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

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Abstract

According to Article 12 of Regulation (EC) No 396/2005, EFSA has reviewed the maximum residue levels (MRLs) currently established at European level for the pesticide active substance chromafenozide. Considering the information provided by Member States, neither EU uses nor import tolerances are currently authorised for chromafenozide within the EU. Furthermore, no MRLs are established by the Codex Alimentarius Commission (Codex maximum residue limits) for this active substance. Therefore, residues of chromafenozide are not expected to occur in any plant or animal commodity and therefore a consumer risk assessment is not required. Nevertheless, the available information allowed EFSA to propose a marker residue definition and a limit of quantification (LOQ) for enforcement against potential illegal uses.

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Keywords: chromafenozide, MRL review, Regulation (EC) No 396/2005, consumer risk assessment, diacylhydrazine, insecticide

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Review of the existing MRLs for chromafenozide

Summary

Chromafenozide was approved on 1 April 2015 by means of Commission Implementing Regulation (EU) 2015/51 under Regulation (EC) No 1107/2009 as amended by Commission Implementing Regulations (EU) No 540/2011 and 541/2011.

As the active substance was approved after the entry into force of Regulation (EC) No 396/2005 on 2 September 2008, the European Food Safety Authority (EFSA) is required to provide a reasoned opinion on the review of the existing maximum residue levels (MRLs) for that active substance in compliance with Article 12(1) of the aforementioned regulation.

As the basis for the MRL review, on 16 April 2018, EFSA initiated the collection of data for this active substance. In a first step, Member States were invited to submit by 16 May 2018 their national Good Agricultural Practices (GAPs), in a standardised way, in the format of specific GAP forms. According to the information provided in the GAP forms, no uses are currently authorised for chromafenozide in the Member States. Moreover, the RMS did not report any uses authorised in third countries that might have a significant impact on international trade.

On the basis of all the data submitted by Member States, EFSA, according to the process, should in principle ask Hungary as the designated RMS, to complete the Pesticide Residues Overview File (PROFile) and to prepare a supporting evaluation report. Nevertheless, since neither the European Union (EU) uses nor import tolerances are currently authorised for chromafenozide, a GAP overview file was provided; however a PROFile was not considered relevant and was not submitted. The evaluation report was provided by the RMS to EFSA on 5 September 2018.

Following a scientific check on the data submitted undertaken by EFSA, no additional clarification/amendment were needed and, on 27 September 2018, the RMS was directly informed of the completeness of the information received.

Based on the information provided by the RMS, Member States and the EURL, and taking into account the conclusions derived by EFSA in the framework of Directive 91/414/EEC, EFSA prepared in September 2018 a draft reasoned opinion, which was circulated to Member States for consultation via a written procedure. Comments received by 29 October 2018 were considered during the finalisation of this reasoned opinion. The following conclusions are derived.

Residues of chromafenozide are not expected to occur in any plant commodity or in any animal product because no uses or import tolerances are currently authorised for chromafenozide in the EU and no codex maximum residue limits (CXLs) are available for this active substance. A risk assessment is therefore in principle not required.

Nevertheless, to assist risk managers in applying the most appropriate enforcement measures (against potential illegal uses), EFSA assessed the available data with particular attention to the analytical methods and the nature of residues in plants and livestock.

According to the results from the available metabolism studies in primary, rotational crops and in animals, the parent compound is considered to be the most adequate marker for enforcement against the potential illegal use of chromafenozide. It is expected that this compound can be enforced with a limit of quantification (LOQ) of 0.01 mg/kg in all plant commodities. For animal commodities, an enforcement method is not available. In the absence of fully validated analytical methods, the default LOQ of 0.01 mg/kg is tentatively proposed.

Considering that the enforcement against potential illegal uses falls under the remit of risk managers, EFSA is not in a position to recommend whether the default MRL of 0.01 mg/kg, as defined by Regulation (EC) No 396/2005, or whether the setting of specific LOQ values for plant and animal commodities should apply. It is noted, however, that for chromafenozide, LOQs of 0.01 mg/kg in plant commodities and in animal commodities, would provide a satisfactory level of protection for the European consumers.
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Background

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

As chromafenozide was approved on 1 April 2015 by means of Commission Implementing Regulation (EU) 2015/51\(^3\) under Regulation (EC) No 1107/2009\(^4\) as amended by Commission Implementing Regulations (EU) No 540/2011\(^5\) and 541/2011\(^6\), EFSA initiated the review of all existing MRLs for that active substance.

