Modification of the existing maximum residue levels for flupyradifurone and DFA in rapeseeds/canola seeds and mustard seeds

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Abstract
In accordance with Article 6 of Regulation (EC) No 396/2005, the applicant Bayer SAS - Crop Science Division submitted a request to the competent national authority in the Netherlands to modify the existing maximum residue levels (MRL) for the active substance flupyradifurone and its metabolite DFA in rapeseeds/canola seeds and mustard seeds. The data submitted in support of the request were found sufficient to derive MRL proposals for both compounds in rapeseeds and mustard seeds. Adequate analytical methods for enforcement are available to control the relevant residues in plant matrices under consideration. Based on the risk assessment results, EFSA concluded that the short-term and long-term intake of residues of flupyradifurone and of its metabolite DFA resulting from the use of flupyradifurone is unlikely to present a risk to consumer health.

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Keywords: flupyradifurone, rapeseeds/canola seeds, mustard seeds, insecticide, MRL, consumer risk assessment

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Summary

In accordance with Article 6 of Regulation (EC) No 396/2005, Bayer SAS - Crop Science Division submitted an application to the competent national authority in the Netherlands (evaluating Member State, EMS) to modify the existing maximum residue levels (MRLs) for the active substance flupyradifurone and its metabolite difluoroacetic acid (DFA) in rapeseeds/canola seeds and mustard seeds. The EMS drafted an evaluation report in accordance with Article 8 of Regulation (EC) No 396/2005, which was submitted to the European Commission and forwarded to the European Food Safety Authority (EFSA) on 11 December 2019. To accommodate for the intended uses of flupyradifurone, the EMS proposed to raise the existing MRLs for flupyradifurone in rapeseeds and mustard seeds from the limit of quantification (LOQ) of 0.01 to 0.3 mg/kg and to raise the existing MRLs for difluoroacetic acid (DFA) in rapeseeds and mustard seeds from the LOQ of 0.05 to 0.3 mg/kg.

EFSA assessed the application and the evaluation report as required by Article 10 of the MRL regulation.

Based on the conclusions derived by EFSA in the framework of the peer review of the pesticides risk assessment under Regulation (EC) No 1107/2009, the data evaluated under previous MRL assessments and the additional data provided by the EMS in the framework of this application, the following conclusions are derived.

The metabolism of flupyradifurone was investigated following foliar applications of the radiolabelled active substance on fruit crops, pulses/oilseeds and cereals, by soil granule/soil drench applications on fruit crops, root crops and cereals and by seed dressing on root crops. The EU pesticides peer review concluded that in primary crops, flupyradifurone was expected to be the major component. Following the soil application, significant proportions of difluoroacetic acid (DFA) were observed; the data from residue trials confirmed that DFA is a relevant plant metabolite of flupyradifurone.

Studies investigating the effect of standard processing conditions on the nature of flupyradifurone (hydrolysis studies) demonstrated that the active substance is stable. Studies investigating the effect of processing on the nature of DFA are not available. However, considering the structural similarity of DFA with trifluoroacetic acid (TFA), which is very stable under hydrolysis conditions, EFSA agrees with the applicant and EMS that DFA is unlikely to degrade under standard hydrolytic conditions.

In rotational crops, the major residues identified were flupyradifurone, its metabolites flupyradifurone-hydroxy, 6-CNA and their conjugates, and DFA. The presence of DFA is mostly the result of its uptake from soil, where DFA is the major metabolite of flupyradifurone.

Based on the metabolic pattern identified in primary and rotational crop metabolism studies, the results of hydrolysis studies, the toxicological significance of metabolites and the capabilities of enforcement analytical methods, the following residue definitions were agreed by the EU pesticides peer review:

- Residue definition for risk assessment: Sum of flupyradifurone and DFA, expressed as flupyradifurone
- Residue definitions for enforcement: 1) Flupyradifurone; 2) DFA, expressed as DFA

The same residue definitions are applicable to rotational crops and processed products.

EFSA concluded that for the crops assessed in this application, metabolism of flupyradifurone in primary and in rotational crops, and the possible degradation in processed products have been addressed and that the previously derived residue definitions are applicable. Sufficienly validated analytical methods based on high-performance liquid chromatography with tandem mass spectrometry (HPLC-MS/MS) are available to quantify residues of flupyradifurone and of DFA in oilseeds according to enforcement residue definitions.

The available data are considered sufficient to derive MRL proposals as well as risk assessment values for flupyradifurone and DFA in mustard seeds and rapeseeds in support of the intended SEU use. The intended NEU use on mustard is not supported by compliant residue trials, whereas for the critical intended NEU use on oilseed rape, an MRL proposal was derived on the basis of a scaled residue data.

Flupyradifurone exhibits high persistency in soil, forming DFA as its major soil metabolite. The formation of DFA in soil results in its uptake in rotational crops. Thus, the MRL proposal for DFA in rapeseeds and mustard seeds would need to account for residues that occur after direct treatment of the crop (primary crop treatment) and from the soil uptake. This estimate would lead to a higher MRL proposal of 0.4 mg/kg. Further risk management discussions are therefore recommended on whether...
MRL should be established to cover residues in rotational crops or whether other risk management options (e.g. plant back restrictions) would be appropriate to avoid DFA residues in untreated crops. 

The occurrence of flupyradifurone and DFA residues in rotational crops was investigated in the framework of the EU pesticides peer review and in the framework of the previous EFSA assessment. A wide range of rotational crop studies were available, which indicate a significant uptake of the metabolite DFA in rotational crops. Consequently, the MRL proposals for DFA in rotational crops were derived in the recent EFSA assessment. Since the annual application rate in the intended good agricultural practices (GAPs) on oilseed rape and mustard is significantly lower than the application rates on primary crops for which the residues of DFA in rotational crops were estimated in the previous EFSA assessment, the magnitude of DFA residues in rotational crops was not re-assessed and the conclusions of the previous EFSA opinion are applicable.

In the framework of the current application, processing studies with rapeseeds and mustard seeds were not submitted and are not required, considering the low contribution of residues in these crops to the total consumer exposure.

Rapeseed meal can be used as feed item, and therefore, a potential carry-over into food of animal origin was assessed. The previous EU livestock dietary burden calculation for the intake of flupyradifurone and DFA residues from imported feed and the EU feed items was updated with residue values for rapeseed meal from the new intended uses. When considering the livestock exposure to DFA residues, also the intake of this metabolite via rotational crops has been considered. The calculated livestock dietary burden exceeded the trigger value of 0.004 mg/kg bw day for all relevant livestock species. Since the contribution of flupyradifurone and DFA residues in rapeseed meal to the total EU livestock dietary burden is insignificant, the magnitude of residues in animal commodities was not further assessed. EFSA concludes that the residues in rapeseeds from the intended uses will not affect the residues in animal commodities as estimated in the previous EFSA assessment.

The toxicological profile of flupyradifurone was assessed in the framework of the EU pesticides peer review and the data were sufficient to derive an acceptable daily intake (ADI) value of 0.064 mg/kg bw per day and an acute reference dose (ARFD) of 0.15 mg/kg bw. The toxicological reference values are also applicable to metabolite DFA.

The consumer risk assessment was performed with revision 3.1 of the EFSA Pesticide Residues Intake Model (PRIMo). EFSA performed two separate consumer exposure calculation scenarios in order to estimate the exposure to flupyradifurone and DFA residues from 1) treated primary crops and animal commodities, and 2) plant commodities that are grown as rotational crops (no primary treatment). Acute exposure was calculated only for the crops under consideration.

The calculated chronic exposure under scenario 1 accounted for a maximum of 54% of the ADI (NL toddler diet). The contribution of residues in rapeseeds and mustard seeds to the total consumer exposure was low: 0.34% of the ADI (NL toddler diet) for rapeseeds and 0.01% of the ADI (GEMS/Food G11 diet) for mustard seeds. No acute consumer intake concerns were identified for flupyradifurone residues in rapeseeds and mustard seeds (individually 0.2% of the ARFD).

The consumer exposure to DFA residues in the crops from the soil uptake (scenario 2) as calculated in the previous EFSA output was not updated, since the uptake of DFA (and flupyradifurone) residues in untreated rotational crops was estimated from more critical flupyradifurone EU uses than the intended uses under consideration. The same conclusions are therefore applicable. The calculated consumer exposure accounted for up to 17% of the ADI (GEMS/Food G06 diet). No acute consumer intake concerns were identified for DFA residues in rapeseeds and mustard seeds from the soil uptake (individually < 0.1% of the ARFD).

The combined chronic exposure to flupyradifurone and DFA residues from the intake of food commodities following primary crop treatments, from the intake of animal commodities and from the intake of food commodities containing residues due to the uptake via soil accounts for a maximum of 69% of the ADI (NL toddler). No acute consumer intake concerns were identified for a combined acute exposure to flupyradifurone and DFA residues from the intake of rapeseeds and mustard seeds treated as primary crops and when grown in a crop rotation.

EFSA concluded that the proposed use of flupyradifurone on oilseed rape and mustard will not result in a consumer exposure exceeding the toxicological reference values and therefore is unlikely to pose a risk to consumers’ health. EFSA concluded that the short-term and long-term intake of residues of flupyradifurone and of its metabolite DFA resulting from the use of flupyradifurone is unlikely to present a risk to consumer health.

