Evaluation of confirmatory data following the Article 12 MRL review for fluroxypyr

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Abstract

The applicant Dow AgroSciences submitted a request to the competent national authority in Germany to evaluate the confirmatory data that were identified for fluroxypyr in the framework of the maximum residue level (MRL) review under Article 12 of Regulation (EC) No 396/2005 as not available. To address the data gaps, a method of analysis for plant matrices, information on metabolism in onions, revised Good Agricultural Practices (GAPs) and residue trials on apples, onions and grass, argumentation regarding the efficiency of the hydrolysis step and information on storage stability in plant matrices and products of animal origin were submitted. A ruminant metabolism study with fluroxypyr-meptyl was available and evaluated. Toxicological information on metabolites identified in the ruminant metabolism study (i.e. fluroxypyr pyridinol and its conjugates) is required to derive a final residue definition for livestock. EFSA recommends reconsideration of the existing MRLs for several plant and animal commodities.

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Summary

The review of existing maximum residue levels (MRLs) for the active substance fluroxypyr according to Article 12 of Regulation (EC) No 396/2005 (MRL review) has been performed in 2013. The European Food Safety Authority (EFSA) identified some information as unavailable (data gaps) and derived tentative MRLs for those uses not fully supported by data but for which no risk to consumers was identified. The following data gaps were identified by EFSA:

1) a confirmatory method, an independent laboratory validation (ILV) and further validation of the hydrolysis step of the method in high water content and dry commodities;
2) a fully validated analytical method for enforcement in high oil content and acidic commodities;
3) representative fluroxypyr metabolism studies covering foliar treatment on root and tuber vegetables and leafy vegetables;
4) eight residue trials complying with the southern outdoor Good Agricultural Practice (GAP) on citrus;
5) the northern outdoor GAP reported on apples should be completed (preharvest interval (PHI) value);
6) seven additional residue trials on apples complying with the southern outdoor GAP on pome fruits; the reported GAP should also be completed (PHI value);
7) eight residue trials complying with the southern outdoor GAP on olives for oil production with a possible extrapolation to table olives; the reported GAP should also be completed (PHI value);
8) four additional residue trials complying with the northern outdoor GAP on onions;
9) three additional residue trials on onions complying with the northern outdoor GAP on garlic and shallots; the reported GAP on garlic and shallots should also be completed (PHI value);
10) two additional residue trials complying with the northern outdoor GAP on spring onions; the reported GAP should also be completed (PHI value);
11) four additional residue trials complying with the northern outdoor GAP and four additional residue trials complying the southern outdoor GAP on grass;
12) clarification on whether the various analytical methods used to analyse the samples from the residue trials on the different supported crops also analyse the esters and conjugates of fluroxypyr;
13) the storage time intervals of samples from the supporting residue trials on apple and onions and whether this period is covered by the available storage stability data;
14) a representative metabolism study to address the fate of fluroxypyr esters in ruminants’ matrices;
15) storage stability data for fluroxypyr residues in animal commodities covering the storage time interval of the residue samples from the cow feeding study.

The MRL modifications proposed following the MRL review have been implemented in the MRL legislation by Commission Regulation (EU) No 2015/1040, including footnotes implementing the data gaps identified by EFSA in points 1, 3, 5, 6, 8, 9, 12, 13, 14 and 15, above, as confirmatory data requirements.

The data gaps identified by EFSA in points 2, 4, 7 and 10 above, for a fully validated analytical method for enforcement of residues in high oil content and acidic commodities, and for residues trials on citrus, spring onions (northern Europe (NEU)) and olives for oil production (with possible extrapolation to table olives), have not been implemented as confirmatory data requirements in the MRL legislation, and Commission Regulation (EU) No 2015/1040 set the MRLs for citrus fruits, spring onions, table olives and olives for oil production at the specific limit of quantification (LOQ).

The applicant Dow AgroSciences submitted an application to the competent national authority in Germany for the evaluation of confirmatory data. To address the confirmatory data requirements, the applicant provided:

- a new method of analysis for the determination of residues in high water content and dry matrices (relevant to data gap number 1);
- a detailed description of the metabolism study of fluroxypyr in onions (relevant to data gap number 3);
- revised NEU and southern Europe (SEU) GAPs for apples, and reside trials on NEU and SEU apples (relevant to data gaps number 5 and 6);
• a revised NEU GAP for bulb onions, and reside trials on NEU onions (relevant to data gaps number 8 and 9);
• argumentation on the degradation of fluroxypyr-meptyl observed in a previously submitted hydrolysis study and in previously submitted metabolism studies, regarding the efficiency of the hydrolysis step (relevant to data gap number 12);
• information on the stability of residues in high water content, high acid content, high oil content and dry matrices (relevant to data gap number 13);
• information on the stability of residues in products of animal origin (bovine muscle, liver and milk and in poultry eggs) (relevant to data gap number 15).

Information to address the data gap identified by EFSA in point 14 above, for a representative metabolism study to address the fate of fluroxypyr esters in ruminants’ matrices was not submitted in the application for the assessment of confirmatory data. However, the following study was provided to the competent national authority in France in the context of a national registration of a plant protection product and was evaluated in the framework of the present confirmatory data assessment in relation to the confirmatory data requirements for MRLs for products of animal origin:

• a metabolism study in ruminants performed with radiolabelled fluroxypyr-meptyl (fluroxypyr methylheptyl) (relevant to data gap number 14).

The data gap identified by EFSA in point 11 above, for residues trials on grass, has not been implemented as a confirmatory data requirement in the MRL legislation; Commission Regulation (EU) No 2015/1040 set the MRLs for products of animal origin at the levels of the tentative MRLs derived in the framework of the MRL review from the GAPs evaluated at European Union (EU) level which were not fully supported by data but for which no risk to consumers was identified. Although not explicitly requested, the applicant provided residue trials in grass. Since the MRLs for animal products need to be reconsidered, taking into account the data available in relation to data requirements 14 and 15, EFSA decided to assess the new residue trials and their impact on the MRLs for products of animal origin.

The rapporteur Member State (RMS) assessed the information submitted by the applicant in an evaluation report, which was submitted to the European Commission and forwarded to EFSA on 11 July 2018. EFSA proceeded with the assessment of the application as requested by the European Commission in accordance with Article 9 of the Regulation. During the detailed assessment, EFSA identified points which needed further clarifications. On 5 March 2019, the RMS Germany submitted a revised evaluation report which addressed the points for clarification and included the additional evaluation report on the fate of fluroxypyr-meptyl in ruminants submitted by France.

It is highlighted that the applicant also submitted additional information which was not requested as confirmatory data in the MRL legislation. Since the applicant did not apply for a modification of the existing MRLs for the related crops, the additional data have not been assessed by EFSA in the framework of the current reasoned opinion.

The data gaps numbers 1, 3, 5, 6, 8, 11, 13 and 15 were sufficiently addressed. The data gap number 12 was not addressed. The data gap number 9 was partially addressed. The data gap number 14 was not satisfactorily addressed. The available information was sufficient to derive MRL proposals for apples and onions; however, further risk management considerations are required in relation to the MRLs for all commodities assessed in the evaluation of confirmatory data. The summary table below provides an overview of the assessment of confirmatory data and the recommended MRL modifications to Regulation (EU) No 396/2005.

The tentative residue definition for products of animal origin should be reconsidered and may need to be revised because the new information on the nature of residue in lactating goats indicates that the metabolite fluroxypyr pyridinol and its conjugates may be present at significant levels. The metabolite fluroxypyr pyridinol (free and conjugated) should be considered for inclusion in the residue definition for risk assessment. Toxicological data on fluroxypyr pyridinol and its conjugates are required to assess whether fluroxypyr pyridinol and its conjugates are of lower, similar or higher toxicity in comparison with the parent fluroxypyr or whether specific reference values should be set.

The calculated dietary burdens exceed the trigger value for ruminant livestock species, and the intakes are driven by residues in grass hay resulting from the existing use of fluroxypyr in grassland assessed in the MRL review. The temporary MRLs for animal commodities and commodities used as feed items could not be confirmed, pending confirmation of the residue definition for risk assessment and for enforcement for products of animal origin (ruminants) and the data gap for toxicological information on the metabolite fluroxypyr pyridinol and its conjugates.
The previous consumer risk assessment was updated, using the supervised trials median residue (STMR) derived from the residue trials on apples and onions. The long-term dietary risk assessment did not include contributions of commodities of animal origin pending on confirmation of the residue definition for risk assessment for products of animal origin and due to lack of information on the toxicological relevance of fluroxypyr pyridinol and its conjugates. Hence, the risk assessment is considered indicative only. No consumer intake concerns were identified.

A short-term (acute) dietary risk assessment may be required for products of animal origin, pending on the data gap for toxicological information on the metabolite fluroxypyr pyridinol and its conjugates and confirmation of the residue definition for risk assessment for products of animal origin (ruminants).

Recommended issues proposed for consideration of follow-up actions:

- The tentative residue definition for products of animal origin (ruminants) should be reconsidered and may need to be revised since the new study on the nature of residue in the lactating goat indicates that the metabolite fluroxypyr pyridinol and its conjugates may be present at significant levels in products of animal origin. The metabolite fluroxypyr pyridinol (free and conjugated) should be considered for inclusion in the residue definition for risk assessment.

- Toxicological data on fluroxypyr pyridinol and its conjugates are required to assess whether fluroxypyr pyridinol and its conjugates are of lower, similar or higher toxicity in comparison with the parent fluroxypyr or whether specific reference values should be set. Consequently, the data gap previously identified in the framework of the renewal of the active substance, for information on the toxicological relevance of the metabolite fluroxypyr pyridinol, is also relevant to uses which would lead to residues in ruminants.

- The assessment of the metabolism study with fluroxypyr-meptyl in lactating goat and toxicological data on fluroxypyr pyridinol and its conjugates should be peer reviewed to revise the residue definition for products of animal origin.

| Code(a) | Commodity | Existing MRL(b) | Proposed MRL | Conclusion/recommendation |
|---------|-----------|----------------|--------------|---------------------------|
| Plant commodities

**Enforcement residue definition:** sum of fluroxypyr, its salts, its esters and its conjugates, expressed as fluroxypyr

| Code(a) | Commodity | Existing MRL(b) | Proposed MRL | Conclusion/recommendation |
|---------|-----------|----------------|--------------|---------------------------|
| 0130010 | Apples    | 0.05* (ft 1)   | (0.02*)      | Further risk management considerations required The confirmatory data requirements for information on analytical methods for enforcement, storage stability, PHI and residue trials have been addressed. The residue trials are sufficient to derive an MRL proposal for apples on the basis of the NEU and SEU GAPs. The data demonstrate that it would be appropriate to lower the MRL to the residue trials LOQ of 0.02 mg/kg. Before lowering the MRL, it should be clarified whether the current MRL needs to be maintained due to a use authorised in one of the Member States after the MRL review was completed which leads to residues greater than 0.02 mg/kg. No consumer intake concerns were identified in the indicative risk assessment. |
| 0220010 | Garlic    | 0.05* (ft 2)   | Further risk management considerations required | The confirmatory data requirements for information on PHIs and residue trials have not been addressed (the NEU GAP for garlic was not completed (PHI value)). Information to support the GAP for garlic (residue trials) was not provided. The confirmatory data requirements for information on analytical methods for enforcement and metabolism have been addressed. The LOQ for the enforcement method is 0.01 mg/kg. Since the confirmatory data requirements are not fully addressed, risk managers may consider the deletion of the existing MRL, replacing it with the LOQ of 0.01 mg/kg. |
| Code<sup>(a)</sup> | Commodity | Existing MRL<sup>(b)</sup> | Proposed MRL | Conclusion/recommendation |
|----------------|------------|--------------------------|--------------|---------------------------|
| 0220020       | Onions     | 0.05* (ft 3)             | (0.01*)      | The confirmatory data requirements for information on analytical methods for enforcement, metabolism, storage stability and residue trials have been addressed. The residue trials are sufficient to derive an MRL proposal for onions on the basis of the revised NEU GAP. For the uses on onions assessed, it is appropriate to lower the MRL to the LOQ of 0.01 mg/kg. Before lowering the MRL, it should be clarified whether the current MRL needs to be maintained due to a use authorised in one of the Member States after the MRL review was completed which leads to residues greater than 0.01 mg/kg. No consumer intake concerns were identified in the indicative risk assessment. |
| 0220030       | Shallots   | 0.05* (ft 4)             | Further risk management considerations required | The confirmatory data requirement for information on PHI and residue trials has not been addressed. The NEU GAP for shallots was not completed (PHI value). Information to support the GAP for shallots (residue trials) was not provided. Since the confirmatory data requirements are not fully addressed, risk managers may consider the deletion of the existing MRL, replacing it with the LOQ of 0.01 mg/kg. |
| 0256070       | Thyme      | 0.05 (ft 5)              | Further risk management considerations required | The confirmatory data requirement for information on the analytical method used in the residue trials has not been addressed. The available information was insufficient to demonstrate that the specific analytical method used in the residue trials was capable to determine the esters and conjugates of fluroxypyr included in the residue definition for enforcement and risk assessment. Validated analytical methods are available for the determination of residues in high water content matrices with an LOQ of 0.01 mg/kg. Since the confirmatory data requirement has not been addressed, risk managers may consider the deletion of the existing MRL, replacing it with the LOQ of 0.01 mg/kg. The data gap for a representative metabolism study covering foliar treatment on leafy crops remains open. However, thyme is a minor use crop and the lack of a metabolism study on leafy crop is considered a minor deviation. |
| 0270060       | Leeks      | 0.3 (ft 6)               | Further risk management considerations required | The confirmatory data requirement for information on the analytical method used in the residue trials has not been addressed. The available information was insufficient to demonstrate that the specific analytical method used in the residue trials was capable to determine the esters and conjugates of fluroxypyr included in the residue definition for enforcement and risk assessment. |
| Code<sup>(a)</sup> | Commodity            | Existing MRL<sup>(b)</sup> | Proposed MRL                  | Conclusion/recommendation                                                                 |
|-----------------|----------------------|-----------------------------|--------------------------------|--------------------------------------------------------------------------------------------|
| 0500010         | Barley               | 0.1 (ft 7)                  | Further risk management       | The confirmatory data requirement for information on the analytical method used in the residue trials has not been addressed. The available information was insufficient to demonstrate that the specific analytical methods used in the residue trials were capable to determine the esters and conjugates of fluroxypyr included in the residue definition for enforcement and risk assessment. Since the confirmatory data requirements are not fully addressed, risk managers may consider the deletion of the existing MRLs for barley, maize/corn, oat, rye, sorghum and wheat, replacing them with the LOQ of 0.01 mg/kg. |
| 0500030         | Maize/corn           | 0.05* (ft 7)                | Further risk management       | The confirmatory data requirement for information on the analytical methods for enforcement has been addressed. The LOQ for the enforcement method is 0.01 mg/kg. |
| 0500050         | Oat                  | 0.1 (ft 7)                  | Further risk management       | The confirmatory data requirements for information on analytical methods for enforcement have been addressed. The LOQ for the enforcement method is 0.01 mg/kg. |
| 0500070         | Rye                  | 0.1 (ft 7)                  | Further risk management       | Since the confirmatory data requirements are not fully addressed, risk managers may consider the deletion of the existing MRLs for barley, maize/corn, oat, rye, sorghum and wheat, replacing them with the LOQ of 0.01 mg/kg. |
| 0500080         | Sorghum              | 0.05* (ft 7)                | Further risk management       | Since the confirmatory data requirements are not fully addressed, risk managers may consider the deletion of the existing MRLs for barley, maize/corn, oat, rye, sorghum and wheat, replacing them with the LOQ of 0.01 mg/kg. |
| 0500090         | Wheat                | 0.1 (ft 7)                  | Further risk management       | The confirmatory data requirement for information on the analytical method used in the residue trials has not been addressed. The available information was insufficient to demonstrate that the specific analytical method used in the residue trials was capable to determine the esters and conjugates of fluroxypyr included in the residue definition for enforcement and risk assessment. Since the confirmatory data requirement has not been addressed, risk managers may consider the deletion of the existing MRL, replacing it with the LOQ due to the lack of supporting data. Validated analytical methods are not available for herbal infusions from flowers. The lowering of the MRL to the default LOQ for this type of matrix could be considered. |
| 0631000         | Herbal infusions from flowers | 2 (ft 8)                  | Further risk management       | The confirmatory data requirement for information on the analytical method used in the residue trials has not been addressed. The available information was insufficient to demonstrate that the specific analytical method used in the residue trials was capable to determine the esters and conjugates of fluroxypyr included in the residue definition for enforcement and risk assessment. Since the confirmatory data requirement has not been addressed, risk managers may consider the deletion of the existing MRL, replacing it with the LOQ due to the lack of supporting data. Validated analytical methods are not available for herbal infusions from flowers. The lowering of the MRL to the default LOQ for this type of matrix could be considered. |
### Animal commodities

**Existing enforcement residue definition:** sum of fluroxypyr and its salts, expressed as fluroxypyr (products of animal origin except honey and other apiculture products) (tentatively derived in the MRL review for ruminants and implemented in Regulation (EC) No 396/2005 for products of animal origin except honey and other apiculture products)