By way of background information, in the framework of Directive 91/414/EEC Chromafenozide was evaluated by Hungary, designated as rapporteur Member State (RMS). Subsequently, a peer review on the initial evaluation of the RMS was conducted by EFSA, leading to the conclusions as set out in the EFSA scientific conclusion (EFSA, 2013). Furthermore, according to the provisions of the approval regulation, confirmatory information was requested, among others, as regards ecotoxicology and environmental fate, to be submitted by 31 March 2017.

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

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 16 April 2018, EFSA initiated the collection of data for this active substance. In a first step, Member States were invited to submit by 16 May 2018 their national Good Agricultural Practices (GAPs), in a standardised way, in the format of specific GAP forms. In the framework of this consultation nine Member States (the Czech Republic, Finland, France, Germany, Ireland, Lithuania, the Netherlands, Spain and Sweden) provided feedback on their national authorisations for chromafenozide. An evaluation report was also submitted by the European Union Reference Laboratories for Pesticides Residues (EURLs, 2018). According to the information provided in the GAP forms, uses are not currently authorised for chromafenozide in Member States. Moreover, the

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1. Regulation (EC) No 396/2005 of the European Parliament and of the Council of 23 February 2005 on maximum residue levels of pesticides in or on food and feed of plant and animal origin and amending Council Directive 91/414/EEC. OJ L 70, 16.3.2005, p. 1-16.
2. Council Directive 91/414/EEC of 15 July 1991 concerning the placing of plant protection products on the market. OJ L 230, 19.8.1991, p. 1-32. Repealed by Regulation (EC) No 1107/2009.
3. Commission Implementing Regulation (EU) 2015/51 of 14 January 2015 approving the active substance chromafenozide, 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 and allowing Member States to extend provisional authorisations granted for that active substance. OJ L 9, 15.1.2015, p. 22-26.
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.
RMS did not report any uses authorised in third countries that might have a significant impact on international trade. On the basis of all the data submitted by Member States, EFSA, according to the process, should in principle ask Hungary as the designated RMS, to complete the PROFile and to prepare a supporting evaluation report. Nevertheless, since neither EU uses nor import tolerances are currently authorised for chromafenozide, a GAP overview file was provided; however, a PROFile was not considered relevant and was not submitted. The evaluation report was provided by the RMS to EFSA on 5 September 2018.

Following a scientific check on the data submitted undertaken by EFSA, no additional clarification/amendment were needed and, on 27 September 2018, the RMS was directly informed of the completeness of the information received.

Based on the information provided by the RMS, Member States and the EURs and taking into account the conclusions derived by EFSA in the framework of Directive 91/414/EEC, EFSA prepared in September 2018 a draft reasoned opinion, which was circulated to Member States for consultation via a written procedure. Comments received by 29 October 2018 were considered during the finalisation of this reasoned opinion.

The evaluation report submitted by the RMS (Hungary, 2018), the GAP overview file and the Member States consultation report (EFSA, 2018) are considered as supporting documents to this reasoned opinion and, thus, are made publicly available. Furthermore, a screenshot of the Report sheet of the EFSA Pesticide Residue Intake Model (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.

The active substance and its use pattern

Chromafenozide is the ISO common name for N'-tert-butyl-5-methyl-N'-(3,5-xyloyl)chromane-6-carbohydrazide (IUPAC). The chemical structure of chromafenozide is reported in Appendix E.

The EU MRLs for chromafenozide are established in Annexes IIIA of Regulation (EC) No 396/2005 an overview of the MRL changes that occurred since the entry into force of the Regulation mentioned above is provided below (Table 1).

| Procedure          | Legal implementation | Remarks                      |
|--------------------|----------------------|------------------------------|
| MRL application    | Commission Implementing Regulation (EU) 2015/401<sup>(a)</sup> | Pome fruits and grapes (EFSA, 2014) |

MRL: maximum residue level.

(a): Commission Regulation (EU) 2015/401 of 25 February 2015 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 acetamiprid, chromafenozide, cyazofamid, dicamba, difenoconazole, fenpyrazamine, fluazinam, formetanate, nicotine, penconazole, pymetrozine, pyraclostrobin, tau-fluvalinate and tebuconazole in or on certain products. OJ L 71, 14.3.2015, p. 114–156.

