Modification of the existing maximum residue level for fluopicolide in chards

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Abstract

In accordance with Article 6 of Regulation (EC) No 396/2005, the competent national authority in Belgium sent an application to modify the existing maximum residue level (MRL) for the active substance fluopicolide in chards. In order to accommodate for the intended use of fluopicolide, the evaluating Member State (EMS) proposed to raise the existing MRLs from 4 mg/kg to 6 mg/kg. Belgium drafted the evaluation report in accordance with Article 8 of Regulation (EC) No 396/2005, which was submitted to the European Commission and forwarded to EFSA. According to EFSA, the data are sufficient to derive a MRL proposal of 6 mg/kg on chards. Adequate analytical enforcement methods are available to control the residues of fluopicolide in chards at the validated limit of quantification (LOQ) of 0.01 mg/kg. Based on the risk assessment results, EFSA concluded that the proposed use of fluopicolide on chards will not result in a consumer exposure exceeding the toxicological reference values and therefore is unlikely to pose a consumer health risk.

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Summary

In accordance with Article 6 of Regulation (EC) No 396/2005, the competent national authority in Belgium, Federal Public Service Health, Food Chain Safety and Environment, hereafter referred to as the evaluating Member State (EMS), compiled an application to modify the existing maximum residue level (MRL) for the active substance fluopicolide in chards. 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) on 8 March 2017. To accommodate for the intended use of fluopicolide, the EMS proposed to raise the existing MRL from 4 mg/kg to 6 mg/kg.

EFSA assessed the application and the evaluation report as required by Article 10 of the MRL regulation. Based on the conclusions derived by EFSA in the framework of Directive 91/414/EEC, the data evaluated under previous MRL assessments the following conclusions are derived.

The metabolism of fluopicolide in primary crops was investigated in crops belonging to the groups of fruit, root and leafy crops.

Studies investigating the effect of processing on the nature of fluopicolide (hydrolysis studies) demonstrated that the active substance is stable.

The metabolism in rotational crops showed to be similar to the pathway observed in primary crops.

Based on the metabolic pattern identified in plant metabolism studies, in hydrolysis studies and the toxicological profile of metabolites, the residue definition for plant products was proposed as fluopicolide for enforcement; for risk assessment, two separate residue definitions were derived (i.e. fluopicolide and its metabolite M-01). These residue definitions are applicable to primary crops, rotational crops and processed products.

EFSA concluded that for the use on the crop under consideration, the agreed residue definitions are applicable.

Sufficiently validated analytical methods, including a multi-residue QuEChERS method using high performance liquid chromatography with tandem mass spectrometry (HPLC–MS/MS) for detection, are available to quantify residues in chards according to the enforcement residue definition at the limit of quantification (LOQ) of 0.01 mg/kg.

The available residue trials are sufficient to derive a MRL proposal of 6 mg/kg for chards and are supported by acceptable storage stability data.

The occurrence of fluopicolide residues in rotational crops was investigated in the framework of the EU pesticides peer review. Based on the available information on the magnitude of residues, it was concluded that low residues of metabolite M-01 may occur in rotational crops. Provided that the active substance is used on chards according to the proposed Good Agricultural Practice (GAP), the exposure to residues of M-01 via rotational crops is expected to be low.

Residues of fluopicolide in commodities of animal origin were not assessed since chards are normally not fed to livestock.

The toxicological profile of fluopicolide was assessed in the framework of the European Union (EU) pesticides peer review under Directive 91/414/EEC, and the data were sufficient to derive an acceptable daily intake (ADI) of 0.08 mg/kg body weight (bw) per day and an acute reference dose (ARfD) of 0.18 mg/kg bw. In addition, an ADI of 0.05 mg/kg bw per day and an ARfD of 0.3 mg/kg bw was proposed for its metabolite M-01 (2,6-dichlorobenzamide).

The consumer risk assessment was performed with revision 2 of the EFSA Pesticide Residues Intake Model (PRIMo). No long-term or acute consumer intake concerns were identified. For fluopicolide, the highest estimated chronic intake accounted for 2.8% of the ADI (WHO Cluster diet B) and the highest acute exposure was calculated to be 30.2% of the ARfD for chards.

For the metabolite M-01, the highest estimated chronic and acute intake from chards only was calculated accounting for less than 0.01% of the ADI and 0.1% of the ARfD. It is noted that the chronic risk assessment for the metabolite M-01 could not be performed as no comprehensive overview is available on the concentration of M-01 in commodities for which the use of fluopicolide is authorised. However, the contribution of M-01 residues in chards to the chronic exposure was calculated to be low (< 0.01% of the ADI) and is unlikely to pose a public health concern.

