REGISTRATION REPORT

Part B

Section 7

Metabolism and Residues

Detailed summary of the risk assessment

Product code: 19202

Product name: **KINVARA**

Chemical active substances:

MCPA, 233 g/L
Fluroxypyr, 50 g/L
Clopyralid, 28 g/L

Central Zone

Zonal Rapporteur Member State: Poland

CORE ASSESSMENT

(Authorization)

Applicant: XXXX

Submission date: 31/01/2024

Evaluation date: October 2024

MS Finalisation date: March 2025

Version history

When	What
31/01/2024	Submission acc. Art. 43 Kinvara
October 2024	Initial RR
March 2025	Post-comments Amendment

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7 Metabolism and residue data (KCA section 6)

7.1 Summary and zRMS Conclusion

The applicant's dRR was not rewritten. In the resulting zRMS' RR all comments /corrections/ add-ons were placed on the grey background. Any colour highlightings with no explanation were removed from the dRR.

7.1.1 Critical GAP(s) and overall conclusion

Selection of critical uses and justification

The critical GAPs with respect to consumer intake and risk assessment for the preparation KINVARA are presented in Table 7-1. They have been selected from the individual GAPs in the Central Zone for cereals and grassland. A list of all intended uses within the Central Zone is given in Part B, Section 0.

Overall conclusion

On the basis of the data provided by the applicant in further part of the report the following general conclusions, in the context of the authorization request, can be set:

MCPA:
The proposed GAP for MCPA in 'KINVARA' on cereals and grassland (1 x 0.699 kg a.s./ha) is less critical than the GAP for MCPA on cereals and grassland (1 x 1.8 kg a.s./ha) supported at Annex I inclusion therefore it will not result in higher livestock intakes of MCPA or MRLs higher than current values in animal commodities. The current animal commodities MRLs will therefore not be exceeded following the use of the Kinvara.
Based on results from residue trials, no MCPA residues in grain are expected. Therefore, MCPA residues are also not expected in processed fractions such as flour or bread.
It is also can be concluded that when Kinvara is used consistently with the intended GAP, MCPA residues in succeeding crops are not expected.

Fluroxypyr:
The requested uses modify the theoretical maximum daily intake for animals (2017) however, the current animal MRLs are sufficient to accommodate the use of KINVARA in accordance with the intended GAP.
The chronic exposure does not exceed 10 % of the ADI, therefore investigation of processing on the nature and magnitude of the residues is not required.
The residues are not expected to be present in rotational crops.

Clopyralid:
After use of Kinvara there is no risk for animal MRLs to be exceeded.
Residues in processed products such as bread and flour tend to be reduced, which means that they do not pose a risk to consumer health if Kinvara is used in accordance with GAP.
Residues in rotational crops arising from the proposed uses of KINVARA are not expected.

Furthermore, the data available are considered sufficient for risk assessment.
An exceedance of the current MRLs for MCPA, fluroxypyr and clopyralid as laid down in the relevant presented below regulations is not expected.
The expected clopyralid MRLs are consistent with the intended uses.
The data on current (taken from EU web on 4.09.2024) and awaited MRLs are shown as follows:
(taken from EU web on 4.09.2024)

Code	Products to which MRLs apply	Fluroxypyr (sum of fluroxypyr, its salts, its esters, and its conjugates, expressed as fluroxypyr)(R),(A) Reg. (EU) 2022/1363 Applicable	MCPA and MCPB (MCPA, MCPB including their salts, esters and conjugates expressed as MCPA)(R),(F) Reg. (EU) No 491/2014 Applicable	Clopyralid Reg. (EU) 2021/1807 Applicable
500090	Wheat	0.1	0.2	3
500010	Barley	0.1	0.2	2
500070	Rye	0.1	0.2	5
500050	Oat	0.1	0.2	3