**General recommendation:** The tentative residue definition for enforcement for ruminants should be reconsidered because the metabolite fluroxypyr pyridinol and its conjugates may be present at significant levels in products of animal origin. Toxicological information on fluroxypyr pyridinol is not available and is required in order to assess whether fluroxypyr pyridinol and its conjugates are of lower, similar or higher toxicity in comparison with the parent fluroxypyr or whether specific reference values should be set.

| Code(a) | Commodity | Existing MRL(b) | Proposed MRL | Conclusion/recommendation |
|---------|------------|----------------|--------------|---------------------------|
| 0900020 | Sugar canes | 0.05* (ft 9) | Further risk management considerations required | The confimatory data requirement for information on the analytical method used in the residue trials has not been addressed. The available information was insufficient to demonstrate that the specific analytical method used in the residue trials was capable to determine the esters and conjugates of fluroxypyr included in the residue definition for enforcement and risk assessment. |
|         |            |                |              | Since the confimatory data requirements are not fully addressed, risk managers may consider the deletion of the existing MRL, replacing it with the LOQ of 0.01 mg/kg. |

| Code(a) | Commodity | Existing MRL(b) | Proposed MRL | Conclusion/recommendation |
|---------|------------|----------------|--------------|---------------------------|
| 1011010 | Swine – muscle | 0.01* (ft 10) | Further risk management considerations required | The confimatory data requirement for information on storage stability has been addressed, demonstrating that residues in bovine muscle, liver and milk, and in poultry eggs were stable for at least 12 months when stored at −18°C |
| 1011020 | Swine – fat | 0.04 (ft 10) | | |
| 1011030 | Swine – liver | 0.04 (ft 10) | | |
| 1011040 | Swine – kidney | 0.06 (ft 10) | | |
| 1011050 | Swine – edible offals | 0.06 (ft 10) | | |
| 1011990 | Swine – others | 0.01* (ft 10) | | |
| 1012010 | Bovine – muscle | 0.01* (ft 10) | | |
| 1012020 | Bovine – fat | 0.06 (ft 10) | | |
| 1012030 | Bovine – liver | 0.07 (ft 10) | | |
| 1012040 | Bovine – kidney | 0.3 (ft 10) | | |
| 1012050 | Bovine – edible offals | 0.3 (ft 10) | | |
| 1012990 | Bovine – others | 0.01* (ft 10) | | |
| 1013010 | Sheep – muscle | 0.01* (ft 10) | | |

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| Code(a) | Commodity  | Existing MRL(b) | Proposed MRL | Conclusion/recommendation |
|--------|------------|----------------|--------------|---------------------------|
| 1013020 | Sheep – fat | 0.06 (ft 10) |              |                           |
| 1013030 | Sheep – liver | 0.07 (ft 10) |              |                           |
| 1013040 | Sheep – kidney | 0.3 (ft 10)  |              |                           |
| 1013050 | Sheep – edible offals | 0.3 (ft 10) |              |                           |
| 1013990 | Sheep – others | 0.01* (ft 10) |              |                           |
| 1014010 | Goat – muscle | 0.01* (ft 10) |              |                           |
| 1014020 | Goat – fat | 0.06 (ft 10) |              |                           |
| 1014030 | Goat – liver | 0.07 (ft 10) |              |                           |
| 1014040 | Goat – kidney | 0.3 (ft 10)  |              |                           |
| 1014050 | Goat – edible offals | 0.3 (ft 10) |              |                           |
| 1014990 | Goat – others | 0.01* (ft 10) |              |                           |
| 1020000 | Milk | 0.06 (ft 10) |              |                           |

(a): Commodity code number according to Annex I of Regulation (EC) No 396/2005.
(b): Existing EU MRL and corresponding footnote on confirmatory data.

ft 1: The European Food Safety Authority identified some information on analytical methods, storage stability, PHI and residue trials as unavailable. When re-viewing the MRL, the Commission will take into account the information referred to in the first sentence, if it is submitted by 1 July 2017, or, if that information is not submitted by that date, the lack of it (Footnote related to data gaps Nos 1, 5, 6 and 13).

ft 2: The European Food Safety Authority identified some information on analytical methods, metabolism, PHI and residue trials as unavailable. When re-viewing the MRL, the Commission will take into account the information referred to in the first sentence, if it is submitted by 1 July 2017, or, if that information is not submitted by that date, the lack of it (Footnote related to data gaps Nos 1, 3 and 9).

ft 3: The European Food Safety Authority identified some information on analytical methods, metabolism, storage stability and residue trials as unavailable. When re-viewing the MRL, the Commission will take into account the information referred to in the first sentence, if it is submitted by 1 July 2017, or, if that information is not submitted by that date, the lack of it (Footnote related to data gaps Nos 1, 3, 8 and 13).

ft 4: The European Food Safety Authority identified some information on analytical methods, metabolism, PHI and residue trials as unavailable. When re-viewing the MRL, the Commission will take into account the information referred to in the first sentence, if it is submitted by 1 July 2017, or, if that information is not submitted by that date, the lack of it (Footnote related to data gaps Nos 1, 3 and 9).

ft 5: The European Food Safety Authority identified some information on the analytical method used in the residue trials as unavailable. When re-viewing the MRL, the Commission will take into account the information referred to in the first sentence, if it is submitted by 1 July 2017, or, if that information is not submitted by that date, the lack of it (Footnote related to data gap No 12).

ft 6: The European Food Safety Authority identified some information on analytical methods, metabolism and the analytical method used in the residue trials as unavailable. When re-viewing the MRL, the Commission will take into account the information referred to in the first sentence, if it is submitted by 1 July 2017, or, if that information is not submitted by that date, the lack of it (Footnote related to data gap Nos 1, 3 and 12).

ft 7: The European Food Safety Authority identified some information on analytical methods and the analytical method used in the residue trials as unavailable. When re-viewing the MRL, the Commission will take into account the information referred to in the first sentence, if it is submitted by 1 July 2017, or, if that information is not submitted by that date, the lack of it (Footnote related to data gaps Nos 1 and 12).

ft 8: The European Food Safety Authority identified some information on the analytical method used in the residue trials as unavailable. When re-viewing the MRL, the Commission will take into account the information referred to in the first sentence, if it is submitted by 1 July 2017, or, if that information is not submitted by that date, the lack of it (Footnote related to data gap No 12).

ft 9: The European Food Safety Authority identified some information on analytical methods and the analytical method used in the residue trials as unavailable. When re-viewing the MRL, the Commission will take into account the information referred to in the first sentence, if it is submitted by 1 July 2017, or, if that information is not submitted by that date, the lack of it (Footnote related to data gap No 12).
to in the first sentence, if it is submitted by 1 July 2017, or, if that information is not submitted by that date, the lack of it (Footnote related to data gaps Nos 1 and 12).

ft 10: The European Food Safety Authority identified some information on storage stability and metabolism as unavailable. When re-reviewing the MRL, the Commission will take into account the information referred to in the first sentence, if it is submitted by 1 July 2017, or, if that information is not submitted by that date, the lack of it (Footnote related to data gaps Nos 14 and 15).
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Assessment

The review of existing maximum residue levels (MRLs) for the active substance fluroxypyr according to Article 12 of Regulation (EC) No 396/20051 (MRL review) has been performed in 2013 (EFSA, 2013). The European Food Safety Authority (EFSA) identified some information as unavailable (data gaps) and derived tentative MRLs for those uses not fully supported by data but for which no risk to consumers was identified. The following data gaps were identified by EFSA:

1) a confirmatory method, an Independent laboratory validation (ILV) and further validation of the hydrolysis step of the method in high water content and dry commodities;
2) a fully validated analytical method for enforcement in high oil content and acidic commodities;
3) representative fluroxypyr metabolism studies covering foliar treatment on root and tuber vegetables and leafy vegetables;
4) eight residue trials complying with the southern outdoor Good Agricultural Practice (GAP) on citrus;
5) the northern outdoor GAP reported on apples should be completed (preharvest interval (PHI) value);
6) seven additional residue trials on apples complying with the southern outdoor GAP on pome fruits; the reported GAP should also be completed (PHI value);
7) eight residue trials complying with the southern outdoor GAP on olives for oil production with a possible extrapolation to table olives; the reported GAP should also be completed (PHI value);
8) four additional residue trials complying with the northern outdoor GAP on onions;
9) three additional residue trials on onions complying with the northern outdoor GAP on garlic and shallots; the reported GAP on garlic and shallots should also be completed (PHI value);
10) two additional residue trials complying with the northern outdoor GAP on spring onions; the reported GAP should also be completed (PHI value);
11) four additional residue trials complying with the northern outdoor GAP and four additional residue trials complying the southern outdoor GAP on grass;
12) clarification on whether the various analytical methods used to analyse the samples from the residue trials on the different supported crops also analyse the esters and conjugates of fluroxypyr;
13) the storage time intervals of samples from the supporting residue trials on apple and onions and whether this period is covered by the available storage stability data;
14) a representative metabolism study to address the fate of fluroxypyr esters in ruminants’ matrices;
15) storage stability data for fluroxypyr residues in animal commodities covering the storage time interval of the residue samples from the cow feeding study;

In addition, EFSA identified a data gap on rotational crop field trials which is relevant for the national authorisations (see below details on additional studies submitted by the applicant).

The MRL modifications proposed following the MRL review have been implemented in the MRL legislation by Commission Regulation (EU) No 2015/10402, including footnotes implementing the data gaps identified by EFSA in points 1, 3, 5, 6, 8, 9, 12, 13, 14 and 15, above, as confirmatory data requirements.

The data gaps identified by EFSA in points 2, 4, 7 and 10 above, for a fully validated analytical method for enforcement of residues in high oil content and acidic commodities, and for residues trials on citrus, spring onions (NEU) and olives for oil production (with possible extrapolation to table olives), have not been implemented as confirmatory data requirements in the MRL legislation; Commission Regulation (EU) No 2015/1040 set the MRLs for citrus fruits, spring onions, table olives and olives for oil production at the specific limit of quantification (LOQ).

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1 Regulation (EC) No 396/2005 of the 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 Commission Regulation (EU) 2015/1040 of 30 June 2015 amending Annexes II, III and V to Regulation (EC) No 396/2005 of the European Parliament and of the Council as regards maximum residue levels for azoxystrobin, dimoxystrobin, fluroxypyr, methoxyfenozide, metrafenone, oxadiargyl and tribenuron in or on certain products. OJ L 167, 1.7.2015, p. 10–56.
Any parties having an interest in maintaining the proposed tentative MRL were requested to address the confirmatory data requirements. In accordance with the specific provisions, the applicant Dow AgroSciences submitted an application to the competent national authority in Germany (designated rapporteur Member State, RMS) for the evaluation of confirmatory data. To address the confirmatory data requirements, the applicant provided:

- a new method of analysis for the determination of residues in high water content and dry matrices (relevant to data gap number 1);
- a detailed description of the metabolism study of fluroxypyr in onions (relevant to data gap number 3);
- revised NEU and southern Europe (SEU) GAPs for apples, and reside trials on NEU and SEU apples (relevant to data gaps number 5 and 6);
- a revised NEU GAP for bulb onions, and reside trials on NEU onions (relevant to data gaps number 8 and 9);
- argumentation on the degradation of fluroxypyr-meptyl observed in a previously submitted hydrolysis study and in previously submitted metabolism studies, regarding the efficiency of the hydrolysis step (relevant to data gap number 12);
- information on the stability of residues in high water content, high acid content, high oil content and dry matrices (relevant to data gap number 13);
- information on the stability of residues in products of animal origin (bovine muscle, liver and milk and in poultry eggs) (relevant to data gap number 15).

Information to address the data gap identified by EFSA in point 14 above, for a representative metabolism study to address the fate of fluroxypyr esters in ruminants’ matrices was not submitted in the application for the assessment of confirmatory data. However, the following study was provided to the competent national authority in France in the context of a national registration of a plant protection product and was evaluated in the framework of the present confirmatory data assessment in relation to the confirmatory data requirements for MRLs for products of animal origin:

- a metabolism study in ruminants performed with radiolabelled fluroxypyr-meptyl (fluroxypyr methylheptyl) (relevant to data gap number 14).³

The data gap identified by EFSA in point 11 above, for residues trials on grass, which is linked to the MRLs for products of animal origin, has not been implemented as a confirmatory data requirement in the MRL legislation; Commission Regulation (EU) No 2015/1040 set the MRLs for products of animal origin at the levels of the tentative MRLs derived in the framework of the MRL review from the GAPs evaluated at European Union (EU) level which were not fully supported by data but for which no risk to consumers was identified. Although not explicitly requested, the applicant provided residue trials in grass. Since the MRLs for animal products need to be reconsidered, taking into account the data available in relation to data requirements 14 and 15, EFSA decided to assess the new residue trials and their impact on the MRLs for products of animal origin.

The RMS assessed the information submitted by the applicant in an evaluation report, which was submitted to the European Commission and forwarded to EFSA on 11 July 2018. The evaluation of confirmatory data was performed in accordance with the procedure set out in the Commission Staff Working Document SANTE/10235/2016 (European Commission, 2016). EFSA proceeded with the assessment of the application as requested by the European Commission in accordance with Article 9 of the Regulation. During the detailed assessment, EFSA identified points which needed further clarifications. On 5 March 2019, the RMS Germany submitted a revised evaluation report which addressed the points for clarification (Germany, 2018) and included the additional evaluation report on the fate of fluroxypyr-meptyl in ruminants submitted by France (France, 2018).

It is highlighted that the applicant also submitted additional information as follows which was not requested as confirmatory data in the MRL legislation:

³ In the framework of the national re-registration of the pesticide product ‘STARANE 200’, France received a metabolism study in ruminants. Since this study is relevant to the data gap number 14, France, as the zonal application rapporteur Member State (zRMS) evaluated the new animal metabolism study in the format of an additional evaluation report, and submitted the assessment to the European Commission and to EFSA on 13 July 2018 (France, 2018). The additional evaluation report of France on the fate of fluroxypyr methylheptyl ester in ruminants was included in the submission of the revised evaluation report by the RMS Germany (Germany, 2018).
• genotoxicity studies on the metabolite fluoroxypr methoxypyridine: in the framework of the renewal of the approval of the active substance fluoroxypr under Regulation (EC) No 1107/2009\(^4\), the notifier was required to submit confirmatory information as regards the toxicological relevance of the metabolites fluoroxypr pyridinol and fluoroxypr methoxypyridine to the Member States, the Commission and EFSA by 31 December 2013. The need to investigate the toxicological relevance of these metabolites was triggered by their potential presence in groundwater\(^5\);
• a revised GAP for citrus, and residue trials on oranges (relevant to data gap number 4 that has not been implemented as a confirmatory data requirement in the MRL legislation);
• residue trials on olives (relevant to data gap number 7 that has not been implemented as a confirmatory data requirement in the MRL legislation);
• a new SEU GAP for bulb onions and reside trials on SEU onions;
• a revised NEU GAP for spring onions/green onions and residue trials on NEU spring onions/green onions (related to data gap number 10 that has not been implemented as a confirmatory data requirement in the MRL legislation); and a new SEU GAP for spring onions/green onions and residue trials on SEU spring onions/green onions;
• rotational crop field trials covering the maximum plateau concentration of fluoroxypr methoxypyridine metabolite in view of its high persistence in soil and in the absence of toxicological data on this metabolite;
• a new method of analysis for the determination of residues in milk and milk products.

Since the applicant did not apply for a modification of the existing MRLs for the related crops, the data mentioned in the bullet points above have not been assessed by EFSA in the framework of the current reasoned opinion.

EFSA based its assessment on the evaluation report submitted by the RMS (Germany, 2018), the evaluation report on the fate of fluoroxypr-mephtyl in ruminants submitted by France (France, 2018), and the reasoned opinion on the MRL review according to Article 12 of Regulation (EC) No 396/2005 (EFSA, 2013), the Conclusion on the peer review of the pesticide risk assessment (EFSA, 2011), the renewal Assessment Report on the active substance fluoroxypr (draft assessment report (DAR)) and its addendum (Ireland, 2009, 2011), the technical report on the outcome of the consultation with Member States, the applicant and EFSA in light of confirmatory data (EFSA, 2015) and the review report finalised in the Standing Committee on the Food Chain and Animal Health at its meeting on 17 June 2011 (European Commission, 2017).

For this application, the data requirements established in Regulation (EU) No 544/2011\(^6\) and the relevant guidance documents at the date of implementation of the confirmatory data requirements by Regulation (EU) No 2015/1040 are applicable. 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\(^7\).

A detailed description of the GAPs for the uses of fluoroxypr, which are relevant for the current confirmatory data evaluation, is reported in Appendix A.

An updated list of end points, including the end points of relevant studies assessed previously and the confirmatory data evaluated in this application, is presented in Appendix B.

The evaluation report submitted by the RMS (Germany, 2018) and the additional evaluation report submitted by the zonal Rapporteur Member (zRMS) (France, 2018) are considered supporting documents to this reasoned opinion and, thus, are made publicly available as a background documents to this reasoned opinion.

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\(^4\) 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

\(^5\) The data gap was addressed by the applicant by providing information to refine the groundwater exposure assessment and defining use conditions that minimise the risk for groundwater contamination (Member States should continue to pay particular attention to the potential contamination of groundwater by metabolite fluoroxypr pyridinol, when the active substance is applied in regions with alkaline or vulnerable soil and/or with vulnerable climatic conditions) (European Commission, 2017).

