIDUES IN LIVESTOCK

	Dietary burden expressed in							
	mg/kg bw per day		mg/kg DM					
Relevant groups (subgroups)	Median	Maximum	Median	Maximum	Most critical subgroup[a]	Most critical commodity[b]	Trigger exceeded (Y/N)	Comments
Cattle (all)	0.002	0.002	0.05	0.05	Dairy cattle	Potato, process waste	N	
Cattle (dairy only)	0.002	0.002	0.04	0.04	Dairy cattle	Potato, process waste	N	
Sheep (all)	0.002	0.002	0.05	0.05	Ram/Ewe	Potato, process waste	N	
Sheep (ewe only)	0.002	0.002	0.05	0.05	Ram/Ewe	Potato, process waste	N	
Swine (all)	0.001	0.001	0.04	0.04	Swine (breeding)	Potato, process waste	N	
Poultry (all)	0.001	0.001	0.01	0.01	Turkey	Potato, culls	N	
Poultry (layer only)	0.000	0.000	0.01	0.01	Poultry layer	Potato, culls	N	
Fish	–	–	–	–	–	–	–	–

Abbreviation: DM, dry matter.

[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
	Lactating ruminants	2.82	7	Study on goat (Latvia, 2017; EFSA, 2017)

Time needed to reach a plateau concentration in milk and eggs (days)	Milk: 2 days	EFSA, 2017
Metabolism in rat and ruminant similar	yes	EFSA, 2017
Can a general residue definition be proposed for animals?	Not triggered	
Animal residue definition for monitoring (RD-Mo)	Not triggered	
Animal residue definition for risk assessment (RD-RA)	Not triggered	
Fat soluble residues	Not triggered	
Methods of analysis for monitoring of residues (analytical technique, matrix groups, LOQs)	Not triggered	

B.3.1.2 | Stability of residues in livestock

Not available and not required since MRLs for livestock commodities are not necessary.

B.4 | CONSUMER RISK ASSESSMENT

B.4.1 | Consumer risk assessment without consideration of the existing CXLs

Not relevant since no ARfD has been considered necessary.

ADI	0.5 mg/kg bw per day (Reg. (EU) 2018/692)
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)	0.5% ADI (PT general population) Major contributors among crops assessed: Wine grapes: 0.4% of ADI Tomatoes: 0.1% of ADI
NEDI (% ADI)	Not assessed in this review.
Assumptions made for the calculations	**Scenario EU:** The calculation is based on the median residue levels derived for raw agricultural commodities, according to the residue definition for enforcement, multiplied by the relevant conversion factors (CFs) for risk assessment. A peeling factor (PeF = 0.17) was applied to cucurbits with inedible peel. The contributions of commodities where no GAP was reported in the framework of the MRL review were not included in the calculation.

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.

Consumer exposure assessment through drinking water resulting from groundwater metabolite(s) according to SANCO/221/2000 rev.10 Final (25/02/2003).

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.4.2. | Consumer risk assessment with consideration of the existing CXLs

Not relevant since no ARfD has been considered necessary.

ADI	0.5 mg/kg bw per day (Reg. (EU) 2018/692)
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 CX:** 0.5% ADI (PT general population) Major contributor among crops assessed: Wine grapes: 0.4% of ADI Tomatoes: 0.1% of ADI
NEDI (% ADI)	Not assessed in this review.
Assumptions made for the calculations	**Scenario CX:** The calculation is based on the median residue levels derived for raw agricultural commodities higher than the derived MRLs, according to the residue definition for enforcement, multiplied by the relevant conversion factors (CFs) for risk assessment derived in the current assessment. A peeling factor (PeF = 0.17) was applied to cucurbits with inedible peel. The contributions of commodities where no GAP was reported in the framework of the MRL review were not included in the calculation.

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

B.4.3. | Consumer risk assessment of metabolite RH-150721 in processed commodities

ARfD	0.22 mg/kg bw (EFSA, 2023)
Highest IESTI, according to EFSA PRIMo (rev.3.1)	**Scenario CX metabolite RH-150721:** Pumpkins (boiled): 49% of ARfD
NESTI (% ARfD)	Not assessed in this review.

Assumptions made for the calculations	**Scenario CX metabolite RH-150721:** The calculation is based on the highest residue levels expected in raw agricultural commodities, considering a full conversion of the parent to the metabolite and a correction factor of 0.95 from the MW metabolite 150721/MW parent.

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

B.5 | Proposed MRLs

Code number	Commodity	Existing EU MRL (mg/kg)	Existing CXL (mg/kg)	Outcome of the review/MRL application	
				MRL (mg/kg)	Comment
Enforcement residue definition: zoxamide (sum of constituent isomers)					
151010	Table grapes	5	5	5	Further consideration needed[a] Data gap # 1
151020	Wine grapes	5	5	5	Further consideration needed[a] Data gap # 1
211000	Potatoes	0.02*	0.02	0.02	Recommended[b]
220010	Garlic	0.02*	–	0.7	Recommended[c]
220020	Onions	0.02*	–	0.7	Recommended[c]
220030	Shallots	0.02*	–	0.7	Recommended[c]
220040	Spring onions/green onions and Welsh onions	0.02*	–	0.02	Further consideration needed[d] Data gap # 2
231010	Tomatoes	0.5	2	2	Recommended[b]
231030	Aubergines/eggplants	0.02*	–	0.5	Further consideration needed[e] Data gap # 3
232010	Cucumbers	2	2	2	Recommended[b]
232020	Gherkins	2	2	2	Recommended[b]
232030	Courgettes	2	2	2	Recommended[b]
233010	Melons	2	2	2	Recommended[f]
233020	Pumpkins	2	2	2	Recommended[f]
233030	Watermelons	2	2	2	Recommended[f]
256020	Chives	30	–	30	Further consideration needed[d] Data gap # 2
1040000	Honey and other apiculture products	0.05*	–	0.2	Further consideration needed[e] Data gap #4
–	Other commodities of plant and/or animal origin	See Reg. 2017/171	–	–	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]MRL is derived from the existing CXL, which is not sufficiently supported by data but for which no risk to consumers is identified; GAP evaluated at EU level, which is also not fully supported by data, would lead to a lower tentative MRL (combination F-V in Appendix E).