A comprehensive assessment of the quantity of M-01 residues in primary and rotational crops and the dietary exposure assessment for M-01 should be performed in the framework of the MRL review.
EFSA concluded that the proposed use of fluopicolide on chards will not result in a consumer exposure exceeding the toxicological reference values, and therefore, it is unlikely to pose a risk to consumer health.

EFSA proposes to amend the existing MRL as reported in the summary table below.

Full details of all endpoints and the consumer risk assessment can be found in Appendices B–D.

### Table: Enforcement residue definition: Fluopicolide

| Code\(^{(a)}\) | Commodity            | Existing EU MRL (mg/kg) | Proposed EU MRL (mg/kg) | Comment/justification |
|---------------|----------------------|-------------------------|-------------------------|-----------------------|
| 0252030       | Chards/beet leaves   | 4                       | 6                       | By extrapolation from indoor residue trials on lettuce (open leaf varieties). MRL of 6 mg/kg covers the indoor and outdoor uses of fluopicolide on chards. Risk for consumers is unlikely. |

MRL: maximum residue level.

\(^{(a)}\): Commodity code number according to Annex I of Regulation (EC) No 396/2005.
Table of contents

Abstract ................................................................................................................................................... 1
Summary ................................................................................................................................................. 3
Assessment ............................................................................................................................................. 6
1. Residues in plants ........................................................................................................................ 7
   1.1. Nature of residues and methods of analysis in plants .............................................................. 7
   1.1.1. Nature of residues in primary crops ....................................................................................... 7
   1.1.2. Nature of residues in rotational crops .................................................................................... 7
   1.1.3. Nature of residues in processed commodities ........................................................................... 7
   1.1.4. Methods of analysis in plants .................................................................................................. 7
   1.1.5. Stability of residues in plants ................................................................................................... 7
   1.1.6. Proposed residue definitions .................................................................................................. 8
   1.2. Magnitude of residues in plants .................................................................................................. 8
   1.2.1. Magnitude of residues in primary crops .................................................................................. 8
   1.2.2. Magnitude of residues in rotational crops ................................................................................. 8
   1.2.3. Magnitude of residues in processed commodities ...................................................................... 8
   1.2.4. Proposed MRLs ....................................................................................................................... 8
2. Residues in livestock ....................................................................................................................... 8
3. Consumer risk assessment ............................................................................................................. 8
4. Conclusion and Recommendations ................................................................................................. 9
References ............................................................................................................................................... 9
Abbreviations ........................................................................................................................................... 10
Appendix A – Summary of intended GAP triggering the amendment of existing EU MRLs .................. 12
Appendix B – List of end points ............................................................................................................ 13
Appendix C – Pesticide Residue Intake Model (PRIMo) .................................................................... 18
Appendix D – Input values for the exposure calculations .................................................................... 20
Appendix E – Used compound codes ................................................................................................. 21
Assessment

Fluopicolide is the ISO common name for 2,6-dichloro-N-[3-chloro-5-(trifluoromethyl)-2-pyridyl methyl]benzamide (IUPAC). The chemical structures of the active substance and its main metabolites are reported in Appendix E.

Fluopicolide was evaluated in the framework of Directive 91/414/EEC with United Kingdom designated as rapporteur Member State (RMS) for the representative use as a foliar treatment on vine and potatoes. The draft assessment report (DAR) prepared by the RMS has been peer reviewed by EFSA (2009b).

Fluopicolide was approved for the use as fungicide on 1 June 2010.

The European Union maximum residue levels (EU MRLs) for fluopicolide are established in Annex III A of Regulation (EC) No 396/2005. The review of existing MRLs according to Article 12 of Regulation (EC) No 396/2005 (MRL review) has not yet been performed. EFSA has issued several reasoned opinions on the modification of MRLs for fluopicolide. The proposals from these reasoned opinions have been considered in recent regulations, for EU MRL legislation.

In accordance with Article 6 of Regulation (EC) No 396/2005, the competent national authority in Belgium, Federal Public Service Public Health, Food Chain Safety and Environment compiled an application to modify the existing MRL for the active substance fluopicolide in chards. The evaluating Member State (EMS) compiled an evaluation report in accordance with Article 6(3) of Regulation (EC) No 396/2005, which was submitted to the European Commission and forwarded to the European Food Safety Authority (EFSA) on 8 March 2017. The application was included in the EFSA Register of Questions with the reference number EFSA-Q-2017-00226 and the following subject:

Fluopicolide: MRL in chards

To accommodate for the intended use of fluopicolide, the EMS proposed to raise the existing MRL from 4 mg/kg to 6 mg/kg.