Code	Products to which MRLs apply	Clopyralid PLAN/2024/791 not yet applicable	Clopyralid Reg. (EU) 2021/1807 applicable
0500010	Barley	2	2
0500020	Buckwheat and other pseudocereals	2	2
0500030	Maize/corn	2	2
0500040	Common millet/proso millet	2	2
0500050	Oat	3	**3**
0500060	Rice	2	2
0500070	Rye	5	5
0500080	Sorghum	2	2
0500090	Wheat	3	**3**
0500990	Others (2)	2	2

The chronic and the short-term intakes of MCPA, fluroxypyr and clopyralid residues are unlikely to present a public health concern. A honey issue is irrelevant since the crops in question are not melliferous ones. In the draft label the applicant proposed 56 days period of withdrawal for feed which was accepted by PL as a typical conservative measure driven by clopyralid half-life. As far as consumer health protection is concerned, PL agrees with the authorization of the intended uses.

Data gaps

Noticed data gaps are none.

Table 7-1: 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 (g/L)**	**method kind**	**growth stage & season**	**number min max**	**interval between applications (min)**	**kg as/hL min max**	**water L/ha min max**	**g as/ha min max**		
1	Wheat, Rye Triticale 0500090 0500070	CEU	KINVARA	F	Annual and perennial broadleaf weeds	ME*	MCPA: 233 FXP: 50 CPD: 28	Spray	BBCH 24-39	1	N/A	-	200-400	MCPA: 699 FXP: 150 CPD: 84	-	
	Barley, Oat 0500010 0500050	CEU	KINVARA	F	Annual and perennial broadleaf weeds	ME*	MCPA: 233 FXP: 50 CPD: 28	Spray	BBCH 24-39	1	N/A	-	200-400	MCPA: 699 FXP: 150 CPD: 84	-	
2,3	Grassland (established and new)	CEU	KINVARA	F	Annual and perennial broadleaf weeds	ME*	MCPA: 233 FXP: 50 CPD: 28	Spray	March - end of September	1	N/A	-	200-400	MCPA: 699 FXP: 150 CPD: 84	7	

* 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
MCPA, FXP fluroxypyr, CPD clopyralid, N/A Not applicable
* see remark on page 25 “additional information”

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 KINVARA is composed of MCPA, fluroxypyr and clopyralid.

Table 7-2: Toxicological reference values for the dietary risk assessment of MCPA, fluroxypyr and clopyralid.

Reference value	Source	Year	Value	Study relied upon	Safety factor
MCPA: *MCPA and MCPB (MCPA, MCPB including their salts, esters and conjugates expressed as MCPA)*					
ADI	Review report; SANCO /4062/2001-final, 11 July 2008 SCoFCAH July 08	2008	0.05 mg/kg bw/d	2 years, rat	100
ARfD	Review report; SANCO /4062/2001-final, 11 July 2008	2008	0.15 mg/kg bw/d	NOEL: 15 mg/kg bw/d for maternal toxicity in rabbit	100
Fluroxypyr: *Fluroxypyr (sum of fluroxypyr, its salt, its esters, and its conjugates, expressed as fluroxypyr)*					
ADI	Review report; SANCO /11019/2001 rev 5, 23 March 2017	2017	0.8 mg/kg bw/d	Rat, 2-year study	100
ARfD	Review report; SANCO /11019/2001 rev 5, 23 March 2017	2017	Not established, not required	-	-
Clopyralid: *Clopyralid*					
ADI	Review report; SANTE /10206/2021 rev 1, 20 May 2021	2021	0.15 mg/kg bw/d	Rat 2-year combined chronic toxicity and carcinogenicity study	100
ARfD	Review report; SANTE /10206/2021 rev 1, 20 May 2021	2021	0.17 mg/kg bw/d	LOAEL: 50 mg/kg bw/d for maternal toxicity in rabbit	300

7.1.2.1 Summary for MCPA

Table 7-3: Summary for MCPA

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	Wheat, Rye, Triticale	Yes	Yes	Yes	Yes	Yes	No	No
	Barley, Oat	Yes	Yes	Yes	Yes	Yes	No	No
2, 3	Grassland	Yes	Yes	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