[b]MRL is derived from the existing CXL, which is supported by data and for which no risk to consumers is identified; GAP evaluated at EU level, which is also fully supported by data, leads to a lower MRL (combination H-VII in Appendix E).

[c]New MRL derived based on a GAP authorised in USA and Canada fully supported by data. No risk to consumers is identified.

[d]GAP evaluated at EU level is not supported by data but no risk to consumers was identified for the existing EU MRL; no CXL is available (combination D-I in Appendix E).

[e]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 E).

[f]MRL is derived from a GAP evaluated at EU level, which is fully supported by data and for which no risk to consumers is identified; existing CXL is covered by the recommended MRL (combination H-III in Appendix E).

[g]There are no relevant authorisations or import tolerances reported at EU level; no CXL is available. Either a specific LOQ or the default MRL of 0.01 mg/kg may be considered (combination A-I in Appendix E).

APPENDIX C

Pesticide Residue Intake Model (PRIMo)

- PRIMo(EU)

European Food Safety Authority

EFSA PRIMo revision 3.1; 2021/01/06

Zoxamide

LOQs (mg/kg) range from:	0.01	to:	0.02
Toxicological reference values			
ADI (mg/kg bw per day):	0.5	ARfD (mg/kg bw):	not necessary
Source of ADI:	EC	Source of ARfD:	EC
Year of evaluation:	Reg. (EU)	Year of evaluation:	Reg. (EU) 2018/692

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)	0.5%	PT general	2.57	0.4%	Wine grapes	0.1%	Tomatoes	0.0%	Table grapes		0.5%
	0.5%	GEMS/Food G06	2.44	0.2%	Tomatoes	0.2%	Table grapes	0.0%	Onions		0.5%
	0.5%	RO general	2.38	0.3%	Wine grapes	0.1%	Tomatoes	0.0%	Onions		0.5%
	0.4%	FR adult	2.18	0.4%	Wine grapes	0.0%	Tomatoes	0.0%	Chives		0.4%
	0.4%	GEMS/Food G07	1.90	0.2%	Wine grapes	0.1%	Tomatoes	0.1%	Table grapes		0.4%
	0.4%	DE child	1.84	0.2%	Table grapes	0.1%	Tomatoes	0.1%	Chives		0.4%
	0.3%	GEMS/Food G15	1.64	0.2%	Wine grapes	0.1%	Tomatoes	0.1%	Table grapes		0.3%
	0.3%	GEMS/Food G08	1.64	0.2%	Wine grapes	0.1%	Tomatoes	0.1%	Table grapes		0.3%
	0.3%	NL toddler	1.63	0.2%	Table grapes	0.1%	Tomatoes	0.0%	Potatoes		0.3%
	0.3%	GEMS/Food G11	1.51	0.2%	Wine grapes	0.1%	Table grapes	0.1%	Tomatoes		0.3%
	0.3%	IE adult	1.46	0.2%	Wine grapes	0.0%	Table grapes	0.0%	Tomatoes		0.3%
	0.3%	DE women 14-50 yr	1.33	0.1%	Wine grapes	0.1%	Tomatoes	0.0%	Table grapes		0.3%
	0.2%	DE general	1.24	0.1%	Wine grapes	0.0%	Tomatoes	0.0%	Table grapes		0.2%
	0.2%	GEMS/Food G10	1.23	0.1%	Tomatoes	0.1%	Wine grapes	0.0%	Table grapes		0.2%
	0.2%	DK adult	1.14	0.1%	Wine grapes	0.0%	Tomatoes	0.0%	Table grapes		0.2%
	0.2%	NL child	1.08	0.2%	Table grapes	0.0%	Tomatoes	0.0%	Potatoes		0.2%
	0.2%	FR child 3 15 yr	1.08	0.1%	Tomatoes	0.1%	Wine grapes	0.1%	Table grapes		0.2%
	0.2%	UK adult	1.07	0.2%	Wine grapes	0.0%	Tomatoes	0.0%	Table grapes		0.2%
	0.2%	UK vegetarian	0.98	0.1%	Wine grapes	0.0%	Tomatoes	0.0%	Table grapes		0.2%
	0.2%	NL general	0.87	0.1%	Wine grapes	0.0%	Table grapes	0.0%	Tomatoes		0.2%
	0.1%	PL general	0.70	0.1%	Tomatoes	0.0%	Table grapes	0.0%	Onions		0.1%
	0.1%	ES adult	0.70	0.1%	Wine grapes	0.1%	Tomatoes	0.0%	Onions		0.1%
	0.1%	IT toddler	0.65	0.1%	Tomatoes	0.0%	Table grapes	0.0%	Onions		0.1%
	0.1%	FR toddler 2 3 yr	0.64	0.0%	Chives	0.0%	Wine grapes	0.0%	Tomatoes		0.1%
	0.1%	FI 3 yr	0.60	0.0%	Tomatoes	0.0%	Table grapes	0.0%	Cucumbers		0.1%
	0.1%	IT adult	0.57	0.1%	Tomatoes	0.0%	Table grapes	0.0%	Onions		0.1%
	0.1%	FI adult	0.57	0.0%	Wine grapes	0.0%	Tomatoes	0.0%	Table grapes		0.1%
	0.1%	DK child	0.56	0.0%	Tomatoes	0.0%	Cucumbers	0.0%	Table grapes		0.1%
	0.1%	UK toddler	0.52	0.0%	Tomatoes	0.0%	Table grapes	0.0%	Onions		0.1%
	0.1%	SE general	0.48	0.1%	Tomatoes	0.0%	Onions	0.0%	Potatoes		0.1%
	0.1%	FI 6 yr	0.46	0.0%	Tomatoes	0.0%	Table grapes	0.0%	Onions		0.1%
	0.1%	ES child	0.45	0.1%	Tomatoes	0.0%	Onions	0.0%	Table grapes		0.1%
	0.1%	FR infant	0.34	0.0%	Chives	0.0%	Courgettes	0.0%	Tomatoes		0.1%
	0.1%	LT adult	0.29	0.0%	Tomatoes	0.0%	Cucumbers	0.0%	Potatoes		0.1%
	0.0%	UK infant	0.23	0.0%	Tomatoes	0.0%	Onions	0.0%	Potatoes		0.0%
	0.0%	IE child	0.09	0.0%	Table grapes	0.0%	Tomatoes	0.0%	Onions		0.0%