EFSA based its assessment on the evaluation report submitted by the EMS (Belgium, 2017), the DAR (and its addendum) prepared under Council Directive 91/414/EEC (United Kingdom, 2005, 2008), the Commission review report on fluopicolide (European Commission, 2010a), the conclusion on the peer review of the pesticide risk assessment of the active substance fluopicolide (EFSA, 2009b), as well as the conclusions from previous EFSA opinions on fluopicolide (EFSA, 2009a, 2011, 2012a, 2012b, 2013, 2014, 2015a, 2015b).

For this application, the data requirements established in Regulation (EU) No 544/2011 and the guidance documents applicable at the date of submission of the application to the EMS are applicable (European Commission, 1997a–g, 2000, 2010a,b, 2017; OECD, 2011, 2016). 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.

The detailed description of the intended use of fluopicolide, which is the basis for the current MRL application, is reported in Appendix A.

A selected list of end points of the studies assessed by EFSA in the framework of this MRL application, review, including the end points of relevant studies assessed previously, submitted in support of the current MRL application, are presented in Appendix B.

The evaluation report submitted by the EMS (Belgium, 2017) and the exposure calculations using the EFSA Pesticide Residues Intake Model version 2 (PRIMo) are considered as supporting documents to this reasoned opinion and, thus, are made publicly available as background documents to this reasoned opinion.

1 Commission Directive 2010/15/EU of 8 March 2010 amending Council Directive 91/414/EEC to include fluopicolide as active substance, OJ L 58, 9.3.2010, p. 5-7.

2 For an overview of all MRL Regulations on this active substance, please consult: http://ec.europa.eu/food/plant/pesticides/eu-pesticides-database/public/?event=pesticide.residue.selection&language=EN

3 Commission Regulation (EU) No 283/2013 of 1 March 2013 setting out the data requirements for active substances, 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. OJ L 93, 3.4.2013, p. 1-84.
1. Residues in plants

1.1. Nature of residues and methods of analysis in plants

1.1.1. Nature of residues in primary crops

In the framework of the peer review under Directive 91/414/EEC, the metabolism of fluopicolide in primary crops was evaluated in the fruit (grapes), leafy (lettuce) and root (potato) crop groups (EFSA, 2009b). Based on these metabolism studies, the residue definition was proposed as fluopicolide for monitoring. Considering the two different toxicological end points set for fluopicolide and its metabolite M-01 (2,6-dichlorobenzamide), two separate residue definitions were proposed for risk assessment, as fluopicolide and M-01, respectively (EFSA, 2009b).

1.1.2. Nature of residues in rotational crops

As chards can be grown in rotation with other plants and both fluopicolide and the M-01 are persistent (DT90 values observed in field soil dissipation studies for both substances exceed 1 year); therefore, the possible occurrence of residues in succeeding crops resulting from the primary use must be investigated.

The metabolism in rotational crops showed to be similar to the pathway observed in primary crops (EFSA, 2009b).

1.1.3. Nature of residues in processed commodities

The effect of processing on the nature of fluopicolide was investigated during the peer review. Fluopicolide was shown to be hydrolytically stable under standard hydrolysis conditions representing pasteurisation, baking/brewing/boiling and sterilisation. Thus, for processed commodities, the same residue definition as for raw agricultural commodities (RACs) is applicable (EFSA, 2009b).

1.1.4. Methods of analysis in plants

Analytical methods for the determination of fluopicolide residues in plant commodities were assessed during the peer review under Directive 91/414/EEC (EFSA, 2009b).

Several analytical methods for the determination of fluopicolide residues in high water-, high acid- and in high starch/high protein-content commodities using gas chromatography with mass spectrometric detection (GC-MSD), liquid chromatography with tandem mass spectrometry (LC-MS/MS) and high performance liquid chromatography with tandem mass spectrometry (HPLC-MS/MS) at limit of quantifications (LOQs) from 0.01 mg/kg (for high water content commodities) to 0.1 mg/kg (for acidic commodities), are available. Independent laboratory validation (ILV) was performed for GC-MSD and HPLC-MS/MS methods. There is also an analytical method for the determination of the metabolite M-01 available (EFSA, 2009b).

The multiresidue QuEChERS method described in the European Standard EN 15662:2008 (CEN, 2008) and using HPLC-MS/MS detection is also applicable to analyse fluopicolide residues in high water-, high acid-, high oil- and in high starch/high protein content matrices at the LOQ of 0.01 mg/kg (EFSA, 2015b).

As chards belong to high water-content commodity group, EFSA concludes that sufficiently validated analytical methods are available for enforcing the proposed MRL for fluopicolide in chards.