7.1.2.2 Summary for fluroxypyr

Table 7-4: Summary for fluroxypyr

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	Wheat, Rye, Triticale	Yes	Yes	Yes	Yes	Yes	No	No
	Barley, Oat	Yes	Yes	Yes	Yes	Yes	No	No
2, 3	Grassland	Yes	Yes	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

7.1.2.3 Summary for clopyralid

Table 7-5: Summary for clopyralid

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	Wheat, Rye, Triticale	Yes	Yes	Yes	Yes	Yes	No	No
	Barley, Oat	Yes	Yes	Yes	Yes	Yes	No	No
2, 3	Grassland	Yes	Yes	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

7.1.2.4 Summary for KINVARA

Table 7-6: Information on KINVARA (KCA 6.8)

Crop	PHI for KINVARA proposed by applicant	PHI/ Withholding period* sufficiently supported for			PHI for KINVARA proposed by zRMS	zRMS Comments (if different PHI proposed)
		MCPA	Fluroxypyr	Clopyralid		
Wheat, Rye, Triticale	F **	Yes	Yes	Yes	none	
Barley, Oat	F **	Yes	Yes	Yes		
Grassland	7 days	Yes	Yes	Yes		

NR: not relevant

* A withholding period has not been specified by the applicant.
** F: PHI is defined by the application stage at last treatment (time elapsing between last treatment and harvest of the crop).

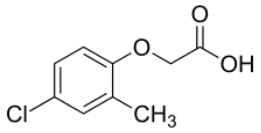
Waiting period before planting succeeding crops		**Overall waiting period proposed by zRMS**
Crop group	**Led by clopyralid**	
All succeeding crops	125 days	-

Assessment

7.2 MCPA

General data on MCPA are summarised in the table below (last updated 2021/10/25).

Table 7-7: General information on MCPA

Active substance (ISO Common Name)	MCPA
IUPAC	4-chloro-*o*-tolyloxyacetic acid
Chemical structure	
Molecular formula	$C_9H_9ClO_3$
Molar mass	200.6 g/mol
Chemical group	Phenoxyacetic herbicides
Mode of action (if available)	Auxin / multifaceted
Systemic	Yes
Company*	Nufarm
Rapporteur Member State (RMS)	PL and NL (as co-RMS) Original: Italy
Approval status	Approved on 01/05/2006 COMMISSION DIRECTIVE 05/57/EC; Reg. (EU)2020/1511 Reg. (EU) 2021/1449 Reg. (EU) No 540/2011
Restriction	Only uses as herbicide may be authorised.
Review Report	SANCO/4062/2001-final, 11 July 2008
Current MRL regulation	Reg. (EU) No 491/2014 Applicable from: 05/06/2014
Peer review of MRLs according to Article 12 of Reg No 396/2005 EC performed	In progress (Last updated: 30/11/2020)
EFSA Journal: Conclusion on the peer review	No
EFSA Journal: Conclusion on article 12	No
Current MRL applications on intended uses	None known

* Notifier in the EU process to whom the a.s. belong(s)

7.2.1 Stability of Residues (KCA 6.1)

7.2.1.1 Stability of residues during storage of samples

Available data

Cereals
No new data submitted in the framework of this application. Storage stability studies of residues in cereals were reviewed during the evaluation for EU approval. The data was acceptable and is summarised in the EU Draft Assessment Reports (DAR).

Table 7-8: 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			
Cereals	High starch content	18 months	MCPA DAR, Vol. 3, B.6, Oct 2003
Grassland	High water content		MCPA DAR

Conclusion on stability of residues during storage

zRMS: The available study investigated the storage stability of MCPA residues in cereal grain as well as forage (DE) – this should be completed here.
Sufficient storage stability data are available to support the intended uses.

A**dditional information**
Storage stability in animal matrices is not a data requirement for KINVARA but should be addressed as part of the renewal of the active ingredient MCPA at EU level. Nevertheless XXXX have a LoA from Nufarm (dated May 2017) indicating access to the MCPA task force renewal data. This provides the applicant access to Annex II renewal data including stability data in animal matrices.