Conclusion:
The estimated long-term dietary intake (TMDI/NEDI/IEDI) was below the ADI.
The long-term intake of residues of Zoxamide 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

As an ARfD is not necessary/not applicable, no acute risk assessment is performed.

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				**IESTI**			
Highest % of ARfD/ADI	Commodities	MRL / input for RA (mg/kg)	Exposure (µg/kg bw)	Highest % of ARfD/ADI	Commodities	MRL / input for RA (mg/kg)	Exposure (µg/kg bw)
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				**IESTI**			
Highest % of ARfD/ADI	Processed commodities	MRL / input for RA (mg/kg)	Exposure (µg/kg bw)	Highest % of ARfD/ADI	Processed commodities	MRL / input for RA (mg/kg)	Exposure (µg/kg bw)
Expand/collapse list							

Conclusion:

- PRIMo(CXL)

European Food Safety Authority

EFSA PRIMo revision 3.1; 2021/01/06

Zoxamide (F)

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

Toxicological reference values

ADI (mg/kg bw per day):	0.5	ARfD (mg/kg bw):	not necessary
Source of ADI:	EC	Source of ARfD:	EC
Year of evaluation:	Reg. (EU) 2018/692	Year of evaluation:	Reg. (EU) 2018/692

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)
0.5%	PT general	2.62	0.4%	Wine grapes	0.0%	Table grapes	0.0%	Tomatoes		0.5%
0.5%	FR adult	2.30	0.4%	Wine grapes	0.0%	Chives	0.0%	Tomatoes		0.5%
0.5%	RO general	2.25	0.3%	Wine grapes	0.1%	Tomatoes	0.0%	Onions		0.5%
0.4%	GEMS/Food G06	2.11	0.2%	Table grapes	0.2%	Tomatoes	0.0%	Onions		0.4%
0.4%	GEMS/Food G07	1.88	0.2%	Wine grapes	0.1%	Table grapes	0.0%	Tomatoes		0.4%
0.4%	DE child	1.82	0.2%	Table grapes	0.1%	Chives	0.0%	Tomatoes		0.4%
0.3%	NL toddler	1.63	0.3%	Table grapes	0.0%	Tomatoes	0.0%	Potatoes		0.3%
0.3%	GEMS/Food G08	1.61	0.2%	Wine grapes	0.1%	Table grapes	0.0%	Tomatoes		0.3%
0.3%	GEMS/Food G15	1.59	0.2%	Wine grapes	0.1%	Table grapes	0.1%	Tomatoes		0.3%
0.3%	IE adult	1.56	0.2%	Wine grapes	0.0%	Table grapes	0.0%	Tomatoes		0.3%
0.3%	GEMS/Food G11	1.49	0.2%	Wine grapes	0.1%	Table grapes	0.0%	Tomatoes		0.3%
0.3%	DE women 14-50 yr	1.33	0.1%	Wine grapes	0.1%	Table grapes	0.0%	Tomatoes		0.3%
0.2%	DE general	1.25	0.1%	Wine grapes	0.0%	Table grapes	0.0%	Tomatoes		0.2%
0.2%	DK adult	1.15	0.2%	Wine grapes	0.0%	Table grapes	0.0%	Tomatoes		0.2%
0.2%	GEMS/Food G10	1.10	0.1%	Wine grapes	0.1%	Tomatoes	0.0%	Table grapes		0.2%
0.2%	UK adult	1.09	0.2%	Wine grapes	0.0%	Tomatoes	0.0%	Table grapes		0.2%
0.2%	NL child	1.09	0.2%	Table grapes	0.0%	Tomatoes	0.0%	Potatoes		0.2%
0.2%	FR child 3 15 yr	1.05	0.1%	Wine grapes	0.1%	Table grapes	0.0%	Tomatoes		0.2%
0.2%	UK vegetarian	0.98	0.1%	Wine grapes	0.0%	Tomatoes	0.0%	Table grapes		0.2%
0.2%	NL general	0.88	0.1%	Wine grapes	0.0%	Table grapes	0.0%	Tomatoes		0.2%
0.1%	ES adult	0.64	0.1%	Wine grapes	0.0%	Tomatoes	0.0%	Onions		0.1%
0.1%	FR toddler 2 3 yr	0.64	0.0%	Chives	0.0%	Wine grapes	0.0%	Tomatoes		0.1%
0.1%	PL general	0.62	0.1%	Table grapes	0.0%	Tomatoes	0.0%	Onions		0.1%
0.1%	FI 3 yr	0.56	0.0%	Table grapes	0.0%	Tomatoes	0.0%	Cucumbers		0.1%
0.1%	IT toddler	0.53	0.1%	Tomatoes	0.0%	Table grapes	0.0%	Courgettes		0.1%
0.1%	FI adult	0.53	0.1%	Wine grapes	0.0%	Tomatoes	0.0%	Table grapes		0.1%
0.1%	DK child	0.51	0.0%	Cucumbers	0.0%	Table grapes	0.0%	Tomatoes		0.1%
0.1%	IT adult	0.49	0.0%	Tomatoes	0.0%	Table grapes	0.0%	Courgettes		0.1%
0.1%	SE general	0.48	0.0%	Tomatoes	0.0%	Onions	0.0%	Gherkins		0.1%
0.1%	UK toddler	0.46	0.0%	Table grapes	0.0%	Tomatoes	0.0%	Onions		0.1%
0.1%	FR infant	0.46	0.0%	Chives	0.0%	Courgettes	0.0%	Wine grapes		0.1%
0.1%	FI 6 yr	0.43	0.0%	Table grapes	0.0%	Tomatoes	0.0%	Cucumbers		0.1%
0.1%	ES child	0.34	0.0%	Tomatoes	0.0%	Onions	0.0%	Table grapes		0.1%
0.0%	LT adult	0.23	0.0%	Tomatoes	0.0%	Cucumbers	0.0%	Potatoes		0.0%
0.0%	UK infant	0.19	0.0%	Tomatoes	0.0%	Onions	0.0%	Potatoes		0.0%
0.0%	IE child	0.08	0.0%	Table grapes	0.0%	Onions	0.0%	Tomatoes		0.0%