1.1.5. Stability of residues in plants

The stability of fluopicolide and its metabolite M-01 residues in plant matrices under storage conditions prior to analysis was assessed during the peer review under Directive 91/414/EEC (EFSA, 2009b). Residues of fluopicolide and its metabolite M-01 were found to be stable at ≤ −18°C for at least 30 months in high water-, high acid- and in high starch content matrices and for at least 18 months in other matrices (wheat straw). In the residue trials submitted in support of the current MRL application (i.e. lettuce), the samples were stored for a maximum period of 10 months under conditions, for which integrity of the samples was demonstrated. Thus, it is concluded that the residue data are valid with regard to storage stability (EFSA, 2015b).
1.1.6. **Proposed residue definitions**

The current residue definition for enforcement set in Regulation (EC) No 396/2005 is identical to the residue definition derived in the peer review.

For chards, EFSA concludes that the metabolism of fluopicolide is sufficiently addressed and the residue definitions for enforcement and risk assessment agreed during the peer review are applicable.

1.2. **Magnitude of residues in plants**

1.2.1. **Magnitude of residues in primary crops**

Eight trials performed on open leaf varieties of lettuce under indoor conditions during the 2012 growing season were submitted. Fluopicolide residues were in the range of 0.18–3.10 mg/kg, resulting in an MRL proposal of 6 mg/kg. Metabolite M-01 was observed in much lower levels, ranging from the LOQ of 0.01 mg/kg up to 0.032 mg/kg.

Since all trials were conducted on open leaf varieties, according to the guidance document SANCO 7525/VI/95-rev. 10.3 (European Commission, 2017) the derived MRL proposal of 6 mg/kg can be extrapolated to chards.

The results of the residue trials, the related risk assessment input values (highest residue (HR), median residue) and the MRL proposals are summarised in Appendix B.1.2.1.

According to the EMS, the analytical method used to analyse the residue trials’ samples has been sufficiently validated and was proven to be fit for purpose.

1.2.2. **Magnitude of residues in rotational crops**

Field trials conducted on winter wheat, spring wheat, beans and cabbage grown in rotation to potatoes treated with four foliar applications of fluopicolide at a total dose rate of 400 g/ha (4 x 100 g/ha) were evaluated during the peer review. At maturity, fluopicolide residues were below the LOQ (≤ 0.01 mg/kg) in all edible crop parts, except in wheat straw (0.12 mg/kg) and metabolite M-01 residues were found in quantifiable levels in wheat straw and cabbage, up to 0.03 and 0.04 mg/kg, respectively (EFSA, 2009b, 2012a).

Considering that the application rate of the intended use of fluopicolide on chards is lower than the one investigated in the peer review (0.5N), EFSA concludes that low residues may occur in rotational crops. Provided that the active substance is used on chards according to the proposed Good Agricultural Practice (GAP), the exposure to residues of M-01 via rotational crops is expected to be low.

A comprehensive assessment of the quantity of M-01 residues in rotational crops and the dietary exposure should be performed in the framework of the MRL review.

1.2.3. **Magnitude of residues in processed commodities**

Specific studies to assess the magnitude of fluopicolide residues during the processing of the crop under consideration were not provided and are not required as the theoretical maximum daily intake (TMDI) for chards amounts to less than 10% of the acceptable daily intake (ADI) (European Commission, 1997d).

1.2.4. **Proposed MRLs**

The available residue trials are sufficient to derive a MRL proposal for chards (see Appendix B.1.2.1).

2. **Residues in livestock**

The assessment of residues in livestock is not relevant to the present application as chards are not used for animal feed purposes.

3. **Consumer risk assessment**

The consumer risk assessment was performed with revision 2 of the EFSA Pesticide PRIMo. This exposure assessment model contains the relevant European food consumption data for different subgroups of the EU population (EFSA, 2007).
For the calculation of chronic exposure, EFSA used the median residue values as derived, respectively, for fluopicolide and M-01 from the residue trials on the crop under consideration and the median residue values reported in previously issued EFSA reasoned opinions (EFSA, 2009a, 2011, 2012a,b, 2013, 2014, 2015a,b). For the remaining commodities of plant and animal origin, the existing MRLs as established in Annex IIIA of Regulation (EC) No 396/2005 were used as input values for fluopicolide. It is noted that the chronic risk assessment for the metabolite M-01 is incomplete and therefore only indicative. It cannot be completed as no comprehensive overview is available on the concentration of M-01 in commodities, for which the use of fluopicolide is authorised. A full chronic risk assessment for M-01 will be performed in the framework of Article 12 of the Regulation (EC) No 396/2005. 

The short-term exposure assessment for fluopicolide and metabolite M-01 was performed for chards in accordance with the internationally agreed methodology. The calculations were based on the HR derived from supervised field trials on open leaf varieties.

The complete list of input values can be found in Appendix D.2.

- **Fluopicolide**

  Long-term consumer intake concerns were not identified for any of the European diets incorporated in the EFSA PRIMo. The total calculated intake accounted for up to 2.8% of the ADI (WHO Cluster diet B). The contribution to the total consumer exposure of residues in chards was negligible (below 0.03% of the ADI (ES adult)). An acute consumer risk was not identified for the crop under consideration. The acute consumer exposure was calculated to be 30.2% of the acute reference dose (ARfD) for chards.