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

Full details of all end points and the consumer risk assessment can be found in Appendices B-D.
| Code<sup>(a)</sup> | Commodity                              | Existing EU MRL (mg/kg) | Proposed EU MRL (mg/kg) | Comment/justification                                                                 |
|-----------------|----------------------------------------|-------------------------|-------------------------|--------------------------------------------------------------------------------------|
| 0401060         | Rapeseeds/canola seeds                 | 0.01*                   | 0.3                     | The submitted data are sufficient to derive an MRL proposal for the intended NEU and SEU uses. Risk for consumers unlikely |
| 0404080         | Mustard seeds                          | 0.01*                   | 0.3                     | The MRL proposal reflects the SEU use. For the NEU use, the data were not sufficient to derive an MRL proposal. Risk for consumers unlikely |

**Enforcement residue definition (2): Difluoroacetic acid (DFA)**

| Code<sup>(a)</sup> | Commodity                              | Existing EU MRL (mg/kg) | Proposed EU MRL (mg/kg) | Comment/justification                                                                 |
|-----------------|----------------------------------------|-------------------------|-------------------------|--------------------------------------------------------------------------------------|
| 0401060         | Rapeseeds/canola seeds                 | 0.05 (ft.1)             | 0.3                     | The MRL proposal does not account for residues which may be taken up by crops from soil which was previously treated with flupyradifurone, which may be expected to contribute up to 0.05 mg/kg in oilseeds grown in soil at the calculated EU soil plateau concentration for flupyradifurone residues. The resulting MRL proposal would be 0.4 mg/kg. Further risk management discussions are therefore recommended on whether MRLs should be established to cover residues in rotational crops or whether other risk management options (e.g. plant back restrictions) would be appropriate to avoid DFA residues in untreated crops |
| 0404080         | Mustard seeds                          | 0.05 (ft.1)             | 0.3                     |                                                                                        |

MRL: maximum residue level; NEU: northern European Union; SEU: southern European Union.

*: Indicates that the MRL is set at the limit of analytical quantification (LOQ).

<sup>(a)</sup>: Commodity code number according to Annex I of Regulation (EC) No 396/2005.

<sup>ft.1</sup>: The European Food Safety Authority identified some information on rotational crops 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 6 April 2018, or, if that information is not submitted by that date, the lack of it. The confirmatory data were sufficiently addressed in the recent EFSA assessment proposing the deletion of the footnote (EFSA, 2020).
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Assessment

The European Food Safety Authority (EFSA) received an application to modify the existing maximum residue levels (MRLs) for flupyradifurone and its metabolite difluoroacetic acid (DFA) in rapeseeds/canola seeds and mustard seeds. The detailed description of the intended uses of flupyradifurone in NEU and SEU on oilseed rape and mustard, which are the basis for the current MRL application, is reported in Appendix A.

Flupyradifurone is the ISO common name for 4-[(6-chloro-3-pyridylmethyl)(2,2-difluoroethyl)amino]furan-2(5H)-one (IUPAC). The chemical structures of the active substance and its main metabolites are reported in Appendix E.

Flupyradifurone was evaluated in the framework of Regulation (EC) No 1107/20099 with the Netherlands designated as rapporteur Member State (RMS) for the representative uses of foliar applications on hops and lettuce. The Draft Assessment Report (DAR) also included a proposal to set maximum residue levels (MRL application), in accordance with Article 11 (2) of the Regulation (EC) 1107/2009. The draft assessment report (DAR) prepared by the RMS has been peer reviewed by EFSA (EFSA, 2015) where some information was identified as unavailable (data gaps) and tentative MRLs were derived for those uses which were not fully supported by data. Flupyradifurone was approved7 for use as insecticide on 9 December 2015.

The MRL proposals for both flupyradifurone and its metabolite difluoroacetic acid (DFA) were implemented in the MRL legislation by Commission Regulation (EU) 2016/4863. The data gaps identified by the peer review as well as residues of flupyradifurone and DFA from new uses and authorised uses in third countries were assessed in a recently issued EFSA reasoned opinion (EFSA, 2020). The MRL proposals have not yet been implemented in the MRL legislation, but the conclusions taken therein will be considered for the present assessment.

In accordance with Article 6 of Regulation (EC) No 396/20054, Bayer SAS - Crop Science Division submitted an application to the competent national authority in the Netherlands (evaluating Member State, EMS) to modify the existing maximum residue levels (MRLs) for the active substance flupyradifurone and its metabolite difluoroacetic acid (DFA) in rapeseeds/canola seeds and mustard seeds. The EMS drafted an evaluation report in accordance with Article 8 of Regulation (EC) No 396/2005, which was submitted to the European Commission and forwarded to the European Food Safety Authority (EFSA) on 11 December 2019. To accommodate for the intended uses of flupyradifurone, the EMS proposed to raise the existing MRLs for flupyradifurone in rapeseeds and mustard seeds from the limit of quantification (LOQ) of 0.01 to 0.3 mg/kg and to raise the existing MRLs for DFA in rapeseeds and mustard seeds from the LOQ of 0.05 to 0.3 mg/kg.

EFSA based its assessment on the evaluation report submitted by the EMS (Netherlands, 2019), the draft assessment report (DAR) (and its addendum) (Netherlands, 2014, 2015) prepared under Regulation (EC) 1107/2009, the Commission review report on flupyradifurone (European Commission, 2015), the conclusion on the peer review of the pesticide risk assessment of the active substance flupyradifurone (EFSA, 2015) as well as the conclusions from previous EFSA opinions on flupyradifurone (EFSA, 2016, 2020).

For this application, the data requirements established in Regulation (EU) No 283/20135 and the guidance documents applicable at the date of submission of the application to the EMS are applicable (European Commission, 2000, 2010a,b, 2017; OECD, 2007a–h, 2008a,b, 2009a,b, 2011, 2013, 2016, 2017).

1 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.
2 Commission Implementing Regulation (EU) 2015/2084 of 18 November 2015 approving the active substance flupyradifurone, 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 302, 19.11.2015, p. 89–92.
3 Commission Regulation (EU) 2016/486 of 29 March 2016 amending Annexes II and III to Regulation (EC) No 396/2005 of the European Parliament and of the Council as regards maximum residue levels for cyazofamid, cycloxydim, difluoroacetic acid, fenoxycarb, flumetrin, flupicicloide, flupyradifurone, fluapyroxad, kresoxim-methyl, mepanipyrim, metalaxyl-M, pendimethalin and tebufentin in or on certain products. OJ L 90, 6.4.2016, p. 1–66.
4 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.
5 Commission Regulation (EU) No 283/2013 of 1 March 2013 setting out the data requirements for active substances, in accordance with Regulation (EC) No 1107/2009 of the European Parliament and of the Council concerning the placing of plant protection products on the market. OJ L 93, 3.4.2013, p. 1–84.
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. A selected list of end points of the studies assessed by EFSA in the framework of this MRL application including the end points of relevant studies assessed previously, are presented in Appendix B.

The evaluation report submitted by the EMS (Netherlands, 2019) and the exposure calculations using the EFSA Pesticide Residues Intake Model (PRIMo) are considered as supporting documents to this reasoned opinion and, thus, are made publicly available as background documents to this reasoned opinion.

1. **Residues in plants**

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

1.1.1. **Nature of residues in primary crops**

Flupyradifurone metabolism in primary crops was investigated in the framework of the EU pesticides peer review in four crop groups either by foliar applications (apple, cotton, rice), by soil granule/drench applications (tomato, potato, rice) and by seed treatment (potato). Studies were conducted using 14C-flupyradifurone labelled on the pyridinyl and furanone moiety. One study on tomato using soil drench application and a 14C-labelling on the difluoroethyl amino group was also submitted (EFSA, 2015).

The metabolism in primary crops was seen to be similar in all plant groups investigated. Flupyradifurone was consistently observed as the major component of the radioactive residues, accounting for ca. 25–88% total radioactive residue (TRR) in all plant parts analysed. Besides flupyradifurone, the following metabolites were identified in different plant matrices: the conjugate flupyradifurone-hydroxy-glycoside, up to 36% TRR in apple leaves, the conjugate CHMP-diglycoside, up to 37% TRR (0.06 mg/kg) and the metabolite 6-CNA in the range of 13–22% TRR in tomato fruit, potato tuber and cotton seed at ca. 0.02 mg/kg, both resulting from the cleavage of the molecule at ethylamine bond and containing the pyridinyl moiety.

In tomato fruits, following the soil drench application, significant proportions (87% TRR) and levels (0.17 mg/kg) of difluoroacetic acid (DFA) were observed. Re-analysing samples from radiolabelled studies for non-radiolabelled DFA residues, the measured DFA residues (expressed as DFA equivalent) were in the range of 0.04–0.23 mg/kg in apple fruits, potato tubers, cotton seeds and rice grains, irrespective of the mode of application.

The peer review concluded that in primary crops, flupyradifurone is not extensively degraded and the metabolism in plants proceed via the hydroxylation of the furanone ring leading to the flupyradifurone-hydroxy metabolite (M8 metabolite) and its glycoside conjugates and via the cleavage of the parent molecule at the ethylamine bond resulting in the formation of metabolites containing the pyridinyl moiety (CHMP-diglycoside, 6-CNA free and conjugated). The furanone counterpart is extensively metabolised and incorporated in natural glycoside or carbohydrate components.

For the intended uses under consideration, it is concluded that the metabolic behaviour of flupyradifurone in primary crops is sufficiently addressed.

1.1.2. **Nature of residues in rotational crops**

The nature of flupyradifurone in rotational crops (turnips, Swiss chard and wheat) was investigated in the framework of the EU pesticides peer review. Flupyradifurone labelled at 14C-pyridinyl and 14C-furanone moiety was applied on a bare soil at an application rate of 436 g/ha. Rotational crops were planted 29, 135 and 296 days after the soil treatment. In rotational crops flupyradifurone and its metabolites flupyradifurone-hydroxy, 6-CNA and their conjugates were found to be the major components of the radioactive residues (EFSA, 2015). These radiolabelled studies did not include the labelling on the difluoroethyl amino group.

Additional field rotational crop studies indicated that DFA is the major component of the residues in rotational crops. The presence of DFA is mostly due to the uptake of residue from soil (EFSA, 2015).

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6 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.
1.1.3. Nature of residues in processed commodities

The effect of processing on the nature of flupyradifurone was investigated in the framework of the EU pesticides peer review (EFSA, 2015). Standard hydrolysis studies showed that flupyradifurone is hydrolytically stable under conditions of pasteurisation, baking/brewing/boiling and sterilisation.