Conclusion:
The estimated long-term dietary intake (TMDI/NEDI/IEDI) was below the ADI.
The long-term intake of residues of Zoxamide (F) 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

As an ARfD is not necessary/not applicable, no acute risk assessment is performed.

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				**IESTI**			
Highest % of ARfD/ADI	Commodities	MRL / input for RA (mg/kg)	Exposure (µg/kg bw)	Highest % of ARfD/ADI	Commodities	MRL / input for RA (mg/kg)	Exposure (µg/kg bw)
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				**IESTI**			
Highest % of ARfD/ADI	Processed commodities	MRL / input for RA (mg/kg)	Exposure (µg/kg bw)	Highest % of ARfD/ADI	Processed commodities	MRL / input for RA (mg/kg)	Exposure (µg/kg bw)
Expand/collapse list							

Conclusion:

- PRIMo(CXL)Zoxamide metabolite RH 150721

European Food Safety Authority

EFSA PRIMo revision 3.1; 2021/01/06

RH-150721

LOQs (mg/kg) range from:	0.01	to:	0.01
Toxicological reference values			
ADI (mg/kg bw per day):	0.04	ARfD (mg/kg bw):	0.22
Source of ADI:	EFSA	Source of ARfD:	EFSA
Year of evaluation:		Year of evaluation:	2023

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)

TMDI/ IEDI (range) in % of ADI
minimum - maximum
6.5%

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%	PT general	2.60	5%	Wine grapes	0.6%	Table grapes	0.4%	Tomatoes		7%
	6%	FR adult	2.28	5%	Wine grapes	0.2%	Chives	0.2%	Table grapes		6%
	5%	RO general	2.20	3%	Wine grapes	0.9%	Tomatoes	0.4%	Onions		5%
	5%	GEMS/Food G06	1.98	2%	Table grapes	2%	Tomatoes	0.4%	Onions		5%
	5%	GEMS/Food G07	1.85	3%	Wine grapes	0.7%	Table grapes	0.5%	Tomatoes		5%
	4%	DE child	1.77	3%	Table grapes	0.8%	Chives	0.5%	Tomatoes		4%
	4%	NL toddler	1.59	3%	Table grapes	0.5%	Tomatoes	0.1%	Potatoes		4%
	4%	GEMS/Food G08	1.56	2%	Wine grapes	0.7%	Table grapes	0.6%	Tomatoes		4%
	4%	GEMS/Food G15	1.55	2%	Wine grapes	0.7%	Table grapes	0.6%	Tomatoes		4%
	4%	IE adult	1.51	3%	Wine grapes	0.5%	Table grapes	0.2%	Tomatoes		4%
	4%	GEMS/Food G11	1.47	2%	Wine grapes	0.9%	Table grapes	0.4%	Tomatoes		4%
	3%	DE women 14-50 yr	1.30	2%	Wine grapes	0.6%	Table grapes	0.4%	Tomatoes		3%
	3%	DE general	1.22	2%	Wine grapes	0.5%	Table grapes	0.3%	Tomatoes		3%
	3%	DK adult	1.13	2%	Wine grapes	0.4%	Table grapes	0.3%	Tomatoes		3%
	3%	UK adult	1.08	2%	Wine grapes	0.2%	Tomatoes	0.1%	Table grapes		3%
	3%	GEMS/Food G10	1.06	0.9%	Wine grapes	0.7%	Tomatoes	0.6%	Table grapes		3%
	3%	NL child	1.06	2%	Table grapes	0.3%	Tomatoes	0.1%	Potatoes		3%
	3%	FR child 3 15 yr	1.01	0.7%	Wine grapes	0.7%	Table grapes	0.4%	Tomatoes		3%
	2%	UK vegetarian	0.95	2%	Wine grapes	0.3%	Tomatoes	0.2%	Table grapes		2%
	2%	NL general	0.87	1%	Wine grapes	0.5%	Table grapes	0.2%	Tomatoes		2%
	2%	ES adult	0.62	0.9%	Wine grapes	0.4%	Tomatoes	0.1%	Onions		2%
	2%	FR toddler 2 3 yr	0.60	0.5%	Chives	0.5%	Wine grapes	0.2%	Tomatoes		2%
	1%	PL general	0.59	0.7%	Table grapes	0.4%	Tomatoes	0.2%	Onions		1%
	1%	FI 3 yr	0.50	0.5%	Table grapes	0.3%	Tomatoes	0.2%	Onions		1%
	1%	FI adult	0.50	0.6%	Wine grapes	0.3%	Tomatoes	0.2%	Table grapes		1%
	1%	IT toddler	0.47	0.7%	Tomatoes	0.2%	Table grapes	0.1%	Courgettes		1%
	1%	UK toddler	0.45	0.5%	Table grapes	0.3%	Tomatoes	0.1%	Onions		1%
	1%	DK child	0.44	0.4%	Table grapes	0.3%	Tomatoes	0.2%	Cucumbers		1%
	1%	IT adult	0.43	0.6%	Tomatoes	0.3%	Table grapes	0.1%	Courgettes		1%
	1%	SE general	0.41	0.4%	Tomatoes	0.2%	Onions	0.1%	Potatoes		1%
	1.0%	FR infant	0.39	0.5%	Chives	0.3%	Courgettes	0.1%	Wine grapes		1.0%
	1.0%	FI 6 yr	0.39	0.4%	Table grapes	0.2%	Tomatoes	0.2%	Onions		1.0%
	0.8%	ES child	0.31	0.5%	Tomatoes	0.1%	Onions	0.1%	Table grapes		0.8%
	0.5%	LT adult	0.20	0.3%	Tomatoes	0.1%	Potatoes	0.1%	Cucumbers		0.5%
	0.5%	UK infant	0.18	0.2%	Tomatoes	0.1%	Onions	0.1%	Potatoes		0.5%
	0.2%	IE child	0.08	0.1%	Table grapes	0.0%	Onions	0.0%	Tomatoes		0.2%