\(^6\) 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.

\(^7\) 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.
1. Mammalian toxicology

In the framework of the renewal of the approval of the active substance fluoroxypry under Regulation (EC) No 1107/2009, specific provisions for confirmatory data requirements were set by Commission Implementing Regulation (EU) No 736/2011\(^8\), including, inter alia, that the notifier shall submit confirmatory information as regards the toxicological relevance of the metabolites fluoroxypry pyridinol and fluoroxypry methoxypyridine to the Member States, the Commission and EFSA by 31 December 2013. The need to investigate the toxicological relevance of these metabolites was triggered by their potential presence in groundwater. The confirmatory data submitted by the applicant were evaluated by the designated RMS, Ireland, and the outcome of the consultation on the pesticide risk assessment in light of the confirmatory data was presented in a technical report of EFSA (EFSA, 2015). Studies on the toxicological relevance of the metabolites fluoroxypry pyridinol and fluoroxypry methoxypyridine were not submitted in the context of the confirmatory data for the approval of the active substance and a toxicological assessment was not provided. The data gap was addressed by the applicant by providing information to refine the groundwater exposure assessment and defining use conditions that minimise the risk for groundwater contamination. Member States were requested to pay particular attention to the potential contamination of groundwater by metabolite fluoroxypry pyridinol, when the active substance is applied in regions with alkaline or vulnerable soil and/or with vulnerable climatic conditions (European Commission, 2017).

In the current application for the evaluation of confirmatory data, the applicant submitted three genotoxicity studies on fluoroxypry methoxypyridine (Germany, 2018). The request for toxicological information on the metabolite fluoroxypry methoxypyridine has not been implemented in the MRL legislation as a confirmatory data requirement and is not relevant the present confirmatory data evaluation. Therefore, the submitted toxicological data on the metabolite fluoroxypry methoxypyridine have not been assessed in the present confirmatory data evaluation.

With regard to the metabolite fluoroxypry pyridinol, no new toxicological studies were submitted in the current application for the evaluation of confirmatory data. EFSA agrees with the assessment of the zRMS France that the new metabolism study on the nature of residue in the lactating goat indicates that fluoroxypry pyridinol and its conjugates may be present at significant levels in products of animal origin, and therefore, the tentative residue definitions for products of animal origin (ruminants) should be reconsidered (France, 2018). Consequently, the previously identified data gap\(^9\) for information on the toxicological relevance of the metabolite fluoroxypry pyridinol is also relevant to uses which would lead to residues in ruminants.

2. Residues in plants

2.1. Nature of residues and methods of analysis in plants

2.1.1. Nature of residues in primary crops

In order to address data gap number 3\(^10\) (representative metabolism studies covering foliar treatment on root and tuber vegetables and leafy vegetables), a detailed assessment of the previously submitted metabolism study of fluoroxypry-meptyl in onions was provided (Germany, 2018). Details of the study are presented in Appendix B.1.1.1. At harvest, the total radioactive residues (TRRs) were low, ranging from 0.004 to 0.04 mg eq./kg. Fluoroxypry-meptyl was rapidly taken up into onion shoots and bulbs where it was converted to free acid and conjugates of the acid. In onions, fluoroxypry is metabolised in the same manner as previously demonstrated in the metabolism studies on spring and winter wheat (Germany, 2018). Therefore, the data gap number 3 was addressed for foliar treatment on root and tuber vegetables, linked to the MRLs for garlic, onions and shallots.

In the MRL review, EFSA also identified data gap number 3 for a representative metabolism study covering foliar treatment on leafy vegetables. A risk management decision was taken that this study is

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\(^8\) Commission Implementing Regulation (EU) No 736/2011 of 26 July 2011 approving the active substance fluoroxypry, 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 195, 27.7.2011, p. 37–41

\(^9\) Data gap identified in the framework of the renewal of the active substance fluoroxypry and set as a confirmatory data requirement by Commission Implementing Regulation (EU) No 736/2011.

\(^10\) Data gap numbers: refer to the list presented in the summary and assessment Sections.
not required for the very minor leafy crops assessed in the MRL review, i.e. thyme and herbal infusions from flowers. For the use on leek (in the leafy crops group), a confirmatory data requirement was set for information on metabolism, in order to confirm the MRL on leek. A representative metabolism study covering foliar treatment on leafy vegetables has not been submitted. However, the information submitted on the metabolism study on onions provides sufficient evidence to support the specific use on leeks, considering the botanical similarity. For future MRL applications for leafy crops, this data gap needs to be addressed.

Overall EFSA concluded that the data gap number 3 for representative metabolism studies was sufficiently addressed for root and tuber vegetables, linked to the MRLs for garlic, onions and shallots, and the specific use linked to the MRL for leek.

2.1.2. Nature of residues in rotational crops
Not relevant for the current assessment.12

2.1.3. Nature of residues in processed commodities
Not relevant for the current assessment.

2.1.4. Methods of analysis in plants
In order to address data gap number 1 which is relevant for the uses in apples, garlic, onions, shallots, leeks, barley, maize, oats, rye, sorghum, wheat and sugar cane (crops belonging to the groups of high water content and dry commodities),10 the applicant provided a new method of analysis using LC-MS/MS (method study ID DOW 091171) for the determination of residues of the ester fluroxypyr-mephtyl, expressed as fluroxypyr acid equivalent, in high water content, high acid content and dry matrices. Details on the analytical method are presented in Appendix B.1.1.1. The new method for high water content and dry matrices includes a hydrolysis step under alkaline conditions (addition of 5 N sodium hydroxide solution and incubation for 2 h at 90°C), in order to cleave the esters and to derive fluroxypyr acid. The method was sufficiently validated with an LOQ 0.01 mg/kg for high water content and dry matrices in accordance with the guidance document on pesticide residue analytical methods SANCO/825/00 rev. 8.1 (European Commission, 2010b). A confirmatory method is available. ILV is available for high water content and dry matrices. EFSA concluded that the data gap number 1 identified in the framework of the MRL review has been addressed.

2.1.5. Stability of residues in plants
The storage stability of fluroxypyr residues in plants stored under frozen conditions was investigated in the framework of the EU pesticides peer review where it was demonstrated that in frozen samples of crops classified as matrices with high water content (wheat forage) and dry matrices (wheat grain), residues were stable for at least 24 months when stored at –18°C (EFSA, 2011). In the current confirmatory data application, the applicant submitted new information on the stability of residues in frozen samples of crops classified as matrices with high water content (corn forage), high acid content (orange fruit and orange peel), high oil content (olive fruit and olive oil) and dry matrices (corn grain), where it was demonstrated that residues were stable for at least 10 months when stored at less than –18°C (Germany, 2018).

In order to address data gap number 13,10 for the storage time intervals of samples from the supporting residue trials on apples and onions and whether this period is covered by the available storage stability data, the applicant provided new reside trials on apples and onions in which the samples were stored under conditions for which integrity of the samples has been demonstrated (see Section 2.2.1). EFSA concluded that data gap number 13 identified in the framework of the MRL review was addressed.

11 Although leeks are considered as leafy crops, metabolism studies in onions are expected to be representative, since both onions and leeks belong to the family of Alliaceae.
12 For rotational crops, the residue definition was proposed on a tentative basis, in view of the high persistence of the metabolite fluroxypyr methoxypropyridine and the absence of toxicological data on this metabolite (EFSA, 2013). Meanwhile, EFSA recommended avoiding rotation with root and tuber crops. When implementing the recommendations of the MRL review, risk managers decided not to request confirmatory data for rotational crop metabolism studies.
2.1.6. Proposed residue definitions

Based on the new data provided with this application (i.e. a detailed description of the metabolism study of fluroxypyr in onions), EFSA confirmed the previously derived residue definition for risk assessment and enforcement for the groups of root and tuber vegetables and cereals (following foliar treatment) as the ‘sum of fluroxypyr, its salts, its esters and its conjugates, expressed as fluroxypyr’.13

This residue definition was also proposed for fruit crops, following soil treatment (EFSA, 2013).14

For the leafy crops, in the absence of metabolism studies covering this crop group, the MRL review proposed to tentatively apply the same residue definition (EFSA, 2013). Following the MRL review, a few MRLs have been set for crops classified as leafy crops, mainly minor crops (i.e. thyme and herbal infusions from flowers). Risk managers decided that for these crops, confirmatory data for metabolism studies are not required. With regard to the MRL for leeks (foliar treatment), a confirmatory data requirement was implemented for information on metabolism. Although a metabolism study in leafy crops is not available, the information submitted on the metabolism study on onions provides sufficient evidence to support the residue definition for the specific use on leeks, considering botanical similarity. The residue definition for risk assessment/enforcement for other leafy crops is tentative.

2.2. Magnitude of residues in plants

2.2.1. Magnitude of residues in primary crops

In order to address the confirmatory data requirements implemented in the MRL legislation, the applicant submitted residue trials performed in apples and NEU bulb onions. In addition, the applicant submitted residue trials performed in grass which are not implemented as confirmatory data requirements, but which were assessed to consider their impact on the livestock dietary burden and the MRLs for products of animal origin. The samples were analysed for the parent compound and the metabolites included in the residue definitions for enforcement and risk assessment. According to the assessment of the evaluating Member State (EMS), the methods used were sufficiently validated and fit for purpose. The samples of these residue trials were stored under conditions for which integrity of the samples has been demonstrated.

A summary of residues data from the supervised residue trials assessed in the evaluation of confirmatory data is presented in Appendix B.1.2.1.

The applicant submitted additional residue trials performed in oranges15, olives, SEU onions and spring onions/green onions which are not required as confirmatory data and have not been assessed in the present confirmatory data evaluation. Further details on these trials are reported in the ER prepared by Germany (Germany, 2018).

Apples

In order to address data gap numbers 5 and 6,8 the applicant provided revised NEU and SEU GAPs for apples (NEU and SEU: 1 × 196 g a.s./ha, PHI 7 days, see also Appendix A) and submitted new NEU and SEU residue trials on apples. The revised NEU and SEU GAPs for apples assessed in the evaluation of confirmatory data are less critical than the GAPs assessed in the MRL review (NEU apples: 1 × 0.30 kg a.s./ha, PHI to be completed; SEU: pome fruits 1 × 0.31 kg a.s./kg, PHI to be completed).

13 When the residue definition proposed in the MRL review was implemented in Regulation (EC) No 396/2005, the EU reference laboratories identified the reference standard for fluroxypyr conjugates as commercially not available. When re-viewing the MRLs, the Commission will take into account the commercial availability of the reference standard referred to in the first sentence by 1 July 2016, or, if that reference standard is not commercially available by that date, the unavailability of it (Commission Regulation (EU) 2015/1040).

14 For the fruit crops assessed in the current application (citrus fruits, pome fruits) (soil treatment), for which no representative metabolism studies are available, the MRL review considered that the metabolism is sufficiently addressed by the fluroxypyr metabolic pathway depicted in the rotational crops after bare soil application.

15 Eight residue trials on oranges are available in compliance with a revised SEU GAP (1 × 300 g a.s./ha, PHI 15 days). The trials were conducted on eight varieties of orange at geographically independent locations in Greece, Italy and Spain in 2014 by banded spray application to soil at growth stages BBCH 80-85. Samples were analysed for fluroxypyr residues in accordance with the residue definition for enforcement and risk assessment. The levels of fluroxypyr residues (expressed as fluroxypyr) were below the LOQ of 0.01 mg/kg in all samples of orange whole fruit. The trials are sufficient to derive risk assessment values and to confirm the existing MRL for oranges at the LOQ of 0.01* mg/kg.
In support of the revised NEU and SEU GAPs, a total of eight GAP compliant residue trials were conducted on apples (196 g fluroxypyr/ha corresponding to 282 g fluroxypyr-meptyl/ha, 1 application, 7-day PHI) (Germany, 2018). Four trials were conducted in NEU (northern France and Poland) in 2014, and four trials were conducted in SEU (southern France, Italy and Spain) in 2014. Applications were performed with banded spray application to soil at growth stages BBCH 85–89 (NEU) or 81–87 (SEU). Sampling was performed at 7-day PHI, and in two trials, each in NEU and SEU residue decline samples were taken at 3-, 10- and 14-day PHIs. The samples were analysed for fluroxypyr-meptyl ester, fluroxypyr and the metabolites included in the residue definition for enforcement and risk assessment determined as fluroxypyr free acid by LC-MS/MS. According to the assessment of the EMS, the method used in the new residue trials was sufficiently validated with an LOQ of 0.01 mg/kg and fit for purpose. The levels of fluroxypyr residues (expressed as fluroxypyr) in apple fruit were below the LOQ of 0.01 mg/kg in all samples.

The newly submitted additional residue trials on apples confirm the results of the trials previously evaluated in the MRL review, where all residue trial results were below the LOQ of 0.02 mg/kg. Overall, the trials submitted for the revised GAP together with the trials submitted in support of the MRL review for the more critical GAP suggest a no-residue situation. Extrapolation of the MRL for apples to the whole group pome fruits is possible (European Commission, 2011).

EFSA concluded that the data gaps numbers 5 and 6 identified in the framework of the MRL review were addressed.

Onions, bulb

In order to address data gap number 8, the applicant provided a revised NEU GAP for bulb onions (1 × 100 g a.s./ha, PHI 90 days) and submitted new residue trials on onions. The revised NEU GAP for bulb onions is less critical than the GAP assessed in the MRL review for bulb onions (GAP: 2 × 0.20 kg a.s./ha, PHI 77 days).

Overall, eight additional GAP compliant residue trials were conducted on onions (100 g fluroxypyr/ha corresponding to 144 g fluroxypyr-meptyl/ha, 1 application, 90-day PHI) (Germany, 2018). The trials were conducted in 2013 and 2014 in northern France, Poland and the United Kingdom. Applications were performed with banded spray application to soil at growth stages BBCH 11–41. Samples were taken 84–91 days after the treatment; two trials each in 2013 and 2014 were designed as residue decline studies with sampling up to 109 days PHI. The samples were analysed for fluroxypyr-meptyl ester, fluroxypyr and the metabolites included in the residue definition for enforcement and risk assessment determined as fluroxypyr free acid by LC-MS/MS. According to the assessment of the EMS, the method used was sufficiently validated with an LOQ of 0.01 mg/kg in onions (whole plant and bulb) and fit for purpose. Residues (expressed as fluroxypyr) were below the LOQ of 0.01 mg/kg in all samples.

Onion is a major crop in the EU, and therefore, a minimum of eight trials are required. Overall, the number and quality of the NEU trials is sufficient to derive an MRL proposal of 0.01 mg/kg, equivalent to the LOQ.

EFSA concluded that the data gap number 8 identified in the framework of the MRL review was addressed.

Garlic and shallots

According to the data gap number 9, the NEU GAP for garlic and shallots should be revised, specifying the PHI. Furthermore, additional residue trials were requested which are representative for the NEU GAP on garlic and shallots. The applicant did not provide the required information/data. Thus, formally, data gap number 9 was not fully addressed.

Considering that for onions the submitted information was sufficient to derive a MRL proposal, extrapolation to garlic and shallots would be possible, if the applicant confirms that the GAP for garlic and shallots is aligned with the GAP for onions.

Grass

The data gap number 11 identified by the MRL review identifying four residues trials on grass in NEU and SEU as missing, has not been implemented as a confirmatory data requirement in the MRL legislation. Commission Regulation (EU) No 2015/1040 set tentative MRLs for products of animal origin derived in the framework of the MRL review from the GAPs evaluated at EU level which were not fully supported by data but for which no risk to consumers was identified.

Although not explicitly requested, the applicant provided a revised GAP and new residue trials in grass. Since the MRLs for animal products need to be reconsidered, taking into account the data
submitted in response to data requirements 14 and 15 (metabolism study in ruminants and storage stability data for animal products), EFSA decided to assess the new residue trials and their impact on the livestock dietary burden and the MRLs for products of animal origin.

The revised GAPs for grass (NEU and SEU: 1 × 300 g a.s./ha, PHI 7 days) are less critical than the GAPs for grass assessed in the MRL review (NEU: 2 × 0.36 kg a.s./kg, PHI 4 days; SEU: 2 × 0.40 kg a.s./kg, PHI 15 days).

In support of the revised NEU and SEU GAPs, eight each GAP compliant residue trials on grass were conducted in NEU and SEU (300 g fluroxypyr a.s./ha corresponding to 431 g fluroxypyr-meptyl/ha, 1 application, 7-day PHI) (Germany, 2018). Trials in NEU (Austria, northern France, Hungary and the United Kingdom) and in SEU (southern France and Italy) were conducted on different varieties of rye and pasture grasses in 2010 (four trials each) and 2011 (four trials each). Applications were performed with spray application to soil at growth stages BBCH 29–77 (NEU) or 42–69 (SEU). Sampling was performed at 0, 1, 3 and 7 days PHI in all trials. The samples were analysed for fluroxypyr-meptyl ester, fluroxypyr and the metabolites included in the residue definition for enforcement and risk assessment determined as fluroxypyr free acid by LC-MS/MS. According to the assessment of the EMS, the methods of analysis used in the 2010 and 2011 trials were both sufficiently validated with an LOQ of 0.01 mg/kg in grass and fit for purpose. The levels of fluroxypyr residues (expressed as fluroxypyr) in grass in GAP compliant residue trials ranged from 3.6 to 19 mg/kg (NEU) and from 1.7 to 15 mg/kg (SEU).