- **M-01 (2,6-dichlorobenzamide)**

  Chronic exposure to M-01 residues in chards is insignificant, expected to be below 0.01% of the ADI.

  An acute consumer risk was not identified; the highest acute exposure was calculated to be 0.2% of the ARfD for chards.

4. **Conclusion and Recommendations**

   The data submitted in support of this MRL application were found to be sufficient to derive an MRL proposal for chards.

   EFSA concluded that the proposed use of fluopicolide on chards will not result in a consumer exposure exceeding the toxicological reference values and therefore is unlikely to pose a risk to consumers’ health.

   The MRL recommendation is summarised in Appendix B.4.

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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
CEN European Committee for Standardisation (Comité Européen de Normalisation)
CF conversion factor for enforcement to risk assessment residue definition
CS capsule suspension
DAR draft assessment report
DAT days after treatment
DT$_{90}$ period required for 90% dissipation (define method of estimation)
EMS evaluating Member State
FAO Food and Agriculture Organization of the United Nations
GAP Good Agricultural Practice
GC gas chromatography
HPLC-MS/MS high-performance liquid chromatography with tandem mass spectrometry
| Abbreviation | Description |
|--------------|-------------|
| HR           | highest residue |
| IEDI         | international estimated daily intake |
| IESTI        | international estimated short-term intake |
| ILV          | independent laboratory validation |
| ISO          | International Organisation for Standardisation |
| IUPAC        | International Union of Pure and Applied Chemistry |
| JMPR         | Joint FAO/WHO Meeting on Pesticide Residues |
| LC           | liquid chromatography |
| LOQ          | limit of quantification |
| MRL          | maximum residue level |
| MS/MS        | tandem mass spectrometry detector |
| NEU          | northern Europe |
| OECD         | Organisation for Economic Co-operation and Development |
| PBI          | plant-back interval |
| PHI          | preharvest interval |
| PRIMo        | (EFSA) Pesticide Residues Intake Model |
| QuEChERS     | Quick, Easy, Cheap, Effective, Rugged, and Safe (analytical method) |
| RA           | risk assessment |
| RAC          | raw agricultural commodity |
| RD           | residue definition |
| RMS          | rapporteur Member State |
| SANCO        | Directorate-General for Health and Consumers |
| SC           | suspension concentrate |
| SEU          | southern Europe |
| STMR         | supervised trials median residue |
| TMDI         | theoretical maximum daily intake |
| WHO          | World Health Organization |
## Appendix A – Summary of intended GAP triggering the amendment of existing EU MRLs

| Crop and/or situation | NEU, SEU, or country | F G or I \(^{(a)}\) | Pest(s) or group of pests controlled | Preparation | Application | Application rate per treatment | PHI (days) \(^{(d)}\) | Remarks |
|-----------------------|----------------------|---------------------|-------------------------------------|-------------|------------------------|-----------------------------|---------------------|---------|
| Chard (NEU)           | G                    | mildew              | SC 62.5 g/l                         | Spraying    | BBCH 14–47            | 1–2                         | 0.1 kg/ha 14       | (+ 625 g/L propamocarb) |

NEU: northern European Union; SEU: southern European Union; MS: Member State; SC: suspension concentrate; 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 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 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                       | Grapes      | Foliar  |                | 21, 28         |         | EFSA (2009b) |
| Root crops                        | Potato      | Post-harvest | 2 × 200 g/ha | 20             |         |         |
| Leafy crops                       | Lettuce     | Foliar/Soil drench | 2 × 200 g/ha | 14, 35         |         |         |

| Rotational crops (available studies) | Crop groups | Crop(s) | Application(s) | PBI (DAT) | Comment | Source |
|--------------------------------------|-------------|---------|----------------|------------|---------|--------|
| Root/tuber crops                     | Radish      | Soil 1 × 0.4 kg/ha | 29, 133, 365 | Bare soil application; [14C]-phenyl and pyridinyl ring labelled fluopicolide | EFSA (2009b) |
| Leafy crops                          | Lettuce     | Soil 1 × 0.4 kg/ha | 29, 133, 365 |         |         |        |
| Cereal (small grain)                 | Wheat       | Soil 1 × 0.4 kg/ha | 29, 133, 365 |         |         |        |

| Processed commodities (hydrolysis study) | Conditions | Stable? | Comment | Source |
|------------------------------------------|------------|--------|---------|--------|
|                                         | Pasteurisation (20 min, 90°C, pH 4) | Yes    |         | EFSA (2009b) |
|                                         | Baking, brewing and boiling (60 min, 100°C, pH 5) | Yes    |         |        |
|                                         | Sterilisation (20 min, 120°C, pH 6) | Yes    |         |        |