7.2.1.2 Stability of residues in sample extracts (KCA 6.1)

Please refer to Section 7.2.1.1 above.

Conclusion on stability of residues in sample extracts

Sufficient data are available to support the intended uses.

zRMS agrees with the above consideration of the applicant.

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

No new data submitted in the framework of this application.

Studies on the metabolism of this active substance in plants were reviewed during the evaluation for EU approval. The data was acceptable and is summarised in the EU Draft Assessment Reports (DAR). The studies are also summarised below.

Table 7-9: 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	Winter wheat	MCPA-uniformly phenyl ring labelled	Foliar, F	Aq. solution of 25% as potassium salts applied at 6.8 L/ha in 1,250 L water	1	1, 25, 49, 102 (green plants, straw , grain)	-	MCPA DAR, Vol. 3, B.6, Oct 2003
	Wheat	MCPA-2-EHE - uniformly phenyl ring labelled	G	1.68 kg acid equivalent/ha	1	7 (forage) 67 (grain and straw)	-	
		MCPA-DMA-uniformly phenyl ring labelled					-	
	Maize, broad bean	MCPA-acid-unspecified label	Foliar, G	500 - 10,000 mg/kg of MCPA Na salt		2, 5, 7	-	

Summary of plant metabolism studies reported in the EU

Residue Definition: *"MCPA its salts, esters and conjugates expressed as MCPA"*

Annex point	IIIA 8.2/01
Reference	MCPA DAR - Vol. 3, B.6, Oct 2003
Title	Investigations into the Metabolism of MCPA in Winter Wheat
Author/Year	Keller W, Otto S (1979)
Guideline	BASF internal method

Method

Test material was MCPA acid (4-Chloro-2-methyl[ring-U^{14}C] phenoxy) acetic acid - Radiochemical purity 98% with a specific activity of 4.1 mCi/mmol (20.3 μCi/mg). A metabolism study was conducted by BASF with MCPA in winter wheat. The investigation provided data on the uptake, distribution and metabolism of ^{14}C-MCPA (uniformly ring labelled) in the forage, grain and straw of wheat. Winter wheat (variety Flanders) was cultivated on a clay loam soil. A mixture of ^{14}C-MCPA and cold MCPA was applied as an aqueous solution of 25% as potassium salts. The treatment was done by leaf spraying at a rate of 6.8 l/ha in 1,250 l water. After sampling at 1, 25 and 49 days after treatment remaining plants were harvested at 102 days. Green plants, straw and grain were then analysed for determination of radioactivity after methanol-water extraction.

Result

^{14}C activity determination after methanol-water extraction in straw and grain

Sampling (days)	^{14}C Total Residues	Unextractable ^{14}C Residues		^{14}C Residues in Extract	
	mg/kg	mg/kg	%	mg/kg	%
1	26.98	0.98	3.6	26.00	96.4
25	2.83	0.45	15.9	2.38	84.1
49	2.21	0.52	23.5	1.69	76.5
102 (straw)	1.29	0.90	69.8	0.39	30.2
102 (grain)	0.03	0.0286	95.3	0.0014	4.7