Grass samples from 7-day PHI were used to prepare silage with a fermentation period of circa 3–6 weeks. The levels of fluroxypyr residues (expressed as fluroxypyr) in grass silage from the GAP compliant residue trials ranged from 10 to 38 mg/kg (NEU) and from 4.3 to 30 mg/kg (SEU). The median processing factor (PF) in the trials for the preparation of silage was calculated as 1.99 (see Appendix B.1.2.3).

Overall, the number and quality of the trials is sufficient to derive risk assessment values (highest residue (HR) and supervised trials median residue (STMR)) for NEU and SEU grass and silage.

In addition, the applicant submitted a further eight each NEU and SEU residue trials on grass conducted at a lower application rate (200 g fluroxypyr a.s./ha corresponding to 288 g fluroxypyr-meptyl/ha, 1 application, 7-day PHI) which are not GAP compliant and therefore were not assessed.

Thyme, leeks, barley, maize/corn, oat, rye, sorghum, wheat, herbal infusions from flowers and sugar canes.

In the framework of the MRL review, EFSA requested clarification on whether the analytical methods used to analyse the samples in the residue trials on the different supported crops also covered the esters and conjugates of fluroxypyr (data gap number 12 (EFSA, 2013). This data gap has been implemented in the MRL legislation by Commission Regulation (EU) No 2015/1040 as a confirmatory data requirement for thyme, leeks, barley, maize/corn, oat, rye, sorghum, wheat, herbal infusions from flowers and sugar canes.

The analytical methods reported for plant products include an extraction in alkaline conditions, followed by an acid hydrolysis step. The applicant provided arguments to demonstrate that in alkaline medium, the fluroxypyr-meptyl ester is likely to be hydrolysed. The study on the hydrolysis of fluroxypyr-meptyl ester in alkaline medium was previously assessed in the framework of the renewal of approval of the active substance under Council Directive 91/414/EEC (Ireland, 2009). Metabolism studies have demonstrated that conjugates of fluroxypyr are cleaved under and bound residues are extracted under acid conditions (Germany, 2018). However, there is insufficient information available on the specific analytical methods used in the residue trials in the crops concerned to be demonstrated that the analyses also covered the esters and conjugates of fluroxypyr. The EMS provided clarification that additional information on whether the specific analytical method used in the residue trials included suitable hydrolysis steps in order to release the analyte from conjugates and esters was not submitted by the applicant. Therefore, it remains unclear whether the analytical methods used in the various

16 The method of analysis used in the 2011 trials (method DOW 091171) was sufficiently validated for the determination of fluroxypyr and its salts, its esters and its conjugates with an LOQ of 0.01 mg/kg in grass and fit for purpose (Germany 2018). The method of analysis used in the 2010 trials (method ERC 97.10, based on method ERC 92.01; Ireland, 2009) involves extraction and maceration with caustic methanol (original study report). The alkaline conditions are expected to hydrolyse the fluroxypyr-meptyl ester and the method has validation with fluroxypyr-meptyl fortification determined as fluroxypyr reported with mean recovery results in grass ranging from 90% to 101% (Ireland, 2009). Although an ILV and further validation of the ester hydrolysis step is missing, this was considered a minor deviation and the analytical method used in the 2010 trials was judged to be satisfactory.
residue trials were sufficiently capable to determine the esters and conjugates of fluroxypyr included in the residue definition for enforcement and risk assessment.

Overall, EFSA concluded that the confirmatory data requirement regarding data gap number 12, for information on the analytical method used in the residue trials for thyme, leeks, barley, maize/corn, oat, rye, sorghum, wheat, herbal infusions from flowers and sugar canes has not been addressed.

2.2.2. Magnitude of residues in rotational crops

In the framework of the MRL review, EFSA identified data gap,\(^{10}\) for rotational crops field trials covering the maximum plateau concentration of fluroxypyr methoxypridine metabolite in view of its high persistence in soil and in the absence of toxicological data on this metabolite, which is not expected to impact on the validity of the MRLs derived but which might have an impact on national authorisations (EFSA, 2013). The MRL review concluded that if this data gap is not addressed in the future, Member States are recommended to withdraw or modify the relevant authorisations at national level. Meanwhile, Member States were also recommended to avoid rotation with root and tuber crops (EFSA, 2013). The data gap for rotational crops field trials has not been implemented as a confirmatory data requirement in the MRL legislation and Commission Regulation (EU) No 2015/1040 set the MRLs for the root and tuber crops under consideration (garlic, shallots, onions and spring onions) at the relevant LOQ. No new studies on rotational crops were submitted in the current application for the evaluation of confirmatory data.

2.2.3. Magnitude of residues in processed commodities

Although not requested as confirmatory data, the applicant provided processing studies in barley grain which demonstrated that malting and brewing to produce beer, milling to produce bran and flour and abrasion to pot barley leads to a reduction of the residues in the processed product (Germany, 2018). The number and quality of the processing studies is sufficient to derive robust PFs which are recommended to be included in Annex VI of Regulation (EC) No 396/2005. The processing study can be used to refine the dietary burden calculation (see Section 3).

The applicant provided silage processing studies with grass used to prepare silage and a median PF for the preparation of grass silage was calculated (see Section 2.2.1).

The relevant PFs are presented in Appendix B.1.2.3.

3. Residues in livestock

3.1. Nature of residues

Metabolism studies for fluroxypyr (as fluroxypyr acid) in livestock (lactating goat, indicative information for laying hens) have been assessed previously in the framework of the EU pesticides peer review (EFSA, 2011). However, from the use of the variant fluroxypyr-meptyl on grass, it was shown that ruminant livestock are mostly exposed to the fluroxypyr esters rather than the fluroxypyr acid. Furthermore, fluroxypyr-meptyl is highly fat soluble (Log P<sub>ow</sub> > 5) contrary to fluroxypyr, and its behaviour in animals is therefore not comparable to that of fluroxypyr (EFSA, 2013). Considering the identified uncertainties and the significant levels of the esters ruminants are likely to be exposed to, the EU pesticides peer review and the MRL review identified the data gap number 14\(^{10}\) requesting a representative metabolism study to address the fate of fluroxypyr esters in ruminants’ matrices. The data gap has been implemented in the MRL legislation as a confirmatory data requirement for information on metabolism linked to the animal commodity MRLs for swine, bovine, sheep, goat and for milks.

Information to address the fate of fluroxypyr esters in ruminants’ matrices was not submitted by the applicant in the framework of the confirmatory data assessment (Germany, 2018). However, a metabolism study with radiolabelled fluroxypyr-meptyl in lactating goat was provided to the competent national authority in France, being the zonal RMS (zRMS) in the context of a national registration of a plant protection product. The metabolism study was assessed by France in relation to the confirmatory data requirement implemented in the MRL legislation and shared with the RMS in the format of an additional evaluation report (France, 2018). The additional evaluation report assessment of France was included in the revised evaluation report submitted by the RMS (Germany, 2018).

The metabolism study was performed with \(^{14}\)C-2,6-ringlabelled fluroxypyr-meptyl at a target dose rate of 90 mg a.s./kg dry feed (1.96 mg/kg body weight (bw) per day, equivalent to fluroxypyr 1.36
mg/kg bw per day) in lactating goat (one animal) for 7 days (France, 2018). Milk, urine and faces were sampled throughout the dosing period. Liver, muscle, fat, kidneys, GI track, GI contents, blood and bile were collected at sacrifice. Samples were stored at −20°C and analysed within 6 months, which is within the period of storage stability demonstrated for products of animal origin (bovine muscle, liver and milk: 12 months at −18°C).

The majority of the dose was excreted in the urine and faeces (40.0% and 30.9%, respectively). Transfer to edible tissues and milk was each < 0.1% of the dose. Total residues of fluroxypyr-meptyl in milk reached plateau levels during the dosing period (day 3) and ranged up to 0.041 mg eq/kg. In tissues, highest residue levels were detected in the kidney, followed by the liver (1.545 and 0.123 mg eq/kg, respectively). Lower residue levels were detected in muscle (loin, flank) and fat (perirenal, subcutaneous) (0.011, 0.012 and 0.036, 0.012 mg eq/kg, respectively).

The parent fluroxypyr-meptyl accounted for 26.6–41.7% TRR in faeces but was not present in edible tissues or milk. Fluroxypyr acid was the major component in all matrices (accounting for 38.6–86.8% TRR in edible tissues and 40.4–61.3% TRR in milk). Fluroxypyr pyridinol (fluroxypyr 2-pyridinol) was detected in all tissues excluding muscle, and was present at significant levels (> 10% TRR and/or 0.01 mg/kg) in liver and kidney (14.5% and 6.9% TRR, respectively). The conjugate fluroxypyr pyridinol glucuronide (fluroxypyr 2-pyridinol glucuronide) was present at significant levels in edible tissues except liver (ranging from 10.4% to 26.5% TRR). Details of the characterisation and identification of radioactive residues are presented in Appendix E.

The proposed primary biotransformation pathway is via cleavage of the hydrocarbon chain to form fluroxypyr acid, and subsequent cleavage of the acid moiety to form fluroxypyr pyridinol, which may undergo glucuronide conjugation (France, 2018). The zRMS France proposed that there may be a second pathway for fluroxypyr-meptyl to form fluroxypyr pyridinol. However, it remains unclear why the levels of fluroxypyr pyridinol in tissues with the exception of muscle were lower in the previously assessed lactating goat metabolism study with fluroxypyr acid despite having been performed at a higher dose (accounting for 2–7% TRR), and why the study with fluroxypyr acid reported no evidence of the conjugate fluroxypyr pyridinol glucuronide (EFSA, 2011; Ireland, 2011).

The RMS Germany concluded that, due to the initial formation of fluroxypyr acid in the goat, the metabolism of fluroxypyr-meptyl in ruminants can be considered qualitatively similar to that of fluroxypyr acid (Germany, 2018). EFSA agrees with the conclusions of the RMS Germany and with the detailed assessment of the zRMS France that the tentative residue definition for products of animal origin should be reconsidered and may need to be revised because the new information on the nature of residue in lactating goats indicates that the metabolite fluroxypyr pyridinol and its conjugates may be present at significant levels. The metabolite fluroxypyr pyridinol (free and conjugated) should be considered for inclusion in the residue definition for risk assessment. However, toxicological data on fluroxypyr pyridinol are not available and it is not possible to conclude whether the toxicity of fluroxypyr pyridinol is covered by the parent fluroxypyr. The assessment of the metabolism study with fluroxypyr-meptyl in lactating goat and toxicological data on fluroxypyr pyridinol and its conjugates should be peer reviewed to revise the residue definition for products of animal origin.

EFSA concluded that the confirmatory data requirements related to data gap number 14 identified in the framework of the MRL review were not satisfactorily addressed to confirm the MRLs for products of animal origin, since there is a data gap for information on the toxicological relevance of the metabolite fluroxypyr pyridinol and its conjugates. Toxicological data on fluroxypyr pyridinol and its conjugates are required to assess whether fluroxypyr pyridinol and its conjugates are of lower, similar or higher toxicity in comparison with the parent fluroxypyr or whether specific reference values should be set.

3.2. Methods of analysis in livestock

Information on methods of analysis for enforcement of residues in food and feed of animal origin was not requested as confirmatory data in the MRL legislation.

The applicant provided supplementary information on a new method of analysis using LC-MS/MS for the determination of residues of fluroxypyr and its salts in milk and milk products, which is based on the method of analysis in plants submitted in the framework of the confirmatory data assessment (see Section 2.1.4). The new method of analysis in milk includes a hydrolysis step in acidic medium to extract bound residues and cleave conjugates. However, in contrast to the method for plant matrices, the method for milk does not require a hydrolysis step in alkaline medium, since esters are not expected in milk. Details on the analytical method are presented in Appendix B.2.1.1. The method was...
sufficiently validated with an LOQ 0.01 mg/kg for the determination of fluroxypyr and its salts in milk (cream, skim milk, whole milk) in accordance with the guidance document on pesticide residue analytical methods SANCO/825/00 rev. 8.1 (European Commission, 2010b). A confirmatory method and ILV are available for milk.

No additional method was submitted for methods of analysis for enforcement of residues in food and feed of animal origin.

3.3. Stability of residues in products of animal origin

In order to address data gap number 15, the applicant submitted new information on the stability of residues in frozen products of animal origin, where it was demonstrated that residues in bovine muscle, liver and milk, and in poultry eggs were stable for at least 12 months when stored at −18°C (Germany, 2018). EFSA concluded that data gap number 15 identified in the framework of the MRL review was addressed.

3.4. Proposed residue definitions

The existing residue definition for enforcement purposes and for risk assessment was tentatively derived in the MRL review, for ruminants as: ‘sum of fluroxypyr and its salts, expressed as fluroxypyr’ (tentative). In the context of the MRL review, a metabolism study in poultry was not triggered, and therefore, no residue definition was proposed for poultry matrices (EFSA, 2013).

Based on the new information available in the context of the present confirmatory data assessment (the new metabolism study on the nature of residue in the lactating goat), EFSA concluded that the previously derived tentative residue definition for risk assessment and enforcement should be reconsidered. The tentative residue definition for products of animal origin (ruminants) may need to be revised because the new metabolism study on the nature of residue in lactating goats indicates that the metabolite fluroxypyr pyridinol and its conjugates may be present at significant levels in products of animal origin (France, 2018). The metabolite fluroxypyr pyridinol (free and conjugated) should be considered for inclusion in the residue definition for risk assessment. However, toxicological information on fluroxypyr pyridinol is not available and is required in order to assess whether fluroxypyr pyridinol and its conjugates are of lower, similar or higher toxicity in comparison with the parent fluroxypyr or whether specific reference values should be set.

EFSA concluded that the tentative residue definition for enforcement purposes and for risk assessment (ruminants) could not be confirmed on the basis of the available information and should be reconsidered, pending on the data gap for toxicological information on the metabolite fluroxypyr pyridinol and its conjugates.

3.5. Magnitude of residues in livestock

The livestock dietary burden was updated according to OECD, 2013 using the risk assessment values derived from the new residue trials on apple and grass, and the PF derived from the silage processing study. EFSA assumes that uses on citrus and cereals have been withdrawn following the MRL review and the contribution to the livestock dietary burden from citrus dried pulp, cereals grain, wheat and rye bran, barley and oat straw, wheat and rye straw was excluded from the livestock dietary burden calculation. The input values for the livestock dietary burden calculations are reported in Appendix D.

The calculated dietary burdens exceed the trigger value of 0.1 mg/kg dry matter (DM) for ruminant livestock species, and the intakes are driven by residues in grass hay resulting from the existing use of fluroxypyr in grassland assessed in the MRL review (see Appendix B.2). Residues of fluroxypyr in apple pomace contribute insignificantly to the existing livestock exposure.

Risk assessment values (STMR and HR) and MRLs could not be derived for commodities of animal origin, pending confirmation of the residue definition for risk assessment and for enforcement for products of animal origin (ruminants) and the data gap for toxicological information on the metabolite fluroxypyr pyridinol and its conjugates.

4. Consumer risk assessment

EFSA updated the previous long-term (chronic) risk assessment using revision 2 of the EFSA PRIMo (EFSA, 2007), taking into account the new data submitted under the present confirmatory data
application. The long-term dietary risk assessment was performed with regard only to consumers’ exposure from products of plant origin. The contributions of commodities of animal origin were not included in the calculation due to lack of information on the toxicological relevance of fluoroxypr pyridinol and its conjugates, and pending on confirmation of the residue definition for risk assessment for products of animal origin. Hence, the risk assessment is considered indicative only. The toxicological reference value for fluoroxypr used in the risk assessment (i.e. acceptable daily intake (ADI) value) was derived in the framework of the EU pesticides peer review (EFSA, 2011). The metabolites included in the risk assessment residue definition for products of plant origin (fluoroxypr salts, esters and conjugates) were considered to be of similar toxicity/not more toxic than the parent compound.

The long-term dietary exposure assessment is based on the median residue levels derived for raw agricultural commodities (apples and onions only). The contributions of commodities where no GAP was reported in the framework of the MRL review were not included in the calculation. The crops citrus fruits, pome fruits except apples, table olives, olives for oil production and spring onions were excluded from the consumer risk assessment because EFSA assumes that uses have been withdrawn following the MRL review. The crops garlic, shallots, thyme, leeks, barley, maize/corn, oat, rye, sorghum, wheat, herbal infusions from flowers and sugar canes were excluded from the consumer risk assessment due to the lack of information to address the confirmatory data. The estimated long-term consumer exposure was below the toxicological reference value; however, the risk assessment was affected by non-standard uncertainties due to the exclusion of the contributions of commodities of animal origin and lack of information on the toxicological relevance of fluoroxypr pyridinol and its conjugates.

A short-term (acute) dietary risk assessment was not performed, and it is not necessary for products of plant origin because an acute reference dose (ARFD) has been considered not required for the active substance fluoroxypr and the metabolites included in the residue definition for risk assessment for plant commodities (EFSA, 2011, European Commission, 2011). However, a short-term (acute) dietary risk assessment may be required for products of animal origin, pending on the data gap for toxicological information on the metabolite fluoroxypr pyridinol and its conjugates and confirmation of the residue definition for risk assessment for products of animal origin (ruminants).