For the purpose of this MRL review, all the uses of chromafenozide currently authorised within the EU as submitted by the Member States during the GAP collection, have been reported by the RMS in the GAP overview file. According to the information provided in the GAP forms, no uses are currently authorised for chromafenozide in Member States and no import tolerance are currently in place. Although MRLs based on a previous MRL application were legally implemented, the uses assessed by EFSA in the past are finally not authorised in any Member State (EFSA, 2014).

Assessment

Considering that no uses are currently authorised for chromafenozide within the European Union, that no codex maximum residue limits (CXLs) are available for this active substance and that no uses authorised in third countries were notified to the RMS, European consumers are not expected to be
exposed to residues of chromafenozide and a consumer risk assessment is, in principle, not required. Risk managers might have interest, however, to enforce against the potential illegal use of chromafenozide within the EU, as well as the presence of illegitimate residue levels in imported products.

Therefore, in order to assist risk managers in applying the most appropriate enforcement measures, EFSA assessed the available data with particular attention to the analytical methods, the toxicological reference values and the nature of residues in plants and livestock.

EFSA has based its assessment on the draft assessment report (DAR) prepared under Council Directive 91/414/EEC (Hungary, 2013a,b), the conclusion on the peer review of the pesticide risk assessment of the active substance chromafenozide (EFSA, 2013) and the previous reasoned opinion on chromafenozide (Hungary, 2013c; EFSA, 2014). The evaluation report submitted by the RMS in the framework of this review (Hungary, 2018) was considered as additional supporting information. 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.

Primary crop metabolism of chromafenozide was investigated after foliar treatment on fruits and fruiting vegetables (apples), pulses and oilseeds (soybeans), cereals (rice) with $^{14}$C-phenyl-labelled chromafenozide and assessed in the framework of the peer review (EFSA, 2013; Hungary, 2013b). It was concluded during the peer review that chromafenozide was not extensively metabolised and thus the majority of the parent compound remained unchanged. The presence of minor degradation products of chromafenozide was attributed most likely not to plant metabolism but to photolysis of chromafenozide on the plant surface. The residue pattern was comparable in the different crops (apple, rice and soybean).

Therefore, based on the available data for the active substance under assessment, the parent compound only is considered to be the most adequate marker for enforcement against the potential illegal use of chromafenozide in plants.

Livestock metabolism of chromafenozide was investigated in lactating goats dosed with labelled $^{14}$C-chromafenozide considering the occurrence of significant residues in fruit pomace (Hungary, 2013b). Upon repeated oral administration of chromafenozide to lactating goats, radioactivity was eliminated almost completely, mainly via the faeces. Transfer of radioactivity to milk was negligible ($< 0.005$ mg eq./kg), and residues in the tissues were also very low (0.05 µg eq./kg in liver) and only the parent was identified or negligible ($< 0.002$ mg eq./kg other edible matrices). Chromafenozide was detected only in liver, and no significant other metabolites were detected in any of the tested matrices. Hence, the residue definition for animal products is proposed as chromafenozide.

An analytical enforcement method is available to monitor chromafenozide residues in high water (apple, pears) and high acid (grape) content commodities with a limit of quantification (LOQ) of 0.01 mg/kg and was assessed during the peer review (EFSA, 2013). The determination is carried out by high-performance liquid chromatography (HPLC) with a diode array detector (DAD) or ultraviolet (UV) detector. A confirmatory high-performance liquid chromatography with tandem mass spectrometry (HPLC-MS/MS) method validated on high water (apple) and high acid (grape) content matrices is available. A new HPLC-MS/MS method monitoring two ion transitions was proposed for enforcement purpose on high water (apple), high acid (grapes), high oil (olive) content commodities and on wheat straw. The method was sufficiently validated in terms of specificity, linearity, precision, accuracy at the LOQ of 0.01 mg/kg (Hungary, 2013c; EFSA, 2014). During the completeness check, information on the availability of analytical methods for the enforcement of chromafenozide was received from the EURLs (EURL, 2018). On the basis of the information provided, liquid chromatography with tandem mass spectrometry (LC-MS/MS) methods are sufficiently validated in plant commodities (high water, high acid, high fat content and dry matrices) at the LOQs of 0.01 (validated in tomato, grapes and almonds) and at a LOQs of 0.005 mg/kg (validated in wheat, rye, oat and rice), respectively.