The effect of processing on the nature of difluoroacetic acid (DFA) has not been investigated. Considering the similarity of the structures between trifluoroacetic acid (TFA) and DFA, the applicant proposed a read-across for both acids. The TFA, due to its stability in environment, has been widely studied and is, due to its structure (complete fluoride ion substitution), very stable and thus has no potential for hydrolytic degradation (Lifongo et al., 2010).

EFSA agrees with the EMS that there is sufficient evidence that difluoroacetic acid is stable under standard hydrolysis conditions.

1.1.4. Methods of analysis in plants

The availability of analytical enforcement methods for the determination of flupyradifurone and DFA in plant matrices was investigated in the framework of the EU pesticides peer review (EFSA, 2015). It was concluded that a method using HPLC-MS/MS is sufficiently validated for the determination of flupyradifurone and DFA residues; LOQs achievable with the method were 0.01 and 0.007 mg/kg7 for flupyradifurone and DFA (expressed as DFA), respectively, in plant matrices with high water (lettuce), high starch (wheat, potato), high acid (oranges) and high oil content (rapeseeds).

EFSA concludes that a sufficiently validated analytical method is available for the enforcement of flupyradifurone and DFA residues in the crops under consideration.

1.1.5. Storage stability of residues in plants

The storage stability of flupyradifurone and DFA has been investigated in the EU pesticides peer review (EFSA, 2015) as well as in the previously issued EFSA reasoned opinion (EFSA, 2020). The freezer storage stability of flupyradifurone and DFA residues is confirmed at –18°C for 52 months in matrices with high water content, high acid content, high oil content, high protein content and high starch content (EFSA, 2020). It was demonstrated that in crops assessed in the framework of this application, residues are stable for at least 52 months when stored at –18°C.

1.1.6. Proposed residue definitions

Based on the metabolic pattern identified in primary and rotational crop metabolism studies, the results of hydrolysis studies, the toxicological significance of metabolites and the capabilities of enforcement analytical methods, the following residue definitions were agreed by the EU pesticides peer review (EFSA, 2015):

- residue definition for risk assessment: sum of flupyradifurone and DFA, expressed as flupyradifurone
- residue definitions for enforcement: 1) flupyradifurone; 2) DFA, expressed as DFA

The same residue definitions are applicable to rotational crops and processed products. The residue definitions set in Regulation (EC) No 396/2005 are identical with the above-mentioned residue definitions for enforcement.

EFSA concludes that these residue definitions are appropriate for the crops under consideration and no further information is required.

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7 According to the EMS, the LOQs in the final addendum to the DAR (Netherlands, 2015) and EFSA conclusion (EFSA, 2015) have been inaccurately reported as the inter laboratory validation experiments the DFA was fortified and analysed as DFA, but expressed as flupyradifurone (Netherlands, 2017). This means that DFA was validated at an LOQ of 0.02 mg/kg in plant matrices and at 0.1 mg/kg in hops, when expressed as flupyradifurone, which would correspond to LOQs of 0.007 mg/kg in plant matrices and 0.03 mg/kg in hops, when expressed as DFA.
1.2. Magnitude of residues in plants

1.2.1. Magnitude of residues in primary crops

Oilseed rape

Intended NEU GAPs:

1) 2 × 37.5 g/ha, interval 14 days, BBCH 65–79, PHI 45 days
2) 2 × 56.25 g/ha, interval 14 days, BBCH 30–49, PHI n.a.
3) 2 × 56.25 g/ha, interval 14 days, BBCH 50–59, PHI n.a.

Intended SEU GAP:

1) 2 × 56.25 g/ha, interval 14 days, BBCH 30–79, PHI 45 days

Mustard

Intended NEU GAP: 2 × 56.25 g/ha, interval 14 days, BBCH 50–59, PHI n.a.

Intended SEU GAP: 2 × 56.25 g/ha, interval 14 days, BBCH 30–79, PHI 45 days

In support of the intended NEU uses, the applicant submitted eight residue trials on oilseed rape, which were conducted in France, Germany and Belgium in 2015 and 2016. Residue trials were designed as decline trials (two/three sampling points at the preharvest intervals (PHIs) of 34–38 days, 42–48 days and 50–54 days) and performed with two applications at a nominal application rate of 56.2 g/ha; the last treatment took place at the BBCH of 73–80.

Residue trials are not fully compliant with any of the intended NEU GAPs reported in the application form. The applicant argues that the GAPs with earlier applications at a higher rate are less critical than the GAP with lower rate but later applications (i.e. GAP with a PHI of 45 days). This is confirmed in residue trials, where at longer PHIs of 50–54 days a decline of residues was observed in all trials, except one. The EMS disagrees with the applicant and concludes that intended NEU GAPs number 2 and 3 are not supported by residue trials.

In order to support the NEU GAP number 1, the EMS proposes and EFSA agrees to apply the proportionality principle to potentially account for residues in oilseed rape at a lower application rate of 37.5 g/ha. From a scaled residue data set, MRL proposals of 0.3 mg/kg for flupyradifurone and of 0.15 mg/kg for DFA are derived.

The applicant proposes that the residue data on rapeseeds are extrapolated to mustard seeds. According to EU Guidance document (European Commission, 2017), such an extrapolation would be acceptable, but the submitted residue trials on oilseed rape do not support the intended NEU GAP on mustard. Thus, the intended NEU GAP on mustard is not supported by residue trials.

In support of the intended SEU use, the applicant submitted in total eight GAP compliant residue trials on oilseed rape. Trials were performed in Spain, Portugal, Italy and France over one growing season of 2016 with two applications at a nominal application rate of 56.2 g/ha. All trials were designed as decline trials, with two/three sampling points 36–40 days, 43–47 days and 49–54 days after the last application; the last treatment took place at the BBCH of 67–80. The applicant proposes that the residue data on rapeseeds are extrapolated to mustard seeds. According to EU Guidance document (European Commission, 2017), such an extrapolation is supported and an MRL of 0.3 mg/kg both for flupyradifurone and DFA is derived on the basis of the intended SEU use of flupyradifurone on oilseed rape and mustard.

The samples of residue trials were stored under conditions for which integrity of the samples has been demonstrated. The samples were analysed for flupyradifurone and difluoroacetic acid (DFA). According to the assessment of the EMS, the methods used were sufficiently validated and fit for purpose (Netherlands, 2019).

1.2.2. Magnitude of residues in rotational crops

Oilseed rape and mustard can be grown in a crop rotation. A wide range of rotational crop field studies were submitted for the EU pesticides peer review and in the framework of the previous EFSA assessments (EFSA, 2015, 2020; Netherlands, 2017). Flupyradifurone was either applied on a bare soil or on a primary crop lettuce at application rates ranging from 125 to 300 g/ha. Studies indicate a significant uptake of metabolite DFA in rotational crops. Consequently, the EU pesticide peer review derived provisional MRLs for difluoroacetic acid in rotational crops (EFSA, 2015). These provisional
MRLs were further assessed by EFSA in the light of rotational crop studies which were submitted by the EMS Netherlands for the assessment of Article 12 confirmatory data and for the setting of MRLs for flupyradifurone and DFA (EFSA, 2020).

Since the total annual application rate in the intended use GAPs on oilseed rape and mustard is significantly lower than the application rates on primary crops for which the residues of DFA in rotational crops were estimated in the previous EFSA assessment (EFSA, 2020), the magnitude of DFA residues in rotational crops was not re-assessed and the conclusions of the previous EFSA opinion are applicable.

1.2.3. Magnitude of residues in processed commodities

Processing studies with rapeseeds and mustard seeds were not submitted in the framework of the current application and are not required considering the low contribution of residues in rapeseeds and mustard seeds to the total consumer exposure. In the previous EFSA output, a wide range of processing studies were assessed, including several oilseeds (soybean, peanut, cotton) and a wide range of processing factors were derived (EFSA, 2020).

1.2.4. Proposed MRLs

The available data are considered sufficient to derive MRL proposals as well as risk assessment values for flupyradifurone and DFA in mustard seeds and rapeseeds on the basis of the intended SEU use. The intended NEU use on mustard is not supported by compliant residue trials, whereas for the critical intended NEU use on oilseed rape, an MRL proposal was derived on the basis of scaled residue data.

When estimating the MRL proposal for DFA, consideration shall be given to possible residues that would occur if oilseed rape and mustard are both 1) treated as primary crop and 2) grown in soil that contains flupyradifurone residues at EU plateau levels. Thus, in order to estimate the MRL for DFA in rapeseeds and mustard seeds, the highest level of DFA expected in the respective rotational crop (oilseed rape) at EU flupyradifurone soil plateau concentrations (0.05 mg/kg; EFSA, 2020) would need to be added to the MRL calculated from the primary crop treatment (0.3 mg/kg). The estimate, when rounded to the next MRL class, would result in an MRL proposal of 0.4 mg/kg for DFA in both oilseeds under consideration. It is noted that the OECD guidance document on rotational crops (OECD, 2018) provides several risk management options for active substances that are likely to lead to residues in rotational crops. One option is the setting of MRLs considering the contribution of residues taken up from the soil. However, risk managers should also discuss the appropriateness of other options described in the OECD guidance document (e.g. plant back restrictions could be imposed to avoid or limit residues in succeeding crops).

The appropriateness of the calculated MRL proposals with regard to consumer health risks is assessed in Section 3.

2. Residues in livestock

Rapeseed meal can be fed to livestock and therefore the possible carry-over of flupyradifurone and DFA residues in commodities of animal origin would need to be assessed. The applicant has reported that the intended use pattern is not intended for harvesting forage as feed item (Netherlands, 2019).

The previous EU livestock dietary burden calculation for the intake of flupyradifurone and DFA residues from imported feed and the EU feed items (EFSA, 2020) was updated with residue values for rapeseed meal from the new intended uses. When considering the livestock exposure to DFA residues, also the intake of this metabolite via rotational crops has been considered.

The livestock exposure was calculated separately for flupyradifurone and the DFA according to the OECD methodology using the EFSA Animal model 2017 (OECD, 2013). For rapeseeds, the input values were as derived from the residue trials under consideration. For remaining feed items, the input values were as reported in Appendix D.1. in the previous EFSA assessment (EFSA, 2020).