5. Conclusion and Recommendations

To address data gaps identified in the framework of the MRL review, the applicant submitted a method of analysis for high water content and dry matrices, a detailed description of the metabolism study in onions, revised GAPs and reside trials on apples, a revised GAP and reside trials on onions, residues trials on grass, argumentation regarding the efficiency of the hydrolysis step in the analytical method and information on storage stability in high water content, high acid content, high oil content and dry matrices and in products of animal origin. In addition, a metabolism study in ruminants with fluoroxypr-mepthyl was provided in the context of a national registration of a plant protection product and was evaluated in the framework of the present confirmatory data assessment.

The data gaps numbers 1, 3, 5, 6, 8, 11, 13 and 15 were sufficiently addressed. The data gap number 12 was not addressed. The data gap number 9 was partially addressed. The data gap number 14 was not satisfactorily addressed. The available information was sufficient to derive MRL proposals for apples and onions; however, further risk management considerations are required in relation to the MRLs for all commodities assessed in the evaluation of confirmatory data. The overview of the assessment of confirmatory data and the recommended MRL modifications are summarised in Appendix B.4.

The tentative residue definition for products of animal origin should be reconsidered and may need to be revised because the new information on the nature of residue in lactating goats indicates that the metabolite fluoroxypr pyridinol and its conjugates may be present at significant levels. The metabolite fluoroxypr pyridinol (free and conjugated) should be considered for inclusion in the residue definition for risk assessment. Toxicological data on fluoroxypr pyridinol and its conjugates are required to assess whether fluoroxypr pyridinol and its conjugates are of lower, similar or higher toxicity in comparison with the parent fluoroxypr or whether specific reference values should be set.

The calculated dietary burdens exceed the trigger value for ruminant livestock species, and the intakes are driven by residues in grass hay resulting from the existing use of fluoroxypr in grassland assessed in the MRL review. The temporary MRLs for animal commodities and commodities used as feed items could not be confirmed, pending confirmation of the residue definition for risk assessment
and for enforcement for products of animal origin (ruminants) and the data gap for toxicological information on the metabolite fluoroxypr pyridinol and its conjugates.

The previous consumer risk assessment was updated, using the risk assessment value (STMR) derived from the residue trials on apples and onions. The long-term dietary risk assessment did not include contributions of commodities of animal origin pending on confirmation of the residue definition for risk assessment for products of animal origin and due to lack of information on the toxicological relevance of fluoroxypr pyridinol and its conjugates. No consumer intake concerns were identified. A short-term (acute) dietary risk assessment may be required for products of animal origin, pending on the data gap for toxicological information on the metabolite fluoroxypr pyridinol and its conjugates and confirmation of the residue definition for risk assessment for products of animal origin (ruminants).

Recommended issues proposed for consideration of follow-up actions:

- The tentative residue definition for products of animal origin (ruminants) should be reconsidered and may need to be revised since the new study on the nature of residue in the lactating goat indicates that the metabolite fluoroxypr pyridinol and its conjugates may be present at significant levels in products of animal origin. The metabolite fluoroxypr pyridinol (free and conjugated) should be considered for inclusion in the residue definition for risk assessment.
- Toxicological data on fluoroxypr pyridinol and its conjugates are required to assess whether fluoroxypr pyridinol and its conjugates are of lower, similar or higher toxicity in comparison with the parent fluoroxypr or whether specific reference values should be set. Consequently, the data gap previously identified in the framework of the renewal of the active substance, for information on the toxicological relevance of the metabolite fluoroxypr pyridinol, is also relevant to uses which would lead to residues in ruminants.
- The assessment of the metabolism study with fluoroxypr-meptyl in lactating goat and toxicological data on fluoroxypr pyridinol and its conjugates should be peer reviewed to revise the residue definition for products of animal origin.

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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
- CF conversion factor for enforcement to risk assessment residue definition
- DAR draft assessment report
- DAT days after treatment
- DM dry matter
- EC emulsifiable concentrate
- EMS evaluating Member State
- FAO Food and Agriculture Organization of the United Nations
- GAP Good Agricultural Practice
- GC-ECD gas chromatography with electron capture detector
- GC-MS gas chromatography with mass spectrometry
- HPLC high-performance liquid chromatography
- 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
- IUPAC International Union of Pure and Applied Chemistry
- LOQ limit of quantification
- MRL maximum residue level
- NEU northern Europe
- OECD Organisation for Economic Co-operation and Development
- PBI plant back interval
| Acronym | Description |
|---------|-------------|
| PF      | processing factor |
| PHI     | preharvest interval |
| $P_{ow}$ | partition coefficient between n-octanol and water |
| PRIMo   | (EFSA) Pesticide Residues Intake Model |
| RA      | risk assessment |
| RAC     | raw agricultural commodity |
| RD      | residue definition |
| RMS     | rapporteur Member State |
| SANCO   | Directorate-General for Health and Consumers |
| SEU     | southern Europe |
| STMR    | supervised trials median residue |
| TRR     | total radioactive residue |
### Appendix A – Summary of GAPs assessed in the evaluation of confirmatory data

| Crop and/or situation | NEU, SEU, MS or country | F, G or I^(a) | Pests or group of pests controlled | Preparation | Application | Application rate per treatment | Remarks |
|-----------------------|-------------------------|--------------|-----------------------------------|-------------|----------------|------------------------------|---------|
|                       |                         |              |                                   | Type(b) | Conc. a.s.(c) | Method kind | Range of growth stages & season^(d) | Number min-max | Interval between application (min) | g a.s./hL/min-max | Water L/ha/min-max | Rate(c) | Unit | PHI (days)^(e) | |
| Apples                | NEU                     | F            | Broad leaf weeds                 | EC        | 250           | Soil treatment, spray application | BBCH 85–87 | 1 | –                     | 70–400 | 196 g a.s./ha | 7       | Banded application (30% total area) |
| Apples                | SEU                     | F            | Broad leaf weeds                 | EC        | 200           | Soil treatment, spray application | BBCH 81–87 | 1 | –                     | 70–400 | 196 g a.s./ha | 7       | Banded application (30% total area) |
| Onions, bulb          | NEU                     | F            | Broad leaf weeds                 | EC        | 333           | Foliar, spray application        | BBCH 13–43 | 1 | –                     | 70–400 | 100 g a.s./ha | 90      | |
| Grassland             | NEU                     | F            | Broad leaf weeds                 | EC        | 200           | Foliar, spray application        | From BBCH 13 | 1 | –                     | 70–400 | 300 g a.s./ha | 7       | |
| Grassland             | SEU                     | F            | Broad leaf weeds                 | EC        | 200           | Foliar, spray application        | From BBCH 13 | 1 | –                     | 70–400 | 300 g a.s./ha | 7       | |

NEU: northern European Union; SEU: southern European Union; MS: Member State.

Note: EFSA assessed the GAPs notified when the Art. 12 MRL review was initiated in 2011, and no information was provided to EFSA that GAPs assessed for deriving MRLs have been amend or withdraw following the amendments to the conditions of approval of the active substance fluroxypyr by Commission Implementing Regulation (EU) 2017/856. The manufacturing impurity N-methyl-2-pyrrolidone (NMP) is classified as toxic for reproduction category 1B under Regulation (EC) No 1272/2008 of the European Parliament and of the Council and must not exceed < 3 g/kg in the technical material. In accordance with the regulation, Member States shall where necessary amend or withdraw authorisations for plant protection products containing fluroxypyr as the active substance by 8 September 2017 and any grace period shall expire by 8 September 2018 at the latest.

(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): The application rates are expressed as fluroxypyr; the formulated product contains the variant fluroxypyr-meptyl; the concentration of the a.s. in the formulation is expressed as fluroxypyr.

(d): 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.

(e): 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)\(^{(a)}\) | Sampling (DAT) | Comment/source |
|----------------------------------|-------------|---------|----------------------------|----------------|----------------|
| Fruit crops                      | Root crops  | Onions  | Foliar, F BBCH 09-13 1 x 0.1 kg, 2 x 0.1 kg, 1 x 0.2 kg or 2 x 0.2 kg fluroxypyr/ha | Plants: 0, 3, 14, 28 Root, bulb, skin, shoots: 3 months, 3.5 months | Radiolabelled active substance: 2,6-14C ring-labelled fluroxypyr-meptyl Germany (2018) |
|                                  | Leafy crops | –       | –                          | –              | –              |
| Cereals/grass                    | Root crops  | Onions  | Foliar, F BBCH 37-39 1 x 0.3 kg fluroxypyr/ha | Whole plant: 0 Stalk and leaves; heads: 28 Straw and grain: 62 | Radiolabelled active substance: 2,6-14C ring-labelled fluroxypyr-meptyl EFSA (2013) |
|                                  | Leafy crops | –       | –                          | –              | –              |
|                                  | Cereals/grass | Winter wheat | Foliar, F BBCH 31 1 x 0.2 kg fluroxypyr/ha | Whole plant: 0, 3, 7, 14, 28 Straw and grain: 104 | Radiolabelled active substance: 2,6-14C ring-labelled fluroxypyr-meptyl EFSA (2013) |
|                                  | Pulses/oilseeds | – | –                          | –              | –              |
|                                  | Miscellaneous | Broadleaved weed species (Galium aparine) | Foliar 1 x 0.15 kg fluroxypyr/ha | 7 | Radiolabelled active substance: not specified Indicative information EFSA (2013) |
|                                  | Miscellaneous | Broadleaved weed species (Stellaria media, Viola arvensis) | Foliar, G 1 x 0.075 kg fluroxypyr/ha | Whole plant: 1, 7 | Radiolabelled active substance: 2,6-14C ring-labelled fluroxypyr-meptyl Indicative information EFSA (2013) |
| Rotational crops (available studies) | Crop groups | Crop(s) | Application(s) | PBI (DAT) | Comment/source |
|-----------------------------------|-------------|---------|----------------|-----------|----------------|
| **Root/tuber crops** | Turnip | Bare soil, F 0.6 kg a.s./ha | 30 120(b) 366 | Radiolabelled active substance: $^{14}$C-pyridinyl labelled fluoroxypr-meptyl Root and tops Harvest intervals: 98, 183, 438 DAT EFSA (2013) |
| | Turnip | Bare soil, F 0.7 kg a.s./ha | 30 120 365 | Radiolabelled active substance: $^{14}$C-pyridinyl labelled fluoroxypr-meptyl Root and tops Harvest intervals: 91, 215, 428 DAT EFSA (2013) |
| **Leafy crops** | Lettuce | Bare soil, F 0.6 kg a.s./ha | 30 120(b) 366 | Radiolabelled active substance: $^{14}$C-pyridinyl labelled fluoroxypr-meptyl Harvest intervals: 86, 113, 128, 156, 200, 225, 422, 443 DAT EFSA (2013) |
| | Lettuce | Bare soil, F 0.7 kg a.s./ha | 30 120 365 | Radiolabelled active substance: $^{14}$C-pyridinyl labelled fluoroxypr-meptyl Harvest intervals: 77, 168, 418 DAT EFSA (2013) |
| **Cereal (small grain)** | Wheat | Bare soil, F 0.6 kg a.s./ha | 30 120(b) 366 | Radiolabelled active substance: $^{14}$C-pyridinyl labelled fluoroxypr-meptyl Grain and straw Harvest intervals: 128, 232, 458 DAT EFSA (2013) |
| | Wheat | Bare soil, F 0.7 kg a.s./ha | 30 120 365 | Radiolabelled active substance: $^{14}$C-pyridinyl labelled fluoroxypr-meptyl Immature plant, grain, chaff and straw Harvest intervals: 83, 156, 202, 289, 414, 467 DAT EFSA (2013) |
| | Corn | Bare soil, F 0.7 kg a.s./ha | 365 | Radiolabelled active substance: $^{14}$C-pyridinyl labelled fluoroxypr-meptyl Fodder and grain Harvest interval: 467 DAT EFSA (2013) |
| **Pulses/oilseeds** | Green beans | Bare soil, F 0.6 kg a.s./ha | 30 366 | Radiolabelled active substance: $^{14}$C-pyridinyl labelled fluoroxypr-meptyl Whole plant and beans Harvest interval: 94, 119, 441, 451 DAT EFSA (2013) |
| | Soya beans | Bare soil, F 0.6 kg a.s./ha | 120(b) | Radiolabelled active substance: $^{14}$C-pyridinyl labelled fluoroxypr-meptyl Beans and trash Harvest interval: 226 DAT EFSA (2013) |
| **Processed commodities (hydrolysis study)** | Conditions | Stable? | Comment/Source |
| | Pasteurisation (20 min, 90°C, pH 4) | Not triggered | – |
| | Baking, brewing and boiling (60 min, 100°C, pH 5) | Not triggered | – |
| | Sterilisation (20 min, 120°C, pH 6) | Not triggered | – |
| | Other processing conditions | – | – |

(a): Outdoor/field application (F) or glasshouse/protected/indoor application (G). (b): The 120 DAT plot was under greenhouse conditions.
Can a general residue definition be proposed for primary crops?

| Inconclusive | Residue definition is applicable to cereals following foliar treatment (EFSA, 2013). Residue definition is applicable to root crops (Germany, 2018) |
|--------------|----------------------------------------------------------------------------------------------------------------------------------|

Rotational crop and primary crop metabolism similar?

| Inconclusive | EFSA (2013) |
|--------------|-------------|

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

| Not triggered | Residues of fluroxypyr slightly exceed 0.1 mg/kg in treated crops assessed in the MRL Review (leeks and camomile) however the chronic exposure is not expected to exceed 10% of the ADI |
|--------------|----------------------------------------------------------------------------------------------------------------------------------|

Plant residue definition for monitoring (RD-Mo)

**Sum of fluroxypyr, its salts, its esters, and its conjugates, expressed as fluroxypyr**.
Residue definition applicable to cereals following foliar treatment (EFSA, 2013) and to root crops following foliar treatment (Germany, 2018) Residue definition applicable to the fruit crops following soil treatment assessed in the current application (apples) The residue definition is sufficiently supported for the specific use by foliar treatment on leek, based on the available metabolism study on onions and considering botanical similarity. The residue definition is tentative for other leafy crops because the data gap for a representative metabolism study covering foliar treatment on leafy crops remains open The residue definition for enforcement set for the primary crops may also apply to the rotational crops on a tentative basis but in view of the high persistence of the metabolite fluroxypyr methoxypyridine and the absence of toxicological data on this metabolite, rotational crops field trials covering the maximum plateau concentration of this metabolite are required. EFSA recommends avoiding rotation with root and tuber crops (EFSA, 2013)

Plant residue definition for risk assessment (RD-RA)

**Sum of fluroxypyr, its salts, its esters, and its conjugates, expressed as fluroxypyr**
Residue definition applicable to cereals following foliar treatment (EFSA, 2013) and to root crops following foliar treatment (Germany, 2018) Residue definition applicable to the fruit crops following soil treatment assessed in the current application (apples) The residue definition is sufficiently supported for the specific use by foliar treatment on leek, based on the available metabolism study on onions and considering botanical similarity. The residue definition is tentative for other leafy crops because the data gap for a representative metabolism study covering foliar treatment on leafy crops remains open The residue definition for risk assessment set for the primary crops may also apply to the rotational crops on a tentative basis but in view of the high persistence of the metabolite fluroxypyr methoxypyridine and the absence of toxicological data on this metabolite, rotational crops field trials covering the maximum plateau concentration of this metabolite are required. EFSA recommends avoiding rotation with root and tuber crops (EFSA, 2013)
Methods of analysis for monitoring of residues (analytical technique, crop groups, LOQs)

**Dry matrices:** GC–MS, LOQ 0.01 mg/kg
Validated for the determination of fluroxypyr and its esters, salts and conjugates in dry commodities (cereal grain). Validation of the hydrolysis step not submitted
Confirmatory method missing
ILV available
(EFSA, 2013)

Matrices with high water content: GC-ECD, LOQ 0.05 mg/kg
Validated for the determination of fluroxypyr and its esters, salts and conjugates in high water content (forage) commodities. Validation of the hydrolysis step not submitted
Confirmatory method missing
ILV missing
(EFSA, 2013)

Matrices with high water content, high acid content and dry matrices: LC–MS/MS, LOQ 0.01 mg/kg (method DOW 091171)
Validated for the determination of fluroxypyr and its salts, its esters and its conjugates in high water content (apple, onion, grass forage), high acid content (grapefruit) and dry matrices (wheat grain, wheat hay)
Confirmatory method available
ILV available for high water content and dry matrices. ILV missing for high acid content matrices
Method applicability not demonstrated for high oil content matrices
(Germany, 2018)

**B.1.1.2. Stability of residues in plants**

| Plant products (available studies) | Category       | Commodity       | T (°C) | Stability period | Value | Unit   | Compounds covered    | Comment/source |
|-----------------------------------|----------------|-----------------|--------|------------------|-------|--------|----------------------|----------------|
|                                   | High water content | Wheat forage   | −18    | 24 months       |       |        | Fluroxypyr residues  | EFSA (2011)    |
|                                   | High water content | Corn forage    | −20    | 11 months       |       |        | Fluroxypyr residues  | Germany (2018) |
|                                   | High oil content   | Olive fruit    | −18    | 10 months       |       |        | Fluroxypyr residues  | Germany (2018) |
|                                   | High acid content  | Orange fruit   | −18    | 10 months       |       |        | Fluroxypyr residues  | Germany (2018) |
|                                   | Processed products | Corn stover    | −20    | 11 months       |       |        | Fluroxypyr residues  | Germany (2018) |

