REGISTRATION REPORT

Part B

Section 7

Metabolism and Residues

Detailed summary of the risk assessment

Product code: GF-4021

Product name: LaDiva

Chemical active substances:

Halauxifen-methyl 10 g a.s./L (9.594 g a.e./L)

Picloram 48 g a.s./L

Aminopyralid 32 g a.s./L

Central Zone

Zonal Rapporteur Member State: Poland

CORE ASSESSMENT

(new submission of the product)

Applicant: Dow AgroSciences

Submission date: November 2020, updated May 2021

MS Finalisation date: October 2021 (initial Core Assessment)

January 2023 (final Core Assessment)

Version history

When	What
November 2020	New submission of GF-4021 to the Central Zone.
October 2021	Initial zRMS assessment. The report in the dRR format has been prepared by the Applicant , therefore all comments, additional evaluations and conclusions of the zRMS are presented in grey commenting boxes. Minor changes are introduced directly in the text and highlighted in grey. Not agreed or not relevant information are ~~struck through and shaded for transparency~~.
November 2022	dRR updated by Applicant
January 2023	Final report (Core Assessment updated following the commenting period). Additional information/assessments included by the zRMS in the report in response to comments received from the cMS and the Applicant are highlighted in yellow. Information no longer relevant ~~is struck through and shaded~~.

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7 Metabolism and residue data (KCA section 6)

7.1 Summary and zRMS Conclusion

7.1.1 Critical GAP(s) and overall conclusion

Selection of critical uses and justification

The critical GAP with respect to consumer intake and risk assessment for the preparation GF-4021 is presented in Table 7.1. It has been selected from the individual GAPs in the central zone for oilseed rape. A list of all intended uses within the central zone is given in Part B, Section 0.

Overall conclusion

The data available are considered sufficient for risk assessment. An exceedance of the current MRLs of 0.05 mg/kg for halauxifen-methyl, 0.03 mg/kg for picloram and 0.05* mg/kg for aminopyralid in rape seeds, as laid down in Reg. (EU) 396/2005, is not expected.

The chronic and the short-term intakes of halauxifen-methyl, picloram and aminopyralid residues are unlikely to present a public health concern.
As far as consumer health protection is concerned, Poland as zRMS agrees with the authorization of the intended uses.

According to available data, the following specific mitigation measure should apply:
Do not grow leafy vegetables in the treated field less than 120 days after application of GF-4021.

Data gaps

Noticed data gaps are: None

Table 7.1.1-1: Acceptability of critical GAPs (and respective fall-back GAPs, if applicable)

1	2	3	4	5	6	7		8				9			10	11
GAP number (see part B.0)*	**Crop and/ or situation ****	**Zone**	**Product code**	**F, Fn, Fpn G, Gn, Gpn or I*****	**Pests or Group of pests controlled**	**Formulation**		**Application**				**Application rate per treatment**			**PHI (days)**	**Conclusion**
						Type	**Conc. of as**	**method kind**	**growth stage & season**	**number min max**	**interval between applications (min)**	**gas/hL min max**	**water L/ha min max**	**gas/ha min max**		
1	Winter oil seed rape Brassica napus BRSNN *MRL code: 041060*	CZ (Poland Germany Czech Republic Slovakia Hungary Romania Slovenia)	GF-4021	F	Broadleaf weeds (post-em) Capsella bursa-pastoris Centaurea cyanus Chenopodium album Descurainina sophia Galeopsis tetrahit Galium aparine Geranium dissectum Geranium pusillum Lamium purpureum Matricaria chamomilla Myosotis arvensis Papaver rhoeas Sonchus arvensis Tripleurospermum perforatum Viola arvensis	EC	10 (9.594 g ae./L) + 32 + 48	Overall, Broadcast foliar spray	BBCH 12-19	a) 1 b) 1	-		100-300	a, b) 2.5 (2.4ae) + 12 + 8	-	A

* Use number(s) in accordance with the list of all intended GAPs in Part B, Section 0 should be given in column 1
** Use also code numbers according to Annex I of Regulation (EU) No 396/2005
*** F: professional field use, Fn: non-professional field use, Fpn: professional and non-professional field use, G: professional greenhouse use, Gn: non-professional greenhouse use, Gpn: professional and non-professional greenhouse use, I: indoor application

Explanation for Column 11 "Conclusion"

A	Exposure acceptable without risk mitigation measures, safe use
R	Further refinement and/or risk mitigation measures required
N	Exposure not acceptable, no safe use

7.1.2 Summary of the evaluation

The preparation GF-4021 is composed of halauxifen methyl, picloram, and aminopyralid.

Table 7.1.2-1: Toxicological reference values for the dietary risk assessment of halauxifen methyl/picloram/aminopyralid

Halauxifen methyl				
Endpoint	**Value**	**Study**	**Safety factor**	**Reference**
Acceptable Daily Intake (ADI)	0.058	Rabbit, developmental toxicity	100	EFSA Journal 2014;12(12):3913
Acute Reference Dose (ARfD)	0.058			
Picloram				
Endpoint	**Value**	**Study**	**Safety factor**	**Reference**
Acceptable Daily Intake (ADI)	0.3	Rabbit developmental + 1-year dog studies	100	EFSA Journal 2009; 7(12):1390 EU Final Review report – 01/26/2018
Acute Reference Dose (ARfD)	0.3			
Aminopyralid				
Endpoint	**Value**	**Study**	**Safety factor**	**Reference**
Acceptable Daily Intake (ADI)	0.26 mg/kg bw/d	Development rabbit study	100	EFSA Journal 2013; 11(9):3352
Acute Reference Dose (ARfD)	0.26 mg/kg bw/d			

7.1.2.1 Summary for Halauxifen-Methyl

Table 7.1.2.1-1: Summary for halauxifen-methyl

Use-No.*	**Crop**	**Plant metabolism covered?**	**Sufficient residue trials?**	**PHI sufficiently supported?**	**Sample storage covered by stability data?**	**MRL compliance**	**Chronic risk for consumers identified?**	**Acute risk for consumers identified?**
1	Winter Oil Seed Rape	Yes	Yes (6 NEU Trials)	Yes	Yes	Yes	No	No

* Use number(s) in accordance with the list of all intended GAPs in Part B, Section 0 should be given in column 1

The effects of processing on the nature of halauxifen-methyl residues have been investigated. Data on effects of processing on the amount of residue have been submitted. These data were not considered for risk assessment.

Residues in succeeding crops have been sufficiently investigated taking into account the specific circumstances of the cGAP uses being considered here. It is very unlikely that residues will be present in succeeding crops.

Considering dietary burden and based on the intended uses, no significant modification of the intake was calculated for livestock. Further investigation of residues as well as the modification of MRLs in commodities of animal origin is therefore not necessary.

7.1.2.2 Summary for Picloram

Table 7.1.2.2-1: Summary for Picloram

Use-No.*	Crop	Plant metabolism covered?	Sufficient residue trials?	PHI sufficiently supported?	Sample storage covered by stability data?	MRL compliance	Chronic risk for consumers identified?	Acute risk for consumers identified?
1	Winter Oil Seed Rape	Yes	Yes (12 NEU trials)	Yes	Yes	Yes	No	No

* Use number(s) in accordance with the list of all intended GAPs in Part B, Section 0 should be given in column 1

As residues of picloram do not exceed the trigger values defined in Reg. (EU) No 283/2013, there is no need to investigate the effect of industrial and/or household processing.

Residues in succeeding crops have been sufficiently investigated taking into account the specific circumstances of the cGAP uses being considered here. On the basis of the available data, the following mitigation measure has been proposed: **do not grow leafy vegetables in the treated field less than 120 days after application of GF-4021**.

Considering dietary burden and based on the intended uses, no significant modification of the intake was calculated for livestock. Further investigation of residues as well as the modification of MRLs in commodities of animal origin is therefore not necessary.

7.1.2.3 Summary for Aminopyralid

Table 7.1.2.3-1: Summary for Aminopyralid

Use-No.*	Crop	Plant metabolism covered?	Sufficient residue trials?	PHI sufficiently supported?	Sample storage covered by stability data?	MRL compliance	Chronic risk for consumers identified?	Acute risk for consumers identified?
1	Winter Oil Seed Rape	Yes	Yes (12 NEU trials)	Yes	Yes	Yes	No	No

* Use number(s) in accordance with the list of all intended GAPs in Part B, Section 0 should be given in column 1

The effects of processing on the nature of aminopyralid residues have been investigated. Data on effects of processing on the amount of residue have been submitted. These data were not considered for risk assessment.

Residues in succeeding crops have been sufficiently investigated taking into account the specific circumstances of the cGAP uses being considered here. A confined rotational crop study (Study title: A confined rotational crop study with ^{14}C-aminopyralid Authors: Sandra Rotondaro, He Wang, Brittany Kish Date: 16 December 2015 Study ID: 120968) has been evaluated by EMS-United Kingdom, 2017.
EMS-UK conclusions (Evaluation Report: "Modification of MRLs for aminopyralid in barley, rye, oats, wheat, sorghum, millet and maize", 2017):
Significant residues (>0.01 mg/kg) are expected in leafy/stem vegetable and cereal (forage, hay and straw) crops grown in rotation at a plant back interval of 30 days following application of 10 g aminopyralid/ha. As such, the current MRL of 0.01 mg/kg for leafy crops and stem vegetables may be exceeded when replanting occurs 30 days after application. On this basis the existing 90 day plant back restriction should remain in place.
Taking into account presented above UK conclusions, in our opinion **90 day plant back restriction** should

remain in place.

Considering dietary burden and based on the intended uses, no significant modification of the intake was calculated for livestock. Further investigation of residues as well as the modification of MRLs in commodities of animal origin is therefore not necessary.

7.1.2.4 Summary for GF-4021

Table 7.1.2.4-1: Information on GF-4021 (KCA 6.8)

Crop	PHI for product code proposed by applicant	PHI/ Withholding period* sufficiently supported for			PHI for GF-4021 proposed by zRMS	zRMS Comments (if different PHI proposed)
		Halauxifen-Methyl	Picloram	Aminopyralid		
Winter Oil Seed Rape Brassica napus BRSNN MRL code: 041060	F** (Max BBCH 30)	F**	F**	F**	F	-

NR: not relevant
* Purpose of withholding period to be specified
** F: PHI is defined by the application stage at last treatment (time elapsing between last treatment and harvest of the crop).

Table 7.1.2.4-2: Waiting periods before planting succeeding crops

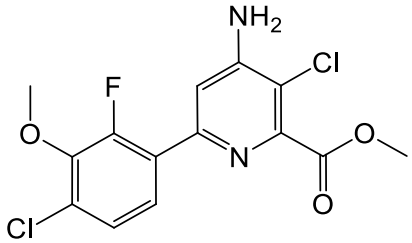
Waiting period before planting succeeding crops				Overall waiting period proposed by zRMS for GF-4021
Crop group	Led by halauxifen-methyl	Led by picloram	Led by amino-pyralid	
Leafy vegetables	NR	120 days	NR	Do not grow leafy vegetables in the treated field less than 120 days after application of GF-4021

NR: not relevant

7.2 Halauxifen-methyl

General data on Halauxifen Methyl are summarized in the table below (last updated 2020/11/10)

Table 7.2-1: General information on Halauxifen Methyl

Active substance (ISO Common Name)	Halauxifen-methyl
IUPAC	methyl 4-amino-3-chloro-6-(4-chloro-2-fluoro-3-methoxy-phenyl)pyridine-2-carboxylate
Chemical structure	
Molecular formula	$C_{14}H_{13}Cl_2FN_2O_3$
Molar mass	347.17 g/mol
Chemical group	Belongs to the new family of 6-arylpicolinate herbicides
Mode of action (if available)	Synthetic auxin herbicide
Systemic	Yes
Company	Dow AgroSciences*
Rapporteur Member State (RMS)	UK
Approval status	Approved by (EU) COMMISSION REGULATION (EU) No 2015/1165) of 15 July 2015. http://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32015R1165&from=EN
Restriction	
Review Report	SANTE/10406/2015, rev. 1, 29 May 2015, 26 January 2018
Current MRL regulation	Regulation (EU) No 2016/67
Peer review of MRLs according to Article 12 of Reg No 396/2005 EC performed	~~Yes~~ No
EFSA Journal : Conclusion on the peer review	Yes **
EFSA Journal: conclusion on article 12	~~Yes **~~ No
Current MRL applications on intended uses	No current MRL application on rape seed. Existing MRL on Oilseeds/canola seeds (0401060) Status: Reasoned opinion available COMMISSION REGULATION (EU) 2016/67 EFSA Journal 2014; 12(12): 3913

* Notifier in the EU process to whom the a.s. belong(s)
** EFSA Journal 2014; 12(12): 3913

7.2.1 Stability of Residues (KCA 6.1)

7.2.1.1 Stability of residues during storage of samples

Available data

No new data submitted in the framework of this application.

Table 7.2.1.1-1: Summary of stability data achieved at ≤ - 18°C (unless stated otherwise)

Matrix	Characteristics of the matrix	Acceptable Maximum Storage duration	Reference
Data relied on in EU			
Plant products			
Lettuce	High Water Content Commodity ~~Crop~~	735 days (approx. 24 Months)	Devine, H. C. (2013) X11393728 (XDE-729 methyl) and X11393729 (XDE-729): Residue Stability Study in Crops under Frozen Storage Conditions, DAS Study ID: 110563 EFSA Journal 2014;12(12):3913
Wheat Grain	High Starch Content Commodity ~~Dry Crop~~	735 days (approx. 24 Months)	
Oilseed rape seed	High oil Content Commodity ~~Oily Crop~~	735 days (approx. 24 Months)	
Oranges	High Acid Content Commodity ~~Crop~~	735 days (approx. 24 Months)	
Animal Products			
Ruminant	Muscle	756 days for XDE-729 Methyl and Halauxifen acid (XDE-729 acid) 742 days for X11449757	Langridge, G. (2014), Frozen Storage Stability of Residues of XDE-729 Methyl Ester, Halauxifen acid (XDE-729 acid) and X11449757 in Animal Matrices – Twenty Four Months Stability Data for XDE-729 Methyl Ester and Halauxifen acid (XDE-729 acid) and Twenty Four Months Stability Data for the Relevant Metabolite, X11449757 DAS Study ID: 110768 EFSA Journal 2014;12(12):3913
Ruminant	Milk	756 days for XDE-729 Methyl and Halauxifen acid (XDE-729 acid) 742 days for X11449757	
Poultry	Liver	756 days for XDE-729 Methyl and Halauxifen acid (XDE-729 acid) 742 days for X11449757	
Poultry	Eggs	756 days for XDE-729 Methyl and Halauxifen acid (XDE-729 acid) 742 days for X11449757	

Conclusion on stability of residues during storage

The results from the final frozen storage stability study in crop matrices indicate that XDE-729 methyl ester and Halauxifen acid (XDE-729 acid) in crop samples from field studies can be stored frozen for at least 24 months (735 days) with no observable degradation of residues.

The results from the final frozen storage stability study in animal matrices show that residues of Halauxifen-methyl (XDE-729 methyl) ester and Halauxifen acid (XDE-729 acid) do not exhibit any significant degradation for at least 756 days and that residues of X11449757 do not exhibit any significant degradation for at least 742 days in bovine muscle, bovine milk, poultry liver and poultry eggs while stored under frozen conditions.

zRMS comments:

The stability of residues for the active substance halauxifen-methyl were reviewed at the EU level.
According to the EFSA Journal 2014;12(12):3913 – "*Peer review of the pesticide risk assessment of the active substance halauxifen-methyl*":

Stability of residues (Annex IIA, point 6 introduction, Annex IIIA, point 8 Introduction)

Plant Matrices: (Ongoing 24 month study. Data collected to approximately 16 months)
Halauxifen-methyl and X11393729 (halauxifen) stable at least 16 months in:
- high-water- (lettuce),
- high starch- (wheat grain),
- high oil (oilseed rape seed) and
- a high acid (oranges) matrices

Animal Tissues (Ongoing 24 month study) Data collected to approximately 12 months)

	Halauxifen-methyl and X11393729 (halauxifen) stable for at least 12 months in bovine muscle, bovine milk, poultry liver, and poultry eggs (data collected to approximately 12 months) - Metabolite X11449757, stable for at least 6 months in bovine muscle, bovine milk, poultry liver, and poultry eggs (data has been collected to approximately 6 months)

The final frozen storage stability studies in crop (Devine, H. C. (2013)) and animal matrices (Langridge, G. (2014)) has been submitted by the applicant and has been evaluated.
A storage stability study of Devine, H. C. (2013) was conducted with X11393728 (XDE-729 methyl ester) and X11393729 (XDE-729 acid) in wheat grain, lettuce, oilseed rape seed and whole oranges to determine the stability of the residues while stored frozen for up to approximately 24 months. Samples were analysed for X11393728 (XDE-729 methyl ester) and X11393729 (XDE-729 acid) after a maximum of 735 days of frozen storage. The results show that residues of X11393728 (XDE-729 methyl ester) and X11393729 (XDE-729 acid) do not exhibit any significant degradation for at least 735 days when stored under frozen conditions in wheat grain, lettuce, oilseed rape seed and whole oranges.
A storage stability study of Langridge, G. (2014) was conducted with XDE-729 methyl ester and XDE-729 acid and with relevant metabolite X11449757, in animal matrices to determine the stability of the residues while stored frozen for up to approximately 24 months. The results show that residues of XDE-729 methyl ester and XDE-729 acid do not exhibit any significant degradation for at least 756 days and that residues of X11449757 do not exhibit any significant degradation for at least 742 days in bovine muscle, bovine milk, poultry liver and poultry eggs while stored under frozen conditions.
The studies have been accepted.
Sufficient stability data are available to support the residue data presented in the present dossier.

7.2.1.2 Stability of residues in sample extracts (KCA 6.1)

Available data
The stability of residues in sample extracts of different crop matrices were also confirmed through the inclusion of the procedural batch recovery samples along with residue sample analyses. Therefore, the supervised residue trials data for the current application are valid with regard to stability of residues in stored sample extracts.

Conclusion on stability of residues in sample extracts
The supervised residue trials data for the current application are valid with regard to stability of residues in stored sample extracts.

zRMS comments:
The supervised residue trials data supporting the current application are valid with regard to stability of residues of halauxifen-methyl in stored samples extracts.

7.2.2 Nature of residues in plants, livestock and processed commodities

7.2.2.1 Nature of residue in primary crops (KCA 6.2.1)

Available data
In addition to studies in wheat (cereals group) and turnips (root and tuber vegetable) that were reviewed during the Annex 1 inclusion of the active substance halauxifen, a new metabolism study in oilseed rape (pulse and oilseed group) has been submitted by the applicant in the framework of this application. These

studies are summarized in the table below. A detailed summary of the new study is provided in Appendix 2.

Table 7.2.2.1-1: Summary of plant metabolism studies

Crop Group	Crop	Label position	Application and sampling details					Reference
			Method, F or G (a)	Rate (kg a.s./ha)	No	Sampling (DAT)	Remarks	
EU data/ EFSA, 2014								
Root and tuber vegetables	Turnips	Phenyl-UL 14C Pyridine 2,6-14C	Foliar app at BBCH 17 (F)	10 g as/ha	1	Immature Roots/Tops (14) Mature Roots/Tops (28)	No apps made that included a safener.	Rotondaro, S. L., (2012), A Nature of the Residue Study with [14C]-XDE-729 Methyl Applied to Turnips, DAS Study ID: 110413 EFSA Journal 2014;12(12):3913
Cereals	Wheat	Phenyl-UL 14C Pyridine 2,6-14C	Foliar app at BBCH 45 (F)	10 g as/ha	1	Forage (49) Hay (75) Straw/grain (89)	Apps made with and without the safener cloquintocet mexyl	Ma, M., Smith, K.P., Jackson, A.U., (2012), A Nature of the Residue Study with [14C]-XR-729 Methyl Applied to Wheat with and Without the Safener Cloquintocet Mexyl (Amended Report), DAS Study ID: 101080 EFSA Journal 2014;12(12):3913
New data submitted in this dRR								
Pulses and oilseeds	Oilseed rape	Phenyl-UL 14C Pyridine 2,6-14C	Foliar app at BBCH 17-19 (fall) or at BBCH 39-40 (spring) (F)	6.0 g as/ha	1	Fall App: Forage (64) Seed (178) Spring App: Forage (27) Seed (53)	One set of plants treated with a single fall app, another set with a single spring app.	LaMar, (2013), The Nature of the Residues of [^{14}C] XDE-729 Methyl (2 Radiolabels) in Oilseed Rape DAS Study ID: 120997

* Outdoor/field application (F) or glasshouse/protected/indoor application (G)

Summary of plant metabolism studies reported in the EU

^{14}C XDE-729 methyl (also referred to as halauxifen methyl) labelled in either the phenyl or pyridine rings was foliar applied to spring wheat (BBCH 45) or to turnips (BBCH 17) grown in outdoor plots at the maximum seasonal rate of 10 g a.i./ha (9.6 g a.e./ha). For wheat, the total radioactive residue (TRR) levels were generally very low and were quantified in samples of forage (7 day PHI, max 0.20 mg eq/kg), hay (24 day PHI, max 0.41 mg eq/kg), straw (84 day PHI, max 0.35 mg eq/kg), and grain (84 day PHI, max ≤ 0.004 mg eq/kg). Likewise, the TRR levels in the harvested turnip commodities were also low as they were 0.001-0.006 mg eq/kg in immature and mature roots and approximately 0.08-0.10 mg eq/kg in immature and mature tops.

The majority of the residues were found to be readily extractable from the commodities of both crops using a mild procedure. Minimal additional residues were extractable using stronger procedures. For wheat, typically 62-77% of the TRR was extracted from the forage, hay and straw samples, while approximately 80% of the TRR was extracted from the immature and mature turnip tops. All extracts were further characterized by HPLC. Grain and turnip root samples were not extracted and characterized due to the low

TRR levels present in both samples.

For both crops, XDE-729 methyl was readily metabolized. In wheat, metabolism proceeds either through dissociation of the ester to produce the XDE-729 acid (X11393729) or through demethylation of the methoxy group on the phenyl ring to produce the metabolite X11406790. Both X11393729 and X11406790 are O-demethylated to form X11449757 and X11406790 can also be conjugated with glucose followed by further conjugation with malonic acid. Metabolism continues through natural incorporation of the radiolabelled carbon into natural plant constituents, such as pectin and lignin. Low levels of the dechlorinated parent ester, metabolite X11861662, were detected and are thought to result from the degradation of the XDE-729 methyl by a photolytic mechanism on the plant surface. The combined effects of metabolism and photolytic degradation coupled with the low application rate resulted in low terminal residues of XDE-729 methyl and metabolites in feed and food commodities.

In turnips, the metabolism of XDE-729 methyl proceeds through N-conjugation of the parent ester with glucose; through dissociation of the parent ester to produce X1139372; or through demethylation of the methoxy group on the phenyl ring to produce the metabolite X11406790. X11406790 is then conjugated with glucose (theorized) followed by further conjugation with malonic acid. X11393729 is also conjugated with glucose, through either the nitrogen or the oxygen. This pathway is considered to be comparable to that seen in wheat.

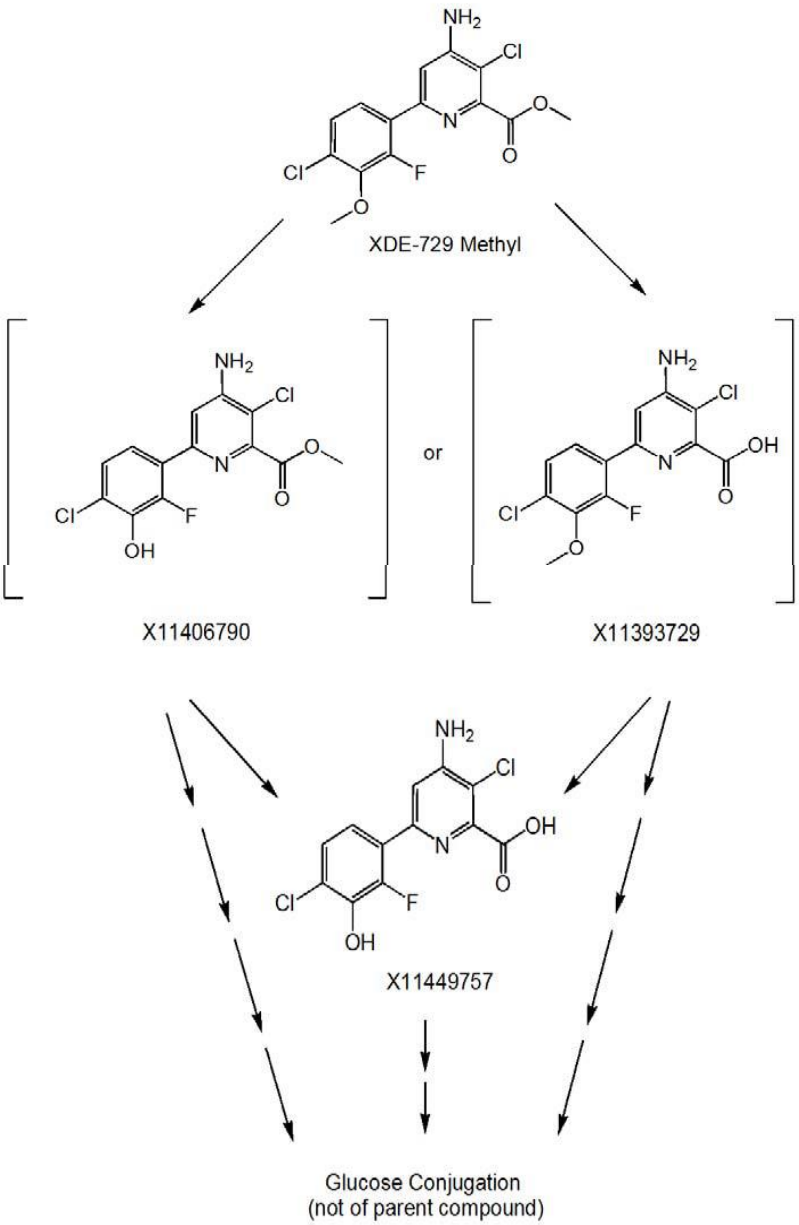
EFSA, 2014:
Primary metabolism of halauxifen-methyl was investigated in the cereal (wheat) and root/tuber (turnip groups. One of the metabolites formed was halauxifen. Having regard to the low total radioactive residues (TRR) observed in grains in the wheat metabolism study (0.002-0.004 mg/kg), these metabolites are not expected to be present in significant levels in cereals so the residue definition for monitoring and risk assessment was proposed as the sum of halauxifen-methyl and halauxifen expressed as halauxifen-methyl, restricted to the cereal group.

Summary of new plant metabolism study on oilseed rape
The new metabolism study was conducted with radiolabelled ^{14}C XDE-729 methyl (methyl 4-amino-3-chloro-6-(4-chloro-2-fluoro-3-methoxyphenyl) pyridine-2-carboxylate) to determine the nature and amount of residue in oilseed rape. The test substance was foliar applied to separate outdoor plots of oilseed rape (OSR) in either the late fall (at BBCH 17- 19) denoted as S1 application or in the early spring (at approx. BBCH 40) denoted as S2 application at the maximum seasonal application rate of 6 g a.i./ha (5.76 a eq/ha). The forage samples from both applications were collected at BBCH 61-69, mature seed and trash samples were collected at BBCH 89. Following collection, the samples were weighed and stored frozen (<-20 °C) pending analysis.
TRR levels in all samples from either the fall or the spring applications were low, approximately 60-70% of the TRR was extracted from the forage samples and 35-40% from the trash samples. Seeds from both applications and trash from fall application were not extracted due to very low residue content (≤0.002

mg eq/kg). Samples of forage and spring trash were extracted with a mixture of acetonitrile/water showed that the residues were readily extractable.
For the fall application, residues in the forage and trash samples were very low (0.001-0.003 mg/kg). Residues in samples from the spring application were moderately higher in the range of 0.016-0.018 mg/kg in forage and 0.024-0.048 mg/kg in trash due to later application.
By HPLC analysis of the extracts several individual components were identified, but no one of the component exceeded 0.002 mg/kg in forage and 0.003 mg/kg in the trash samples.
Unchanged parent XDE-729 methyl was not detected in any of the extracts, while all of the extracts appeared to contain low levels (0.002 mg/kg or less) of the XDE-729 acid (X11393729) in which the aryl methoxy group had been O-demethylated (X11449757).
Enzyme hydrolysis work with one of the spring trash extracts using β-glucosidase suggested the presence of several low-level glucose conjugates; however, the aglycone portion of these conjugates could not be identified.

From the study it can be seen that the metabolism of XDE-729 in oilseed rape involves hydrolysis of the parent XDE-729 and O-demethylation of the methoxy ether moiety to give X11449757. Possible intermediates in the formation of X11449757, compounds X11406790 (the O-desmethyl parent ester) and X11393729 (the parent XDE-729 acid), were not observed. As it was shown by the enzymatic hydrolysis, several glucose conjugates are formed further. The structures of the conjugated species could not be identified.
Given the nearly negligible residues seen in the two raw agricultural commodities of oilseed rape (forage and seed), it is proposed that the only residue components that need to be included in any analytical method that is developed for these commodities are the parent XDE-729 methyl and XDE-729 acid. No hydrolysis step needs to be included in any such method. It is likewise proposed that the residue definition for oilseed rape for both monitoring and risk assessment purposes be established as the sum of XDE-729 methyl and XDE-729 acid (X11393729) expressed as XDE-729 equivalents. The metabolic pathway seen in this study is comparable to the pathways seen for XDE-729 in cereals (wheat) and in root and tuber crops (turnips).
Due to the low TRR levels in all the forage samples and to the fact that oilseed rape trash is not a recognized raw agricultural commodity, no additional extraction and characterization work was deemed necessary for any of the residue.

Figure 7.2.2.1-1: Proposed metabolic pathway



Conclusion on metabolism in primary crops

The metabolic pathway was proposed based on this study. A single application of 6 g as/ha resulted in residue levels of levels in seeds of rape typically ≤0.001 mg eq/kg, and maximum 0.007 mg eq/kg forage XDE-729 methyl equivalents. Due to the low TRR levels in all the seed samples as well as in the trash sample from the fall application, these samples were not extracted and analyzed. Residues from the spring application samples were extractable using mild procedure. Radiolabelled residue levels in seed were typically ≤0.001 mg eq/kg and no further analysis was conducted. Given the low initial TRR levels in all the forage samples, no additional work was necessary to further characterize the non-extractable residues since all were at or below 0.007 mg eq/kg. Extraction of select samples with acetonitrile/water released 37.9-69.7% TRR.

Metabolites of XDE-729 methyl in oilseed rape were characterized via HPLC, TLC, and enzymatic hydrolysis. Based on the initial HPLC analyses, only the O-demethylated parent acid (X11449757) was observed and was targeted for isolation and structure confirmation. XDE-729 methyl was not observed in any of the sample. In addition to X11449757, an additional 3-6 unidentified components were observed in

the extracts. Quantification of these residues showed X11445797 to not be present at levels in excess of 0.001 mg/kg, while the maximum level of any of the unidentified components was 0.002 mg/kg. The fact that the residue profiles were comparable in all of the samples regardless of the position on the radiolabel in the test material with which they were treated confirms that the bond between the two ring systems was not cleaved.
The results indicate that the metabolism of XDE-729 methyl proceeds through hydrolysis of the methyl ester and O-demethylation of the aryl methoxy group to give X11449757. The two possible intermediates in this process, the parent XDE-729 acid (X11393729) and the O-demethyl parent ester (X11406790), were not observed in any of the sample extracts. Further metabolism involves glucose conjugation of multiple metabolites; however, the structures of the conjugated species could not be analysed.

Based on the results from NOR studies run in representative crops from three crop groupings (cereals, root and tuber vegetables, pulses and oilseeds) that showed the total radioactive residues in all raw agricultural commodities to be low (<0.01 mg eq/kg in all commodities having possible direct human consumption) and that further showed a similar residue profile in all three crop groupings, it can be proposed that the current residue definition in place for cereals includes all treated crops. Thus, the proposed residue definition for both monitoring and risk assessment for all crops is halauxifen-methyl and compound X11393729 (halauxifen) expressed as halauxifen-methyl equivalents.

zRMS comments:

The metabolism of halauxifen-methyl was evaluated during the Annex I inclusion.
According to the EFSA Journal 2014;12(12):3913 – "Peer review of the pesticide risk assessment of the active substance halauxifen-methyl":
"Primary metabolism of halauxifen-methyl was investigated in the cereal (wheat) and root/tuber (turnip) groups. It is also noted that an oilseed rape study is available but not submitted or evaluated. One of the metabolites formed was halauxifen. The chlorinated and fluorinated phenyl and pyridyl ring remain intact in all of the identified metabolites, but their toxicological profile was concluded to be not sufficiently addressed. Having regard to the low total radioactive residues (TRR) observed in grains in the wheat metabolism study (0.002 to 0.004 mg eq/kg), these metabolites are not expected to be present in significant levels in cereals and therefore, the residue definition for monitoring and risk assessment was proposed as the sum of halauxifen-methyl and X11393729 (halauxifen) expressed as halauxifen-methyl, restricted to the cereal group only. Any further uses on cereals or other crops will need further consideration of these metabolites."

The residue definitions for plant agreed for monitoring and risk assessment (EFSA Journal 2014;12(12):3913):
Sum halauxifen-methyl and X11393729 (halauxifen), expressed as halauxifen-methyl (restricted to cereals).
According to the Reg. (EU) 2016/67 the residue definitions for plant for monitoring:
Halauxifen-methyl (sum of halauxifen-methyl and X11393729 (halauxifen), expressed as halauxifen-methyl)

In addition to studies in wheat (cereals group) and turnips (root and tuber vegetable) that were reviewed during the Annex 1 inclusion of the active substance halauxifen-methyl, a new metabolism study in oilseed rape (pulse and oilseed group) has been submitted by the Applicant in the framework of this application ("*The nature of the Residues of ^{14}C] XDE-729 Methyl (2 Radiolabels) in Oilseed Rape*" LaMar, J. E.; 2013). The study in oilseeds has not yet evaluated in EFSA.

In our opinion the evaluation of metabolism study of halauxifen-methyl in the new crop group (oilseed) and the setting residue definition should be carried out at the EU level and the active substance level, not at the level of plant protection product registration in the Central Zone.
However, it should be noted that several countries in Central Europe have authorized plant protection products containing halauxifen-methyl for use as a herbicide in oilseed rape. It should be noted too that Halauxifen is not on EFSA list for peer review and there is no open question for MRL setting meaning EFSA will not look at this substance soon.
Taking into above account zRMS-PL has evaluated the study.
The results from NOR studies run in representative crops from three crop groupings (cereals, root and tuber vegetables, pulses and oilseeds) showed the total radioactive residues in all raw agricultural commodities be low (<0.01 mg eq/kg in all commodities having possible direct human consumption) and that further showed a similar residue profile in all three crop groupings **(**in group of cereals, of roots crop and group of pulses and oilseeds crops).
Considering the above, the same residue definition for halauxifen-methyl for a group of pulses and oilseeds crops can be proposed and adopted as the residue definition for halauxifen-methyl for a group of cereals. Thus, the proposed residue definition for both monitoring and risk assessment for new group of crops is

halauxifen-methyl and compound X11393729 (halauxifen) expressed as halauxifen-methyl.

Remark:
Similar conclusions were drawn by zRMS-Denmark (GF-3447, 2017) and zRMS-France (GF-3447, 2018).

7.2.2.2 Nature of residue in rotational crops (KCA 6.6.1)

Available data

No new data concerning the nature of residues in rotational crops are being submitted in the framework of this application.

Table 7.2.2.2-1: Summary of metabolism studies in rotational crops

Crop group	Crop	Label position	Application and sampling details					Reference
			Method, F or G *	Rate (kg a.s./ha)	Sowing intervals (DAT)	Harvest Intervals (DAT)	Remarks	
EU data, EFSA 2014								
Leafy vegetables	Lettuce	Phenyl-UL 14C Pyridine 2,6-14C	Single app to sandy loam soil (F)	10 g ae/ha	14, 90 and 270	Immature at BBCH 41-43 Mature at BBCH 49	90-day lettuce was initially planted outdoors but was moved indoors before reaching maturity. The 270-day crop was grown indoors.	Rotondaro, S. L., (2011), A Confined Rotational Crop Study with [14C]-XDE-729 Methyl Ester , DAS Study ID: 101635 EFSA Journal 2014;12(12):3913
Root and tuber vegetables	Radish	Phenyl-UL 14C Pyridine 2,6-14C	Single app to sandy loam soil (F)	10 g ae/ha	14, 90 and 270	Mature root and tops at BBCH 49	The 270-day crop was grown indoors.	
Cereals	Wheat	Phenyl-UL 14C Pyridine 2,6-14C	Single app to sandy loam soil (F)	10 g ae/ha	14, 90 and 270	Forage at BBCH 25 Hay at BBCH 61-85 Straw and grain at BBCH 89	90-day wheat was planted outdoors but moved indoors before the	

* Outdoor/field application (F) or glasshouse/protected/indoor application (G). While all plots were initially treated and maintained outdoors, they were moved indoors at 140 days after treatment due to the onset of cold weather and were maintained in a greenhouse for the next 221 days. At that time, the box containing the 270-day plant-back wheat was returned back outdoors for the harvest of hay, grain and straw.

Summary of plant metabolism studies reported in the EU

XDE-729 methyl radiolabelled in either the phenyl or pyridine ring was applied to plots of bare sandy loam soil at the rate of 10 g a.e./ha. At three plant-back intervals (14, 90, and 270 days) radishes, lettuce, and wheat were sown. For the first plant back interval, the crops were grown outdoors to maturity at Ricerca, Ohio, USA. Due to the onset of colder fall temperatures, the lettuce and wheat boxes for the 90-day interval were moved indoors in order for the crops to reach maturity. All 270-day crops were planted indoors where the lettuce and radish crops grew to maturity. Wheat was moved back outdoors after collection of the forage samples and the crop grown to maturity. Plot maintenance simulated typical cultural practices.

From each plant-back interval, immature lettuce, mature lettuce, mature radish tops, mature radish roots, wheat forage, wheat hay, and wheat grain and straw were harvested. The harvested crops were milled and

combusted to determine Total Radioactive Residue levels. All crop fractions harvested contained less than 0.01 mg/kg XDE-729 methyl equivalents and were therefore not analyzed further.
It is unlikely that crops rotated into wheat fields treated with XDE-729 at 10 g a.e./ha would result in detectible levels of XDE-729 methyl or metabolites in any Raw Agricultural Commodity. Because of the low residue levels in all crops at all plant-back intervals, a metabolic pathway has not been proposed, and a succeeding residue trials crop study and tolerance/MRL are not necessary for succeeding crops.
It is noted that the Environmental Fate assessment (Section B.8.3 iv) has concluded that high levels of unextracted residues may accumulate at up to 3.83 times the initial parent dose (although there is some uncertainty about this level of accumulation). Uniform Principles relating to unextracted residues state that no authorisation can be granted in the case of high unextracted residue, unless it can be scientifically demonstrated that there is no accumulation in soil at such levels that unacceptable residues in succeeding crops occur. In this instance, given the results of the rotational crop metabolism study confirmed that levels of TRR in all crop samples were very low, and at a level that did not need further characterisation, it can be concluded that, despite accumulation in the soil, it is reasonable to conclude that unacceptable residues will not occur in succeeding crops.

Conclusion on metabolism in rotational crops
Residues in rotational crops were investigated in wheat, lettuce and radish following a single application to bare ground soil at 10 g a.e./ha and plant back intervals (PBI) of 14, 90 and 270 days. Irrespective of the plant back interval, the maximum total radioactive residue (TRR) was found to be 0.001 mg eq/ha in the different plant matrices analyzed. Therefore, it can be concluded that significant residues will not occur in rotational crops when the active substance is applied according to the representative uses.

zRMS comments:

The metabolism of halauxifen-methyl in rotational crops was evaluated at EU level.
According to the EFSA Journal 2014;12(12):3913 – "Peer review of the pesticide risk assessment of the active substance halauxifen-methyl":
"Residues in rotational crops were investigated in wheat, lettuce and radish following a single application to bare soil at 10 g/ha and for plant back intervals (PBI) of 10, 90 and 240 days. Irrespective of the plant back intervals, the maximum TRR was found to be 0.001 mg/kg in the different plant matrices analysed for. Therefore, it can be concluded that significant residues will not occur in rotational crops when the active substance is applied according to the representative uses."
No residues are expected in rotational crops. No waiting periods beyond normal agricultural practice are proposed for succeeding crops to be planted.
The metabolic pathway in rotational plant is sufficiently addressed and no additional metabolism studies are necessary to support the intended uses for GF-4021.

7.2.2.3 Nature of residues in processed commodities (KCA 6.5.1)

Available data
No new data concerning the nature of residues in processed commodities were submitted in the framework

of this application.

Table 7.2.2.3-1: Nature of the residues in processed commodities

Conditions (Duration, Temperature, pH)	Identified compound(s) (%)	Reference
EU data, EFSA 2014		
Pasteurisation (20 minutes, 90°C, pH 4)	XDE-729 methyl (99%), degradate X11393729 (1.6%)	Ma, M., Balcer, J.L., (2011), Processing Study to Determine the Nature of Residues of [14C]-XDE-729 Methyl and [14C]-X11393729 Following Industrial or Household Preparation, DAS Study ID: 110369 EFSA Journal 2014;12(12):3913
Baking, boiling, brewing (60 minutes, 100°C, pH 5)	XDE-729 methyl (93.7%), degradate X11393729 (6.3%)	
Sterilisation (20 minutes, 120°C, pH 6)	XDE-729 methyl (69.2%), degradate X11393729 (29.6%)	
Work with degradate (^{14}C X-11393729)		
EU Data, EFSA 2014		
Pasteurisation (20 minutes, 90°C, pH 4)	X11393729 (100%)	Ma, M., Balcer, J.L., (2011), Processing Study to Determine the Nature of Residues of [14C]-XDE-729 Methyl and [14C]-X11393729 Following Industrial or Household Preparation, DAS Study ID: 110369 EFSA Journal 2014;12(12):3913
Baking, boiling, brewing (60 minutes, 100°C, pH 5)	X11393729 (100%)	
Sterilisation (20 minutes, 120°C, pH 6)	X11393729 (100%)	

Conclusion on nature of residues in processed commodities

A nature of the residues in processed commodities study was conducted to simulate the conditions of pasteurization, sterilization and baking, brewing and boiling. Studies were conducted using ^{14}C XDE-729-methyl and with its sole processing degradate, ^{14}C X11393739 (also referred to as XDE-729 or halauxifen). Under conditions representative of processing operations, ^{14}C-XDE-729 methyl is degraded with increased pH and temperature, with formation of one degradate, X11393729, accounting for up to 29.6% of the total radioactivity. ^{14}C-X11393729 can be regarded as stable to hydrolysis. Recoveries of radioactive during each for each material tested were ≥ 97.9%. Therefore, hydrolysis during RAC processing operations does not significantly affect the nature of the residues since both XDE-729-methyl and X11393739 are already included in the residue definition for crops.

zRMS comments:

The effect of processing on the nature of residues was investigated in the framework of the approval of halauxifen-methyl. In the EFSA Journal 2014;12(12):3913 it is stated that halauxifen-methyl was degraded to halauxifen (X11393729) under standard hydrolysis conditions. Halauxifen (X11393729) can be regarded as stable to hydrolysis.

Since all residues in seed of oilseed rape are < 0.02 mg/kg and no residues of halauxifen exceeding 0.1 mg/kg are expected in the treated crops, further considerations about the effects of processing are not required in the framework of this dossier.

7.2.2.4 Conclusion on the nature of residues in commodities of plant origin (KCA 6.7.1)

Table 7.2.2.4-1: Summary of the nature of residues in commodities of plant origin

Endpoints	
Plant groups covered	Cereals (Wheat) Root and tuber vegetables (Turnip) Pulses and Oilseeds (Oilseed rape)
Rotational crops covered	Yes
Metabolism in rotational crops similar to metabolism in primary crops?	Due to the low residue levels in all crops fractions (TRR < 0.01 mg eq/kg) at all plant-back intervals, a metabolic pathway has not been proposed.
Processed commodities	Halauxifen-methyl is degraded to X11393729 (halauxifen) under standard hydrolysis conditions. X11393729 (halauxifen) can be regarded as stable to hydrolysis.
Residue pattern in processed commodities similar to pattern in raw commodities?	Yes No change needed in the residue definition.
Plant residue definition for monitoring	Sum of Halauxifen-methyl and compound X11393739 (halauxifen) expressed as halauxifen-methyl equivalents (EFSA Journal 2014, 12(11):3913) * Halauxifen-methyl (sum of halauxifen-methyl and X11393729 (halauxifen), expressed as halauxifen-methyl) **
Plant residue definition for risk assessment	Sum of Halauxifen-methyl and compound X11393739 (halauxifen) expressed as halauxifen-methyl equivalents (EFSA Journal 2014, 12(11):3913) *
Conversion factor from enforcement to RA	None ~~No processing factor was proposed as residues were all below the LOQ in both the raw agricultural commodity (grain) and in the processed commodities.~~

* Currently established only for cereals.
** According to the Reg. (EU) 2016/67

7.2.2.5 Nature of residues in livestock (KCA 6.2.2-6.2.5)

Available data

No new animal metabolism data are submitted in the framework of this application.

Table 7.2.2.5-1: Summary of animal metabolism studies

Group	Species	Label position	No of animal	Application details		Sample details		Reference
				Rate (mg/kg bw/d)	Duration (days)	Commodity	Time of sampling	
EU data, EFSA 2014								
Lactating ruminants	Goat	Phenyl-UL 14C Pyridine 2,6-14C	2 (one for each label)	PH Label: 10.25 mg/kg of dry matter/day PY Label: 11.17 mg/kg of dry matter/day	5	Milk	twice daily	Rotondaro, S., Adelfinskaya, Y.A., (2011), A Nature of the Residue Study in the Ruminant with [14C]-XR-729 Methyl Ester, DAS Study ID: 101389 EFSA Journal 2014;12(12):3913
						Urine and faeces	daily	
						Tissues (liver, kidney, fat (3 types), muscle (2 types) and GI tract contents)	at sacrifice (6-8 Hrs after final dose)	
Laying poultry	Hens	Phenyl-UL 14C Pyridine 2,6-14C	10 per group (one group per label)	PH Label: 11.3 mg/kg of dry matter/day PY Label: 11.6 mg/kg of dry matter/day	7	Eggs	daily	Rotondaro, S., Adelfinskaya, Y.A (2011), A Nature of the Residue Study in the Laying Hen with [14C]-XR-729 Methyl Ester, DAS Study ID: 101390 EFSA Journal 2014;12(12):3913
						Excreta	daily	
						Tissues (Liver, fat muscle (types) and skin with fat)	at sacrifice (6-9 Hrs after final dose)	

Metabolism in animals has been thoroughly characterized in rats, poultry and lactating ruminants. Since metabolism is similar in the animals tested, no further studies are required in swine. Based on the proposed uses of XDE-729, no study is fish is needed.

Summary of animal metabolism studies reported in the EU

For the study in ruminants, lactating goats were dosed for 5 consecutive days with ^{14}C XDE-729 methyl at a nominal dose of 10-11 mg/kg dry feed/day which is approximately 476 times higher than the maximum theoretical dietary burden in dairy cows. Analyses of the samples collected throughout the study showed most of the recovered radioactivity to be accounted for in the excreta and contents of the GI tract, while less than 0.5% of the total was accounted for in the collected milk and edible tissue samples. Residues in milk appeared to plateau within about 3-4 days after the initiation of dosing at a level of 0.01 mg/kg or less. For tissues, the highest residues were observed in kidney (≤ 0.121 mg/kg) and liver (≤ 0.077 mg/kg), while residues in fat and muscle were generally at or below 0.010 mg/kg. Residues in all samples analyzed were readily extractable (generally *ca* 85% of the TRR or higher) using mild procedures. Characterization of these residues showed that, once absorbed, XDE-729 methyl is readily metabolized by demethylation to give either the parent acid (X11393729) or the desmethyl parent ester (X11406790), or both to give the O-desmethyl parent acid (X11449757). These metabolites were further metabolized to give sulphate or glucuronic acid conjugates.

For the study in poultry, laying hens were dosed for 7 consecutive days with ^{14}C XDE-729 methyl at a nominal dose of 11 mg/kg dry feed/day which is about 600 times higher than the maximum theoretical dietary burden to hens. Analyses of the samples collected throughout the study showed most of the recovered radioactivity to be accounted for in the excreta, while only about 0.1% of the total was accounted

for in the egg and edible tissue samples combined. While it was not possible to determine if residue levels in eggs plateaued during the study, they remained low throughout and still did not exceed 0.003 mg/kg by the end if the study. For tissues, residue levels were highest in liver (≤ 0.046 mg/kg) and were at or below *ca* 0.01 mg/kg in all the other samples. Residues in all samples analyzed were readily extractable (generally *ca* 70-90% of the TRR) using mild procedures. Characterization of these residues showed that, once absorbed, XDE-729 methyl was readily metabolized by demethylation to give either the parent acid (X11393729) or the desmethyl parent ester (X11406790), or both to give the O-desmethyl parent acid (X11449757). These metabolites were further metabolized to primarily give sulphate conjugates.

Other than the fact that no glucuronic acid conjugates were seen in the poultry study, the metabolic pathways seen in poultry and ruminants were the same and likewise were the same as that seen in the rat. Based on those similarities, an additional study in swine is not necessary.

While EFSA initially expressed concern that the two animal metabolites containing the chlorinated and fluorinated phenyl and pyridyl rings may have some additive toxicity, it was ultimately concluded that because the proposed use on cereals results in residues that are so low that they do not trigger the need for livestock feeding studies (i.e. no residues are expected to be found in products of animal origin), there is no need to set MRLs or a residue definition for products of animal origin.

Conclusion on metabolism in livestock

Given the low residue levels seen in treated crop commodities that might be fed to animals along with the fact that orally administered doses of XDE-729 methyl are not readily accumulated in the edible commodities of animals, residues in meat, milk and eggs are considered to likely be below any practical limit of detection. As such, there was no actual need for the applicant to conduct either animal metabolism studies or animal feeding studies based on the current proposed uses for XDE-729 methyl. Thus, no residue definitions for products of animal origin were proposed as, based on the representative uses, the setting of MRLs for animal products was considered unnecessary.

Considering the intended uses for GF-4021, residue of halauxifen methyl in rapeseed has an insignificant impact to the total livestock exposure. Thus, no further animal metabolism data are required in the framework of this application.

zRMS comments:

The metabolism of halauxifen-methyl was evaluated in the framework of the approval of halauxifen-methyl. In the EFSA Journal 2014;12(12):3913 it is stated that *Metabolism studies on goat and hen were submitted, although the need for animal metabolism studies was not triggered. No residue definitions for products of animal origin were proposed as, based on the representative uses, the setting of MRLs for animal products was concluded to be unnecessary and since the toxicological profile of some metabolites was considered not sufficiently addressed.*

Taking into account the intended uses for product GF-4021, it should be noted that the residue of halauxifen- methyl in oilseed rape has a negligible impact on the overall exposure of livestock.

Since no residues are expected to be found in products of animal origin, there is no need to set MRLs or a residue definition for products of animal origin and further considerations are not required in the framework of this dossier.

7.2.2.6 Conclusion on the nature of residues in commodities of animal origin (KCA 6.7.1)

Table 7.2.2.6-1: Summary on the nature of residues in commodities of animal origin

	Endpoints
Animals covered	Lactating goats
	Laying hens
Time needed to reach a plateau concentration	Milk: 3 days
	Eggs: definite plateau was not reached; However, due to the low level of residues found (max ca. 0.003 mg/kg Halauxifen-methyl equivalents) and given the study was conducted at 625 times the maximum theoretical burden to hens, it was concluded that despite not reaching the plateau, the study was fit for purpose to support the proposed GAP.
Animal residue definition for monitoring	No residue definition proposed since no detectable residues are anticipated in products of animal origin. (EFSA, 2014) halauxifen-methyl (sum of halauxifen-methyl and X11393729 (halauxifen), expressed as halauxifen-methyl) (Reg. (EU) 2016/67)
Animal residue definition for risk assessment	No residue definition proposed since no detectable residues are anticipated in products of animal origin. (EFSA, 2014)
Conversion factor	None (EFSA, 2014)
Metabolism in rat and ruminant similar	Yes (No metabolism study in swine is needed.)
Fat soluble residue	Not conclude on

7.2.3 Magnitude of residues in plants (KCA 6.3)

7.2.3.1 Summary of European data and new data supporting the intended uses

Data, previously evaluated by zRMS, France (RR, GF-3447, 2019) are relied upon for this application. Study RDE-15-20345 (evaluated by zRMS, France (RR, GF-3447, 2019)) on the magnitude of residue has been submitted by the applicant in the framework of this application for GF-4021. This study is summarized in the Table below and the detailed assessment is presented in Appendix 2.

Six NEU and ten SEU trials are submitted, in all instances no residues of halauxifen-methyl or halauxifen acid were detected in the seed or straw samples. As a no residue situation is observed, a reduce data package is considered sufficient to support the intended use of halauxifen-methyl on oilseed rape.