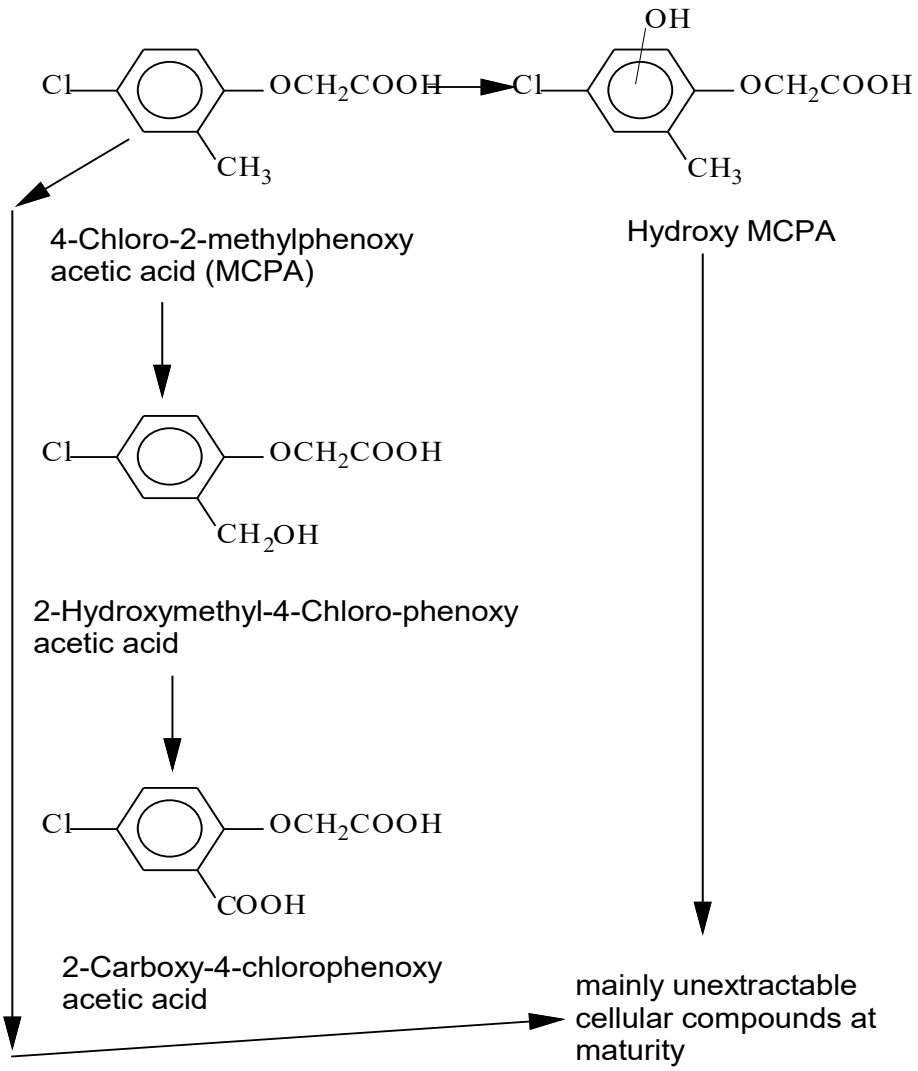
From the table above (radioactivity determination after extraction), it appears that wheat grains have extremely low total residues content (0.03 mg/kg). Only 4.7% are extractable with aqueous methanol at harvest. In the straw 30% of total residues are extractable. The rate of degradation of MCPA in the plant is high (table below, distribution of residues after HPLC). The resulting metabolites were identified in wheat as parent MCPA acid (A1), Hydroxy-MCPA (A2), 2-carboxy-4-chlorophenoxyacetic acid (A3), 2-hydroxymethyl-4-chlorophenoxyacetic acid (A5) and an unknown compound (A4). Identification of radioactivity in ^{14}C-MCPA treated wheat after HPLC separation and GC-MS characterisation.

Distribution of ^{14}C residues after HPLC

Component	1 day mg/kg	25 day mg/kg	49 day mg/kg	102 days
A1 mg/kg	24.10	0.72	0.56	0.09
A2 mg/kg	0.17	0.19	0.12	0.02
A3 mg/kg	0.13	0.14	0.08	0.04
A4 mg/kg	0.27	0.22	0.14	0.04
A5 mg/kg	1.59	0.98	0.56	0.20

MCPA is hydroxylated at the methyl group with formation of 2-hydroxymethyl-4-chloro-phenoxyacetic acid (A5). This metabolite, together with unchanged MCPA, constitutes approximately 75% of the residues extractable from straw with aqueous methanol at harvest. 2-Carboxy-4-chlorophenoxyacetic acid was identified as a further metabolite (A3) and constitutes nearly 10% of the residues extractable from straw with aqueous methanol at harvest. The hydroxylation of the aromatic ring observed to a slight extent is obviously a minor metabolic pathway in the plant.