For animal commodities, validated analytical methods for enforcement are not available (Hungary, 2013a,b; EURLs, 2018).

It is expected that chromafenozide can be enforced with an LOQ of 0.01 mg/kg in all plant commodities. For animal commodities, in the absence of fully validated analytical methods, the default LOQ of 0.01 mg/kg is tentatively proposed.

The toxicological assessment of chromafenozide was peer reviewed under Directive 91/414/EEC, which resulted in an acceptable daily intake (ADI) being established at 0.27 mg/kg body weight (bw) per day and an acute reference dose (ARfD) not being considered necessary (EFSA, 2013).

Chronic exposure calculations were performed using revision 2 of the EFSA PRIMo (EFSA, 2007). In order to assess whether the reported LOQ values are sufficiently protective for European consumers,
chronic and acute intake calculations were performed. These calculations were carried out assuming residues present at the LOQ of 0.01 mg/kg in all plant commodities and at the default LOQ of 0.01 mg/kg in all commodities of animal origin.

The calculated exposures were compared with the toxicological reference values for chromafenozide. The highest chronic exposure was calculated for UK infants, representing 0.3% of the ADI. EFSA highlights that this calculation does not reflect real exposure of consumers to chromafenozide residues. This theoretical calculation only indicates that the above reported LOQ values would provide a satisfactory level of protection for European consumers.

Conclusions and Recommendations

Residues of chromafenozide are not expected to occur in any plant commodity or in any animal product because no uses or import tolerances are currently authorised for chromafenozide in the EU and no CXLs are available for this active substance. A risk assessment is therefore in principle not required.

Nevertheless, to assist risk managers in applying the most appropriate enforcement measures (against potential illegal uses), EFSA assessed the available data with particular attention to the analytical methods and the nature of residues in plants and livestock.

According to the results from the available metabolism studies in primary, rotational crops and in animals, the parent compound is considered to be the most adequate marker for enforcement against the potential illegal use of chromafenozide. It is expected that this compound can be enforced with an LOQ of 0.01 mg/kg in all plant commodities. For animal commodities, an enforcement method is not available. In the absence of fully validated analytical methods, the default LOQ of 0.01 mg/kg is tentatively proposed.

Considering that the enforcement against potential illegal uses falls under the remit of risk managers, EFSA is not in a position to recommend whether the default MRL of 0.01 mg/kg, as defined by Regulation (EC) No 396/2005, or whether the setting of specific LOQ values for plant and animal commodities should apply. It is noted however that for chromafenozide, LOQs of 0.01 mg/kg in plant commodities and in animal commodities, would provide a satisfactory level of protection for the European consumers.

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Abbreviations

a.s. active substance
ADI acceptable daily intake
ARfd acute reference dose
BBCH growth stages of mono- and dicotyledonous plants
bw body weight
CXL codex maximum residue limit
DAD diode array detector
DAR draft assessment report
DAT days after treatment
DB dietary burden
DM dry matter
eq. residue expressed as a.s. equivalent
EURLs European Union Reference Laboratories for Pesticide Residues (former CRLs)
GAP Good Agricultural Practice
HPLC–MS/MS high-performance liquid chromatography with tandem mass spectrometry
IEDI international estimated daily intake
ILV independent laboratory validation
InChiKey International Chemical Identifier Key
ISO International Organisation for Standardization
IUPAC International Union of Pure and Applied Chemistry
LC–MS/MS liquid chromatography with tandem mass spectrometry
LOQ limit of quantification
Mo monitoring
MRL maximum residue level
MS Member States
NEDI national estimated daily intake
NTMDI national theoretical maximum daily intake
OECD Organisation for Economic Co-operation and Development
PBI plant-back interval
PHI preharvest interval
PRIMo (EFSA) Pesticide Residues Intake Model
PROFile (EFSA) Pesticide Residues Overview File
RA risk assessment
RD residue definition
RMS rapporteur Member State
SANCO Directorate-General for Health and Consumers
SMILES simplified molecular-input line-entry system
TMDI theoretical maximum daily intake
UV ultraviolet (detector)
Appendix A – Summary of authorised uses considered for the review of MRLs