Table 7.2.3.1-1: Summary of EU reported and new data supporting the intended uses of GF-4021 and conformity to existing MRL

Commodity	Source	Residue zone (N-EU, S-EU, EU, outside EU)	Evaluation GAP Halauxifen-methyl Residue levels (mg/kg) E = according to enforcement residue definition RA = according to risk assessment residue definition	STMR (mg/kg)	HR (mg/kg)	Unrounded OECD calculator MRL (mg/kg)	Current EU MRL (mg/kg) *	MRL compliance
Oilseed rape seeds	RR GF-3447, France, 2018 (RDE-15-20345)	N-EU	GAP: 0.5 L/ha (4.8 g ae/ha of halauxifen-methyl and 24 g ae/ha of picloram), BBCH 16-30, outdoor E: 6 x ND (6x <0.02) RA: 6 x ND (6x <0.02)	E: 0.02 RA: 0.02	E: 0.02 RA: 0.02	0.02	0.05	Yes
		S-EU	GAP: 0.5 L/ha (4.8 g ae/ha of halauxifen-methyl and 24 g ae/ha of picloram), BBCH 16-30, outdoor E: 10 x ND (10x <0.02) RA: 10 x ND (10x < 0.02)	E: 0.02 RA: 0.02	E: 0.02 RA: 0.02	0.02	0.05	Yes

* Source of EU MRL: Part A of Annex I to Reg. 396/2005
** No MRL set for OSR straw in EU, data submitted for completeness.

7.2.3.2 Conclusion on the magnitude of residues in plants

According to the available data, the intended use on oilseed rape is considered acceptable. The data submitted show that no exceedance of the MRL will occur. The use is considered acceptable.

zRMS comments:

The intended use for GF-4021 is oilseed rape. Oilseed rape is the major crop in northern Europe (EU guideline Document SANCO 7525/VI/95-rev.10.3 of 13 June 2017). A minimum of eight trials are required.

Table 7.1: Intended cGAP for GF-4021

Crop	Number of applications	Application rate per treatment (gai/ha)	Interval between application	Growth stage at last application	PHI (days)
Oilseed rape	1	Halauxifen-methyl: 2.5 g ae/ha + Picloram: 12 g ae/ha + Aminopyralid: 8 g ae/ha	N/A	BBCH 12-19	-

Study RDE-15-20345 (evaluated by zRMS, France (RR, GF-3447, 2019)) on the magnitude of residue has been submitted by the applicant in the framework of this application for GF-4021.
Sixteen residue trials: 6 NEU and 10 SEU were conducted on oilseed rape. The product was applied ones to oilseed rape at maximum application rate of 5 g halauxifen-methyl/ha. The application was done up to BBCH 30. It cover the intended GAP (one application, rate 2.5 g halauxifen-methyl/ha, BBCH 12-19).
The maximum frozen storage period of samples prior to the analysis was 375 days. All residue data reported within the present submission are covered by the storage period.
Residues of halauxifen and halauxifen-methyl were determined according to method described in Dow AgroSciences Study Number 110005. The limit of quantification was 0.01 mg/kg for all analytes.
Levels of residue are below the LOQ of 0.02 mg/kg for halauxyfen-methyl (sum of halauxyfen-methyl and halauxyfen acid; expressed as halauxyfen methyl) for all the submitted trials.
According to the SANTE/2019/12752 if the residue levels in plants or plant products are lower than the limit of quantification (LOQ), the number of independent trials may be reduced. The number of trials shall not be below the minimum of four per zone for major crops. So there are sufficient residue trials to support the intended use of halauxyfen methyl on oilseed rape.

The value of EU MRL for halauxifen-methyl on oilseed rape equals 0.05 mg/kg (Regulation (EU) 2016/67). The residues arising from the proposed use will not exceed the MRL established for oilseeds.
The current EU MRL for halauxifen-methyl is sufficient to support the proposed use.
Additionally it should be mentioned that oilseed rape straws are not fed to animals. Therefore, no consideration about this item is required.

No additional data are required.

7.2.4 Magnitude of residues in livestock

7.2.4.1 Dietary burden calculation

As no residues were detected in any of the samples for which processing factors are applied, in accordance with the instructions detailed in the animal model, 2017, a processing factor of 1 has been used.

Table 7.2.4.1-1: Input values for the dietary burden calculation (considering the uses authorized in the country of the zRMS/authorized within the zone/evaluated in Art. 12 procedure and the uses under consideration)

Feed Commodity	Median dietary burden		Maximum dietary burden	
	Input value (mg/kg)	Comment	Input value (mg/kg)	Comment
Enforcement / Monitoring and Risk assessment residue definition: ~~halauxifen-methyl and halauxifen acid, expressed as halauxifen equivalents~~ halauxifen-methyl (sum of halauxifen-methyl and X11393729 (halauxifen), expressed as halauxifen-methyl) (Reg. (EU) 2016/67)				

Feed Commodity	Median dietary burden		Maximum dietary burden	
	Input value (mg/kg)	Comment	Input value (mg/kg)	Comment
Barley straw	0.02	STMR (EFSA, 2014)	0.05	HR (EFSA, 2014)
Triticale, rye and wheat straw	0.02	STMR (EFSA, 2014)	0.03	HR (UK, 2014)
Barley, triticale, rye and wheat grain	0.02	STMR (EFSA, 2014)	0.02	STMR (EFSA, 2014)
Brewer's grain, dried	0.02 ~~0.07 (0.02 x3.3)~~	STMR (EFSA, 2014) ~~x default PF~~	0.02 ~~0.07 (0.02 x 3.3)~~	STMR (EFSA, 2014) ~~x default PF~~
Canola meal	0.02 ~~0.04 (0.02* x 2)~~	STMR (EFSA, 2014) ~~x default PF~~	0.02 ~~0.04 (0.02* x 2)~~	STMR (EFSA, 2014) ~~x default PF~~
Distiller's grain, dried	0.02 ~~0.07 (0.02* x 3.3)~~	STMR (EFSA, 2014) ~~x default PF~~	0.02 ~~0.07 (0.02* x 3.3)~~	STMR (EFSA, 2014) ~~x default PF~~
Rape meal	0.02 ~~0.04 (0.02* x 2)~~	STMR (EFSA, 2014) ~~x default PF~~	0.02 ~~0.04 (0.02* x 2)~~	STMR (EFSA, 2014) ~~x default PF~~
Wheat gluten meal	0.02 ~~0.04 (0.02* x 1.8)~~	STMR (EFSA, 2014) ~~x default PF~~	0.02 ~~0.04 (0.02* x 1.8)~~	STMR (EFSA, 2014) ~~x default PF~~
Wheat milled by-products	0.02 ~~0.14 (0.02* x 7)~~	STMR (EFSA, 2014) ~~x default PF~~	0.02 ~~0.14 (0.02* x 7)~~	STMR (EFSA, 2014) ~~x default PF~~

N.B. In the absence of specific processing studies, default (EFSA) processing factors (PFs) were used in the calculation

Table 7.2.4.1-2: Results of the dietary burden calculation

New data requirements (Regulation (EU) No 283/2013)

Relevant groups	Dietary burden expressed in mg/kg bw per day		Dietary burden expressed in mg/kg DM		Most critical diet (a)	Most critical commodity		Trigger exceeded (Yes/No) 0.004 mg/kg bw
	Median	Maximum	Median	Maximum				
Cattle (all diets)	0,002	0,003	0,06	0,07	Dairy cattle	Wheat	milled bypdts	No
Cattle (dairy only)	0,002	0,003	0,06	0,07	Dairy cattle	Wheat	milled bypdts	No
Sheep (all diets)	0,004	0,005	0,09	0,11	Lamb	Wheat	milled bypdts	Yes
Sheep (ewe only)	0,003	0,003	0,08	0,10	Ram/Ewe	Wheat	milled bypdts	No
Swine (all diets)	0,003	0,003	0,09	0,09	Swine (finishing)	Wheat	milled bypdts	No
Poultry (all diets)	0,003	0,003	0,05	0,05	Poultry layer	Wheat	milled bypdts	No
Poultry (layer only)	0,003	0,003	0,05	0,05	Poultry layer	Wheat	milled bypdts	No

(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".

Based on the intakes calculated above, animal intakes are below the trigger values of 0.004 mg/kg bw/day (Reg. (EU) 283/2013) for all animals except lamb. In order to estimate the contribution of halauxifen methyl residues in rape seed to the total livestock dietary exposure, zRMS calculated a second scenario (scenario 2) without rape seed. Results of scenario 2 are presented thereafter in Table 7.2.4-3:

Table 7.2.4.1-3: Results of the dietary burden calculation

New data requirements (Regulation (EU) No 283/2013)

Relevant groups	Dietary burden expressed in mg/kg bw per day		Dietary burden expressed in mg/kg DM		Most critical diet (a)	Most critical commodity		Trigger exceeded (Yes/No) 0.004 mg/kg bw
	Median	Maximum	Median	Maximum				
Cattle (all diets)	0,002	0,003	0,06	0,07	Dairy cattle	Wheat	milled bypdts	No
Cattle (dairy only)	0,002	0,003	0,06	0,07	Dairy cattle	Wheat	milled bypdts	No
Sheep (all diets)	0,004	0,005	0,09	0,11	Lamb	Wheat	milled bypdts	Yes
Sheep (ewe only)	0,003	0,003	0,08	0,10	Ram/Ewe	Wheat	milled bypdts	No
Swine (all diets)	0,003	0,003	0,09	0,09	Swine (finishing)	Wheat	milled bypdts	No
Poultry (all diets)	0,003	0,003	0,05	0,05	Poultry layer	Wheat	milled bypdts	No
Poultry (layer only)	0,003	0,003	0,05	0,05	Poultry layer	Wheat	milled bypdts	No

(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".

From the comparison of the two scenarios it appears that the contribution of rape seed to the total livestock exposure is insignificant. Therefore, France as zRMS is of the opinion that it is not necessary to further investigate the need to modify the existing MRLs for commodities of animal origin in the framework of the current application.

Table 7.2.4.1-4: Results of the dietary burden calculation

Relevant groups	Dietary burden expressed in				Most critical diet (a)	Most critical commodity (b)		Trigger exceeded (Yes/No)
	mg/kg bw per day		mg/kg DM					0.004
	Median	Maximum	Median	Maximum				mg/kg bw
Cattle (all diets)	0.001	0.001	0.02	0.04	Dairy cattle	Barley	straw	No
Cattle (dairy only)	0.001	0.001	0.02	0.04	Dairy cattle	Barley	straw	No
Sheep (all diets)	0.001	0.002	0.03	0.05	Lamb	Barley	straw	No
Sheep (ewe only)	0.001	0.002	0.03	0.05	Ram/Ewe	Barley	straw	No
Swine (all diets)	0.000	0.001	0.01	0.02	Swine (finishing)	Barley	grain	No
Poultry (all diets)	0.000	0.002	0.01	0.03	Poultry layer	Wheat gluten	meal	No
Poultry (layer only)	0.000	0.002	0.01	0.03	Poultry layer	Wheat gluten	meal	No

(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".

7.2.4.2 Livestock feeding studies (KCA 6.4.1-6.4.3)

Available data – EFSA, 2014
No new data were submitted in the framework of this application.

No livestock feeding studies are required since residues were not detected in oilseed rape seeds, and halauxifen-methyl residues in livestock diets would not reach a level where feeding studies would be triggered.

Conclusion on feeding studies
The requested uses (or the new mode of calculation) modify the theoretical maximum daily intake for animals, but regarding available feeding data, there is no risk for animal MRL to be exceeded.
The calculated livestock dietary burden does not exceed the trigger value of 0.004 mg/kg bw/day except for lamb. However, it appears that the impact of halauxifen methyl residues in rape seed to the total livestock exposure was insignificant. Therefore, the modification of the MRLs for commodities of sheep and goat origin is not further investigated in the framework of the current application.
No further data are required and no exceedance of the in force MRLs is expected.

zRMS comments:
Information given by the Applicant is sufficient and zRMS-Poland agrees with presented above conclusions. No further data are required.

7.2.5 Magnitude of residues in processed commodities (Industrial Processing and/or Household Preparation) (KCA 6.5.2-6.5.3)

7.2.5.1 Available data for all crops under consideration

Available data – EFSA, 2014
No new data were submitted in the framework of this application, as residues of halauxifen did not exceed 0.1 mg/kg in the treated crop. There is consequently no need to further investigate the effect of industrial and/or household processing on the magnitude of halauxifen methyl residues.

7.2.5.2 Conclusion on processing studies

Processing studies are not required as they are not expected to affect the outcome of the risk assessment. No residues of halauxifen exceeding 0.1 mg/kg are expected in the treated crops. There is consequently no need to further investigate the effect of industrial and/or household processing on the magnitude of halauxifen methyl residues.

zRMS comments:
Information given by the Applicant is sufficient. Since all residues in seed of oilseed rape are < 0.02 mg/kg and no residues of halauxifen exceeding 0.1 mg/kg are expected in the treated crops, further considerations about the effects of processing are not required in the framework of this dossier. No further data are required.

7.2.6 Magnitude of residues in representative succeeding crops

Residues in rotational crops were investigated in wheat, lettuce and radish following a single application to bare soil at 10 g/ha and for plant back intervals (PBI) of 10, 90 and 240 days. Irrespective of the plant back intervals, the maximum TRR was found to be 0.001 mg/kg in the different plant matrices analysed for. Therefore, it can be concluded that significant residues will not occur in rotational crops when the active substance is applied according to the representative uses.

7.2.6.1 Field rotational crop studies (KCA 6.6.2)

Available data – EFSA, 2014
No new data submitted in the framework of this application.

Conclusion on rotational crops studies
Results from the confined rotational crop study on wheat, radish and lettuce, following application at 10 g/ha and PBI of 14, 90 and 240 days, indicated that all TRRs were ≤0.001 mg/kg in all plants fractions at all PBIs, therefore no field residue trials with succeeding crops are necessary. Specific plant-back restrictions related to the use of GF-4021 are therefore not required, provided that GF-4021 is applied in compliance with the GAPs evaluated in the framework of this review.

zRMS comments:

Information given by the Applicant is sufficient.
No residues are expected in rotational crops at all investigated PBIs (PBI of 14, 90 and 240 days), therefore no field residue trials with succeeding crops are necessary.
No waiting periods beyond normal agricultural practice are proposed for succeeding crops to be planted.
No further data are required.

7.2.7 Other / special studies (KCA6.10, 6.10.1)

The available data for the active substance sufficiently address aspects of the residue situation that might arise from the use of GF-4021. Therefore, other special studies are not needed.

Considering oilseed rape can be seen as a worst-case scenario for foraging honeybees. If the highest residue level in aerial parts of plants is equal to or above the threshold value of 0.05 mg/kg but below 0.5 mg/kg, an MRL proposal could be made based on the highest residue and on the hypothesis of a transfer factor of 1 from aerial parts to honey depending on the outcome of the risk assessment and if the MRL is safe for consumers (SANTE/11956/2016 rev.9).

In available oilseed rape residue studies where whole plant samples were harvested during flowering (BBCH 60-69) study RDE-15-20400 (150534) can be referenced. The application timing of RDE-15-20400 (150534) was conducted at a more critical GAP than that proposed for GF-4021 with a more critical application rate of 4.8 g ae/ha compared to 2.4 g ae/ha and a more critical application timing at growth stage of BBCH 50 compared to BBCH 19 for uses of GF-4021. Residue values in oilseed rape whole plants ranged from ND (<0.003 mg/kg) to 0.023 mg/kg in samples harvested between BBCH 53 – 59 at 7 days after application and ranged from ND (<0.003 mg/kg) to <0.01 mg/kg in samples harvested between BBCH 63-67 (flowering) at 14-15 days after application, demonstrating a rapid decline in residues, and expected residues in aerial parts (flowers) of <0.01 mg/kg. Given that the highest residue of halauxifen-methyl detected was 0.023 mg/kg in whole plants (sampled at BBCH 59, just prior to flowering) and <0.01 mg/kg in whole plants including flowers which are below the default honey MRL of 0.05 mg/kg a proposal can be made that the default honey MRL remains sufficient and an exceedance of this MRL is not expected. Further, a honey MOR study is not required within in the framework of this application.

The available data for the active substance sufficiently address aspects of the residue situation that might arise from the use of GF-4021. Therefore, other special studies are not needed.

zRMS comments:
According to the „Technical guidelines for determining the magnitude of pesticide residues in honey and setting Maximum Residue Levels in honey“ (SANTE/11956/2016 rev. 9; 14 September 2018) residues in honey can occur when a substance with systemic properties is applied prior to the flowering stage (before BBCH 60), of a crop which is foraged by bees.
Halauxifen-methyl is a substance with systemic properties. Oilseed rape is a melliferous crop with high melliferous capacity. Residues in honey could be therefore expected.
Applicant provided data showing that for GF-4021 applied according the submitted GAP, the MRL for halauxifen-methyl can be expected to below 0.05 mg/kg for honey and bee products.

No additional data are required.

7.2.8 Estimation of exposure through diet and other means (KCA 6.9)

Toxicological reference values relevant for dietary risk assessment are reported in the summary of the evaluation (see 7.1.2).

7.2.8.1 Input values for the consumer risk assessment: Halauxifen-methyl

The input values in the following table were used to estimate consumer risk using the EFSA PRIMo Rev 3.1. All assessments follow the Tier I approach and are based on published MRL values (for all commodities) and assume no dissipation of residues. The acute dietary assessments are performed only for the consumption of commodities for which GAPs are notified.

Table 7.2.8.1-1: Input values for the consumer risk assessment: Halauxifen-methyl

Commodity	Chronic risk assessment		Acute risk assessment	
	Input value (mg/kg)	Comment	Input value (mg/kg)	Comment
Halauxifen-methyl (sum of halauxifen-methyl and X11393729 (halauxifen), expressed as halauxifen-methyl)				
Citrus fruits, Pome fruits; Stone fruits; Berries and small fruits; and Miscellaneous fruits	0.02*	* Indicates that the MRL is set at the limit of analytical quantification (EU Pesticides Database, accessed October 28, 2019)	Acute risk assessment was undertaken only with regard to the crops under consideration.	
Tree nuts	0.05*			
VEGETABLES, FRESH OR FROZEN (except Leaf vegetables (f) herbs and edible flowers)	0.02*			
Leaf vegetables (f) herbs and edible flowers	0.05*			
PULSES	0.02*			
OILSEEDS AND OILFRUITS	0.05*		0.05*	MRL for rapeseeds (EU Pesticides Database, accessed October 28, 2019)
CEREALS	0.02*		Acute risk assessment was undertaken only with regard to the crops under consideration.	
TEAS, COFFEE, HERBAL INFUSIONS, AND COCOA	0.1*			
HOPS (dried)	0.1*			
SPICES (except horseradish)	0.1*			
Horseradish	0.14			
SUGAR PLANTS	0.02*			
PRODUCTS OF ANIMAL ORIGIN -TERRESTRIAL ANIMALS except Honey and other apiculture products	0.02*			
Honey and other apiculture products	0.05*			

7.2.8.2 Conclusion on consumer risk assessment: Halauxifen-methyl

Extensive calculation sheets are presented in Appendix 3.

The highest Theoretical Maximum Daily Intake (TMDI) is 4% of the ADI for the Netherlands toddler. The highest contribution (2% ADI) is from cattle milk. Children have the highest International Estimated Short-Term Intake (IESTI) for unprocessed commodities at 0.1% of the ARfD for the consumption of rapeseeds/canola seeds, and for processed commodities at 0.1% of the ARfD for the consumption of rapeseeds/oils.

Table 7.2.8.2-1: Consumer risk assessment: Halauxifen-methyl

TMDI (% ADI) according to EFSA PRIMo	4% (based on NL toddler)
IESTI (% ARfD) according to EFSA PRIMo	Unprocessed Commodities: 0.1% based on consumption of rapeseeds/canola seeds by children Processed Commodities: 0.1% based on consumption of rapeseeds/oils by children

The proposed uses of halauxifen-methyl in the formulation GF-4021 do not represent unacceptable acute and chronic risks for the consumer.

zRMS comments:

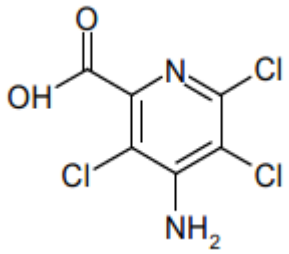
The consumer risk assessments were performed with revision 3.1 of the EFSA Pesticide Residues Intake Model (PRIMo). The calculation of the TMDI using EFSA model (version 3.1) and MRLs according to Reg. (EU) 2016/67 led to a utilisation of the ADI of 4% with the NL toddler being the population group with the highest value. For this diet, the highest contributor is Milk: Cattle with 2% of the ADI.
The intended uses will not result in a consumer chronic exposure exceeding the ADI.

For the calculation of the acute exposure the MRL has been used only for the use under consideration. The highest International Estimated Short-Term Intake (IESTI) is at 0.1% and 0.05% of the ARfD for the consumption of rapeseeds/canola by children and by adults respectively.
The proposed uses of halauxifen-methyl in the formulation GF-4021 do not represent unacceptable acute and chronic risks for the consumer.

7.3 Picloram

General data on picloram are summarized in the table below (last updated 2020/11/10)

Table 7.3-1: General information on picloram

Active substance (ISO Common Name)	Picloram
IUPAC	4-amino-3,5,6-trichlorpyridine-2-carboxylic acid
Chemical structure	
Molecular formula	$C_6H_3Cl_3N_2O_2$
Molar mass	241.46
Chemical group	Pyridines
Mode of action (if available)	Picloram is a systemic herbicide that deregulates plant growth through an 'auxinic' mode of action. It is absorbed by leaves and roots, translocated both acropetally and basipetally and accumulates in meristematic tissues of plants.
Systemic	Yes
Company	Dow AgroSciences*
Rapporteur Member State (RMS)	Poland (Co-RMS: Czech Republic) *Remark: the original RMS was the United Kingdom (UK)*
Approval status	Approved In force legislation: COMMISSION DIRECTIVE 2010/39/EU of 22 June 2010 (Original inclusion: COMMISSION DIRECTIVE 2008/69/EC of 1 July 2008.)
Restriction	Only uses as herbicide may be authorised.
Review Report	SANCO/835/08 – final.
Current MRL regulation	Regulation (EU) 2021/1531 ~~Reg (EU) 2016/1~~ ~~Reg. (EU) 2021/1531 – not yet applicable; new MRL values for Picloram will apply from 10/10/2021~~
Peer review of MRLs according to Article 12 of Reg No 396/2005 EC performed	in progress EFSA-Q-2009-00112
EFSA Journal : Conclusion on the peer review	Yes**
EFSA Journal: conclusion on article 12	Yes**
Current MRL applications on intended uses	NO – current MRL in oilseeds is compliant Oilseeds/canola seeds (0401060) Status: Reasoned opinion available Reg (EU) 2016/1 Reg (EU) No 737/2014 Reg (EU) No 839/2008 Reg (EU) No 149/2008

* Notifier in the EU process to whom the a.s. belong(s)
** EFSA Journal 2009; 7(12): 1390

7.3.1 Stability of Residues (KCA 6.1)

7.3.1.1 Stability of residues during storage of samples

Available data

No new data submitted in the framework of this application.

Table 7.3.1-1: Summary of stability data achieved at ≤ - 18°C (unless stated otherwise)

Matrix	Characteristics of the matrix	Acceptable Maximum Storage duration	Reference
Data relied on in EU EFSA, 2009			
Plant products			
Wheat Green Forage	High content water commodity	Approximately 36 Months (1096 Days)	S.Dolder, (2003), Frozen Storage Stability of Pic1oram in Wheat Green Forage, Wheat Straw, Wheat Grain, Soil, Water, Oilseed Rape Grain and Oilseed Rape Hay, DAS Study ID: 980075 EFSA Journal 2009; 7(12): 1390
Wheat Straw	~~Dry commodity~~ No group	Approximately 36 Months (1097 Days)	
Wheat Grain	~~Dry commodity~~ High starch commodity	Approximately 36 Months (1096 Days)	
Oilseed Rape Seed	High oil content commodity	Approximately 24 Months (728 Days)	
Oilseed Rape Hay	No group	Approximately 24 Months (731 Days)	
Animal Products			
Ruminant	Milk	Approximately 15 Months (447 Days)	Bjerke, E., (1988), Stability of Picloram In Milk and Egg Whites Stored Frozen, DAS Study ID: GHC-2079 EFSA Journal 2009; 7(12): 1390
Poultry	Egg	Approximately 19 Months (559 Days)	

Conclusion on stability of residues during storage

The results from the frozen storage stability study in crop matrices indicate that Picloram in crop samples from field studies can be stored frozen for at least 24-36 months with no observable degradation of residues.

The results from the frozen storage stability study in animal matrices show that residues of Picloram do not exhibit any significant degradation for at least 15 months in milk and 19 months in eggs while stored under frozen conditions.
Since crop samples were kept frozen for a maximum of 348 days in the submitted super-vised residue trials, sufficient stability data are available to support the residue data presented for GF-4021.

zRMS comments:

The stability of residues for the active substance picloram were reviewed at the EU level.
In the EFSA Journal 2013; 11(10):3439 it is concluded that the storage stability of picloram in primary crops was investigated in the DAR under Directive 91/414/EEC (United Kingdom, 2007). Residues of picloram were found to be stable at ≤ -20°C for up to 36 months in wheat forage, straw and grain samples and up to 24 months for oilseed rape seed and hay (in matrices with high oil content as well in dry matrices). As the supervised residue trial samples were stored under conditions for which integrity of the samples was demonstrated, it is concluded that the residue data are valid with regard to storage stability.
Additionally, picloram was also demonstrated to be stable in milk for up to 447 days and in egg whites for up to 559 days (EFSA Journal 2009; 7(12):1390).
No additionally data are required.

7.3.1.1 **Stability of residues in sample extracts** (KCA 6.1)

Available data
The stability of residues in sample extracts of different crop matrices were also confirmed through the inclusion of the procedural batch recovery samples along with the residue sample analyses. Therefore, the supervised residue trials data for the current application are valid with regard to stability of residues in stored sample extracts.

Conclusion on stability of residues in sample extracts
The supervised residue trials data for the current application are valid with regard to stability of residues in stored sample extracts.

zRMS comments:
The supervised residue trials data supporting the current application are valid with regard to stability of residues of picloram in stored samples extracts.

7.3.2 Nature of residues in plants, livestock and processed commodities

7.3.2.1 Nature of residue in primary crops (KCA 6.2.1)

Available data
No new data submitted in the framework of this application.

Table 7.3.2.1-1: Summary of plant metabolism studies

Crop Group	Crop	Label position	Application and sampling details					Reference
			Method, F or G (a)	Rate (kg a.s./ha)	No	Sampling (DAT)	Remarks	
EU data, EFSA 2009								
Pulses and oilseed	Oilseed rape	2,6-^{14}C pyridine ring	Foliar app at BBCH 33 (F)	40 g as/ha	1	Immature plants (1 (21 h), 30 (fractionated into leaves, stem and flower buds), 50 (fractionated into leaves, stem and pods)) Mature Roots/Tops (84, fractionated into stem, chaff and seeds)		Stenner, S. S., (2002), Metabolism of Picloram in Spring Oilseed Rape Following A Foliar Application, DAS Study ID: 000299 EFSA Journal 2009; 7(12): 1390
Cereals	Wheat	2,6-^{14}C pyridine ring	Foliar app at BBCH 13-22 (tillering) (F)	26 g a.s./ha and 53 g a.s./ha, separately	1	Forage (38) Straw/grain/chaff (104)	The plants were grown under outdoor screenhouse conditions. Two plots were treated, one at 1N and one at 2N rate.	Stenner, S. S. (1992), [14C] Picloram: Nature of the Residue in Wheat - MET92030, RES92105, HWI 6397-111, DAS Study ID: GH-C 2942

* Outdoor/field application (F) or glasshouse/protected/indoor application (G)

Summary of plant metabolism studies reported in the EU (EFSA, 2009)

The metabolism and distribution of picloram was investigated in oilseed rape and wheat. Picloram labelled in the 2,6-position of the ring was applied to oilseed rape at a rate of 1.7-fold the intended rate, and to wheat at the normal field rate (1N) as well as twice the intended rate (2N).

Total residues in oilseed rape plants at harvest (PHI 84 days) were accounting for 0.1 mg/kg and in the seeds for less than 0.01 mg/kg. Hence no further attempt was made to characterise or identify residues in the seed. In stem and chaff samples the main components identified were picloram (28% to 54% TRR), and a conjugated residue which released unchanged picloram (24% to 56%) when subjected to basic or acidic hydrolysis. A metabolite PYR was present in stem and chaff samples at very low levels (<0.005 mg/kg). The RMS concluded that the postulated metabolite 4-amino-3,5-dichloro-6-hydroxypicolinic acid (6-OH) was not detected in any samples, and that evidence of the metabolite 4-amino-2,3,5-trichloropyridine (PYR) was found in stem and chaff samples at maturity but not at levels considered of significance.

Total residues in wheat grain at harvest (PHI 104 days) were 0.05 mg/kg (1N) and 0.09 mg/kg (2N), and in straw 0.34 mg/kg (1N) and 0.52 mg/kg (2N), respectively. The majority of the TRR (75-90%) in straw and grain could be extracted with successive extraction steps. Hydrolysis of extracts using acid, alkali or β-glucosidase released parent picloram. Direct hydrolysis of samples of straw, grain and forage revealed the major component found in all samples to be parent picloram. The 6-OH metabolite and PYR were found at trace levels (≤0.002 mg/kg).

Both the oilseed rape and wheat studies demonstrate that picloram is not degraded but quickly forms conjugates in plant material. Hydrolysis of these conjugates releases picloram.

Conclusion on metabolism in primary crops

The metabolism and distribution of picloram was investigated in oilseed rape and wheat. Both studies demonstrated that picloram is not degraded but quickly forms conjugates in plant material. Hence, the residue definition for risk assessment was agreed as picloram, free and conjugated expressed as picloram.
Plant residue definitions were set as "picloram" for monitoring and "picloram free and conjugated expressed as picloram" for risk assessment.
The metabolic pathway of picloram in plant is sufficiently addressed and no additional metabolism studies are necessary to support the intended uses for GF-4021.

zRMS comments:

The metabolism of picloram in primary crops (oilseed rape and wheat) was evaluated by the RMS (United Kingdom, 2007, 2009) and reviewed by EFSA (EFSA, 2009) in the framework of the peer review under Directive 91/414/EEC.

The peer review proposed to set the residue definition for risk assessment as picloram, free and conjugated expressed as picloram whereas no final residue definition for enforcement was derived pending confirmatory data on the method of analysis (EFSA 2009).
Considering that the confirmatory data submitted to the EMS confirmed that the method of analysis, which was also used for analysing the residue trials, determines both free and conjugated picloram, EFSA proposes to include picloram conjugates in the residue definition for enforcement.
However, as the current residue definition for enforcement set in Regulation (EC) No 396/2005 comprises parent picloram only, a modification of the residue definition requires to assess the impact on the existing MRLs. Currently barley, maize, oats, sorghum, wheat, other cereals, ~~and~~ sugar cane and flowering brassica are the only crops for which MRLs have been set above the LOQ. If the picloram conjugates are included in the residue definition as proposed by the EFSA, the existing MRLs for these crops might need to be revised. Thus, EFSA proposes to amend the residue definition in the framework of the MRL review under Article 12 of Regulation (EC) No 396/2005; only on this occasion a full overview will be available on the authorised GAPs and the relevant residue trials which will allow to take a final decision on the MRLs needed. For the current MRL application the existing enforcement residue definition should be considered.
EFSA concludes that the metabolism of picloram in rape seed is sufficiently addressed. As long as the MRL review under Article 12 of Regulation (EC) No 396/2005 is not yet finalised, the existing enforcement residue definition can be maintained (i.e. parent picloram), but in future the picloram conjugates should be included in the

enforcement residue definition. For risk assessment, the residue definition is agreed to be the sum of picloram and its conjugates, expressed as picloram.
No additional metabolism studies are necessary to support the intended uses for GF-4021.

7.3.2.2 Nature of residue in rotational crops (KCA 6.6.1)

Available data

New data submitted in the framework of this application. ~~No~~

Table 7.3.2.2-1: Summary of metabolism studies in rotational crops

Crop group	Crop	Label position	Application and sampling details					Reference
			Method, F or G *	Rate (kg a.s./ha)	Sowing intervals (DAT)	Harvest Intervals (DAT)	Remarks	
EU data, EFSA 2009								
Leafy vegetables	Mustard green	2,6-^{14}C pyridine ring	Single app to sandy loam soil (F)	583 g as/ha	30, 120, and 365	Mature	Outdoor screened enclosure.	Kimmel, E. ; Aldcroft, K. S. ; Ewing, A.L., (1993), A Confined Rotational Crop Study With 14C-Picloram Using Turnips, Mustard Greens, Wheat, and Corn - MET9106; Ptrl No. 311W, DAS Study ID GH-C 2971R EFSA Journal 2009; 7(12): 1390
Root and tuber vegetables	Turnip	2,6-^{14}C pyridine ring	Single app to sandy loam soil (F)	583 g as/ha	30, 120, and 365	Mature root and tops	Outdoor screened enclosure.	
Cereals	Wheat	2,6-^{14}C pyridine ring	Single app to sandy loam soil (F)	583 g as/ha	30, 120, and 365	Forage, Straw, chaff and grain at maturity	Outdoor screened enclosure.	
Oilseed	Maize	2,6-^{14}C pyridine ring	Single app to sandy loam soil (F)	583 g as/ha	30, 120, and 365	Forage (silage-stage, R5), mature (R6 divided into fodder, grain, and cobs	Outdoor screened enclosure.	
Leafy vegetables	Lettuce	2,6-^{14}C	Single app to sandy loam soil (F)	25 g ae/ha	30, 60, 335	Immature and Mature		Croffie, J. W., Adelfinskaya, Y., Hastings, M; (2016). A Confined Rotational Crop Study with 14C-Picloram. DAS Study No. 130200
Root and tuber vegetables	Radish	2,6-^{14}C	Single app to sandy loam soil (F)	25 g ae/ha	30, 60	Mature root and tops		
Cereals	Wheat	2,6-^{14}C	Single app to sandy loam soil (F)	25 g ae/ha	30, 60, 335	Forage, Hay, Straw, and grain at maturity		

* Outdoor/field application (F) or glasshouse/protected/indoor application (G)

Summary of plant rotational metabolism studies reported in the EU

In a GLP study conducted in 1991, radio-labelled picloram labelled in the 2, 6 position of the ring (radiochemical purity 99.7%) was applied as a spray to confined plots containing sandy loam soil at a rate of 0.583 kg/ha (ca 25N). The soil was allowed to age for 30, 120 and 365 days and was lightly cultivated

prior to planting. Crops of wheat (var. Len), corn/maize (var. Hybrid 3751), mustard green (var. Southern Giant Curled Long Standing) and turnip (var. Seven Top) were planted for each plant back interval.

As summarized by EFSA, (EFSA Journal 2009; 7(12):1390):
The TRR in cereal forage and straw were generally seen to decline with longer plant back intervals. The TRR for cereal grain and turnip tops for the 120-day plant back interval were higher than those found at other the plant back intervals. The TRR in turnip roots remained relatively stable across all plant back intervals.
Generally, the residue profile was similar across all crops. In most cases parent picloram was the major residue found. Acid hydrolysis of extracts released further picloram, indicating that metabolites A, B and C were most likely conjugates of picloram. Metabolite PYR was found in wheat, maize and turnip samples, but in all cases, it was present at low levels.
It has been concluded that picloram, and possibly any conjugates found in the soil, are readily transported into succeeding crops. The vast majority of radioactivity is present as picloram or conjugates of picloram. The metabolism in succeeding crops is similar to that seen in primary crops. Thus, the same residue definition as for primary crops is appropriate.
Residues above the limit of quantification (LOQ) may be expected in rotational crops. The PRAPeR 70 meeting of experts agreed that the confined rotational crop study could be used to conduct a risk assessment and to propose MRLs for certain rotational crops.

A new confined rotational crop study was conducted with a single application of ^{14}C-Picloram at a target rate of 25 g a.i./ha made to the surface of bare soil plots. For the purpose of renewal of a.s. approval, these studies were considered as acceptable. Wheat, radishes, and lettuce were planted at intervals of 30, 60, and 335 days after application. Results were consistent with the previous confined crop rotational study which was conducted at the higher rotational cropland use rate of 661 g a.i./ha; the Picloram levels (free plus conjugated) in the new confined crop rotational study were similar to those observed in the previous study when application rate was normalized to a 1N rate. In the new study, at all plant back intervals, total Picloram residues (free plus conjugated) in wheat grain were lower than the existing EU MRL (0.2 mg/kg). Although a 90- to 120-d plant back interval was not conducted in the current study, significant residue decline from the 60- to the 335-d PBIs would indicate that application to oilseed rape at 25 g a.i./ha, including consideration of crop intercept, followed by planting the field with wheat after 120 days, the total Picloram residues in wheat grain at 120-d plant back interval would be significantly lower than the existing EU MRL. Following a 335-d plant back interval, residues in root and leafy vegetables were lower than the previous study, at less than 0.01 mg/kg total Picloram.
The majority of the residue, generally >70% of the TRR was characterized as Picloram or conjugates of Picloram. Individual conjugates were not identified.
The longest laboratory DT_{90} was greater than 700 days and the longest DT_{90} field in soil was found to be 163 days. It is therefore possible that > 10% of the applied active substance as its relevant metabolites or degradation products could still remain in soil at replanting of succeeding crops.
In a confined crop rotation study, radio-labelled picloram was applied to the soil at a rate 25-fold the intended application rate. The soil was allowed to age for 30, 120 and 365 days and was lightly cultivated prior to planting. Crops of wheat, maize, mustard green and turnip were planted for each plant back interval. The TRR in cereal forage and straw were generally seen to decline with longer plant back intervals. The TRR for cereal grain and turnip tops for the 120-day plant back interval were higher than those found at other plant back intervals. The TRR in turnip roots remained relatively stable across all plant back intervals.

Generally, the residue profile was similar across all crops. In most cases parent picloram was the major residue found. Acid hydrolysis of extracts released further picloram, indicating that metabolites A, B and C were most likely conjugates of picloram. Metabolite PYR was found in wheat, maize and turnip samples, but in all cases, it was present at low levels.

It has been concluded that picloram, and possibly any conjugates formed in the soil, are readily transported into succeeding crops. The vast majority of radioactivity is present as picloram or conjugates of picloram.

The metabolism in succeeding crops is similar to that seen in primary crops. Thus, the same residue definition as for primary crops is appropriate.

Residues above the LOQ may be expected in rotational crops. The PRAPeR 70 meeting of experts agreed that the confined crop rotation study could be used to conduct a risk assessment and to propose MRLs for certain rotational crops. Nevertheless, rotational field crop studies should be submitted to either confirm the proposed MRLs or to modify the proposed MRLs if necessary. The TRR observed in the ether partition fraction in the rotational crop study is considered to be a worst-case assumption for the residues of free and conjugated picloram. On this basis, the PRAPeR 70 meeting of experts proposed provisional MRLs for fruiting vegetables, brassica vegetables, leafy vegetables, stem vegetables, herbal infusion and spices, legume vegetables, pulses, cereal grains, root vegetables and oilseeds. The occurrence of picloram residues in rotational crops was investigated in the framework of the peer review and referred to a single application of picloram on rape seed every three years.

Conclusion on metabolism in rotational crops

In a confined crop rotation study metabolism in succeeding crops was found to be similar to that seen in primary crops. In the tested rotational cereal, oilseed and root crops the vast majority of radioactivity was present as picloram or conjugates of picloram. Residues above the limit of quantification (LOQ) may be expected in rotational crops.

On the basis of the new confined study the 335-day plant-back interval, total free plus conjugated Picloram residues in all human-consumed crops were ≤0.015 mg/kg. Residues in animal feed commodities were also low.

Metabolism in succeeding crops is similar to that seen in primary crops. The same residue definitions as for primary crops apply.

The metabolic pathway in rotational plant is sufficiently addressed and no additional metabolism studies are necessary to support the intended uses for GF-4021.

zRMS comments:

The metabolism of picloram in rotational crops was evaluated at EU level.

In EFSA Journal 2009; 7(12):1390 it is concluded that in a confined crop rotation study metabolism in succeeding crops was found to be similar to that seen in primary crops. In the tested rotational cereal, oilseed and root crops the vast majority of radioactivity was present as picloram or conjugates of picloram. Residues above the limit of quantification (LOQ) may be expected in rotational crops. On the basis of the confined study default levels were derived for several rotational crops to conduct a risk assessment and to propose maximum residue limits (MRLs). Nevertheless, rotational field crop studies should be submitted to confirm the proposed MRLs, or to modify the proposed MRLs if necessary.

The data on metabolism and distribution of picloram in succeeding crops demonstrate that the metabolism of the active substance in rotational crops is similar to the pathway observed in primary crops. Thus, the same residue definition applies (EFSA, 2009).

Oilseed rape can be grown in rotation with other plants. EFSA concluded in EFSA Journal 2013; 11(10):3439 that *The soil degradation studies demonstrated that the degradation rate of picloram is moderate; the maximum field DT_{90} (considered only valid for application rates up 52 g/ha) was 163 days (EFSA, 2009), which is above the trigger value of 100 days. Thus, further studies investigating the nature and magnitude of the compound uptake in rotational crops are required (EC, 1997c).*

Applicant submitted in the framework of this application an additional confined rotational crop study performed at 1N rate. The assessment of the study is presented in Appendix 2. It should be noted that the results are in line with the previous confined crop rotational study. In a confined crop rotation study metabolism in succeeding crops was found to be similar to that seen in primary crops.

The metabolic pathway in rotational plant is sufficiently addressed and no additional metabolism studies are necessary to support the intended uses for GF-4021.

7.3.2.3 Nature of residues in processed commodities (KCA 6.5.1)

Available data
No new data submitted in the framework of this application.

Conclusion on nature of residues in processed commodities
Data on the effects of industrial- and household processing on residues were not required.

zRMS comments:
Since all residues in seed of oilseed rape are < 0.01 mg/kg and no residues of picloram exceeding 0.1 mg/kg are expected in the treated crops and TMDI is below 10% of the ADI, further considerations about the effects of processing are not required in the framework of this dossier.

7.3.2.4 Conclusion on the nature of residues in commodities of plant origin KCA 6.7.1)

Table 7.3.2.4-1: Summary of the nature of residues in commodities of plant origin

Endpoints	
Plant groups covered	Pulses and Oilseeds (Oilseed rape) Cereals (Wheat)
Rotational crops covered	Yes
Metabolism in rotational crops similar to metabolism in primary crops?	Yes
Processed commodities	not required
Residue pattern in processed commodities similar to pattern in raw commodities?	Not applicable
Plant residue definition for monitoring	Picloram, pending the MRL review under Article 12 of Regulation (EC) No 396/2005 (EFSA 2013) Picloram ~~(Reg. (EU) 2016/1)~~ Reg. (EU) 2021/1531
Plant residue definition for risk assessment	Picloram, free and conjugated expressed as picloram (EFSA 2009)
Conversion factor from enforcement to RA	None

7.3.2.5 Nature of residues in livestock (KCA 6.2.2-6.2.5)

Available data
No new data submitted in the framework of this application.

Table 7.3.2.5-1: Summary of animal metabolism studies

Group	Species	Label position	No of animal	Application details		Sample details		Reference
				Rate (mg/kg bw/d)	Duration (days)	Commodity	Time of sampling	
EU data, EFSA 2009								
Lactating ruminants	Goat	2,6-^{14}C	1 dosed	1200 mg/kg feed	4	Milk	Twice daily	Yackovich, P. R. ; Byrne, S. L., (1992), Nature of Residues of 14C Labelled Picloram in the Lactating , DAS Study ID: MET92043 EFSA Journal 2009; 7(12): 1390
						Urine and faeces	Twice daily	
						Tissues (muscle (leg and loin), fat (omental and renal), liver, kidney, and GI tract and contents)	at sacrifice (*ca* 23 hours after final dose)	
Laying poultry	Hens	2,6-^{14}C	5 per group (3 groups)	45 mg/kg feed	7	Eggs (separated into whites and yolks)	Twice daily	Yackovich, P.R.; Miller, J. H., (1992), The Fate of 14C Labelled Picloram Fed To Laying Hens, DAS Study ID: GH-C 1827 EFSA Journal 2009; 7(12): 1390
						Excreta	Twice daily	
						Tissues (muscle (breast and thigh), skin, liver, kidney, fat, blood, heart, abdominal egg yolks, gizzard, GI tract contents)	at sacrifice (*ca* 23 hours after final dose)	

7.3.2.6 Conclusion on the nature of residues in commodities of plant origin KCA 6.7.1)

Table 7.3.2.4-1: Summary of the nature of residues in commodities of plant origin

Endpoints	
Plant groups covered	Pulses and Oilseeds (Oilseed rape) Cereals (Wheat)
Rotational crops covered	Yes
Metabolism in rotational crops similar to metabolism in primary crops?	Yes
Processed commodities	not required
Residue pattern in processed commodities similar to pattern in raw commodities?	Not applicable
Plant residue definition for monitoring	Picloram, pending the MRL review under Article 12 of Regulation (EC) No 396/2005 (EFSA 2013) Picloram ~~(Reg. (EU) 2016/1)~~ Reg. (EU) 2021/1531
Plant residue definition for risk assessment	Picloram, free and conjugated expressed as picloram (EFSA 2009)
Conversion factor from enforcement to RA	None

7.3.2.7 Nature of residues in livestock (KCA 6.2.2-6.2.5)

Available data

No new data submitted in the framework of this application.

Table 7.3.2.5-1: Summary of animal metabolism studies

Group	Species	Label position	No of animal	Application details		Sample details		Reference
				Rate (mg/kg bw/d)	Duration (days)	Commodity	Time of sampling	
EU data, EFSA 2009								
Lactating ruminants	Goat	2,6-^{14}C	1 dosed	1200 mg/kg feed	4	Milk	Twice daily	Yackovich, P. R. ; Byrne, S. L., (1992), Nature of Residues of 14C Labelled Picloram in the Lactating , DAS Study ID: MET92043 EFSA Journal 2009; 7(12): 1390
						Urine and faeces	Twice daily	
						Tissues (muscle (leg and loin), fat (omental and renal), liver, kidney, and GI tract and contents)	at sacrifice (*ca* 23 hours after final dose)	
Laying poultry	Hens	2,6-^{14}C	5 per group (3 groups)	45 mg/kg feed	7	Eggs (separated into whites and yolks)	Twice daily	Yackovich, P.R.; Miller, J. H., (1992), The Fate of 14C Labelled Picloram Fed To Laying Hens, DAS Study ID: GH-C 1827 EFSA Journal 2009; 7(12): 1390
						Excreta	Twice daily	
						Tissues (muscle (breast and thigh), skin, liver, kidney, fat, blood, heart, abdominal egg yolks, gizzard, GI tract contents)	at sacrifice (*ca* 23 hours after final dose)	

Summary of animal studies reported in the EU

On the basis of the proposed MRLs in rotational crops the experts considered livestock intake that was found to be significant for ruminants.

The metabolism and distribution of picloram was investigated in lactating ruminants and poultry.

One lactating goat was dosed daily by capsule for four consecutive days at a dose rate of 1200 mg/kg diet as received (17.4 mg/kg BW). The majority (*ca* 90%) of the dose administered was excreted, mainly in the urine. Residues in milk were seen to increase after dosing, declining rapidly prior to the next dose. The higher residue levels seen after dosing did not increase significantly with successive doses, indicating that a steady state was reached by the second day of dosing. The highest levels of the TRR were found in the kidney.

The major component identified in all tissues was the parent picloram accounting for 88% TRR (0.16 mg/kg) for milk, 97% TRR (0.25 mg/kg) for muscle, 88% TRR (3.03 mg/kg) for kidney, 56% TRR (0.076 mg/kg) for liver and 45% TRR (0.01 mg/kg) for fat. In both fat and liver, a significant proportion of the radioactivity was initially assigned as non-polar residues (47% TRR, 0.011 mg/kg for fat and 21% TRR, 0.028 mg/kg for liver). Further analysis by HPLC showed the non-polar fractions to consist of many components with a chromatographic profile similar to the non-polar impurities found in the original test material. This radioactivity is considered by the notifier to be due to impurities and not to metabolites of

picloram.

Laying hens were dosed orally by capsule for seven consecutive days at a rate of 45 mg/kg diet as received. The majority (*ca* 85-90%) of the dose administered was excreted. Residues in egg whites reached a plateau after 2-3 days, however residues in egg yolks did not reach a plateau during the dosing period studied. The highest levels of the TRR in tissues consumed by humans were found in the kidney.

Extractability was high for all tissues studied (>95%). In all tissues the major component identified was unchanged parent picloram. No further work was conducted to identify or characterise the remaining radioactivity, since the corresponding TRR values were low (ranging from <0.01 – 0.024 mg/kg).

Picloram was not metabolised to any significant degree in goats and poultry. Based on the metabolism data submitted, residues in animal products should be defined as picloram for both risk assessment and monitoring purposes.

EFSA, 2013
Since rape seed and its by-products are used as feed products, a potential carry-over into food of animal origin was assessed. The calculated livestock dietary burden exceeded the trigger value of 0.1 mg/kg (dry matter) for all relevant species but was mainly driven by the existing MRLs for feed products. The impact of picloram residues in rape seed to the total livestock exposure was insignificant and therefore the modification of the MRLs for commodities of animal origin is not further investigated in the framework of the current application.
No MRL is necessary for animal products since residues are unlikely to be significant. The addendum has not been peer reviewed, however EFSA has verified the assessment provided and agrees with the conclusion that residues in animal products are expected to be less than 0.01 mg/kg.

Conclusion on metabolism in livestock
The metabolism and distribution of picloram was investigated in lactating ruminants and poultry. Picloram was not metabolised to any significant degree in goats and poultry. Based on the metabolism data submitted, residues in animal products should be defined as picloram for both risk assessment and monitoring purposes. A re-assessment of residues in food of animal origin after the experts' meeting (Addendum 6, July 2009) indicated that residues in products of animal origin are unlikely to be significant.

zRMS comments:

The metabolism of picloram was evaluated in the framework of the approval of picloram. In the EFSA Journal 2009; 7(12):1390 it is stated that *The metabolism and distribution of picloram was investigated in lactating ruminants and poultry.(…) Based on the metabolism data submitted, residues in animal products should be defined as* ***picloram*** *for both risk assessment and monitoring purposes.*
EFSA concluded that residues in animal products are expected to be less than 0.01 mg/kg (EFSA, 2009).
Additionally, according to the EFSA Journal 2013; 11(10):3439: *The impact of picloram residues in rape seed to the total livestock exposure was insignificant and therefore the modification of the MRLs for commodities of animal origin is not further investigated in the framework of the current application.*

Taking into account the intended uses for product GF-4021, it should be noted that the residue of picloram in oilseed rape has a negligible impact on the overall exposure of livestock.
Further considerations are not required in the framework of this dossier.

7.3.2.8 Conclusion on the nature of residues in commodities of animal origin (KCA 6.7.1)

Table 7.3.2.6-1: Summary on the nature of residues in commodities of animal origin

	Endpoints
Animals covered	Lactating goats
	Laying hens
Time needed to reach a plateau concentration	2 days in milk
	2-3 days in egg whites, egg yolks did not reach a after 7 days
Animal residue definition for monitoring	Picloram (EFSA 2009) Reg. (EU) 2021/1531
Animal residue definition for risk assessment	Picloram (EFSA 2009)
Conversion factor	None (EFSA 2009)
Metabolism in rat and ruminant similar	Yes (EFSA 2009) No metabolism study in swine is needed.
Fat soluble residue	No (EFSA 2009)

7.3.3 Magnitude of residues in plants (KCA 6.3)

7.3.3.1 Summary of European data and new data supporting the intended uses

The MRL for picloram in oilseed rape is based on a critical GAP of one application at a rate of 24 g ae/ha at growth stage BBCH 50. The evaluation leading to the current MRL for picloram in oilseed rape is presented in the RMS 2012 and EFSA 2013. The critical GAP upon which the EU MRL for picloram was set covers the use of GF-4021 proposed in this submission.

Sufficient trials on oilseed rape were previously presented and evaluated in the RMS 2012 and EFSA 2013. A summary of the residue trial data for oilseed rape is provided in the Table below.

Data, previously evaluated by zRMS, France (RR, GF-3447, 2019) are also relied upon for this application. Study RDE-15-20345 (evaluated by zRMS, France (RR, GF-3447, 2019)) on the magnitude of residue has been submitted by the applicant in the framework of this application for GF-4021. This study is summarized in the Table below and the detailed assessment is presented in Appendix 2. The GAP proposed for GF-4021 results in an application rate for picloram that is less intensive (1 x 12 g ae/ha) than that which the EU MRL is based (1 x 24 g ae/ha). Consequently, the existing proposed EU MRL of 0.03 mg/kg for picloram and the associated critical GAP upon which it is based fully covers the proposed GAP for GF-4021 in this submission with regard to picloram and will not lead to residues exceeding the

proposed EU MRL. The detailed assessment of these studies is presented in Appendix 2.

Table 7.3.3.1-1: Summary of EU reported and new data supporting the intended uses of GF-4021 and conformity to existing MRL

Commodity	Source	Residue zone (N-EU, S-EU, EU, outside EU)	Evaluation GAP Picloram Residue levels (mg/kg) E = according to enforcement residue definition RA = according to risk assessment residue definition	STMR (mg/kg)	HR (mg/kg)	Unrounded OECD calculator MRL (mg/kg)	Current EU MRL (mg/kg) *	MRL compliance
Oilseed rape seeds	EFSA, 2013, MRL ER (UK), 2012	N-EU	GAP on which MRL/EU a.s. assessment is based: 1 x 24 g ae/ha, BBCH 50, outdoor E & RA: 7 x <0.01, 0.02 ~~RA: 7 x <0.01, 0.02~~	0.01	0.02	0.03	0.03	Yes
	RR GF-3447, France, 2018 (RDE-15-20345)	N-EU	Trials GAP: 0.5 L/ha (4.8 g ae/ha of halauxifen-methyl and 24 g ae/ha of picloram), BBCH 16-30, (including 6N at BBCH 19-30), outdoor E & RA: 6 x <0.01	0.01*	0.01*	0.01*	0.03	Yes
	RR GF-3447, France, 2018 (RDE-15-20345)	S-EU	Trials GAP: 0.5 L/ha (4.8 g ae/ha of halauxifen-methyl and 24 g ae/ha of picloram), BBCH 16-30, (including 8S at BBCH 19-30), outdoor E & RA: 10x <0.01	0.01*	0.01*	0.01*	0.03	Yes

* Source of EU MRL: Regulation (EU) 2021/1531 ~~Part A of Annex I to Reg. 396/2005~~

7.3.3.2 Conclusion on the magnitude of residues in plants

According to the available data, the intended use on oilseed rape is considered acceptable, for outdoor uses.