Conclusion:
The estimated long-term dietary intake (TMDI/NEDI/IEDI) was below the ADI.
The long-term intake of residues of RH-150721 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.

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)
49%	Pumpkins / boiled	2 / 1.21	107
16%	Wine grapes / juice	5 / 0.79	34
11%	Courgettes / boiled	2 / 0.69	25
3%	Shallots / boiled	0.7 / 0.42	6.8
2%	Tomatoes / juice	2 / 0.2	3.7
1%	Gherkins / pickled	2 / 0.1	2.4
0.8%	Potatoes / fried	0.02 / 0.02	1.8
0.8%	Tomatoes / sauce/puree	2 / 0.19	1.8
0.3%	Potatoes / dried (flakes)	0.02 / 0.04	0.56

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)
30%	Pumpkins / boiled	2 / 1.21	67
18%	Wine grapes / wine	5 / 4.12	39
11%	Table grapes / raisins	5 / 19.38	24
7%	Wine grapes / juice	5 / 0.79	16
7%	Courgettes / boiled	2 / 0.69	16
2%	Onions / boiled	0.7 / 0.42	3.9
1%	Shallots / boiled	0.7 / 0.42	2.6
0.7%	Tomatoes / sauce/puree	2 / 0.19	1.5
0.04%	Potatoes / chips	0.02 / 0.01	0.08
0.02%	Potatoes / dried (flakes)	0.02 / 0.04	0.05

Conclusion:

The estimated short-term intake (IESTI) exceeded the toxicological reference value for 1 commodities.

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

APPENDIX D

Input values for the exposure calculations

D.1 | LIVESTOCK DIETARY BURDEN CALCULATIONS

Feed commodity	Median dietary burden		Maximum dietary burden	
	Input value[a] (mg/kg)	Comment	Input value[a] (mg/kg)	Comment
Risk assessment residue definition—sum of zoxamide and RH-141452, expressed as zoxamide				
Potato, culls	0.01*	STMR	0.01*	HR
Potato, processed waste	0.01*	STMR	0.01*	STMR
Potato, dried pulp	0.01*	STMR	0.01*	STMR

Abbreviations: HR, highest residue; PF, processing factor; STMR, supervised trials median residue.

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

[a]Figures in the table are rounded to 2 digits, but the calculations are normally performed with the actually calculated values (which may contain more digits). To reproduce dietary burden calculations, the unrounded values need to be used.

D.2 | CONSUMER RISK ASSESSMENT WITHOUT CONSIDERATION OF THE EXISTING CXLS

Commodity	Chronic risk assessment	
	Input value[a] (mg/kg)	Comment
Risk assessment residue definition – sum of zoxamide and RH-141452, expressed as zoxamide		
Table grapes	0.77	$STMR_{Mo}$ (tentative) × CF (1.0)
Wine grapes	0.77	$STMR_{Mo}$ (tentative) × CF (1.0)
Potatoes	0.01*	$STMR_{Mo}$ × PF (1.0)
Garlic	0.22	$STMR_{Mo}$ × CF (1.2)
Onions	0.22	$STMR_{Mo}$ × CF (1.2)
Shallots	0.22	$STMR_{Mo}$ × CF (1.2)
Spring onions/green onions and Welsh onions	0.02	EU MRL
Tomatoes	0.34	$STMR_{Mo}$ × CF (1.1)
Aubergines/eggplants	0.154	$STMR_{Mo}$ (tentative) × CF (1.1)
Cucumbers	0.09	$STMR_{Mo}$ × CF (1.6)
Gherkins	0.09	$STMR_{Mo}$ × CF (1.6)
Courgettes	0.09	$STMR_{Mo}$ × CF (1.6)
Melons	0.02	$STMR_{Mo}$ × PeF (0.17) × CF (1.3)
Pumpkins	0.02	$STMR_{Mo}$ × PeF (0.17) × CF (1.3)
Watermelons	0.02	$STMR_{Mo}$ × PeF (0.17) × CF (1.3)
Chives	30	EU MRL
Honey	0.01	$STMR_{Mo}$ (tentative)

Abbreviation: PeF, peeling factor.

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

[a]Figures in the table are rounded to 2 digits, but the calculations are normally performed with the actually calculated values (which may contain more digits). To reproduce a PRIMo calculation, the unrounded values need to be used.