Can a general residue definition be proposed for primary crops? Yes
Rotational crop and primary crop metabolism similar? Yes
Residue pattern in processed commodities similar to residue pattern in raw commodities? Yes
Plant residue definition for monitoring (RD-Mo) Fluopicolide
Plant residue definition for risk assessment (RD-RA) Fluopicolide and M-01 (2,6-dichlorobenzamide), to be considered separately
Methods of analysis for monitoring of residues (analytical technique, crop groups, LOQs) Matrices with high water-, high oil-, high acid- and high starch/high protein-content matrices: GC–MSD, LOQ 0.01 mg/kg
ILV available for GC–MSD and HPLC–MS/MS.

DAT: days after treatment; PBI: plant-back interval; GC–MSD: gas chromatography with mass spectrometric detection; HPLC-MS/MS: high-performance liquid chromatography with tandem mass spectrometry; LOQ: limit of quantification; ILV: independent laboratory validation.
### B.1.1.2. Stability of residues in plants

| Plant products (available studies) | Category                  | Commodity                | T (°C)    | Stability (Months) |
|-----------------------------------|---------------------------|--------------------------|-----------|-------------------|
| High water content                | Cabbage                   | ≤ −18°C                  | 30        |
| High starch                       | Wheat grain, potato       | ≤ −18°C                  | 30        |
| High acid content                 | Grapes                    | ≤ −18°C                  | 30        |
| Others                            | Wheat straw               | ≤ −18°C                  | 18        |

Storage stability data on fluopicolide and M-01 (2,6-dichlorobenzamide), respectively. (EFSA, 2009b)
B.1.2. Magnitude of residues in plants

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

| Commodity | Region/Indoor\(^{(a)}\) | Residue levels observed in the supervised residue trials (mg/kg) | Comments | Calculated MRL (mg/kg) | HR\(^{(b)}\) (mg/kg) | STMR\(^{(c)}\) (mg/kg) | CF\(^{(d)}\) |
|-----------|--------------------------|---------------------------------------------------------------|----------|------------------------|---------------------|---------------------|---------|
| Chards    | Indoor                   | Fluopicolide: 0.18, 0.21, 0.27, 0.30, 0.49, 1.10, 2.80, 3.10, M-01: 4 \(\times\) < 0.01; 0.01; 0.014, 0.018, 0.032 | All the trials were conducted on open leaf varieties of lettuce and can therefore be extrapolated to chards according to the current extrapolation rules. A MRL of 6 mg/kg is therefore proposed for chards. | 6 | 3.1 | 0.4 | – |
|           |                          |                                                               |          | –                     | 0.032               | 0.01                | –       |

MRL: maximum residue level.

(a): NEU: Outdoor trials conducted in northern Europe, SEU: Outdoor trials conducted in southern Europe, Indoor: indoor EU trials or Country code: if non-EU trials.
(b): Highest residue according to the residue definition for monitoring.
(c): Supervised trials median residue according to the residue definition for monitoring.
(d): Conversion factor to recalculate residues according to the residue definition for monitoring to the residue definition for risk assessment.
B.1.2.2. Residues in rotational crops

Confined rotational crop study (quantitative aspect)

Considering that the confined rotational crops studies were conducted with a bare soil application of fluopicolide at a rate of 400 g a.s./ha, i.e. 2N rate the intended application rate for the use on chards, residue levels > 0.01 mg/kg are expected in edible parts of the rotational crops conducted on winter wheat, spring wheat, beans and cabbage grown in rotation to potatoes treated at a total dose rate of 400 g a.s./ha. Significant residue levels are unlikely to occur in rotational crops provided that the active substance is used on chards according to the proposed GAP.

Field rotational crop study

Field trials were conducted on winter wheat, spring wheat, beans and cabbage grown in rotation to potatoes treated at a total dose rate of 400 g a.s./ha. Significant residue levels are unlikely to occur in rotational crops provided that the active substance is used on chards according to the proposed GAP.

a.s: active substance; GAP: Good Agricultural Practice.

B.1.2.3. Processing factors

Not relevant.

B.2. Residues in livestock

Not relevant.