The data submitted show that no exceedance of the MRL will occur.
The uses are considered acceptable.

zRMS comments:

The intended use for GF-4021 is oilseed rape. Oilseed rape is the major crop in northern Europe (EU guideline Document ~~SANCO/7525/VI/95-rev.10.3 of 13 June 2017~~ SANTE/2019/12752). A minimum of eight trials are required.

Table 7.2: Intended cGAP for GF-4021

Crop	Number of applications	Application rate per treatment (gai/ha)	Interval between application	Growth stage at last application	PHI (days)
Oilseed rape	1	Halauxifen-methyl: 2.5 g ae/ha + Picloram: 12 g ae/ha + Aminopyralid: 8 g ae/ha	N/A	BBCH 12-19	-

Study RDE-15-20345 (evaluated by zRMS, France (RR, GF-3447, 2019)) on the magnitude of residue has been submitted by the applicant in the framework of this application for GF-4021.
Sixteen residue trials: 6 NEU and 10 SEU were conducted on oilseed rape. The product was applied ones to oilseed rape at maximum application rate of 24 g picloram/ha. The application was done up to BBCH 30. It covers the intended GAP (one application, rate 12 g picloram/ha, BBCH 12-19).
The maximum frozen storage period of samples prior to the analysis was 375 days. All residue data reported within the present submission are covered by the storage period.
Residues of picloram were determined according to method described in Dow AgroSciences Study Number 120610. The limit of quantification was 0.01 mg/kg.
Levels of residue are below the LOQ of 0.01 mg/kg for picloram for all the submitted trials.
According to the SANTE/2019/12752 if the residue levels in plants or plant products are lower than the limit of quantification (LOQ), the number of independent trials may be reduced. The number of trials shall not be below the minimum of four per zone for major crops. So there are sufficient residue trials to support the intended use of picloram on oilseed rape.

The value of EU MRL for picloram on oilseed rape equals 0.03 mg/kg (Regulation (EU) 2021/1531 ~~2016/1~~). The residues arising from the proposed use will not exceed the MRL established for oilseeds.
The current EU MRL for picloram is sufficient to support the proposed use.
Additionally it should be mentioned that oilseed rape straws are not fed to animals. Therefore, no consideration about this item is required.

No additional data are required.

7.3.4 Magnitude of residues in livestock

7.3.4.1 Dietary burden calculation

Table 7.3.4.1-1: Input values for the dietary burden calculation

Feed Commodity	Median dietary burden		Maximum dietary burden	
	Input value (mg/kg)	Comment	Input value (mg/kg)	Comment
Risk assessment residue definition: the sum of picloram and its conjugates, expressed as picloram				
Barley, corn (field and pop), oats, sorghum, triticale and wheat grain	0.2	EU MRL	0.2	EU MRL
Brewer's grain, dried	0.66 (0.2 x 3.3)	EU MRL x default PF	0.66 (0.2 x 3.3)	EU MRL x default PF
Canola meal	0.02 (0.01* x 2)	STMR (EFSA, 2013) x default PF	0.02 (0.01* x 2)	STMR (EFSA, 2013) x default PF
Corn, field / milled by-products	0.20 (0.2 x 1)	EU MRL x default PF	0.20 (0.2 x 1)	EU MRL x default PF
Corn, field / hominy meal	1.20 (0.2 x 6)	EU MRL x default PF	1.20 (0.2 x 6)	EU MRL x default PF
Corn, field / gluten feed	0.50 (0.2 x 2.5)	EU MRL x default PF	0.50 (0.2 x 2.5)	EU MRL x default PF
Corn, field / gluten, meal	0.20 (0.2 x 1)	EU MRL x default PF	0.20 (0.2 x 1)	EU MRL x default PF
Distiller's grain, dried	0.66 (0.2 x 3.3)	EU MRL x default PF	0.66 (0.2 x 3.3)	EU MRL x default PF
Rape meal	0.02 (0.01* x 2)	STMR (EFSA, 2013) x default PF	0.02 (0.01* x 2)	STMR (EFSA, 2013) x default PF
Wheat gluten meal	0.36 (0.2 x 1.8)	EU MRL x default PF	0.36 (0.2 x 1.8)	EU MRL x default PF
Wheat milled by-products	1.40 (0.2 x 7)	EU MRL x default PF	1.40 (0.2 x 7)	EU MRL x default PF

N.B. In the absence of specific processing studies, default (EFSA) processing factors (PFs) were used in the calculation.

The results of the dietary burden calculations are summarised in the following tables.

Table 7.3.4.1-2: Results of the dietary burden calculation

Old data requirements (Regulation (EU) No 544/2011)

Relevant groups	Dietary burden expressed in mg/kg bw per day		Dietary burden expressed in mg/kg DM		Most critical diet (a)	Most critical commodity		Trigger exceeded (Yes/No) 0.10 mg/kg DM
	Median	Maximum	Median	Maximum				
Cattle (all diets)	0,022	0,022	0,64	0,64	Beef cattle	Wheat	milled bypdts	Yes
Cattle (dairy only)	0,022	0,022	0,57	0,57	Dairy cattle	Wheat	milled bypdts	Yes
Sheep (all diets)	0,039	0,039	0,91	0,91	Lamb	Wheat	milled bypdts	Yes
Sheep (ewe only)	0,024	0,024	0,73	0,73	Ram/Ewe	Wheat	milled bypdts	Yes
Swine (all diets)	0,027	0,027	0,91	0,91	Swine (breeding)	Wheat	milled bypdts	Yes
Poultry (all diets)	0,034	0,034	0,50	0,50	Poultry layer	Wheat	milled bypdts	Yes
Poultry (layer only)	0,034	0,034	0,50	0,50	Poultry layer	Wheat	milled bypdts	Yes

(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 DM per day".

Based on the intakes calculated above, picloram intakes exceed the trigger values of 0.1 mg/kg DM (Reg. (EU) 544/2011) for all relevant species. Therefore, feeding studies are required.

However, EFSA stated in the modification of the MRL on rape seed and mustard seed that the contribution of rapeseed is insignificant and therefore EFSA did not investigated further the need to modify the existing MRLs for commodities of animal origin. Indeed, as it can be seen in Table 7.3.4.**1-3**, animal exposures are unchanged when removing rape seed meal from their diets.

Table 7.3.4.1-3: Results of the dietary burden calculation – scenario 2: without rape seed meal

Old data requirements (Regulation (EU) No 544/2011)

Relevant groups	Dietary burden expressed in mg/kg bw per day		Dietary burden expressed in mg/kg DM		Most critical diet (a)	Most critical commodity		Trigger exceeded (Yes/No) 0.10 mg/kg DM
	Median	Maximum	Median	Maximum				
Cattle (all diets)	0,022	0,022	0,64	0,64	Beef cattle	Wheat	milled bypdts	Yes
Cattle (dairy only)	0,022	0,022	0,57	0,57	Dairy cattle	Wheat	milled bypdts	Yes
Sheep (all diets)	0,039	0,039	0,91	0,91	Lamb	Wheat	milled bypdts	Yes
Sheep (ewe only)	0,024	0,024	0,73	0,73	Ram/Ewe	Wheat	milled bypdts	Yes
Swine (all diets)	0,027	0,027	0,91	0,91	Swine (breeding)	Wheat	milled bypdts	Yes
Poultry (all diets)	0,034	0,034	0,50	0,50	Poultry layer	Wheat	milled bypdts	Yes
Poultry (layer only)	0,034	0,034	0,50	0,50	Poultry layer	Wheat	milled bypdts	Yes

(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 DM per day".

Although animal intakes exceed the trigger value for all animal groups, results of both tested scenarios indicate that the contribution of rape seed meal to the total livestock exposure is insignificant. Therefore, no further considerations about livestock are required in this dossier.

A comprehensive assessment, taking into account all authorized uses and the supporting studies will be performed in the framework of the MRL review under Article 12 of regulation (EC) N°396/2005.

7.3.4.2 Livestock feeding studies (KCA 6.4.1-6.4.3)

Available data - EFSA Reasoned Opinion, 2013

In order to estimate the contribution of picloram residues in rape seed to the total livestock dietary exposure, EFSA calculated a second scenario (scenario 2) without rape seed.

The results indicate that the trigger value of 0.1 mg/kg dry matter (DM) is exceeded for all animal

commodities in both scenarios. From the comparison of the two scenarios it is evident that the contribution of the rape seed to the total livestock exposure is insignificant. Therefore, EFSA did not further investigate the need to modify the existing MRLs for commodities of animal origin in the framework of the current application. A comprehensive assessment, taking into account all authorised uses and the supporting studies will be performed in the framework of the MRL review under Article 12 of Regulation (EC) No 396/2005.

No livestock feeding studies are required since residues in oilseed rape seed are low and picloram residues in livestock diets would not reach a level where feeding studies would be required. Therefore, no studies are submitted in the framework of this application.

Conclusion on feeding studies

The requested uses (or the new mode of calculation) modify the theoretical maximum daily intake for animals, but regarding available feeding data, there is no risk for animal MRL to be exceeded.

In the framework of the modification of the MRL on rape seed and mustard seed that the contribution of rapeseed was deemed insignificant (EFSA, 2013). Therefore, the modification of the MRLs for commodities of animal origin is not further investigated in the framework the MRL modification.
The input values used in the framework of the MRL modification cover the intended uses under assessment in the present application. Therefore, the same conclusions can be drawn.

No further data are required. The requested uses (or the new mode of calculation) modify the theoretical maximum daily intake for animals, but regarding available feeding data, there is no risk for animal MRL to be exceeded.

zRMS comments:
Information given by the Applicant is sufficient and zRMS-Poland agrees with presented above conclusions. No further data are required.

7.3.5 Magnitude of residues in processed commodities (Industrial Processing and/or Household Preparation) (KCA 6.5.2-6.5.3)

Available data – EFSA Reasoned Opinion, 2013
No new data submitted in the framework of this application.

7.3.5.1 Available data for all crops under consideration

Available data – EFSA Reasoned Opinion, 2013
No new data were submitted in the framework of this application.

7.3.5.2 Conclusion on processing studies

Processing studies are not required as they are not expected to affect the outcome of the risk assessment. No residues of picloram exceeding 0.1 mg/kg are expected in the treated crops. There is consequently no need to further investigate the effect of industrial and/or household processing.

zRMS comments:
Information given by the Applicant is sufficient. Since all residues in seed of oilseed rape are < 0.01 mg/kg and no residues of picloram exceeding 0.1 mg/kg are expected in the treated crops and TMDI is below 10% of the ADI, further considerations about the effects of processing are not required in the framework of this dossier. No further data are required.

7.3.6 Magnitude of residues in representative succeeding crops

The use of picloram assessed in the peer review referred to a single application of picloram on oilseed rape every three years at an application rate of 0.024 kg a.s./ha and the latest growth stage BBCH 31. The applicant now applies for the use of picloram on oilseed rape every year at a less intensive application rate (0.012 kg a.s./ha), with the last application done at the growth stage of BBCH 19.

The new field rotational crop studies investigating the magnitude of picloram residues in rotational crops were submitted by applicant to support the use of picloram on rape seed every year. zRMS France evaluated these studies (GF-3447 RR) and they are summarised in A 2.2.6.1.

Presented data demonstrate that following application of picloram at 25 g ai/ha and planting leafy vegetable, root crops or cereals at about 120 days later, the predicted residues in root, leafy vegetable and cereals crops will be below 0.01 mg/kg.
Based on the results of these new field rotational crop studies and based on the proposed critical GAP for GF-4021, a waiting period beyond normal crop harvest for oil seed rape is not specified since soil residues are expected to be sufficiently low by the time treated oilseed rape is harvested.
However, label should include a statement that in case of necessity for termination of plantation treated with GF-4021 because of crops damages caused by frost, diseases or insects, do not plant succeeding crops until 120 days since use of GF-4021 (zRMS France, GF-3447).

7.3.6.1 Field rotational crop studies (KCA 6.6.2)

As mentioned in section 7.3.2.2, according to the results of the confined rotational crop study submitted in the framework of picloram's inclusion process, residues above the LOQ may be expected in rotational crops. The PRAPeR 70 meeting of experts agreed that the confined crop rotation study could be used to conduct a risk assessment and to propose MRLs for certain rotational crops. Nevertheless, EFSA recommended the submission of rotational field crop studies to either confirm the proposed MRLs, or to modify the proposed MRLs if necessary (EFSA, 2009).

Thus, two new field rotational crops studies investigating the magnitude of residues have been submitted to confirm the MRLs in rotational crops. These studies have been performed according to the intended cGAP (1 x 24 g a.s./ha, applied at BBCH 30)

The new field rotational crop studies investigating the magnitude of picloram residues in rotational crops were submitted by applicant to support the use of picloram on rape seed every year. zRMS evaluated these studies and they are summarised in A 2.2.6.1.

Both studies are deemed acceptable. Samples of wheat, turnip and kale were planted 30, 120 or 335 days after application of picloram to bare soil. No residues above the LoQ were measure in any of the 120-day and 335-day samples. However, quantified residues were observed in 30-day PBI samples.

Among 30-day PBI samples, none of the animal feed commodities (that are wheat whole plant that can be assimilated to wheat forage, wheat straw and turnip tops) presented residue levels higher than the trigger value of 0.05 mg/kg. As regards food commodities, residue levels exceeding the trigger value of 0.01 mg/kg were found in 30 DAT wheat grain and 30 DAT kale leaves and reached 0.02 mg/kg and 0.03 mg/kg, respectively. Nevertheless, picloram was applied to bare soil in both studies; this worst-case scenario does not take into account the foliar interception that may occur during plant treatment. Picloram is intended to be applied from BBCH 12 to BBCH 30 (see Part B, Section 0). According to the Generic Guidance to FOCUS groundwater scenarios (version 1.1, April 2002), foliar intercepts of 40% and 80% can be considered for oilseed rape during leaf development (BBCH 10-19) and stem elongation (BBCH 20-39), respectively. Consequently, a worst case foliar interception of 40% has been considered to refine the residue levels estimated in rotational crops, Details of the calculations can be found in Table 7.3.6.**1**.

Table 7.3.6.1-1: refinement of 30-day PBI sample results taking into consideration foliar interception

Crop group	Crop commodity	HR (mg/kg)	40% foliar inter-cept	EU MRL *(Reg. (EU) 2016/1)*	MRL exceedance?
Cereals	Wheat whole plant	0.05	0.03	N/A - feeding commodity	
	Wheat grain	**0.02**	0.012	0.2 (1) or 0.01* (2)	No
	Wheat straw	0.02	0.012	N/A - feeding commodity	
Root and tuber vegetables	Turnip roots	0.01	0.006	0.01*	No
	Turnip tops	0.04	0.024	N/A - feeding commodity	
Leafy vegetables	Kale leaves	**0.03**	**0.018**	0.01*	**Yes**

(1). Barley, maize, oats, sorghum, wheat, other cereals
(2). Buckwheat and other pseudo-cereals, common millet/proso millet, rice, rye

Once results refined in order to take into consideration foliar intercept, the trigger value of 0.01 mg/kg remains exceeded in kale leaves. Thus, an MRL exceedance cannot be excluded in leafy vegetables.

Conclusion on rotational crops studies

Based on the results of these new field rotational crop studies and based on the proposed critical GAP for GF-4021, a waiting period beyond normal crop harvest for oil seed rape is not specified since soil residues are expected to be sufficiently low by the time treated oilseed rape is harvested.
However, label should include a statement that in case of necessity for termination of plantation treated with GF-4021 because of crops damages caused by frost, diseases or insects, do not plant succeeding crops until 120 days since use of GF-4021(zRMS France, GF-3447).

No further data are required in the framework of this dossier. According to the results of the newly submitted studies (previously evaluated in RR GF-3447 dRR, France), zRMS proposed not to grow leafy vegetables in the treated field less than 120 days after application of GF-3447.
Moreover, final report of DAS Study ID 140651 should be submitted post-authorisation.

zRMS comments:

According to EFSA (EFSA Journal 2009; 7(12):1390) it has been concluded that picloram, and possibly any conjugates formed in the soil, are readily transported into succeeding crops. The vast majority of radioactivity is present as picloram or conjugates of picloram. The metabolism in succeeding crops is similar to that seen in primary crops. Thus, the same residue definition as for primary crops is appropriate.
According to the EFSA Journal 2013;11(10):3439:
*No rotational field crops studies investigating the magnitude of residues are available. The use of picloram assessed in the peer review referred to a single application of picloram on oilseed rape every three years at an application rate of 0.024 kg a.s./ha and the latest growth stage BBCH 31. The applicant now applies for the use of picloram on oilseed rape every year at the same application rate, but with the last application done at the growth stage of BBCH 50. During the peer review, provisional MRLs were proposed for certain rotational crops, based on the rotational crop metabolism study summarised under 3.1.2.2 and considering the intended GAP defined as a single triennial application (i.e. 0.07 mg/kg for fruiting vegetables, brassica vegetables, leafy vegetables, stem vegetables, herbal infusion and spices; 0.02 mg/kg for legume vegetables, pulses, cereal grains; 0.01*mg/kg for root vegetables and oilseeds) (EFSA, 2009). MRLs on these crops are currently set at the LOQ. Label restrictions are proposed now by the applicant to ensure that residues in rotational crops do not exceed the current MRLs. The EMS agreed with these restrictions and considered that setting of MRLs in rotational crops should be dealt under the article 12 review (United Kingdom, 2013). EFSA is of the opinion that in order to properly assess the magnitude of picloram residues in rotational crops, the applicant should submit a rotational crop field study according to EU guidelines and reflecting the critical GAP for picloram on a primary annual crop. The EMS has indicated that the applicant is undertaking a further confined rotational study at 1N rate to further address the potential for residues in rotational crops. EFSA notes that the data requirement for rotational crop studies will be reconsidered in the framework of the MRL review of picloram according to Article 12 of Regulation (EC) No 396/2005. As long as these data are not available, Member States when granting authorisations should consider the setting of appropriate restrictions in order to avoid possible contamination of crops grown in rotation on soil that was previously treated with picloram which exceed the current MRLs.*

Two new field rotational crop studies investigating the magnitude of picloram residues in rotational crops were submitted by applicant to support the use of picloram on rape seed every year. These studies have been performed according to the following GAP: 1 x 24 g a.s./ha, applied at BBCH 30. zRMS France evaluated these studies (GF-3447 RR, 2018). As requested by zRMS France, Applicant additionally submitted final report of DAS Study ID 140651. The detailed evaluation of these two field rotational crop studies have been presented in Appendix 2.
The information provided above by Applicant in point 7.3.6 is included in the zRMS-France evaluation (2018) and is therefore acceptable and sufficient to support the intended uses for GF-4021. zRMS-PL agrees with conclusions presented by zRMS-France (S-EU) in Registration Report for GF-3447 (2018), and with agreed endpoint.

According to the results of the newly submitted studies, zRMS-Poland, like zRMS-France, proposed not to grow leafy vegetables in the treated field less than 120 days after application of GF-4021.

7.3.7 Other / special studies (KCA6.10, 6.10.1)

~~The available data for the active substance sufficiently address aspects of the residue situation that might arise from the use of GF-4021. Therefore, other special studies are not needed.~~

Oilseed rape is a melliferous plant and that therefore, data needs to be presented to show that for GF-4021 applied according the submitted GAP, the MRL can be expected to below 0.05 mg/kg for honey and bee products.
Although as stated, picloram residues levels in the trials in RDE 15-20345 at 0, 7 and 14 days after application did show levels in excess of 0.05 mg/kg the latest application across the trials was BBCH 30, which even when the latest whole plant sampling of 14 days is taken into account is a significant period away from the start of flowering in oilseed rape (BBCH 61).
There were limited sampling points however, it can be readily seen in the data that across the trials there was a significant decline in the picloram residue levels from the day 0 over the 14-day sampling period.

Additionally, the oilseed rape nature of residues study cited in section 7.3.2.1 (000299) is presented but not summarized at it has been evaluated and used at the EU level. In this study the application of picloram was made at 40 g as/ha (>3.3 times the GF-4021 rate) at BBCH 33 (GF-4120 BBCH range 12-19), Samples were taken at regular intervals including at flower bud formation. The level of picloram detected at this sampling point was 0.070 mg/kg.

By scaling (proportionality principle) this residue level for picloram to the max rate in GF-4021 of 12 g/ha the residue level would be around 0.021 mg/kg.
Therefore, it can be reasonably expected that based on this data that the level of picloram available in the flowers would be well below 0.05 and that an exceedance of the MRL in honey and other bee products would not occur.

zRMS comments:
According to the „Technical guidelines for determining the magnitude of pesticide residues in honey and setting Maximum Residue Levels in honey“ (SANTE/11956/2016 rev. 9; 14 September 2018) residues in honey can occur when a substance with systemic properties is applied prior to the flowering stage (before BBCH 60), of a crop which is foraged by bees.
Picloram is a substance with systemic properties. Oilseed rape is a melliferous crop with high melliferous capacity. Residues in honey could be therefore expected.
Applicant provided data showing that for GF-4021 applied according the submitted GAP, the MRL for picloram can be expected to below 0.05 mg/kg for honey and bee products.
No other special studies are needed.

7.3.8 Estimation of exposure through diet and other means (KCA 6.9)

Toxicological reference values relevant for dietary risk assessment are reported in the summary of the evaluation (see 7.1.2).

7.3.8.1 Input values for the consumer risk assessment: Picloram

The input values in the following table were used to estimate consumer risk using the EFSA PRIMo Rev 3.1. All assessments follow the Tier I approach and are based on published MRL values (Reg. (EU) 2021/1531) and assume no dissipation of residues. The acute dietary assessments are performed only for the consumption of commodities for which GAPs are notified.

Table 7.3.8.1-1: Input values for the consumer risk assessment: Picloram

Commodity	Chronic risk assessment		Acute risk assessment	
	Input value (mg/kg)	Comment	Input value (mg/kg)	Comment
Picloram				
FRUITS, FRESH or FROZEN; TREE NUTS	0.01*	* Indicates that the MRL is set at the limit of analytical quantification (Reg. (EU) 2021/1531)	Acute risk assessment was undertaken only with regard to the crops under consideration.	
VEGETABLES, FRESH OR FROZEN (except flowering brassica)	0.01*			
Flowering Brassica	0.08			
PULSES	0.01*			
OILSEEDS AND OIL FRUITS (except rapeseeds/canola seeds, mustard seeds, and borage seeds)	0.01*			
Rapeseeds/canola seeds, mustard seeds, and borage seeds	0.03		0.01	STMR for rapeseed (EFSA Journal 2013; 11(10):3439)
CEREALS (except barley,	0.01*		Acute risk assessment was undertaken only	

Commodity	Chronic risk assessment		Acute risk assessment	
	Input value (mg/kg)	Comment	Input value (mg/kg)	Comment
maize/corn, oat, sorghum, wheat, and others)			with regard to the crops under consideration.	
Barley, maize/corn, oat, sorghum, wheat, and others	0.2			
TEAS, COFFEE, HERBAL INFUSIONS, AND COCOA	0.01*			
HOPS (dried)	0.01*			
SPICES (except horseradish)	0.01*			
Horseradish	0.07			
SUGAR PLANTS (except sugar canes)	0.01*			
Sugar canes	0.05			
PRODUCTS OF ANIMAL ORIGIN -TERRESTRIAL ANIMALS except muscle, kidney, edible offals, ruminant fat, milk, honey and other apiculture products	0.01*			
Muscle, and ruminant fat	0.2			
Kidney	5.0			
Edible offals (other than liver and kidney	0.5			
Milk, Honey and other apiculture products	0.05*			

7.3.8.2 Conclusion on consumer risk assessment: Picloram

Extensive calculation sheets are presented in Appendix 3.

The highest Theoretical Maximum Daily Intake (TMDI) is 2% of the ADI for the Netherlands toddler. The highest contribution (1% of the ADI) is from cattle milk. Children have the highest International Estimated Short-Term Intake (IESTI) for unprocessed commodities at < 0.01% of the ARfD for the consumption of rapeseeds/canola seeds, and for processed commodities at < 0.01% of the ARfD for the consumption of rapeseeds/oils.

Table 7.3.8.2-1: Consumer risk assessment: Picloram

TMDI (% ADI) according to EFSA PRIMo	2% (based on NL toddler)
IESTI (% ARfD) according to EFSA PRIMo	Unprocessed Commodities: < 0.01% based on consumption of rapeseeds/canola seeds by children Processed Commodities: < 0.01% based on consumption of rape-seeds/oils by children

The proposed uses of picloram in the formulation GF-4021 do not represent unacceptable chronic and acute dietary risk for the consumer.

zRMS comments:

The consumer risk assessments were performed with revision 3.1 of the EFSA Pesticide Residues Intake Model (PRIMo). The calculation of the TMDI using EFSA model (version 3.1) and MRLs according to Reg. (EU) ~~2016/1~~

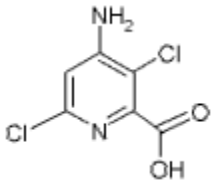
2021/1531 led to a utilisation of the ADI of 2% with the NL toddler being the population group with the highest value. For this diet, the highest contributor is Milk: Cattle with 1% of the ADI.
The intended uses will not result in a consumer chronic exposure exceeding the ADI.

For the calculation of the acute exposure the MRL has been used only for the use under consideration. The highest International Estimated Short-Term Intake (IESTI) is at 0.01% of the ARfD for the consumption of rapeseeds/canola by children and by adults.
The proposed uses of picloram in the formulation GF-4021 do not represent unacceptable acute and chronic risks for the consumer.

7.4 Aminopyralid

General data on aminopyralid are summarized in the table below (last updated 2016/04/13)

Table 7.4-1: General information on aminopyralid

Active substance (ISO Common Name)	Aminopyralid
IUPAC	4-amino-3,6-dichloropyridine-2-carboxylic acid
Chemical structure	
Molecular formula	$C_6H_4C_{12}N_2O_2$
Molar mass	207.026 g/mol
Chemical group	Pyridine carboxylic acid group
Mode of action (if available)	In susceptible plant species aminopyralid induces an epinastic response (i.e. stimulation of cell elongation and premature senescence, particularly in meristematic tissue) leading to secession of growth and rapid necrosis.
Systemic	Yes
Company (ies)	Dow AgroSciences*
Rapporteur Member State (RMS)	UK At present - Finland
Approval status	Approved Date of (01/01/2015) Commission Directive 2002/64/EC
Restriction	None
Review Report	SANCO/11423/2014 – rev. 1 11/07/2014
Current MRL regulation	Regulation (EU) 2021/1841 ~~Regulation (EU) 2017/171~~ ~~New MRL Regulation published: Commission Regulation (EU) 2019/1015 of 20 June 2019.~~
Peer review of MRLs according to Article 12 of Reg No 396/2005 EC performed	Reasoned Opinion on the review of the existing maximum residue levels for aminopyralid according to Article 12 of Regulation (EC) No 396/2005. EFSA Journal 2020;18(8):6229, 45 pp. https://doi.org/10.2903/j.efsa.2020.6229
EFSA Journal : Conclusion on the peer review	Yes, EFSA 2013
EFSA Journal: conclusion on article 12	Yes, See below
Current MRL applications on intended uses	EFSA-Q-2014-00594 All commodities Status: Evaluation ongoing

* Notifier in the EU process to whom the a.s. belong(s)
** If yes: see list of references

7.4.1 Stability of Residues (KCA 6.1)

7.4.1.1 Stability of residues during storage of samples

Available data

Two new stability studies have been submitted by the applicant in the framework of this application. Results

are summarized in the Table below. The detailed assessment of these studies are presented in Appendix 2.

Table 7.4.1.1-1: Summary of stability data achieved at ≤ - 18°C (unless stated otherwise)

Matrix	Characteristics of the matrix	Acceptable Maximum Storage duration	Reference
Data relied on in EU			
Plant products			
Wheat Straw	~~Dry crop~~ No group	Approximately 16 months	Lindsay, D. A., (2004). Frozen Storage Stability of XDE-750 in Range Land and Pasture Grass and Hay and Wheat Straw and Wheat Grain DAS Study ID: 030004 EFSA Journal 2013; 11(9): 3352
Wheat Grain	~~Non-oily grain~~ High starch commodity	Approximately 16 months	
Grass Forage	High water crop	Approximately 16 months	
Grass Hay	~~High water crop~~ No group	Approximately 16 months	
New Data			
Oilseed Rape Oil	~~High oil crop~~ Processed product	Approximately 25 months	Machado, G., (2013). Frozen Storage Stability of Aminopyralid (XDE-750) in Rape Forage, Seed and Oil DAS Study ID: 110634
Oilseed Rape Forage	High water crop	Approximately 25 months	
Oilseed Rape Seed	High oil crop	Approximately 25 months	
Barley Grain	~~Non-oily grain~~ High starch commodity	Approximately 6 months	Lindner, M., (2014). Storage Stability Study for Residues of Aminopyralid in Barley Grain, Malt Sprouts, Spent Grains, Yeast and Beer Study ID: S08-02908
Malt Sprouts	Processed product	Approximately 6 months	
Spent Grain	Processed product	Approximately 6 months	
Yeast	Processed product	Approximately 6 months	
Beer	Processed product	Approximately 6 months	
Animal Products			
Not required as animal tissue samples were analyzed within 30 days of collection.			

Conclusion on stability of residues during storage

The results from the final frozen storage stability study in crop matrices indicate that aminopyralid in crop samples from field studies can be stored frozen for at least 16 months with no observable degradation of residues.

Since animal tissue samples were not stored longer than 30 days following collection, no frozen storage stability determination is required for animal tissue samples.

zRMS comments:

The stability of residues for the active substance aminopyralid were reviewed at the EU level.
According to the EFSA Journal 2013;11(9):3352 – "*Peer review of the pesticide risk assessment of the active substance aminopyralid*":

Stability of residues (Annex IIA, point 6 introduction, Annex IIIA, point 8 Introduction)

Residues of aminopyralid stable at least 16 months in matrices with:
- high water content: (forage and grass)
- high starch content: (wheat grain) and
- dry matrices: (straw, hay),

when stored at -20°C.

EFSA concluded in EFSA Journal 2020;18(8):6229 that *The storage stability of aminopyralid residues was investigated in wheat (grain, forage, hay and straw) and grass (forage) in the framework of the peer review (EFSA,*

2013b; United Kingdom, 2013) and in rapeseed (forage, seeds, rape oil) in a new study submitted under this review, however not peer reviewed (Finland, 2020).
In high water content and dry commodities, the available studies demonstrated storage stability for aminopyralid for a period of 16 months when stored at –20°C, while in high oil content matrices, the new study reported by Finland demonstrates the storage stability for up to 25 months.

Two new stability studies have been submitted by the Applicant in the framework of this application and has been evaluated.
Residues of aminopyralid were stable for at least 25 months in oilseed rape (forage, seed and oil) matrices when stored deep frozen at -20 °C (Machado, G. B., 2013). More details are presented in Appendix 2, in point A 2.3.1.1.1.1.
Study (Lindner, M., 2014) meets the OECD guideline 506 requirements. Samples were analysed for aminopyralid and its conjugates, determined as aminopyralid. Residues of aminopyralid were stable in barley grain, malt sprouts, spent grains, yeast and beer for 6 months following storage at ≤ -18°C. More details are presented in Appendix 2, in point A 2.3.1.1.1.2.
The studies have been accepted.

The stability studies are not required as animal tissue samples were analyzed within 30 days of collection.

Sufficient stability data are available to support the residue data presented in the present dossier.

7.4.1.2 Stability of residues in sample extracts (KCA 6.1)

Available data
The stability of residues in sample extracts of different crop/animal matrices were also confirmed through the inclusion of the procedural batch recovery samples along with residue sample analyses. Therefore, the supervised residue trials data for the current application are valid with regard to stability of residues in stored sample extracts.

Conclusion on stability of residues in sample extracts
The supervised residue trials data for the current application are valid with regard to stability of residues in stored sample extracts.

zRMS comments:

The supervised residue trials data supporting the current application are valid with regard to stability of residues of aminopyralid in stored samples extracts.

7.4.2 Nature of residues in plants, livestock and processed commodities

7.4.2.1 Nature of residue in primary crops (KCA 6.2.1)

Available data
No new data submitted in the framework of this application.

Table 7.4.2.1-1: Summary of plant metabolism studies

Crop Group	Crop	Label position	Application and sampling details					Reference
			Method, F or G (a)	Rate (kg a.s./ha)	No	Sampling (DAT)	Remarks	
EU data								
Cereals	Grass	2- and 6-positions on the pyridine ring	F	0.360 (1.8N rate)	1	0, 7, 14, 21, 42	Fresh grass harvested at each sampling. Sub-sample of 42 DAT grass dried to	UK, 2013 DAR 2008 EFSA, 2013 EFSA, 2020

							produce corresponding hay sample.	
Cereals	Spring wheat	2- and 6-positions on the pyridine ring	F	0.040 (4N rate)	1	0, 14, 35, 86	Forage harvested at 0 and 14 DAT, hay harvested 35 DAT, straw and grain harvested 86 DAT.	UK, 2013 DAR 2008 EFSA, 2013 EFSA, 2020
				0.080 (8N rate)	1	0, 14, 35, 86		
Pulses & Oilseeds	Oilseed rape	2- and 6-positions on the pyridine ring	F	0.014	1	0, 7, 14, 28, 62	Immature plants collected at 0, 7, 14, 28 DAA. Mature whole plants were separated into seeds and remainder of aerial portions plant.	France, 2011 EFSA, 2020

Summary of plant metabolism studies reported in the EU

The data summarised in the aminopyralid DAR are sufficient to describe the distribution and expression of residues in plants (cereals), and no further studies are submitted. The proposed residue definition in plants is aminopyralid and its conjugates, expressed as aminopyralid.

As summarized in the EFSA 2020 Reasoned Opinion:

The metabolism of aminopyralid was investigated in three varieties of grass and in cereals (United Kingdom, 2006, 2013) and assessed in the framework of the peer review (EFSA, 2013b). In both studies, aminopyralid radiolabelled in the positions 2 and 6 of the pyridine ring of the molecule, was applied as a single foliar treatment.

In the first study, after one foliar application of 360 g a.s./ha on common pasture grasses, most of the radioactive residues were extracted (90–99% of the total radioactive residues; TRR). In fresh grass, residue levels ranged from 19 to 37 mg eq/kg 7 days after treatment (DAT), decreasing to 5–7 mg eq/kg 42 DAT. In hay 42 DAT, residues were higher ranging from 13 to 23 mg eq/kg. In all three varieties, the major component identified in fresh grass was parent aminopyralid, accounting for 48–68% TRR 7 days after treatment and decreasing to 22–31% TRR (up to 35% TRR in hay) after 42 days. The decrease of the parent, unconjugated aminopyralid, was balanced with a constant increase of the conjugated fraction mostly composed of glucose conjugates, from 19–39% TRR to 50–60% TRR (EFSA, 2013b).

In a second study, wheat was treated with one foliar application of 40 g a.s./ha (4N the application rate of the GAP on cereals) and 80 g a.s./ha (8N rate). Total residue levels of aminopyralid in grain were 0.039 to 0.084 mg eq/kg (at 4N rate and 8N rate, respectively), while total radioactive residues were higher in forage (up to 0.87 mg eq/kg), hay (up to 0.69 mg eq/kg) and straw (up to 0.62 mg eq/kg). A similar profile as in grass was observed in wheat, with a steady decrease of unconjugated aminopyralid, from 87–90% TRR in forage (0 DAT) to 8–11% TRR in straw (86 DAT), compensated by an increase of the conjugated fractions, similarly composed of glucose conjugates of aminopyralid, from 7–9% TRR to 63–70% TRR (EFSA, 2013b).

The metabolism of aminopyralid was also investigated in oilseeds and assessed in the framework of a previous MRL application but not peer reviewed (France, 2011; EFSA, 2012). After one foliar treatment on rapeseed with 14 g a.s./ha of aminopyralid radiolabelled in the positions 2 and 6 of the pyridine ring, total residue levels from successive sampling decreased from 0.08 mg eq/kg to 0.04 mg eq/kg in immature plants and were 0.003 mg eq/kg in mature seeds. The major components identified were also unconjugated aminopyralid (up to 78% TRR just after application) and its conjugates (up to 60% TRR at harvest) which were released as aminopyralid upon hydrolytic extraction conditions (France, 2011; EFSA, 2012). As it

was observed in the wheat and grass studies, residue levels of the unconjugated aminopyralid declined while at longer harvest intervals the levels of conjugates increased.

The metabolic pathway of aminopyralid was similar in cereals, grass and oilseeds.

Conclusion on metabolism in primary crops
It was concluded in EFSA 2013 that:

'Metabolism in plants was investigated in cereals only, on wheat and three different varieties of grass, using a single application of ^{14}C-aminopyralid labelled in the 2 and 6 position of the pyridine ring. Samples were collected just after application and at regular intervals up to 42 for grass and 86 days for wheat.

In grasses, most of the radioactive residues were extracted by means of solvents and non-extractable residues remained below 5% TRR. Parent aminopyralid was identified as the major component of the residues, accounting for 48-68% TRR 7 days after application, with a steady decrease to 22-31% TRR after 42 days. The decrease of the parent was balanced with a constant increase of the chromatographic fraction C3, from 19-39% TRR to 50-60% TRR. Following either acid or base hydrolysis, the C3 fraction was identified as mostly composed of glucose conjugates of aminopyralid. The base hydrolysis was shown to be more efficient in releasing conjugates, since in the 21-day rye grass extracts, 75- 88% of the radioactivity was released as aminopyralid under base hydrolysis, while only 50- 60% were released under acidic conditions. A similar profile was observed in the wheat study. A constant decrease from 87-90% TRR in forage to 8-11% TRR in straw was observed for aminopyralid, compensated by a steady increase of the HPLC fractions 1 and 5 from 5% to 23-37% TRR. Acid and base treatments confirmed these chromatographic fractions to be mainly composed of conjugates of aminopyralid, and to a lower extent, of hydroxyl-aminopyralid. As for grass, a significant part of the residues in wheat was present as conjugates of aminopyralid. At harvest, 49% and 72% of the radioactivity present in the straw and grain, respectively, was released as aminopyralid after hydrolysis, as against only 16% and 11% TRR following solvent extractions'.

The proposed residue definition in plants is aminopyralid (sum of aminopyralid, its salts and its conjugates, expressed as aminopyralid). This is aligned with Regulation (EU) 2021/1841. ~~aminopyralid and its conjugates, expressed as aminopyralid.~~

zRMS comments:

The metabolism of aminopyralid was investigated in three varieties of grass and in cereals (United Kingdom, 2006, 2013) and assessed in the framework of the peer review (EFSA, 2013). In both studies, aminopyralid radiolabelled in the positions 2 and 6 of the pyridine ring of the molecule, was applied as a single foliar treatment.
EFSA concluded in EFSA Journal 2020;18(8):6229 that The metabolism of aminopyralid was also investigated in oilseeds and assessed in the framework of a previous MRL application but not peer reviewed (France, 2011; EFSA, 2012). After one foliar treatment on rapeseed with 14 g a.s./ha of aminopyralid radiolabelled in the positions 2 and 6 of the pyridine ring, total residue levels from successive sampling decreased from 0.08 mg eq/kg to 0.04 mg eq/kg in immature seeds and were 0.003 mg eq/kg in mature seeds. The major components identified were also unconjugated aminopyralid (up to 78% TRR just after application) and its conjugates (up to 60% TRR at harvest) which were released as aminopyralid upon hydrolytic extraction conditions (France, 2011; EFSA, 2012). As it was observed in the wheat and grass studies, residue levels of the unconjugated aminopyralid declined while at longer harvest intervals the levels of conjugates increased.
The metabolic pathway of aminopyralid was similar in cereals, grass and oilseeds.

The residue definitions for plant agreed for monitoring and risk assessment (EFSA Journal 2020;18(8):6229):
Based on the metabolism studies, unconjugated aminopyralid is not a sufficient marker as its conjugates were found to represent a major part of the radioactive residues. Both parent and its conjugated are toxicologically relevant and thus should be considered in the consumer exposure.
Therefore, the residue definition for enforcement and risk assessment in cereals/grass and oilseeds is proposed as ***the sum of aminopyralid and its conjugates, expressed as aminopyralid****. This residue definition was already proposed during the peer review (in cereals only) and supported in all assessments performed in the framework of previous MRL applications. It is noted that* ***the residue definition for enforcement currently established in the***

Regulation (EC) 396/2005 (Regulation (EU) 2021/1841) is ~~limited to the parent only~~ Aminopyralid (sum of aminopyralid, its salts and its conjugates, expressed as aminopyralid).

7.4.2.2 Nature of residue in rotational crops (KCA 6.6.1)

Available data

No new data submitted in the framework of this application.

Table 7.4.2.2-1: Summary of metabolism studies in rotational crops

Crop group	Crop	Label position	Application and sampling details					Reference
			Method, F or G *	Rate (kg a.s./ha)	Sowing intervals (DAT)	Harvest Intervals (DAT)	Remarks	
EU data								
Leafy vegetables	Lettuce	2- and 6-positions on the pyridine ring	F	0.010	90	0, 90, 140 and 151	Immature and mature lettuce harvested	UK, 2013 DAR 2008 EFSA, 2013
					120	0, 120, 166, 179		
Root and tuber vegetables	Turnip				90	0, 90, 129 and 179	Immature and mature (tops and roots) harvested	UK, 2013 DAR 2008 EFSA, 2013
					120	0, 120, 163, 193		
Cereals	Sorghum				90	90, 119, 187, 217	Early and late forage, stover and grain harvested.	UK, 2013 DAR 2008 EFSA, 2013
					120	0, 120, 154, 200, 230		

* Outdoor/field application (F) or glasshouse/protected/indoor application (G)

Summary of plant metabolism studies reported in the EU

A confined rotational crop study summarised in the EU DAR involved a single application of aminopyralid at 10 g ae/ha in order to investigate the potential for residues in succeeding crops. In this study representative crops (lettuce, turnips and sorghum) were seeded 90 and 120 days after application of radiolabelled-aminopyralid. Results indicate that any residues related to aminopyralid that are found in rotational crops planted into treated fields between 90 and 120 days after application will be very low, ranging from <0.001 mg/kg to <0.030 mg/kg. The rotational crop metabolism study has shown that the only component that would be taken up from the soil is aminopyralid. The conclusion presented in the DAR indicates that residues of aminopyralid are considered unlikely to arise in rotational crops and would not be expected to present a consumer exposure concern.

Although there is no specific data on levels of aminopyralid taken up at 30 days, based on available data the DAR indicates that the residues would be similarly low based on the soil residue profile. Therefore, for purposes of residues, a replanting interval of 30 days is expected to be adequate.

Results from the confined rotational crop residue study indicated that that residues of aminopyralid are considered unlikely to arise in rotational crops and would not be expected to present a consumer exposure concern. It is considered that no field magnitude of residue studies are required in rotational crops to support the use of aminopyralid in cereals and no further studies are submitted.

Conclusion on metabolism in rotational crops

The data summarised in the EU DAR are sufficient to describe the potential for residues of aminopyralid in succeeding crops based on the proposed GAP for GF-1810 and no further studies are required or

submitted.

Residues of aminopyralid are considered unlikely to arise in rotational crops and would not be expected to present a consumer exposure concern.

zRMS comments:

The metabolism of aminopyralid in rotational crops was evaluated at EU level.
According to the EFSA Journal 2020;18(8):6229 – "Review of the existing MRLs for aminopyralid":
"Aminopyralid is authorised on crops that may be grown in rotation. The field DT90 reported in the soil degradation studies evaluated in the framework of the peer review was 116 days (EFSA, 2013b).
Therefore, the possible occurrence of residues in rotational crops needs to be assessed. One confined rotational crop study with aminopyralid radiolabelled in the positions 2 and 6 of the pyridine ring of the molecule was available for this review (EFSA, 2013b; United Kingdom, 2013). In this study, aminopyralid was applied at a low rate of 10 g a.s./ha onto bare soil. Crops were planted at nominal plant-back intervals (PBI) of 90 and 120 DAT. Crops planted at each interval consisted of leafy vegetables (lettuce), roots (turnip) and cereals (sorghum). Residues in all crops were generally low, ranging from < 0.001 to 0.006 mg eq/kg in edible parts of the crops and reaching up to 0.03 mg eq/ kg in feed items (sorghum forage and stover). The major compounds further characterised were aminopyralid (free or conjugated) and it was concluded that the metabolic pathway was similar as in primary crops."
The data on metabolism and distribution of aminopyralid in succeeding crops demonstrate that the metabolism of the active substance in rotational crops is similar to the pathway observed in primary crops. Thus, **the same residue definition is applicable for rotational crops** (United Kingdom, 2012).

7.4.2.3 Nature of residues in processed commodities (KCA 6.5.1)

Available data
One ~~new~~ hydrolysis study has been submitted by the applicant in the framework of this application. This study is summarized in the table below. ~~The detailed results of this study are presented in Appendix 2.~~

Table 7.4.2.3-1: Nature of the residues in processed commodities

Conditions (Duration, Temperature, pH)	Identified compound(s) (%)	Reference
New data		
Pasteurisation (20 minutes, 90°C, pH 4)	Parent (101%)	Rotondaro, S.L., Adusumilli, H., 2012, 110709
Baking, boiling, brewing (60 minutes, 100°C, pH 5)	Parent (100%)	Rotondaro, S.L., Adusumilli, H., 2012, 110709
Sterilisation (20 minutes, 120°C, pH 6)	Parent (100%)	Rotondaro, S.L., Adusumilli, H., 2012, 110709

Overall material balance for the aminopyralid experiments averaged 98.5%. Material balance averaged 98.6%, 96.5%, and 100% at pH 4, 5, and 6, respectively.

After processing, the samples were analysed by HPLC, comparing retention times with an authentic standard. In the ^{14}C-aminopyralid pH 4, 5 and 6 heated replicates, 101, 100, 100% of the radioactivity remained as ^{14}C-aminopyralid (average replicates/dose solution); these values take into account the purity of the dose solution.

Conclusion on nature of residues in processed commodities
Hydrolysis during RAC processing operations does not significantly affect the nature of the residues as defined by the residue definition.

zRMS comments:

EFSA concluded in EFSA Journal 2012;10(9):2894 that specific studies to assess the magnitude of aminopyralid residues during the processing of rape seed are not necessary as the residue levels in raw agricultural commodities (RAC) did not exceed the trigger value of 0.1 mg/kg and the total theoretical maximum daily intake (TMDI) amounts to less than 10% of the ADI (EC, 1997d). Considering the low log Po/w of -1.76 to -2.96 for pH of 5 to 9 (ref. DAR) it is not expected that aminopyralid residues accumulate in oil produced from treated rape seed.
Additionally according to the EFSA Journal 2020;18(8):6229 – "Review of the existing MRLs for aminopyralid":
Studies investigating the nature of aminopyralid residues in processed commodities were assessed in the framework of a previous application to modify MRLs in cereals (United Kingdom, 2017; EFSA, 2019b), however, not peer reviewed. These studies were conducted with radiolabelled aminopyralid in the positions 2 and 6 of the pyridine ring simulating representative hydrolytic conditions for pasteurisation (20 min at 90°C, pH 4), boiling/brewing/baking (60 min at 100°C, pH 5) and sterilization (20 min at 120°C, pH 6). Aminopyralid was stable to hydrolysis under standard conditions of pasteurisation, baking/brewing/boiling and sterilisation.
The UK conclusions (2017) of the study (Rotondaro, S.L., Adusumilli, H., 2012, 110709):
Under conditions representing pasterurisation, baking, brewing and boiling, and sterilization aminopyralid was found to be hydrolytically stable. The residue definition agreed for risk assessments for plants is therefore applicable to processed commodities i.e.
~~*Sum of aminopyralid and its conjugates expressed as aminopyralid.*~~
Aminopyralid (sum of aminopyralid, its salts and its conjugates, expressed as aminopyralid).

Further considerations about the effects of processing are not required in the framework of this dossier.

7.4.2.4 Conclusion on the nature of residues in commodities of plant origin (KCA 6.7.1)

Table 7.4.2.4-1: Summary of the nature of residues in commodities of plant origin

Endpoints	
Plant groups covered	Cereals (grass and wheat) Pulses and oilseed (oilseed rape)
Rotational crops covered	Leafy crop (lettuce), root crop (turnip), cereals (sorghum), 10 g a.s./ha, PBI, 90 and 120 days
Metabolism in rotational crops similar to metabolism in primary crops?	Yes
Processed commodities	Aminopyralid is stable under standard hydrolysis conditions
Residue pattern in processed commodities similar to pattern in raw commodities?	Yes~~*~~
Plant residue definition for monitoring	~~Sum of aminopyralid and its conjugates expressed as aminopyralid (EFSA Journal 2013;11(9):3352) **~~ ~~Aminopyralid according to Reg. (EC) No 396/2005~~ Aminopyralid (sum of aminopyralid, its salts and its conjugates, expressed as aminopyralid) (Reg. (EU) 2021/1841).
Plant residue definition for risk assessment	~~Sum of aminopyralid and its conjugates expressed as aminopyralid (EFSA Journal 2013;11(9):3352) ***~~ Aminopyralid (sum of aminopyralid, its salts and its conjugates, expressed as aminopyralid).
Conversion factor from enforcement to RA	None (EFSA 2013)

7.4.2.5 Nature of residues in livestock (KCA 6.2.2-6.2.5)

Available data
No new data submitted in the framework of this application.

Table 7.4.2.5-1: Summary of animal metabolism studies

Group	Species	Label position	No of animal	Application details		Sample details		Reference
				Rate (mg/kg bw/d)	Duration (days)	Commodity	Time of sampling	
EU data								
Lactating ruminants	Goat	Aniline ring and triazole ring	2	0.5~~11~~ mg/kg bw/d* ~~per day~~	≥6	Milk	twice daily	UK, 2015; EFSA, 2013 EFSA, 2020
						Urine and faeces	daily	
						Tissues	at sacrifice	
Laying poultry	Hens	Aniline ring and triazole ring	10	~~Twice daily at 0.579~~ 0.79 mg/kg bw/d~~ay~~*	≥7	Eggs	twice daily	UK, 2015; EFSA, 2013 EFSA, 2020
						Excreta	twice daily	
						Tissues	at sacrifice	

~~* assuming a body weight of 1.9 kg (SANCO/7021/VI/95 rev. 4)~~
* EFSA Journal 2020;18(8):6229

Summary of animal metabolism studies reported in the EU
It was concluded in EFSA 2013 that:

'Based on the highest residue value observed in grass, the intake by cattle was calculated to be 21.3 mg/kg DM for cattle. A goat metabolism was therefore submitted, conducted at the dose of 17.6 mg/kg DM over 6 consecutive days (ca 0.8N). Aminopyralid was intensively excreted in faeces and urine and no more than 0.07% of the administered dose was recovered in milk and edible matrices. TRRs in milk, liver, muscle and fat were below 0.009 mg/kg and the characterisation of residues was therefore only attempted in kidney where 80% TRR was identified as aminopyralid. Although, no residue intake is foreseen by poultry, a metabolism study on laying hen was provided, conducted at the dose rate of 11.6 mg/kg DM over 7 consecutive days. As previously for ruminants, aminopyralid was almost totally excreted, and all TRRs in eggs and tissues were significantly below 0.01 mg/kg, in the range of <0.002 to 0.004 mg/kg. No characterisation of residues was performed in any of these samples. The animal residue definition for monitoring and risk assessment was proposed as aminopyralid'.

Conclusion on metabolism in livestock
No separate or supplemental studies on metabolism, distribution and expression of aminopyralid residues in livestock were conducted or are required to describe the behaviour of aminopyralid in the formulated product GF-4021 for the uses proposed in this document.

The data summarised in the aminopyralid DAR are sufficient to describe the distribution and expression of residues in livestock, and no further studies are submitted. For products of animal origin, the proposed residue definition is the parent molecule, aminopyralid.

zRMS comments:

The metabolism of aminopyralid was evaluated at the EU level and conclusions are presented in the Peer review of the pesticide risk assessment of the active substance aminopyralid. Information provided by Applicant is sufficient.
For products of animal origin, the proposed residue definition is the parent molecule, aminopyralid.
No further data are required to support the proposed uses.

7.4.2.6 Conclusion on the nature of residues in commodities of animal origin (KCA 6.7.1)

Table 7.4.2.6-1: Summary on the nature of residues in commodities of animal origin

	Endpoints
Animals covered	Lactating goats
	Laying hens
Time needed to reach a plateau concentration	2 days in milk
	5-7 days in eggs
Animal residue definition for monitoring	Aminopyralid (EFSA 2013, EFSA 2020* and Reg. (EU) 2021/1841)
Animal residue definition for risk assessment	Aminopyralid (EFSA 2013, EFSA 2020*)
Conversion factor	None (EFSA 2013, EFSA 2020*)
Metabolism in rat and ruminant similar	Yes
Fat soluble residue	No

*EFSA Journal 2020;18(8):6229

7.4.3 Magnitude of residues in plants (KCA 6.3)

7.4.3.1 Summary of European data and new data supporting the intended uses

No new data are submitted in the framework of this application.