The results of the dietary burden calculations, which are presented in Appendix B, Section B.2, indicated significant exposure to residues of flupyradifurone and DFA, exceeding the trigger value of...
0.004 mg/kg bw per day for all livestock species. Since the contribution of flupyradifurone and DFA residues in rapeseed meal to the total EU livestock dietary burden is insignificant, the magnitude of residues in animal commodities was not further assessed.

EFSA concludes that the residues in rapeseeds from the intended uses will not affect the residues in animal commodities as estimated in the previous EFSA assessment.

3. Consumer risk assessment

The consumer risk assessment was performed with revision 3.1 of the EFSA Pesticide Residues Intake Model (PRIMo). This exposure assessment model contains the relevant European food consumption data for different subgroups of the EU population (EFSA, 2018, 2019).

The toxicological reference values for flupyradifurone used in the risk assessment (i.e. ADI of 0.064 mg/kg bw per day and ARfD of 0.15 mg/kg bw) were derived in the framework of the EU pesticides peer review (European Commission, 2015). The peer review also assessed toxicological studies submitted for metabolite DFA and concluded that the reference values of parent are applicable to DFA (EFSA, 2015). The residue definition for risk assessment refers to the sum of flupyradifurone and DFA, expressed as flupyradifurone.

The previous consumer exposure assessment performed in the EFSA opinion on the modification of MRLs for flupyradifurone and DFA (EFSA, 2020) was updated with risk assessment values for rapeseeds and mustard seeds as derived from the submitted residue trials.

EFSA performed two separate consumer exposure calculations in order to estimate the exposure from primary crops (including also animal products) and rotational crops, to provide risk managers additional information to decide on risk management options as regards residues in rotational crops, e.g. whether MRLs should be established to cover residues in rotational crops or whether other restrictions would be appropriate to avoid residues in untreated crops. The calculated exposures were then compared with the toxicological reference values as derived for flupyradifurone.

Scenario 1: Exposure to residues from treated primary plant commodities and from the intake of animal commodities

In order to estimate chronic and acute consumer exposure to residues of flupyradifurone and DFA, the STMR values as derived for rapeseeds and mustard seeds from the submitted residue trials (Table B.1.2.1) were used as input values. For the remaining plant and animal commodities, the input values were as reported in the previous EFSA assessment (EFSA, 2020). For those commodities on which no uses of flupyradifurone are authorised in EU, no input values were used in the consumer exposure calculation.

The calculated chronic exposure accounted for a maximum of 54% of the ADI (NL toddler diet). The contribution of residues in rapeseeds and mustard seeds to the total consumer exposure was low: 0.34% of the ADI (NL toddler) for rapeseeds and 0.01% of the ADI (GEMS/Food G11 diet) for mustard seeds.

No acute consumer intake concerns were identified for flupyradifurone residues in rapeseeds and mustard seeds (individually 0.2% of the ARfD).

Scenario 2: Exposure to residues of DFA (and of flupyradifurone on lettuce and barley) from the intake of plant commodities that are grown as rotational crops (no primary treatment)

The exposure assessment as calculated in the previous EFSA output (EFSA, 2020) was not updated, since the uptake of DFA (and flupyradifurone) residues in untreated rotational crops was estimated from more critical flupyradifurone EU uses than the intended uses under consideration. The same conclusions are therefore applicable. The consumer exposure from the chronic intake of DFA residues taken up by crops from the soil which was previously treated with flupyradifurone accounted for up to 17% of the ADI (GEMS/Food G06 diet).

The contribution of residues in untreated rapeseeds and mustard seeds from the soil uptake of residues to the acute consumer exposure was individually below 0.1% of the ARfD.

An overview of input values for consumer exposure assessment is provided in Appendix D.2. For further details on the exposure calculations, screenshots of the Report sheets of the PRIMo are presented in Appendix C.

The combined chronic exposure to flupyradifurone and DFA residues from the intake of food commodities following primary crop treatments, from the intake of animal commodities and from the intake of food commodities containing residues due to the uptake via soil accounts for a maximum of 69% of the ADI (NL toddler diet). No acute consumer intake concerns were identified for a combined
acute exposure to flupyradifurone and DFA residues from the intake of rapeseeds and mustard seeds treated as primary crops and when grown in a crop rotation.

4. Conclusion and Recommendations

The data submitted in support of this MRL application were found to be sufficient to derive an MRL proposal for flupyradifurone and DFA in rapeseeds/canola seeds and mustard seeds on the basis of the intended EU uses.

EFSA concluded that the proposed uses of flupyradifurone on oilseed rape and mustard will not result in a consumer exposure exceeding the toxicological reference values and therefore is unlikely to pose a risk to consumers’ health. EFSA concluded that the short-term and long-term intake of residues of flupyradifurone and of its metabolite DFA resulting from the use of flupyradifurone is unlikely to present a risk to consumer health.

The MRL recommendations are summarised in Appendix B.4.

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Abbreviations

| Abbreviation | Description |
|--------------|-------------|
| a.s. | active substance |
| ADI | acceptable daily intake |
| ARFD | acute reference dose |
| BBCH | growth stages of mono- and dicotyledonous plants |
| bw | body weight |
| CAS | Chemical Abstract Service |
| CF | conversion factor for enforcement to risk assessment residue definition |
| Acronym | Full Form |
|---------|-----------|
| CS      | capsule suspension |
| CV      | coefficient of variation (relative standard deviation) |
| DALA    | days after last application |
| DAR     | draft assessment report |
| DAT     | days after treatment |
| DM      | dry matter |
| DP      | dustable powder |
| DS      | powder for dry seed treatment |
| EC      | emulsifiable concentrate |
| EDI     | estimated daily intake |
| EMS     | evaluating Member State |
| GAP     | Good Agricultural Practice |
| GS      | growth stage |
| HPLC    | high-performance liquid chromatography |
| HPLC-MS | high-performance liquid chromatography with mass spectrometry |
| HPLC-MS/MS | high-performance liquid chromatography with tandem mass spectrometry |
| HR      | highest residue |
| ISO     | International Organisation for Standardisation |
| IUPAC   | International Union of Pure and Applied Chemistry |
| LC      | liquid chromatography |
| LOQ     | limit of quantification |
| MRL     | maximum residue level |
| MS      | Member States |
| MS      | mass spectrometry detector |
| MS/MS   | tandem mass spectrometry detector |
| MW      | molecular weight |
| NEU     | northern Europe |
| OECD    | Organisation for Economic Co-operation and Development |
| PBI     | plant back interval |
| PF      | processing factor |
| PHI     | preharvest interval |
| RA      | risk assessment |
| RD      | residue definition |
| RMS     | rapporteur Member State |
| SC      | suspension concentrate |
| SL      | soluble concentrate |
| SP      | water-soluble powder |
| STMR    | supervised trials median residue |
| TAR     | total applied radioactivity |
| TRR     | total radioactive residue |
| WHO     | World Health Organization |
| Crop and/or situation | NEU, SEU, MS or country | Preparation | Type | Conc. a.s. | Method kind | Range of growth stages & season | Number min-max | Interval between application (min) | g a.s./L min-max | Water L/ha min-max | Rate | Unit | PHI (days) | Remarks |
|-----------------------|-------------------------|-------------|------|------------|-------------|-------------------------------|----------------|----------------------------------|----------------|-----------------|-------|-------|-----------|---------|
| Oilseed rape NEU (CZ, HU, LV, NL, PL, RO, SK, SL) | NEU (CZ, HU, LV, NL, PL, RO, SK, SL) | EC 85 | Foliar treatment – broadcast spraying | 30-49 | 2 | 14 | 9.375-28.125 | 200-600 | 56.25 | g a.s./ha | n.a. |
| Oilseed rape NEU (LV, PL, RO) | NEU (LV, PL, RO) | EC 85 | Foliar treatment – broadcast spraying | 50-59 | 2 | 14 | 9.375-28.125 | 200-600 | 56.25 | g a.s./ha | n.a. |
| Oilseed rape NEU (CZ, HU, LV, NL, PL, RO, SK, SL) | NEU (CZ, HU, LV, NL, PL, RO, SK, SL) | EC 85 | Foliar treatment – broadcast spraying | 65-79 | 2 | 14 | 6.25-18.75 | 200-600 | 37.5 | g a.s./ha | 45 | Identified as critical NEU GAP |
| Oilseed rape SEU (BG, ES, HR) | SEU (BG, ES, HR) | EC 85 | Foliar treatment – broadcast spraying | 30-79 | 2 | 14 | 9.375-28.125 | 200-600 | 56.25 | g a.s./ha | 45 |
| Mustard NEU (LV, PL, RO) | Mustard NEU (LV, PL, RO) | EC 85 | Foliar treatment – broadcast spraying | 50-59 | 2 | 14 | 9.375-28.125 | 200-600 | 56.25 | g a.s./ha | n.a. |
| Mustard SEU (BG, ES, HR) | Mustard SEU (BG, ES, HR) | EC 85 | Foliar treatment – broadcast spraying | 30-79 | 2 | 14 | 9.375-28.125 | 200-600 | 56.25 | g a.s./ha | 45 |

MRL: maximum residue level; GAP: Good Agricultural Practice; NEU: northern European Union; SEU: southern European Union; MS: Member State; a.s.: active substance; EC: emulsifiable concentrate.
(a): Outdoor or field use (F), greenhouse application (G) or indoor application (I).
(b): CropLife International Technical Monograph no 2, 7th Edition. Revised March 2017. Catalogue of pesticide formulation types and international coding system.
(c): Growth stage range from first to last treatment (BBCH Monograph, Growth Stages of Plants, 1997, Blackwell, ISBN 3-8263-3152-4), including, where relevant, information on season at time of application.
(d): PHI – minimum preharvest interval.
**Appendix B – List of end points**