ADI: acceptable daily intake; GC–MS: gas chromatography with mass spectrometry; ILV: independent laboratory validation; GC–ECD: gas chromatography with electron capture detector; LC–MS/MS: liquid chromatography with tandem mass spectrometry; LOQ: limit of quantification
### 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/Source                                                                                                                                                                                                                                                                                                                                                       | Calculated MRL (mg/kg) | HR(b) (mg/kg) | STMR(c) (mg/kg) | CF(d) |
|-----------------|------------------|----------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------|--------------|----------------|-------|
| Apples          | NEU              | Trials application rate 1 × 400 g a.s./ha (Germany, 2013): 4 × < 0.02 Trials application rate 1 × 196 g a.s./ha (Germany, 2018): 4 × < 0.01 | Residue trials on apples performed in accordance with the critical GAPs assessed in the MRL review (NEU: 1 × 0.30 kg a.s./ha; SEU: 1 × 0.31 kg a.s./kg) are sufficiently compliant with the less critical revised NEU GAP on apples assessed in the evaluation of confirmatory data (1 × 196 g a.s./ha, PHI 7 days) since a no residue situation is expected. Reduced number of SEU trials is sufficient since a no residue situation is expected MRL proposed at the higher of the LOQs from the residue trials of 0.02* mg/kg | 0.02*                 | 0.02         | 0.01           | –     |
|                 | SEU              | Trials application rate 1 × 250 g a.s./kg (Germany, 2013): 1 × < 0.02 Trials application rate 1 × 196 g a.s./ha (Germany, 2018): 4 × < 0.01 |                                                                                                                                                                                                                                                                                                                                                                    |                        |              |                |       |
| Onions, bulb    | NEU              | Trials application rate 1 × 400 g a.s./ha, PHI 77–95 days (Germany, 2013): 4 × < 0.01 Trials application rate 1 × 100 g a.s./ha, PHI 90 days (Germany, 2018): 4 × < 0.01 | Residue trials on NEU onions performed in accordance with the critical NEU GAP assessed in the MRL review (1 × 0.40 kg a.s./ha, PHI 77–95 days) are sufficiently compliant with the less critical revised NEU GAP on bulb onions assessed in the evaluation of confirmatory data (1 × 100 g a.s./ha, PHI 90 days) since a no residue situation is expected. MRL proposed at the LOQs of 0.01* mg/kg | 0.01*                 | 0.01         | 0.01           | –     |
### Evaluation of confirmatory data following the Article 12 MRL review for fluroxypyr

| Commodity | Region/indoor(a) | Residue levels observed in the supervised residue trials (mg/kg) | Comments/Source | Calculated MRL (mg/kg) | HR(b) (mg/kg) | STMR(c) (mg/kg) | CF(d) |
|-----------|------------------|---------------------------------------------------------------|-----------------|------------------------|---------------|----------------|-------|
| Grasses   | NEU              | Grass: 3.6, 5.7, 10, 10.8, 11.6, 15, 16, 18.8                  | Residue trials on grass compliant with revised GAP on grass assessed in the evaluation of confirmatory data (1 × 300 g a.s./ha, PHI 7 days) | –          | Grass: 18.8    | Grass: 11.2    | –     |
|           |                  | Silage: 15, 10, 25, 18.6, 26.7, 38, 14, 30.6                 |                 |                        | Silage: 38    | Silage: 21.8    |       |
|           | SEU              | Grass: 1.7, 5.4, 8.1, 9.5, 11, 12, 14, 14.5                  | Residue trials on grass compliant with revised GAP on grass assessed in the evaluation of confirmatory data (1 × 300 g a.s./ha, PHI 7 days) | –          | Grass: 14.5    | Grass: 10.25   | –     |
|           |                  | Silage: 4.3, 23.4, 6.5, 16.8, 26, 22, 27, 29.7              |                 |                        | Silage: 29.7  | Silage: 22.7    |       |

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

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

(b): Highest residue. The highest residue for risk assessment refers to the whole commodity.

(c): Supervised trials median residue. The median residue for risk assessment refers to the whole commodity.

(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

| Residues in rotational and succeeding crops expected based on confined rotational crop study? |
| Inconclusive |

In view of the high persistence of the metabolite fluroxypyr methoxypyridine and the absence of toxicological data on this metabolite, rotational crops field trials covering the maximum plateau concentration of this metabolite are required (EFSA, 2013).

| Residues in rotational and succeeding crops expected based on field rotational crop study? |
| Inconclusive |

Data gap for rotational crops field trials covering the maximum plateau concentration of fluroxypyr methoxypyridine metabolite in view of its high persistence in soil and in absence of toxicological data on this metabolite (EFSA, 2013).

B.1.2.3. Processing factors

| Processed commodity | Number of valid studies<sup>a</sup> | Processing Factor (PF) | CF<sub>P</sub><sup>b</sup> | Comment/source |
|---------------------|-----------------------------|-------------------------|------------------|----------------|
|                     | Individual values           | Median PF               |                  |                |
| Barley/malt         | 3                           | 0.31, 0.5, 1.24         | 0.5              | 1 Germany (2018) |
| Barley/beer         | 3                           | 0.032, < 0.22, < 0.40  | 0.22             | 1 Germany (2018) |
| Barley/pot barley   | 3                           | < 0.091, 0.24, 0.36    | 0.24             | 1 Germany (2018) |
| Barley/bran         | 3                           | 0.73, 0.82, 1.54       | 0.82             | 1 Germany (2018) |
| Barley/flour        | 3                           | < 0.12, 0.17, 0.26     | 0.17             | 1 Germany (2018) |
| Grass, silage       | 16                          | 0.80, 0.88, 1.63, 1.72, 1.75, 1.77, 1.83, 1.93, 2.05, 2.30, 2.36, 2.50, 2.53, 2.53, 4.17, 4.33 | 1.99             | 1 Germany (2018) EFSA calculated the processing factors using studies submitted in support of the present application |
| Grass, hay          | 7                           | Not reported           | 4.43             | 1 EFSA (2013) |

<sup>a</sup>: Studies with residues in the RAC at or close to the LOQ were disregarded (unless concentration may occur).

<sup>b</sup>: Conversion factor for risk assessment in the processed commodity; median of the individual conversion factors for each processing residues trial.

B.2. Residues in livestock

Dietary burden calculation according to OECD, 2013.

| Relevant groups | Dietary burden expressed in | Most critical diet<sup>a</sup> | Most critical commodity<sup>b</sup> | Trigger exceeded (Yes/No) 0.10 mg/kg DM | Previous assessment Max burden mg/kg DM (EFSA, 2013) |
|-----------------|-----------------------------|-----------------|------------------------------|-----------------------------------|-----------------------------------------------|
|                 | mg/kg bw per day           | mg/kg DM        | Median | Maximum | Median | Maximum | Dairy cattle | Grass | hay | Yes | 86.34 |
| Cattle (all     | 1.301                       | 2.184           | 33.83 | 56.79   |       |        | Yes     | 86.34 |
| Cattle (dairy   | 1.301                       | 2.184           | 33.83 | 56.79   |       |        | Yes     | 86.34 |
| Cattle (ewe     | 1.692                       | 2.839           | 50.75 | 85.18   |       |        | Yes     |       |
| Sheep (ewe      | 1.692                       | 2.839           | 50.75 | 85.18   |       |        | Yes     |       |
| Sheep (all      | 0.260                       | 0.437           | 11.28 | 18.93   |       |        | Yes     | 12.91 |
| Swine (all      |                             |                 |       |        |       |        |         |       |
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 |
|------------------------------|--------|-------------------------|-----------------|----------------|
| Laying hen                   | Fluroxypyr: dose not reported | 10 | Informative only; no characterisation of the nature of residues (EFSA, 2011) |
| Lactating ruminants (cow)    | Fluroxypyr: dose not reported | single dose | Informative only; no characterisation of the nature of residues (EFSA, 2011) |
| Lactating ruminants (goat)   | Fluroxypyr: 4.3-5.2 mg/kg bw per d or 16.4 mg/kg bw per d | 4 | EFSA (2011, 2013) |
| Lactating ruminants (goat)   | Fluroxypyr-meptyl: 1.96 mg/kg bw per d (equivalent to fluroxypyr: 1.36 mg/kg bw per d) | 7 | Label position: 14C-2,6-ringlabelled fluroxypyr-meptyl (France, 2018) (See Appendix E for summary of the characterisation and identification of radioactive residues) |
| Pig                          | –      | –                       | –               | –              |
| Fish                         | –      | –                       | –               | –              |

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

- Milk: 3
- Eggs: –

Metabolism in rat and ruminant similar

- Inconclusive

Based on the data gap set for metabolism data in ruminants, the MRL review was unable to conclude whether the metabolic pathways in rodents and ruminants are comparable and whether a pig metabolism study is required or not (EFSA, 2013)
### Animal residue definition for monitoring (RD-Mo)

**Residue definition for monitoring (tentatively derived in the MRL review)**
- Ruminants: sum of fluroxypyr and its salts, expressed as fluroxypyr (tentative) (EFSA, 2013)
- Poultry: in the context of the MRL review a metabolism study in poultry was submitted but not triggered and therefore no residue definition was proposed for poultry matrices (EFSA, 2013)

**Residue definition for monitoring implemented in Regulation (EC) No 396/2005): sum of fluroxypyr and its salts, expressed as fluroxypyr (products of animal origin except honey and other apiculture products)**

**Residue definition for risk assessment (evaluation of confirmatory data following the MRL review)**
- The tentative residue definition for enforcement purposes and for risk assessment (ruminants) could not be confirmed and should be reconsidered, pending on the data gap for toxicological information on the metabolite fluroxypyr pyridinol and its conjugates

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

**Residue definition for risk assessment (tentatively derived in the MRL review)**
- Ruminants: sum of fluroxypyr and its salts, expressed as fluroxypyr (tentative) (EFSA, 2013)
- Poultry: in the context of the MRL review a metabolism study in poultry was submitted but not triggered and therefore no residue definition was proposed for poultry matrices (EFSA, 2013)

**Residue definition for risk assessment (evaluation of confirmatory data following the MRL review)**
- The tentative residue definition for risk assessment (ruminants) could not be confirmed and should be reconsidered, pending on the data gap for toxicological information on the metabolite fluroxypyr pyridinol and its conjugates

### Fat soluble residues

|   | Yes |
|---|-----|
| Fat soluble residues | Fluroxypyr-meptyl is highly fat soluble (log $P_{ow} > 5$) (EFSA, 2013). |

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

- **Milk, Muscle, Fat, Liver, Kidney:** GC–MS, LOQ 0.01 mg/kg. Confirmatory method available
  - ILV available (EFSA, 2013)
- **Eggs, Muscle, Fat, Liver:** HPLC–MS/MS, LOQ 0.01 mg/kg. Confirmatory method available
  - ILV available (EFSA, 2013)
- **Milk:** LC–MS/MS, LOQ 0.01 mg/kg. Validated for the determination of fluroxypyr and its salts in milk (cream, skim milk, whole milk). Confirmatory method available
  - ILV available (Germany, 2018)

**MRL:** maximum residue level; GC–MS/MS: gas chromatography with tandem mass spectrometry; ILV: independent laboratory validation; HPLC–MS/MS: high-performance liquid chromatography with tandem mass spectrometry; LOQ: limit of quantification.
B.2.1.2. Stability of residues in livestock

| Animal products (available studies) | Animal | Commodity | T (°C) | Stability period Value | Compounds covered | Comment/source |
|------------------------------------|--------|-----------|--------|------------------------|-------------------|---------------|
|                                    | Bovine | Muscle    | –18    | 12 Months              | Fluroxypyr residues | Germany (2018) |
|                                    | Bovine | Liver     | –18    | 12 Months              | Fluroxypyr residues | Germany (2018) |
|                                    | Bovine | Milk      | –18    | 12 Months              | Fluroxypyr residues | Germany (2018) |
|                                    | Poultry| Eggs      | –18    | 12 Months              | Fluroxypyr residues | Germany (2018) |

B.2. Magnitude of residues in livestock

B.2.2.1. Summary of the residue data from livestock feeding studies

Risk assessment values (STMR and HR) and MRLs could not be derived for products of animal origin, pending confirmation of the residue definition for risk assessment and for enforcement for products of animal origin (ruminants) and the data gap for toxicological information on the metabolite fluroxypyr pyridinol and its conjugates.

B.3. Consumer risk assessment

ARfD

Not established, not required for the active substance fluroxypyr and the metabolites included in the residue definition for risk assessment for plant commodities (EFSA, 2011)

Data gap for toxicological information on the metabolite fluroxypyr pyridinol and its conjugates

Highest IESTI, according to EFSA PRIMo

A short-term (acute) dietary risk assessment is not necessary for products of plant origin because an ARfD has been considered not required for the active substance fluroxypyr and the metabolites included in the residue definition for risk assessment for plant commodities.

A short-term (acute) dietary risk assessment may be required for products of animal origin, pending on the data gap for toxicological information on the metabolite fluroxypyr pyridinol and its conjugates and confirmation of the residue definition for risk assessment for products of animal origin (ruminants)

Assumptions made for the calculations

Not relevant
ADI 0.8 mg/kg bw per day (fluroxypyr acid) (EFSA, 2011)

Highest IEDI, according to EFSA PRIMo <0.1% ADI (diet)
Contribution of crops assessed:
- Apples: <0.1% of ADI
- Onions: <0.1% of ADI

Assumptions made for the calculations:
The long-term dietary risk assessment was performed with regard only to consumers’ exposure from products of plant origin. The contributions of commodities of animal origin were not included in the calculation due to lack of information on the toxicological relevance of fluroxypyr pyridinol and its conjugates, and pending on confirmation of the residue definition for risk assessment for products of animal origin. Hence, the risk assessment is considered indicative only.
The calculation is based on the median residue levels derived for raw agricultural commodities.
The contributions of commodities where no GAP was reported in the framework of the MRL review were not included in the calculation.
Citrus fruits, pome fruits except apples, table olives, olives for oil production and spring onions were excluded from the consumer risk assessment because EFSA assumes that uses have been withdrawn following the MRL review.
Garlic, shallots, thyme, leeks, barley, maize/corn, oat, rye, sorghum, wheat, herbal infusions from flowers and sugar canes were excluded from the consumer risk assessment due to the lack of information to address the confirmatory data requirements.

B.4. Recommended MRLs

| Code | Commodity | Existing MRL | Proposed MRL | Conclusion/recommendation |
|------|-----------|--------------|--------------|---------------------------|
| 0130010 | Apples | 0.05* (ft 1) | (0.02*) Further risk management considerations required | The confirmatory data requirements for information on analytical methods for enforcement, storage stability, PHI and residue trials have been addressed.

The residue trials are sufficient to derive an MRL proposal for apples on the basis of the NEU and SEU GAPs. The data demonstrate that it would be appropriate to lower the MRL to the residue trials LOQ of 0.02 mg/kg. Before lowering the MRL, it should be clarified whether the current MRL needs to be maintained due to a use authorised in one of the Member States after the MRL review was completed which leads to residues greater than 0.02 mg/kg.

No consumer intake concerns were identified in the indicative risk assessment.