### A.1. Authorised outdoor uses in northern EU

| Crop and/or situation | MS or country | F or G or I\(^{(a)}\) | Pests or group of pests controlled | Preparation | Application | Application rate per treatment |
|-----------------------|---------------|----------------------|----------------------------------|-------------|----------------|-------------------------------|
|                        |               |                      |                                  | Type\(^{(b)}\) | Conc. a.s. | Method kind | Range of growth stages & season\(^{(c)}\) | Number min-max | Interval between application (min) | a.s./L ha min-max | Water L/ha min-max | Rate and unit | PHI (days)\(^{(d)}\) | Remarks |
|                        |               |                      |                                  | Type(b) | Conc. a.s. | Method kind | Range of growth stages & season(c) | Number min-max | Interval between application (min) | a.s./L ha min-max | Water L/ha min-max | Rate and unit | PHI (days)(d) | Remarks |

No authorised uses are reported by European MSs.

MS: Member State; a.s.: active substance.
(a): Outdoor or field use (F), greenhouse application (G) or indoor application (I).
(b): CropLife International Technical Monograph no 2, 6th Edition. Revised May 2008. Catalogue of pesticide.
(c): Growth stage range from first to last treatment (BBCH Monograph, Growth Stages of Plants, 1997, Blackwell, ISBN 3-8263-3152-4), including, where relevant, information on season at time of application.
(d): PHI: minimum preharvest interval.

### A.2. Authorised outdoor uses in southern EU

| Crop and/or situation | MS or country | F or G or I\(^{(a)}\) | Pests or group of pests controlled | Preparation | Application | Application rate per treatment |
|-----------------------|---------------|----------------------|----------------------------------|-------------|----------------|-------------------------------|
|                        |               |                      |                                  | Type\(^{(b)}\) | Conc. a.s. | Method kind | Range of growth stages & season\(^{(c)}\) | Number min-max | Interval between application (min) | a.s./L ha min-max | Water L/ha min-max | Rate and unit | PHI (days)\(^{(d)}\) | Remarks |
|                        |               |                      |                                  | Type(b) | Conc. a.s. | Method kind | Range of growth stages & season(c) | Number min-max | Interval between application (min) | a.s./L ha min-max | Water L/ha min-max | Rate and unit | PHI (days)(d) | Remarks |

No authorised uses are reported by European MSs.

MS: Member State; a.s.: active substance.
(a): Outdoor or field use (F), greenhouse application (G) or indoor application (I).
(b): CropLife International Technical Monograph no 2, 6th Edition. Revised May 2008. Catalogue of pesticide.
(c): Growth stage range from first to last treatment (BBCH Monograph, Growth Stages of Plants, 1997, Blackwell, ISBN 3-8263-3152-4), including, where relevant, information on season at time of application.
(d): PHI: minimum preharvest interval.
### A.3. Authorised indoor uses (and post-harvest uses) in EU

| Crop and/or situation | MS or country | F | G | I | Pests or group of pests controlled | Preparation | Application | Application rate per treatment | PHI (days) | Remarks |
|-----------------------|--------------|---|---|---|-----------------------------------|-------------|-------------|---------------------------------|------------|---------|
|                       |              |   |   |   |                                   | 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 |             |
|                       |              |   |   |   |                                   |             |            |           |                                   |            |                     |               |               |              |             |

No authorised uses are reported by European MSs.

MS: Member State; a.s.: active substance.
(a): Outdoor or field use (F), greenhouse application (G) or indoor application (I).
(b): CropLife International Technical Monograph no 2, 6th Edition. Revised May 2008. Catalogue of pesticide.
(c): Growth stage range from first to last treatment (BBCH Monograph, Growth Stages of Plants, 1997, Blackwell, ISBN 3-8263-3152-4), including, where relevant, information on season at time of application.
(d): PHI: minimum preharvest interval.

### A.4. Import tolerance

| Crop and/or situation | MS or country | F | G | I | Pests or group of pests controlled | Preparation | Application | Application rate per treatment | PHI (days)(d) | Remarks |
|-----------------------|--------------|---|---|---|-----------------------------------|-------------|-------------|---------------------------------|------------|---------|
|                       |              |   |   |   |                                   | 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 |             |
|                       |              |   |   |   |                                   |             |            |           |                                   |            |                     |               |               |              |             |

No authorised uses are reported by European MSs.