**B.1. Residues in plants**

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

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

| Primary crops (available studies) | Crop groups | Crop(s) | Application(s) | Sampling | Comment/Source |
|-----------------------------------|-------------|---------|----------------|----------|----------------|
| Fruit crops                       | Apple       | Foliar  | a) 1 × 86 g/ha meter canopy height (CH); BBCH 69 b) 2 × 86 g/ha/m CH; BBCH 69 | a) 89 DAT b) 14 DALA | Radiolabelled active substance: [furanone-4-14C] -, [pyridinylmethyl-14C] flupyradifurone (Netherlands, 2014; EFSA, 2015) |
|                                  | Tomato      | Soil drench, 2 × 300 g/ha, BBCH 14-15 and 51-59, interval 14 days | 56-92 DALA | Radiolabelled active substance: [furanone-4-14C], [pyridinylmethyl-14C] and [ethyl-1-14C] flupyradifurone (Netherlands, 2014; EFSA, 2015) |
| Root crops                       | Potato      | In furrow, 1 × 626 g/ha, BBCH 03 | 97 DAT | Radiolabelled active substance: [furanone-4-14C] and [pyridinylmethyl-14C] flupyradifurone (Netherlands, 2014; EFSA, 2015) |
|                                  |             | Seed treatment, 1 × 254 g/ha, BBCH 03 | 97 DAT | |
| Cereals/ grass                    | Rice        | Foliar  | 175 g/ha, BBCH 13-15 + 240 g/ha, BBCH 87-89 | 29 DALA | Radiolabelled active substance: [furanone-4-14C] and [pyridinylmethyl-14C] flupyradifurone (Netherlands, 2014; EFSA, 2015) |
|                                  |             | Soil (granules) at planting, 1 × 409-434 g/ha, BBCH 13-15 | 127 DALA | Radiolabelled active substance: [furanone-4-14C] and [pyridinylmethyl-14C] flupyradifurone (Netherlands, 2014; EFSA, 2015) |
| Pulses/oilseeds                  | Cotton      | Foliar  | a) 1 × 210 g/ha, BBCH 15-18 b) 210 g/ha, BBCH 15-18 + 175 g/ha, BBCH 95-97 | a) 169 DAT b) 14-15 DALA | Radiolabelled active substance: [furanone-4-14C] and [pyridinylmethyl-14C] flupyradifurone (Netherlands, 2014; EFSA, 2015) |
| Rotational crops (available studies) | Crop groups | Crop(s) | Application(s) | PBI (DAT) | Comment/Source |
| Root/tuber crops                 | Turnips     | Soil, 436 g/ha | 29, 135 and 296 | Radiolabelled active substance: [furanone-4-14C] and [pyridinylmethyl-14C] flupyradifurone (Netherlands, 2014; EFSA, 2015) |
| Leafy crops                      | Swiss chard |             |               |         |               |
| Cereal (small grain)             | Wheat       |             |               |         |               |

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### Processed commodities (hydrolysis study)

| Conditions | Stable? | Comment/Source |
|------------|---------|----------------|
| Pasteurisation (20 min, 90°C, pH 4) | Flupyradifurone: yes DFA: not investigated | EFSA (2015) |
| Baking, brewing and boiling (60 min, 100°C, pH 5) | Flupyradifurone: yes DFA: not investigated | EFSA (2015) |
| Sterilisation (20 min, 120°C, pH 6) | Flupyradifurone: yes DFA: not investigated | EFSA (2015) |

| Other processing conditions | – | – |

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### Can a general residue definition be proposed for primary crops?

- Yes  EFSA (2015)

### Rotational crop and primary crop metabolism similar?

- Yes  EFSA (2015)

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

- Yes  EFSA (2015)

### Plant residue definition for monitoring (RD-Mo)

Two separate residue definitions (EFSA, 2015):

1. Flupyradifurone
2. Difluoroacetic acid (DFA), expressed as DFA

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

Sum of flupyradifurone and DFA, expressed as flupyradifurone (EFSA, 2015)

- Flupyradifurone. Matrices with high water content (lettuce), high starch content (wheat, potato), high acid content (oranges), high oil content (rapeseeds): HPLC-MS/MS, LOQ 0.01 mg/kg. Hops: 0.05 mg/kg.
- DFA*. Matrices with high water content (lettuce), high starch content (wheat, potatoes), high acid content (oranges), high oil content (rapeseeds): HPLC-MS/MS, LOQ 0.007 mg/kg. Hops: 0.03 mg/kg.

* According to the Evaluation report from the Netherlands (2017), the LOQs in the final addendum to the DAR (Netherlands, 2015) and EFSA conclusion (EFSA, 2015) have been inaccurately reported since in the validation experiments the DFA was fortified and analysed as DFA, but expressed as flupyradifurone (Netherlands, 2017). This means that DFA was validated at an LOQ of 0.02 mg/kg in plant matrices and at 0.1 mg/kg in hops, when expressed as flupyradifurone, which would correspond to LOQs of 0.007 mg/kg in plant matrices and 0.03 mg/kg in hops, when expressed as DFA.

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DAT: days after treatment; DALA: days after last application; BBCH: growth stages of mono- and dicotyledonous plants; PBI: plant-back interval; HPLC–MS/MS: high performance liquid chromatography with tandem mass spectrometry; LOQ: limit of quantification.
## 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                | Spinach, sugar cane, tomato | –18                 | 52     | Months                 |      | Flupyradifurone, DFA             | EFSA (2020)    |
| High oil content                  | Soybean seed              | –18                 | 52     | Months                 |      | Flupyradifurone, DFA             |                |
| High protein content              | Bean seed                 | –18                 | 52     | Months                 |      | Flupyradifurone, DFA             |                |
| Dry/High starch                   | Wheat grain               | –18                 | 52     | Months                 |      | Flupyradifurone, DFA             |                |
| High acid content                 | Oranges                   | –18                 | 52     | Months                 |      | Flupyradifurone, DFA             |                |
| Other                             | Coffee bean               | –18                 | 52     | Months                 |      | Flupyradifurone, DFA             |                |
## B.1.2. Magnitude of residues in plants

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

| Commodity          | Region/indoor<sup>(a)</sup>                                                                 | Residue levels observed in the supervised residue trials (mg/kg) | Comments/Source                                                                 | Calculated MRL (mg/kg) | HR<sup>(b)</sup> (mg/kg) | STMR<sup>(c)</sup> (mg/kg) |
|--------------------|-----------------------------------------------------------------------------------------------|------------------------------------------------------------------|---------------------------------------------------------------------------------|------------------------|-------------------------|--------------------------|
| **Enforcement residue definition (Mo):** 1) Flupyradifurone (F); 2) Difluoroacetic acid (DFA), expressed as DFA  
**Risk assessment residue definition (RA):** Sum of flupyradifurone and DFA, expressed as flupyradifurone |
| Rapeseeds          | NEU (Intended use GAP: 2 × 37.5 g/ha, interval 14 days, BBCH 65–79, PHI 45 days)             | Unscaled trials (2 × 56.25 g/ha, BBCH of 73–80, PHI 45 days)     | Residue trials on oilseed rape scaled by a scaling factor of 0.667 to the application rate of 37.5 g/ha in order to comply with the critical GAP  |
|                    | ***Mo***: 1) 2 × 0.066; 0.088; 0.12; 0.13; 2 × 0.15; 0.21  
|                    | **RA**: 2 × 0.25; 2 × 0.27; 0.31; 2 × 0.35; 0.50  
|                    | Scaled:                                                                                   |                                                                  |                                                                                  | 1) 0.3                  | Mo: F: 0.14             | Mo: F: 0.08               |
|                    | ***Mo***: 2) 0.04; 0.048; 0.063; 2 × 0.068; 0.075; 0.075<sup>(e)</sup>; 0.095  
|                    | **RA**: 2 × 0.17; 2 × 0.18; 0.21; 2 × 0.23; 0.33                                        |                                                                  |                                                                                  | 2) 0.15                | RA: 0.33                | RA: 0.19                |
|                    | NEU (Intended use GAP: 2 × 56.25 g/ha, interval 14 days, BBCH 30–49, PHI n.a.)           | No residue trials submitted.                                     |                                                                                  | --                     | --                      | --                       |
|                    | NEU (Intended use GAP: 2 × 56.25 g/ha, interval 14 days, BBCH 50–59, PHI n.a.)         | No residue trials submitted.                                     |                                                                                  | --                     | --                      | --                       |
| Mustard seeds      | NEU (Intended use GAP: 2 × 56.25 g/ha, interval 14 days, BBCH 50–59; PHI n.a.)          | No residue trials submitted.                                     |                                                                                  | --                     | --                      | --                       |
| 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) |
|---------------|--------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------|------------------------|----------------------|------------------------|
| Rapeseeds    | SEU (Intended use GAP: 2 × 56.25 g/ha, interval 14 days, BBCH 30–79, PHI 45 days)           | Mo: 1) 0.024; 0.036; 0.058; 0.066; 2 × 0.11; 0.13; 0.16\(^{(d)}\)  
2) 0.015; 0.033 0.05\(^{(e)}\); 0.057; 0.063; 0.06; 0.088; 0.16\(^{(d)}\)  
RA: 0.069; 0.21; 2 × 0.22; 0.28; 0.30; 0.32; 0.63\(^{(d)}\) | Residue trials on oilseed rape compliant with the SEU GAP  
Residue data extrapolation to mustard seeds possible. | 1) 0.3  
2) 0.3 | Mo: F: 0.16  
DFA: 0.16 | RA: 0.63 |

**MRL:** maximum residue level; **GAP:** Good Agricultural Practice; **BBCH:** growth stages of mono- and dicotyledonous plants; **Mo:** monitoring; **RA:** risk assessment; **PHI:** preharvest interval; **n.a.:** not applicable.

\(^{(a)}\): 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.

\(^{(b)}\): HR: Highest residue. The highest residue for risk assessment refers to the whole commodity and not to the edible portion.

\(^{(c)}\): STMR: Supervised trials median residue. The median residue for risk assessment refers to the whole commodity and not to the edible portion.