D.3 | CONSUMER RISK ASSESSMENT WITH CONSIDERATION OF THE EXISTING CXLS

Commodity	Chronic risk assessment	
	Input value[a] (mg/kg)	Comment
Risk assessment residue definition – sum of zoxamide and RH-141452, expressed as zoxamide		
Table grapes	0.83	$STMR_{Mo}$ (CXL) (tentative) × CF (1.0)
Wine grapes	0.83	$STMR_{Mo}$ (CXL) (tentative) × CF (1.0)
Potatoes	0.01	$STMR_{Mo}$ (CXL) × CF (1.0)
Garlic	0.22	$STMR_{Mo}$ × CF (1.2)

(Continued)

	Chronic risk assessment	
Commodity	**Input value[a] (mg/kg)**	**Comment**
Onions	0.22	$STMR_{Mo}$ × CF (1.2)
Shallots	0.22	$STMR_{Mo}$ × CF (1.2)
Spring onions/green onions and Welsh onions	0.02	EU MRL
Tomatoes	0.20	$STMR_{Mo}$ (CXL) × CF (1.1)
Aubergines/eggplants	0.154	$STMR_{Mo}$ (tentative) × CF (1.1)
Cucumbers	0.06	$STMR_{Mo}$ (CXL) × CF (1.6)
Gherkins	0.23	$STMR_{Mo}$ (CXL) × CF (1.6)
Courgettes	0.23	$STMR_{Mo}$ (CXL) × CF (1.6)
Melons	0.02	$STMR_{Mo}$ × PeF (0.17) × CF (1.3)
Pumpkins	0.02	$STMR_{Mo}$ × PeF (0.17) × CF (1.3)
Watermelons	0.02	$STMR_{Mo}$ × PeF (0.17) × CF (1.3)
Chives	30	EU MRL
Honey	0.01	$STMR_{Mo}$ (tentative)

Abbreviation: PeF, peeling factor.

[a]Figures in the table are rounded to 2 digits, but the calculations are normally performed with the actually calculated values (which may contain more digits). To reproduce a PRIMo calculation, the unrounded values need to be used.

D.4 | CONSUMER RISK ASSESSMENT OF METABOLITE RH-150721 IN PROCESSED COMMODITIES WITH CONSIDERATION OF THE EXISTING CXLS

	Acute risk assessment	
Commodity	**Input value[a] (mg/kg)**	**Comment**
Risk assessment residue definition 2 – RH-150721		
Table grapes/raisins	19.4	HR-RAC × CRF × PF
Wine grapes/wine	4.1	HR-RAC × CRF
Wine grapes/juice	0.79	STMR-RAC × CRF
Potatoes/chips	0.01*	STMR-RAC × CRF
Potatoes/dried (flakes)	0.04	STMR-RAC × CRF × PF
Potatoes/fried	0.02	HR-RAC × CRF
Onions/boiled	0.42	HR-RAC × CRF
Shallots/boiled	0.42	HR-RAC × CRF
Tomatoes/sauce/puree	0.19	STMR-RAC × CRF
Tomatoes/juice	0.20	STMR-RAC × CRF
Gherkins/pickled	0.10	HR-RAC × CRF × PF
Courgettes/boiled	0.70	HR-RAC × CRF
Pumpkins/boiled	1.2	HR-RAC × CRF

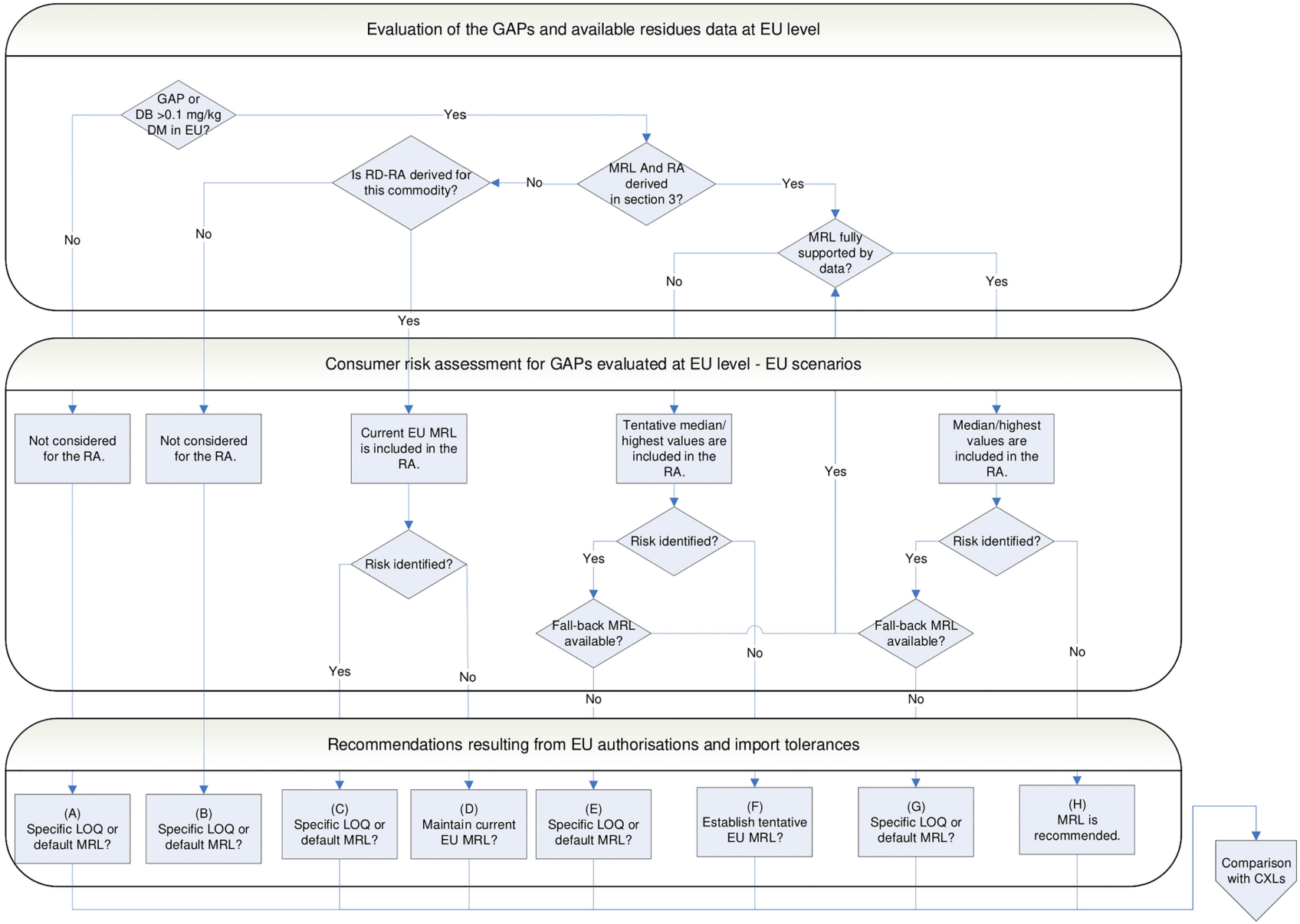
Abbreviations: CRF, correction factor of 0.95 based on the MW metabolite RH-150721/MW parent; PF, processing factor.