MS: Member State; a.s.: active substance.
(a): Outdoor or field use (F), greenhouse application (G) or indoor application (I).
(b): CropLife International Technical Monograph no 2, 6th Edition. Revised May 2008. Catalogue of pesticide.
(c): Growth stage range from first to last treatment (BBCH Monograph, Growth Stages of Plants, 1997, Blackwell, ISBN 3-8263-3152-4), including, where relevant, information on season at time of application.
(d): PHI: minimum preharvest interval.
Appendix B – List of end points

B.1. Residues in plants

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

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

| Primary crops (available studies) | Crop groups | Crop(s) | Application(s) | Sampling (DAT) | Comment/source |
|----------------------------------|-------------|---------|----------------|----------------|----------------|
| Fruit crops                      | Apple       |         | 1 x 100 g a.s./ha, 2 x 100 g a.s./ha, 1 x 465 g a.s./ha | 0, 14, 30, 62 | Radiolabelled chromafenozide: phenyl-14C-chromafenozide (Hungary, 2013a) |
| Cereals/grass                    | Rice        |         | 1 x 100 g a.s./ha, 1 x 500 g a.s./ha | 0, 13, 29 | Radiolabelled chromafenozide: phenyl-14C-chromafenozide (Hungary, 2013a) |
| Pulses/oilseeds                 | Soybean     |         | 1 x 100 g a.s./ha, 1 x 500 g a.s./ha | 0, 14, 27, 60 | Radiolabelled chromafenozide: phenyl-14C-chromafenozide (Hungary, 2013a) |

| Rotational crops (available studies) | Crop groups | Crop(s) | Application(s) | PBI (DAT) | Comment/source |
|-------------------------------------|-------------|---------|----------------|-----------|----------------|
|                                     |             |         |                |           | No data available and not required (EFSA, 2013) |

| Processed commodities (hydrolysis study) | Conditions | Stable? | Comment/source |
|-----------------------------------------|------------|---------|----------------|
| Pasteurisation                          | (20 min, 90°C, pH 4) | Yes | Radiolabelled 14C-chromafenozide was stable during processing in apple juice heated at temperatures up to 60 to 85°C for 2 min (EFSA, 2013; Hungary, 2013a) |
| Baking, brewing and boiling             | (60 min, 100°C, pH 5) | Not triggered | (EFSA, 2013) |
| Sterilisation                           | (20 min, 120°C, pH 6) | Not triggered | (EFSA, 2013) |
Can a general residue definition be proposed for primary crops?
Yes EFSA (2013)

Rotational crop and primary crop metabolism similar?
Not applicable EFSA (2013)

Residue pattern in processed commodities similar to residue pattern in raw commodities?
Not applicable EFSA (2013)

Plant residue definition for monitoring (RD-Mo)
Chromafenozide

Plant residue definition for risk assessment (RD-RA)
Not relevant for enforcement against illegal uses.

Methods of analysis for monitoring of residues (analytical technique, matrix groups, LOQs)
Matrices with high water and high acid content:
- HPLC-DAD/UV, LOQ of 0.01 mg/kg, validated for apples, grapes; confirmatory method (HPLC–MS/MS) and ILV available noting that the data gap identified during the peer review concerning verification of the extraction efficiency is still open (EFSA, 2013, 2014; Hungary, 2013a, 2018)

Matrices with high water, high acid, high oil content and dry matrices:
- HPLC–MS/MS, LOQ of 0.01 mg/kg, sufficiently on high water (apple), high acid (grapes), high oil (olive) content commodities and on wheat straw (Hungary, 2013a)
- LC–MS/MS, LOQ of 0.01 mg/kg validated for high acid, high water and high oil content matrices (on tomato, grapes and almonds) and a LOQ of 0.005 mg/kg for dry commodities validate on wheat, rye, oat and rice (EURLs, 2018)

a.s.: active substance; DAT: days after treatment; PBI: plant-back interval; HPLC–MS/MS: high-performance liquid chromatography with tandem mass spectrometry; LC–MS/MS: liquid chromatography with tandem mass spectrometry; LOQ: limit of quantification; ILV: independent laboratory validation; DAD: diode array detector; UV: ultraviolet.

B.1.2. Magnitude of residues in plants
Not relevant since neither EU uses nor import tolerances are currently authorised for chromafenozide.