\(^{(d)}\): Residue trial value higher at a longer PHI of 49 days.

\(^{(e)}\): Residue trial value higher at a longer PHI of 52 days.
B.1.2.2. Residues in rotational crops

| Residues in rotational and succeeding crops expected based on confined rotational crop study? | Yes | EFSA (2015) |
|---|---|---|
| Yes, of the metabolite DFA | Field rotational crop studies in NEU/SEU at 200 g/ha on bare soil (25–30 days PBI) or on lettuce as primary crop (61–145 and 266–329 days PBI) indicate residues of flupyradifurone in edible matrices at ≤ 0.01 mg/kg, except in lettuce head (0.03 mg/kg (one sample)) and in barley straw (two samples 0.02 and 0.04 mg/kg). Metabolite DFA was present at significant levels, requiring setting of MRLs for this compound in rotational crops (EFSA, 2015).

Field rotational crop studies, performed at 300 g/ha on bare soil (21–30, 107–204 and 273–365 days PBI) or at 175–185 g/ha on bare soil (107–204 and 273–365 days PBI) (EFSA, 2020; Netherlands, 2017). Residues of flupyradifurone were < LOQ of 0.01 mg/kg in all crops at all plant back intervals, except in one sample of barley grain (0.01 mg/kg, second rotation) and in barley straw (0.02 and 0.03 mg/kg second rotation and 0.02 mg/kg third rotation). Residues of DFA (expressed as DFA, mg/kg) were as follows:

**21–30 days PBI**
- Strawberry: mature: < 0.007; 0.07; 0.1; 0.12
- immature: 0.056; 0.08; 0.009; 0.08
- Cauliflower/broccoli: mature: 2 x 0.02; 0.05; 0.07
- immature: 0.025; 0.059; 0.042; 0.056

**107–204 days PBI**
- Potato: mature: 0.01; 0.02; 0.03; 0.07
- immature: 0.012; 0.042; 0.088; 0.016
- Strawberry: mature: 0.01; 0.05; 0.06; 0.12
- immature: < 0.007; 0.04; 0.07; 0.12
- Cauliflower/broccoli: mature: 0.01; 0.035; 0.04; 0.06
- immature: 0.015; 0.048; 0.029; 0.06
- Barley grain: 0.04; 0.05; 0.09; 0.12
- Barley straw: 3 x < 0.03; 0.04
- Rapeseeds: 0.009; 0.01; 0.02
- Maize grain: < 0.007; 0.02; 0.035; 0.04

**273–365 days PBI**
- Potato: mature: < 0.007; 2 x 0.01; 0.015
- immature: < 0.007; 0.011; 0.018; 0.019
- Strawberry: mature: 2 x < 0.007; 0.02; 0.08
- immature: < 0.007; 0.017; 0.024; 0.026
- Cauliflower/broccoli: mature: 0.008; 0.015; 0.02; 0.03
- immature: 0.007; 0.041; 0.016; 0.018
- Barley grain: 0.03; 0.04; 0.06; 0.09
- Barley straw: 4 x < 0.03
- Rapeseeds: 2 x 0.007; 0.013
- Maize grain: < 0.007; 0.01; 0.02; 0.03

LOQ: limit of quantification; NEU: northern European Union; SEU: southern European Union; PBI: plant-back interval; DFA: difluoroacetic acid; MRL: maximum residue level.

B.1.2.3. Processing factors

No processing studies were submitted in the framework of the present MRL application.
B.2. Residues in livestock

Dietary burden calculation according to OECD, 2013.
Calculations performed with Animal model 2017.9

- Flupyradifurone

| Relevant groups | Dietary burden expressed in | Most critical diet(a) | Most critical commodity(b) | Trigger exceeded (Yes/No) | Previous assessment (EFSA, 2020) |
|-----------------|-----------------------------|------------------------|---------------------------|--------------------------|---------------------------------|
|                 | mg/kg bw per day, mg/kg DM  |                        |                           |                          |                                 |
|                 | Median                       | Maximum                | Median                    | Maximum                  |                                 |
| Cattle (all diets) | 0.063                        | 0.170                  | 1.78                      | 5.60                     |                                 |
| Dairy cattle    |                              |                        | Kale                      | Leaves                   | Y                               |
| Sheep (ewes only) | 0.045                        | 0.155                  | 1.36                      | 3.86                     | Y                               |
| Swine (all diets) | 0.028                        | 0.097                  | 1.21                      | 4.22                     | Y                               |
| Poultry (all diets) | 0.037                        | 0.078                  | 0.52                      | 1.10                     | Y                               |

bw: body weight; DM: dry matter.
(a): When several diets are relevant (e.g. cattle, sheep and poultry ‘all diets’), the most critical diet is identified from the maximum dietary burdens expressed as ‘mg/kg bw per day’.
(b): The most critical commodity is the major contributor identified from the maximum dietary burden expressed as ‘mg/kg bw per day’.

- Difluoroacetic acid (DFA), expressed as DFA

| Relevant groups | Dietary burden expressed in | Most critical diet(a) | Most critical commodity(b) | Trigger exceeded (Yes/No) | Previous assessment (EFSA, 2020) |
|-----------------|-----------------------------|------------------------|---------------------------|--------------------------|---------------------------------|
|                 | mg/kg bw per day, mg/kg DM  |                        |                           |                          |                                 |
|                 | Median                       | Maximum                | Median                    | Maximum                  |                                 |
| Cattle (all diets) | 0.038                        | 0.057                  | 1.14                      | 1.99                     | Y                               |
| Dairy cattle    |                              |                        | Swede                     | Roots                    | Y                               |
| Sheep (all diets) | 0.039                        | 0.065                  | 0.99                      | 1.60                     | Y                               |
| Lamb            |                              |                        | Swede                     | Roots                    | Y                               |

9 https://ec.europa.eu/food/plant/pesticides/max_residue_levels/guidelines_en
| Relevant groups                  | Dietary burden expressed in | Most critical diet (a) | Most critical commodity (b) | Trigger exceeded (Yes/No) | Previous assessment (EFSA, 2020) |
|--------------------------------|-----------------------------|------------------------|----------------------------|----------------------------|---------------------------------|
|                                | Median | Maximum | Median | Maximum | mg/kg bw per day | mg/kg DM |                       |                             |                                 |
| Sheep (ewe only)               | 0.033  | 0.053   | 0.99   | 1.60    | Ram/Ewe         | Swede    | Roots                   | Y                            | 0.053                          |
| Swine (all diets)              | 0.022  | 0.044   | 0.87   | 1.66    | Swine (finishing) | Swede    | Roots                   | Y                            | 0.044                          |
| Poultry (all diets)            | 0.036  | 0.050   | 0.53   | 0.73    | Poultry layer   | Swede    | Roots                   | Y                            | 0.050                          |
| Poultry (layer only)           | 0.036  | 0.050   | 0.53   | 0.73    | Poultry layer   | Swede    | Roots                   | Y                            | 0.050                          |

bw: body weight; DM: dry matter.
(a): When several diets are relevant (e.g. cattle, sheep and poultry ‘all diets’), the most critical diet is identified from the maximum dietary burdens expressed as ‘mg/kg bw per day’.
(b): The most critical commodity is the major contributor identified from the maximum dietary burden expressed as ‘mg/kg bw per day’.
B.3. Consumer risk assessment

Residue definition for risk assessment: Sum of flupyradifurone and DFA, expressed as flupyradifurone

### ARfD

- **Highest IESTI, according to EFSA PRIMo**
  - **Scenario 1)** Exposure from residues in treated primary plant commodities and animal commodities
    - Contribution of crops assessed:
      - Rapeseeds: 0.2% of the ARfD
      - Mustard seeds: 0.2% of the ARfD
  - **Scenario 2)** Exposure from residues in rotational crops (no primary treatment)
    - Contribution of crops assessed:
      - Rapeseeds: 0.08% of the ARfD
      - Mustard seeds: 0.06% of the ARfD
  - Combined acute exposure:
    - Rapeseeds: 0.28% of the ARfD
    - Mustard seeds: 0.26% of the ARfD

### Assumptions made for the calculations

- The exposure assessment was performed only for residues in rapeseeds and mustard seeds.
- In scenario 1, the input value was the STMR value as derived from the residue trials.
- The input values in scenario 2 were as reported in the EFSA recent output (EFSA, 2020) and estimated in untreated oilseed grown in a crop rotation.
- Calculations performed with PRIMo revision 3.1

### ADI

- **Highest IEDI, according to EFSA PRIMo**
  - **Scenario 1)** Exposure from residues in animal commodities and treated primary plant commodities (expressed as % of ADI):
    - 54% NL toddler diet
    - Maximum contribution of the commodities assessed:
      - Rapeseeds: 0.34% of the ADI (NL toddler)
      - Mustard seeds: 0.01% of the ADI (GEMS/Food G11 diet).
  - **Scenario 2)** Exposure from residues in rotational crops (no treatment) (expressed as % of ADI):
    - 17% GEMS G06 diet
    - 15% NL toddler diet
    - Maximum contribution of the commodities assessed:
      - Rapeseeds: 0.13% of the ADI (NL toddler)
      - Mustard seeds: 0.002% of the ADI (GEMS/Food G11 diet).
  - **Combined chronic exposure:**
    - 69% NL toddler diet
Assumptions made for the calculations

Scenario 1: The calculation is based on the median residue levels expected in crop from primary treatment only. For rapeseeds and mustard seeds, the input values were the STMR as derived from the submitted residue trials. For remaining commodities of plant and animal origin the input values were as reported in the previous EFSA assessment (EFSA, 2020). For those commodities on which no uses of flupyradifurone are authorised in EU, no input values were used in the consumer exposure calculation.

Scenario 2: The calculation is based on DFA and flupyradifurone residues (STMR) taken up via roots by annual crops grown in soil containing residues at the soil plateau concentrations. The perennial crops and animal commodities were excluded from the exposure calculation. For rapeseeds and mustard seeds, the input value was as reported in the previous EFSA assessment for untreated oilseeds that was grown in a crop rotation; for remaining commodities, the input values were as reported in the previous EFSA assessment (EFSA, 2020).