The MRL for aminopyralid in oilseed rape is based on a critical GAP of one application at a rate of 12 g ae/ha at growth stage BBCH 50. The evaluation leading to the current MRL for aminopyralid in oilseed rape is presented in the EFSA Reasoned Opinion on the modification of the existing MRL for aminopyralid in rape seed, 2012. The critical GAP upon which the EU MRL for aminopyralid was set covers the use of GF-4021 proposed in this submission.

Sufficient trials on oilseed rape were previously presented and evaluated in the EFSA 2012. A summary of the residue trial data for oilseed rape is provided in the Table below.

Table 7.4.3.1-1: Summary of EU reported and new data supporting the intended uses of GF-4021 and conformity to existing MRL

Commodity	Source	Residue zone (N-EU, S-EU, EU, outside EU)	Evaluation GAP Picloram Residue levels (mg/kg) E = according to enforcement residue definition RA = according to risk assessment residue definition	STMR (mg/kg)	HR (mg/kg)	Unrounded OECD calculator MRL (mg/kg)	Current EU MRL (mg/kg) *	MRL compliance
Oilseed rape seeds	EFSA, 2012, MRL ER (FR), 2012**	N-EU	GAP on which MRL/EU a.s. assessment is based: 1 x 12 g ae/ha, BBCH 50, outdoor E: 11 x <0.01, 0.02 RA: 11 x <0.01, 0.02	0.01	0.02	0.03	0.0~~3~~5	Yes
	EFSA, 2012, MRL ER (FR), 2012**	S-EU	GAP on which MRL/EU a.s. assessment is based: 1 x 12 g ae/ha, BBCH 50, outdoor E: 6 x <0.01, 4 x 0.01, 0.02 RA: 6 x <0.01, 4 x 0.01, 0.02	0.01	0.02	0.03	0.0~~3~~5	Yes

* Source of EU MRL: Part A of Annex I to Reg. 396/2005
EFSA Journal 2012;10(9):2894

** Trials were analysed for the extended residue definition anticipating the future change of the enforcement residue definition as proposed in the EU peer review (i.e., sum of aminopyralid and its conjugates, expressed as aminopyralid).

7.4.3.2 Conclusion on the magnitude of residues in plants

According to the available data, the intended uses on oilseed rape are considered acceptable, for outdoor uses. The data submitted show that no exceedance of the MRL will occur. The uses are considered acceptable.

zRMS comments:

The intended use for GF-4021 is oilseed rape. Oilseed rape is the major crop in northern Europe (EU guideline Document ~~SANCO 7525/VI/95 rev.10.3 of 13 June 2017~~ SANTE/2019/12752). A minimum of eight trials are required.

Table 7.3: Intended cGAP for GF-4021

Crop	Number of applications	Application rate per treatment (gai/ha)	Interval between application	Growth stage at last application	PHI (days)
Oilseed rape	1	Halauxifen-methyl: 2.5 g ae/ha + Picloram: 12 g ae/ha + Aminopyralid: 8 g ae/ha	N/A	BBCH 12-19	-

A total of 12 residue trials on rape seed (N-EU) were available, all based on a GAP that is more critical (higher rates and later application timings) than the GAP proposed for the product GF-4021. However, these trials support the existing MRL for aminopyralid and are therefore fully adequate to support the intended use on rape seed.
The residue trials on oilseed rape were previously presented and evaluated in the EFSA 2012.
EMS-France conclusions (2011):

In support of the proposed GAP, a total of 11 residue trials on rape seed carried out in Southern Europe and a total of 12 residues trials on rape seed carried out in Northern Europe have been provided by the applicant. They were carried out with a single application at 10.9 to 19 g a.s./ha from BBCH 31 up to BBCH 50 using SL or SC formulations. Samples of whole plant were harvested from a couple hours up to 85 days after application and mature seeds and rest of plant were harvested 64 to 119 days after application. Trials data are summarized in Table 7.3-9.

All the submitted trials were performed according to the proposed GAP, except for 4 trials in which the application rate was more critical (outside the 25% margin). However, as residue levels in these trials are below the LOQ in mature seeds and show similar residue levels to other trials performed at 12 g as/ha (+/-25%), then these trials are considered acceptable. Enough trials have been provided to modify the current MRL on rape seed.
According to the EFSA Journal 2012;10(9):289: *No storage stability data have been provided for high oil content commodities. The EMS considered this data gap as a minor deficiency.*

Applicant submitted additional storage stability studies. Residues of aminopyralid were stable for at least 25 months in oilseed rape (forage, seed and oil) matrices when stored deep frozen at -20 °C (Machado, G. B., 2013).
All residue data reported within the present submission are covered by the storage period.

Residue trial samples have been analysed for aminopyralid and its conjugates by LC-MS/MS with an LOQ of 0.01 mg/kg, using methods GRM 02.31 or GRM07.07. Validation data have been provided and considered sufficient to validate the method used.

All the samples were analysed for aminopyralid and its conjugates, determined as aminopyralid. Residues of aminopyralid were from <0.01 to 0.02 mg/kg in oilseed rape.

The value of EU MRL for aminopyralid on oilseed rape equals 0.05~~0~~ mg/kg (Regulation (EU) ~~2019/1015~~ 2021/1841). The residues arising from the proposed use will not exceed the MRL established for oilseeds.
The current EU MRL for aminopyralid is sufficient to support the proposed use.
Additionally it should be mentioned that oilseed rape straws are not fed to animals. Therefore, no consideration about this item is required.

No additional data are required.

7.4.4 Magnitude of residues in livestock

7.4.4.1 Dietary burden calculation

The use of GF-4021 may result in residues of aminopyralid in animal feed items, therefore the possible transfer of residues in animal commodities from the proposed uses should be considered. Livestock intake calculations and feeding studies undertaken are provided below.

For dietary burden calculation reference is made to the recent EFSA Review of the existing maximum residue levels for aminopyralid according to Article 12 of Regulation (EC) No 396/2005, 2020. Below are the input values used for calculation of the livestock dietary burden.

Table 7.4.4.1-10: Input values for the dietary burden calculation

Feed Commodity	Median dietary burden		Maximum dietary burden	
	Input value (mg/kg)	Comment	Input value (mg/kg)	Comment
Risk assessment residue definition: Sum of aminopyralid and its conjugates expressed as aminopyralid				
Barley straw	0.04	Median residue (EFSA, 2020)	0.13	Highest residue (EFSA, 2020)
Corn, field stover (fodder)	0.01*	Median residue (EFSA, 2020)	0.12	Highest residue (EFSA, 2020)
Corn, pop stover (fodder)	0.01*	Median residue (EFSA, 2020)	0.12	Highest residue (EFSA, 2020)
Grass forage (fresh)	1.19	Median residue (EFSA, 2020)	4.26	Highest residue (EFSA, 2020)
Grass hay	4.17	Median residue x PF (3.5) (EFSA, 2020)	14.91	Highest residue x PF (3.5) (EFSA, 2020)
Grass silage	1.9	Median residue x PF (1.6) (EFSA, 2020)	6.82	Highest residue x PF (1.6) (EFSA, 2020)
Millet straw (fodder, dry)	0.01*	Median residue (EFSA, 2020)	0.12	Highest residue (EFSA, 2020)
Oat straw	0.05	Median residue (EFSA, 2020)	0.27	Highest residue (EFSA, 2020)
Rye straw	0.05	Median residue (EFSA, 2020)	0.27	Highest residue (EFSA, 2020)
Sorghum, grain stover	0.01*	Median residue (EFSA, 2020)	0.12	Highest residue (EFSA, 2020)
Triticale straw	0.05	Median residue (EFSA, 2020)	0.27	Highest residue (EFSA, 2020)
Wheat straw	0.05	Median residue (EFSA, 2020)	0.27	Highest residue (EFSA, 2020)
Barley grain	0.04	Median residue (EFSA, 2020)	0.04	Median residue (EFSA, 2020)
Corn, field (Maize) grain	0.01*	Median residue (EFSA, 2020)	0.01	Median residue (EFSA, 2020)

Feed Commodity	Median dietary burden		Maximum dietary burden	
	Input value (mg/kg)	Comment	Input value (mg/kg)	Comment
Corn, pop grain	0.01*	Median residue (EFSA, 2020)	0.01	Median residue (EFSA, 2020)
Millet grain	0.01*	Median residue (EFSA, 2020)	0.01	Median residue (EFSA, 2020)
Oat grain	0.04	Median residue (EFSA, 2020)	0.04	Median residue (EFSA, 2020)
Rye grain	0.04	Median residue (EFSA, 2020)	0.04	Median residue (EFSA, 2020)
Sorghum grain	0.01*	Median residue (EFSA, 2020)	0.01*	Median residue (EFSA, 2020)
Triticale grain	0.01*	Median residue (EFSA, 2020)	0.01*	Median residue (EFSA, 2020)
Wheat grain	0.01*	Median residue (EFSA, 2020)	0.01*	Median residue (EFSA, 2020)
Brewer's grain dried	0.13	Median residue x PF (3.3) (EFSA, 2020)	0.13	Median residue x PF (3.3) (EFSA, 2020)
Canola (Rapeseed) meal	0.02	Median residue x PF (2) (EFSA, 2020)	0.02	Median residue x PF (2) (EFSA, 2020)
Corn, field milled by-pdts	0.01*	Median residue x PF (1) (EFSA, 2020)	0.01*	Median residue x PF (1) (EFSA, 2020)
Corn, field hominy meal	0.06	Median residue x PF (6) (EFSA, 2020)	0.06	Median residue x PF (6) (EFSA, 2020)
Corn, field gluten feed	0.03	Median residue x PF (2.5) (EFSA, 2020)	0.03	Median residue x PF (2.5) (EFSA, 2020)
Corn, field gluten, meal	0.01*	Median residue x PF (1) (EFSA, 2020)	0.01*	Median residue x PF (1) (EFSA, 2020)
Distiller's grain dried	0.03	Median residue x PF (3.3) (EFSA, 2020)	0.03	Median residue x PF (3.3) (EFSA, 2020)
Rape meal	0.02	Median residue x PF (2) (EFSA, 2020)	0.02	Median residue x PF (2) (EFSA, 2020)
Wheat gluten meal	0.02	Median residue x PF (1.8) (EFSA, 2020)	0.02	Median residue x PF (1.8) (EFSA, 2020)
Wheat milled by-pdts	0.02	Median residue x PF (2.4) (EFSA, 2020)	0.02	Median residue x PF (2.4) (EFSA, 2020)

Table 7.4.4.1-11: Results of the dietary burden calculation

The dietary burden calculations have been performed using the EFSA animal dietary burden and MRL calculations (2017) based on the intake values according to the OECD Guidance Document on Residues in Livestock, Series on testing and assessment No. 64, Series on pesticides No. 32 and Pesticides No. 73 (ENV/JM/MONO(2013)8) and are presented below.

Relevant groups	Dietary burden expressed in				Most critical diet (a)	Most critical commodity (b)		Trigger exceeded (Yes/No)
	mg/kg bw per day		mg/kg DM					0.004
	Median	Maximum	Median	Maximum				mg/kg bw
Cattle (all diets)	0.11	0.39	2.89	10.3	Dairy cattle	Grass	forage (fresh)	Yes
Cattle (dairy only)	0.11	0.39	2.89	10.3	Dairy cattle	Grass	forage (fresh)	Yes
Sheep (all diets)	0.15	0.54	4.53	16.2	Lamb	Grass	forage (fresh)	Yes
Sheep (ewe only)	0.15	0.54	4.53	16.2	Ram/Ewe	Grass	forage (fresh)	Yes
Swine (all diets)	0.02	0.08	1.00	3.45	Swine (finishing)	Grass	silage	Yes
Poultry (all diets)	0.004	0.006	0.06	0.08	Poultry layer	Wheat	straw	No
Poultry (layer only)	0.004	0.006	0.06	0.08	Poultry layer	Wheat	straw	No

(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".

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7.4.4.2 Livestock feeding studies (KCA 6.4.1-6.4.3)

Available data
No new data were submitted in the framework of this application.

Conclusion on feeding studies
In the framework of the EFSA, 2020 peer review, a feeding study was performed with dairy cows (United Kingdom, 2006). In these studies, aminopyralid was administered using different dosing levels ranging from 32.8 mg/kg DM (equivalent to 1.26 mg/kg body weight (bw) per day) to 644.7 mg/kg DM (equivalent to 24.8 mg/kg bw per day), corresponding to 3.2N to 62.9N the maximum dietary burden calculated for dairy cattle. In this study, samples of tissues and milk were analysed for aminopyralid and the results confirmed the intensive excretion of aminopyralid observed in the metabolism study.
The study performed on dairy cows was used to derive MRL and risk assessment values for all commodities of ruminants, in compliance with the latest recommendations on this matter (FAO, 2009).
Since extrapolation from ruminants to pigs is acceptable, results of the livestock feeding study on ruminants were relied upon to derive the MRL and risk assessment values in pigs. Significant levels of aminopyralid are only expected in kidney, where the mean levels were 0.07 and 0.15 mg/kg for the two lowest dose rates. For milk and all other tissues of ruminants, no residues were found above the LOQ at any dosing levels and MRLs can be proposed at the LOQ (0.01 mg/kg). All the samples analysed were stored for less than 30 days, thus decline of residues during storage of the trial samples is not expected.
No study was available for poultry; however, MRLs are not required since poultry are not expected to be exposed to significant levels of aminopyralid residues (EFSA, 2020).

The requested uses (or the new mode of calculation) modify the theoretical maximum daily intake for animals, but regarding available feeding data, there is no risk for animal MRL to be exceeded.

zRMS comments:
Information given by the Applicant is sufficient and zRMS-Poland agrees with presented above conclusions. No further data are required.

7.4.5 Magnitude of residues in processed commodities (Industrial Processing and/or Household Preparation) (KCA 6.5.2-6.5.3)

7.4.5.1 Available data for all crops under consideration

No new data were submitted in the framework of this application.

7.4.5.2 Conclusion on processing studies

Processing studies are not required as they are not expected to affect the outcome of the risk assessment.

zRMS comments:

Since no residues of aminopyralid exceeding 0.1 mg/kg are expected in the treated crops and TMDI is below 10% of the ADI, further considerations about the effects of processing are not required in the framework of this dossier.
No further data are required.

7.4.6 Magnitude of residues in representative succeeding crops

The crops under consideration can be grown in rotation.

Considering available data dealing with nature of residues (see 7.2.2.2), no study dealing with magnitude of residues in succeeding crops is needed.

A new confined rotational crop study has been submitted. Lettuce, turnips and sorghum were planted 30, 120 and 365 days after the application of 63.9 g/ha of aminopyralid in bare soil. Due to phytotoxic effects, lettuce did not grow at the tested plant back intervals of 30, 120 or 180 days; thus, the study design was modified, replacing lettuce with mustard, which was planted at PBI 300 and 365 days. Residues in green mustard (mature and immature) were found at 0.024–0.027 mg eq/kg at PBI 300 days and 0.084–0.088 mg/kg at PBI 365 days. Residues of aminopyralid were determined in turnip leaves at 0.270 mg eq/kg and 0.334 mg eq/kg at PBI 30 and 120 days, respectively, and 0.038 mg eq/kg and 0.034 mg eq/kg at PBI 30 and 120 days, respectively, in turnip roots. In wheat (forage, straw, hay and grain), the highest residues found in all crop products at 120 days PBI (0.095 mg eq/kg in wheat forage; 0.658 mg eq/kg in wheat hay; 0.555 mg eq/kg in wheat straw; 0.033 mg eq/kg in wheat grain). The level of details reported in the ER (United Kingdom, 2017) was limited. For example, information regarding the characterization of the residues of aminopyralid in rotated crops was considered insufficient to draw a robust conclusion. However, considering that this study is overdosed in comparison with the GAPs under assessment by a factor of 6 (6N rate), it is concluded that this study gives an indication that residues in crops growing in rotational may occur at more than 0.01 mg/kg if the application is performed following the GAPs under assessment (EFSA, 2019).

zRMS comments:

A confined rotational crop study (Study title: A confined rotational crop study with ^{14}C-aminopyralid Authors: Sandra Rotondaro, He Wang, Brittany Kish Date: 16 December 2015 Study ID: 120968) has been evaluated by EMS-United Kingdom, 2017.
EMS-UK conclusions (Evaluation Report: "Modification of MRLs for aminopyralid in barley, rye, oats, wheat, sorghum, millet and maize", 2017):
Significant residues (>0.01 mg/kg) are expected in leafy/stem vegetable and cereal (forage, hay and straw) crops grown in rotation at a plant back interval of 30 days following application of 10 g aminopyralid/ha. As such, the current MRL of 0.01 mg/kg for leafy crops and stem vegetables may be exceeded when replanting occurs 30 days after application. On this basis the existing 90 day plant back restriction should remain in place.

Taking into account presented above UK conclusions, in our opinion 90 day plant back restriction should remain in place for aminopyralid. However, based on the discussion in 7.3.6, a plant back restriction of 120d is recommended for the GF-4021 product driven by picloram.

7.4.6.1 Field rotational crop studies (KCA 6.6.2)

Available data
No new data submitted in the framework of this application.

Conclusion on rotational crops studies
Specific plant-back restrictions related to the use of GF-4021 are therefore not required, provided that GF-4021 is applied in compliance with the GAPs evaluated in the framework of this review.

zRMS comments:

See point 7.4.6.
Taking into account presented above UK conclusions, in our opinion 90 day plant back restriction should remain in place.

7.4.7 Other / special studies (KCA6.10, 6.10.1)

~~The available data for the active substance sufficiently address aspects of the residue situation that might arise from the use of GF-4021. Therefore, other special studies are not needed.~~

Assessment of residues in whole plant data at flowering for aminopyralid
The application of aminopyralid to winter oilseed rape is early (max. BBCH 19), which is not during the flowering period of the crop and during which time bees are not actively foraging. A selection of residue decline trials (see table 1) sampled oilseed rape whole plants during the flowering period of the crop (BBCH 60-69) following application of aminopyralid at BBCH 31-51. These residues represent a worst case compared to the residues expected in pollen and nectar that have the potential to be transferred to honey arising from the proposed GF-4021 GAP as:

i) application timing in residue data assessed below was at a growth stage closer to flowering (BBCH 31-51) compared to the proposed GF-4021 GAP (BBCH 12-19);
ii) application was at an exaggerated rate (12 to 19 g a.e./ha) compared to the intended GF-4021 GAP (8 g a.e./ha);
iii) whole plants were analysed and you would not expect all the residue determined in a whole plant to be transferred to honey;
iv) GF-4021 is intended for application to winter OSR, the residue data assessed in table 1 are associated with trials on spring OSR. It is expected that aminopyralid residues would be lower in winter OSR due to the crop's hibernation period, which extends the duration between application and flowering therefor allowing further residue degradation to occur.

Correcting for the exaggerated application rate (proportionality principle), the scaled residues in whole plants were in the range 0.018 to 0.049 mg/kg, which are within the default MRL in honey (0.05* mg/kg). Therefore, residues in honey exceeding the default MRL as a result of the intended renewal GAP on oilseed rape are not expected assuming a maximum application rate of 8 g a.e./ha up to BBCH 19 as this application scenario is far less critical relative to the data assessed in Table 1 (especially with respect to application timing).

Table 7.4.7-1: Residues of aminopyralid in whole plant at flowering adjusted to the 8 g a.e./ha GF-4021 GAP.

Study	Residue in Whole Plant at Flowering (mg/kg)	Trial ID	BBCH at Harvest	Study App rate (g a.e./ha)	GF-4021 cGAP rate (g a.e./ha)	Scale factor	Residue (mg/kg) Scaled to 8 g a.e./ha
GHE-P-11273 CEMS-2698	0.05	CEMS-2698A	65	18	8[(a)]	0.445	0.022
	0.04	CEMS-2698A	69	18		0.445	0.018
GHE-P-11493 CEMS-2965	0.06	CEMS-2965A	68	13		0.616	0.037
	0.06		68	19		0.422	0.025
	0.08	CEMS-2965B	69	13		0.616	0.049
	0.08		69	19		0.422	0.034
GHE-P-12499 CEMS-4348	0.056	CEMS-4348B	61	12		0.668	0.037
	0.051	CEMS-4348D	61	12		0.668	0.034
	0.033	CEMS-4348D	65	12		0.668	0.022

[(a)] Lower rate also exists for GF-4021 where the application rate is 6.3 g a.e./ha – the information above is protective of this.

Based on available data and the argumentation above, the applicant proposes the default MRL of 0.05* mg/kg should be applied to honey.

CONCLUSION

Based on the assessment of more critical residue data, the applicant strongly believes that the likelihood of observing an aminopyralid MRL exceedance in honey is negligible following GAP compliant application of GF-4021.

RESIDUES DATA FROM SUPERVISED TRIALS – SUMMARY CEMS-2698A

Active substance (common name):	**Aminopyralid**	Commercial Product (name):	GF-1634
Crop/Crop group:	**Oilseed rape**	Other active substance in the formulation (common name and content):	Clopyralid 240 g ae/L Picloram 80 g ae/L
Responsible body for reporting (name & address):	Dow AgroSciences, 3B Park Square, Milton Park, Abingdon, Oxon, OX14 4RN, UK	Producer of commercial product	Dow AgroSciences
Content of active substance (g/Kg or g/L):	Aminopyralid 60 g ae/L	Indoor/Glasshouse/Outdoor:	Outdoor
Formulation number:	GF-1634	Residues calculated as:	Aminopyralid 1-butyl ester
Formulation (e.g. WP):	SL (soluble concentrate)	Residue method and LOQ	GRM 02.31: 0.01 mg/kg
		Study no. / Dow Agrosciences Report Reference:	CEMS-2698/ GHE-P-11273

1	2	3	4	5			6		7	8	9	10	11
Trial code/ Location, Country	Crop/Variety	Date of: 1) Sowing or Planting 2) Flowering 3) Harvest	Method of Treatment	Application rate per treatment			No. of trt(s)	Dates of treat-ments	Growth stage at treatments	Portion ana-lysed	Residues (mg/kg)	PHI (days)	Remarks:
	(a)	(b)	(c)	kg a.s./hL	Water (L/ha)	kg a.e./ha		(d)	(e)	(a)	(h)	(f)	(g)
CEMS-2698A GHE-P-11273 Burweg, D-21709, Lower Saxony, Germany	Oilseed rape/ Artus	07 Sep 200 Not applicable 27 July 2005	Broadcast application using a small plot sprayer	-	304	0.018	1	04 Apr 2005	BBCH 50-51	Whole plant	ND 0.78 0.05 0.04 0.02	0- 0+ 28 60 85	Storage: 248d
										Seed	<0.01	114	
										Rest of plant	0.01	114	

(a) According to EEC and Codex classifications (both) should be used.
(b) Only if relevant.
(c) High or low volume spraying, spreading, dusting etc, overall, broad-cast, - type of equipment must be indicated.
(d) Year must be indicated.
(e) BBCH Monograph, Growth Stages of Plants, 1997, Blackwell, ISBN 3-8263-3152-4
(f) Minimum number of days after last application (Label pre-harvest interval, PHI, underline)
(g) Remarks may include: climatic conditions: references to analytical method; information concerning the metabolites included, method of storage, storage stability, analysis date and analytical method.
(h) Residues expressed on a dry weight basis if applicable.

RESIDUES DATA FROM SUPERVISED TRIALS – SUMMARY CEMS-2965A

Active substance (common name):	**Aminopyralid**	Commercial Product (name):	GF-1633
Crop/Crop group:	**Oilseed rape**	Other active substance in the formulation (common name and content):	Clopyralid 240 g ae/L Picloram 80 g ae/L
Responsible body for reporting (name & address):	Dow AgroSciences, 3B Park Square, Milton Park, Abingdon, Oxon, OX14 4RN, UK	Producer of commercial product	Dow AgroSciences
Content of active substance (g/Kg or g/L):	Aminopyralid 40 g ae/L	Indoor/Glasshouse/Outdoor:	Outdoor
Formulation number:	GF-1633	Residues calculated as:	Aminopyralid 1-butyl ester
Formulation (e.g. WP):	SL (soluble concentrate)	Residue method and LOQ	GRM 02.31: 0.01 mg/kg
		Study no. / Dow Agrosciences Report Reference:	CEMS-2965/ GHE-P-11493

1	2	3	4	5			6		7	8	9	10	11
Trial code/ Location, Country	Crop/Variety	Date of: 1) Sowing or Planting 2) Flowering 3) Harvest	Method of Treatment	Application rate per treatment			No. of trt(s)	Dates of treat-ments	Growth stage at treatments	Portion ana-lysed	Residues (mg/kg)	PHI (days)	Remarks:
	(a)	(b)	(c)	kg a.e./hL	Water (L/ha)	kg a.e./ha		(d)	(e)	(a)	(h)	(f)	(g)
GHE-P-11493 Burweg, D-21709, Lower Saxony, Germany	Oilseed rape/ Ti-tan	03 Sep 2005 Not applicable 21 July 2006	Broadcast application using a small plot sprayer	-	219	0.013	1	25 Apr 2006	BBCH 50	Whole plant	ND 0.32 0.06 0.01 0.02	0- 0+ 27 59 70	Storage: 218d
										Seed	ND	87	
										Rest of plant	<0.01	87	
				-	212	0.019	1	25 Apr 2006	BBCH 50	Whole plant	ND 0.46 0.06 0.02 0.01	0- 0+ 27 59 70	
										Seed	ND	87	
										Rest of plant	0.02	87	

(a) According to EEC and Codex classifications (both) should be used.
(b) Only if relevant.
(c) High or low volume spraying, spreading, dusting etc, overall, broad-cast, - type of equipment must be indicated.
(d) Year must be indicated.
(e) BBCH Monograph, Growth Stages of Plants, 1997, Blackwell, ISBN 3-8263-3152-4
(f) Minimum number of days after last application (Label pre-harvest interval, PHI, underline)
(g) Remarks may include: climatic conditions: references to analytical method; information concerning the metabolites included, method of storage, storage stability, analysis date and analytical method.
(h) Residues expressed on a dry weight basis if applicable.

RESIDUES DATA FROM SUPERVISED TRIALS – SUMMARY CEMS-2965B

Active substance (common name):	**Aminopyralid**	Commercial Product (name):	GF-1633
Crop/Crop group:	**Oilseed rape**	Other active substance in the formulation (common name and content):	Clopyralid 240 g ae/L Picloram 80 g ae/L
Responsible body for reporting (name & address):	Dow AgroSciences, 3B Park Square, Milton Park, Abingdon, Oxon, OX14 4RN, UK	Producer of commercial product	Dow AgroSciences
Content of active substance (g/Kg or g/L):	Aminopyralid 40 g ae/L	Indoor/Glasshouse/Outdoor:	Outdoor
Formulation number:	GF-1633	Residues calculated as:	Aminopyralid 1-butyl ester
Formulation (e.g. WP):	SL (soluble concentrate)	Residue method and LOQ	GRM 02.31: 0.01 mg/kg
		Study no. / Dow Agrosciences Report Reference:	CEMS-2965/ GHE-P-11493

1	2	3	4	5			6		7	8	9	10	11
Trial code/ Location, Country	Crop/Variety	Date of: 1) Sowing or Planting 2) Flowering 3) Harvest	Method of Treatment	Application rate per treatment			No. of trt(s)	Dates of treatments	Growth stage at treatments	Portion analysed	Residues (mg/kg)	PHI (days)	Remarks:
	(a)	(b)	(c)	kg a.e./hL	Water (L/ha)	kg a.e./ha		(d)	(e)	(a)	(h)	(f)	(g)
GHE-P-11493 Konin, PL-62-045, Wielkopolska, Poland	Oilseed rape/ Californium	21 Aug 2005 Not Applicable 3) 19 July 2006	Broadcast application using a small plot sprayer	-	209	0.013	1	27 Apr 2006	BBCH 50-51	Whole plant	ND 0.16 0.08 0.06 0.04	0- 0+ 28 60 75	Storage: 217d
										Seeds	<0.01	83	
										Rest of plant	0.08	83	
				-	210	0.019	1	27 Apr 2006	BBCH 50-51	Whole plant	ND 0.33 0.08 0.05 0.06	0- 0+ 28 60 75	
										Seeds	<0.01	83	
										Rest of plant	0.08	83	

(a) According to EEC and Codex classifications (both) should be used.
(b) Only if relevant.
(c) High or low volume spraying, spreading, dusting etc, overall, broadcast, - type of equipment must be indicated.
(d) Year must be indicated.
(e) BBCH Monograph, Growth Stages of Plants, 1997, Blackwell, ISBN 3-8263-3152-4
(f) Minimum number of days after last application (Label pre-harvest interval, PHI, underline)
(g) Remarks may include: climatic conditions: references to analytical method; information concerning the metabolites included, method of storage, storage stability, analysis date and analytical method.
(h) Residues expressed on a dry weight basis if applicable.

RESIDUES DATA FROM SUPERVISED TRIALS – SUMMARY CEMS-4348B

Active substance (common name):	**Aminopyralid**	Commercial Product (name):	GF-1633
Crop/Crop group:	**Oilseed rape**	Other active substance in the formulation (common name and content):	Clopyralid 240 g ae/L Picloram 80 g ae/L
Responsible body for reporting (name & address):	Dow AgroSciences, 3B Park Square, Milton Park, Abingdon, Oxon, OX14 4RN, UK	Producer of commercial product	Dow AgroSciences
Content of active substance (g/Kg or g/L):	Aminopyralid 40 g ae/L	Indoor/Glasshouse/Outdoor:	Outdoor
Formulation number:	GF-1633	Residues calculated as:	Aminopyralid 1-butyl ester
Formulation (e.g. WP):	SL (soluble concentrate)	Residue method and LOQ	GRM 07.07: 0.01 mg/kg
		Study no. / Dow Agrosciences Report Reference:	CEMS-4348/ GHE-P-12499

1	2	3	4	5			6		7	8	9	10	11
Trial code/ Location, Country	Crop/Variety	Date of: 1) Sowing or Planting 2) Flowering 3) Harvest	Method of Treatment	Application rate per treatment			No. of trt(s)	Dates of treatments	Growth stage at treatments	Portion analysed	Residues (mg/kg)	PHI (days)	Remarks:
	(a)	(b)	(c)	kg a.e./hL	Water (L/ha)	kg a.e./ha		(d)	(e)	(a)	(h)	(f)	(g)
GHE-P-12499 F-01560, Cormoz, Ain, France	Oilseed rape/ Adriana	03 Sep 2008 From 25 Mar 2009 3) 16 July 2009	Boom sprayer (3m width) with 6 flat fan Lechler, LD015F110 nozzles	0.0060	198	0.0118	1	20 Mar 2009	BBCH 31	Whole plant	0.477 0.147 0.056	0 13 27	Storage: 241d
										Seeds	<0.01 ND	105 118	
										Rest of plant	0.013 0.011	105 118	

(a) According to EEC and Codex classifications (both) should be used.
(b) Only if relevant.
(c) High or low volume spraying, spreading, dusting etc, overall, broadcast, - type of equipment must be indicated.
(d) Year must be indicated.
(e) BBCH Monograph, Growth Stages of Plants, 1997, Blackwell, ISBN 3-8263-3152-4
(f) Minimum number of days after last application (Label pre-harvest interval, PHI, underline)
(g) Remarks may include: climatic conditions: references to analytical method; information concerning the metabolites included, method of storage, storage stability, analysis date and analytical method.
(h) Residues expressed on a dry weight basis if applicable.

RESIDUES DATA FROM SUPERVISED TRIALS – SUMMARY CEMS-4348D

Active substance (common name):	**Aminopyralid**	Commercial Product (name):	GF-1633
Crop/Crop group:	**Oilseed rape**	Other active substance in the formulation (common name and content):	Clopyralid 240 g ae/L Picloram 80 g ae/L
Responsible body for reporting (name & address):	Dow AgroSciences, 3B Park Square, Milton Park, Abingdon, Oxon, OX14 4RN, UK	Producer of commercial product	Dow AgroSciences
Content of active substance (g/Kg or g/L):	Aminopyralid 40 g ae/L	Indoor/Glasshouse/Outdoor:	Outdoor
Formulation number:	GF-1633	Residues calculated as:	Aminopyralid 1-butyl ester
Formulation (e.g. WP):	SL (soluble concentrate)	Residue method and LOQ	GRM 07.07: 0.01 mg/kg
		Study no. / Dow Agrosciences Report Reference:	CEMS-4348/ GHE-P-12499

1	2	3	4	5			6		7	8	9	10	11
Trial code/ Location, Country	Crop/Variety	Date of: 1) Sowing or Planting 2) Flowering 3) Harvest	Method of Treatment	Application rate per treatment			No. of trt(s)	Dates of treatments	Growth stage at treatments	Portion analysed	Residues (mg/kg)	PHI (days)	Remarks:
	(a)	(b)	(c)	kg a.e./hL	Water (L/ha)	kg a.e./ha		(d)	(e)	(a)	(h)	(f)	(g)
GHE-P-12499 F-82700, St. Porquier, Midi-Pyrénéés, France	Oilseed rape/ Corail	16 Oct 2008 Not recorded 03 July 2009	Boom sprayer (3m width) with 6 flat fan Lurmark, LD015F110 nozzles	0.0060	196	0.0118	1	13 Mar 2009	BBCH 39	Whole plant	0.108 0.051 0.033	0 14 28	Storage: 248d
										Seed	0.007 0.011	98 112	
										Rest of plant	0.022 0.021	98 112	

(a) According to EEC and Codex classifications (both) should be used.
(b) Only if relevant.
(c) High or low volume spraying, spreading, dusting etc, overall, broadcast, - type of equipment must be indicated.
(d) Year must be indicated.
(e) BBCH Monograph, Growth Stages of Plants, 1997, Blackwell, ISBN 3-8263-3152-4
(f) Minimum number of days after last application (Label pre-harvest interval, PHI, underline)
(g) Remarks may include: climatic conditions: references to analytical method; information concerning the metabolites included, method of storage, storage stability, analysis date and analytical method.
(h) Residues expressed on a dry weight basis if applicable. Residues in [italics] have been proportioned to the cGAP.

zRMS comments:
According to the „Technical guidelines for determining the magnitude of pesticide residues in honey and setting Maximum Residue Levels in honey“ (SANTE/11956/2016 rev. 9; 14 September 2018) residues in honey can occur when a substance with systemic properties is applied prior to the flowering stage (before BBCH 60), of a crop which is foraged by bees.
Aminopyralid is a substance with systemic properties. Oilseed rape is a melliferous crop with high melliferous capacity. Residues in honey could be therefore expected.
Applicant provided argumentation and additionally data on residues in whole plant data at flowering for aminopyralid showing that for GF-4021 applied according the submitted GAP, the MRL for aminopyralid can be expected to below 0.05 mg/kg for honey and bee products.
No other special studies are needed.

7.4.8 Estimation of exposure through diet and other means (KCA 6.9)

Toxicological reference values relevant for dietary risk assessment are reported in the summary of the evaluation (see 7.1.2).

7.4.8.1 Input values for the consumer risk assessment: Aminopyralid

The input values in the following table were used to estimate consumer risk using the EFSA PRIMo Rev 3.1. All assessments follow the Tier I approach and are based on published MRL values (Reg. (EU) 2021/1841) and assume no dissipation of residues. The acute dietary assessments are performed only for the consumption of commodities for which GAPs are notified.

Table 7.4.8.1-1: Input values for the consumer risk assessment: Aminopyralid

Commodity	Chronic risk assessment		Acute risk assessment	
	Input value (mg/kg)	Comment	Input value (mg/kg)	Comment
Aminopyralid (sum of aminopyralid, its salts and its conjugates, expressed as aminopyralid)				
FRUITS, FRESH or FROZEN (except Tree Nuts, Table Olives, Avocados)	0.01*	* Indicates that the MRL is set at the limit of analytical quantification (Reg. (EU) 2021/1841)	Acute risk assessment was undertaken only with regard to the crops under consideration.	
Tree Nuts, Table Olives, Avocados	0.05*			
VEGETABLES, FRESH OR FROZEN (except herbs and edible flowers)	0.01*			
Herbs and edible flowers	0.02*			
PULSES	0.05*			
OILSEEDS AND OIL FRUITS	0.05*			
Rapeseeds/canola seeds	0.05*		0.01	STMR for rapeseeds (EFSA Journal 2020; 18(8):6229)
CEREALS (except barley, maize/corn, millet, oat, rye, sorghum, and wheat)	0.05*		Acute risk assessment was undertaken only with regard to the crops under consideration.	
Barley, oat, and rye	0.15			

Commodity	Chronic risk assessment		Acute risk assessment	
	Input value (mg/kg)	Comment	Input value (mg/kg)	Comment
Maize/corn, common millet/proso millet, and sorghum	0.05			
Wheat	0.1			
TEAS, COFFEE, HERBAL INFUSIONS, AND COCOA	0.05*			
HOPS (dried)	0.05*			
SPICES (except horseradish)	0.05*			
Horseradish	0.02			
SUGAR PLANTS	0.01*			
PRODUCTS OF ANIMAL ORIGIN - TERRESTRIAL ANIMALS				
All animals except Poultry				
Muscle and fat	0.1			
Liver	0.05			
Kidney and Edible Offals	1.0			
Others	0.05*			
Poultry Muscle, Fat, & Kidney	0.01*			
Poultry Liver, Edible Offals, Others	0.05*			
Milk	0.02			
Birds eggs	0.01*			
Honey and other apiculture products	0.05*			
Amphibians & reptiles, terrestrial invertebrates, and wild terrestrial vertebrate animals	0.01*			

7.4.8.2 Conclusion on consumer risk assessment: Aminopyralid

Extensive calculation sheets are presented in Appendix 3.

The highest Theoretical Maximum Daily Intake (TMDI) is 1% of the ADI for the Netherlands toddler. The highest contribution (0.5% of the ADI) is from cattle milk. Children have the highest International Estimated Short-Term Intake (IESTI) for unprocessed commodities at 0.01% of the ARfD for the consumption of rapeseeds/canola seeds, and for processed commodities at < 0.01% of the ARfD for the consumption of rapeseeds/oils.

Table 7.4.8.2-1: Consumer risk assessment: Aminopyralid

TMDI (% ADI) according to EFSA PRIMo	1% (based on NL toddler)
IESTI (% ARfD) according to EFSA PRIMo	Unprocessed Commodities: 0.01% based on consumption of rapeseeds/canola seeds by children Processed Commodities: < 0.01% based on consumption of rapeseeds/oils by children

The proposed uses of aminopyralid in the formulation GF-4021 do not represent unacceptable chronic and acute dietary risk for the consumer.

zRMS comments:

The consumer risk assessments were performed with revision 3.1 of the EFSA Pesticide Residues Intake Model (PRIMo). The calculation of the TMDI using EFSA model (version 3.1) and MRLs according to Reg. (EU) ~~2019/1015~~ 2021/1841 led to a utilisation of the ADI of 1% with the NL toddler being the population group with the highest value. For this diet, the highest contributor is Milk: Cattle with 0.5% of the ADI.
The intended uses will not result in a consumer chronic exposure exceeding the ADI.

For the calculation of the acute exposure the MRL has been used only for the use under consideration. The highest International Estimated Short-Term Intake (IESTI) is at 0.02% and 0.01% of the ARfD for the consumption of rapeseeds/canola by children and by adults respectively.
The proposed uses of aminopyralid in the formulation GF-4021 do not represent unacceptable acute and chronic risks for the consumer.

Combined exposure and risk assessment

From a scientific point of view, it is regarded necessary to take into account potential combination effects. However, the evaluation of cumulative or synergistic effects as requested by Art. 4 (3b) of Regulation (EC) No. 1107/2009 should only be performed when harmonised "scientific methods accepted by the Authority to assess such effects are available."
Currently, no EU-harmonized guidance is available on the risk assessment of combined exposure to multiple active substances; this approach is not mandatory at EU level.

The product is a mixture of three active substances (halauxifen-methyl, picloram, and aminopyralid). An acute reference dose has been allocated for all three, therefore, a combined acute exposure can be considered.

7.4.9 Acute consumer risk assessment from combined exposure

In a first step, dose-addition of residues of the individual active substances is assumed by making use of the Hazard Index (HI) concept. The Hazard Quotient (HQ) is calculated for all active substances in the PPP that are acutely toxic by performing deterministic IESTI/NESTI calculations with the calculation models EFSA PRIMO (rev.3.1) and appropriate national models, if required, and dividing the individual exposure levels by the respective ARfD. Addition of the individual HQs irrespective of any considerations on phenomenological effects or mode(s)/mechanisms of action results in the HI. The results of the HQ/HI calculations are summarized in the following table.

Table 7.4.9-1: Acute consumer risk assessment from combined exposure

Crop	Active Ingredient	HQ (based on IESTI according to EFSA PRIMo)
Unprocessed Commodities: Consumption of rapeseeds/canola seeds by Children	Halauxifen-methyl	0.001
	Picloram	0.0001
	Aminopyralid	0.0001
	Cumulative risk (HI)	**0.0012**
Processed Commodities: Consumption of rapeseeds/oils by Children	Halauxifen-methyl	0.001
	Picloram	0.0001
	Aminopyralid	0.0001

Crop	Active Ingredient	HQ (based on IESTI according to EFSA PRIMo)
	Cumulative risk (HI)	**0.0012**

The Hazard Index is <1. Thus, combined exposure to all active substances in GF-4021 is not expected to present a consumer risk. No further refinement of the assessment is required.

7.4.10 Chronic consumer risk assessment from combined exposure

The uses under consideration provide only a minor contribution to the overall chronic exposure of consumers to pesticide residues. The issue requires a more universal consideration and possibly the generic usage of monitoring data. A harmonised approach is not yet available, and currently no specific consideration is warranted in the scope of this evaluation.

zRMS comments:
Information given by the Applicant is sufficient and zRMS-Poland agrees with presented above conclusions.

7.6 References

Halauxifen-methyl

EC (European Commission), 2015. Review report for the active substance halauxifen-methyl Finalised in the Standing Committee on Plants, Animals, Food and Feed at its meeting on 29 May 2015 in view of the approval of halauxifen-methyl as active substance in accordance with Regulation (EC) No 1107/2009. SANTE/10406 /2015 rev. 1, 29 May 2015

EFSA (European Food Safety Authority), 2014. Conclusion on the peer review of the pesticide risk assessment of the active substance halauxifen-methyl (XDE-729 methyl). EFSA Journal 2014;12(12):3913, 93 pp. doi:10.2903/j.efsa.2014.3913 Available online: www.efsa.europa.eu/efsajournal

United Kingdom, 2013. Draft Assessment Report (DAR) on the active substance halauxifen-methyl prepared by the rapporteur Member State United Kingdom, in the framework of Directive 91/414/EEC, December 2013. Available online: www.efsa.europa.eu.

United Kingdom, 2014. Final Addendum to the Draft Assessment Report (DAR) on halauxifen-methyl, compiled by EFSA, October 2014. Available online: www.efsa.europa.eu.

Picloram

EC (European Commission), 2010. Review report for the active substance picloram. Finalised in the Standing Committee on the Food Chain and Animal Health at its meeting on 14 March 2008 in view of the inclusion of picloram in Annex I of Council Directive 91/414/EEC. SANCO/835/2008-Final, 11 May 2010, 8 pp.

EFSA (European Food Safety Authority), 2009. Conclusion on the peer review of the pesticide risk assessment of the active substance picloram. EFSA Journal 2009; 7(12):1390, 78 pp.

EFSA (European Food Safety Authority), 2013. Reasoned opinion on the modification of the existing MRLs for picloram in rape seed and mustard seed. EFSA Journal 2013;11(10):3439, 27 pp. doi:10.2903/j.efsa.2013.3439

United Kingdom, 2007. Draft assessment report on the active substance picloram prepared by the rapporteur Member State the United Kingdom in the framework of Council Directive 91/414/EEC, April 2007.

United Kingdom, 2009. Addendum to the draft assessment report on the active substance picloram prepared by the rapporteur Member State the United Kingdom in the framework of Council Directive 91/414/EEC, April 2009.

United Kingdom, 2012. Evaluation report on the modification of MRLs for picloram in oilseed rape prepared by the evaluating Member State United Kingdom under Article 8 of Regulation (EC) No 396/2005, 24 September 2012, 32pp

EFSA Journal 2012;10(9):2894 - Modification of the existing MRL for aminopyralid in rape seed. Available online: www.efsa.europa.eu.

EFSA Journal 2013;11(9):3352 - Peer review of the pesticide risk assessment of the active substance aminopyralid. Available online: www.efsa.europa.eu.

EFSA Journal 2020;18(8):6229 - Review of the existing MRLs for aminopyralid. Available online: www.efsa.europa.eu.

General documents

EC (European Commission), 1996. Appendix G. Livestock Feeding Studies. 7031/VI/95 rev.4. Available online: http://ec.europa.eu/food/plant/protection/resources/publications_en.htm

EC (European Commission), 1997a. Appendix A. Metabolism and distribution in plants. 7028/IV/95-rev.3. Available online: http://ec.europa.eu/food/plant/protection/resources/publications_en.htm

EC (European Commission), 1997b. Appendix B. General recommendations for the design, preparation and realization of residue trials. Annex 2. Classification of (minor) crops not listed in the Appendix of Council Directive 90/642/EEC. 7029/VI/95-rev.6. Available online: http://ec.europa.eu/food/plant/protection/resources/publications_en.htm

EC (European Commission), 1997c. Appendix C. Testing of plant protection products in rotational crops. 7524/VI/95-rev.2. Available online http://ec.europa.eu/food/plant/protection/resources/publications_en.htm

EC (European Commission), 1997d. Appendix E. Processing studies. 7035/VI/95-rev.5. Available online: http://ec.europa.eu/food/plant/protection/resources/publications_en.htm

EC (European Commission), 1997e. Appendix F. Metabolism and distribution in domestic animals. 7030/VI/95-rev.3. Available online: http://ec.europa.eu/food/plant/protection/resources/publications_en.htm

EC (European Commission), 1997f. Appendix H. Storage stability of residue samples. 7032/VI/95-rev.5. Available online: http://ec.europa.eu/food/plant/protection/resources/publications_en.htm

EC (European Commission), 1997g. Appendix I. Calculation of maximum residue level and safety intervals. 7039/VI/95. As amended by the document: classes to be used for the setting of EU pesticide maximum residue levels (MRLs). SANCO 10634/2010. Available online: http://ec.europa.eu/food/plant/protection/resources/publications_en.htm

EC (European Commission), 2000. Residue analytical methods. For pre-registration data requirement for Annex II (part A, section 4) and Annex III (part A, section 5 of Directive 91/414. SANCO/3029/99-rev.4. Available online: http://ec.europa.eu/food/plant/protection/resources/publications_en.htm

EC (European Commission), 2004. Residue analytical methods. For post-registration control. SANCO/825/00-rev.7. Available online: http://ec.europa.eu/food/plant/protection/resources/publications_en.htm

EC (European Commission), 2010. Classes to be used for the setting of EU pesticide Maximum Residue Levels (MRLs). SANCO 10634/2010 Rev. 0, finalized in the Standing Committee on the Food Chain and Animal Health at its meeting of 23-24 March 2010. Available online: http://ec.europa.eu/food/plant/protection/resources/publications_en.htm

EC (European Commission), 2017. Appendix D. Guidelines on comparability, extrapolation, group tolerances and data requirements for setting MRLs. 7525/VI/95-rev.10.3. Available online: http://ec.europa.eu/food/plant/protection/resources/publications_en.htm

FAO (Food and Agriculture Organization of the United Nations), 2009. Submission and evaluation of pesticide residues data for the estimation of Maximum Residue Levels in food and feed. Pesticide Residues. 2nd Ed. FAO Plant Production and Protection Paper 197, 264 pp.

Appendix 1 Lists of data considered in support of the evaluation

List of data submitted by the applicant and relied on

Data point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Vertebrate study Y/N	Owner
KCP 8 (KCA 6.1)	Machado, G.	2013	Frozen Storage Stability of Aminopyralid (XDE-750) in Rape Forage, Seed and Oil DAS Report No.: 110634 Dow AgroSciences Ind. Ltd. GLP (Y/N): Y Published (Y/N): N	N	Corteva Agriscience (Dow AgroSciences)
KCP 8 (KCA 6.1)	Lindner, M.	2014	Storage Stability Study for Residues of Aminopyralid in Barley Grain, Malt Sprouts, Spent Grains, Yeast and Beer DAS Report No.: S08-02908 Eurofins Agroscience Services Chem GmbH GLP (Y/N): Y Published (Y/N): N	N	Corteva Agriscience (Dow AgroSciences)
KCP 8 (KCA 6.1)	Delmotte, R.	2016	Title: Magnitude of the Residues of Halauxifen-methyl and Picloram in Oilseed rape (RAC Whole Plant, Seed and Straw), following One Application of GF-3447, Northern and Southern Europe – 2015 RDE-15-20345. DAS Report No.: 150006 Source: Dow AgroSciences GLP (Y/N): Y Published (Y/N): N	N	Corteva Agriscience (Dow AgroSciences)
KCP 8 (KCA 6.2.1)	LaMar, J. E.	2013	The Nature of the Residues of [^{14}C] XDE-729 Methyl (2 Radiolabels) in Oilseed Rape DAS Study No. 120997 PTRL West GLP/GEP (Y/N): Yes Published (Y/N): No	N	Corteva Agriscience (Dow AgroSciences)
KCP 8 (KCP 6.5.1)	Croffie, J. W., Adelfinskaya, Y., Hastings, M.	2016	A Confined Rotational Crop Study with 14C-Picloram. DAS Report No.: 130200 Research for Hire GLP (Y/N): Y Published (Y/N): N	N	Corteva Agriscience (Dow AgroSciences)

Data point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Vertebrate study Y/N	Owner
KCP 8 (KCA 6.6.2)	White, T.	2017	Determination of residues of picloram in winter and spring wheat grown as rotational crops after one application of GF-224 to bare soil at eight sites in Northern Europe and eight sites in Southern Europe 2014 – 2016 DAS Report No.: 140642 Dow AgroSciences GLP (Y/N): Y Published (Y/N): N	N	Corteva Agriscience (Dow AgroSci-ences)
KCP 8 (KCA 6.6.2)	White, T.	2019	Determination of Residues of Picloram in Rotational Crops (Wheat, Turnip and Kale) After One Application of GF-224 to Bare Soil at Two Sites in Northern Europe and Two Sites in Southern Europe 2014-2017. DAS Report No.: 140651 Eurofins Agroscience Services Ltd. GLP (Y/N): Y Published (Y/N): N	N	Corteva Agriscience (Dow AgroSci-ences)

List of data submitted or referred to by the applicant and relied on, but already evaluated at EU peer review

Data point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Vertebrate study Y/N	Owner
KCA 6.1	Devine, H. C.	2013	X11393728 (XDE-729 methyl) and X11393729 (XDE-729): Residue Stability Study in Crops under Frozen Storage Conditions DAS Report No.: 110563 Dow AgroSciences LLC GLP (Y/N): Y Published (Y/N): N	N	Corteva Agriscience (Dow AgroSciences)
KCA 6.1	Langridge, G	2014	Frozen Storage Stability of Residues of XDE-729 Methyl Ester, XDE-729 Acid and X11449757 in Animal Matrices – Twenty-Four Months Stability Data for XDE-729 Methyl Ester and XDE-729 Acid and Twenty-Four Months Stability Data for the Relevant Metabolite, X11449757 DAS Report No.: 110768 Dow AgroSciences LLC GLP (Y/N): Y Published (Y/N): N	N	Corteva Agriscience (Dow AgroSciences)
KCA 6.1	Dolder, S.	2003	Frozen Storage Stability ofPic1oram in Wheat Green Forage, Wheat Straw, Wheat Grain, Soil, Water, Oilseed Rape Grain and Oilseed Rape Hay DAS Report No.: 980075 Dow AgroSciences LLC GLP (Y/N): Y Published (Y/N): N	N	Corteva Agriscience (Dow AgroSciences)
KCA 6.1	Bjerke, E.	1988	Stability of Picloram In Milk and Egg Whites Stored Frozen DAS Report No.: GH-C 2079 Dow AgroSciences LLC GLP (Y/N): Y Published (Y/N): N	N	Corteva Agriscience (Dow AgroSciences)
KCA 6.1	Lindsay, D.	2004	Frozen Storage Stability of XDE-750 in Range Land and Pasture Grass and Hay and Wheat Straw and Wheat Grain Frozen Storage Conditions DAS Report No.: 030004 Dow AgroSciences LLC GLP (Y/N): Y Published (Y/N): N	N	Corteva Agriscience (Dow AgroSciences)

Data point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Vertebrate study Y/N	Owner
KCA 6.2.1	Rotondaro, S. L. and el.	2012	A Nature of the Residue Study with [14C]-XDE-729 Methyl Applied to Turnips. DAS Report No.: 110413 Dow AgroSciences LLC GLP (Y/N): Y Published (Y/N): N	N	Corteva Agriscience (Dow AgroSciences)
KCA 6.2.1	Ma, M., Smith, K.P., Jackson, A.U.	2012	A Nature of the Residue Study with [14C]-XR-729 Methyl Applied to Wheat with and without the Safener Cloquintocet Mexyl (Amended Report). DAS Report No.: 101080 (Amended report). Research for Hire GLP (Y/N): Y Published (Y/N): N	N	Corteva Agriscience (Dow AgroSciences)
KCA 6.6.2	Rotondaro, S.L.	2011	A Confined Rotational Crop Study with [14C]-XDE-729 Methyl Ester. DAS Report No.: 101635, 026108. Ricerca GLP (Y/N): Y Published (Y/N): N	N	Corteva Agriscience (Dow AgroSciences)
KCA 6.5.1	Ma, M., Balcer, J.L.	2011	Processing Study to Determine the Nature of Residues of 14C-XDE-729 Methyl and 14C-X11393729 Following Industrial or Household Preparation. DAS Report No.: 110369. Dow AgroSciences LLC GLP (Y/N): Y Published (Y/N): N	N	Corteva Agriscience (Dow AgroSciences)
KCA 6.2.3	Rotondaro, S.L and Adelfinskaya Y. A.	2011	A Nature of the Residue Study in the Ruminant with [14C]-XR-729 Methyl Ester. DAS Report No.: 101389. Southwest Bio-Labs, Inc. GLP (Y/N): Y Published (Y/N): N	N	Corteva Agriscience (Dow AgroSciences)
KCA 6.2.2	Rotondaro, S., Adelfinskaya, Y.A.	2011	A Nature of the Residue Study in the Laying Hen with [14C]-XR-729 Methyl Ester. DAS Report No.: 101390. Southwest Bio-Labs, Inc. GLP (Y/N): Y Published (Y/N): N	N	Corteva Agriscience (Dow AgroSciences)

Data point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Vertebrate study Y/N	Owner
KCA 7.2.1	Norr, C.	2001	Metabolism of picloram in spring oilseed rape following a foliar application. DAS Report No. 000299; 0C0003 (FBRC); GH-C 5391 Federal Biological Research Centre for Agriculture and Forestry (BBA), Berlin, Germany GLP (Y/N): Y Published (Y/N): N	N	Corteva Agriscience (Dow AgroSci-ences)
KCA 7.2.1	Stenner, S. S.	1992	[^{14}C] picloram: Nature of the residue in wheat - MET92030, RES92105, HWI 6397-111. DAS Report No.: GH-C 2942 Hazleton Wisconsin, Inc, Madison, Wisconsin, United States; Plant Sciences Inc, Watsonville, California, United States GLP (Y/N): Y Published (Y/N): N	N	Corteva Agriscience (Dow AgroSci-ences)
KCA 7.6.1	Kimmel, E.; Aldcroft, K. S.; Ewing, A.L.	1993	A confined rotational crop study with ^{14}C-picloram using turnips, mustard greens, wheat, and corn - MET9106; Ptrl No. 311W. DAS Report No. GH-C 2971R PTRL West Inc, Richmond , California, United States GLP (Y/N): YES Published (Y/N): NO	N	Corteva Agriscience (Dow AgroSci-ences)
KCA 7.2.3	Yackovich, P. R.; Byrne, S. L.	1992	Nature of residues of ^{14}C labelled picloram in the lactating goat. DAS Report No. MET92043 GLP (Y/N): Y Published (Y/N): N	N	Corteva Agriscience (Dow AgroSci-ences)
KCA 7.2.2	Yackovich, P.R.; Miller, J. H.	1986	The fate of ^{14}C labelled picloram fed to laying hens. DAS Report No. GH-C 1827 The Dow Chemical Company GLP/GEP (Y/N): N (prior to GLP) Published (Y/N): N	N	Corteva Agriscience (Dow AgroSci-ences)
KCA 6.5.1	Rotondaro, S.; Adusu-milli, H.	2012	Processing Study to Determine the Nature of Residues of 14C-Aminopyralid Following Industrial or Household Preparation. DAS Report No.: 110709. Dow AgroSciences LLC GLP (Y/N): Y Published (Y/N): N	N	Corteva Agriscience (Dow AgroSci-ences)

Data point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Vertebrate study Y/N	Owner
KCA 7.4.2	Linder, S. J.; Balcer, J. L	2007	A Nature of the Residue Study with 14C Labeled Aminopyralid Applied to Oilseed Rape Corteva Report No.: 060011 Corteva Agriscience LLC GLP (Y/N): Y Published (Y/N): N	N	Corteva Agriscience (Dow AgroSci-ences)
KCA 7.2.7	Delmotte, R.	2015	Magnitude of the Residues of Halauxifen-methyl and Clopyralid in Oilseed rape (RAC Whole Plant, Seed and Straw), following One Application of GF-3488, Northern Europe – 2015 Corteva Report No.: 150534 Corteva Agriscience LLC GLP (Y/N): Y Published (Y/N): N	N	Corteva Agriscience (Dow AgroSci-ences)

List of data submitted by the applicant and not relied on

Data point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Vertebrate study Y/N	Owner
-	-	-	-	-	-

List of data relied on and not submitted by the applicant but necessary for evaluation

Data point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Vertebrate study Y/N	Owner
-	-	-	-	-	-

Appendix 2 Detailed evaluation of the additional studies relied upon

A 2.1 Halauxifen-methyl

A 2.1.1 Stability of residues

A 2.1.1.1 Stability of residues during storage of samples

A 2.1.2 Nature of residues in plants, livestock and processed commodities

A 2.1.2.1 Nature of residue in plants

A 2.1.2.1.1 Nature of residue in primary crops

Only one new study dealing with the nature of residues in primary crops is included in this petition.