ARfD: acute reference dose; bw: body weight; IESTI: international estimated short-term intake; PRIMo: (EFSA) Pesticide Residues Intake Model; ADI: acceptable daily intake; IEDI: international estimated daily intake; MRL: maximum residue level; HR: highest residue; GAP: Good Agricultural Practice.
| Code<sup>a</sup> | Commodity | Existing MRL<sup>b</sup> | Proposed MRL | Conclusion/recommendation |
|----------------|-----------|-------------------------|--------------|---------------------------|
| 0220010        | Garlic    | 0.05<sup>*</sup> (ft 2) | Further risk management considerations required | The confirmatory data requirements for information on PHI and residue trials have not been addressed (the NEU GAP for garlic was not completed (PHI value)). Information to support the GAP for garlic (residue trials) was not provided. Since the confirmatory data requirements are not fully addressed, risk managers may consider the deletion of the existing MRL, replacing it with the LOQ of 0.01 mg/kg. |
| 0220020        | Onions    | 0.05<sup>*</sup> (ft 3) | (0.01*) Further risk management considerations required | The confirmatory data requirements for information on analytical methods for enforcement, metabolism, storage stability and residue trials have been addressed. The residue trials are sufficient to derive an MRL proposal for onions on the basis of the revised NEU GAP. For the uses on onions assessed, it is appropriate to lower the MRL to the LOQ of 0.01 mg/kg. Before lowering the MRL, it should be clarified whether the current MRL needs to be maintained due to a use authorised in one of the Member States after the MRL review was completed which leads to residues greater than 0.01 mg/kg. No consumer intake concerns were identified in the indicative risk assessment. |
| 0220030        | Shallots  | 0.05<sup>*</sup> (ft 4) | Further risk management considerations required | The confirmatory data requirement for information on PHI and residue trials has not been addressed. The NEU GAP for shallots was not completed (PHI value). Information to support the GAP for shallots (residue trials) was not provided. Since the confirmatory data requirements are not fully addressed, risk managers may consider the deletion of the existing MRL, replacing it with the LOQ of 0.01 mg/kg. |
| 0256070        | Thyme     | 0.05 (ft 5)            | Further risk management considerations required | The confirmatory data requirement for information on the analytical method used in the residue trials has not been addressed. The available information was insufficient to demonstrate that the specific analytical method used in the residue trials was capable to... |
| Code(a) | Commodity | Existing MRL(b) | Proposed MRL | Conclusion/recommendation |
|---------|-----------|----------------|--------------|---------------------------|
| 0270060 | Leeks     | 0.3 (ft 6)     | Further risk management considerations required | The confirmatory data requirement for information on the analytical method used in the residue trials has not been addressed. The available information was insufficient to demonstrate that the specific analytical method used in the residue trials was capable to determine the esters and conjugates of fluroxypyr included in the residue definition for enforcement and risk assessment. The confirmatory data requirement for information on metabolism has been sufficiently addressed for the specific use in leek following foliar treatment. The data gap for a representative metabolism study covering foliar treatment on leafy crops remains open. However, information submitted on the metabolism study on onions provides sufficient evidence to support the specific use on leeks, considering the botanical similarity. The confirmatory data requirement for information on analytical methods for enforcement has been addressed. The LOQ for the enforcement method is 0.01 mg/kg. Since the confirmatory data requirements are not fully addressed, risk managers may consider the deletion of the existing MRL, replacing it with the LOQ of 0.01 mg/kg. |
| 0500010 | Barley    | 0.1 (ft 7)     | Further risk management considerations required | The confirmatory data requirements for information on the analytical method used in the residue trials have not been addressed. The available information was insufficient to demonstrate that the specific analytical methods used in the residue trials were capable to determine the esters and conjugates of fluroxypyr included in the residue definition for enforcement and risk assessment. The confirmatory data requirements for information on analytical methods for enforcement have been addressed. The LOQ for the enforcement method is 0.01 mg/kg. Since the confirmatory data requirements are not fully addressed, risk managers may consider the deletion of the existing MRL, replacing it with the LOQ of 0.01 mg/kg. |
| 0500030 | Maize/corn| 0.05*(c)       | Further risk management considerations required | The confirmatory data requirements for information on the analytical method used in the residue trials have not been addressed. The available information was insufficient to demonstrate that the specific analytical methods used in the residue trials were capable to determine the esters and conjugates of fluroxypyr included in the residue definition for enforcement and risk assessment. The confirmatory data requirements for information on analytical methods for enforcement have been addressed. The LOQ for the enforcement method is 0.01 mg/kg. Since the confirmatory data requirements are not fully addressed, risk managers may consider the deletion of the existing MRL, replacing it with the LOQ of 0.01 mg/kg. |
| 0500050 | Oat       | 0.1 (ft 7)     | Further risk management considerations required | The confirmatory data requirements for information on the analytical method used in the residue trials have not been addressed. The available information was insufficient to demonstrate that the specific analytical methods used in the residue trials were capable to determine the esters and conjugates of fluroxypyr included in the residue definition for enforcement and risk assessment. The confirmatory data requirements for information on analytical methods for enforcement have been addressed. The LOQ for the enforcement method is 0.01 mg/kg. Since the confirmatory data requirements are not fully addressed, risk managers may consider the deletion of the existing MRL, replacing it with the LOQ of 0.01 mg/kg. |
| 0500070 | Rye       | 0.1 (ft 7)     | Further risk management considerations required | The confirmatory data requirements for information on the analytical method used in the residue trials have not been addressed. The available information was insufficient to demonstrate that the specific analytical methods used in the residue trials were capable to determine the esters and conjugates of fluroxypyr included in the residue definition for enforcement and risk assessment. The confirmatory data requirements for information on analytical methods for enforcement have been addressed. The LOQ for the enforcement method is 0.01 mg/kg. Since the confirmatory data requirements are not fully addressed, risk managers may consider the deletion of the existing MRL, replacing it with the LOQ of 0.01 mg/kg. |
| Code<sup>(a)</sup> | Commodity | Existing MRL<sup>(b)</sup> | Proposed MRL | Conclusion/recommendation |
|----------------|-----------|----------------------------|--------------|---------------------------|
| 0500080 | Sorghum | 0.05<sup>*</sup> (ft 7) | Further risk management considerations required | consider the deletion of the existing MRLs for barley, maize/corn, oat, rye, sorghum and wheat, replacing them with the LOQ of 0.01 mg/kg |
| 0500090 | Wheat | 0.1 (ft 7) | Further risk management considerations required |
| 0631000 | Herbal infusions from flowers | 2 (ft 8) | Further risk management considerations required | The confirmatory data requirement for information on the analytical method used in the residue trials has not been addressed. The available information was insufficient to demonstrate that the specific analytical method used in the residue trials was capable to determine the esters and conjugates of fluroxypyr included in the residue definition for enforcement and risk assessment. Since the confirmatory data requirement has not been addressed, risk managers may consider the deletion of the existing MRL, replacing it with the LOQ due to the lack of supporting data. Validated analytical methods are not available for herbal infusions from flowers. The lowering of the MRL to the default LOQ for this type of matrix could be considered. The data gap for a representative metabolism study covering foliar treatment on leafy crops remains open. However, herbal infusions from flowers are a minor use commodity and the lack of a specific metabolism study is considered a minor deviation |
| 0900020 | Sugar canes | 0.05<sup>*</sup> (ft 9) | Further risk management considerations required | The confirmatory data requirement for information on the analytical method used in the residue trials has not been addressed. The available information was insufficient to demonstrate that the specific analytical method used in the residue trials was capable to determine the esters and conjugates of fluroxypyr included in the residue definition for enforcement and risk assessment. The confirmatory data requirement for information on analytical methods for enforcement has been addressed. The LOQ for the enforcement method is 0.01 mg/kg. Since the confirmatory data requirements are not fully addressed, risk managers may consider the deletion of the existing MRL, replacing it with the LOQ of 0.01 mg/kg |

**Animal commodities**

**Existing enforcement residue definition:** sum of fluroxypyr and its salts, expressed as fluroxypyr (products of animal origin except honey and other apiculture products) (tentatively derived in the MRL review for ruminants and implemented in Regulation (EC) No 396/2005 for products of animal origin except honey and other apiculture products)

**General recommendation:** The tentative residue definition for enforcement for ruminants should be reconsidered because the metabolite fluroxypyr pyridinol and its conjugates may be present at significant levels in products of animal origin. Toxicological information on fluroxypyr pyridinol is not available and is required in order to assess whether fluroxypyr pyridinol and its conjugates are of lower, similar or higher toxicity in comparison with the parent fluroxypyr or whether specific reference values should be set.
| Code(a) | Commodity | Existing MRL(b) | Proposed MRL | Conclusion/recommendation |
|---------|------------|----------------|--------------|--------------------------|
| 1011010 | Swine – muscle | 0.01* (ft 10) | Further risk management considerations required | The confirmatory data requirement for information on storage stability has been addressed, demonstrating that residues in bovine muscle, liver and milk, and in poultry eggs were stable for at least 12 months when stored at –18°C. The confirmatory data requirement for information on metabolism has not been satisfactorily addressed to confirm the tentative residue definition for products of animal origin. Information available on the fate of fluoroxypry esters in ruminants’ matrices demonstrates that the metabolite fluoroxypry pyridinol and its conjugates are present at significant levels in products of animal origin. Since information on the toxicological relevance of the metabolite fluoroxypry pyridinol and its conjugates is not available, a final residue definition cannot be derived. Since the confirmatory data requirements are not fully addressed, risk managers may consider to revoke or restrict the uses on grassland, which is the major driver of residues in products on animal origin. Risk managers may consider the deletion of the existing MRLs for products of animal origin, replacing them with the LOQ of 0.01 mg/kg, which is achievable with routine analytical methods. |
| 1011020 | Swine – fat | 0.04 (ft 10) | | |
| 1011030 | Swine – liver | 0.04 (ft 10) | | |
| 1011040 | Swine – kidney | 0.06 (ft 10) | | |
| 1011050 | Swine – edible offals | 0.06 (ft 10) | | |
| 1011990 | Swine – others | 0.01* (ft 10) | | |
| 1012010 | Bovine – muscle | 0.01* (ft 10) | | |
| 1012020 | Bovine – fat | 0.06 (ft 10) | | |
| 1012030 | Bovine – liver | 0.07 (ft 10) | | |
| 1012040 | Bovine – kidney | 0.3 (ft 10) | | |
| 1012050 | Bovine – edible offals | 0.3 (ft 10) | | |
| 1012990 | Bovine – others | 0.01* (ft 10) | | |
| 1013010 | Sheep – muscle | 0.01* (ft 10) | | |
| 1013020 | Sheep – fat | 0.06 (ft 10) | | |
| 1013030 | Sheep – liver | 0.07 (ft 10) | | |
| 1013040 | Sheep – kidney | 0.3 (ft 10) | | |
| 1013050 | Sheep – edible offals | 0.3 (ft 10) | | |
| 1013990 | Sheep – others | 0.01* (ft 10) | | |
| 1014010 | Goat – muscle | 0.01* (ft 10) | | |
| 1014020 | Goat – fat | 0.06 (ft 10) | | |
| 1014030 | Goat – liver | 0.07 (ft 10) | | |
| 1014040 | Goat – kidney | 0.3 (ft 10) | | |
| 1014050 | Goat – edible offals | 0.3 (ft 10) | | |
| 1014990 | Goat – others | 0.01* (ft 10) | | |
| 1020000 | Milk | 0.06 (ft 10) | | |

(a): Commodity code number according to Annex I of Regulation (EC) No 396/2005.
(b): Existing EU MRL and corresponding footnote on confirmatory data.

1: The European Food Safety Authority identified some information on analytical methods, storage stability, PHI and residue trials as unavailable. When re-viewing the MRL, the Commission will take into account the information referred to in the

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first sentence, if it is submitted by 1 July 2017, or, if that information is not submitted by that date, the lack of it. (Footnote related to data gaps Nos 1, 5, 6 and 13).

ft 2: The European Food Safety Authority identified some information on analytical methods, metabolism, PHI and residue trials as unavailable. When re-viewing the MRL, the Commission will take into account the information referred to in the first sentence, if it is submitted by 1 July 2017, or, if that information is not submitted by that date, the lack of it. (Footnote related to data gaps Nos 1, 3 and 9).

ft 3: The European Food Safety Authority identified some information on analytical methods, metabolism, storage stability and residue trials as unavailable. When re-viewing the MRL, the Commission will take into account the information referred to in the first sentence, if it is submitted by 1 July 2017, or, if that information is not submitted by that date, the lack of it. (Footnote related to data gaps Nos 1, 3, 8 and 13).

ft 4: The European Food Safety Authority identified some information on analytical methods, metabolism, PHI and residue trials as unavailable. When re-viewing the MRL, the Commission will take into account the information referred to in the first sentence, if it is submitted by 1 July 2017, or, if that information is not submitted by that date, the lack of it. (Footnote related to data gaps Nos 1, 3 and 9).

ft 5: The European Food Safety Authority identified some information on the analytical method used in the residue trials as unavailable. When re-viewing the MRL, the Commission will take into account the information referred to in the first sentence, if it is submitted by 1 July 2017, or, if that information is not submitted by that date, the lack of it. (Footnote related to data gap No 12).

ft 6: The European Food Safety Authority identified some information on analytical methods, metabolism and the analytical method used in the residue trials as unavailable. When re-viewing the MRL, the Commission will take into account the information referred to in the first sentence, if it is submitted by 1 July 2017, or, if that information is not submitted by that date, the lack of it. (Footnote related to data gaps Nos 1, 3 and 12).

ft 7: The European Food Safety Authority identified some information on analytical methods and the analytical method used in the residue trials as unavailable. When re-viewing the MRL, the Commission will take into account the information referred to in the first sentence, if it is submitted by 1 July 2017, or, if that information is not submitted by that date, the lack of it. (Footnote related to data gaps Nos 1 and 12).

ft 8: The European Food Safety Authority identified some information on the analytical method used in the residue trials as unavailable. When re-viewing the MRL, the Commission will take into account the information referred to in the first sentence, if it is submitted by 1 July 2017, or, if that information is not submitted by that date, the lack of it. (Footnote related to data gap No 12).

ft 9: The European Food Safety Authority identified some information on analytical methods and the analytical method used in the residue trials as unavailable. When re-viewing the MRL, the Commission will take into account the information referred to in the first sentence, if it is submitted by 1 July 2017, or, if that information is not submitted by that date, the lack of it. (Footnote related to data gaps Nos 1 and 12).

ft 10: The European Food Safety Authority identified some information on storage stability and metabolism as unavailable. When re-viewing the MRL, the Commission will take into account the information referred to in the first sentence, if it is submitted by 1 July 2017, or, if that information is not submitted by that date, the lack of it. (Footnote related to data gaps Nos 14 and 15).
Appendix C – Pesticide Residue Intake Model (PRiMo)

Fluroxypyr

Status of the active substance: Code no.
LOQ (mg/kg bw): 0.01 Proposed LOQ

Toxicological end points
ADI (mg/kg bw per day):
0.8 Proposed ADI
ARfD (mg/kg bw):
n.n. Proposed ARfD

Source of ADI: EFSA
Source of ARfD: EFSA
Year of evaluation: 2011

No of diets exceeding ADI:

Chronic risk assessment – refined calculations

| Commodity/group of commodities | highest contributor to MS diet in % of ADI | 2nd contributor to MS diet in % of ADI | 3rd contributor to MS diet in % of ADI | pTMRLs at LOQ in % of ADI |
|--------------------------------|------------------------------------------|----------------------------------------|----------------------------------------|----------------------------|
| DE child                      | 0.0                                      | 0.0                                    | 0.0                                    | FRUIT (FRESH OR FROZEN)    |
| NL child                      | 0.0                                      | 0.0                                    | 0.0                                    | FRUIT (FRESH OR FROZEN)    |
| FR toddler                    | 0.0                                      | 0.0                                    | 0.0                                    | FRUIT (FRESH OR FROZEN)    |
| DK child                      | 0.0                                      | 0.0                                    | 0.0                                    | FRUIT (FRESH OR FROZEN)    |
| FR infant                     | 0.0                                      | 0.0                                    | 0.0                                    | FRUIT (FRESH OR FROZEN)    |
| PL general population         | 0.0                                      | 0.0                                    | 0.0                                    | FRUIT (FRESH OR FROZEN)    |
| UK Toddler                    | 0.0                                      | 0.0                                    | 0.0                                    | FRUIT (FRESH OR FROZEN)    |
| LT adult                      | 0.0                                      | 0.0                                    | 0.0                                    | FRUIT (FRESH OR FROZEN)    |
| WHO Cluster diet B            | 0.0                                      | 0.0                                    | 0.0                                    | FRUIT (FRESH OR FROZEN)    |
| UK Infant                     | 0.0                                      | 0.0                                    | 0.0                                    | FRUIT (FRESH OR FROZEN)    |
| SE general population 90th percentile | 0.0                                      | 0.0                                    | 0.0                                    | FRUIT (FRESH OR FROZEN)    |
| NL general                    | 0.0                                      | 0.0                                    | 0.0                                    | FRUIT (FRESH OR FROZEN)    |
| IT General population         | 0.0                                      | 0.0                                    | 0.0                                    | FRUIT (FRESH OR FROZEN)    |
| ES child                      | 0.0                                      | 0.0                                    | 0.0                                    | FRUIT (FRESH OR FROZEN)    |
| WHO cluster diet E            | 0.0                                      | 0.0                                    | 0.0                                    | FRUIT (FRESH OR FROZEN)    |
| WHO cluster diet D            | 0.0                                      | 0.0                                    | 0.0                                    | FRUIT (FRESH OR FROZEN)    |
| WHO regional European diet    | 0.0                                      | 0.0                                    | 0.0                                    | FRUIT (FRESH OR FROZEN)    |
| IT kids/toddler               | 0.0                                      | 0.0                                    | 0.0                                    | FRUIT (FRESH OR FROZEN)    |
| IE adult                      | 0.0                                      | 0.0                                    | 0.0                                    | FRUIT (FRESH OR FROZEN)    |
| ES adult                      | 0.0                                      | 0.0                                    | 0.0                                    | FRUIT (FRESH OR FROZEN)    |
| DK adult                      | 0.0                                      | 0.0                                    | 0.0                                    | FRUIT (FRESH OR FROZEN)    |
| IT adult                      | 0.0                                      | 0.0                                    | 0.0                                    | FRUIT (FRESH OR FROZEN)    |
| WHO Cluster diet F            | 0.0                                      | 0.0                                    | 0.0                                    | FRUIT (FRESH OR FROZEN)    |
| UK vegetarian                 | 0.0                                      | 0.0                                    | 0.0                                    | FRUIT (FRESH OR FROZEN)    |
| FR all population             | 0.0                                      | 0.0                                    | 0.0                                    | FRUIT (FRESH OR FROZEN)    |
| UK Adult                      | 0.0                                      | 0.0                                    | 0.0                                    | FRUIT (FRESH OR FROZEN)    |
| FI adult                      | 0.0                                      | 0.0                                    | 0.0                                    | FRUIT (FRESH OR FROZEN)    |

Conclusion:
The estimated Theoretical Maximum Daily Intakes (TMDI), based on pTMRLs were below the ADI. A long-term intake of residues of Fluroxypyr is unlikely to present a public health concern.