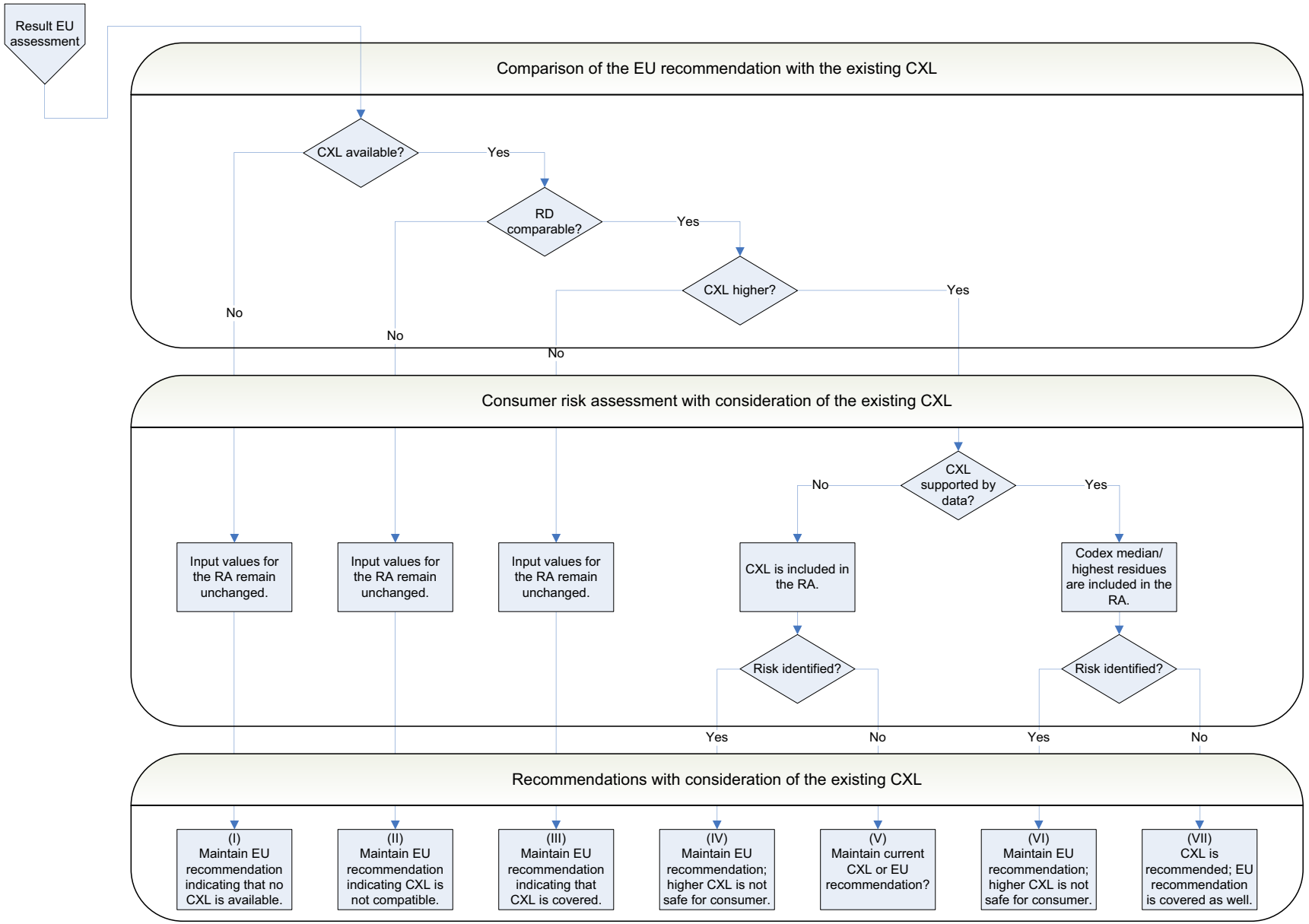
*Indicates that the input value is proposed at the limit of quantification.

[a]Figures in the table are rounded to 2 digits, but the calculations are normally performed with the actually calculated values (which may contain more digits). To reproduce a PRIMo calculation, the unrounded values need to be used.