A 2.1.2.1.1.1 Oilseed Rape

Comments of zRMS:	A metabolism study was conducted with [phenyl-^{14}C]XDE-729 methyl and [pyridine-^{14}C]XDE-729 methyl applied as a foliar spray directly onto oilseed rape. The [^{14}C-]XDE-729 methyl application solutions were prepared to mimic a GF-2630 EC formulation. The study design consisted of five test plots: one control and four treated (one for each radiolabel applied in the fall referred to as S-1, and one for each radiolabel applied in the spring referred to as S-2). Approximately 25% of the whole plants were harvested at the forage stage. Seed was harvested at maturity along with stems and leaves (trash). Total radioactive residues in oilseed rape were as follows: PH S-1 forage, (0.002 mg eq/kg), PY S-1 forage (0.003 mg eq/kg), S-1 seed (<0.001 mg eq/kg for both radiolabels), PH S-1 trash (0.001 mg eq/kg), PY S-1 trash (0.002 mg eq/kg), PH S-2 forage (0.016 mg eq/kg), PY S-2 forage (0.018 mg eq/kg), PH S-2 seed (0.001 mg eq/kg), PY S-2 seed (0.002 mg eq/kg), PH S-2 trash (0.024 mg eq/kg) and PY S-2 trash (0.048 mg eq/kg). Extraction of select samples with acetonitrile/water released 37.9-69.7% TRR. Metabolites of XDE-729 methyl in oilseed rape were characterized via HPLC, TLC, and enzymatic hydrolysis. XDE-729 methyl was not observed in any matrix. Residue levels were low in general with no single residue exceeding 0.001 mg eq/kg or 30.5% TRR. X11449757 was present in low levels (0.001 mg eq/kg, 4.5-10.7% TRR, trace amounts also possible in S-1 forage). Other minor residues were hydrolyzed by treatment with β-glucosidase suggesting glucose conjugation of unknown residues. The metabolic pathway for XDE-729 methyl involves the hydrolysis of the methyl ester and demethylation of the methoxy ether moieties to X11449757. Intermediates X11406790 and X11393729 were not observed. Further metabolism involves glucose conjugation of multiple metabolites although structures of the conjugated species are not known. The metabolic pathway seen in this study is comparable to the pathways seen for XDE-729 in cereals (wheat) and in root and tuber crops (turnips). It should be noted that no new metabolites in this study were identified compare to the previously assessed study by the RMS in wheat and turnip. **ZRMS-Poland is of the opinion that the presented metabolism in oilseed rape (group of pulses and oilseeds crops) is similar to that in wheat (group of cereals) and turnip (group of roots crop). Considering the above, the same residue definition for halauxifen-methyl for a group of pulses and oilseeds crops can be proposed and adopted as the residue definition for halauxifen-methyl for a group of cereals.** <u>Remark:</u> Similar conclusions were drawn by zRMS-Denmark (GF-3447, 2017) and zRMS-France (GF-3447, 2018).

Reference:	7.2.2.1
Report	The Nature of the Residues of [^{14}C] XDE-729 Methyl (2 Radiolabels) in Oilseed Rape; LaMar, J. E.; 2013; DAS Study No. 120997
Guideline(s):	Yes – OECD 501
Deviations:	No
GLP:	Yes
Acceptability:	Yes

Executive Summary

CITATION

LaMar, J. E.; 2013; The Nature of the Residues of [^{14}C] XDE-729 Methyl (2 Radiolabels) in Oilseed Rape; PTRL West; Lab Study No. 2370W; DAS Study No. 120997; 16 December 2013; Unpublished

COMPLIANCE

Guideline(s):	OECD 501 (EC Working Document 7028/VI/95, Appendix A, rev. 3, 22/7/97)
US EPA Guideline(s):	OPPTS 860.1300
Deviations:	There were no deviations from the test guidelines
Dates of work:	06 November 2012 (first application) to mid-August 2013 (exact completion date for the experimental work was not indicated in the report)
GLP status:	Yes
Number of pages in final report:	158

BACKGROUND INFORMATION

XDE-729 (halauxifen) is a systemic, post-emergent herbicide that belongs to the auxin family of herbicides. This compound was initially developed for the control of broadleaf weeds in spring and winter cereals and is currently under development as a mixture with florasulam for broadleaf weed control in spring and winter cereals.

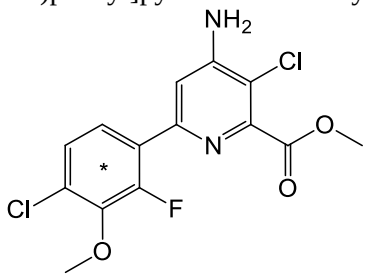
MATERIALS AND METHODS

Test Item(s)

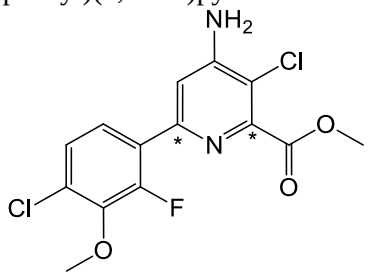
Non-radiolabelled test item #1

ISO Common name:	Halauxifen
Test item (chemical/other name):	XDE-729 Methyl (Halauxifen Methyl)
Purity:	The analytical standard used as part of this study had a purity of 99.1%.
Description (physical state):	White powder at 24.4 °C.
Lot/batch no.:	201001134-26 (TSN 031117-0005)
CAS no.:	943831-98-9
SMILES string	Not Available

Radiolabelled test item #1

Name:	[Phenyl-^{14}C] XDE-729 Methyl
Test item (chemical/other name):	Methyl 4-amino-3-chloro-6-(4-chloro-2-fluoro-3-methoxy(UL-^{14}C)phenyl]pyridine-2-carboxylate
Structural formula: Position of labelling (*)	
Lot/batch no.:	INV303547 (XX3-122713-68)
Radiochemical purity:	99.0%
Specific radioactivity:	39.9 mCi/mmol

Radiolabelled test item #2

Name:	[Pyridine-^{14}C] XDE-729 Methyl
Test item (chemical/other name):	Methyl 4-amino-3-chloro-6-(4-chloro-2-fluoro-3-methoxy-phenyl)(2,6-^{14}C)pyridine-2-carboxylate
Structural formula: Position of labelling (*)	
Lot/batch no.:	INV303546 (DE3-130593-42)
Radiochemical purity:	≥98.7%
Specific radioactivity:	27.9 mCi/mmol

Methods

Test Site Information

Testing environment:	Outdoor test plots
Container description:	The test plots consisted of five, above ground, wooden boxes that each had a surface area of 1 m^2 and a depth of *ca* 0.5 m. One box served as a control and two boxes (one for each label) were treated in the late fall and the other two in the early spring.
Soil type:	sandy loam
Soil characteristics:	0.75% OM pH 7.4 CEC – 9.3 meq/100 g
Any adverse weather conditions:	There were no adverse meteorological abnormalities that impacted the study.
Any adverse insect or disease problems:	There were no insect or disease problems that adversely impacted the study.

Study Use Pattern

Application method:	Foliar spray to immature plants.	
Formulation type:	Emulsifiable Concentrate (EC) (GF-2630)	
Application rate:	6.0 g as/ha (5.76 g ae/ha) per application (This was the targeted rate. The actual rate was 6.86-6.93 g as/ha or 6.58-6.65 g ae/ha.)	
Number of applications:	A single application was made to each plot.	
Timing of applications	The fall application was made on 06 November 2012 when the plants were at growth stage BBCH 17-19. The spring application was made on 16 April 2013 when the plants were at growth stage BBCH 39-40.	
PHI:	Fall Application:	Forage – 64 DAA Seed and Trash – 178 DAA
	Spring Application:	Forage – 27 DAA Seed and Trash – 53 DAA

Test System

Organism (*Species*):	Oilseed Rape (*Brassica napus*)
Variety:	No variety was provided in the field report for this study.
Crop group:	Oilseed and Pulse
Growth stage at application:	BBCH 17-19 (Fall application) BBCH 39-40 (Spring application)
Harvested RAC:	Both recognized RAC's for oilseed rape (forage and mature seed) were collected. In addition, the remaining stems and leaves (referred to as "trash") at the time of the final harvest were also collected
Growth stage at harvest:	The forage samples from both applications were at BBCH 64-67 when collected. The growth stage at the time the mature seed and trash samples were collected was BBCH 89.
Harvesting procedure:	Forage samples were collected by cutting off *ca* 25% of the plants in each plot at a height of 2-3 cm above the soil line using a grape knife. The collected plants were then cut into 10-15 cm segments using scissors and this material then placed into labelled Ziploc plastic bags prior to weighing and freezing. Seed pods were collected from the mature plants using pruning shears. The pods were opened manually allowing the seeds to fall into a tared container. After hand removal of any extraneous plant material, the seeds were weighed and then transferred to a labelled Ziploc bag prior to freezing. The remaining stems and leaves at the time the seeds were harvested were collected and handled in a manner similar to that described for the forage samples.

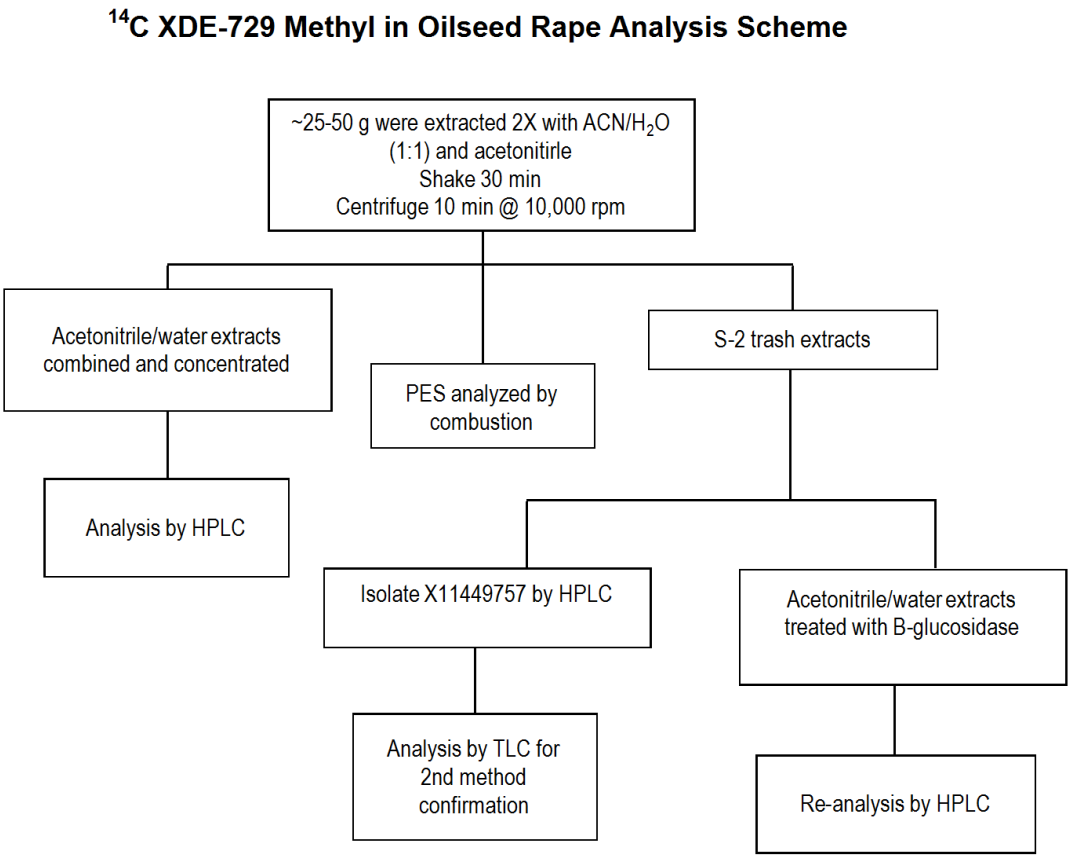
Sample Handling and Preparation

Following collection, the samples were weighed and stored frozen at the field site prior to shipping frozen to the nearby analytical facility using refrigerated trucks. All samples were received in good (frozen) condition at the analytical facility within one day or less of shipping. Upon receipt, the samples were reweighed and then cryogenically milled to a fine particle size in the presence of dry ice. After allowing any remaining dry ice to sublime overnight in a freezer, the samples were reweighed and then stored frozen (<-20 °C) pending analysis.

Extraction of Sample Residues

Due to the low TRR levels in all the seed samples as well as in the trash sample from the fall application, these samples were not extracted and analyzed. All other samples were extracted as outlined in the following flow diagram. In general, 25-50 g portions of the milled forage and trash samples were extracted by shaking twice for 30 minutes with acetonitrile/water (1:1) followed by once with acetonitrile. The solids from each step were removed by centrifugation and the resulting supernatants decanted and the three extracts pooled. After determining the final volume of the pooled extract, aliquots were removed for LSC analysis. Portions of these extracts (typically *ca* 100 mL) were concentrated by rotary evaporation to remove most of the acetonitrile and a portion of the remaining aqueous fraction prepared for HPLC analysis. The post-extraction solids (PES) were allowed to air dry prior to weighing and submitting for combustion analysis in order to determine the remaining radioactive residue.

Figure 2.1.2.1.1.1-1: Flow diagram for the extraction of Oilseed Rape Forage and Trash



Analyses of Non-Extractable Residues

Given the low initial TRR levels in all the forage samples, no additional work was necessary to further characterize the nonextractable residues since all were at or below 0.007 mg eq/kg. No additional work was done with the non-extractable residues in the trash samples since OSR trash is not considered to be a raw agricultural commodity.

Enzyme or Acid Hydrolysis of Suspected Conjugate Fractions

No acid hydrolysis work was done with any of the sample extracts. A portion of the concentrated extract from the spring treated PH-trash sample, however, was subjected to enzyme hydrolysis using β-glucosidase. For this work, an aliquot of the extract was evaporated to dryness and the resulting residue redissolved in 800 µL of 0.1 M sodium acetate buffer (pH 5). After 20 mg of the enzyme, the sample was incubated for 4 hours at 37 °C after which 10 L of formic acid was added in order to stop enzymatic activity. The sample was then assayed by HPLC and the results compared to the initial analysis of this extract.

Metabolite Isolation and Identification

A total of six reference standards were available for use in this study. Included were standards for the parent XDE-729 ester; the parent XDE-729 acid (X11393729); the O-demethylated parent ester (X11406790); the O-demethylated parent acid (X11449757); the deschloro parent ester (X11861662); and the deschloro parent acid (X11861663). HPLC retention time comparisons were made between these reference standards and the radioactive peaks in the chromatograms in order to provide initial tentative identifications.

Based on the initial HPLC analyses, only the O-demethylated parent acid (X11449757) was observed and was targeted for isolation and structure confirmation. This was accomplished using extracts of the phenyl-labelled spring trash sample. Portions of this extract were subjected to repetitive HPLC analysis that

included collection and pooling of the X11449757 fraction from each analysis. The pooled isolated fraction was concentrated to near dryness and the sample subjected to comparative TLC analysis in order to obtain structure confirmation.

Analytical Methodology

Total ^{14}C measurements

All liquid based samples were directly radioassayed by liquid scintillation counting. Typically, triplicate aliquots were dispensed into plastic or glass vials and scintillation cocktail added. Samples were analyzed in a Beckman series LS6000 or LS6500 liquid scintillation counter using blank scintillation cocktail for background subtraction. The LSC spectrometer provided quench curve correction via a series of quenched standard solutions containing a known amount of ^{14}C radioactivity.

Total radioactivity in all plant samples both before and after extraction was determined by combustion analysis using a Harvey Biological Oxidizer. Typically, 3-5 aliquots weighing *ca* 250 mg each were combusted for 3 to 4 minutes and the $^{14}CO_2$ trapped in 15-mL of Carbon-14 Cocktail. These trapped samples were then radioassayed by LSC. Combustion efficiency was routinely determined for each set of samples (typically >96%) and the dpm values in the combusted samples adjusted accordingly.

High performance liquid chromatography (HPLC) for quantitation

HPLC analyses of all sample extracts were accomplished using a Phenomenex Synergi Hydro-RP column (150 x 3.3 mm i.d., 4.0 µm; 1.0 mL/min; UV detection at 254 nm) that was eluted with a four step, non-linear gradient using mixtures of water and acetonitrile containing 0.1% formic acid.

Thin-layer chromatography (TLC)

TLC analyses used for metabolite ID confirmation were carried out using 20 x 20 cm silica gel 60 TLC plates with F254 indicator that were developed one time in acetone/isopropanol/acetic acid (7/2/0.5). Reference standards were detected via UV exposure, while radioactive zones were detected by exposing plates to phosphor imaging screens and then scanning with a Storm 820 phosphor imager system with ImageQuant software.

RESULTS AND DISCUSSION

Results of In-Life Phase

Analyses of the spray solutions for total radioactivity showed that for both the fall and spring applications, each of the four test plots was treated with *ca* 114-115% of the intended amounts of test material. This was equivalent to a total seasonal rate of 6.86-6.93 g as/ha (6.59-6.65 g ae/ha) that was applied to each plot. Purity analyses of the post application retainer samples of the spray solutions (all were ≥98.7% pure) verified the stability of the ^{14}C test material during the application process.

No abnormal weather conditions were experienced during the in-life phase of this study and likewise no disease or insect problems were encountered. All crops appeared to grow normally.

Total Radioactive Residue (TRR) Levels

TRR levels in all samples, expressed as mg/kg of parent equivalents are shown below.

Table A.2.1.2.1.1.1-1: Total radioactive residues (TRRs) in matrices of oilseed rape following a single application of ^{14}C XDE-729

Matrix	Timing and Application No.	PHI (days)	Total Radioactive Residue (mg a.i./kg)	
			Phenyl Label (PH)	Pyridine Label (PY)
Fall Forage	Single app at BBCH 17-19	64	0.002	0.003
Fall Seed	Single app at BBCH 17-19	178	<LOD [a]	<LOD
Fall Trash	Single app at BBCH 17-19	178	0.001	0.002
Spring Forage	Single app at BBCH 39-40	27	0.016	0.018
Spring Seed	Single app at BBCH 39-40	53	0.001	0.002
Spring Trash	Single app at BBCH 39-40	53	0.024	0.048

[a] Limit of Detection which was set at 2 times the background level.

TRR levels in all samples from either the fall or spring applications were low, with comparable levels seen in the corresponding samples from each application regardless of the position of the radiolabel in the ^{14}C

test material. This indicated that both ring systems stayed intact and that there was no cleavage of the bond between the two rings.
For both applications, there was negligible translocation of residues into the developing seeds as the TRR levels in all seed samples were 0.001 mg/kg or less. For the fall application, residues in the forage and trash samples were likewise very low (0.001-0.003 mg/kg). For the corresponding samples from the spring application, residues were moderately higher as there were in the range of 0.016-0.018 mg/kg in forage and 0.024-0.048 mg/kg in trash. The moderately higher residues seen in these latter two samples was assumed to be due to the fact that the plants for the spring application were treated at a later growth stage than those for the fall application and thus intercepted more of the spray solution and the resulting residues experienced less growth dilution between the time of application and the time of harvest.

Distribution of Residues Following Extraction
The percentage of the residues that were readily extractable using acetonitrile/water from each of the forage samples from the fall and spring applications as well as from the trash samples from the spring application, expressed both as a percentage of the total sample residue and as mg/kg of parent equivalents, is shown below in Tables 2 and 3. Due to the low TRR levels in both seed samples as well as the fall trash sample, none of these materials were extracted and analyzed.

Table A.2.1.2.1.1.1-2: Distribution of the parent and the metabolites in oilseed rape forage following a single fall or spring application of 14C XDE-729

Metabolite Fraction	PH-Fall Forage		PY-Fall Forage		PH Spr. Forage		PY Spr. Forage	
	%TRR	mg/kg	%TRR	mg/kg	%TRR	mg/kg	%TRR	mg/kg
Extractable RA	69.7	0.001	64.7	0.002	57.3	0.008	58.7	0.010
XDE-729 Methyl	ND	ND	ND	ND	ND	ND	ND	ND
X11449757	10.8	<0.001	5.4	<0.001	10.7	0.001	6.1	0.001
Unknwn at 17 Min	10.8	<0.001	5.4	<0.001	9.5	0.001	6.6	0.001
Unknwn at 20 Min	ND	ND	8.4	<0.001	8.7	0.001	10.9	0.002
Unknwn at 23 Min	30.4	0.001	9.8	<0.001	ND	ND	7.0	0.001
Unknwn at 24 Min	ND	ND	15.2	<0.001	11.4	0.002	8.7	0.001
Unknwn at 25 Min	17.6	<0.001	20.6	<0.001	7.5	0.001	8.4	0.001
Unknwn at 26 Min	ND	ND	ND	ND	9.5	0.001	ND	ND
Non-retained RA	ND	ND	ND	ND	ND	ND	10.8	0.002
Extracted Solids	30.3	<0.001	35.3	0.001	42.7	0.006	41.3	0.007

ND = Not Detected

Table A.2.1.2.1.1.1-3: Distribution of the parent and the metabolites in oilseed rape trash following a single fall or spring application of 14C XDE-729

Metabolite Fraction	PH-Fall Trash		PY-Fall Trash		PH Spr. Trash		PY Spr. Trash	
	%TRR	mg/kg	%TRR	mg/kg	%TRR	mg/kg	%TRR	mg/kg
Extractable RA	NA	--	NA	--	37.9	0.010	40.4	0.020
XDE-729 Methyl	--	--	--	--	ND	ND	ND	ND
X11449757	--	--	--	--	7.0	0.002	4.5	0.002
Unknwn at 17 Min	--	--	--	--	6.3	0.002	4.4	0.002
Unknwn at 20 Min	--	--	--	--	6.9	0.002	3.7	0.002
Unknwn at 23 Min	--	--	--	--	7.1	0.002	6.3	0.003
Unknwn at 24 Min	--	--	--	--	10.6	0.003	7.1	0.003
Unknwn at 25 Min	--	--	--	--	ND	ND	ND	ND
Non-retained RA	--	--	--	--	ND	ND	6.8	0.003
Extracted Solids	--	--	--	--	62.1	0.017	59.6	0.029

NA = Not Analyzed (residues too low)
ND = Not Detected

For both the fall and spring forage samples, *ca* 60-70% of the TRR was extractable using the mild procedures employed for this study. The level of extractable radioactivity in the spring trash samples was moderately lower at *ca* 35-40% of the TRR. This moderate drop off was not unexpected as such decreases in extractability are often seen as treated plant material gets closer to maturity and begins to senesce.
Due to the low initial TRR levels in all the forage samples and to the fact that oilseed rape trash is not a recognized raw agricultural commodity, no additional extraction and characterization work was deemed necessary for any of the residues remaining in the post extraction solids.

Characterisation and Identification of Residues

Aliquots of all extracts of the spring and fall forage samples and of the spring trash samples were concentrated and analyzed directly by HPLC without any intermediate cleanup step. The distribution of the radioactivity in these extracts among parent XDE-729 methyl and its metabolites, expressed as both a percentage of the TRR and as mg/kg of parent equivalents, are shown above in Tables 2 and 3. The data for the forage sample residues are further summarized in Table 4 to show the amounts of the residue that were identified and characterized and to show the accountability of the residues during the extraction process. A comparable table was not prepared for the spring trash samples since OSR trash is not a recognized agricultural commodity and since these samples were only extracted in order to serve as a potential source of residues for metabolite identification purposes.
Results of the HPLC analyses of the forage extracts showed the residues in all samples to be multicomponent, with the only fraction matching one of the available reference standards being X11449757 (formed following cleavage of the methyl ester and O-demethylation of the methoxy group on the phenyl ring from the parent test material). No residues of the unchanged XDE-729 methyl were observed in any of the forage samples. In addition to X11449757, an additional 3-6 unidentified components were observed in the extracts, most of which were slightly less polar in nature than X11449757. Quantitation of these residues showed X11445797 to not be present at levels in excess of 0.001 mg/kg, while the maximum level of any of the unidentified components was 0.002 mg/kg. The fact that the residue profiles were comparable in all of the samples regardless of the position on the radiolabel in the test material with which they were treated confirms that the bond between the two ring systems was not cleaved.
As shown in Table 3, the residue profiles in the extracts of the spring OSR trash samples were comparable to that seen in the forage samples. This suggests that XDE-729 was not more extensively metabolized as the plants matured.

Table A.2.1.2.1.1.1-4: Summary of characterisation and identification of radioactive residues in the forage from oilseed rape plants treated with a single fall or spring application of 14C XDE-729 at a rate of 6.0 g as/ha

	PH-Fall Forage (0.002 mg/kg)		PY-Fall Forage (0.003 mg/kg)		PH Spr. Forage (0.016 mg/kg)		PY Spr. Forage (0.018 mg/kg)	
	%TRR	mg/kg	%TRR	mg/kg	%TRR	mg/kg	%TRR	mg/kg
XDE-729 Methyl	ND	ND	ND	ND	ND	ND	ND	ND
X11449757	10.8	<0.001	5.4	<0.001	10.7	0.001	6.1	0.001
Unknwn at 17 Min	10.8	<0.001	5.4	<0.001	9.5	0.001	6.6	0.001
Unknwn at 20 Min	ND	ND	8.4	<0.001	8.7	0.001	10.9	0.002
Unknwn at 23 Min	30.4	0.001	9.8	<0.001	ND	ND	7.0	0.001
Unknwn at 24 Min	ND	ND	15.2	<0.001	11.4	0.002	8.7	0.001
Unknwn at 25 Min	17.6	<0.001	20.6	<0.001	7.5	0.001	8.4	0.001
Unknwn at 26 Min	ND	ND	ND	ND	9.5	0.001	ND	ND
Non-retained RA	ND	ND	ND	ND	ND	ND	10.8	0.002
Total Identified	10.8	<0.001	5.4	<0.001	10.7	0.001	6.1	0.001
Total Characterized	58.8	0.001	59.4	0.002	46.6	0.006	52.4	0.008
Total Extractable	69.7	0.001	64.7	0.002	57.3	0.008	58.7	0.010
Unextracted (PES)[1]	30.3	<0.001	35.3	0.001	42.7	0.006	41.3	0.007
Accountability[2]	50.0	0.001	100.0	0.003	87.5	0.014	94.4	0.017

[1] Residues remaining after exhaustive extractions.
[2] Accountability = (Total extractable + Total unextractable)/(TRRs from combustion analysis) * 100
ND = Not Detected

While only about half of the radioactivity thought to be present in the PH-Fall forage sample was accounted for following extraction, this recovery was not considered to be out of line given the low combustion TRR value in the sample (0.002 mg/kg). Recoveries in the other three samples were considered to be nearly quantitative given the low combustion TRR values in the samples and thus all percentage TRR values for the samples were normalized. The mg/kg values shown for each component were based on the recovered TRR values rather than the initial combustion TRR values.

Results of Enzyme Hydrolysis Work

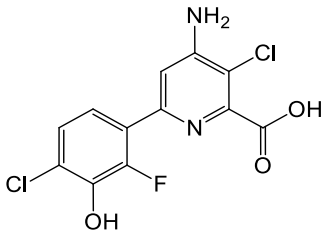
A portion of the extract of the spring PH-trash sample was subjected to enzyme hydrolysis using β-glucosidase as previously described. Results of this work showed two moderately polar components with retention times of *ca* 15 and 17 minutes appeared to be converted to additional residues that eluted with retention times of *ca* 23 and 24 minutes (low to moderate levels of radioactivity were already present in these two regions prior to the hydrolysis step). These results suggested the presence of possible glucose conjugates in the treated samples. Since none of the available reference standards eluted in the 23- or 24-minute region of the HPLC chromatogram, it was not possible to determine the structure of the conjugated residue components.

Metabolite Identification

While the levels of all the observed metabolite fractions in the forage and trash extracts were low (none in forage exceeded 0.002 mg/kg), one was a chromatographic match by reverse phase HPLC with the reference standard for X11449757. As previously described, this fraction was isolated from the extract of the spring PH-trash sample by making repetitive shots of this extract on HPLC and the collected fraction of interest then analyzed by normal phase (silica gel) TLC. This analysis confirmed that the isolated metabolite chromatographed with the same R_f as that for the X11449757 reference standard. This was considered to be positive confirmation of this metabolite as X11449757.

The structure, chemical name and the common name used in the study report for the residue component that was identified during this study is shown below.

Table A.2.1.2.1.1.1-5: Identification of compounds from metabolism study

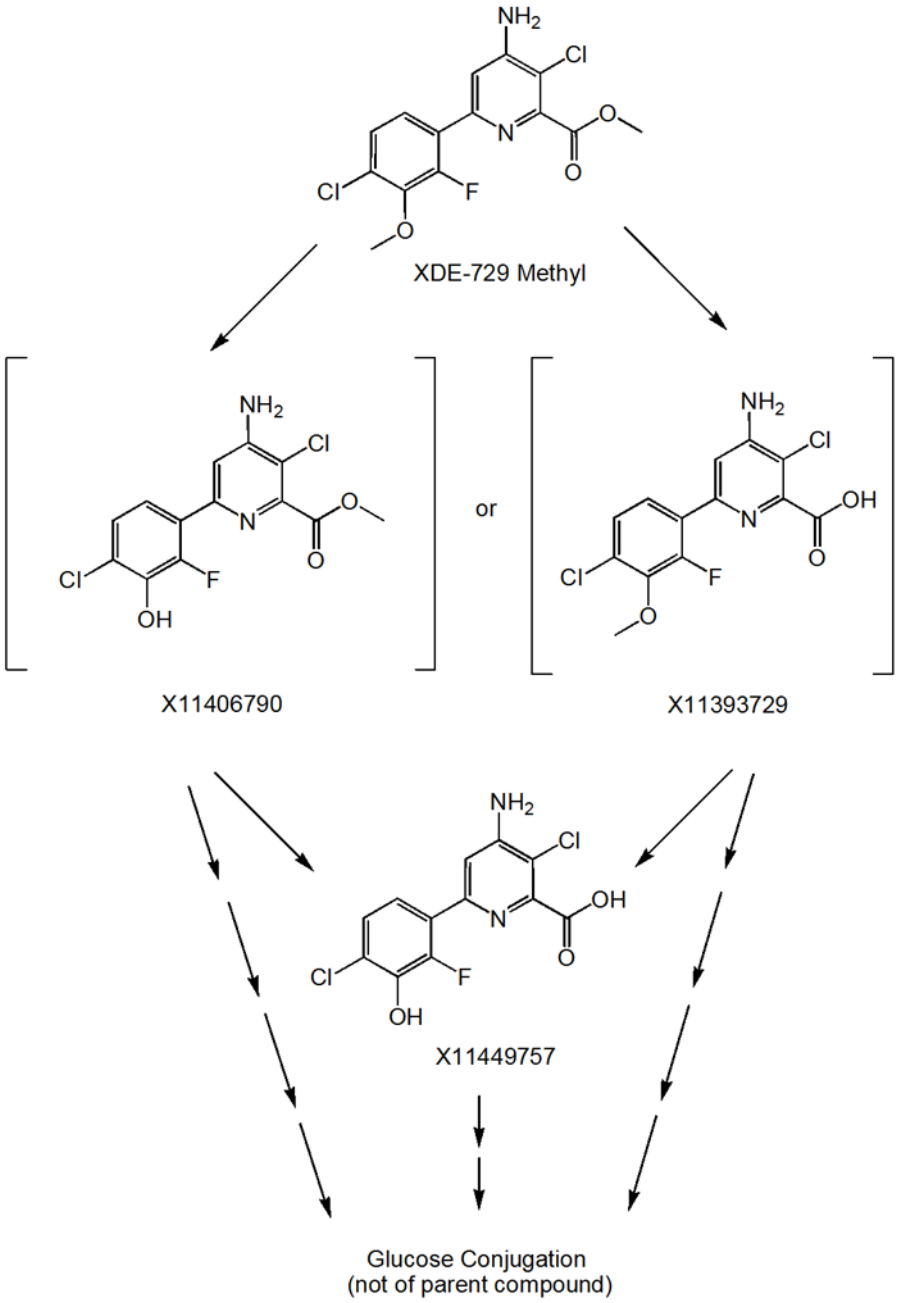
Common name/code number	Chemical name	Chemical structure
X11449757	4-amino-3-chloro-6-(4-chloro-2-flouro-3-hydroxyphenyl)-picolinic acid	

Metabolic Pathway

The proposed metabolic pathway elucidated during this study is shown below. As indicated, the metabolism of XDE-729 methyl proceeds through hydrolysis of the methyl ester and O-demethylation of the aryl methoxy group to give X11449757. The two possible intermediates in this process, the parent XDE-729 acid (X11393729) and the O-demethyl parent ester (X11406790), were not observed in any of the sample extracts. Further metabolism involves glucose conjugation of multiple metabolites; however, the structures of these conjugated moieties could not be determined due to the low levels at which they were present

The metabolic pathway determined in this study was comparable to that seen in earlier metabolism studies run using wheat (1) and turnips (2). In both of those studies, the two proposed intermediates from the current study, X11393729 and X11406790, were both actually at higher levels than X11449757 and there was more extensive glucose conjugation of the metabolites.

Figure 2.1.2.1.1.1-2: Proposed metabolic pathway of XDE-729 methyl in oilseed rape



Storage Stability

Since all samples were initially extracted and analyzed within 22 days following harvest and since all samples were stored frozen at all times following harvest, no special work was needed to confirm storage stability.

CONCLUSION

Foliar applications of ^{14}C XDE-729 to oilseed rape in either the spring or fall at levels that were about 15% higher than the maximum seasonal GAP rate of 6.0 g as/ha resulted in negligible residues in seed (<LOD-0.002 mg/kg) and nearly negligible residues in forage (0.002-0.003 mg/kg from the fall application and 0.016-0.018 mg/kg from the spring application). Residues in the remaining stems and leaves at harvest

(referred to as trash) were likewise low (0.001-0.002 mg/kg for the fall application and 0.024-0.048 mg/kg for the spring application). The similarity in residue levels in the corresponding samples at each sampling interval regardless of the position of the label in the ^{14}C test material suggested that the bond between the two ring systems in the molecule was not cleaved.

Extraction of both the spring and fall forage samples and the spring trash samples with a mixture of acetonitrile/water showed *ca* 60-70% of the TRR in the forage samples and *ca* 35-40% of the trash residues to be readily extractable. The moderate decline in the levels of readily extractable radioactivity between the forage and trash samples was not unexpected as such decreases are often observed as plant material gets closer to maturity and begins to senesce.
HPLC analyses of the extracts of the forage and trash samples showed both to consist of the same multiple radioactive components, with no individual component in the forage samples observed at a level in excess of 0.002 mg/kg and no individual component in trash observed at a level in excess of 0.003 mg/kg. No unchanged parent XDE-729 methyl was observed in any of the extracts, while all of the extracts appeared to contain low levels (0.002 mg/kg or less) of the parent XDE-729 acid in which the aryl methoxy group had been O-demethylated (X11449757).
Enzyme hydrolysis work with one of the spring trash extracts using β-glucosidase suggested the presence of several low level glucose conjugates; however, the aglycone portion of these conjugates could not be identified.

Based on the results from this study, the metabolic pathway for XDE-729 in oilseed rape involves hydrolysis of the methyl ester and O-demethylation of the methoxy ether moiety to give X11449757. Possible intermediates in the formation of X11449757, compounds X11406790 (the O-desmethyl parent ester) and X11393729 (the parent XDE-729 acid), were not observed. Further metabolism appeared to involve the formation of glucose conjugates, although the structures of the conjugated species could not be identified. The metabolic pathway seen in this study is comparable to the pathways seen for XDE-729 in cereals (wheat) and in root and tuber crops (turnips).
Given the nearly negligible residues seen in the two raw agricultural commodities of oilseed rape (forage and seed), it is proposed that the only residue components that need to be included in any analytical method that is developed for these commodities are the parent XDE-729 methyl and XDE-729 acid. No hydrolysis step needs to be included in any such method. It is likewise proposed that the residue definition for oilseed rape for both monitoring and risk assessment purposes be established as the sum of XDE-729 methyl and XDE-729 acid (X11393729) expressed as XDE-729 equivalents. This residue definition is the same as that proposed for cereals.

A 2.1.3 Magnitude of residues in plants

A 2.1.3.1 Oilseed Rape

Table A.2.3.1-1: Comparison of intended and critical EU GAPs

Type of GAP	Number of applications	Application rate per treatment (gai/ha)	Interval between application	Growth stage at last application	PHI (days)
cGAP EU (dRR, 2016)	1	Picloram: 24 g ae/ha + Halauxifen-methyl: 4.8 g ae/ha	N/A	BBCH 30	N/A
cGAP EU (EFSA, 2013, MRL ER (UK), 2012)	1	Picloram: 24 g ae/ha	N/A	BBCH 50	N/A
Intended cGAP (2*)	1	Halauxifen-methyl: 2.5 g ae/ha + Picloram: 12 g ae/ha + Aminopyralid: 8 g ae/ha	N/A	BBCH 12-19	-

* Use number(s) in accordance with the list of all intended GAPs in Part B, Section 0

A 2.1.3.1.1 Magnitude of Residues - Study 150006 (RDE-15-20345).

Comments of zRMS:	Sixteen residue trials: 6 NEU and 10 SEU were conducted on oilseed rape during 2014 and 2015 seasons to determine the magnitude of halauxifen and halauxifen-methyl after one spraying application with 4.8 g ae/ha of halauxifen-methyl and 24 g ae/ha of picloram with application at BBCH 16-30. Residues of halauxifen and halauxifen-methyl were determined according to method described in Dow AgroSciences Study Number 110005. The LOQ for all compounds was 0.01 mg/kg for oilseed rape. Concurrent recoveries obtained during the conduct of this study were acceptable with mean values in the range 70-110%. All RSD values were below 20%. Levels of residue are below the LOQ of 0.02 mg/kg for halauxyfen-methyl (sum of halauxyfen-methyl and halauxyfen acid; expressed as halauxyfen methyl) for all trials. The maximum frozen storage period of samples prior to the analysis was 375 days. All residue data reported within the present submission are covered by the storage period. The study is acceptable. <u>Remark:</u> In Northern Europe, each trial consisted in two treated plots corresponding to two different date of treatment. Thus, as the two plots are located at the same experimental site but correspond to different experimental conditions, the highest level of residues between the two treated plots has been selected for the assessment. Lines describing the plots whose results are not taken into consideration have been greyed out.

Reference:	KCA 6.3.1
Report	Magnitude of the Residues of Halauxifen-Methyl and Picloram in Oilseed Rape (RAC Whole Plant, Seed and Straw), Following One Application of GF-3447, Northern and Southern Europe – 2015, R. Demotte, 2016, Report No. RDE-15-20345, DAS Study ID 150006
Guideline(s):	Guideline 7029/VI/95 (rev. 5) to Directive 91/414/EEC and Regulations (EU) 283/2013 and 284/2013 implementing Regulation (EC) 1107/2009
Deviations:	No
GLP:	Yes
Acceptability:	Yes

Sixteen trials were located in Northern and Southern Europe (France, United Kingdom, Poland, Spain, Italy and Greece) in 2014-2015. Seven trials were Decline Curve trials and nine were harvest trials.

In Northern Europe (trials FR01 to PL06), three plots were established in each trial. U plot was left untreated. T1 plot was treated once with GF-3447, at a late autumn timing (November- December 2014) with a BBCH crop stage between 16 and 30. T2 plot was treated once with GF-3447, with maximum BBCH growth stage of 30 and before 28th February 2015.

In Southern Europe (trials FR07 to GR16), two plots were established in each trial. U plot was left untreated. T plot was treated once with GF-3447, with maximum BBCH growth stage of 30 and before 28th February 2015.

At every application, the target dose of GF-3447 was 0.5 L/ha (corresponding to 4.8 g ae/ha of halauxifen-methyl and 24 g ae/ha of picloram). Applications were carried out using boom sprayers in order to reproduce a normal agricultural application technique on a small-scale size. In each trial, one application was made on T1 and T2 or T plots. Amounts of mixture applied ranged from 161 to 406 L/ha.
On trials FR02, GB04, PL06, FR09, ES12, IT13, IT14, GR15 and GR16, one sampling of seeds and straw was taken at harvest in each plot.

On trials FR01, GB03 and PL05, specimens were taken at 7 occasions: whole plants were taken at 0, 7 and

14 days after application on plots U, T1 and T2. Seeds and straw were taken 7 days before harvest, at commercial harvest and at 3 and 7 days after harvest.

On trials FR07, FR08 and ES10 and ES11 specimens were taken at 7 occasions: whole plants were taken at 0, 7 and 14 days after application on plots U and T. Seeds and straw were taken 7 days before harvest, at commercial harvest and at 3 and 7 days after harvest.

All the specimens were placed into labelled plastic bags, weighed and double bagged. Specimens were frozen and shipped on freezer truck. They were delivered to analytical site on July 07th and 14th 2015, August 04th, 10th and 12th 2015, September 01st 2015 and October 07th 2015.

The maximum frozen storage period of samples prior to the analysis was 375 days.
A frozen storage stability study CEMS-4957 was conducted by CEMAS on XDE-729 methyl and XDE-729 acid. CEMS-4957 was reported on 19-Aug-2013 and showed that residues of X11393728 (XDE-729 methyl ester) and X11393729 (XDE-729 acid) do not exhibit any significant degradation when stored under frozen conditions for up to 735 days in wheat grain, lettuce, oilseed rape seed and whole oranges.

A frozen storage stability study 980075 was conducted by Dow AgroSciences on picloram. 980075 was reported on 20-May-2003 and showed that residues of picloram do not exhibit any significant degradation when stored under frozen conditions for up to 1096 days in wheat green forage, straw and grain.

Halauxifen (XDE-729)
All samples were analysed for XDE-729 methyl (X11393728) and XDE-729 acid (X11393729) using the analytical method described in Dow AgroSciences Study Number 110005, “Determination of Residues of XDE-729 Methyl Ester and XDE-729 Acid in Agricultural Commodities and Wheat Processed Products using Online Solid-Phase Extraction and Liquid Chromatography with Tandem Mass Spectrometry”. The limit of detection (LOD) and limit of quantitation (LOQ) were 0.003 mg/kg and 0.01 mg/kg, respectively. Recoveries in whole plants averaged 87%, in straw 98% and 90% in seeds for halauxifen-methyl, and averaged 86% in whole plants, 99% in straw and 100% in seeds, for halauxifen-acid.

Picloram
All samples were analysed for picloram using Dow AgroSciences study number 120610, “Method Validation Study for the Determination of Residues of Clopyralid and Picloram in Agricultural Commodities by LC-MS/MS”. The limit of detection (LOD) and limit of quantitation (LOQ) were 0.003 mg/kg and 0.01 mg/kg, respectively. Recoveries in whole plants averaged 91%, in straw 101% and 78% in seeds.

Residue in untreated specimens
No residue of halauxifen-methyl was detected (<LOD) in any untreated specimens. No residue of halauxifen-acid and picloram were detected (< LOD) in any untreated specimens, with exceptions of some specimens with residue between LOD and LOQ.