B.2. Residues in livestock

B.2.1. Nature of residues and methods of analysis in livestock

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

| Livestock (available studies) | Animal     | Dose (mg/kg bw per day) | Duration (days) | Comment/Source                                                                 |
|-----------------------------|------------|-------------------------|-----------------|-------------------------------------------------------------------------------|
| Lactating goats             | 0.006      | 7                       | Radiolabelled $^{14}$C-chromafenozide, goat 1; 76 kg (Hungary, 2013a)         |
|                             | 0.42       | 7                       | Radiolabelled $^{14}$C-chromafenozide, goat 2; 54 kg (Hungary, 2013a)         |

bw: body weight.
Time needed to reach a plateau concentration in milk and eggs (days)

| | Milk | Eggs |
|---|---|---|
| Milk | A plateau level of approximately 0.004 µg eq/g milk was reached after approximately 2 days (Hungary, 2013a) | No data |
| Eggs | Similar profile was observed in the goat and rat study with chromafenozide only identified as the major compound (EFSA, 2013) | No data |

Metabolism in rat and ruminant similar

| | Yes |
|---|---|
| Yes | EFSA (2013) |

Can a general residue definition be proposed for animals?

| | Yes |
|---|---|
| Yes | EFSA (2013) |

Animal residue definition for monitoring (RD-Mo)

| | Chromafenozide |
|---|---|
| Chromafenozide | Not relevant for enforcement against illegal uses |

Animal residue definition for risk assessment (RD-RA)

| | Not relevant for enforcement against illegal uses |
|---|---|

Fat soluble residues

| | No |
|---|---|
| No | EFSA (2013) |

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

| | Not available |
|---|---|
| Not available | |

B.2.2. Magnitude of residues in livestock

Not relevant since neither EU uses nor import tolerances are currently authorised for chromafenozide.

B.3. Consumer risk assessment

Not relevant since no ARfD has been considered necessary.

| | Not considered necessary (EFSA, 2013) |
|---|---|
| ARfD | |

ADI

| 0.27 mg/kg bw per day (EFSA, 2013) |
|---|
| 0.27 mg/kg bw per day (EFSA, 2013) |

TMDI according to EFSA PRIMo

| Not assessed in this review |
|---|
| Not assessed in this review |

NTMDI, according to (to be specified)

| Not assessed in this review |
|---|
| Not assessed in this review |

Highest IEDI, according to EFSA PRIMo (rev. 2)

| 0.3% ADI (UK, infants) |
|---|
| 0.3% ADI (UK, infants) |

NEDI (% ADI)

| Not assessed in this review |
|---|
| Not assessed in this review |

Assumptions made for the calculations

The calculation is based on the LOQs for enforcement according to the available analytical methods for plant commodities and on the default LOQ for animal commodities.

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. IEDI: international estimated daily intake.
## Appendix C – Pesticide Residue Intake Model (PRIMo) PRIMo(EU)

### Chromafenozide

| Status of the active substance: Code no. | LOQ (mg/kg bw): | Proposed LOQ: | ADI (mg/kg bw per day): | ARfD (mg/kg bw): |
|----------------------------------------|-----------------|---------------|------------------------|-----------------|
| Code no.                               | 0.27            |               | 0.27                   | n.n.            |
| Source of ADI: EFSA                    | Source of ADI: EFSA |
| Year of evaluation: 2013               | Year of evaluation: 2013 |

### Toxicological end points

| TMDI (range) in % of ADI | Minimum – maximum |
|--------------------------|-------------------|
| Chromafenozide           |                   |

### Chronic risk assessment – refined calculations

| Commodity/group of commodities | TMDI (range) in % of ADI | Minimum – maximum |
|--------------------------------|--------------------------|-------------------|
| Milk and cream                | 0.0                      |                   |
| Potatoes                      | 0.0                      |                   |
| Wheat                         | 0.0                      |                   |

### Conclusion:

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

| Commodity | pTMRL/threshold MRL (mg/kg) | No of commodities for which ARfD/ADI is exceeded (IESTI 1) | No of commodities for which ARfD/ADI is exceeded (IESTI 2) | No of commodities for which ARfD/ADI is exceeded (IESTI 1) | No of commodities for which ARfD/ADI is exceeded (IESTI 2) |
|-----------|----------------------------|----------------------------------------------------------|----------------------------------------------------------|----------------------------------------------------------|----------------------------------------------------------|
| Processed commodities | pTMRL/ARfD | --- | --- | --- | --- |