APPENDIX E

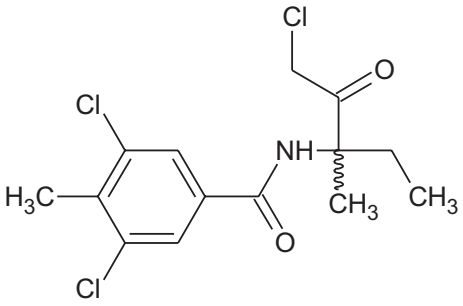
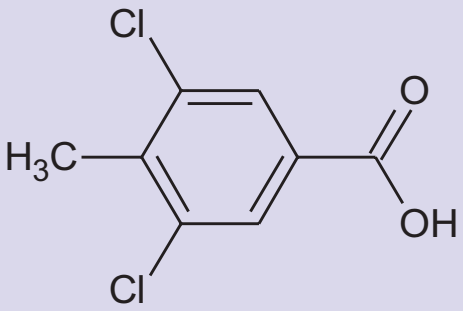
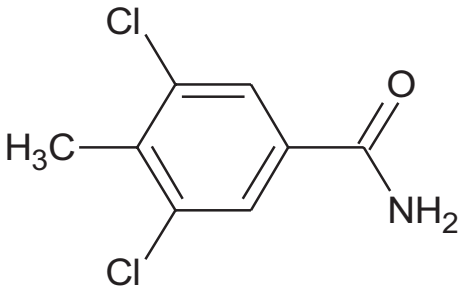
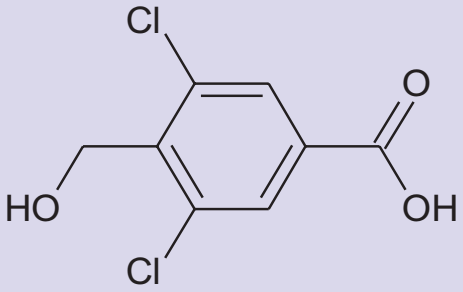
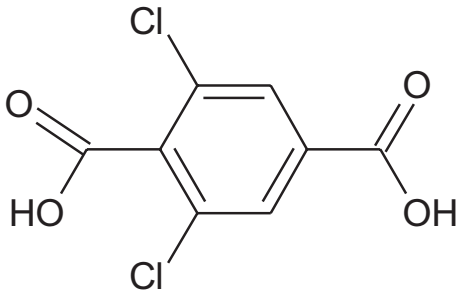
Decision tree for deriving MRL recommendations



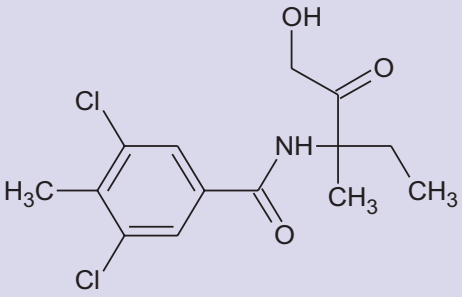
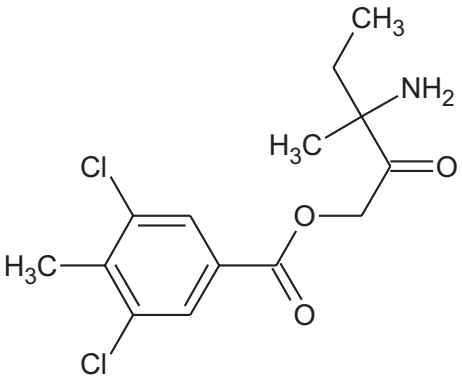
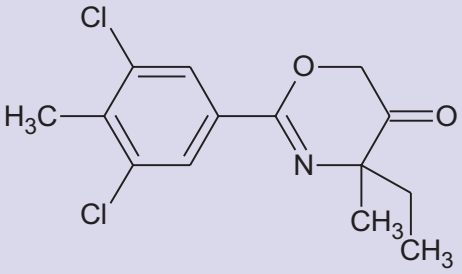

Result EU assessment
Comparison of the EU recommendation with the existing CXL
CXL available?
Yes
No
RD comparable?
Yes
No
CXL higher?
Yes
No
Consumer risk assessment with consideration of the existing CXL
CXL supported by data?
No
Yes
Input values for the RA remain unchanged.
Input values for the RA remain unchanged.
Input values for the RA remain unchanged.
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.

APPENDIX F

Used compound codes

Code/trivial name[a]	IUPAC name/SMILES notation/InChiKey[b]	Structural formula[c]
Zoxamide	3,5-dichloro-*N*-[(1*RS*)-3-chloro-1-ethyl-1-methyl-2-oxopropyl]-4-methylbenzamide SOUGWDPPRBKJEX-UHFFFAOYSA-N Clc1cc(cc(Cl)c1C)C(=O)NC(C)(CC)C(=O)CCl	
RH-24549 RH-4549	3,5-dichloro-4-methylbenzoic acid GBEJAEMDMASLJL-UHFFFAOYSA-N Clc1cc(cc(Cl)c1C)C(=O)O	
RH-139432	3,5-dichloro-4-methylbenzamide SPTGJWNMECZLCA-UHFFFAOYSA-N Clc1cc(cc(Cl)c1C)C(N)=O	
RH-141452 RH-1452 M-17 in rat	3,5-dichloro-4-hydromethyl benzoic acid WWKBFQWNMXRYAY-UHFFFAOYSA-N OCc1c(Cl)cc(cc1Cl)C(=O)O	
RH-141455 RH-1455	2,6-dichlorobenzene-1,4-dicarboxylic acid LJUJMEBEACINIP-UHFFFAOYSA-N OC(=O)c1c(Cl)cc(cc1Cl)C(=O)O	

(Continued)

Code/trivial name[a]	IUPAC name/SMILES notation/InChiKey[b]	Structural formula[c]
RH-141288	3,5-dichloro-*N*-(1-hydroxy-3-methyl-2-oxopentan-3-yl)-4-methylbenzamide XAPGELGSWBCKEV-UHFFFAOYSA-N Clc1cc(cc(Cl)c1C)C(=O)NC(C)(CC)C(=O)CO	
RH-150721	3-amino-3-methyl-2-oxopentyl 3,5-dichloro-4-methylbenzoate SLDKOOMBYWXHGS-UHFFFAOYSA-N Clc1cc(cc(Cl)c1C)C(=O)OCC(=O)C(C)(N)CC	
RH-129151	2-(3,5-dichloro-4-methylphenyl)-4-ethyl-4-methyl-4*H*-1,3-oxazin-5(6*H*)-one RONWHACIFRLANZ-UHFFFAOYSA-N CCC1(C)N=C(OCC1=O)c1cc(Cl)c(C)c(Cl)c1	

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

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

[b]ACD/Name 2021.1.3 ACD/Labs 2021.1.3 (File Version N15E41, Build 123232, 7 July 2021).

[c]ACD/ChemSketch 2021.1.3 ACD/Labs 2021.1.3 (File Version C25H41, Build 123835, 28 August 2021).