Table A.2.3.1.1-1: Summary of the study RDE-15-20345 trials – Residues of halauxifen-methyl and halauxifen-acid

Trial No./ Location/ EU zone/ Year	Commodity/ Variety (a)	Date of 1.Sowing or planting 2.Flowering 3. Harvest (b)	Application rate per treatment			Dates of treatment or no. of treatments and last date (c)	Growth stage at last treatment or date	Portion analyzed	Residues (mg/kg)		PHI (days) (d)	Details on trial (e)
			g a.e./ ha	Water (l/ha)	g a.e./hl				halauxifen-methyl	halauxifen-acid		
RDE-15-20345 FR01 49700 Doué la Fontaine, Pays de la Loire (EU Northern Zone)	Winter oilseed rape / DK Expertise	1) 05/09/14 2) 08/04/15 to 20/04/15 3) 06/07/15	4.8	161	2.98	04 Dec 14	BBCH 18-19	Whole plant Whole plant Whole plant Seeds Seeds Seeds Seeds Straw Straw Straw Straw	0.226 0.077 0.038 ND ND ND ND ND ND ND ND	ND ND ND ND ND ND ND ND ND ND ND	0 7 14 203 211 214 218 203 211 214 218	Residue method and LOQ: 110005 / 0.01 mg/kg Max frozen storage time prior to analysis: 334 days formulation (type): GF-3447 (EC)
RDE-15-20345 FR01 49700 Doué la Fontaine, Pays de la Loire (EU Northern Zone)	Winter oilseed rape / DK Expertise	1) 05/09/14 2) 08/04/15 to 20/04/15 3) 06/07/15	4.90	164	2.99	19 Feb 15	BBCH 27-29	Whole plant Whole plant Whole plant Seeds Seeds Seeds Seeds Straw Straw Straw Straw	0.204 0.015 0.010 ND ND ND ND ND ND ND ND	ND ND ND ND ND ND ND ND ND ND ND	0 8 14 126 134 137 141 126 134 137 141	Residue method and LOQ: 110005 / 0.01 mg/kg Max frozen storage time prior to analysis: 257 days Formulation (type): GF-3447 (EC)
RDE-15-20345 FR02 08300 Tagnon, Champagne-Ardenne (EU Northern Zone)	Winter oilseed rape / DK Exstorm	1) 23/08/14 2) 20/04/15 to 04/05/15 3) 22/07/15	5.08	239	2.13	26 Nov 14	BBCH 19	Seeds Straw	ND ND	ND ND	238 238	Residue method and LOQ: 110005 / 0.01 mg/kg Max frozen storage time prior to analysis: 120 days Formulation (type): GF-3447 (EC)

Trial No./ Location/ EU zone/ Year	Commodity/ Variety	Date of 1.Sowing or planting 2.Flowering 3. Harvest	Application rate per treatment			Dates of treatment or no. of treatments and last date	Growth stage at last treatment or date	Portion analyzed	Residues (mg/kg)		PHI (days)	Details on trial
			g a.e./ ha	Water (l/ha)	g a.e./hl				halauxifen-methyl	halauxifen-acid		
	(a)	(b)				(c)					(d)	(e)
RDE-15-20345 FR02 08300 Tagnon, Champagne-Ardenne (EU Northern Zone)	Winter oilseed rape / DK Exstorm	1) 23/08/14 2) 20/04/15 to 04/05/15 3) 22/07/15	4.56	214	2.13	19 Feb 15	BBCH 19	Seeds Straw	ND ND	ND ND	153 153	Residue method and LOQ: 110005 / 0.01 mg/kg Max frozen storage time prior to analysis: 128 days Formulation (type): GF-3447 (EC)

Trial No./ Location/ EU zone/ Year	Commodity/ Variety	Date of 1.Sowing or planting 2.Flowering 3. Harvest	Application rate per treatment			Dates of treatment or no. of treatments and last date	Growth stage at last treatment or date	Portion analyzed	Residues (mg/kg)		PHI (days)	Details on trial
			g a.e./ ha	Water (l/ha)	g a.e./hl				halauxifen-methyl	halauxifen-acid		
	(a)	(b)				(c)					(d)	(e)
RDE-15-20345 GB03 OX27 7LT Bucknell, Oxfordshire (EU Northern Zone)	Winter oilseed rape / Harper	1) 04/09/14 2) not recorded 3) 30/07/15	4.66	194	2.4	04 Dec 14	BBCH 17-18	Whole plant Whole plant Whole plant Seeds Seeds Seeds Seeds Straw Straw Straw Straw	0.224 0.056 0.031 ND ND ND ND ND ND ND ND	ND ND ND ND ND ND ND ND ND ND ND	0 7 14 225 232 235 238 225 232 235 238	Residue method and LOQ: 110005 / 0.01 mg/kg Max frozen storage time prior to analysis: 334 days formulation (type): GF-3447 (EC)

Trial No./ Location/ EU zone/ Year	Commodity/ Variety	Date of 1.Sowing or planting 2.Flowering 3. Harvest	Application rate per treatment			Dates of treatment or no. of treatments and last date	Growth stage at last treatment or date	Portion analyzed	Residues (mg/kg)		PHI (days)	Details on trial
			g a.e./ ha	Water (l/ha)	g a.e./hl				halauxifen-methyl	halauxifen-acid		
	(a)	(b)				(c)					(d)	(e)
RDE-15-20345 GB03 OX27 7LT Bucknell, Oxfordshire (EU Northern Zone)	Winter oilseed rape / Harper	1) 04/09/14 2) not recorded 3) 30/07/15	4.96	207	2.4	17 Feb 15	BBCH 19	Whole plant Whole plant Whole plant Seeds Seeds Seeds Seeds Straw Straw Straw Straw	0.207 0.034 0.014 ND ND ND ND ND ND ND ND	ND ND ND ND ND ND ND ND ND ND ND	0 7 14 150 157 160 163 150 157 160 163	Residue method and LOQ: 110005 / 0.01 mg/kg Max frozen storage time prior to analysis: 259 days formulation (type): GF-3447 (EC)
RDE-15-20345 GB04 LU6 3QZ Kensworth, Bedfordshire (EU Northern Zone)	Winter oilseed rape / Charger	1) 16/08/14 2) Not Recorded 3) 01/08/15	5.00	208	2.4	01 Dec 14	BBCH 18	Seeds Straw	ND ND	ND ND	239 239	Residue method and LOQ: 110005 / 0.01 mg/kg Max frozen storage time prior to analysis: 114 days Formulation (type): GF-3447 (EC)

Trial No./ Location/ EU zone/ Year	Commodity/ Variety	Date of 1.Sowing or planting 2.Flowering 3. Harvest	Application rate per treatment			Dates of treatment or no. of treatments and last date	Growth stage at last treatment or date	Portion analyzed	Residues (mg/kg)		PHI (days)	Details on trial
			g a.e./ ha	Water (l/ha)	g a.e./hl				halauxifen-methyl	halauxifen-acid		
	(a)	(b)				(c)					(d)	(e)
RDE-15-20345 GB04 LU6 3QZ Kensworth, Bedfordshire (EU Northern Zone)	Winter oilseed rape / Charger	1) 16/08/14 2) Not Recorded 3) 01/08/15	4.56	190	2.4	18 Feb 15	BBCH 19-30	Seeds Straw	ND ND	ND ND	160 160	Residue method and LOQ: 110005 / 0.01 mg/kg Max frozen storage time prior to analysis: 122 days Formulation (type): GF-3447 (EC)
RDE-15-20345 PL05 64-840 Nowe Brzeźno, Wielkopolska (EU Northern Zone)	Winter oilseed rape / Granat	1) 30/08/14 2) 27/04/15 to 17/05/15 3) 29/07/15	4.50	281	1.60	20 Nov 14	BBCH 16-18	Whole plant Whole plant Whole plant Seeds Seeds Seeds Seeds Straw Straw Straw Straw	0.179 0.112 0.101 ND ND ND ND ND ND ND ND	ND (0.004) (0.005) ND ND ND ND ND ND ND ND	0 7 15 245 251 254 258 245 251 254 258	Residue method and LOQ: 110005 / 0.01 mg/kg Max frozen storage time prior to analysis: 348 days formulation (type): GF-3447 (EC)
RDE-15-20345 PL05 64-840 Nowe Brzeźno, Wielkopolska (EU Northern Zone)	Winter oilseed rape / Granat	1) 30/08/14 2) 27/04/15 to 17/05/15 3) 29/07/15	4.40	275	1.60	23 Feb 15	BBCH 30	Whole plant Whole plant Whole plant Seeds Seeds Seeds Seeds Straw Straw Straw Straw	0.174 0.048 0.031 ND ND ND ND ND ND ND ND	ND (0.006) (0.006) ND ND ND ND ND ND ND ND	0 7 14 150 156 159 163 150 156 159 163	Residue method and LOQ: 110005 / 0.01 mg/kg Max frozen storage time prior to analysis: 263 days formulation (type): GF-3447 (EC)

Trial No./ Location/ EU zone/ Year	Commodity/ Variety	Date of 1.Sowing or planting 2.Flowering 3. Harvest	Application rate per treatment			Dates of treatment or no. of treatments and last date	Growth stage at last treatment or date	Portion analyzed	Residues (mg/kg)		PHI (days)	Details on trial
			g a.e./ ha	Water (l/ha)	g a.e./hl				halauxifen-methyl	halauxifen-acid		
	(a)	(b)				(c)					(d)	(e)
RDE-15-20345 PL06 63-040 Michalów, Wielkopolska (EU Northern Zone)	Winter oilseed rape / DK Exprit	1) 29/08/14 2) 20/04/15 to 05/05/15 3) 22/07/15	4.85	303	1.60	26 Nov 14	BBCH 18	Seeds Straw	ND ND	ND ND	239 239	Residue method and LOQ: 110005 / 0.01 mg/kg Max frozen storage time prior to analysis: 119 days formulation (type): GF-3447 (EC)
RDE-15-20345 PL06 63-040 Michalów, Wielkopolska (EU Northern Zone)	Winter oilseed rape / DK Exprit	1) 29/08/14 2) 20/04/15 to 05/05/15 3) 22/07/15	4.90	307	1.60	27 Feb 15	BBCH 20	Seeds Straw	ND ND	ND ND	146 146	Residue method and LOQ: 110005 / 0.01 mg/kg Max frozen storage time prior to analysis: 127 days formulation (type): GF-3447 (EC)
RDE-15-20345 FR07 13150 Tarascon, Provence Alpes Côte d'Azur (EU Southern Zone)	Winter oilseed rape / Athletic Royal	1) 25/08/14 2) 15/04/15 to 05/05/15 3) 15/06/15	4.82	302	1.60	19 Feb 15	BBCH 30	Whole plant Whole plant Whole plant Seeds Seeds Seeds Seeds Straw Straw Straw Straw	0.088 (0.007) ND ND ND ND ND ND ND ND ND	ND ND ND ND ND ND ND ND ND ND ND	0 7 14 110 117 120 124 110 117 120 124	Residue method and LOQ: 110005 / 0.01 mg/kg Max frozen storage time prior to analysis: 267 days formulation (type): GF-3447 (EC)

Trial No./ Location/ EU zone/ Year	Commodity/ Variety	Date of 1.Sowing or planting 2.Flowering 3. Harvest	Application rate per treatment			Dates of treatment or no. of treatments and last date	Growth stage at last treatment or date	Portion analyzed	Residues (mg/kg)		PHI (days)	Details on trial
			g a.e./ ha	Water (l/ha)	g a.e./hl				halauxifen-methyl	halauxifen-acid		
	(a)	(b)				(c)					(d)	(e)
RDE-15-20345 FR08 31330 Grenade sur Garonne, Midi Pyrénées (EU Southern Zone)	Winter oilseed rape / DK Explicit	1) 25/09/14 2) 15/04/15 to 29/04/15 3) 27/06/15	4.63	193	2.40	09 Feb 15	BBCH 30	Whole plant Whole plant Whole plant Seeds Seeds Seeds Seeds Straw Straw Straw Straw	0.121 0.012 (0.004) ND ND ND ND ND ND ND ND	ND ND ND ND ND ND ND ND ND ND ND	0 7 14 133 140 143 147 133 140 143 147	Residue method and LOQ: 110005 / 0.01 mg/kg Max frozen storage time prior to analysis: 277 days formulation (type): GF-3447 (EC)
RDE-15-20345 FR09 31290 Montgaillard Lauragais, Midi Pyrénées (EU Southern Zone)	Winter oilseed rape / DK Exstorm	1) 29/08/14 2) 13/04/15 to 26/04/15 3) 28/06/15	5.03	210	2.40	09 Feb 15	BBCH 30	Seeds Straw	ND ND	ND ND	141 141	Residue method and LOQ: 110005 / 0.01 mg/kg Max frozen storage time prior to analysis: 153 days formulation (type): GF-3447 (EC)
RDE-15-20345 ES10 41400 Ecija, Andalucia (Sevilla) (EU Southern Zone)	Winter oilseed rape / NXH 214	1) 07/11/14 2) 10/03/15 to 10/04/15 3) 25/05/15	4.86	254	1.91	04 Feb 15	BBCH 30	Whole plant Whole plant Whole plant Seeds Seeds Seeds Seeds Straw Straw Straw Straw	0.151 (0.005) ND ND ND ND ND ND ND ND ND	ND ND ND ND (0.004) ND (0.003) ND ND ND ND	0 7 14 140 111 114 118 140 111 114 118	Residue method and LOQ: 110005 / 0.01 mg/kg Max frozen storage time prior to analysis: 282 days formulation (type): GF-3447 (EC)

Trial No./ Location/ EU zone/ Year	Commodity/ Variety	Date of 1.Sowing or planting 2.Flowering 3. Harvest	Application rate per treatment			Dates of treatment or no. of treatments and last date	Growth stage at last treatment or date	Portion analyzed	Residues (mg/kg)		PHI (days)	Details on trial
			g a.e./ ha	Water (l/ha)	g a.e./hl				halauxifen-methyl	halauxifen-acid		
	(a)	(b)				(c)					(d)	(e)
RDE-15-20345 ES11 24713 Sueros de Cepeda, León (EU Southern Zone)	Winter oilseed rape / Hidromel	1) 21/09/14 2) April to May 2015 3) 08/07/15	4.79	299	1.60	11 Feb 15	BBCH 17	Whole plant Whole plant Whole plant Seeds Seeds Seeds Seeds Straw Straw Straw Straw	0.147 0.025 (0.007) ND ND ND ND ND ND ND ND	ND ND ND ND ND ND ND ND ND ND ND	0 7 14 152 159 163 166 152 159 163 166	Residue method and LOQ: 110005 / 0.01 mg/kg Max frozen storage time prior to analysis: 275 days formulation (type): GF-3447 (EC)
RDE-15-20345 ES12 24765 Redelda de la Valduerna, León (EU Southern Zone)	Winter oilseed rape / Expertise	1) 30/09/14 2) April 2015 3) 10/07/15	4.85	303	1.60	11 Feb 15	BBCH 17	Seeds Straw	ND ND	ND ND	149 149	Residue method and LOQ: 110005 / 0.01 mg/kg Max frozen storage time prior to analysis: 143 days formulation (type): GF-3447 (EC)
RDE-15-20345 IT13 20871 Vimercate, Lombardy (EU Southern Zone)	Winter oilseed rape / PR45 W04	1) 25/09/14 2) 20/04/15 to 06/05/15 3) 11/06/15	4.70	294	1.60	26 Jan 15	BBCH 22-24	Seeds Straw	ND ND	ND ND	134 134	Residue method and LOQ: 110005 / 0.01 mg/kg Max frozen storage time prior to analysis: 174 days formulation (type): GF-3447 (EC)

Trial No./ Location/ EU zone/ Year	Commodity/ Variety (a)	Date of 1.Sowing or planting 2.Flowering 3. Harvest (b)	Application rate per treatment			Dates of treatment or no. of treatments and last date (c)	Growth stage at last treatment or date	Portion analyzed	Residues (mg/kg)		PHI (days) (d)	Details on trial (e)
			g a.e./ ha	Water (l/ha)	g a.e./hl				halauxifen-methyl	halauxifen-acid		
RDE-15-20345 IT14 27028 San Martino Siccomario, Lombardy (EU Southern Zone)	Winter oilseed rape / PR44 W29	1) 04/10/14 2) 15/04/15 to 30/04/15 3) 12/06/15	4.86	304	1.60	27 Jan 15	BBCH 23-24	Seeds Straw	ND ND	ND ND	134 134	Residue method and LOQ: 110005 / 0.01 mg/kg Max frozen storage time prior to analysis: 173 days formulation (type): GF-3447 (EC)
RDE-15-20345 GR15 57200 Drymos, Central Macedonia (EU Southern Zone)	Winter oilseed rape / Edimax CL	1) 01/10/14 2) 01/04/15 to 25/04/15 3) 25/05/15 to 15/06/15	4.83	403	1.20	20 Feb 15	BBCH 22-23	Seeds Straw	ND ND	ND ND	109 109	Residue method and LOQ: 110005 / 0.01 mg/kg Max frozen storage time prior to analysis: 174 days formulation (type): GF-3447 (EC)
RDE-15-20345 GR16 62045 Lefkothea, Central Macedonia (EU Southern Zone)	Winter oilseed rape / Nelson	1) 10/10/14 2) 01/04/15 to 25/04/15 3) 25/05/15 to 15/06/15	4.86	406	1.20	20 Feb 15	BBCH 22-23	Seeds Straw	ND ND	ND ND	111 111	Residue method and LOQ: 110005 / 0.01 mg/kg Max frozen storage time prior to analysis: 242 days formulation (type): GF-3447 (EC)

(a) According to CODEX Classification / Guide
(b) Only if relevant
(c) Year must be indicated
(d) Days after last application (Label pre-harvest interval, PHI, underline)
(e) Remarks may include: Climatic conditions; Reference to analytical method and information which metabolites are included

A 2.1.4 Magnitude of residues in livestock

Not required for the characterization of the product.

A 2.1.5 Other/Special Studies

No other/special studies required for the current submission.

A 2.2 Picloram

A 2.2.1 Stability of residues

No new study submitted.

A 2.2.1.1 Stability of residues during storage of samples

Not required for the characterization of the product.

A 2.2.2 Nature of residues in plants, livestock and processed commodities

A 2.2.2.1 Nature of residue in plants

Not required for the characterization of the product.

A 2.2.2.1.1 Nature of residue in rotational crops

Comments of zRMS:	The purpose of this study was to determine the amount, nature and distribution of residues in the raw agricultural commodities of three rotational crops, wheat, lettuce, and radish (a cereal, a leafy vegetable and a root crop, respectively) planted in a sandy loam soil at 30, 60 and 335 days after treatment (DAT) with a single soil application of ^{14}C-picloram at a target rate of 25 g ai/ha. This study was conducted to requirements to determine the nature, amount and distribution of residues in raw agricultural commodities of rotational crops outlined in the OECD Guidance Document 502 for Metabolism in Rotational Crops (2007). No deficiencies have been identified. However, as some data on the field phase of the study were not provided or clear enough, the study is used only as additional information. The study is acceptable as informative. Remark: Similar conclusions were drawn by zRMS-France (GF-3447, 2018).

Reference:	
Report	A Confined Rotational Crop Study with ^{14}C-Picloram, Croffie, J.W., 2016, Study ID: 130200
Guideline(s):	Yes, OECD Guidance Document 502 for Metabolism in Rotational Crops (Issued 8 January 2007)
Deviations:	No (none mentioned)
GLP:	Yes
Acceptability:	Supplementary

Materials and methods

Study design

Pyridine-labelled ^{14}C-Picloram was soil-applied as a potassium hydroxide (KOH) salt to confined plots of sandy loam soil at a rate of 25 g a.i./ha for crops that may be rotated. After aging the test plots for plant-back intervals of 30, 60, and 335 days after treatment (DAT), radishes (Cherry Belle Radish), lettuce (Buttercrunch Lettuce), and wheat (Ultra Wheat) were planted into the plots. The crops were grown outdoors to maturity at Research For Hire located in Porterville, California, USA. Plot maintenance simulated typical cultural practices.

Crops were selected as representative of small grain, leafy vegetable, and root crop. Eleven boxes were treated, ten in the spring and one in the fall. Of the spring application boxes, four boxes were planted with lettuce (one box for 30-d PBI, one for both 30- and 335-d PBIs, and two for a 60-d PBI). Four boxes were designated for radish (one box for 30-d PBI, one for both 30- and 335-d PBIs, and two other for 60-d PBI) and two boxes were designated for wheat (one box for 30-d PBI and box for 30- and 335-d PBIs). A separate box was planted with wheat at a 60-day PBI, following a fall application.
A total of two additional boxes were used to grow control (untreated) crops.

Sample collection
The untreated samples were collected prior to treated samples and handled/stored separately. Equipment was cleaned prior to and after each sampling event. Separate equipment was used for each plot. Each sample was placed into a tared, pre-labelled, plastic Ziploc bag, which was then placed into a pre-labelled, plastic-lined cloth residue bag. After the weights were recorded, the bagged samples were placed into frozen storage. The forage wheat samples were cut with scissors approximately 3 cm above the soil surface. The lettuce was cut with scissors approximately 3 cm above the soil surface and then placed into sample bags. Mature radishes were pulled from the ground and the roots were cut with scissors into a foil lined tray and brought back to the lab and hand washed with water then patted dry with a paper towel. The tops and roots were placed into separate sample bags. The wheat hay samples were cut with scissors approximately 1 1/2 inches (4.5 cm) above the soil surface into labelled plastic trash bags. The fresh weight was recorded, and then the hay was laid on butcher paper in the RFH greenhouses and allowed to dry. The grain heads were cut first with scissors and placed into a large plastic bag. Then the straw was cut approximately 1 inch (3 cm) above the soil surface. The grain was separated from the chaff using a grain thresher. The chaff was added to the straw sample.

Sample milling
The samples were removed from frozen storage, pre-weighed, chopped into smaller pieces if needed, and milled with dry ice, to maintain a frozen state during milling, returned to frozen storage to allow for sublimation of the dry ice (typically two days), post weighed, and returned to frozen storage pending shipment to Dow AgroSciences (DAS).
The entire sample was processed when the total sample weighed less than 1000.0 grams. When the total sample weighed more than 1000.0 grams random grab samples were collected from the bulk until reaching 1000.0 grams. The selected portion to be processed was composed of approximately 10 random grab samples from the bulk sample. The remaining sample was stored frozen at RFH, pending permission for disposal from study director at DAS. Homogenized samples were shipped to DAS on dry ice using an overnight courier.

Sample extraction and analysis
At all plant-back intervals, samples that equalled or exceeded 0.010 mg eq./kg were subjected to neutral solvent extraction (ASE, 80:20 acetonitrile:water). As necessary, the post-extracted tissue samples were further extracted with base (100:1 methanol/10 N NaOH). The neutral extracts were further treated with base (MeOH/10 N NaOH 100:1) then acid (1 N HCl) in an attempt to liberate picloram from conjugates. TRR in extracted samples was then analysed by HPLC.

Sample Storage Conditions
Samples, including milled tissue, extracts, and post-extracted samples, were stored in freezers (approximately -10 to -30 °C) when not in the process of analysis.

Results and discussion
Table A 5 presents the distribution of the TRR within the crop harvests. Residues in crops at all plant-back times ranged from 0.001 to 0.494 mg eq./kg (picloram equivalents). Residues in immature lettuce, wheat forage, hay, straw and grain showed a significant decline with an increase in the plant-back interval. Residues in mature lettuce and radish tops showed moderate increases from the 30-d plant-back interval to the 60-d plant-back interval. All crops showed significant decrease in the residues from the 60-d plant back interval to the 335-d plant-back interval.

Table A.2.2.2.1.1-1: Total Radioactive Residues (TRRs) in lettuce, radish and wheat commodities

Matrix	TRR (ppm)		
	30-day Plant-back interval	60-day Plant-back interval	335-day Plant-back interval
Immature lettuce	0.023	0.019	0.005
Mature lettuce	0.014	0.018	0.002
Mature radish tops	0.029	0.039	0.008
Mature radish roots	0.002	0.002	0.001
Wheat forage	0.077	0.065	0.021
Wheat hay	0.494	0.255	0.058
Wheat straw	0.403	0.327	0.104
Wheat grain	0.126	0.054	0.020

All crop samples that contained residues of 0.010 mg picloram equivalents/kg (mg eq/kg) or higher were characterized. Residue levels in radish roots at all plant-black intervals were below 0.010 mg eq/kg and were not subjected to characterization. Results of characterisation are displayed in Table A 7 to Table A13.

Table A.2.2.2.1.1-2: Summary of characterization and identification of Radioactive Residues in immature lettuce following application of radiolabelled picloram at 25 g as/ha

Compound	30d immature lettuce TRR = 0.023 ppm		60d immature lettuce TRR = 0.019 ppm		335d immature lettuce TRR = 0.005 ppm	
	% TRR	ppm	% TRR	ppm	% TRR	ppm
Picloram (total free and conjugated) = total identified	72.4	0.016	99.8	0.019	N/A	N/A
Total characterized	2.9	0.001	3.6	0.001	N/A	N/A
Total extractable	80	0.018	92.0	0.018	N/A	N/A
Unextractable (PES)*	9.0	0.002	9.9	0.002	N/A	N/A
Accountability**	89.0	0.020	101.9	0.020	N/A	N/A

N/A: Not analysed due to low residues parent
* Residues remaining after exhaustive extractions.
** Accountability = (Total extractable + Total unextractable) / (TRRs from combustion analysis) * 100.

Table A.2.2.2.1.1-3: Summary of characterization and identification of Radioactive Residues in mature lettuce following application of radiolabelled picloram at 25 g as/ha

Compound	30d mature lettuce TRR = 0.013 ppm		60d mature lettuce TRR = 0.018 ppm		335d mature lettuce TRR = 0.002 ppm	
	% TRR	ppm	% TRR	ppm	% TRR	ppm
Picloram (total free and conjugated) = total identified	77.0	0.010	84.4	0.015	N/A	N/A
Total characterized	2.5	0.000	0.0	0.000	N/A	N/A
Total extractable	89.8	0.012	90.4	0.016	N/A	N/A
Unextractable (PES)*	17.3	0.002	11.8	0.002	N/A	N/A
Accountability**	107.1	0.014	102.2	0.018	N/A	N/A

N/A: Not analysed due to low residues parent
* Residues remaining after exhaustive extractions.
** Accountability = (Total extractable + Total unextractable) / (TRRs from combustion analysis) * 100.

Table A.2.2.2.1.1-4: Summary of characterization and identification of Radioactive Residues in mature radish tops following application of radiolabelled picloram at 25 g as/ha

Compound	30d radish tops TRR = 0.029 ppm		60d radish tops TRR = 0.039 ppm		335d radish tops TRR = 0.008 ppm	
	% TRR	ppm	% TRR	ppm	% TRR	ppm
Picloram (total free and conjugated) = total identified	84.9	0.025	75.7	0.029	N/A	N/A
Total characterized	0.0	0.000	12.0	0.005	N/A	N/A
Total extractable	90.8	0.027	83.3	0.032	N/A	N/A
Unextractable (PES)*	4.5	0.001	10.8	0.004	N/A	N/A
Accountability**	95.2	0.028	94.1	0.036	N/A	N/A

N/A: Not analysed due to low residues parent
* Residues remaining after exhaustive extractions.
** Accountability = (Total extractable + Total unextractable) / (TRRs from combustion analysis) * 100.

Table A.2.2.2.1.1-5: Summary of characterization and identification of Radioactive Residues in wheat forage following application of radiolabelled picloram at 25 g as/ha

Compound	30d wheat forage TRR = 0.077 ppm		60d wheat forage TRR = 0.065 ppm		335d wheat forage TRR = 0.021 ppm	
	% TRR	ppm	% TRR	ppm	% TRR	ppm
Picloram (total free and conjugated) = total identified	83.5	0.064	109.1	0.071	103.8.	0.022
Total characterized	6.0	0.005	0.0	0.000	0.0	0.000
Total extractable	84.7	0.065	94.6	0.061	97.6	0.020
Unextractable (PES)*	8.7	0.007	4.3	0.003	3.4	0.001
Accountability**	93.5	0.072	98.9	0.064	101.0	0.021

* Residues remaining after exhaustive extractions.
** Accountability = (Total extractable + Total unextractable) / (TRRs from combustion analysis) * 100.

Table A.2.2.2.1.1-6: Summary of characterization and identification of Radioactive Residues in wheat hay following application of radiolabelled picloram at 25 g as/ha

Compound	30d wheat hay TRR = 0.494 ppm		60d wheat hay TRR = 0.255 ppm		335d wheat hay TRR = 0.058 ppm	
	% TRR	ppm	% TRR	ppm	% TRR	ppm
Picloram (total free and conjugated) = total identified	85.0	0.420	70.9	0.181	95.8	0.056
Total characterized	7.5	0.037	23.1	0.059	>100	N/A
Total extractable	92.5	0.457	94.0	0.240	94.3	0.055
Unextractable (PES)*	5.3	0.026	4.9	0.012	6.7	0.004
Accountability**	98.4	0.486	103.9	0.265	101.4	0.059

N/A: Not analysed due to low residues parent
* Residues remaining after exhaustive extractions.
** Accountability = (Total extractable + Total unextractable) / (TRRs from combustion analysis) * 100.

Table A.2.2.2.1.1-7: Summary of characterization and identification of Radioactive Residues in wheat straw following application of radiolabelled picloram at 25 g as/ha

Compound	30d wheat straw TRR = 0.403 ppm		60d wheat straw TRR = 0.327 ppm		335d wheat straw TRR = 0.104 ppm	
	% TRR	ppm	% TRR	ppm	% TRR	ppm
Picloram (total free and conjugated) = total identified	72.7	0.293	54.5	0.178	43.7	0.045
Total characterized	19.6	0.079	41.4	0.135	47.6	0.050
Total extractable	92.3	0.372	95.9	0.314	91.3	0.096
Unextractable (PES)*	5.9	0.024	7.1	0.023	4.6	0.005
Accountability**	100.2	0.404	105.3	0.344	98.9	0.103

* Residues remaining after exhaustive extractions.
** Accountability = (Total extractable + Total unextractable) / (TRRs from combustion analysis) * 100.

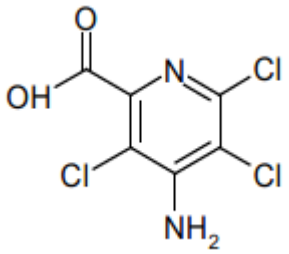
Table A.2.2.2.1.1-8: Summary of characterization and identification of Radioactive Residues in wheat grain following application of radiolabelled picloram at 25 g as/ha

Compound	30d wheat grain TRR = 0.126 ppm		60d wheat grain TRR = 0.054 ppm		335d wheat grain TRR = 0.020 ppm	
	% TRR	ppm	% TRR	ppm	% TRR	ppm
Picloram (total free and conjugated) = total identified	79.7	0.100	85.6	0.046	76.3	0.015
Total characterized	6.4	0.008	3.8	0.002	16.5	0.003
Total extractable	86.1	0.108	89.4	0.048	92.8	0.018
Unextractable (PES)*	4.6	0.006	7.8	0.004	1.0	0.000
Accountability**	94.9	0.119	94.0	0.050	99.4	0.020

* Residues remaining after exhaustive extractions.
** Accountability = (Total extractable + Total unextractable) / (TRRs from combustion analysis) * 100.

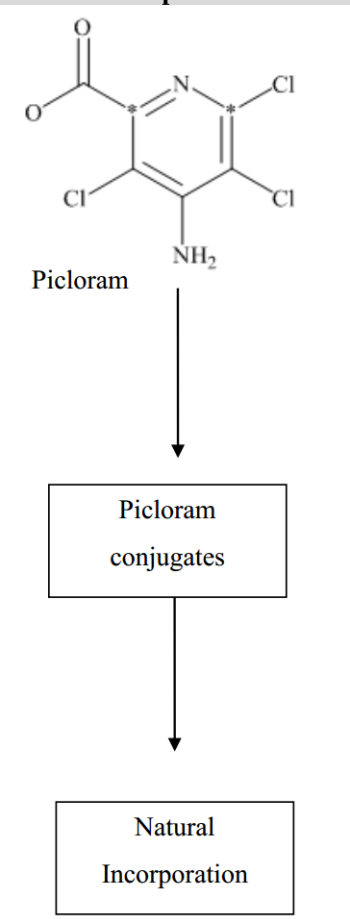
In all characterized matrices, HPLC analysis confirmed that the major component was picloram, free or conjugated in all extracts (base, neutral and hydrolyzed neutral extracts).

Table A.2.2.2.1.1-9: Identification of compounds from metabolism study

Common name/code Figure B.3.1.-1. ID No.	Chemical name (IUPAC)	Chemical structure
Picloram	4-amino-3,5,6-trichloropyridine-2-carboxylic acid	

The proposed metabolic pathway is presented in Figure A.2.2.2.1.1-1. As shown in the diagram, the metabolism of picloram is mainly through formation of conjugates.

Figure A.2.2.2.1.1-1: Proposed Metabolic Profile of picloram in rotational crops



Conclusions

The majority of the residue, generally >70% of the TRR, was characterized and identified as picloram or conjugates of picloram. Individual conjugates were not identified. Results were consistent with the previous Confined Rotational Crop study which was conducted at the higher rate of 583 g a.s./ha.

A 2.2.3 Magnitude of residues in plants

A 2.2.3.1 Oilseed Rape

Table A.2.2.3.1-1: Comparison of intended and critical EU GAPs

Type of GAP	Number of applications	Application rate per treatment (gai/ha)	Interval between application	Growth stage at last application	PHI (days)
cGAP EU (dRR, 2016)	1	Picloram: 24 g ae/ha + Halauxifen-methyl: 4.8 g ae/ha	N/A	BBCH 30	N/A
cGAP EU (EFSA, 2013, MRL ER (UK), 2012)	1	Picloram: 24 g ae/ha	N/A	BBCH 50	N/A
Intended cGAP (2*)	1	Halauxifen-methyl: 2.5 g ae/ha + **Picloram: 12 g ae/ha** + Aminopyralid: 8 g ae/ha	N/A	BBCH 12-19	-

* Use number(s) in accordance with the list of all intended GAPs in Part B, Section 0

A 2.2.3.1.1 Magnitude of residues – Study 150006 (RHE-15-20345)

Comments of zRMS:	Sixteen residue trials: 6 NEU and 10 SEU were conducted on oilseed rape during 2014 and 2015 seasons to determine the magnitude of picloram after one spraying application with 4.8 g ae/ha of halauxifen-methyl and 24 g ae/ha of picloram with application at BBCH 16-30. Residues of picloram, free and conjugates, were determined according to method described in Dow AgroSciences Study Number 120610. The LOQ for all compounds was 0.01 mg/kg for oilseed rape. Concurrent recoveries obtained during the conduct of this study were acceptable with mean values in the range 70-110%. All RSD values were below 20%. Levels of residue are below the LOQ of 0.01 mg/kg for picloram (free and conjugated, expressed as picloram) for all trials. The maximum frozen storage period of samples prior to the analysis was 375 days. All residue data reported within the present submission are covered by the storage period. The study is acceptable. <u>Remark:</u> In Northern Europe, each trial consisted in two treated plots corresponding to two different date of treatment. Thus, as the two plots are located at the same experimental site but correspond to different experimental conditions, the highest level of residues between the two treated plots has been selected for the assessment. Lines describing the plots whose results are not taken into consideration have been greyed out.

Reference:	KCA 6.3.1
Report	Magnitude of the Residues of Halauxifen-Methyl and Picloram in Oilseed Rape (RAC Whole Plant, Seed and Straw), Following One Application of GF-3447, Northern and Southern Europe – 2015, R. Demotte, 2016, Report No. RDE-15-20345, DAS Study ID 150006
Guideline(s):	Guideline 7029/VI/95 (rev. 5) to Directive 91/414/EEC and Regulations (EU) 283/2013 and 284/2013 implementing Regulation (EC) 1107/2009
Deviations:	No
GLP:	Yes

Acceptability: Yes

Sixteen trials were located in Northern and Southern Europe (France, United Kingdom, Poland, Spain, Italy and Greece) in 2014-2015. Seven trials were Decline Curve trials and nine were harvest trials.

In Northern Europe (trials FR01 to PL06), three plots were established in each trial. U plot was left untreated. T1 plot was treated once with GF-3447, at a late autumn timing (November- December 2014) with a BBCH crop stage between 16 and 30. T2 plot was treated once with GF-3447, with maximum BBCH growth stage of 30 and before 28th February 2015.

In Southern Europe (trials FR07 to GR16), two plots were established in each trial. U plot was left untreated. T plot was treated once with GF-3447, with maximum BBCH growth stage of 30 and before 28th February 2015.

At every application, the target dose of GF-3447 was 0.5 L/ha (corresponding to 4.8 g ae/ha of halauxifen-methyl and 24 g ae/ha of picloram). Applications were carried out using boom sprayers in order to reproduce a normal agricultural application technique on a small-scale size. In each trial, one application was made on T1 and T2 or T plots. Amounts of mixture applied ranged from 161 to 406 L/ha.
On trials FR02, GB04, PL06, FR09, ES12, IT13, IT14, GR15 and GR16, one sampling of seeds and straw was taken at harvest in each plot.

On trials FR01, GB03 and PL05, specimens were taken at 7 occasions: whole plants were taken at 0, 7 and 14 days after application on plots U, T1 and T2. Seeds and straw were taken 7 days before harvest, at commercial harvest and at 3 and 7 days after harvest.

On trials FR07, FR08 and ES10 and ES11 specimens were taken at 7 occasions: whole plants were taken at 0, 7 and 14 days after application on plots U and T. Seeds and straw were taken 7 days before harvest, at commercial harvest and at 3 and 7 days after harvest.

All the specimens were placed into labelled plastic bags, weighed and double bagged. Specimens were frozen and shipped on freezer truck. They were delivered to analytical site on July 07th and 14th 2015, August 04th, 10th and 12th 2015, September 01st 2015 and October 07th 2015.

The maximum frozen storage period of samples prior to the analysis was 375 days.
A frozen storage stability study CEMS-4957 was conducted by CEMAS on XDE-729 methyl and XDE-729 acid. CEMS-4957 was reported on 19-Aug-2013 and showed that residues of X11393728 (XDE-729 methyl ester) and X11393729 (XDE-729 acid) do not exhibit any significant degradation when stored under frozen conditions for up to 735 days in wheat grain, lettuce, oilseed rape seed and whole oranges.

A frozen storage stability study 980075 was conducted by Dow AgroSciences on picloram. 980075 was reported on 20-May-2003 and showed that residues of picloram do not exhibit any significant degradation when stored under frozen conditions for up to 1096 days in wheat green forage, straw and grain.

Halauxifen (XDE-729)
All samples were analysed for XDE-729 methyl (X11393728) and XDE-729 acid (X11393729) using the analytical method described in Dow AgroSciences Study Number 110005, “Determination of Residues of XDE-729 Methyl Ester and XDE-729 Acid in Agricultural Commodities and Wheat Processed Products using Online Solid-Phase Extraction and Liquid Chromatography with Tandem Mass Spectrometry”. The limit of detection (LOD) and limit of quantitation (LOQ) were 0.003 mg/kg and 0.01 mg/kg, respectively.
Recoveries in whole plants averaged 87%, in straw 98% and 90% in seeds for halauxifen-methyl, and averaged 86% in whole plants, 99% in straw and 100% in seeds, for halauxifen-acid.

Picloram
All samples were analysed for picloram using Dow AgroSciences study number 120610, “Method Validation Study for the Determination of Residues of Clopyralid and Picloram in Agricultural

Commodities by LC-MS/MS". The limit of detection (LOD) and limit of quantitation (LOQ) were 0.003 mg/kg and 0.01 mg/kg, respectively. Recoveries in whole plants averaged 91%, in straw 101% and 78% in seeds.

Residue in untreated specimens

No residue of halauxifen-methyl was detected (<LOD) in any untreated specimens. No residue of halauxifen-acid and picloram were detected (< LOD) in any untreated specimens, with exceptions of some specimens with residue between LOD and LOQ.

Table A.2.2.3.1.1-1: Summary of the study RDE-15-20345 trials – Residues of picloram

Trial No./ Location/ EU zone/ Year	Commodity/ Variety	Date of 1.Sowing or planting 2.Flowering 3. Harvest	Application rate per treatment			Dates of treatment or no. of treatments and last date	Growth stage at last treatment or date	Portion analyzed	Residues (mg/kg)	PHI (days)	Details on trial
			g a.e./ ha	Water (l/ha)	g a.e./hl				Picloram free and conjugated, expressed as picloram		
	(a)	(b)				(c)				(d)	(e)
RDE-15-20345 FR01 49700 Doué la Fontaine, Pays de la Loire (EU Northern Zone)	Winter oilseed rape / DK Expertise	1) 05/09/14 2) 08/04/15 to 20/04/15 3) 06/07/15	24.05	161	14.94	04 Dec 14	BBCH 18-19	Whole plant Whole plant Whole plant Seeds Seeds Seeds Seeds Straw Straw Straw Straw	1.007 0.342 0.285 ND ND ND ND ND ND ND ND	0 7 14 203 211 214 218 203 211 214 218	Residue method and LOQ: 120610 / 0.01 mg/kg Max frozen storage time prior to analysis: 361 days formulation (type): GF-3447 (EC)
RDE-15-20345 FR01 49700 Doué la Fontaine, Pays de la Loire (EU Northern Zone)	Winter oilseed rape / DK Expertise	1) 05/09/14 2) 08/04/15 to 20/04/15 3) 06/07/15	24.53	164	14.96	19 Feb 15	BBCH 27-29	Whole plant Whole plant Whole plant Seeds Seeds Seeds Seeds Straw Straw Straw Straw	0.756 0.294 0.273 (0.004) ND (0.004) ND 0.016 0.021 0.013 0.020	0 8 14 126 134 137 141 126 134 137 141	Residue method and LOQ: 120610 / 0.01 mg/kg Max frozen storage time prior to analysis: 284 days formulation (type): GF-3447 (EC)
RDE-15-20345 FR02 08300 Tagnon, Champagne-Ardenne (EU Northern Zone)	Winter oilseed rape / DK Exstorm	1) 23/08/14 2) 20/04/15 to 04/05/15 3) 22/07/15	25.44	239	10.64	26 Nov 14	BBCH 19	Seeds Straw	ND (0.003)	238 238	Residue method and LOQ: 120610 / 0.01 mg/kg Max frozen storage time prior to analysis: 124 days formulation (type): GF-3447 (EC)

Trial No./ Location/ EU zone/ Year	Commodity/ Variety	Date of 1.Sowing or planting 2.Flowering 3. Harvest	Application rate per treatment			Dates of treatment or no. of treatments and last date	Growth stage at last treatment or date	Portion analyzed	Residues (mg/kg)	PHI (days)	Details on trial
			g a.e./ ha	Water (l/ha)	g a.e./hl				Picloram free and conjugated, expressed as picloram		
	(a)	(b)				(c)				(d)	(e)
RDE-15-20345 FR02 08300 Tagnon, Champagne-Ardenne (EU Northern Zone)	Winter oilseed rape / DK Exstorm	1) 23/08/14 2) 20/04/15 to 04/05/15 3) 22/07/15	22.80	214	10.65	19 Feb 15	BBCH 19	Seeds Straw	ND 0.018	153 153	Residue method and LOQ: 120610 / 0.01 mg/kg Max frozen storage time prior to analysis: 152 days formulation (type): GF-3447 (EC)
RDE-15-20345 GB03 OX27 7LT Bucknell, Oxfordshire (EU Northern Zone)	Winter oilseed rape / Harper	1) 04/09/14 2) not recorded 3) 30/07/15	23.33	194	12.03	04 Dec 14	BBCH 17-18	Whole plant Whole plant Whole plant Seeds Seeds Seeds Seeds Straw Straw Straw Straw	0.814 0.308 0.286 ND ND ND ND (0.004) ND (0.004) (0.005)	0 7 14 225 232 235 238 225 232 235 238	Residue method and LOQ: 120610 / 0.01 mg/kg Max frozen storage time prior to analysis: 361 days formulation (type): GF-3447 (EC)
RDE-15-20345 GB03 OX27 7LT Bucknell, Oxfordshire (EU Northern Zone)	Winter oilseed rape / Harper	1) 04/09/14 2) not recorded 3) 30/07/15	24.82	207	11.99	17 Feb 15	BBCH 19	Whole plant Whole plant Whole plant Seeds Seeds Seeds Seeds Straw Straw Straw Straw	0.894 0.607 0.445 0.005) (0.005) ND (0.003) (0.007) 0.012 0.015 0.018	0 7 14 150 157 160 163 150 157 160 163	Residue method and LOQ: 120610 / 0.01 mg/kg Max frozen storage time prior to analysis: 286 days formulation (type): GF-3447 (EC)

Trial No./ Location/ EU zone/ Year	Commodity/ Variety	Date of 1.Sowing or planting 2.Flowering 3. Harvest	Application rate per treatment			Dates of treatment or no. of treatments and last date	Growth stage at last treatment or date	Portion analyzed	Residues (mg/kg)	PHI (days)	Details on trial
			g a.e./ ha	Water (l/ha)	g a.e./hl				Picloram free and conjugated, expressed as picloram		
	(a)	(b)				(c)				(d)	(e)
RDE-15-20345 GB04 LU6 3QZ Kensworth, Bedfordshire (EU Northern Zone)	Winter oilseed rape / Charger	1) 16/08/14 2) Not Recorded 3) 01/08/15	25.01	208	12.02	01 Dec 14	BBCH 18	Seeds Straw	ND 0.011	239 239	Residue method and LOQ: 120610 / 0.01 mg/kg Max frozen storage time prior to analysis: 118 days formulation (type): GF-3447 (EC)
RDE-15-20345 GB04 LU6 3QZ Kensworth, Bedfordshire (EU Northern Zone)	Winter oilseed rape / Charger	1) 16/08/14 2) Not Recorded 3) 01/08/15	22.80	190	12.00	18 Feb 15	BBCH 19-30	Seeds Straw	ND 0.021	160 160	Residue method and LOQ: 120610 / 0.01 mg/kg Max frozen storage time prior to analysis: 146 days formulation (type): GF-3447 (EC)
RDE-15-20345 PL05 64-840 Nowe Brzeźno, Wielkopolska (EU Northern Zone)	Winter oilseed rape / Granat	1) 30/08/14 2) 27/04/15 to 17/05/15 3) 29/07/15	22.51	281	8.01	20 Nov 14	BBCH 16-18	Whole plant Whole plant Whole plant Seeds Seeds Seeds Seeds Straw Straw Straw Straw	0.398 0.326 0.308 (0.005) ND (0.003) ND 0.026 0.021 0.012 0.020	0 7 15 245 251 254 258 245 251 254 258	Residue method and LOQ: 120610 / 0.01 mg/kg Max frozen storage time prior to analysis: 375 days formulation (type): GF-3447 (EC)

Trial No./ Location/ EU zone/ Year	Commodity/ Variety	Date of 1.Sowing or planting 2.Flowering 3. Harvest	Application rate per treatment			Dates of treatment or no. of treatments and last date	Growth stage at last treatment or date	Portion analyzed	Residues (mg/kg)	PHI (days)	Details on trial
			g a.e./ ha	Water (l/ha)	g a.e./hl				Picloram free and conjugated, expressed as picloram		
	(a)	(b)				(c)				(d)	(e)
RDE-15-20345 PL05 64-840 Nowe Brzeźno, Wielkopolska (EU Northern Zone)	Winter oilseed rape / Granat	1) 30/08/14 2) 27/04/15 to 17/05/15 3) 29/07/15	22.03	275	8.01	23 Feb 15	BBCH 30	Whole plant Whole plant Whole plant Seeds Seeds Seeds Seeds Straw Straw Straw Straw	1.039 0.140 0.213 (0.004) ND ND (0.004) 0.028 0.039 0.035 0.039	0 7 14 150 156 159 163 150 156 159 163	Residue method and LOQ: 120610 / 0.01 mg/kg Max frozen storage time prior to analysis: 287 days formulation (type): GF-3447 (EC)
RDE-15-20345 PL06 63-040 Michalów, Wielkopolska (EU Northern Zone)	Winter oilseed rape / DK Exprit	1) 29/08/14 2) 20/04/15 to 05/05/15 3) 22/07/15	24.29	303	8.02	26 Nov 14	BBCH 18	Seeds Straw	ND 0.015	239 239	Residue method and LOQ: 120610 / 0.01 mg/kg Max frozen storage time prior to analysis: 145 days formulation (type): GF-3447 (EC)
RDE-15-20345 PL06 63-040 Michalów, Wielkopolska (EU Northern Zone)	Winter oilseed rape / DK Exprit	1) 29/08/14 2) 20/04/15 to 05/05/15 3) 22/07/15	24.53	307	7.99	27 Feb 15	BBCH 20	Seeds Straw	ND 0.046	146 146	Residue method and LOQ: 120610 / 0.01 mg/kg Max frozen storage time prior to analysis: 165 days formulation (type): GF-3447 (EC)

Trial No./ Location/ EU zone/ Year	Commodity/ Variety	Date of 1.Sowing or planting 2.Flowering 3. Harvest	Application rate per treatment			Dates of treatment or no. of treatments and last date	Growth stage at last treatment or date	Portion analyzed	Residues (mg/kg)	PHI (days)	Details on trial
			g a.e./ ha	Water (l/ha)	g a.e./hl				Picloram free and conjugated, expressed as picloram		
	(a)	(b)				(c)				(d)	(e)
RDE-15-20345 FR07 13150 Tarascon, Provence Alpes Côte d'Azur (EU Southern Zone)	Winter oilseed rape / Athletic Royal	1) 25/08/14 2) 15/04/15 to 05/05/15 3) 15/06/15	24.14	302	7.99	19 Feb 15	BBCH 30	Whole plant Whole plant Whole plant Seeds Seeds Seeds Seeds Straw Straw Straw Straw	0.589 0.040 0.102 (0.005) ND ND (0.0003) 0.016 0.012 0.015 0.014	0 7 14 110 117 120 124 110 117 120 124	Residue method and LOQ: 120610 / 0.01 mg/kg Max frozen storage time prior to analysis: 291 days formulation (type): GF-3447 (EC)
RDE-15-20345 FR08 31330 Grenade sur Garonne, Midi Pyrénées (EU Southern Zone)	Winter oilseed rape / DK Explicit	1) 25/09/14 2) 15/04/15 to 29/04/15 3) 27/06/15	23.18	193	12.01	09 Feb 15	BBCH 30	Whole plant Whole plant Whole plant Seeds Seeds Seeds Seeds Straw Straw Straw Straw	0.860 0.412 0.267 (0.005) ND ND ND 0.059 0.041 0.040 0.043	0 7 14 133 140 143 147 133 140 143 147	Residue method and LOQ: 120610 / 0.01 mg/kg Max frozen storage time prior to analysis: 301 days formulation (type): GF-3447 (EC)
RDE-15-20345 FR09 31290 Montgaillard Lauragais, Midi Pyrénées (EU Southern Zone)	Winter oilseed rape / DK Exstorm	1) 29/08/14 2) 13/04/15 to 26/04/15 3) 28/06/15	25.15	210	11.98	09 Feb 15	BBCH 30	Seeds Straw	ND (0.006)	141 141	Residue method and LOQ: 120610 / 0.01 mg/kg Max frozen storage time prior to analysis: 190 days formulation (type): GF-3447 (EC)

Trial No./ Location/ EU zone/ Year	Commodity/ Variety	Date of 1.Sowing or planting 2.Flowering 3. Harvest	Application rate per treatment			Dates of treatment or no. of treatments and last date	Growth stage at last treatment or date	Portion analyzed	Residues (mg/kg)	PHI (days)	Details on trial
			g a.e./ ha	Water (l/ha)	g a.e./hl				Picloram free and conjugated, expressed as picloram		
	(a)	(b)				(c)				(d)	(e)
RDE-15-20345 ES10 41400 Ecija, Andalucia (Sevilla) (EU Southern Zone)	Winter oilseed rape / NXH 214	1) 07/11/14 2) 10/03/15 to 10/04/15 3) 25/05/15	24.34	254	9.58	04 Feb 15	BBCH 30	Whole plant Whole plant Whole plant Seeds Seeds Seeds Seeds Straw Straw Straw Straw	1.131 0.507 0.288 ND ND ND ND 0.103 0.090 0.062 0.065	0 7 14 140 111 114 118 140 111 114 118	Residue method and LOQ: 120610 / 0.01 mg/kg Max frozen storage time prior to analysis: 306 days formulation (type): GF-3447 (EC)
RDE-15-20345 ES11 24713 Sueros de Cepeda, León (EU Southern Zone)	Winter oilseed rape / Hidromel	1) 21/09/14 2) April to May 2015 3) 08/07/15	23.95	299	8.01	11 Feb 15	BBCH 17	Whole plant Whole plant Whole plant Seeds Seeds Seeds Seeds Straw Straw Straw Straw	0.946 0.486 0.255 ND ND ND ND 0.068 0.083 0.062 0.044	0 7 14 152 159 163 166 152 159 163 166	Residue method and LOQ: 120610 / 0.01 mg/kg Max frozen storage time prior to analysis: 299 days formulation (type): GF-3447 (EC)
RDE-15-20345 ES12 24765 Redelda de la Valduerna, León (EU Southern Zone)	Winter oilseed rape / Expertise	1) 30/09/14 2) April 2015 3) 10/07/15	24.29	303	5.02	11 Feb 15	BBCH 17	Seeds Straw	ND 0.032	149 149	Residue method and LOQ: 120610 / 0.01 mg/kg Max frozen storage time prior to analysis: 180 days formulation (type): GF-3447 (EC)

Trial No./ Location/ EU zone/ Year	Commodity/ Variety	Date of 1.Sowing or planting 2.Flowering 3. Harvest	Application rate per treatment			Dates of treatment or no. of treatments and last date	Growth stage at last treatment or date	Portion analyzed	Residues (mg/kg)	PHI (days)	Details on trial
			g a.e./ ha	Water (l/ha)	g a.e./hl				Picloram free and conjugated, expressed as picloram		
	(a)	(b)				(c)				(d)	(e)
RDE-15-20345 IT13 20871 Vimercate, Lombardy (EU Southern Zone)	Winter oilseed rape / PR45 W04	1) 25/09/14 2) 20/04/15 to 06/05/15 3) 11/06/15	23.52	294	8.00	26 Jan 15	BBCH 22-24	Seeds Straw	(0.006) 0.010	134 134	Residue method and LOQ: 120610 / 0.01 mg/kg Max frozen storage time prior to analysis: 211 days formulation (type): GF-3447 (EC)
RDE-15-20345 IT14 27028 San Martino Siccomario, Lombardy (EU Southern Zone)	Winter oilseed rape / PR44 W29	1) 04/10/14 2) 15/04/15 to 30/04/15 3) 12/06/15	24.34	304	8.01	27 Jan 15	BBCH 23-24	Seeds Straw	(0.004) 0.028	134 134	Residue method and LOQ: 120610 / 0.01 mg/kg Max frozen storage time prior to analysis: 210 days formulation (type): GF-3447 (EC)
RDE-15-20345 GR15 57200 Drymos, Central Macedonia (EU Southern Zone)	Winter oilseed rape / Edimax CL	1) 01/10/14 2) 01/04/15 to 25/04/15 3) 25/05/15 to 15/06/15	24.19	403	6.00	20 Feb 15	BBCH 22-23	Seeds Straw	ND ND	109 109	Residue method and LOQ: 120610 / 0.01 mg/kg Max frozen storage time prior to analysis: 211 days formulation (type): GF-3447 (EC)

Trial No./ Location/ EU zone/ Year	Commodity/ Variety	Date of 1.Sowing or planting 2.Flowering 3. Harvest	Application rate per treatment			Dates of treatment or no. of treatments and last date	Growth stage at last treatment or date	Portion analyzed	Residues (mg/kg)	PHI (days)	Details on trial
			g a.e./ ha	Water (l/ha)	g a.e./hl				Picloram free and conjugated, expressed as picloram		
	(a)	(b)				(c)				(d)	(e)
RDE-15-20345 GR16 62045 Lefkothea, Central Macedonia (EU Southern Zone)	Winter oilseed rape / Nelson	1) 10/10/14 2) 01/04/15 to 25/04/15 3) 25/05/15 to 15/06/15	24.34	406	6.00	20 Feb 15	BBCH 22-23	Seeds Straw	ND 0.012	111 111	Residue method and LOQ: 120610 / 0.01 mg/kg Max frozen storage time prior to analysis: 209 days formulation (type): GF-3447 (EC)

(a) According to CODEX Classification / Guide
(b) Only if relevant
(c) Year must be indicated
(d) Days after last application (Label pre-harvest interval, PHI, underline)
(e) Remarks may include: Climatic conditions; Reference to analytical method and information which metabolites are included

A 2.2.4 Magnitude of residues in livestock

A 2.2.4.1 Livestock feeding studies

Not required for the characterization of the product.

A 2.2.5 Magnitude of residues in representative succeeding crops

A 2.2.5.1 Field rotational crop studies

Comments of zRMS:

The new field rotational crop studies investigating the magnitude of picloram residues in rotational crops were submitted by Applicant to support the use of picloram on rape seed every year. zRMS- France evaluated these studies (GF-3447, 2018).
zRMS-France conclusions (GF-3447, 2018):
Both studies are deemed acceptable. Samples of wheat, turnip and kale were planted 30, 120 or 335 days after application of picloram to bare soil. No residues above the LoQ were measure in any of the 120-day and 335-day samples. However, quantified residues were observed in 30-day PBI samples.
Among 30-day PBI samples, none of the animal feed commodities (that are wheat whole plant that can be assimilated to wheat forage, wheat straw and turnip tops) presented residue levels higher than the trigger value of 0.05 mg/kg. As regards food commodities, residue levels exceeding the trigger value of 0.01 mg/kg were found in 30 DAT wheat grain and 30 DAT kale leaves and reached 0.02 mg/kg and 0.03 mg/kg, respectively. Nevertheless, picloram was applied to bare soil in both studies; this worst case scenario does not take into account the foliar interception that may occur during plant treatment. Picloram is intended to be applied from BBCH 12 to BBCH 30 (see Part B, Section 0). According to the Generic Guidance to FOCUS groundwater scenarios (version 1.1, April 2002), foliar intercepts of 40% and 80% can be considered for oilseed rape during leaf development (BBCH 10-19) and stem elongation (BBCH 20-39), respectively. Consequently, a worst case foliar interception of 40% has been considered to refine the residue levels estimated in rotational crops, Details of the calculations can be found in Table 7.3.6-1.

Table 7.3.6-1: *Refinement of 30-day PBI sample results taking into consideration foliar interception*

Crop group	***Crop commodity***	***HR (mg/kg)***	***40% foliar intercept***	***EU MRL (Reg. (EU) 2016/1)***	***MRL exceedance?***
Cereals	*Wheat whole plant*	*0.05*	*0.03*	*N/A - feeding commodity*	
	Wheat grain	***0.02***	*0.012*	*0.2 (1) or 0.01* (2)*	*No*
	Wheat straw	*0.02*	*0.012*	*N/A - feeding commodity*	
Root and tuber vegetables	*Turnip roots*	*0.01*	*0.006*	*0.01**	*No*
	Turnip tops	*0.04*	*0.024*	*N/A - feeding commodity*	
Leafy vegetables	*Kale leaves*	***0.03***	***0.018***	*0.01**	***Yes***

(1). Barley, maize, oats, sorghum, wheat, other cereals
(2). Buckwheat and other pseudo-cereals, common millet/proso millet, rice, rye

Once results refined in order to take into consideration foliar intercept, the trigger value of 0.01 mg/kg remains exceeded in kale leaves. Thus, an MRL exceedance cannot be excluded in leafy vegetables.
zRMS-PL agrees with conclusions presented by zRMS-France (S-EU) in Registration Report for GF-3447, 2018, and with agreed endpoint. zRMS-France proposed not to grow leafy vegetables in the treated field less than 120 days after application of GF-3447.