The proposed degradation pathway of MCPA in winter wheat is:



Conclusion
Wheat grains have extremely low total residues content (0.03 mg/kg). Therefore, the study is acceptable.

Annex Point	IIIA 8.2/02
Reference	MCPA DAR - Vol. 3, B.6, Oct 2003
Title	Nature of the residue of ^{14}C-2-Methyl-4-Chlorophenoxyacetic Acid (^{14}C-MCPA as the dimethylamine salt (^{14}C-MCPA DMA) and the 2-Ethylhexyl ester (^{14}C-MCPA 2-EHE) in wheat
Author/Year	Patrick J. Sabourin (1995)
Guideline	GLP

Method
Test materials were the 2-ethylhexyl ester of 2-methyl-4-chlorophenoxyacetic acid (MCPA 2-EHE) and the dimethylamine salt of MCPA (MCPA DMA) both uniformly ring label. Radiochemical purity 98% in both materials with a specific activity of 18.1 μCi/mg for MCPA DMA and 15.7 μCi/mg for MCPA 2-EHE.
A metabolism study was conducted in wheat, growing under greenhouse conditions. Both forms of MCPA were tested to provide data on the uptake, distribution and metabolism of ^{14}C-MCPA DMA and ^{14}C-MCPA

2-EHE in the forage, grain and straw of wheat. The treatment consisted of one foliar spray application of either ^{14}C-MCPA DMA or ^{14}C-MCPA 2-EHE at a rate of 1.68 kg of acid equivalent (MCPA acid) per ha. Sampling of the total radiolabelled residue (TRR) was done in the forage harvested 7 days after treatment and in grain and straw at harvested at 67 days.

Result & Conclusion
The residue in forage and straw of wheat treated with either form of MCPA was qualitatively similar except for a higher proportion of parent, MCPA, in the forage and straw of ^{14}C-MCPA DMA treated wheat. The residue profiles in grain were similar for either form of MCPA. Analysis of sample extracts by HPLC and TLC confirmed the presence of MCPA, 2-carboxy-4-chlorophenoxyacetic acid (CCPA) and 2-hydroxy-4chlorophenoxyacetic acid (2HMCPA), a glucose conjugate of 2HMCPA, and MCPA/2HMCPA conjugates in all samples. Post extracted forage and straw samples were subjected to chemical hydrolysis to free bound residues. Analysis of the hydrolysates of the bound residue in forage and straw demonstrated the presence of conjugated forms of MCPA, 2HMCPA and CCPA. The study is acceptable.

Annex Point	IIIA 8.2/03
Reference	MCPA DAR - Vol. 3, B.6, Oct 2003
Title	The Uptake, Metabolism and Phytotoxicity of MCPA in Plants
Author/Year	Achhireddy N, Kirkwood RC, Fletcher W W, *J. of Pesticide Science* 9; pp 617-622/ (1984)
Guideline	University of Strathclyde internal method used. Guidelines not given

Method
Test material was ^{14}C-MCPA acid, specific activity: 6.0 mCi/mmol. (position of labelling not specified). The phototoxicity of MCPA as related to the translocation and metabolism in maize (C4 plant) and broad bean (C3 plant) was studied under controlled environmental conditions. In a heated greenhouse (22 ± 2°C) Maize plants (*Zea mays L.*) and broad bean (*Vicia faba L.*) were sprayed at the 4 leaf-stage with concentrations of MCPA Na salt of 500; 1,000; 5,000 and 10,000 mg/kg. 2; 5 and 7 days after treatment samples were taken. After extraction procedures distribution of MCPA in the plant was examined.