Combined long-term exposure assessment was calculated by summing up exposure for individual diets from residues in primary crop and from residues in rotational crop (sum of scenario 1 and scenario 2).

All calculations were performed with PRIMo rev. 3.1

ARfD: acute reference dose; bw: body weight; IESTI: international estimated short-term intake; PRIMo: pesticide residue intake model; STMR: supervised trials median residue; ADI: acceptable daily intake; IEDI: international estimated daily intake; STMR: supervised trials median residue; GEMS/Food Global Environment Monitoring System – Food Contamination Monitoring and Assessment Programme.

B.4. Recommended MRLs

| Code(a) | Commodity                  | Existing EU MRL (mg/kg) | Proposed EU MRL (mg/kg) | Comment/justification                                                                 |
|--------|----------------------------|-------------------------|-------------------------|--------------------------------------------------------------------------------------|
| 0401060| Rapeseeds/canola seeds     | 0.01*                   | 0.3                     | The submitted data are sufficient to derive an MRL proposal for the intended NEU and SEU uses. Risk for consumers unlikely |
| 0404080| Mustard seeds              | 0.01*                   | 0.3                     | The MRL proposal reflects the SEU use. For the NEU use, the data were not sufficient to derive an MRL proposal. Risk for consumers unlikely |

| Enforcement residue definition (2): Difluoroacetic acid (DFA) |
|---------------------------------------------------------------|
| Code(a) | Commodity                  | Existing EU MRL (mg/kg) | Proposed EU MRL (mg/kg) | Comment/justification                                                                 |
|--------|----------------------------|-------------------------|-------------------------|--------------------------------------------------------------------------------------|
| 0401060| Rapeseeds/canola seeds     | 0.05 (ft.1)             | 0.3                     | The MRL proposal does not account for residues which may be taken up by crops from soil which was previously treated with flupyradifurone, which may be expected to contribute up to 0.05 mg/kg in oilseeds grown in soil at the calculated EU soil plateau concentration for flupyradifurone residues. The resulting MRL proposal would be 0.4 mg/kg. Further risk management discussions are therefore recommended on whether MRLs should be established to cover residues in rotational crops or whether other risk management options (e.g. plant back restrictions) would be appropriate to avoid DFA residues in untreated crops |
| 0404080| Mustard seeds              | 0.05 (ft.1)             | 0.3                     |                                                                                      |

*: Indicates that the MRL is set at the limit of analytical quantification (LOQ).  
(a): Commodity code number according to Annex I of Regulation (EC) No 396/2005.  
ft.1: The European Food Safety Authority identified some information on rotational crops 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 6 April 2018, or, if that information is not submitted by that date, the lack of it. The confirmatory data were sufficiently addressed in the recent EFSA assessment proposing the deletion of the footnote (EFSA, 2020).
## Appendix C – Pesticide Residue Intake Model (PRIMo)

### Scenario 1

**LOQs (mg/kg) range from:**
- 0.01 to: 0.05

**ADI (mg/kg bw per day):**
- 0.064

**ARfD (mg/kg bw):**
- 0.15

**Source of ADI:**
- EC

**Source of ARfD:**
- EC

**EFSA PRIMo revision 3.1; 2018/08/18**

**Year of evaluation:**
- 2015

#### No of diets exceeding the ADI:
---

#### Calculated exposure (% of ADI)

| Commodity/group of commodities | Exposure (% of ADI) | Highest contributor to MS diet (% of ADI) | 2nd contributor to MS diet (% of ADI) | 3rd contributor to MS diet (% of ADI) |
|-------------------------------|--------------------|------------------------------------------|--------------------------------------|--------------------------------------|
| Wheat                         | 54% 34.34         | 5%                                        | 4%                                    | Wheat 0.3% 53%                        |
| Bovine: Muscle/meat           | 30% 19.32         | 3%                                        | 5%                                    | Bovine: Muscle/meat 0.1% 30%         |
| Apples                        | 27% 17.42         | 21%                                       | 4%                                    | Apples 0.2% 27%                      |
| Wheat                         | 27% 17.42         | 10%                                       | 4%                                    | Wheat 0.2% 27%                       |
| Wheat                         | 26% 16.86         | 16%                                       | 3%                                    | Bovine: Muscle/meat 0.1% 26%         |
| Wheat                         | 25% 15.74         | 15%                                       | 4%                                    | Bovine: Muscle/meat 0.1% 25%         |
| Wheat                         | 23% 14.18         | 14%                                       | 4%                                    | Bovine: Muscle/meat 0.1% 23%         |
| Wheat                         | 21% 12.94         | 12%                                       | 4%                                    | Bovine: Muscle/meat 0.1% 21%         |
| Wheat                         | 21% 12.94         | 12%                                       | 4%                                    | Bovine: Muscle/meat 0.1% 21%         |
| Wheat                         | 20% 11.88         | 11%                                       | 4%                                    | Bovine: Muscle/meat 0.1% 20%         |
| Wheat                         | 20% 11.88         | 11%                                       | 4%                                    | Bovine: Muscle/meat 0.1% 20%         |
| Wheat                         | 20% 11.88         | 11%                                       | 4%                                    | Bovine: Muscle/meat 0.1% 20%         |
| Wheat                         | 20% 11.88         | 11%                                       | 4%                                    | Bovine: Muscle/meat 0.1% 20%         |
| Wheat                         | 20% 11.88         | 11%                                       | 4%                                    | Bovine: Muscle/meat 0.1% 20%         |
| Wheat                         | 20% 11.88         | 11%                                       | 4%                                    | Bovine: Muscle/meat 0.1% 20%         |
| Wheat                         | 20% 11.88         | 11%                                       | 4%                                    | Bovine: Muscle/meat 0.1% 20%         |

#### Chronic risk assessment: JMPR methodology (RED/MDG)

| Commodity/group of commodities | Calculated exposure (% of ADI) | Exposure resulting from | Exposure resulting from |
|-------------------------------|--------------------------------|-------------------------|-------------------------|
| Wheat                         | 54% 34.34         | 54%                     | 54%                     |
| Bovine: Muscle/meat           | 30% 19.32         | 30%                     | 30%                     |
| Apples                        | 27% 17.42         | 27%                     | 27%                     |
| Wheat                         | 27% 17.42         | 27%                     | 27%                     |
| Wheat                         | 26% 16.86         | 26%                     | 26%                     |
| Wheat                         | 25% 15.74         | 25%                     | 25%                     |
| Wheat                         | 23% 14.18         | 23%                     | 23%                     |
| Wheat                         | 21% 12.94         | 21%                     | 21%                     |
| Wheat                         | 21% 12.94         | 21%                     | 21%                     |
| Wheat                         | 20% 11.88         | 20%                     | 20%                     |
| Wheat                         | 20% 11.88         | 20%                     | 20%                     |
| Wheat                         | 20% 11.88         | 20%                     | 20%                     |
| Wheat                         | 20% 11.88         | 20%                     | 20%                     |
| Wheat                         | 20% 11.88         | 20%                     | 20%                     |
The acute risk assessment is based on the ARfD. The calculation is based on the large portion of the most critical consumer group.

### Results for children

| Commodities                  | MRL/ADI (mg/kg) | Exposure (µg/kg bw) | Highest % of ARfD/ADI | Commodities                  | MRL/ADI (mg/kg) | Exposure (µg/kg bw) | Highest % of ARfD/ADI |
|------------------------------|-----------------|---------------------|-----------------------|------------------------------|-----------------|---------------------|-----------------------|
| 0.2% Rapeseeds/canola seeds  | 0.3/0.23        | 0.32                | 0.2%                  | Rapeseeds/canola seeds       | 0.3/0.23        | 0.32                | 0.1%                  |
| 0.2% Mustard seeds           | 0.3/0.23        | 0.23                | 0.1%                  | Sorghum                      | 0.01/0.64       | 0.19                | 0.1%                  |

Total number of commodities exceeding the ARfD/ADI in children and adult diets (IESTI calculation): 2

### Results for adults

| Commodities                  | MRL/ADI (mg/kg) | Exposure (µg/kg bw) | Highest % of ARfD/ADI | Commodities                  | MRL/ADI (mg/kg) | Exposure (µg/kg bw) | Highest % of ARfD/ADI |
|------------------------------|-----------------|---------------------|-----------------------|------------------------------|-----------------|---------------------|-----------------------|
| 0.03% Carob (st johns bread) | 0.05/0.05       | 0.04                | 0.03%                 | Carob (st johns bread)       | 0.05/0.05       | 0.04                | 0.03%                 |

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

### Conclusion:

The estimated short-term intake (IESTI) exceeded the toxicological reference value for 2 commodities.