Reference:	KCA 6.6.2
Report	Determination of residues of picloram in winter and spring wheat grown as rotational crops after one application of GF-224 to bare soil at eight sites in Northern Europe and eight sites in Southern Europe 2014 - 2016, T. White, 2017, Study Number: S14-01961, DAS Study ID 140642
Guideline(s):	OECD (2009) Guidance document on Overview of Residues Chemistry Studies, OECD Test Guideline 509: Crop Field trials OECD (2011) Guidance document on Crop Field trials, SANCO/3029/99 rev. 4, Guideline 7029/VI/95 (REV. 5) to Directive 91/414/EEC and Regulations (EU) 283/2013 and 284/2013 implementing Regulation (EC) 1107/2009
Deviations:	Only two rotational intervals (nominally 120 and 330 days) were studied. According to the OECD 504 the limited field study calls for use of three rotational intervals. The rotated crops should be planted after the minimum rotational interval that could be expected as part of agricultural practice, e.g., 30 days for assessing circumstances of crop failure.
GLP:	Yes
Acceptability:	Yes

Materials and methods

The purpose of this study was to determine the magnitude of residues of picloram in the raw agricultural commodities of winter and spring wheat drilled/planted at different intervals after a single broadcast application of GF-224 to bare soil.

The field portion of this study was conducted on winter and spring wheat under open field conditions in 16 trials during 2014 – 2016. The trials took place in regions of the UK, France, Denmark, Poland, Hungary, Spain and Italy that are typical of Northern and Southern European wheat growing areas.

To determine the magnitude of residues of picloram in wheat, grown as rotational crops, trials were carried out based on a critical GAP with one application of GF-224 at 0.35 L/ha (23.5 g a.e./ha picloram) to bare soil. Following the application, the rotational crops have been drilled / planted to the plots at various intervals. Crops have been drilled at 113-333 days after the application. Grain and straw samples were collected from each crop at BBCH 89.

Residues of picloram were determined using a validated analytical method (reported in Dow AgroSciences study no. 120610 / ABC study no. 68930) using liquid chromatography with electrospray ionisation (ESI) with tandem mass spectrometry (LC-MS/MS). The limit of detection (LOD) and limit of quantitation (LOQ) for picloram in all matrices were 0.003 mg/kg and 0.01 mg/kg, respectively.

Recoveries in wheat grain averaged 95% for picloram. Recoveries in wheat straw averaged 85% for picloram.
The maximum period of frozen storage between sampling and extraction for picloram was 347 days.

Results and discussions

Residues of picloram in wheat grain and straw, following one application of GF-224 to bare soil, a formulation containing picloram, are presented in Table A 8.

Table A.2.2.5.1-1: Residues of picloram in rotational crops

Sample code	Commodity	Picloram application rate (g as/ha)	Timing	Plant back interval (DAA)	**Residue levels (mg/kg)**
					Picloram
S14-01961-01, UK					
L14-01961-01-002A	Wheat Grain	23.9	BBCH 89 (NCH)	118	ND

L14-01961-01-004A	Wheat Straw	23.9	BBCH 89 (NCH)	118	ND
S14-01961-02, Denmark					
L14-01961-02-002A	Wheat Grain	24.2	BBCH 89 (NCH)	113	ND
L14-01961-02-006A		23.6	BBCH 89 (NCH)	325	ND
L14-01961-02-004A	Wheat Straw	24.2	BBCH 89 (NCH)	113	ND
L14-01961-02-008A		23.6	BBCH 89 (NCH)	325	ND
S14-01961-03, Hungary					
L14-01961-03-002A	Wheat Grain	24.3	BBCH 89 (NCH)	140	ND
L14-01961-03-006A		25.2	BBCH 89 (NCH)	301	ND
L14-01961-03-004A	Wheat Straw	24.3	BBCH 89 (NCH)	140	ND
L14-01961-03-008A		25.2	BBCH 89 (NCH)	301	ND
S14-01961-04, Hungary					
L14-01961-04-002A	Wheat Grain	24.1	BBCH 89 (NCH)	140	ND
L14-01961-04-004A	Wheat Straw	24.1	BBCH 89 (NCH)	140	ND
L14-01961-04-008A		24.1	BBCH 89 (NCH)	301	ND
S14-01961-05, Germany					
L14-01961-05-002A	Wheat Grain	24.3	BBCH 89 (NCH)	124	ND
L14-01961-05-006A		26.9	BBCH 89 (NCH)	333	<0.0100 (0.0097)
L14-01961-05-004A	Wheat Straw	24.3	BBCH 89 (NCH)	124	ND
L14-01961-05-008A		26.9	BBCH 89 (NCH)	333	<0.0100 (0.0081)
S14-01961-06, Germany					
L14-01961-06-002A	Wheat Grain	24.0	BBCH 89 (NCH)	132	ND
L14-01961-06-006A		24.2	BBCH 89 (NCH)	311	ND
L14-01961-06-004A	Wheat Straw	24.0	BBCH 89 (NCH)	132	ND
L14-01961-06-008A		24.2	BBCH 89 (NCH)	311	ND
S14-01961-07, Northern France					
L14-01961-07-002A	Wheat Grain	25.1	BBCH 89 (NCH)	118	ND
L14-01961-07-006A		23.8	BBCH 89 (NCH)	300	ND
L14-01961-07-004A	Wheat Straw	25.1	BBCH 89 (NCH)	118	ND
L14-01961-07-008A		23.8	BBCH 89 (NCH)	300	ND
S14-01961-08, Poland					
L14-01961-08-002A	Wheat Grain	23.9	BBCH 89 (NCH)	121	ND
L14-01961-08-006A		23.0	BBCH 89 (NCH)	307	ND
L14-01961-08-004A	Wheat Straw	23.9	BBCH 89 (NCH)	121	ND
L14-01961-08-008A		23.0	BBCH 89 (NCH)	307	ND
S14-01961-09, Southern France					
L14-01961-09-002A	Wheat Grain	25.5	BBCH 89 (NCH)	119	ND
L14-01961-09-006A		21.5	BBCH 89 (NCH)	330	ND
L14-01961-09-004A	Wheat Straw	25.5	BBCH 89 (NCH)	119	ND
L14-01961-09-008A		21.5	BBCH 89 (NCH)	330	ND
S14-01961-10, Southern France					
L14-01961-10-006A	Wheat Grain	24.7	BBCH 89 (NCH)	316	ND
L14-01961-10-008A	Wheat Straw	24.7	BBCH 89 (NCH)	316	ND
S14-01961-11, Southern France					
L14-01961-11-006A	Wheat Grain	25.1	BBCH 89 (NCH)	300	ND
L14-01961-11-008A	Wheat Straw	25.1	BBCH 89 (NCH)	300	<0.0100 (0.0043)
S14-01961-12, Spain					
L14-01961-12-002A	Wheat Grain	24.8	BBCH 89 (NCH)	129	ND
L14-01961-12-006A		24.8	BBCH 89 (NCH)	305	ND
L14-01961-12-004A	Wheat Straw	24.8	BBCH 89 (NCH)	129	<0.0100 (0.0046)
L14-01961-12-008A		24.8	BBCH 89 (NCH)	305	ND
S14-01961-13, Spain					
L14-01961-13-002A	Wheat Grain	24.5	BBCH 89 (NCH)	126	ND
L14-01961-13-006A		24.5	BBCH 89 (NCH)	301	ND
L14-01961-13-004A	Wheat Straw	24.5	BBCH 89 (NCH)	126	ND
L14-01961-13-008A		24.5	BBCH 89 (NCH)	301	ND
S14-01961-14, Spain					
L14-01961-14-002A	Wheat Grain	24.2	BBCH 89 (NCH)	127	ND
L14-01961-14-004A	Wheat Straw	24.2	BBCH 89 (NCH)	127	ND
S14-01961-15, Italy					
L14-01961-15-002A	Wheat Grain	25.9	BBCH 89 (NCH)	126	ND
L14-01961-15-006A		25.2	BBCH 89 (NCH)	315	ND
L14-01961-15-004A	Wheat Straw	25.9	BBCH 89 (NCH)	126	ND
L14-01961-15-008A		25.2	BBCH 89 (NCH)	315	ND

S14-01961-16, Italy					
L14-01961-16-002A	Wheat Grain	25.5	BBCH 89 (NCH)	131	ND
L14-01961-16-006A		24.9	BBCH 89 (NCH)	300	ND
L14-01961-16-004A	Wheat Straw	25.5	BBCH 89 (NCH)	131	ND
L14-01961-16-008A		24.9	BBCH 89 (NCH)	300	ND
S14-01961-17, France					
L14-01961-17-002A	Wheat Grain	25.4	BBCH 89 (NCH)	127	ND
L14-01961-17-004A	Wheat Straw	25.4	BBCH 89 (NCH)	127	ND
S14-01961-18, France					
L14-01961-18-002A	Wheat Grain	25.2	BBCH 89 (NCH)	118	ND
L14-01961-18-004A	Wheat Straw	25.2	BBCH 89 (NCH)	118	ND

DAA = Days after application
ND = Not detected, less than the LOD (<0.003 mg/kg for picloram). Residues of less than the LOQ of 0.01 mg/kg for picloram, but equal to or greater than the LOD are shown in parentheses.
NCH = Normal Commercial Harvest

Conclusion

The results of the study show that residues of picloram in wheat grain taken at normal commercial harvest for plot / treatment 3(300-333 days plant back interval) ranged from <LOD (<0.003 mg/kg) to <0.0100 (0.0097) mg/kg.
Residues of picloram in wheat straw taken at normal commercial harvest for plot / treatment 3 (300-333 days plant back interval) ranged from <LOD (<0.003 mg/kg) to <0.0100 (0.0081) mg/kg.
Residues of picloram in wheat grain taken at normal commercial harvest for plot / treatment 4 (113-140 days plant back interval) had residues of <LOD (<0.003 mg/kg).
Residues of picloram in wheat straw taken at normal commercial harvest for plot / treatment 4 (113-140 days plant back interval) ranged from <LOD (<0.003 mg/kg) to <0.0100 (0.0046) mg/kg.

Reference:	KCA 6.6.2
Report	Determination of Residues of Picloram in Rotational Crops (Wheat, Turnip and Kale) After One Application of GF-224 to Bare Soil at Two Sites in Northern Europe and Two Sites in Southern Europe 2014 – 2017, T. White, 2016, INTERIM REPORT No. S14-01962, DOW AGROSCIENCES REFERENCE ID 140651
Report	Determination of Residues of Picloram in Rotational Crops (Wheat, Turnip and Kale) After One Application of GF-224 to Bare Soil at Two Sites in Northern Europe and Two Sites in Southern Europe 2014 – 2017, **T. White, 2019, FINAL REPORT**, No. S14-01962, DOW AGROSCIENCES REFERENCE ID 140651
Guideline(s):	EU 1999: 1607/VI/97, OECD (2009) Guidance document on Overview of Residues Chemistry Studies, OECD Test Guideline 509: Crop Field trials OECD (2011), Guidance document on Crop Field trials SANCO/3029/99 rev. 4, Guideline 7029/VI/95 (REV. 5) to Directive 91/414/EEC and Regulations (EU) 283/2013 and 284/2013 implementing Regulation (EC) 1107/2009
Deviations:	Yes S14-01962-03: Only kale samples were collected from plots U1, 3, 5 and 6 due to the failure of the wheat and turnip crops. These crops shall be repeated and will be reported in the final report. S14-01962-04: A fifth trial (S14-01962-05) is also in progress on the same site as trial S14-01962-04 in order to repeat the turnip crop of trial S14-01962-04.
GLP:	Yes
Acceptability:	Yes

Materials and methods

To determine maximum picloram residue levels in rotational crops (wheat, turnip and kale), field trials were established in which one application of GF-224, a soluble (liquid) concentrate (SL) formulation containing picloram at a nominal concentration of 67 g a.e./L and clopyralid at a nominal concentration of 267 g a.e./L, was applied to bare soil on each plot at set intervals prior to the planting of the crops. Trials were conducted at four sites: one in the UK (S14-01962-01), one in Germany (S14-01962-02), one in Spain (S14-01962-03) and one in Southern France (S14-01962-04). Each site had a control plot and four treated plots. A fifth trial (S14-01962-05) is in progress on the same site as trial S14-01962-04 in order to repeat the turnip crop of trial S14-01962-04. This will not be included in interim report.

One application of GF-224 was applied at a target rate of 0.35 L product/ha (23.5 g a.e./ha picloram) to all treated plots in each trial.
Following the applications, the rotational crops have been drilled / planted to the plots at various intervals (differing intervals per plot). Crops have been drilled at 29-33, 111-132 and 330-336 after the application.

Residues of picloram were determined using a validated analytical method (reported in ABC study no. 68930 / Dow AgroSciences study code 120610) using Liquid Chromatography Mass Spectrometry (LC-MS/MS). The limit of detection (LOD) and limit of quantitation (LOQ) for picloram in wheat whole plant, grain and straw, turnip roots and tops, including leaves and kale leaves were 0.003 mg/kg and 0.01 mg/kg, respectively.
Recoveries in wheat whole plant averaged 91% for picloram. Recoveries in wheat grain averaged 94 % for picloram. Recoveries in wheat straw averaged 79% for picloram. Recoveries in turnip roots averaged 82 % for picloram. Recoveries in turnip tops, including leaves average 91 % for picloram. Recoveries in kale leaves averaged 93% for picloram.

The maximum period of frozen storage for picloram was 559~~307~~ days. All samples analyzed over 307 days were reanalysis of controls samples, in which all results were ND and were consistent with the initial analysis performed within 307 days.

A frozen storage stability study (980075) of residues of picloram in wheat (green forage, straw and grain), oilseed rape (grain and hay), soil and water was conducted. The stability of residues was studied for three years in wheat, soil and water and for two years in oilseed rape. The results of the study indicate that residues of picloram are stable when stored frozen in wheat (green forage, straw and grain), soil and water for at least 36 months (1095 days) and in oilseed rape (grain and hay) for at least 24 months (728 days).

In addition, frozen storage stability data collected within the ^{14}C confined rotational crop study (GH-C 2971R) demonstrates that wheat straw, corn grain, mustard green foliage, and turnip roots are stable for at least 11 months when stored frozen at -18°C. Therefore, the frozen storage stability data for turnip roots from the ^{14}C CRC study supports the maximum storage duration for turnip roots from the rotational crop study 140651 (263 days).

While kale leaf and turnip top frozen storage stability data is not directly available, frozen storage stability data for two high water content commodities (wheat forage (980075) and mustard green foliage (GH-C 3971R) is available and demonstrates that picloram is stable in high water content commodities for at least 11 months.

Results and Discussions

Analyte residues were not detected above the analytical method LOQ or LOD in any of untreated samples. This data indicates that untreated control plots and samples have remained uncontaminated through the course of the study so far.

Residue data for the treated specimens are summarized in the following Tables:

Summary of Residues in Treated Wheat, Turnip and Kale (drilled 2015) Following One Application of GF-224 to Bare Soil Trial S14-01962-01, UK (Plots 3, 5 and 6)

Plot	DALA (days) Range	Matrix	Residue Levels (mg/kg) Picloram
3 (330-336 days plant back interval)	BBCH 32	Wheat Whole Plant	ND
	BBCH 89 (NCH)	Wheat Grain	ND
	BBCH 89 (NCH)	Wheat Straw	ND
	BBCH 49 (NCH)	Turnip roots	ND
	BBCH 49 (NCH)	Turnip tops, including leaves	ND
	BBCH 49 (NCH)	Kale leaves	ND
5 (111-132 days plant back interval)	BBCH 32	Wheat Whole Plant	ND
	BBCH 89 (NCH)	Wheat Grain	ND
	BBCH 89 (NCH)	Wheat Straw	ND
	BBCH 49 (NCH)	Turnip roots	ND
	BBCH 49 (NCH)	Turnip tops, including leaves	ND
	BBCH 49 (NCH)	Kale leaves	ND
6 (29-33 days plant back interval)	BBCH 32	Wheat Whole Plant	<0.0100 (0.0057)
	BBCH 89 (NCH)	Wheat Grain	<0.0100 (0.0068)
	BBCH 89 (NCH)	Wheat Straw	<0.0100 (0.0078)
	BBCH 49 (NCH)	Turnip roots	ND
	BBCH 49 (NCH)	Turnip tops, including leaves	<0.0100 (0.0053)
	BBCH 49 (NCH)	Kale leaves	ND

ND = Not detected, less than LOD (0.003 mg/kg)
Results in parentheses are between LOD and LOQ
NCH = Normal Commercial Harvest

Summary of Residues in Treated Wheat, Turnip and Kale (drilled 2015) Following One Application of GF-224 to Bare Soil Trial S14-01962-02, Germany (Plots 3, 5 and 6)

Plot	DALA (days) Range	Matrix	Residue Levels (mg/kg) Picloram
3 (330-336 days plant back interval)	BBCH 32	Wheat Whole Plant	<0.0100 (0.0038)
	BBCH 89 (NCH)	Wheat Grain	<0.0100 (0.0064)
	BBCH 89 (NCH)	Wheat Straw	ND
	BBCH 49 (NCH)	Turnip roots	ND
	BBCH 49 (NCH)	Turnip tops, including leaves	<0.0100 (0.0070)
	BBCH 49 (NCH)	Kale leaves	<0.0100 (0.0063)
5 (111-132 days plant back interval)	BBCH 32	Wheat Whole Plant	<0.0100 (0.0036)
	BBCH 89 (NCH)	Wheat Grain	ND
	BBCH 89 (NCH)	Wheat Straw	ND
	BBCH 49 (NCH)	Turnip roots	ND
	BBCH 49 (NCH)	Turnip tops, including leaves	<0.0100 (0.0043)
	BBCH 49 (NCH)	Kale leaves	<0.0100 (0.0032)
6 (29-33 days plant back interval)	BBCH 32	Wheat Whole Plant	0.0491
	BBCH 89 (NCH)	Wheat Grain	0.0233
	BBCH 89 (NCH)	Wheat Straw	0.0196
	BBCH 49 (NCH)	Turnip roots	0.0110
	BBCH 49 (NCH)	Turnip tops, including leaves	0.0422
	BBCH 49 (NCH)	Kale leaves	0.0277

ND = Not detected, less than LOD (0.003 mg/kg)
Results in parentheses are between LOD and LOQ
NCH = Normal Commercial Harvest

Summary of Residues in Treated Wheat, Turnip and Kale (drilled 2015) Following One Application of GF-224 to Bare Soil Trial S14-01962-03, Spain (Plots 3, 5 and 6)

Plot	DALA (days) Range	Matrix	Residue Levels (mg/kg) Picloram
3 (330-336 days plant back interval)	BBCH 32	Wheat Whole Plant	ND
	BBCH 89 (NCH)	Wheat Grain	N/A
	BBCH 89 (NCH)	Wheat Straw	N/A
	BBCH 49 (NCH)	Turnip roots	N/A
	BBCH 49 (NCH)	Turnip tops, including leaves	N/A
	BBCH 49 (NCH)	Kale leaves	ND
5 (111-132 days plant back interval)	BBCH 32	Wheat Whole Plant	<0.0100 (0.0060)
	BBCH 89 (NCH)	Wheat Grain	N/A
	BBCH 89 (NCH)	Wheat Straw	N/A
	BBCH 49 (NCH)	Turnip roots	N/A
	BBCH 49 (NCH)	Turnip tops, including leaves	N/A
	BBCH 49 (NCH)	Kale leaves	<0.0100 (0.0087)
6 (29-33 days plant back interval)	BBCH 32	Wheat Whole Plant	N/A
	BBCH 89 (NCH)	Wheat Grain	N/A
	BBCH 89 (NCH)	Wheat Straw	N/A
	BBCH 49 (NCH)	Turnip roots	N/A
	BBCH 49 (NCH)	Turnip tops, including leaves	N/A
	BBCH 49 (NCH)	Kale leaves	0.0144

ND = Not detected, less than LOD (0.003 mg/kg)
Results in parentheses are between LOD and LOQ
NCH = Normal Commercial Harvest
N/A = Not yet analysed – crop sub-plot being repeated (will be included in the final report)

Summary of Residues in Treated Wheat, Turnip and Kale (drilled 2015) Following One Application of GF-224 to Bare Soil Trial S14-01962-04, Southern France (Plots 3, 5 and 6)

Plot	DALA (days) Range	Matrix	Residue Levels (mg/kg) Picloram
3 (330-336 days plant back interval)	BBCH 32	Wheat Whole Plant	ND
	BBCH 89 (NCH)	Wheat Grain	ND
	BBCH 89 (NCH)	Wheat Straw	ND
	BBCH 49 (NCH)	Turnip roots	N/A
	BBCH 49 (NCH)	Turnip tops, including leaves	N/A
	BBCH 49 (NCH)	Kale leaves	ND
5 (111-132 days plant back interval)	BBCH 32	Wheat Whole Plant	ND
	BBCH 89 (NCH)	Wheat Grain	ND
	BBCH 89 (NCH)	Wheat Straw	ND
	BBCH 49 (NCH)	Turnip roots	N/A
	BBCH 49 (NCH)	Turnip tops, including leaves	N/A
	BBCH 49 (NCH)	Kale leaves	ND
6 (29-33 days plant back interval)	BBCH 32	Wheat Whole Plant	0.0496
	BBCH 89 (NCH)	Wheat Grain	0.0116
	BBCH 89 (NCH)	Wheat Straw	0.0158
	BBCH 49 (NCH)	Turnip roots	N/A
	BBCH 49 (NCH)	Turnip tops, including leaves	N/A
	BBCH 49 (NCH)	Kale leaves	ND

ND = Not detected, less than LOD (0.003 mg/kg)
Results in parentheses are between LOD and LOQ
NCH = Normal Commercial Harvest
N/A = Not yet analysed – crop sub-plot being repeated (will be included in the final report)

Conclusion
Residues of picloram in wheat whole plant taken at BBCH 32 for plot / treatment 3 (330-336 days plant back interval) ranged from <LOD (<0.003 mg/kg) to 0.0038 mg/kg, which is <LOQ of 0.01 mg/kg; for plot / treatment 5 (111-132 days plant back interval) ranged from <LOD (<0.003 mg/kg) to 0.006 mg/kg, which is <LOQ of 0.01 mg/kg; and for plot / treatment 6 (29-33 days plant back interval) ranged from 0.0057 mg/kg, which is <LOQ of 0.01 mg/kg, to 0.0496 mg/kg.

Residues of picloram in wheat grain taken at normal commercial harvest for plot / treatment 3 (330-336 days plant back interval) ranged from <LOD (<0.003 mg/kg) to 0.0064 mg/kg which is <LOQ of 0.01 mg/kg; for plot / treatment 5 (111-132 days plant back interval) all samples analyzed had residues of <LOD (<0.003 mg/kg); and for plot / treatment 6 (29-33 days plant back interval) ranged from 0.0068 mg/kg, which is <LOQ of 0.01 mg/kg, to 0.0233 mg/kg.

Residues of picloram in wheat straw taken at normal commercial harvest for plot / treatment 3 (330-336 days plant back interval) had residues of <LOD (<0.003 mg/kg); for plot / treatment 5 (111-132 days plant back interval) all samples analyzed had residues of <LOD (<0.003 mg/kg); and for plot / treatment 6 (29-33 days plant back interval) ranged from 0.0078 mg/kg, which is <LOQ of 0.01 mg/kg, to 0.0196 mg/kg.

Residues of picloram in turnip roots taken at normal commercial harvest for plot / treatment 3 (330-336 days plant back interval) had residues of <LOD (<0.003 mg/kg); for plot / treatment 5 (111-132 days plant back interval) all samples analyzed had residues of <LOD (<0.003 mg/kg); and for plot / treatment 6 (29-33 days plant back interval) ranged from <LOD (<0.003 mg/kg) to 0.0110 mg/kg.

Residues of picloram in turnip tops, including leaves, taken at normal commercial harvest for plot / treatment 3 (330-336 days plant back interval) ranged from <LOD (<0.003 mg/kg) to 0.007 mg/kg, which is <LOQ of 0.01 mg/kg; for plot / treatment 5 (111-132 days plant back interval) ranged from <LOD (<0.003 mg/kg) to 0.0043 mg/kg, which is <LOQ of 0.01 mg/kg; and for plot / treatment 6 (29-33 days plant back interval) ranged from 0.0053 mg/kg, which is <LOQ of 0.01 mg/kg, to 0.0422 mg/kg.

Residues of picloram in kale leaves taken at normal commercial harvest for plot / treatment 3 (330-336 days plant back interval) ranged from <LOD (<0.003 mg/kg) to 0.0063 mg/kg, which is <LOQ of 0.01 mg/kg; for plot / treatment 5 (111-132 days plant back interval) ranged from <LOD (<0.003 mg/kg) to 0.0087 mg/kg, which is <LOQ of 0.01 mg/kg; and for plot / treatment 6 (29-33 days plant back interval) ranged from <LOD (<0.003 mg/kg) to 0.0277 mg/kg.

A 2.2.5.1.1 Nature of residues in processed commodities

No new study submitted.

Comments of zRMS:	See point A 2.2.2.1.1

CITATION
Croffie, J. W., Adelfinskaya, Y., Hastings, M; 2016; A Confined Rotational Crop Study with 14C-Picloram; Dow AgroSciences, LLC; DAS Study No. 13020; 28 April 2016; Unpublished

COMPLIANCE

Guideline(s):	OECD 502
US EPA Guideline(s):	OCSPP 860.1850, OPPTS 860.
Deviations:	none
Dates of work:	21 February 2013 to 28 April 2016
GLP status:	Yes
Number of pages in final report:	129

BACKGROUND INFORMATION

Picloram is a selective systemic herbicide, effective in the control of many annual and perennial broad-leaved weeds on grassland and non-crop areas and may also be used for selective weed control in certain agronomic row crops, including oilseed rape and field corn. Picloram is currently Annex 1 listed. The mode of action is Herbicide-Synthetic Auxin.

The laboratory aerobic soil DT_{50} was found to be rate-dependent and has a faster degradation at lower application rates.

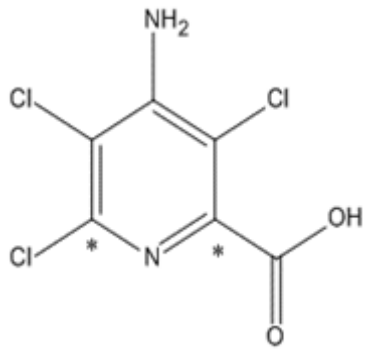
MATERIALS AND METHODS

Test Item(s)

Non-radiolabelled test item #1

ISO Common name:	Picloram
Test item (chemical/chemical/another name):	4-amino-3,5,6-trichloro-2-pyridinecarboxylic acid
Purity:	99.7%
Description (physical state):	Not reported
Lot/batch no.:	TSN029006-0001 (DE3-137773-20)
CAS no.:	1918-02-1
SMILES string	Clc1c(c(c(nc1C(=O)O)Cl)Cl)N

Radiolabelled test item #1

Name:	14C-picloram
Test item (chemical/chemical/another name):	4-amino-3,5,6-trichloro(2,6-14C2)pyridine-2-carboxylic acid
Structural formula:	
Position of labelling (*)	
Lot/batch no.:	INV304760
Radiochemical purity:	99.7%
Specific radioactivity:	31.9 mCi/mmol

Methods

Test Site Information

Testing environment:	outdoor test plots	
Container description:	1.5 x 0.9 m, surface area 1.39 m^2, 7 used	
Soil type:	sandy loam	
Soil characteristics:	% sand	73
	% silt	21
	% clay	6
	% OM:	0.92
	pH (1:1 soil: water)	6.9
	CEC (meq/100 g)	13.4
Any adverse weather conditions:	no	
Any adverse insect or disease problems:	no	

Study Use Pattern

Application method:	soil-applied
Formulation type:	KOH salt
Application rate:	25 g ai/ha
Number of plant-back intervals:	3
Plant-back intervals:	30, 60, 335 days
Plot maintenance during fallow periods:	Irrigated weekly during fallow periods

Test System

Table A.2.2.5.1.1-1: Crop information

Crop/ crop group	Variety	Plant-back intervals (days)	Growth stage at harvest	Harvested RAC	Harvesting procedure
Lettuce/ leafy vegetable	Butter-crunch	30	BBCH 44	Immature	cut with scissors
		30	BBCH 49	mature	cut with scissors
		60	BBCH 44	Immature	cut with scissors
		60	BBCH 49	mature	cut with scissors
		335	BBCH 44	Immature	cut with scissors
		335	BBCH 49	mature	cut with scissors
Radish/ root crop	Cherry Belle	30	BBCH 49	mature radish	pulled up, tops & roots separated by cutting with scissors
		60	BBCH 49	mature radish	pulled up, tops & roots separated by cutting with scissors
		335	BBCH 49	mature radish	pulled up, tops & roots separated by cutting with scissors
Wheat/ cereal	Ultra	30	BBCH 34	forage	cut with scissors
			BBCH 83	hay	cut with scissors, dried
			BBCH 89	straw & grain	cut off heads, separated grain, cut straw
		60	BBCH 34	forage	cut with scissors
			BBCH 83	hay	cut with scissors, dried
			BBCH 89	straw & grain	cut off heads, separated grain, cut straw
		335	BBCH 34	forage	cut by hand
			BBCH 83	hay	cut by hand, dried
			BBCH 89	straw & grain	cut off heads, separated grain, cut straw

Sample Handling and Preparation

The untreated samples were collected prior to treated samples and handled/stored separately. Each sample was placed into a tared, pre-labelled, plastic Ziploc bag, which was then placed into a pre-labelled, plastic-lined cloth residue bag. After the weights were recorded, the bagged samples were placed into frozen storage. The forage wheat samples were cut with scissors approximately 3 cm above the soil surface. The lettuce was cut with scissors approximately 3 cm above the soil surface and then placed into sample bags. Mature radishes were pulled from the ground and the roots were cut with scissors into a foil lined tray and brought back to the lab and hand washed with water then patted dry with a paper towel. The tops and roots were placed into separate sample bags. The wheat hay samples were cut with scissors approximately 1 1/2 inches (4.5 cm) above the soil surface into labelled plastic trash bags. The fresh weight was recorded, and then the hay was laid on butcher paper in the RFH greenhouses and allowed to dry. The grain heads were cut first with scissors and placed into a large plastic bag. Then the straw was cut approximately 1 inch (3 cm) above the soil surface. The grain was separated from the chaff using a grain thresher. The chaff was added to the straw sample.

In general, the samples were removed from frozen storage, pre-weighed, chopped into smaller pieces if needed, and milled with dry ice, to maintain a frozen state during milling, returned to frozen storage to allow for sublimation of the dry ice (typically two days), post weighed, and returned to frozen storage pending shipment to Dow AgroSciences (DAS). The entire sample was processed when the total sample weighed less than 1000.0 grams. When the total sample weighed more than 1000.0 grams random grab samples were collected from the bulk until reaching 1000.0 grams. The selected portion to be processed was composed of approximately 10 random grab samples from the bulk sample. The remaining sample was stored frozen at RFH, pending permission for disposal from study director at DAS. Homogenized samples were shipped to DAS on dry ice using an overnight courier.

Generally, five to ten aliquots of approximately 0.2 g were combusted to determine the radioactive residues in the samples.

Extraction of Sample Residues

Neutral organic solvent extraction (EX1-EX4)

An accelerated solvent extractor (Dionex model ASE 350) was used to extract the milled samples. The sample, approximately 2-10 grams, was weighed directly into a 34 mL ASE cell and loaded on to a Dionex ASE 350 to be extracted. Each sample was subjected to four sequential ASE extractions, twice with 80/20 acetonitrile/water at 40 °C (EX1 & EX2), then twice with 80/20 acetonitrile/water at 70 °C (EX3 & EX4). The four ASE extracts per sample were collected into individual vials.

Volumes of each ASE extract were calculated by measured mass and density. The ASE extract volumes, per extraction, were typically about 30 to 50 mL. The four ASE extracts were combined and concentrated. Solid phase extraction (SPE) was conducted on the ASE extracts containing significant radioactivity, and SPE fractions were prepared for HPLC analysis using the procedure described below.

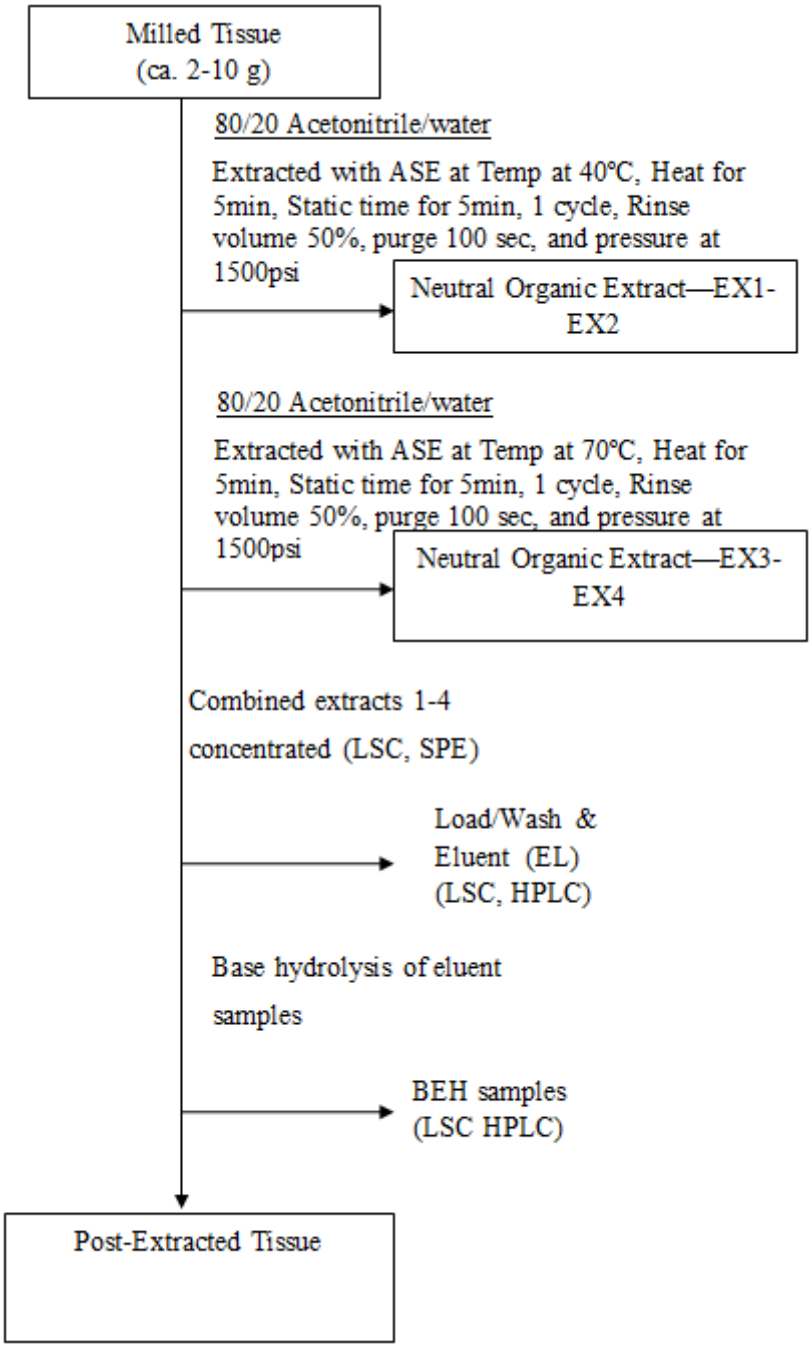
The tissue remaining after the four sequential ASE extractions was air-dried and weighed. At least five aliquots (0.1-0.3 g) were analyzed by oxidative combustion to determine the amount of non-extractable radioactive residue.

Base extraction

Those post-extracted tissues containing greater than 10% of the TRR (generally wheat hay, straw and grain samples) were further extracted with base by aliquoting a sample of the air-dried tissue and adding approximately 10 mL of methanol/ NaOH (100:1). The tissue, along with the solvent, were then blended for approximately 60 seconds at 13,000 rpm using an Omni-mixer homogenizer. The blended tissue was then shaken at ambient temperature for 1 hour and allowed to react without shaking overnight (or least twelve hours). The sample was then centrifuged (approximately 5 minutes at approximately 2000 rpm) and the supernatant was removed by vacuum filtration. The supernatant samples were then analyzed by LSC. The supernatant samples were then concentrated (using a Turbo Vap evaporator) at 40 ºC 5 psi to near dryness. Approximately 0.5-0.8 mL of 1 N HCl was added to each sample to adjust pH. The concentrated supernatant samples were then subjected to SPE procedure as described below.

A second base extraction was performed (BEX2, BEXR2 samples) on the post-extracted pellet to try and remove any additional radioactivity. The procedure was the same as above except in the second base extraction the post-extracted pellet tissue samples were shaken firmly for 4 hours at 55 ºC. After sitting for at least twelve hours the procedure continued on as mentioned above for the first base extraction and the tissue was combusted. The extracts were analyzed by LSC.

Figure A.2.2.5.1.1-1: Flow diagram for the extraction of crop fractions



Analyses of Non-Extractable Residues

No additional work was done with the non-extractable residues since they represented <10% of the TRR and <0.01 mg/kg in human food and <0.050 mg/kg in animal feed commodities.

Base Hydrolysis of Suspected Conjugate Fractions

After SPE, an aliquot (0.25-0.5 mL) of the elution samples, from the neutral extraction only, were concentrated by nitrogen jet at 40 ºC. Approximately 2 mL of methanol/10 N NaOH (100:1) was added to the concentrated samples. The sample was then shaken at ambient temperature for 1 hour and allowed to react, without shaking, overnight (or least twelve hours). The samples were then concentrated further using a turbo evaporator at 40 ºC to approximately 50 µL. After concentration, approximately 1 mL of 1 N HCl and approximately 0.2 mL of acetonitrile was added to each sample. The sample was then centrifuged (approximately 5 minutes @ 14,000 rpm) and the supernatant was transferred to a new vial. The supernatants were analyzed by LSC and HPLC.

Extraction and Clean-up Procedures for Metabolite Identification
A picloram reference standard was available. Retention time comparisons were made between this reference standard and the retention times of radioactive peaks in the chromatograms to provide identifications using HPLC methods.

Analytical Methodology
Total ^{14}C measurement
The liquid scintillation counters automatically converted the radioactivity counting rate in counts per minute (cpm) to disintegrations per minute (dpm) using an external standard to correct for sample quenching. The instrument was calibrated at least every six months with a set of ten quenched standards. Each day of use, the instrument was normalized, and its performance was checked with respect to background cpm value, unquenched standard cpm value, and quenched standard dpm value for a range of quenched standards. The quenched standards are certified by comparison to Standard Reference Material 4222C, (National Institute of Standards and Technology. Gaithersburg, MD). The scintillation counters used were Tri Carb 2910 TRs (PerkinElmer Inc. Massachusetts, USA). The dpm value for an extraction sample was determined by LSC after diluting an appropriate aliquot of the sample with ScintiSafe Plus™ 50% scintillation cocktail (Fisher Scientific, Fair Lawn, NJ) and counting for at least five minutes.

Solid phase extraction (SPE) for neutral extracts EX1-EX4
The general clean-up procedure for the extracts was with a Strata-X SPE (1 g, 20 mL, 8B-S100-JEG, Phenomenex Inc., Torrance, California, USA).
For each sample, the remainder of the ASE extracts EX1 through EX4 after the removal of aliquots for LSC analysis (typically between 20 and 40 mL for each extract) were combined, adding a "keeper" of approximately 100 µL of methanol: glycerol (80:20, v/wt) and concentrated until only aqueous remained using a Rocket Evaporator (Genevac Limited, Ipswich, UK) set at approximately 40 °C. Once concentrated, the extracts were brought to a volume of approximately 6 or 10 mL using HPLC grade water. Concentrated HCl was added to each extract to make samples approximately 1 N, then capped and briefly sonicated to mix. To each SPE cartridge, 3M™ Empore™ Filter Aid was added at a depth of approximately 1 cm. The SPE cartridges were conditioned with acetonitrile (12 or 20 mL) followed by HPLC grade water (2 x 12 or 20 mL). The prepared samples were applied to the conditioned SPE, eluted at approx. 2 mL/min, collecting the eluate. The SPE was dried for 10 seconds after the SPE had eluted. The sample vials were rinsed with approximately 6 or 10 mL of 1 N HCl and transferred to the SPE cartridge, and eluted at approx. 2 mL/min, pooling with the load eluate. The sample vials were then rinsed again with HPLC grade water (4 x 6 or 10 mL). The SPE cartridge was dried under full vacuum for approximately 10 seconds. These combined sample applications were considered the load/wash portions. A fresh collection vial was added, and the cartridge was eluted, at approx. 2 mL/min, with 90/10 acetonitrile/water (3 x 4 or 2 x 7 & 1 x 6 mL). This portion was considered the eluate. Triplicate aliquots were taken of the load/wash and eluent for analysis by LSC. After the addition of 100 µL of a methanol/glycerol (80/20) solution, only the elution samples were concentrated to near dryness using a Rocket Evaporator (Genevac Limited, Ipswich, UK). The concentrated elution samples were reconstituted with first acetonitrile then water (both with 0.1% formic acid) and centrifuged (5 minutes @ 14,000 rpm) to remove particulates. Triplicate aliquots of each reconstituted elution sample supernatant were analyzed by LSC and by HPLC.

Solid phase extraction (SPE) for base extracts (BEX & BEX2)
The general clean-up procedure for the extracts was with a Strata-X SPE (1 g, 20 mL, 8B-S100-JEG, Phenomenex Inc., Torrance, California, USA).
The base extracts were first concentrated by turbo evaporator to near dryness. The pH was adjusted to approximately (0-1) using 1 N HCl. The samples were then brought to a volume of approximately 10 mL by adding 1 N HCl. To each SPE cartridge, 3M™ Empore™ Filter Aid was added at a depth of approximately 1 cm. The SPE cartridges were conditioned with acetonitrile (20 mL) followed by HPLC grade water (2 x 20 mL). The prepared sample was applied to the conditioned SPE, eluted at approx. 2 mL/min, collecting the eluate. The SPE was dried for 10 seconds after the SPE had eluted. The sample vial was rinsed with approximately 10 mL of 1 N HCl and transferred to the SPE cartridge, and eluted at approx. 2 mL/min, pooling with the load eluate. This portion was considered the load/wash sample. The SPE cartridge was dried under full vacuum for 10 seconds. A fresh collection vial was added and the Strata-X SPE was

eluted, at approx. 2 mL/min, with HPLC grade water (4 x 10 mL). This portion was named "wash 2". The SPE cartridge was dried under full vacuum for 10 seconds. A fresh collection vial was added and the Strata-X SPE was eluted, at approx. 2 mL/min, sequentially with 90/10 acetonitrile/water (2 x 7 mL and 1 x 6 mL). This portion was named "1st eluate". The SPE cartridge was dried under full vacuum just long enough to remove most of the liquid. A fresh collection vial was added and the Strata-X SPE was eluted, at approx. 2 mL/min, sequentially with methanol (2 x 7 mL and 1 x 6 mL). This portion was named "2nd eluate". Triplicate aliquots were taken of the load/wash, wash 2, and 1st and 2nd eluents for analysis by LCS. After the addition of 100 µL of a methanol/glycerol (80/20) solution to the 1st elution samples, these were concentrated to near dryness using a Rocket Evaporator (Genevac Limited, Ipswich, UK). The concentrated elution samples were reconstituted at a ratio of 8/2 with water and acetonitrile (both with 0.1% formic acid) and centrifuged (5 minutes @ 14,000 rpm) to remove particulates. Triplicate aliquots of each reconstituted elution sample were analyzed by LSC and by HPLC.

High performance liquid chromatography (HPLC) for quantitation

HPLC analyses of all sample extracts following SPE clean-up were accomplished using a Phenomenex Synergi Hydro-RP column (150 x 4.6 mm i.d.,); 1.0 mL/min; UV detection at 254 nm) and a twostep, linear gradient.

Mass spectral analysis (LC/MS) for identification of transformation products

Whenever possible, initial metabolite identification was accomplished by co-chromatography with available reference standards using HPLC. Structure confirmation of any such tentatively identified components as well as the identification of any significant fraction that did not co-elute with a standard was accomplished by liquid chromatography coupled with tandem mass spectrometry (LC/MS/MS) with electrospray ionization (ESI).

RESULTS AND DISCUSSION

Results of In-Life Phase

Radiochemical purity of the test substance prior to application was determined to be 99.5% (average of three analyses), by HPLC, for a separate aliquot of the ^{14}C-picloram. The specific activity was unchanged at 293,288 dpm/µg (31.90 mCi/mmol) for the applied ^{14}C-picloram substance.

The ^{14}C-picloram was applied in the spring for radishes, lettuce, and 30- and 335-d plant-back wheat. However, the spring-application was too late in the growing season to enable wheat growth following a 60-d plant-back interval (PBI), therefore a separate application and subsequent planting was conducted in the autumn. The spring application solution contained 109.2% of the target amount of formulated picloram, whereas the fall application contained 94.7%. Each plot received 3.80 mg (Spring) or 3.30 mg (Fall) of ^{14}C-picloram, equivalent to 27.3 g ai/ha (Spring) and 23.7 g ai/ha (Fall). The applications were at a seasonal 1X rate. Radiochemical purity and stability of the formulated application solution post-application for the spring was 91.2% and 92.2%, and for the fall it was 91.8% and 93.4%, for the 14C-picloram. Pre-application retainer sample analyses were similar at 92.0% and 92.1% for spring and 94.9% and 90.9% for fall ^{14}C-picloram, indicating stability of picloram during storage and application.

The spring-application was too late in the growing season to enable wheat growth following a 60-d plant-back interval, therefore a separate application and subsequent planting was conducted in the autumn.

Total Radioactive Residue (TRR) Levels

TRR levels in all samples, expressed as mg/kg of parent equivalents below.

Table A.2.2.5.1.1-2: Total radioactive residues (TRRs) in matrices

Sample	30-d plant-back interval	60-d plant-back interval	335-d plant-back interval
	mg eq/kg	mg eq/kg	mg eq/kg
immature lettuce	0.023	0.019	0.005
mature lettuce	0.013	0.018	0.002
mature radish tops	0.029	0.039	0.008
mature radish roots	0.002	0.002	0.001
wheat forage	0.077	0.065	0.021
wheat hay	0.494	0.255	0.058
wheat straw	0.403	0.327	0.104
wheat grain	0.126	0.054	0.020

Residues in crops at all plant-back times ranged from 0.001 to 0.494 mg eq./kg (picloram equivalents). Residues in lettuce, radishes and wheat forage and grain were generally less than those in wheat hay and straw. Residues in immature lettuce, wheat forage, hay, straw and grain showed a significant decline with an increase in the plant-back interval. Residues in mature lettuce and radish tops showed moderate increases from the 30-d plant-back interval to the 60-d plant-back interval. All crops showed significant decrease in the residues from the 60-d plant back interval to the 335-d plant-back interval.

Distribution of Residues Following Extraction

In general, greater than 80% of the total radioactive residue was extracted using a neutral solvent, with the exception of wheat hay and straw in which approximately 70-80% of the TRR was extracted, and wheat grain where even lower levels, 34-40% of the TRR, were extracted. For most samples, the extraction rates were comparable among the 30, 60, and 335 DAT plant back intervals.

Recoveries from the SPE cartridge were good, generally greater than 90%. The radioactivity was found to be mostly in the eluent fractions. A hydrolysis of the eluent samples only, was performed as described.

In general, the base extraction of wheat hay and straw yielded approximately 12-19% of the total radioactive residue during the first base extraction. The first base extracts of wheat grain contained approximately 35-46% for all plant-back intervals. In the second base extraction, for wheat hay and straw an additional 2-4% of the TRR was removed. The second base extractions of wheat grain contained approximately 11-17% of the TRR. HPLC analysis confirmed that the major component in the base extracts was picloram.

Table A.2.2.5.1.1-3: Distribution of the parent and the metabolites in rotational crop matrices when dosed with 14C-labeled picloram

Metabolite Fraction	30D Immature Lettuce		60D Immature Lettuce		335D Immature Lettuce	
	%TRR	µg eq/g	%TRR	µg eq/g	%TRR	µg eq/g
TRR	100	0.023	100	0.019	100	0.005
80/20 ACN/H20 ASE Extract (EX1-EX4)	80.0	0.018	92.0	0.018	NA	NA
100:1 MeOH/NaOH Extract (BEX/BEXR)	NA	NA	NA	NA	NA	NA
Total Extractable	80.0	0.018	92.0	0.018	NA	NA
Total analyzed by HPLC	75.3	0.017	103.4	0.020	NA	NA
Total free & conjugated picloram	72.4	0.016	99.8	0.019	NA	NA
Total Characterized	2.9	0.001	3.6	0.001	NA	NA
Unextractable (PES)[1]	9.0	0.002	9.9	0.002	NA	NA
Accountability[2]	89.0	0.020	101.9	0.020	NA	NA

NA = not analyzed, due to low residues present
[1] Residues remaining after exhaustive extractions.
[2] Accountability = (Total extractable + Total unextractable)/(TRRs from combustion analysis) * 100.

Table A.2.2.5.1.1-4: Distribution of the parent and the metabolites in rotational crop matrices when dosed with 14C-labeled picloram

Metabolite Fraction	30D Mature Lettuce		60D Mature Lettuce		335D Mature Lettuce	
	%TRR	µg eq/g	%TRR	µg eq/g	%TRR	µg eq/g
TRR	100	0.013	100	0.018	100	0.002
80/20 ACN/H20 ASE Extract (EX1-EX4)	89.8	0.012	90.4	0.016	NA	NA
100:1 MeOH/NaOH Extract (BEX/BEXR)	NA	NA	NA	NA	NA	NA
Total Extractable	89.8	0.012	90.4	0.016	NA	NA
Total analyzed by HPLC	79.5	0.010	84.4	0.015	NA	NA
Total free & conjugated picloram	77.0	0.010	84.4	0.015	NA	NA
Total Characterized	2.5	0.000	0.0	0.000	NA	NA
Unextractable (PES)[1]	17.3	0.002	11.8	0.002	NA	NA
Accountability[2]	107.1	0.014	102.2	0.018	NA	NA

NA = not analyzed, due to low residues present
[1] Residues remaining after exhaustive extractions.
[2] Accountability = (Total extractable + Total unextractable)/(TRRs from combustion analysis) * 100.

Table A.2.2.5.1.1-5: Distribution of the parent and the metabolites in rotational crop matrices when dosed with 14C-labeled picloram

Metabolite Fraction	30D Radish Tops		60D Radish Tops		335D Radish Tops	
	%TRR	µg eq/g	%TRR	µg eq/g	%TRR	µg eq/g
TRR	100	0.029	100	0.039	100	0.008
80/20 ACN/H20 ASE Extract (EX1-EX4)	90.8	0.027	83.3	0.032	NA	NA
100:1 MeOH/NaOH Extract (BEX/BEXR)	NA	NA	NA	NA	NA	NA
Total Extractable	90.8	0.027	83.3	0.032	NA	NA
Total analyzed by HPLC	84.9	0.025	87.7	0.034	NA	NA
Total free & conjugated picloram	84.9	0.025	75.7	0.029	NA	NA
Total Characterized	0.0	0.000	12.0	0.005	NA	NA
Unextractable (PES)[1]	4.5	0.001	10.8	0.004	NA	NA
Accountability[2]	95.2	0.028	94.1	0.036	NA	NA

NA = not analyzed, due to low residues present
[1] Residues remaining after exhaustive extractions.
[2] Accountability = (Total extractable + Total unextractable)/(TRRs from combustion analysis) * 100.

Table A.2.2.5.1.1-6: Distribution of the parent and the metabolites in rotational crop matrices when dosed with 14C-labeled picloram

Metabolite Fraction	30D Wheat Forage		60D Wheat Forage (fall)		335D Wheat Forage	
	%TRR	µg eq/g	%TRR	µg eq/g	%TRR	µg eq/g
TRR	100	0.077	100	0.065	100	0.021
80/20 ACN/H20 ASE Extract (EX1-EX4)	84.7	0.065	94.6	0.061	97.6	0.020
100:1 MeOH/NaOH Extract (BEX/BEXR)	NA	NA	NA	NA	NA	NA
Total Extractable	84.7	0.065	94.6	0.061	97.6	0.020
Total analyzed by HPLC	89.5	0.069	109.1	0.071	103.8	0.022
Total free & conjugated picloram	83.5	0.064	109.1	0.071	103.8	0.022
Total Characterized	6.0	0.005	0.0	0.000	0.0	0.000
Unextractable (PES)[1]	8.7	0.007	4.3	0.003	3.4	0.001
Accountability[2]	93.5	0.072	98.9	0.064	101.0	0.021

NA = not analyzed, due to low residues present
[1] Residues remaining after exhaustive extractions.
[2] Accountability = (Total extractable + Total unextractable)/(TRRs from combustion analysis) * 100.