Result
Examination of the distribution of ^{14}C-MCPA within the test species revealed differentials in translocation. In the broad bean the ^{14}C accumulates rather in the shoot and the root apices. Absorption was greater in maize than in the broad bean. The release of ^{14}C-CO_2 from MCPA was greater in broad bean than in maize indicating faster rates of breakdown of MCPA in the broad bean. Most of the radioactivity found in the ether extracts was not identified. In maize 24% of the applied radioactivity was identified as MCPA and in broad bean 32%. These figures confirm the results previously mentioned in the metabolism study conducted with winter wheat.

Conclusion
As the metabolism study in wheat showed a rapid degradation of MCPA via compounds of no toxicological importance and no residues were found at harvest in edible parts of plant origin food, the residue should be defined as MCPA only. No metabolites need to be included in any analytical methods for checking the MRLs values. The study is acceptable.

Conclusion on metabolism in primary crops

The requested uses in the GAP table are accommodated by the plant metabolism data previously reviewed at EU level, therefore the existing residue definitions apply.

7.2.2.2 Nature of residue in rotational crops (KCA 6.6.1)

Available data

No new data submitted in the framework of this application.

Data on the nature and magnitude of residues was reviewed during the EU approval of MCPA and was considered to be acceptable to support the respective representative uses.

MCPA was shown not to be persistent in soil degradation studies presented. Succeeding crops are planted after harvest of the previous crop at least 4 months after MCPA treatment, and it would be expected that MCPA would have totally broken down and therefore not available for translocation. Nevertheless, a confined rotational crop study and a study investigating the long-term effect of repeated applications of MCPA on succeeding crops were reviewed during the Annex I inclusion on MCPA and are discussed in section 7.2.6.

Conclusion on metabolism in rotational crops

Data on the nature of residues reviewed during the Annex I inclusion of MCPA is acceptable to support the proposed uses.

7.2.2.3 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

Based on results from residue trials conducted to date, no MCPA residues are expected at or above the limit of detection. It is therefore unlikely that MCPA residues will be detected in processed fractions such as flour or bread. Therefore, no study has been conducted regarding the effects of industrial processing and household preparation on the nature and magnitude of MCPA residues.

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

Table 7-10: Summary of the nature of residues in commodities of plant origin

Endpoints (MCPA)	
Plant groups covered	Cereals (Wheat, Maize) Pulses (Broad bean)
Rotational crops covered	-
Metabolism in rotational crops similar to metabolism in primary crops?	-
Processed commodities	-
Residue pattern in processed commodities similar to pattern in raw commodities?	-
Plant residue definition for monitoring	MCPA and MCPB (MCPA, MCPB including their salts, esters and conjugates expressed as MCPA) (Reg. (EU) No 491/2014)

Endpoints (MCPA)	
Plant residue definition for risk assessment	MCPA and MCPB (MCPA, MCPB including their salts, esters and conjugates expressed as MCPA) No EFSA proposal.
Conversion factor from enforcement to RA	None

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

Available data

No new data submitted in the framework of this application.

Studies on the metabolism of this active substance in livestock (rat, hen and goat) were reviewed during the evaluation for EU approval. The data was acceptable and is summarised in the EU Draft Assessment Reports (DAR). In addition, further new data that supported the MCPA-AIR III Task Force Renewal Application, dated 24th April 2013, not previously submitted for Annex I inclusion of MCPA, is included below.

Summary of animal metabolism studies reported in the EU

Residue Definition: *"MCPA its salts, esters and conjugates expressed as MCPA"*

Annex Point	IIIA 8.2/05
Reference	MCPA: SCIENTIFIC REPORT OF EFSA The 2009 European Union Report on Pesticide Residues in Food: EFSA Journal 2011;9(11):2430 & MCPA-AIR III Task Force Renewal Application, 24th April 2013
Title	Absorption, distribution, metabolism and excretion in the rat
Author/Year	XXXX (1995)
Guideline	GLP
Annex Point	IIIA 8.2/06
Reference	MCPA:SCIENTIFIC REPORT OF EFSA The 2009 European Union Report on Pesticide Residues in Food: EFSA Journal 2011;9(11):2430
Title	Interspecies Comparison of Metabolism
Author/Year	XXXX (2000)
Guideline	Not GLP

Conclusion

In rats: 70 - 90 % as unchanged MCPA in the urine; 2-7% HMCPA (hydroxymethyl derivative); traces of glycine conjugate. In dogs: 30 % unchanged MCPA, 6,5% HMCPA , 12 - 38% glycine conjugates. In humans high level of conjugation may occur (56-73 % conjugates in a volunteer).