For processed commodities, the toxicological reference value was exceeded in one or several cases.
Scenario 2

Flupyradifurone

Functioning of health protection | 0.044
Toxicological reference values
ADI (mg/kg bw per day): 0.064
LOQ (mg/kg): 0.01
Source of ADI: EC
Source of ADH: EC
Year of evaluation: 2015
Year of evaluation: 2015

No of diets exceeding the ADI : ---

Calculated exposure (% of ADI) MS Diet
Exposure (% of ADI) MS Diet
Highest contributor to MS diet (in % of ADI)
2nd contributor to MS diet (in % of ADI)
3rd contributor to MS diet (in % of ADI)

Commodity/group of commodities
MRLs set at the LOQ (in % of ADI)
Commodities not under assessment (in % of ADI)

| Commodity/group of commodities | MRLs set at the LOQ (in % of ADI) | Commodities not under assessment (in % of ADI) |
|--------------------------------|----------------------------------|-----------------------------------------------|
| Watermelons                    | 17%                              | ---                                            |
| Potatoes                        | 15%                              | ---                                            |
| Cucumbers                       | 11%                              | ---                                            |
| Sweet potatoes                  | 11%                              | ---                                            |
| Tomatoes                        | 10%                              | ---                                            |
| Potatoes                        | 10%                              | ---                                            |
| Tomatoes                        | 10%                              | ---                                            |
| Beans                           | 9%                               | ---                                            |
| Other cereals                   | 9%                               | ---                                            |
| Tomatoes                        | 9%                               | ---                                            |
| Tomatoes                        | 9%                               | ---                                            |
| Tomatoes                        | 9%                               | ---                                            |
| Tomatoes                        | 9%                               | ---                                            |
| Beans                           | 8%                               | ---                                            |
| Tomatoes                        | 8%                               | ---                                            |
| Tomatoes                        | 7%                               | ---                                            |
| Tomatoes                        | 7%                               | ---                                            |
| Tomatoes                        | 7%                               | ---                                            |
| Wheat                           | 7%                               | ---                                            |
| Tomatoes                        | 6%                               | ---                                            |
| Wheat                           | 6%                               | ---                                            |
| Tomatoes                        | 5%                               | ---                                            |
| Tomatoes                        | 4%                               | ---                                            |
| Tomatoes                        | 4%                               | ---                                            |
| Wheat                           | 4%                               | ---                                            |
| Tomatoes                        | 3%                               | ---                                            |
| Tomatoes                        | 3%                               | ---                                            |
| Tomatoes                        | 3%                               | ---                                            |
| Wheat                           | 3%                               | ---                                            |
| Tomatoes                        | 2%                               | ---                                            |
| Tomatoes                        | 2%                               | ---                                            |
| Tomatoes                        | 2%                               | ---                                            |
| Wheat                           | 2%                               | ---                                            |
| Tomatoes                        | 1%                               | ---                                            |
| Tomatoes                        | 1%                               | ---                                            |
| Tomatoes                        | 1%                               | ---                                            |
| Tomatoes                        | 1%                               | ---                                            |

Conclusion:
DE women 14-50 yr UK adult DK adult Tomatoes Wheat

Flupyradifurone Toxicological reference values
Refined calculation mode
Chronic risk assessment: JMPR methodology (IEDI/TMDI)

Modifications of the existing MRLs for Flupyradifurone and DFA in various crops

Input values
Details-acute risk assessment/children Details-acute risk assessment/adults
Details-chronic risk

Supplementary results–

Comments:
Exposure from residues in rotational crops (no treatment)

From data recorded the ADI:

Details – acute risk assessment/children
Details – acute risk assessment/adults

Supplementary results–

Details – chronic risk

Modifications of the existing MRLs for Flupyradifurone and DFA in various crops
The acute risk assessment is based on the ARfD. The calculation is based on the large portion of the most critical consumer group.

### Results for all crops

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

| IESTI | MRL/input | Exposure | IESTI | MRL/input | Exposure |
|-------|-----------|----------|-------|-----------|----------|
| Highest % of ARfD/ADI | Commodities | for RA (mg/kg) | (µg/kg bw) | Commodities | for RA (mg/kg) | (µg/kg bw) |
| 0.08% | Rapeseeds/canola seeds | 0.01/0.09 | 0.12 | 0.06% | Sunflower seeds | 0.01/0.09 | 0.09 |
| 0.06% | Mustard seeds | 0.01/0.09 | 0.09 | 0.04% | Sesame seeds | 0.01/0.09 | 0.06 |

Expand/collapse list

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

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

| IESTI | MRL/input | Exposure | IESTI | MRL/input | Exposure |
|-------|-----------|----------|-------|-----------|----------|
| Highest % of ARfD/ADI | Processed commodities | for RA (mg/kg) | (µg/kg bw) | Commodities | for RA (mg/kg) | (µg/kg bw) |
| 0.0% | Rapeseeds/oils | 0.01/0.09 | 0.05 | 0.0% | Rapeseeds/oils | 0.01/0.09 | 0.05 |

Expand/collapse list

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

D.1. Livestock dietary burden calculations

| Feed commodity | Median dietary burden | Maximum dietary burden |
|----------------|-----------------------|------------------------|
|                | Input value (mg/kg)   | Comment                | Input value (mg/kg) | Comment |
| **Flupyradifurone** |                       |                        |                      |         |
| Rapseed meal   | 0.18                  | STMR × PF\(^{(a)}\)    | 0.18                 | STMR × PF\(^{(a)}\) |
| Remaining feed items | Input values as reported in Appendix D.1 of the EFSA reasoned opinion on the setting of import tolerances, modification of existing maximum residue levels and evaluation of confirmatory data following the Article 12 MRL review for flupyradifurone and DFA (EFSA, 2020) | |

| **Difluoroacetic acid (DFA), expressed as DFA** | | |
|-------------------------------------------------|------------------------|
| Rapseed meal                                    | 0.12                   | STMR × PF\(^{(a)}\)    | 0.12                 | STMR × PF\(^{(a)}\) |
| Remaining feed items                            | Input values as reported in Appendix D.1 of the EFSA reasoned opinion on the setting of import tolerances, modification of existing maximum residue levels and evaluation of confirmatory data following the Article 12 MRL review for flupyradifurone and DFA (EFSA, 2020) | |

STMR: supervised trials median residue; PF: processing factor; MRL: maximum residue level.

\(^{(a)}\): For rapseed meal in the absence of processing factor supported by data, a default processing factor of 2 was included in the calculation to consider the potential concentration of residues in meal.

D.2. Consumer risk assessment

**Scenario 1:** Exposure to residues from the intake of primary crops and commodities of animal origin

| Commodity                       | Chronic risk assessment | Acute risk assessment |
|---------------------------------|-------------------------|-----------------------|
|                                 | Input value (mg/kg)     | Comment               | Input value (mg/kg) | Comment |
| **Risk assessment residue definition:** Sum of flupyradifurone and DFA, expressed as flupyradifurone | | |
| Rapseeds, mustard seeds         | 0.23                    | STMR (rapseeds)       | 0.23                 | STMR (rapseeds) |
| Commodities of plant and animal origin | STMR | Appendix D.2 of EFSA reasoned opinion (EFSA, 2020)\(^{(a)}\) | Acute consumer exposure was performed only for the crops under consideration | |

STMR: supervised trials median residue.

\(^{(a)}\): In melons, the STMR value used in the calculation was 0.31 mg/kg, noting a mistaken value reported in Appendix D.2 of EFSA reasoned opinion (EFSA, 2020).
**Scenario 2:** Exposure to flupyradifurone and DFA residues (expressed as flupyradifurone) from rotational crops

| Commodity                                  | Chronic risk assessment | Acute risk assessment               |
|--------------------------------------------|-------------------------|-------------------------------------|
| Commodity Chronic risk assessment          | Input value (mg/kg)     | Comment                             |
| Commodity Acute risk assessment            | Input value (mg/kg)     | Comment                             |
| Risk assessment residue definition: Sum of flupyradifurone and DFA, expressed as flupyradifurone |                         |                                     |
| Rapeseeds, mustard seeds                   | 0.09                    | STMR in rotational crop rapeseed at EU plateau (EFSA, 2020) | 0.09 | STMR in rotational crop rapeseed at EU plateau (EFSA, 2020) |
| Commodities of plant and animal origin     | STMR                    | Appendix D.2 of EFSA reasoned opinion (EFSA, 2020)              | Acute consumer exposure was performed only for the crops under consideration |

STMR: supervised trials median residue.
## Appendix E – Used compound codes

| Code/trivial name<sup>(a)</sup> | IUPAC name/SMILES notation/InChiKey<sup>(b)</sup> | Structural formula<sup>(c)</sup> |
|--------------------------------|-----------------------------------------------|---------------------------------|
| **flupyradifurone**<sup>(a)</sup> | 4-[(6-chloro-3-pyridylmethyl)(2,2-difluoroethyl)amino]furan-2(5H)-one | ![Structural formula](image) |
|                                | FC(F)CN(Cc1ccc(Cl)nc1)C1=CC(=O)OC1 | ![Structural formula](image) |
|                                | QOYTRGOFZNKF-UHFFFAOYSA-N                  | ![Structural formula](image) |
| **DFA**                        | Difluoroacetic acid                        | ![Structural formula](image) |
|                                | FC(F)C(=O)O                               | ![Structural formula](image) |
|                                | PBWZKZYHONABLN-UHFFFAOYSA-N               | ![Structural formula](image) |
| **TFA**                        | Trifluoroacetic acid                       | ![Structural formula](image) |
|                                | FC(F)(F)(=O)O                             | ![Structural formula](image) |
|                                | DTQVDTLACAAQTR-UHFFFAOYSA-N               | ![Structural formula](image) |
| **6-CNA**                      | 6-chloronicotinic acid                     | ![Structural formula](image) |
|                                | OC(=O)c1ccnc(Cl)c1                       | ![Structural formula](image) |
|                                | UAWMVMPAYRWUFX-UHFFFAOYSA-N               | ![Structural formula](image) |
| **CHMP**                       | (6-chloropyridin-3-yl)methanol             | ![Structural formula](image) |
| **6-CPA**                      | OCc1ccnc(Cl)c1                           | ![Structural formula](image) |
| **6-chloro-picolylalcohol**    | GOXYBEWXWMJLJB-UHFFFAOYSA-N               | ![Structural formula](image) |
| **flupyradifurone-hydroxy**    | 4-[[6-chloropyridin-3-yl)methyl](2,2-difluoroethyl)amino]-5-hydroxyfuran-2(5H)-one | ![Structural formula](image) |
| **M8 metabolite**              | OC2OC(=O)C1=C2N(CC(F)F)Cc1ccnc(Cl)nc1     | ![Structural formula](image) |
|                                | VCISBQOTABLQEA-UHFFFAOYSA-N               | ![Structural formula](image) |

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

<sup>(a)</sup> The metabolite name in bold is the name used in the conclusion.

<sup>(b)</sup> ACD/Name 2018.2.2 ACD/Labs 2018 Release (File version N50E41, Build 103230, 21 July 2018).

<sup>(c)</sup> ACD/ChemSketch 2018.2.2 ACD/Labs 2018 Release (File version C60H41, Build 106041, 7 December 2018).