Table A.2.2.5.1.1-7: Distribution of the parent and the metabolites in rotational crop matrices when dosed with 14C-labeled picloram

Metabolite Fraction	30D Wheat Hay		60D Wheat Hay (fall)		335D Wheat Hay	
	%TRR	µg eq/g	%TRR	µg eq/g	%TRR	µg eq/g
TRR	100	0.494	100	0.255	100	0.058
80/20 ACN/H20 ASE Extract (EX1-EX4)	77.3	0.382	75.2	0.192	80.0	0.047
100:1 MeOH/NaOH Extract (BEX/BEXR)	12.7	0.063	15.2	0.39	12.1	0.007
100:1 MeOH/NaOH Extract (BEX2/BEXR2)	2.5	0.012	3.6	0.009	2.2	0.001
Total Extractable	92.5	0.457	94.0	0.240	94.3	0.055
Total analyzed by HPLC (EX1-EX4)	77.2	0.382	52.4	0.134	76.5	0.045
Total picloram[1] (EX1-EX4)	74.2	0.367	54.0	0.138	85.6	0.050
Total analyzed by HPLC (BEX/BEXR)	10.1	0.050	13.9	0.035	10.2	0.006
Total picloram (BEX/BEXR)	8.5	0.042	13.2	0.034	10.2	0.006
Total analyzed by HPLC (BEX2/BEXR2)	2.3	0.011	3.7	0.009	NA	NA
Total picloram (BEX2/BEXR2)	2.3	0.011	3.7	0.009	NA	NA
Total free & conjugated picloram[2]	85.0	0.420	70.9	0.181	95.8	0.056
Total Characterized[5]	7.5	0.037	23.1	0.059	>100	NA
Unextractable (PES) [3]	5.3	0.026	4.9	0.012	6.7	0.004
Accountability[4]	98.4	0.486	103.9	0.265	101.4	0.059

NA = not analyzed, due to low residues present
[1] Total free + conjugated picloram, after hydrolysis, in the neutral extracts
[2] Total free + conjugated picloram, after hydrolysis of the neutral extract, plus both base extracts.
[3] Residues remaining after exhaustive extractions.
[4] Accountability = (Total neutral extractable + Total neutral unextractable)/(TRRs from combustion analysis) * 100 (does not include base extraction).
[5] Total Characterized is extractable residue not associated with picloram, free or conjugated. Equals Total extractable – Total free & conjugated picloram.

Table A.2.2.5.1.1-8: Distribution of the parent and the metabolites in rotational crop matrices when dosed with 14C-labeled picloram

Metabolite Fraction	30D Wheat Straw		60D Wheat Straw (fall)		335D Wheat Straw	
	%TRR	µg eq/g	%TRR	µg eq/g	%TRR	µg eq/g
TRR	100	0.403	100	0.327	100	0.104
80/20 ACN/H_20 ASE Extract (EX1-EX4)	70.3	0.283	76.1	0.249	70.6	0.074
100:1 MeOH/NaOH Extract (BEX/BEXR)	18.6	0.075	16.5	0.054	17.9	0.019
100:1 MeOH/NaOH Extract (BEX2/BEXR2)	3.4	0.014	3.3	0.011	2.8	0.003
Total Extractable	92.3	0.372	95.9	0.314	91.3	0.096
Total analyzed by HPLC (EX1-EX4)	64.3	0.259	72.0	0.235	73.1	0.076
Total picloram[1] (EX1-EX4)	54.7	0.220	38.6	0.126	27.8	0.029
Total analyzed by HPLC (BEX/BEXR)	17.7	0.071	15.5	0.051	16.6	0.017
Total picloram (BEX/BEXR)	15.8	0.064	14.1	0.046	15.9	0.017
Total analyzed by HPLC (BEX2/BEXR2)	2.2	0.009	1.8	0.006	NA	NA
Total picloram (BEX2/BEXR2)	2.2	0.009	1.8	0.006	NA	NA
Total free & conjugated picloram [2]	72.7	0.293	54.5	0.178	43.7	0.045
Total Characterized[5]	19.6	0.079	41.4	0.135	47.6	0.050
Unextractable (PES) [3]	5.9	0.024	7.1	0.023	4.6	0.005
Accountability[4]	100.2	0.404	105.3	0.344	98.9	0.103

NA = not analyzed, due to low residues present

[1] Total free + conjugated picloram, after hydrolysis, in the neutral extracts

[2] Total free + conjugated picloram, after hydrolysis of the neutral extract, plus both base extracts.

[3] Residues remaining after exhaustive extractions.

[4] Accountability = (Total neutral extractable + Total neutral unextractable)/(TRRs from combustion analysis) * 100 (does not include base extraction).

[5] Total Characterized is extractable residue not associated with picloram, free or conjugated. Equals Total extractable – Total free & conjugated picloram.

Table A.2.2.5.1.1-9: Distribution of the parent and the metabolites in rotational crop matrices when dosed with 14C-labeled picloram

Metabolite Fraction	30D Wheat Grain		60D Wheat Grain (fall)		335D Wheat Grain	
	%TRR	µg eq/g	%TRR	µg eq/g	%TRR	µg eq/g
TRR	100	0.126	100	0.054	100	0.020
80/20 ACN/H20 ASE Extract (EX1-EX4)	39.5	0.050	37.4	0.020	34.0	0.007
100:1 MeOH/NaOH Extract (BEX/BEXR)	35.4	0.044	45.7	0.025	41.8	0.008
100:1 MeOH/NaOH Extract (BEX2/BEXR2)	11.2	0.014	6.3	0.003	17.0	0.003
Total Extractable	86.1	0.108	89.4	0.048	92.8	0.018
Total analyzed by HPLC (EX1-EX4)	39.9	0.050	33.0	0.018	28.6	0.006
Total picloram[1] (EX1-EX4)	38.8	0.049	36.3	0.019	31.7	0.006
Total analyzed by HPLC (BEX/BEXR)	33.0	0.041	49.3	0.026	44.6	0.009
Total picloram (BEX/BEXR)	29.4	0.037	49.3	0.026	44.6	0.009
Total analyzed by HPLC (BEX2/BEXR2)	13.0	0.016	NA	NA	NA	NA
Total picloram (BEX2/BEXR2)	11.5	0.014	NA	NA	NA	NA
Total free & conjugated picloram[2]	79.7	0.100	85.6	0.046	76.3	0.015
Total Characterized[5]	6.4	0.008	3.8	0.002	16.5	0.003
Unextractable (PES)[3]	4.6	0.006	7.8	0.004	1.0	0.000
Accountability[4]	94.9	0.119	94.0	0.050	99.4	0.020

NA = not analyzed, due to low residues present

[1] Total free + conjugated picloram, after hydrolysis, in the neutral extracts

[2] Total free + conjugated picloram, after hydrolysis of the neutral extract, plus both base extracts.

[3] Residues remaining after exhaustive extractions.

[4] Accountability = (Total neutral extractable + Total neutral unextractable)/(TRRs from combustion analysis) * 100 (does not include base extraction).

[5] Total Characterized is extractable residue not associated with picloram, free or conjugated. Equals Total extractable – Total free & conjugated picloram.

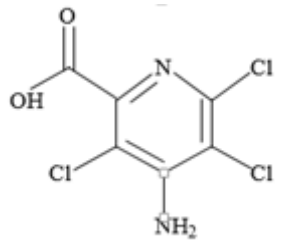
Characterization and Identification of Residues

The neutral organic extracts (not hydrolysed) contained a major component eluting with picloram, plus several peaks eluting near picloram. The major component in the hydrolysed samples was identified as free picloram, by retention time match to the reference standard run co-currently with the samples. Therefore, nearly all of the residues in the neutral extract were characterized as picloram and conjugates of picloram. The identity of picloram was confirmed by LC-MS/MS.

Metabolite Identification

Picloram was identified in the neutral and hydrolysed neutral extracts of 60D- radish tops and wheat hay base extracted tissue based on retention time match to the standard. The conjugated picloram metabolites were not identified.

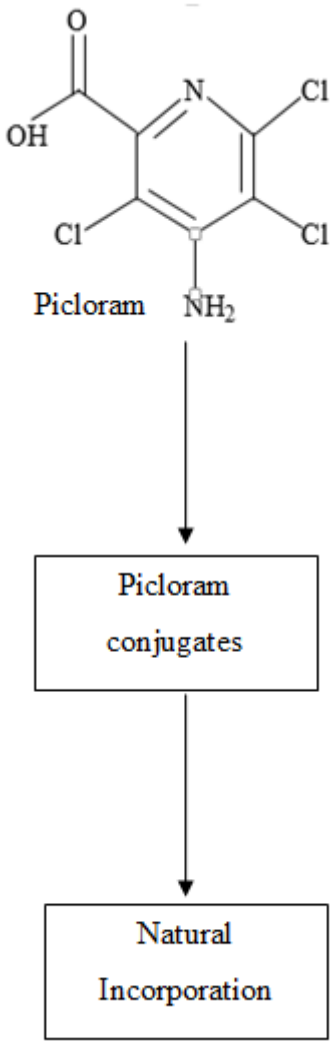
Table A.2.2.5.1.1-10: Identification of compounds from rotational crop study

Common name/code number	Chemical name	Chemical structure
Picloram	4-amino-3,5,6-trichloro-2-pyridinecarboxylic acid	

Metabolic Pathway

The metabolism of picloram is mainly through formation of conjugates. In addition, the ^{14}C-picloram levels (free plus conjugated) in the current CRC were similar to those observed in the previous study when the application rate was normalized to a 1N rate.

Figure A.2.2.5.1.1-2: Proposed metabolic pathway of test item in rotational crops



Storage Stability

Storage stability data for sample tissues is provided below. Extracts were analyzed immediately, and storage stability is neither applicable nor required. All samples and extracts were stored frozen at approximately -10 to -30 °C when not in use. Initial extractions of all samples occurred within approximately 23-128 days after harvest. HPLC analysis for % TRR determination was completed within 20 weeks of sample harvest. Wheat hay samples were re-analyzed within 22 weeks to confirm values. This demonstrated stability of the tissue under the frozen storage conditions for the storage interval.

Table A.2.2.5.1.1-11: Summary of storage stability

Matrix	Storage temp. (°C)	Actual Study Duration (days)	Interval of Demonstrated Storage Stability (days)
Tissues	-10 to -30	135-152	152
Extracts	-10 to -30	NA	NA

(T) = Tissues (E) = Extracts

CONCLUSION

Total residues in all crops were highest at the 30 DAT plant-back intervals and were substantially lower at 60 and 335 DAT. In general, residues were higher in wheat hay and straw than in other crops from the same plant-back interval.

The majority of the residue, generally >70% of the TRR was characterized as picloram or conjugates of picloram. Individual conjugates were not identified.

By the 335-day Plant-Back Interval, total free plus conjugated picloram residues in all human-consumed crops were ≤0.015 mg/kg. Residues in animal feed commodities were also low.

A 2.2.6 Other/Special Studies

Not required for the characterization of the product.

A 2.3 Aminopyralid

A 2.3.1 Stability of residues

~~Not required for the characterization of the product.~~

A 2.3.1.1 Stability of residues during storage of samples

A 2.3.1.1.1 Storage stability of residues in plant products

A 2.3.1.1.1.1 Residue Stability Study in Crops under Frozen Storage Conditions - Study 110634

Comments of zRMS:	A storage stability study was conducted with aminopyralid (XDE-750) in grain, forage and oil of rape to determine the stability of the residue while stored frozen for up to approximately 25 months using analytical method described on GRM 07.07 report. An analytical method GRM 07.07 using LCMS/MS and its ILV have been fully validated for the determination of aminopyralid and its conjugates in fatty products (as rape seed) with LOQ = 0.01 mg/kg. According to the OECD 506 samples should be spiked at 10x the limit of quantitation (LOQ) of the method for each analyte in order to adequately determine the stability of the residues under storage conditions and duplicate samples of every commodity at each time point for all components of the residue definitions need to be analysed. In this study triplicate storage stability samples were analysed. Oil seed rape fractions (oil, forage and seed) were fortified with aminopyralid at 0.10 µg/g. The averaged values for triplicate storage stability samples analysed were 103%, 102% and 99% for rape seed, forage and oil respectively once corrected for concurrent recoveries. No significant decline in concentration was observed over the course of 25 months. zRMS-Poland agrees with zRMS – France conclusions presented below: "*No data concerning samples freezing (within 24 hours after collection) are available in the study.* *Residue amount in stored samples were corrected with recovery rate of freshly fortified samples. Nevertheless, raw data of residue amount uncorrected was also presented in the study.* *Recovery rate of stored samples were calculated compared to fortification level of 0.1 mg/kg but not calculated compared to residue levels for storage time T0.* *Nevertheless, these are minor deficiencies and FR considers this study as valid."* The results of the study indicate that residues of aminopyralid are stable in fractions of oil seed rape for at least 769 days when stored at approximately -20°C. The study is acceptable.

Reference:	KCP 8.1.1 (KCA 6.1)
Report	Frozen Storage Stability of Aminopyralid (XDE-750) in Rape Forage, Seed and Oil. Machado, G.B.; 2013. DAS Report No.: 110634
Guideline(s):	EPA OPPTS 860.1380, Amending Council Directive 91/414/EEC, EC Commission Directive 96/68/EC and 7032/VI/95 ver. 5.
Deviations:	- The r-square value for 11 months' time point analysis does not meet the values described on SOP. - Missing data for oil samples at 18 months' time point.
GLP:	Yes
Acceptability:	Yes

A storage stability study has been conducted with aminopyralid in rape forage, seed and oil matrices to determine the stability of the residues while stored frozen. The stability of the compounds was investigated for at least twenty-five months. All samples were weighed into individual high density polyethylene (HDPE) containers, fortified at 0.10 µg/g and stored in a temperature-monitored freezer at approximately -20 °C. Samples were analysed at 0 days, 34 days, 59 days (61 days for oil samples), 183 days, 335 days, 560 days (rape forage and seed only) and 769 days of frozen storage after fortification. Analysis data shows that residues of aminopyralid are stable for at least 25 months in oil seed rape fractions stored under frozen conditions.

Materials and method

Residues of aminopyralid were measured using analytical method GRM 07.07. Residues of aminopyralid were extracted from rape seed and forage by homogenising and shaking with 0.1 N sodium hydroxide. Oil matrices were extracted by shaking with acetone and evaporating an aliquot to dryness. A liquid/liquid extraction with water and hexane then took place and the aminopyralid was partitioned into the water layer. Any base-labile conjugates were hydrolysed to yield free aminopyralid by adding sodium hydroxide solution.

An aliquot of the crop or oil extracts were then acidified with hydrochloric acid and the solution heated at 80 °C for 90 minutes. During this acidic hydrolysis, bound residues of aminopyralid were further solubilised and acid-labile residues were hydrolysed to yield free aminopyralid. The sample was purified using a mixed-mode polymeric anion exchange solid-phase extraction (SPE) plate.

After elution from the SPE plate with an ethyl acetate/trifluoroacetic acid (99:1) solution, a stable-isotope labelled internal standard ($^{13}C_2$ $^{2}H^{15}N$-aminopyralid) was added, and the eluate is then evaporated to dryness. The residue was reconstituted in an acetonitrile/pyridine/1-butanol (22:2:1) solution, and derivatised with butyl chloroformate to form the 1-butyl esters (1-BE) of the analyte and internal standard. After derivatisation, the mixture was diluted with a methanol/water (40:60) with 0.05% formic acid and 5 mM ammonium formate solution and then analysed by liquid chromatography with positive-ion electrospray tandem mass spectrometry (LC/MS/MS).

Chromatographic analysis was performed using a Zorbax Stable Bond C8, 75 x 4.6 mm, 3.5-µm column coupled to an Agilent liquid chromatographic system and an MDS/SCIEX API 4000 LC/MS/MS system.

Results

The efficiency of the analytical method was determined at the time of analysis of each sampling event by creating three concurrent recovery samples and analysing them according to the method as described above. For all matrices the average recovery of the concurrent recoveries fortified with 0.10 µg/g of aminopyralid was 83% with a standard deviation of 10%.

Based upon the results obtained from the analysis of the concurrent recoveries, it was determined that the analytical method was acceptable for the determination of aminopyralid in oil seed rape fractions.

The averaged values for triplicate storage stability samples analysed were 103%, 102% and 99% for rape seed, forage and oil respectively once corrected for concurrent recoveries. No significant decline in concentration was observed over the course of 25 months.

In addition to a reagent blank, each sampling event contained a control, three concurrent recoveries and a total of three stability samples per matrix.

Table A.2.3.1.1.1.1-1: Concurrent recoveries of Aminopyralid.

Matrix	Sampling event (day)	Amount fortified (µg/g)	Amount found (µg/g)	Recovery	Average recovery (SD)
				(%)	

rape seed	0 0 0 36 36 36 59 59 59 183 183 183 335 335 335 560 560 560 769 769 769	0.10	0.0942 0.0846 0.0951 0.0759 0.0748 0.0734 0.0863 0.0799 0.0820 0.0881 0.0901 0.0983 0.0786 0.0767 0.0769 0.0844 0.0753 0.0719 0.0749 0.0766 0.0750	94 85 95 76 75 73 86 80 82 88 90 98 79 77 77 84 75 72 75 77 75	82 (8)
rape forage	0 0 0 36 36 36 59 59 59 183 183 183 335 335 335 560 560 560 769 769 769	0.10	0.0806 0.0814 0.0745 0.0800 0.0779 0.0804 0.0836 0.0727 0.0822 0.0879 0.0812 0.0817 0.0842 0.0860 0.0853 0.0962 0.0886 0.0869 0.0708 0.0720 0.0726	81 81 75 80 78 80 84 73 82 88 81 82 84 86 85 96 89 87 71 72 73	81 (6)
rape seed oil	0 0 0 36 36 36 61 61 61 183 183 183 335 335 335 769 769 769	0.10	0.0846 0.0833 0.0814 0.0928 0.0882 0.0781 0.1074 0.1080 0.9890 0.1142 0.1007 0.0813 0.0813 0.0835 0.0817 0.0729 0.0746 0.0702	85 83 81 93 88 78 107 108 99 114 101 81 81 83 82 73 75 70	88 (13)

Table A.2.3.1.1.1.1-2: Results of Frozen Storage Stability for Aminopyralid Residues

Matrix	Days of frozen storage	Spike level (µg/g)	Uncorrected found (µg/g)	Corrected found (µg/g)	Corrected found average (µg/g)	% Remaining (corrected)	% Remaining average
Rape seed	0	0.10	0.0890	0.0974	0.0962	97	96
	0		0.0900	0.0986		99	
	0		0.0846	0.0926		93	
	36		0.0834	0.1116	0.1064	112	106
	36		0.0745	0.0998		100	
	36		0.0804	0.1077		108	
	59		0.0868	0.1050	0.1060	105	106
	59		0.0896	0.1084		108	
	59		0.0864	0.1046		105	
	183		0.0931	0.1012	0.1053	101	105
	183		0.0958	0.1041		104	
	183		0.1018	0.1107		111	
	335		0.0717	0.0926	0.1006	93	101
	335		0.0748	0.0967		97	
	335		0.0873	0.1127		113	
	560		0.0906	0.1173	0.1047	117	105
	560		0.0613	0.0794		79	
	560		0.0907	0.1174		117	
	769		0.0800	0.1060	0.1052	106	105
	769		0.0802	0.1062		106	
	769		0.0781	0.1035		103	
rape forage	0	0.10	0.0822	0.0975	0.0983	98	98
	0		0.0770	0.0954		95	
	0		0.0754	0.1021		102	
	36		0.0845	0.1065	0.1031	106	103
	36		0.0811	0.1023		102	
	36		0.0798	0.1005		101	
	59		0.0809	0.1016	0.1013	102	101
	59		0.0825	0.1035		104	
	59		0.0788	0.0989		99	
	183		0.0980	0.1172	0.1093	117	109
	183		0.0904	0.1080		108	
	183		0.0859	0.1027		103	
	335		0.0858	0.1007	0.1001	101	100
	335		0.0844	0.0991		99	
	335		0.0856	0.1004		100	
	560		0.0908	0.1003	0.0988	100	99
	560		0.0882	0.0973		97	
	560		0.0895	0.0989		99	
	769		0.0735	0.1024	0.1006	102	101
	769		0.0716	0.0998		100	
	769		0.0715	0.0996		100	
Rape seed oil	0	0.10	0.0782	0.1019	0.1001	102	100
	0		0.0865	0.1004		100	
	0		0.0883	0.0981		98	
	36		0.0833	0.0965	0.1000	96	100
	36		0.0903	0.1046		105	
	36		0.0853	0.0988		99	
	61		0.1096	0.1047	0.1012	105	101
	61		0.1136	0.1086		109	
	61		0.0945	0.0903		90	
	183		0.1064	0.0990	0.0932	99	93
	183		0.1009	0.0938		94	
	183		0.0934	0.0869		87	
	335		0.0879	0.1069	0.1045	107	104
	335		0.0864	0.1051		105	
	335		0.0834	0.1014		101	
	769		0.0727	0.1002	0.0965	100	96
	769		0.0676	0.0931		93	
	769		0.0698	0.0961		96	

Conclusion

Residues of aminopyralid were stable in rape seed, rape forage, and rape seed oil months and were found

to be stable for at least 769 days following storage at ≤ -18°C.

zRMS Conclusion (France, ANSES)
No data concerning samples freezing (within 24 hours after collection) are available in the study.
Residue amount in stored samples were corrected with recovery rate of freshly fortified samples. Nevertheless, raw data of residue amount uncorrected was also presented in the study.
Recovery rate of stored samples were calculated compared to fortification level of 0.1 mg/kg but not calculated compared to residue levels for storage time T0.
Nevertheless, these are minor deficiencies and FR considers this study as valid.

A 2.3.1.1.1.2 Study S08-02908

Comments of zRMS:	A deep-freezer storage stability study was conducted with aminopyralid in five different beer processing matrices. For this purpose control (untreated) samples of barley grain, malt sprouts, spent grains, yeast and beer were fortified with 0.10 mg/kg of the test substance and stored at ≤ -18 °C over a period of six months. On day 0 six freshly fortified specimens of each matrix were analysed for residues of aminopyralid. On each of the projected sampling timings, i.e. at 3 and 6 months, three stored fortified specimens, three freshly fortified specimens as well as one untreated control specimen were analysed. Analysis was performed using the extraction procedure and LC-MS/MS detection. The analytical method was previously validated at Eurofins | Dr. Specht GLP GmbH under study no. GAB-0871. Samples were analysed for aminopyralid and its conjugates, determined as aminopyralid. Mean recoveries for each of the testing points were all in the range between 70 and 110% with relative standard deviations ≤ 20%. Study meets the OECD guideline 506 requirements. Residues of aminopyralid were stable in barley grain, malt sprouts, spent grains, yeast and beer for 6 months following storage at ≤ -18°C. The study is acceptable.

Reference:	KCP 8.1.1/1
Report	Storage stability study for residues of Aminopyralid in barley grain, malt sprouts, spent grains, yeast and beer, Lindner, M., 2014, S08-02908 (GAB-0872).
Guideline(s):	Yes (EU Directive 91/414/EEC as amended by 96/46/EC, EU guidance document 7032/VI/95 rev. 5, 22/07/1997, Appendix H of EC document 1607/VI/97, rev.2, OECD guideline 506, adopted 16-Oct-2007, for the testing of chemicals; stability in pesticide residues in stored commodities and EPA residue chemistry test guideline OPPTS 860.1380, Aug-1996).
Deviations:	No
GLP:	Yes
Acceptability:	Yes

Materials and methods
Samples of barley grain, malt sprouts, spent grains, yeast and beer were fortified with aminopyralid at 0.1 mg/kg and stored in a freezer at ≤ -18°C. Samples were analysed immediately after fortification with aminopyralid (without storage) and after 3- and 6-months storage for all five matrices.

All the samples were analysed for aminopyralid and its conjugates, determined as aminopyralid. The samples were extracted with 0.1 N sodium hydroxide, during which any bound residue and base labile conjugates were hydrolysed to yield free aminopyralid. An aliquot of each extract was then acidified with hydrochloric acid prior to incubation at 80°C for 90 minutes. During the acid hydrolysis, bound residues of

aminopyralid were further solubilised and any acid labile conjugates hydrolysed to free aminopyralid. Each sample was then purified using mixed mode polymeric anion-exchange solid phase extraction. After elution from the SPE cartridge with an ethyl acetate/trifluoroacetic acid (99:1) solution, a stable-isotope labelled internal standard ($^{13}C_{22}H_{15}N$-aminopyralid) was added and the eluate was then evaporated to dryness. The residue was reconstituted in an acetonitrile/pyridine/1-butanol (22:2:1) solution, and derivatised with butyl chloroformate to form the 1-butyl ester of the analyte and internal standard prior to quantification by LC MS/MS.

Results and discussions

Residues of aminopyralid were stable in barley grain, malt sprouts, spent grains, yeast and beer for 6 months following storage at ≤ -18°C.

Table A.2.3.1.1.1.2-1: Summary of concurrent recoveries of aminopyralid from barley processing commodities.

Matrix	Spike level (mg/kg)	Storage Interval (days)	Sample size (n)	Individual procedural recoveries (%)	Mean ± std dev
Aminopyralid					
Barley grain	0.1	0	6	93, 102, 101, 103, 102, 107	101
	0.1	90	3	106, 100, 89	98
	0.1	180	3	84, 92, 99	92
Malt sprouts	0.1	0	6	87, 83, 85, 86, 87, 86	86
	0.1	89	3	74, 76, 70	73
	0.1	179	3	65, 85, 93	81
Spent grains	0.1	0	6	94, 93, 98, 89, 83, 84	90
	0.1	89	3	91, 105, 96	99
	0.1	180	3	87, 102, 101	97
Yeast	0.1	0	6	97, 86, 96, 100, 94, 97	95
	0.1	84	3	100, 109, 96	102
	0.1	175	3	101, 113, 107	107
Beer	0.1	0	6	84, 85, 93, 100, 105, 106	96
	0.1	84	3	105, 102, 103	103
	0.1	175	3	104, 122, 102	109

Table A.2.3.1.1.1.2-1: Stability of aminopyralid residues in barley processing commodities following storage at ≤ -18°C.

Matrix	Spike level (mg/kg)	Storage interval (days)	Individual recovered residues (mg/kg)	Individual recoveries (%)
Aminopyralid				
Barley grain	0.1	0	0.094, 0.103, 0.102, 0.104, 0.103, 0.108	93, 102, 101, 103, 102, 107
	0.1	90	0.089, 0.090, 0.107	90, 90, 108
	0.1	180	0.103, 0.088, 0.071	103, 88, 71
Malt sprouts	0.1	0	0.090, 0.086, 0.088, 0.089, 0.090, 0.089	87, 83, 85, 86, 87, 86
	0.1	89	0.072, 0.081, 0.083	68, 77, 79
	0.1	179	0.082, 0.073, 0.068	83, 74, 68
Spent grains	0.1	0	0.095, 0.094, 0.099, 0.091, 0.085, 0.085	94, 93, 98, 89, 83, 84
	0.1	89	0.099, 0.113, 0.107	101, 114, 109
	0.1	180	0.116, 0.099, 0.094	118, 101, 96

Matrix	Spike level (mg/kg)	Storage interval (days)	Individual recovered residues (mg/kg)	Individual recoveries (%)
Yeast	0.1	0	0.099, 0.089, 0.099, 0.102, 0.096, 0.099	97, 86, 96, 100, 94, 97
	0.1	84	0.113, 0.110, 0.106	112, 109, 105
	0.1	175	0.099, 0.109, 0.108	101, 111, 110
Beer	0.1	0	0.086, 0.086, 0.095, 0.101, 0.107, 0.108	84, 85, 93, 100, 105, 106
	0.1	84	0.101, 0.104, 0.103	101, 104, 102
	0.1	175	0.068, 0.096, 0.101	71, 99, 104

Conclusion
Residues of aminopyralid were stable in barley grain, malt sprouts, spent grains, yeast and beer for 6 months following storage at ≤ -18°C.

A 2.3.2 Nature of residues in plants, livestock and processed commodities

Not required for the characterization of the product.

A 2.3.3 Stability of residues

Not required for the characterization of the product.

A 2.3.4 Nature of residues in plants, livestock and processed commodities

Not required for the characterization of the product.

Appendix 3 Pesticide Residue Intake Model (PRIMo)

A 3.1 TMDI calculations

European Food Safety Authority

EFSA PRIMo revision 3.1; 2019/03/19

Halauxifen-methyl (sum of halauxifen-methyl and X11393729 (halauxifen), expressed as halauxifen-

LOQs (mg/kg) range from:	0.02	to:	0.10
Toxicological reference values			
ADI (mg/kg bw/day):	0.058	ARfD (mg/kg bw):	0.058
Source of ADI:	EFSA	Source of ARfD:	EFSA
Year of evaluation:	2014	Year of evaluation:	2014

Input values

Details - chronic risk assessment

Supplementary results - chronic risk assessment

Details - acute risk assessment/children

Details - acute risk assessment/adults

Comments:

Normal mode

Chronic risk assessment: JMPR methodology (IEDI/TMDI)

No of diets exceeding the ADI : ---

TMDI/NEDI/IEDI calculation (based on average food consumption)

Calculated exposure (% of ADI)	MS Diet	Expsoure (µg/kg bw per day)	Highest contributor to MS diet (in % of ADI)	Commodity / group of commodities	2nd contributor to MS diet (in % of ADI)	Commodity / group of commodities	3rd contributor to MS diet (in % of ADI)	Commodity / group of commodities	Exposure resulting from MRLs set at the LOQ (in % of ADI)	Exposure resulting from commodities not under assessment (in % of ADI)
4%	NL toddler	2.58	2%	Milk: Cattle	0.4%	Apples	0.2%	Maize/corn	4%	0.2%
2%	NL child	1.41	0.8%	Milk: Cattle	0.3%	Sugar beet roots	0.2%	Apples	2%	0.1%
2%	DE child	1.28	0.7%	Milk: Cattle	0.4%	Apples	0.1%	Wheat	2%	0.2%
2%	UK infant	1.22	1%	Milk: Cattle	0.1%	Potatoes	0.1%	Wheat	2%	0.1%
2%	FR toddler 2 3 yr	1.13	1%	Milk: Cattle	0.1%	Apples	0.1%	Wheat	2%	0.1%
2%	FR child 3 15 yr	1.13	0.8%	Milk: Cattle	0.2%	Wheat	0.1%	Sugar beet roots	2%	0.2%
2%	GEMS/Food G11	0.98	0.3%	Soyabeans	0.3%	Milk: Cattle	0.1%	Potatoes	2%	0.1%
2%	UK toddler	0.90	0.7%	Milk: Cattle	0.1%	Wheat	0.1%	Potatoes	2%	0.1%
2%	GEMS/Food G10	0.88	0.3%	Soyabeans	0.2%	Milk: Cattle	0.1%	Wheat	2%	0.1%
2%	GEMS/Food G08	0.88	0.2%	Milk: Cattle	0.2%	Soyabeans	0.1%	Wheat	2%	0.2%
2%	GEMS/Food G07	0.88	0.2%	Milk: Cattle	0.2%	Soyabeans	0.1%	Wheat	2%	0.1%
1%	GEMS/Food G15	0.85	0.2%	Milk: Cattle	0.2%	Wheat	0.1%	Soyabeans	1%	0.2%
1%	GEMS/Food G06	0.84	0.2%	Wheat	0.1%	Tomatoes	0.1%	Soyabeans	1%	0.3%
1%	DK child	0.82	0.4%	Milk: Cattle	0.2%	Rye	0.2%	Wheat	1%	0.3%
1%	ES child	0.78	0.4%	Milk: Cattle	0.2%	Wheat	0.1%	Cocoa beans	1%	0.2%
1%	RO general	0.78	0.4%	Milk: Cattle	0.2%	Wheat	0.1%	Potatoes	1%	0.2%
1%	DE women 14-50 yr	0.75	0.4%	Milk: Cattle	0.2%	Sugar beet roots	0.1%	Apples	1%	0.1%
1%	SE general	0.75	0.4%	Milk: Cattle	0.2%	Bovine: Muscle/meat	0.1%	Potatoes	1%	0.1%
1%	DE general	0.73	0.4%	Milk: Cattle	0.1%	Sugar beet roots	0.1%	Apples	1%	0.1%
1%	FI adult	0.71	1.0%	Coffee beans	0.0%	Potatoes	0.0%	Rye	1%	0.0%
1%	IE adult	0.69	0.2%	Milk: Cattle	0.1%	Sweet potatoes	0.1%	Wheat	1%	0.1%
1%	NL general	0.65	0.3%	Milk: Cattle	0.1%	Sugar beet roots	0.1%	Potatoes	1%	0.1%
1%	FR infant	0.59	0.6%	Milk: Cattle	0.1%	Potatoes	0.1%	Apples	1%	0.0%
0.8%	FR adult	0.45	0.2%	Milk: Cattle	0.1%	Wine grapes	0.1%	Wheat	0.8%	0.1%
0.8%	PT general	0.44	0.2%	Potatoes	0.1%	Wheat	0.1%	Wine grapes	0.8%	0.1%
0.7%	ES adult	0.43	0.2%	Milk: Cattle	0.1%	Wheat	0.0%	Oranges	0.7%	0.1%
0.6%	FI 3 yr	0.36	0.2%	Potatoes	0.0%	Bananas	0.0%	Wheat	0.6%	0.1%
0.6%	IT toddler	0.33	0.2%	Wheat	0.1%	Other cereals	0.0%	Tomatoes	0.6%	0.2%
0.6%	DK adult	0.33	0.2%	Milk: Cattle	0.0%	Potatoes	0.0%	Wheat	0.6%	0.1%
0.6%	LT adult	0.33	0.1%	Milk: Cattle	0.1%	Potatoes	0.1%	Apples	0.6%	0.1%
0.5%	UK vegetarian	0.30	0.1%	Milk: Cattle	0.1%	Wheat	0.0%	Potatoes	0.5%	0.1%
0.5%	FI 6 yr	0.29	0.1%	Potatoes	0.0%	Cocoa beans	0.0%	Wheat	0.5%	0.1%
0.5%	UK adult	0.28	0.1%	Milk: Cattle	0.1%	Wheat	0.0%	Potatoes	0.5%	0.1%
0.4%	IT adult	0.25	0.1%	Wheat	0.0%	Tomatoes	0.0%	Apples	0.4%	0.1%
0.3%	PL general	0.20	0.1%	Potatoes	0.1%	Apples	0.0%	Tomatoes	0.3%	
0.3%	IE child	0.16	0.1%	Milk: Cattle	0.0%	Wheat	0.0%	Potatoes	0.3%	0.0%

Conclusion:
The estimated long-term dietary intake (TMDI/NEDI/IEDI) was below the ADI.
The long-term intake of residues of Halauxifen-methyl (sum of halauxifen-methyl and X11393729 (halauxifen), expressed as halauxifen-methyl) is unlikely to present a public health concern.

European Food Safety Authority

EFSA PRIMo revision 3.1; 2019/03/19

Picloram

LOQs (mg/kg) range from:	0.01	to:	0.05
Toxicological reference values			
ADI (mg/kg bw/day):	0.3	ARfD (mg/kg bw):	0.3
Source of ADI:	EU Final Review	Source of ARfD:	EU Final Review Report
Year of evaluation:	2018	Year of evaluation:	2018

Input values

Details - chronic risk assessment

Supplementary results - chronic risk assessment

Details - acute risk assessment/children

Details - acute risk assessment/adults

Comments:

Normal mode

Chronic risk assessment: JMPR methodology (IEDI/TMDI)

No of diets exceeding the ADI : ---

TMDI/NEDI/IEDI calculation (based on average food consumption)

Calculated exposure (% of ADI)	MS Diet	Expsoure (µg/kg bw per day)	Highest contributor to MS diet (in % of ADI)	Commodity / group of commodities	2nd contributor to MS diet (in % of ADI)	Commodity / group of commodities	3rd contributor to MS diet (in % of ADI)	Commodity / group of commodities	Exposure resulting from MRLs set at the LOQ (in % of ADI)	Exposure resulting from commodities not under assessment (in % of ADI)
2%	NL toddler	6.27	1.0%	Milk: Cattle	0.5%	Maize/corn	0.3%	Wheat	1%	0.0%
1%	UK infant	3.40	0.6%	Milk: Cattle	0.2%	Wheat	0.1%	Bovine: Muscle/meat	0.7%	
1%	FR child 3 15 yr	3.19	0.4%	Milk: Cattle	0.3%	Wheat	0.1%	Bovine: Muscle/meat	0.5%	0.0%
1%	NL child	3.00	0.4%	Milk: Cattle	0.3%	Wheat	0.1%	Swine: Muscle/meat	0.5%	0.0%
1.0%	FR toddler 2 3 yr	2.90	0.5%	Milk: Cattle	0.2%	Wheat	0.1%	Bovine: Muscle/meat	0.6%	0.0%
0.9%	DK child	2.62	0.3%	Wheat	0.2%	Milk: Cattle	0.1%	Swine: Muscle/meat	0.3%	0.0%
0.9%	DE child	2.59	0.3%	Milk: Cattle	0.3%	Wheat	0.0%	Poultry: Muscle/meat	0.4%	0.0%
0.9%	ES child	2.57	0.3%	Wheat	0.2%	Milk: Cattle	0.1%	Bovine: Muscle/meat	0.3%	
0.8%	UK toddler	2.44	0.3%	Milk: Cattle	0.3%	Wheat	0.1%	Bovine: Muscle/meat	0.4%	
0.8%	RO general	2.43	0.3%	Wheat	0.2%	Milk: Cattle	0.1%	Swine: Muscle/meat	0.3%	
0.8%	GEMS/Food G15	2.42	0.3%	Wheat	0.1%	Milk: Cattle	0.1%	Swine: Muscle/meat	0.2%	0.0%
0.8%	GEMS/Food G06	2.41	0.5%	Wheat	0.1%	Maize/corn	0.0%	Milk: Cattle	0.1%	0.0%
0.8%	GEMS/Food G07	2.38	0.3%	Wheat	0.1%	Milk: Cattle	0.1%	Poultry: Muscle/meat	0.2%	0.0%
0.8%	GEMS/Food G08	2.35	0.3%	Wheat	0.1%	Swine: Muscle/meat	0.1%	Milk: Cattle	0.2%	0.0%
0.8%	SE general	2.31	0.3%	Bovine: Muscle/meat	0.2%	Wheat	0.2%	Milk: Cattle	0.3%	
0.8%	GEMS/Food G10	2.27	0.3%	Wheat	0.1%	Poultry: Muscle/meat	0.1%	Milk: Cattle	0.2%	0.0%
0.7%	GEMS/Food G11	2.22	0.2%	Wheat	0.1%	Milk: Cattle	0.1%	Swine: Muscle/meat	0.2%	
0.6%	IT toddler	1.72	0.4%	Wheat	0.1%	Other cereals	0.0%	Tomatoes	0.0%	
0.6%	DE general	1.67	0.2%	Milk: Cattle	0.1%	Wheat	0.1%	Swine: Muscle/meat	0.3%	0.0%
0.5%	DE women 14-50 yr	1.62	0.2%	Milk: Cattle	0.1%	Wheat	0.1%	Swine: Muscle/meat	0.3%	0.0%
0.5%	NL general	1.48	0.1%	Milk: Cattle	0.1%	Wheat	0.1%	Swine: Muscle/meat	0.2%	0.0%
0.5%	ES adult	1.41	0.2%	Wheat	0.1%	Milk: Cattle	0.0%	Bovine: Muscle/meat	0.1%	
0.5%	IE adult	1.41	0.2%	Wheat	0.1%	Milk: Cattle	0.0%	Bovine: Muscle/meat	0.2%	
0.4%	FR infant	1.30	0.3%	Milk: Cattle	0.1%	Wheat	0.0%	Swine: Muscle/meat	0.3%	0.0%
0.4%	FR adult	1.18	0.1%	Wheat	0.1%	Milk: Cattle	0.0%	Swine: Muscle/meat	0.1%	0.0%
0.4%	PT general	1.05	0.3%	Wheat	0.0%	Maize/corn	0.0%	Potatoes	0.1%	
0.3%	IT adult	1.05	0.3%	Wheat	0.0%	Other cereals	0.0%	Tomatoes	0.0%	
0.3%	DK adult	0.93	0.1%	Milk: Cattle	0.1%	Wheat	0.1%	Swine: Muscle/meat	0.1%	
0.3%	LT adult	0.84	0.1%	Wheat	0.1%	Milk: Cattle	0.1%	Swine: Muscle/meat	0.1%	
0.3%	UK adult	0.81	0.1%	Wheat	0.0%	Milk: Cattle	0.0%	Bovine: Muscle/meat	0.1%	
0.2%	UK vegetarian	0.69	0.1%	Wheat	0.1%	Milk: Cattle	0.0%	Potatoes	0.1%	
0.2%	FI 3 yr	0.52	0.1%	Wheat	0.0%	Oat	0.0%	Potatoes	0.0%	0.0%
0.2%	IE child	0.52	0.1%	Wheat	0.1%	Milk: Cattle	0.0%	Swine: Muscle/meat	0.1%	
0.1%	FI 6 yr	0.39	0.1%	Wheat	0.0%	Oat	0.0%	Potatoes	0.0%	0.0%
0.1%	FI adult	0.22	0.0%	Wheat	0.0%	Coffee beans	0.0%	Oat	0.0%	0.0%
0.0%	PL general	0.10	0.0%	Potatoes	0.0%	Apples	0.0%	Tomatoes	0.0%	

Conclusion:
The estimated long-term dietary intake (TMDI/NEDI/IEDI) was below the ADI.
The long-term intake of residues of Picloram is unlikely to present a public health concern.

European Food Safety Authority

EFSA PRIMo revision 3.1; 2019/03/19

Aminopyralid

LOQs (mg/kg) range from:	0.01	to:	0.05
Toxicological reference values			
ADI (mg/kg bw/day):	0.26	ARfD (mg/kg bw):	0.26
Source of ADI:	EFSA Journal	Source of ARfD:	EFSA Journal
Year of evaluation:	2013; 11(9):3352	Year of evaluation:	'2013; 11(9):3352

Input values

Details - chronic risk assessment

Supplementary results - chronic risk assessment

Details - acute risk assessment/children

Details - acute risk assessment/adults

Comments:

Normal mode

Chronic risk assessment: JMPR methodology (IEDI/TMDI)

No of diets exceeding the ADI : ---

TMDI/NEDI/IEDI calculation (based on average food consumption)

Calculated exposure (% of ADI)	MS Diet	Expsoure (µg/kg bw per day)	Highest contributor to MS diet (in % of ADI)	Commodity / group of commodities	2nd contributor to MS diet (in % of ADI)	Commodity / group of commodities	3rd contributor to MS diet (in % of ADI)	Commodity / group of commodities	Exposure resulting from MRLs set at the LOQ (in % of ADI)	Exposure resulting from commodities not under assessment (in % of ADI)
1%	NL toddler	2.88	0.5%	Milk: Cattle	0.2%	Wheat	0.1%	Maize/corn	0.2%	0.0%
0.8%	DK child	2.09	0.3%	Rye	0.2%	Wheat	0.1%	Milk: Cattle	0.1%	0.0%
0.6%	UK infant	1.63	0.3%	Milk: Cattle	0.1%	Wheat	0.1%	Bovine: Edible offals (other than liver	0.1%	
0.6%	NL child	1.62	0.2%	Milk: Cattle	0.2%	Wheat	0.0%	Swine: Muscle/meat	0.2%	0.0%
0.6%	FR child 3 15 yr	1.61	0.2%	Wheat	0.2%	Milk: Cattle	0.1%	Bovine: Muscle/meat	0.1%	0.0%
0.6%	DE child	1.46	0.2%	Wheat	0.2%	Milk: Cattle	0.0%	Apples	0.2%	0.0%
0.6%	GEMS/Food G08	1.44	0.2%	Wheat	0.1%	Swine: Muscle/meat	0.1%	Barley	0.1%	0.0%
0.5%	FR toddler 2 3 yr	1.41	0.2%	Milk: Cattle	0.1%	Wheat	0.0%	Bovine: Muscle/meat	0.1%	0.0%
0.5%	GEMS/Food G15	1.37	0.2%	Wheat	0.1%	Swine: Muscle/meat	0.1%	Milk: Cattle	0.1%	0.0%
0.5%	GEMS/Food G11	1.35	0.1%	Wheat	0.1%	Soyabeans	0.1%	Milk: Cattle	0.2%	
0.5%	GEMS/Food G07	1.31	0.2%	Wheat	0.0%	Milk: Cattle	0.0%	Swine: Muscle/meat	0.1%	0.0%
0.5%	GEMS/Food G06	1.30	0.3%	Wheat	0.0%	Maize/corn	0.0%	Soyabeans	0.1%	0.0%
0.5%	GEMS/Food G10	1.28	0.2%	Wheat	0.1%	Soyabeans	0.0%	Milk: Cattle	0.2%	0.0%
0.5%	ES child	1.26	0.2%	Wheat	0.1%	Milk: Cattle	0.1%	Bovine: Muscle/meat	0.1%	
0.5%	SE general	1.23	0.2%	Bovine: Muscle/meat	0.1%	Wheat	0.1%	Milk: Cattle	0.1%	
0.5%	UK toddler	1.23	0.2%	Milk: Cattle	0.2%	Wheat	0.0%	Bovine: Muscle/meat	0.1%	
0.4%	RO general	1.16	0.2%	Wheat	0.1%	Milk: Cattle	0.0%	Swine: Muscle/meat	0.1%	
0.4%	DE general	0.99	0.1%	Milk: Cattle	0.1%	Wheat	0.0%	Swine: Muscle/meat	0.1%	0.0%
0.4%	IE adult	0.95	0.1%	Wheat	0.0%	Sheep: Edible offals (other than liver and k	0.0%	Milk: Cattle	0.1%	
0.4%	DE women 14-50 yr	0.94	0.1%	Milk: Cattle	0.1%	Wheat	0.0%	Swine: Muscle/meat	0.1%	0.0%
0.3%	NL general	0.84	0.1%	Wheat	0.1%	Milk: Cattle	0.0%	Swine: Muscle/meat	0.1%	0.0%
0.3%	IT toddler	0.78	0.3%	Wheat	0.0%	Other cereals	0.0%	Tomatoes	0.0%	
0.3%	ES adult	0.75	0.1%	Wheat	0.0%	Milk: Cattle	0.0%	Bovine: Muscle/meat	0.1%	
0.3%	FR adult	0.68	0.1%	Wheat	0.0%	Milk: Cattle	0.0%	Swine: Muscle/meat	0.1%	0.0%
0.3%	PT general	0.65	0.2%	Wheat	0.0%	Potatoes	0.0%	Wine grapes	0.1%	
0.2%	FR infant	0.61	0.1%	Milk: Cattle	0.0%	Wheat	0.0%	Swine: Muscle/meat	0.0%	0.0%
0.2%	LT adult	0.59	0.1%	Rye	0.0%	Wheat	0.0%	Swine: Muscle/meat	0.0%	
0.2%	DK adult	0.55	0.0%	Wheat	0.0%	Milk: Cattle	0.0%	Swine: Muscle/meat	0.0%	
0.2%	FI adult	0.51	0.1%	Coffee beans	0.0%	Rye	0.0%	Wheat	0.1%	0.0%
0.2%	IT adult	0.50	0.2%	Wheat	0.0%	Tomatoes	0.0%	Apples	0.0%	
0.2%	FI 3 yr	0.48	0.0%	Wheat	0.0%	Rye	0.0%	Oat	0.1%	0.0%
0.2%	UK adult	0.40	0.1%	Wheat	0.0%	Bovine: Muscle/meat	0.0%	Milk: Cattle	0.0%	
0.2%	UK vegetarian	0.40	0.1%	Wheat	0.0%	Milk: Cattle	0.0%	Beans	0.0%	
0.1%	FI 6 yr	0.38	0.0%	Wheat	0.0%	Rye	0.0%	Oat	0.1%	0.0%
0.1%	IE child	0.26	0.0%	Wheat	0.0%	Milk: Cattle	0.0%	Swine: Muscle/meat	0.0%	
0.0%	PL general	0.10	0.0%	Potatoes	0.0%	Apples	0.0%	Tomatoes	0.0%	

Conclusion:
The estimated long-term dietary intake (TMDI/NEDI/IEDI) was below the ADI.
The long-term intake of residues of Aminopyralid is unlikely to present a public health concern.

A 3.2 IEDI calculations

Not applicable since TMDI < 100% of ADI for all active substances

A 3.3 IESTI calculations - Raw commodities

Halauxifen-methyl

Acute risk assessment /children	Acute risk assessment / adults / general population
Details - acute risk assessment /children	Details - acute risk assessment/adults

The acute risk assessment is based on the ARfD.
The calculation is based on the large portion of the most critical consumer group.

Show results for all crops

Unprocessed commodities

Results for children				**Results for adults**			
No. of commodities for which ARfD/ADI is exceeded (IESTI):			---	No. of commodities for which ARfD/ADI is exceeded (IESTI):			---
IESTI				**IESTI**			
Highest % of ARfD/ADI	Commodities	MRL / input for RA (mg/kg)	Exposure (µg/kg bw)	Highest % of ARfD/ADI	Commodities	MRL / input for RA (mg/kg)	Exposure (µg/kg bw)
0.1%	Rapeseeds/canola	0.05 / 0.05	0.07	0.05%	Rapeseeds/canola seeds	0.05 / 0.05	0.03
Expand/collapse list							
Total number of commodities exceeding the ARfD/ADI in children and adult diets (IESTI calculation)							

Picloram

Acute risk assessment /children	Acute risk assessment / adults / general population
Details - acute risk assessment /children	Details - acute risk assessment/adults

The acute risk assessment is based on the ARfD.
The calculation is based on the large portion of the most critical consumer group.

Show results of IESTI calculation only for crops with GAPs under assessment

Unprocessed commodities

Results for children				**Results for adults**			
No. of commodities for which ARfD/ADI is exceeded (IESTI):			---	No. of commodities for which ARfD/ADI is exceeded (IESTI):			---
IESTI				**IESTI**			
Highest % of ARfD/ADI	Commodities	MRL / input for RA (mg/kg)	Exposure (µg/kg bw)	Highest % of ARfD/ADI	Commodities	MRL / input for RA (mg/kg)	Exposure (µg/kg bw)
0.00%	Rapeseeds/canola	0.03 / 0.01	0.01	0.00%	Rapeseeds/canola seeds	0.03 / 0.01	0.01
Expand/collapse list							
Total number of commodities exceeding the ARfD/ADI in children and adult diets (IESTI calculation)							

Aminopyralid

Acute risk assessment /children	Acute risk assessment / adults / general population
Details - acute risk assessment /children	Details - acute risk assessment/adults

The acute risk assessment is based on the ARfD.
The calculation is based on the large portion of the most critical consumer group.

Show results of IESTI calculation only for crops with GAPs under assessment

Unprocessed commodities

Results for children				**Results for adults**			
No. of commodities for which ARfD/ADI is exceeded (IESTI):			---	No. of commodities for which ARfD/ADI is exceeded (IESTI):			---
IESTI				**IESTI**			
Highest % of ARfD/ADI	Commodities	MRL / input for RA (mg/kg)	Exposure (µg/kg bw)	Highest % of ARfD/ADI	Commodities	MRL / input for RA (mg/kg)	Exposure (µg/kg bw)
0.01%	Rapeseeds/canola seeds	0.05 / 0.01	0.01	0.00%	Rapeseeds/canola seeds	0.05 / 0.01	0.01
Expand/collapse list							
Total number of commodities exceeding the ARfD/ADI in children and adult diets (IESTI calculation)							

A 3.4 IESTI calculations - Processed commodities

Halauxifen-methyl

Processed commodities								
	Results for children				**Results for adults**			
	No of processed commodities for which ARfD/ADI is exceeded (IESTI):			---	No of processed commodities for which ARfD/ADI is exceeded (IESTI):			---
	IESTI				**IESTI**			
	Highest % of ARfD/ADI	Processed commodities	MRL / input for RA (mg/kg)	Exposure (µg/kg bw)	Highest % of ARfD/ADI	Processed commodities	MRL / input for RA (mg/kg)	Exposure (µg/kg bw)
	0.1%	Rapeseeds / oils	0.05 / 0.1	0.03	#NUM!	#NUM!	#NUM!	#NUM!
	#NUM!	#NUM!	#NUM!	#NUM!	#NUM!	#NUM!	#NUM!	#NUM!
	Expand/collapse list							

Conclusion:
No exceedance of the toxicological reference value was identified for any unprocessed commodity.
A short term intake of residues of Halauxifen-methyl (sum of halauxifen-methyl and X11393729 (halauxifen), expressed as halauxifen-methyl) is unlikely to
For processed commodities, no exceedance of the ARfD/ADI was identified.

Picloram

Processed commodities	Results for children				Results for adults			
	No of processed commodities for which ARfD/ADI is exceeded (IESTI):			---	No of processed commodities for which ARfD/ADI is exceeded (IESTI):			---
	IESTI				**IESTI**			
	Highest % of ARfD/ADI	Processed commodities	MRL / input for RA (mg/kg)	Exposure (µg/kg bw)	Highest % of ARfD/ADI	Processed commodities	MRL / input for RA (mg/kg)	Exposure (µg/kg bw)
	0.0%	Rapeseeds / oils	0.03 / 0.06	0.02	#NUM!	#NUM!	#NUM!	#NUM!
	#NUM!	#NUM!	#NUM!	#NUM!	#NUM!	#NUM!	#NUM!	#NUM!
	Expand/collapse list							

Conclusion:
No exceedance of the toxicological reference value was identified for any unprocessed commodity.
A short term intake of residues of Picloram is unlikely to present a public health risk.
For processed commodities, no exceedance of the ARfD/ADI was identified.

Aminopyralid

Processed commodities	Results for children				Results for adults			
	No of processed commodities for which ARfD/ADI is exceeded (IESTI):			---	No of processed commodities for which ARfD/ADI is exceeded (IESTI):			---
	IESTI				**IESTI**			
	Highest % of ARfD/ADI	Processed commodities	MRL / input for RA (mg/kg)	Exposure (µg/kg bw)	Highest % of ARfD/ADI	Processed commodities	MRL / input for RA (mg/kg)	Exposure (µg/kg bw)
	0.0%	Rapeseeds / oils	0.05 / 0.02	0.01	#NUM!	#NUM!	#NUM!	#NUM!
	Expand/collapse list							

Conclusion:
No exceedance of the toxicological reference value was identified for any unprocessed commodity.
A short term intake of residues of Aminopyralid is unlikely to present a public health risk.
For processed commodities, no exceedance of the ARfD/ADI was identified.