B.3. Consumer risk assessment

ARfD

Fluopicolide: 0.18 mg/kg bw (European Commission, 2010a)
Metabolite M-01: 0.3 mg/kg bw (European Commission, 2010a)

Highest IESTI, according to EFSA PRIMo

Fluopicolide:
Chards: 30.2% of ARfD
Metabolite M-01:
Chards: 0.2% of ARfD

Assumptions made for the calculations

The calculation is based on the highest residue levels expected in chards.
Modification of the existing MRL for fluopicolide in chards

ADI

| Metabolite | M-01: 0.05 mg/kg bw per day (European Commission, 2010a) |

Highest IEDI, according to EFSA PRIMo

| Metabolite | Fluopicolide: 2.8% ADI (WHO Cluster diet B) |
| Contribution of chards: | < 0.03% of ADI (ES adult) |

| Metabolite M-01 | Chards: < 0.01% of ADI |

Assumptions made for the calculations

The calculation is based on the median residue levels derived respectively for fluopicolide and M-01 for raw agricultural commodities for those commodities where data were insufficient to derive an MRL proposal, EFSA considered the existing EU MRL as established in Annex IIIA of Regulation (EC) No 396/2005.

It is noted that the chronic risk assessment for the metabolite M-01 considered residues in chards only as no comprehensive overview is available on the concentration of M-01 in commodities for which the use of fluopicolide is authorised.

Toxicological studies performed on metabolites

Not applicable

B.4. Recommended MRLs

| Code(a) | Commodity | Existing EU MRL (mg/kg) | Proposed EU MRL (mg/kg) | Comment/justification |
|---------|-----------|------------------------|-------------------------|-----------------------|
| 0252030 | Chards/beet leaves | 4 | 6 | By extrapolation from indoor residue trials on lettuce (open leaf varieties). MRL of 6 mg/kg covers the indoor uses of fluopicolide on chards. Risk for consumers is unlikely |

MRL: maximum residue level.

(a): Commodity code number according to Annex I of Regulation (EC) No 396/2005.
### Fluopicolide

**Toxicological end points**

| ADI (mg/kg bw per day) | LOQ (mg/kg bw) | Proposed LOQ |
|------------------------|----------------|--------------|
| 0.08                   | 0.01           |              |

**Source of ADI:** EC

**Source of ARfD:** EC

| Year of evaluation | ADI (mg/kg bw per day) | LOQ (mg/kg bw) | Proposed LOQ |
|--------------------|-------------------------|----------------|--------------|
| 2010a              | 0.08                    | 0.01           |              |

| Year of evaluation | ADI (mg/kg bw per day) | LOQ (mg/kg bw) | Proposed LOQ |
|--------------------|-------------------------|----------------|--------------|
| 2010a              | 0.08                    | 0.01           |              |

#### Status of the active substance:
- included

#### Code no.
- LOQ (mg/kg bw): 0.01
- Proposed LOQ: 0.08

#### ARfD (mg/kg bw):
- 0.18

#### Source of ADI:
- EC

#### Source of ARfD:
- EC

#### Year of evaluation:
- 2010a

### Chronic risk assessment – refined calculations

| TMDI (range in % of ADI) | MS Diet | 2nd contributor to MS diet | Commodity/ group of commodities |
|--------------------------|---------|----------------------------|---------------------------------|
| 0.6                      | Tobacco | 0.5                        | Lettuce                         |
| 0.7                      | Milk and cream | 0.4                      | Table grapes                    |
| 0.8                      | Milk and cream | 0.2                      | Spaghetti                       |
| 0.9                      | Sugar beet | 0.5                      | Milk and cream                  |
| 0.6                      | Table grapes | 0.4                      | Milk and cream                  |
| 0.7                      | Milk and cream | 0.4                      | Sugar beet (root)               |
| 0.8                      | Milk and cream | 0.1                      | Tea                             |
| 0.9                      | Milk and cream | 0.1                      | Table grapes                    |
| 0.6                      | Milk and cream | 0.1                      | Milk and cream                  |
| 0.7                      | Milk and cream | 0.1                      | Tomato                          |
| 0.8                      | Milk and cream | 0.2                      | Tomato                          |
| 0.9                      | Other lettuce and other salad | 0.1              | Broccoli                       |
| 0.6                      | Milk and cream | 0.1                      | Lettuce                         |
| 0.7                      | Milk and cream | 0.1                      | Milk and cream                  |
| 0.8                      | Milk and cream | 0.2                      | Other lettuce and other salad   |
| 0.6                      | Lettuce | 0.1                        | Cucurbits – edible peel         |
| 0.7                      | Lettuce | 0.1                        | Tomato                          |
| 0.8                      | Milk and cream | 0.2                      | Milk and cream                  |
| 0.9                      | Milk and cream | 0.3                      | Tomato                          |
| 0.6                      | Lettuce | 0.1                        | Tomato                          |
| 0.7                      | Lettuce | 0.1                        | Tomato                          |
| 0.8                      | Milk and cream | 0.1                      | Tomato                          |
| 0.9                      | Milk and cream | 0.2                      | Tomato                          |
| 0.6                      | Milk and cream | 0.2                      | Tomato                          |
| 0.7                      | Milk and cream | 0.1                      | Tomato                          |
| 0.8                      | Milk and cream | 0.1                      | Tomato                          |
| 0.9                      | Milk and cream | 0.1                      | Tomato                          |

#### Conclusion:
The estimated Theoretical Maximum Daily Intakes (TMDI), based on pTMRLs were below the ADI. A long-term intake of residues of Fluopicolide is unlikely to present a public health concern.
The acute risk assessment is based on the ARfD. For each commodity, the calculation is based on the highest reported MS consumption per kg bw and the corresponding unit weight from the MS with the critical consumption. If no data on the unit weight was available from that MS, an average European unit weight was used for the IESTI calculation.