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Acute risk assessment/children – refined calculations

| Unprocessed commodities | Processed commodities |
|-------------------------|-----------------------|
| 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 Commodities | Threshold MRL (mg/kg) |
| Highest % of ARfD/ADI Commodities | pTMRL/Threshold MRL (mg/kg) |
| Highest % of ARfD/ADI Commodities | pTMRL/Threshold MRL (mg/kg) |
| Highest % of ARfD/ADI Commodities | pTMRL/Threshold MRL (mg/kg) |
| Highest % of ARfD/ADI Commodities | pTMRL/Threshold MRL (mg/kg) |

No of critical MRLs (IESTI 1): --

No of critical MRLs (IESTI 2): --

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): --

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

**pTMRL: provisional temporary MRL**

***) pTMRL: provisional temporary MRL for unprocessed commodity.

Conclusion:

As no ARfD was considered necessary, it is concluded that the short-term intake of Fluroxypyr residues is unlikely to present a public health concern.

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.
### Appendix D – Input values for the exposure calculations

#### D.1. Livestock dietary burden calculations

| Feed commodity | Median dietary burden | Maximum dietary burden |
|----------------|-----------------------|------------------------|
|                | Input value (mg/kg)   | Comment                | Input value (mg/kg)   | Comment                |
| Citrus, dried pulp | –                     | EFSA assumes that uses have been withdrawn following the MRL review | –                     | EFSA assumes that uses have been withdrawn following the MRL review |
| Apple, pomace     | 0.01                  | STMR<sup>(a)</sup>     | 0.01                  | STMR<sup>(a)</sup>     |
| Cereals, grain    | –                     | EFSA assumes that uses have been withdrawn following the MRL review | –                     | EFSA assumes that uses have been withdrawn following the MRL review |
| Wheat and rye bran| –                     |                        | –                     |                        |
| Barley and oat straw |                      |                        | –                     |                        |
| Wheat and rye straw|                       |                        | –                     |                        |
| Grass (fresh)     | 11.2                  | STMR (NEU trials)      | 18.8                  | HR (NEU trials)        |
| Grass, silage     | 22.3                  | STMR grass, fresh, NEU trials (11.2) × PF (1.99) | 37.4                  | HR grass, fresh, NEU trials (18.8) × PF (1.99) |
| Grass, hay        | 49.6                  | STMR grass, fresh, NEU trials (11.2) × PF (4.43; EFSA, 2013) | 83.3                  | HR grass, fresh, NEU trials (18.8) × PF (4.43; EFSA, 2013) |

Risk assessment residue definition: sum of fluroxypyr, its salts, its esters and its conjugates, expressed as fluroxypyr.

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

(a): For fruit pomace, no default processing factor was applied because residues are expected to be below the LOQ.

Concentration of residues in these commodities is therefore not expected.

#### D.2. Consumer risk assessment

| Commodity               | Chronic risk assessment | Acute risk assessment |
|-------------------------|-------------------------|-----------------------|
|                         | Input value (mg/kg)     | Comment               | Input value (mg/kg) | Comment               |
| Citrus fruits           | –                       | EFSA assumes that uses have been withdrawn following the MRL review | –                       |                        |
| Apples and pome fruits  | 0.01                    | STMR                  | –                       |                        |
| Olives                  | –                       | EFSA assumes that uses have been withdrawn following the MRL review | –                       |                        |
| Garlic                  | –                       | Excluded from the consumer risk assessment due to the lack of information to address the confirmatory data requirements and EFSA assumes the uses will be revoked | –                       |                        |
| Onions                  | 0.01                    | STMR                  | –                       |                        |

Residue definition for risk assessment: sum of fluroxypyr, its salts, its esters and its conjugates, expressed as fluroxypyr. Applicable to cereals following foliar treatment and to root and tuber vegetables following foliar treatment. Applicable to the fruit crops following soil treatment assessed in the current application (apples). Applicable to the specific use in leek following foliar treatment. Tentative for other leafy crops following foliar treatment assessed in the current application (thyme and herbal infusions from flowers).

A short-term (acute) dietary risk assessment is not necessary for plant commodities because an ARfD has been considered not required due to the toxicological profile for the active substance fluroxypyr.

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### Commodity Risk Assessment

| Commodity              | Chronic risk assessment Comment                                                                 | Acute risk assessment Comment                      |
|------------------------|--------------------------------------------------------------------------------------------------|---------------------------------------------------|
| Shallots               | Excluded from the consumer risk assessment due to the lack of information to address the confirmatory data requirements and EFSA assumes the uses will be revoked |                                                   |
| Spring onions          | EFSA assumes that uses have been withdrawn following the MRL review                             |                                                   |
| Thyme                  | Excluded from the consumer risk assessment due to the lack of information to address the confirmatory data requirements and EFSA assumes the uses will be revoked |                                                   |
| Leeks                  | EFSA assumes that uses have been withdrawn following the MRL review                             |                                                   |
| Olives for oil production |                                                                                               |                                                   |
| Barley                 | Excluded from the consumer risk assessment due to the lack of information to address the confirmatory data requirements and EFSA assumes the uses will be revoked |                                                   |
| Maize/corn             |                                                                                                 |                                                   |
| Oat                    |                                                                                                 |                                                   |
| Rye                    |                                                                                                 |                                                   |
| Sorghum                |                                                                                                 |                                                   |
| Wheat                  |                                                                                                 |                                                   |
| Herbal infusions from flowers |                                                                                             |                                                   |
| Sugar canes            |                                                                                                 |                                                   |

**Residue definition for risk assessment:** Ruminants: sum of fluroxypyr and its salts, expressed as fluroxypyr (tentatively derived in the MRL review)

**General recommendation:** The tentative residue definition for risk assessment (ruminants) should be reconsidered because the metabolite fluroxypyr pyridinol and its conjugates may be present at significant levels in products of animal origin. Toxicological information on fluroxypyr pyridinol is not available and is required in order to assess whether fluroxypyr pyridinol and its conjugates are of lower, similar or higher toxicity in comparison with the parent fluroxypyr or whether specific reference values should be set.

A short-term dietary risk assessment may be required for products of animal origin, pending confirmation of the residue definition for risk assessment for products of animal origin (ruminants) and the data gap toxicological information on the metabolite fluroxypyr pyridinol and its conjugates.
### Appendix E – Summary of the livestock metabolism study assessed under the current application

**Table E.1:** Nature of the Residue in the Lactating Goat; Summary of the characterisation and identification of radioactive residues in goat milk following oral dose of $^{14}$C-fluroxypyr-meptyl at 90 mg/kg per day for 7 days (France, 2018)

| Metabolite                                                                 | Approx. retention time (min) | Milk, day 1 (8 h) | Milk, day 4 (80 h) | Milk, day 6 (128 h) |
|---------------------------------------------------------------------------|------------------------------|-------------------|--------------------|---------------------|
|                                                                           | % TRR | mg eq/kg | % TRR | mg eq/kg | % TRR | mg eq/kg |
| Total radioactive residue (TRR)                                           | 100.0 | 0.017    | 100.0 | 0.040    | 100.0 | 0.041    |
| Total extractable                                                         | 99.2  | 0.016    | 95.7  | 0.037    | 87.0  | 0.036    |
| Total extractable analysed by HPLC<sup>A</sup>                            | 63.1  | 0.011    | 76.2  | 0.030    | 77.2  | 0.032    |
| Fluroxypyr-meptyl (Fluroxypyr MHE)                                        | 24.0  | ND       | ND    | ND       | ND    | ND       |
| Unknown component<sup>B</sup>                                             | 1.5   | 22.7     | 0.004 | 14.9     | 0.006 | 13.0     | 0.005   |
| Minor unknown component                                                   | 2.2   | ND       | ND    | ND       | ND    | ND       |
| Fluroxypyr pyridinol glucuronide conjugate (Fluroxypyr 2-pyridinol glucuronide conjugate) | 11.0  | ND       | ND    | ND       | ND    | ND       |
| Fluroxypyr pyridinol (Fluroxypyr 2-pyridinol)                             | 15.0  | ND       | ND    | ND       | ND    | 8.6      | 0.004   |
| **Fluroxypyr** (Fluroxypyr acid)                                          | 16.0  | 40.4     | 0.007 | 61.3     | 0.024 | 55.6     | 0.023   |
| Total identified                                                          | 40.4  | 0.007    | 61.3  | 0.024    | 64.2  | 0.027    |
| Total unextractable                                                        | < LOQ | < LOQ    | 4.3   | 0.002    | 20.2  | 0.008    |
| Accountability<sup>C</sup>                                                | 99.2  | 0.016    | 100.0 | 0.039    | 107.2 | 0.044    |

ND: Not detected.

Components in bold were detected at levels > 10% TRR and/or 0.010 mg/kg.

<sup>A</sup>: Total extractable after combining and concentration steps, taking into account gains and losses at each stage.

<sup>B</sup>: Considered to consist of multiple components following isolation of this polar region in the liver and analysis by the Primesep AB method.

<sup>C</sup>: Total extractable + Total unextractable.
Table E.2: Nature of the Residue in the Lactating Goat; Summary of the characterisation and identification of radioactive residues in goat liver, kidney and loin muscle following oral dose of $^{14}$C-fluroxypyr-meptyl at 90 mg/kg per day for 7 days (France, 2018)

| Metabolite | Approx. retention time (min) | Liver % TRR | mg eq/kg | Kidney % TRR | mg eq/kg | Muscle, loin % TRR | mg eq/kg |
|------------|-----------------------------|-------------|----------|--------------|----------|-------------------|----------|
| Total radioactive residue (TRR) | | 100.0 | 0.123 | 100.0 | 1.545 | 100.0 | 0.011 |
| Total extractable | | 73.3 | 0.090 | 94.1 | 1.453 | 138.7 | 0.015 |
| Total extractable analysed by HPLC$^A$ | | 65.8 | 0.081 | 88.5 | 1.367 | 81.4 | 0.009 |
| Fluroxypyr-meptyl (Fluroxypyr MHE) | | 24.0 | ND | ND | ND | ND | ND |
| Unknown component$^B$ | | 1.5 | ND | ND | ND | ND | ND |
| Minor unknown | | 2.2 | ND | ND | ND | ND | ND |
| Fluroxypyr pyridinol glucuronide conjugate | | 11.0 | ND | ND | 17.7 | 0.274 | 10.4 | 0.001 |
| (Fluroxypyr 2-pyridinol glucuronide conjugate)$^C$ | | 15.0 | 14.5 | 0.018 | 6.9 | 0.107 | ND | ND |
| Fluroxypyr pyridinol | | 16.0 | 38.6 | 0.048 | 63.8 | 0.986 | 71.0 | 0.008 |
| (Fluroxypyr 2-pyridinol) | | | | | | | | |
| Fluroxypyr | | | | | | | | |
| (Fluroxypyr acid) | | | | | | | | |
| Total identified | | 53.1 | 0.066 | 88.5 | 1.367 | 81.4 | 0.009 |
| Total extractable by protease$^D$ | | 23.7 | 0.029 | NA | NA | NA | NA |
| Total unextractable | | 12.0 | 0.015 | 2.4 | 0.037 | < LOQ | < LOQ |
| Accountability$^E$ | | 109.0 | 0.134 | 96.5 | 1.490 | 138.7 | 0.015 |

NA: Not Applicable
Components in bold were detected at levels > 10% TRR and/or 0.010 mg/kg.
A: Total extractable after combining and concentration steps, taking into account gains and losses at each stage.
B: Demonstrated to consist of multiple components following isolation and analysis by HPLC Method 3, each at < 6% of the TRR (0.007 mg eq/kg).
C: Identified based on retention time with the component identified in kidney by LC-MS analysis.
D: Protease extraction carried out on the post-extracted solid. The protease extract was reconstituted for HPLC analysis but no components were identified as all were below LOQ (LOQ ≥ 0.001 mg eq/kg). After protease extraction, a second PES remained and contained 15.2% TRR (0.019 mg eq/kg).
E: Total extractable + Total unextractable.
Table E.3: Nature of the residue in the lactating goat; summary of the characterisation and identification of radioactive residues in goat flank muscle, perirenal fat and subcutaneous fat following oral dose of $^{14}$C-fluroxypyr-meptyl at 90 mg/kg per day for 7 days (France, 2018)

| Metabolite                                                   | Approx. retention time (min) | Muscle, flank |                |                | Fat, perirenal |                |                | Fat, subcutaneous |                |
|--------------------------------------------------------------|-----------------------------|--------------|----------------|----------------|----------------|----------------|----------------|------------------|----------------|
|                                                               | % TRR | mg eq/kg | % TRR | mg eq/kg | % TRR | mg eq/kg | % TRR | mg eq/kg |
| Total radioactive residue (TRR)                              |       |          |       |          |       |          |       |          |
| Total extractable                                            |       |          |       |          |       |          |       |          |
| Total extractable analysed by HPLC$^A$                       |       |          | 98.4 | 0.012    | 119.4 | 0.043    | 73.8 | 0.009    |
| Fluroxypyr-meptyl (Fluroxypyr MHE)                           | 24.0  | ND       | ND    | ND       | ND    | ND       | ND    | ND       |
| Unknown component                                            | 1.5   | ND       | ND    | ND       | ND    | ND       | ND    | ND       |
| Minor unknown                                                | 2.2   | ND       | ND    | ND       | ND    | ND       | ND    | ND       |
| Fluroxypyr pyridinol conjugate                               |       | 11.0     | 26.5 | 0.003    | 26.4 | 0.010    | 10.9 | 0.001    |
| Fluroxypyr pyridinol (Fluroxypyr 2-pyridinol)                | 15.0  | ND       | ND    | 6.2      | 0.002 | 5.1      | 0.001 |
| Fluroxypyr (Fluroxypyr acid)                                 | 16.0  | 71.9     | 0.009 | 86.8     | 0.031 | 57.9     | 0.007 |
| Total identified                                             |       |          | 98.4 | 0.012    | 119.4 | 0.043    | 73.8 | 0.009    |
| Total unextractable                                          |       | < LOQ    | < LOQ | < LOQ    | < LOQ | < LOQ    | < LOQ |
| Accountability$^C$                                           |       | 110.7    | 0.014 | 153.2    | 0.056 | 94.1     | 0.011 |

NA: Not Applicable.
Components in bold were detected at levels > 10% TRR and/or 0.010 mg/kg.
A: Total extractable after combining and concentration steps, taking into account gains and losses at each stage.
B: Identified based on retention time with the component identified in kidney by LC-MS analysis.
C: Total extractable + Total unextractable.
# Appendix F – Used compound codes

| Code/trivial name(a) | IUPAC name/SMILES notation/InChiKey(b) | Structural formula(c) |
|----------------------|--------------------------------------|-----------------------|
| Fluroxypyr          | 4-amino-3,5-dichloro-6-fluoro-2-pyridyloxyacetic acid | ![Structural formula](image) |
| Fluroxypyr          | O=C(O)COc1nc(F)c(Cl)c(N)c1Cl               |                       |
|                     | MEFQWPUMEMWTJP-UHFFFAOYSA-N               |                       |
| Fluroxypyr-meptyl   | (RS)-1-methylheptyl 4-amino-3,5-dichloro-6-fluoro-2-pyridyloxyacetate | ![Structural formula](image) |
| Fluroxypyr-MHE      | CC(CCCCCC)OC(-O)COc1nc(F)c(Cl)c(N)c1Cl |                       |
| Fluroxypyr-methylheptyl | OLZQTUCTGLFTQ-UHFFFAOYSA-N              |                       |
| Fluroxypyr 1-methylheptyl | ZKJARVBUEBZJZT-UHFFFAOYSA-N |                       |
| Fluroxypyr-butoxypropyl | (RS)-2-butoxy-1-methylethyl 4-amino-3,5-dichloro-6-fluoro-2-pyridyloxyacetate | ![Structural formula](image) |
| Fluroxypyr-BPE      | CC(COC(CCC)OC(-O)COc1nc(F)c(Cl)c(N)c1Cl |                       |
|                     | ZKFARSBUEBZJZT-UHFFFAOYSA-N               |                       |
| Fluroxypyr pyridinol | 4-amino-3,5-dichloro-6-fluoropyridin-2-ol | ![Structural formula](image) |
| Fluroxypyr 2-pyridinol | Nc1c(Cl)c(F)nc(O)c1Cl                  |                       |
|                     | JPMASQTVFRLSAR-UHFFFAOYSA-N              |                       |
| N-methyl-2-pyrrolidone | 1-methyl-2-pyrrolidinone                | ![Structural formula](image) |
| NMP                 | O=C1CCCN1C                             |                       |
|                     | SECSVLQFMRJ-M-UHFFFAOYSA-N              |                       |
| Fluroxypyr methoxypyridine | 3,5-dichloro-2-fluoro-6-methoxypyridin-4-amine | ![Structural formula](image) |
| DMP                 | Clc1c(N)c(Cl)c(F)nc1OC                 |                       |
|                     | XBFLRBRESHZOLD-UHFFFAOYSA-N            |                       |

(a): The metabolite name in bold is the name used in the reasoned opinion.
(b): ACD/Name 2018.2.2 ACD/Labs 2018 Release (File version N50E41, Build 103230, 21 July 2018).
(c): ACD/ChemSketch 2018.2.2 ACD/Labs 2018 Release (File version C60H41, Build 106041, 7 December 2018).