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

| Commodity | pTMRL/threshold MRL (mg/kg) | No of commodities for which ARfD/ADI is exceeded (IESTI 1) | No of commodities for which ARfD/ADI is exceeded (IESTI 2) | No of commodities for which ARfD/ADI is exceeded (IESTI 1) | No of commodities for which ARfD/ADI is exceeded (IESTI 2) |
|-----------|----------------------------|----------------------------------------------------------|----------------------------------------------------------|----------------------------------------------------------|----------------------------------------------------------|
| Processed commodities | pTMRL/ARfD | --- | --- | --- | --- |

---

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

***) pTMRL: provisional temporary MRL.

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**Conclusion:**

As no ARfD was considered necessary, it is concluded that the short-term intake of Chromafenozide residues is unlikely to present a public health concern.
Appendix D – Decision tree for deriving MRL recommendations

Evaluation of the GAPs and available residues data at EU level

1. GAP or DB > 0.1 mg/kg QM in EU?
   - Yes → MRL derived in Section 3?
   - No → GAP or DB > 0.1 mg/kg QM in EU?

2. MRL derived in Section 3?
   - Yes → MRL fully supported by data?
   - No → Not considered for the RA.

3. MRL fully supported by data?
   - Yes → Fall-back MRL available?
   - No → Not considered for the RA.

4. Fall-back MRL available?
   - Yes → Median/highest values are included in the RA.
   - No → Not considered for the RA.

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

1. Risk identified?
   - Yes → Median/highest values are included in the RA.
   - No → Not considered for the RA.

2. Tentative median/highest values are included in the RA.
   - Yes → Fall-back MRL available?
   - No → Not considered for the RA.

3. Fall-back MRL available?
   - Yes → MRL is recommended.
   - No → Not considered for the RA.

4. Median/highest values are included in the RA.
   - Yes → Fall-back MRL available?
   - No → Not considered for the RA.

5. Fall-back MRL available?
   - Yes → MRL is recommended.
   - No → Not considered for the RA.

Recommendations resulting from EU authorisations and import tolerances

1. (A) Specific LOQ or default MRL?
2. (B) Specific LOQ or default MRL?
3. (C) Maintain current EU MRL?
4. (D) Specific LOQ or default MRL?
5. (E) Establish tentative EU MRL?
6. (F) Specific LOQ or default MRL?
7. (G) MRL is recommended.
Review of the existing MRLs for chromafenozide

Comparison of the EU recommendation with the existing CXL

- CXL available?
  - Yes:
    - RD comparable?
      - Yes:
        - CXL higher?
          - Yes: Maintain EU recommendation; higher CXL is safe for consumer.
          - No: Maintain EU recommendation; EU recommendation is covered as well.
        - No: CXL is included in the RA.
      - No: Risk identified?
        - Yes: CXL supported by data?
          - Yes: Codex median/highest residues are included in the RA.
          - No: CXL is included in the RA.
        - No: Risk identified?
          - Yes: CXL higher?
            - Yes: Maintain EU recommendation; higher CXL is safe for consumer.
            - No: Maintain current CXL or EU recommendation.
          - No: Maintain current CXL or EU recommendation.
    - No: Input values for the RA remain unchanged.
  - No: Input values for the RA remain unchanged.

Consumer risk assessment with consideration of the existing CXL

- CXL supported by data?
  - Yes: Codex median/highest residues are included in the RA.
  - No: CXL is included in the RA.

- Risk identified?
  - Yes: Maintain EU recommendation; higher CXL is not safe for consumer.
  - No: Input values for the RA remain unchanged.

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 E – Used compound codes

| Code/trivial name<sup>(a)</sup> | IUPAC name/SMILES notation/InChiKey<sup>(b)</sup> | Structural formula<sup>(c)</sup> |
|-------------------------------|---------------------------------------------|---------------------------------|
| Chromafenozide               | $N'$-tert-butyl-5-methyl-$N'$-(3,5-xyloyl)chromane-6-carbohydrazide  
Cc1cc(C)cc(c1)C(=O)N(NC(=O)c2ccc3OCCCc3c2C)C(C)(C)C  
HPNSNYBUACDFDR-UHFFFAOYSA-N | ![Structural formula image](image_url) |

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

(a): The metabolite name in bold is the name used in the conclusion.
(b): ACD/Name 2017.2.1 ACD/Labs 2017 Release (File version N40E41, Build 96719, 6 September 2017).
(c): ACD/ChemSketch 2017.2.1 ACD/Labs 2017 Release (File version C40H41, Build 99535, 14 February 2018).