In the IESTI 1 calculation, the variability factors were 10, 7 or 5 (according to JMPR manual 2002); for lettuce, a variability factor of 5 was used.

In the IESTI 2 calculations, the variability factors of 10 and 7 were replaced by 5. For lettuce, the calculation was performed with a variability factor of 3.

Threshold MRL, is the calculated residue level which would lead to an exposure equivalent to 100% of the ARfD.

| 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): |
|------------------------------------------------------------|------------------------------------------------------------|------------------------------------------------------------|------------------------------------------------------------|
| **Highest % of ARfD/ADI** | **Processed commodities** | **Processed commodities** | **Processed commodities** |
| **Commodities** | **pTMRL/ threshold MRL (mg/kg)** | **Commodities** | **pTMRL/ threshold MRL (mg/kg)** | **Commodities** | **pTMRL/ threshold MRL (mg/kg)** | **Commodities** | **pTMRL/ threshold MRL (mg/kg)** |
| Beet leaves (chard) | 3.1/- | Beet leaves (chard) | 3.1/- | Beet leaves (chard) | 3.1/- |
| Beet leaves | 22.9 | Fried potatoes | 0.0 | Fried potatoes | 0.01/- |
| Potato puree (flakes) | 0.1/- |
| Carrot, juice | 0.15/- |
| Celeriac juice | 0.15/- |
| Potato puree (flakes) | 0.01/- |
| Fried potatoes | 0.01/- |

No exceedance of the ARfD/ADI was identified for any unprocessed commodity.

For Fluopicolide, IESTI 1 and IESTI 2 were calculated for food commodities for which pTMRLs were submitted and for which consumption data are available.

For each commodity, the calculation is based on the highest reported MS consumption per kg bw and the corresponding unit weight from the MS with the critical consumption. If no data on the unit weight was available from that MS, an average European unit weight was used for the IESTI calculation.

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

Not relevant.

D.2. Consumer risk assessment

| Commodity | Chronic exposure assessment | Acute exposure assessment |
|-----------|----------------------------|--------------------------|
|           | Input (mg/kg) | Comment | Input (mg/kg) | Comment |
| **Risk assessment residue definition 1: fluopicolide** | | | |
| Chards    | 0.40         | STMR    | 3.1          | HR      |
| Commodities in previous Reasoned Opinions under Article 10 of Reg. 396/2005 | See table 5 from the Reasoned Opinion under Article 10 of Reg. 396/2005 (EFSA, 2015b) | Acute risk assessment only for the crop under consideration |
| Other commodities of plant and animal origin | MRL | MRLs in Regulation (EU) 1003/2016 |
| **Risk assessment residue definition 2: Metabolite M-01 (2,6-dichlorobenzamide)** | | | |
| Chards    | 0.01         | STMR    | 0.032        | HR      |
| Commodities in previous Reasoned Opinions under Article 10 of Reg. 396/2005 | See table 5 from the Reasoned Opinion under Article 10 of Reg. 396/2005 (EFSA, 2015b) | Acute risk assessment only for the crop under consideration |

STMR: supervised trials median residue; HR: highest residue; MRL: maximum residue level.
### Appendix E – Used compound codes

| Code/trivial name | Chemical name/SMILES notation<sup>(a)</sup> | Structural formula<sup>(a)</sup> |
|-------------------|---------------------------------------------|---------------------------------|
| Fluopicolide      | 2,6-Dichloro-N-[3-chloro-5-(trifluoromethyl)-2-pyridylimethyl]benzamide  
\[\text{Cl}c2cccc(\text{Cl})c2\text{C}(=\text{O})\text{NC}c1\text{ncc(cc1Cl)}\text{C(F)}(\text{F})\text{F}\]  

![Structural formula of Fluopicolide](image1)  
| M-01 or BAM       | 2,6-Dichlorobenzamide  
\[\text{O}--\text{C(N)c1c(Cl)cccc1Cl}\]  

![Structural formula of M-01 or BAM](image2) |

SMILES: simplified molecular-input line-entry system.

<sup>(a)</sup>: (ACD/ChemSketch, Advanced Chemistry Development, Inc., ACD/Labs Release: 12.00 Product version: 12.00 (Build 29305, 25 Nov 2008).