Annex Point	IIIA 8.2/08
Reference	MCPA DAR – Vol. 3, B.6, Oct 2003
Title	Nature of the residue study of ^{14}C-2-Methyl-4-chlorophenoxyacetic acid (^{14}C-MCPA) using egg-laying white Leghorn hens.
Author/Year	XXXX (1995)
Guideline	GLP

Annex Point	IIIA 8.2/09
Reference	MCPA DAR - Vol. 3, B.6, Oct 2003
Title	Supplemental Report to: Nature of the residue study of ^{14}C-MCPA using egg-laying white leghorn hens
Author/Year	XXXX (1996)
Guideline	GLP

Annex Point	IIIA 8.2/11
Reference	MCPA DAR – Vol. 3, B.6, Oct 2003
Title	Nature of the residue study of ^{14}C-2-Methyl-4-chlorophenoxyacetic acid (^{14}C-MCPA) using lactating goats.
Author/Year	XXXX (1995)
Guideline	GLP

According to the MCPA-AIR III Task Force Renewal Application in 24th April 2013, metabolism in livestock is similar to that in rats therefore no metabolism study in pigs is required.

Conclusion on metabolism in livestock

The requested uses in the GAP table are accommodated by the livestock metabolism data previously re-viewed at EU level, therefore the existing residue definitions apply.

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

Table 7-11: Summary on the nature of residues in commodities of animal origin

	Endpoints (MCPA)
Animals covered	Lactating goats
	Laying hens
Time needed to reach a plateau concentration	-
	-
Animal residue definition for monitoring	MCPA, MCPB and MCPA thioethyl expressed as MCPA. (Reg. (EU) No 491/2014)
Animal residue definition for risk assessment	MCPA, MCPB and MCPA thioethyl expressed as MCPA. (Reg. (EU) No 491/2014)
Conversion factor	None
Metabolism in rat and ruminant similar	Yes
Fat soluble residue	Yes

zRMS agrees with the above consideration of the applicant.

7.2.3 Magnitude of MCPA residues in plants (KCA 6.3)

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

Studies on the magnitude of residues resulting from the proposed uses of KINVARA that have been previously evaluated at EU level are summarised in the table below. In addition, new grassland trials previously submitted to the UK in 2020 are summarised here and in Appendix 2. Supervised field trials of all 3 active substances were performed to cover the uses applied for.

Table 7-12: Summary of EU reported and new data supporting the intended uses of KINVARA and conformity to existing MRL (MCPA)

Commodity	Source	Residue zone (N-EU, S-EU, EU, ~~outside EU~~)	Evaluation GAP Residue levels (mg/kg) [(a)]	STMR (mg/kg)	HR (mg/kg)	Unrounded OECD calculator MRL (mg/kg)	Current EU MRL (mg/kg)	MRL compliance
Wheat grain→ Triticale, rye grain	Witte, A. (2015) TRC14-045	NEU	Trials GAP: 1 x 0.631-0.731 kg a.s./ha, BBCH 39, outdoor 3x <LOD, <0.01	-				
	Overall supporting data for cGAP	NEU	**KINVARA cGAP: 1 x 0.699 kg a.s./ha, BBCH 39** 3x <LOD, <0.01	<0.01	<0.01	0.01*	0.2	Yes
Wheat straw→ triticale, rye straw	Witte, A. (2015) TRC14-045	NEU	Trials GAP: 1 x 0.631-0.731 kg a.s./ha, BBCH 39, outdoor 0.14, 0.30, 0.93, 1.47	-				
	Overall supporting data for cGAP	NEU	**KINVARA cGAP: 1 x 0.699 kg a.s./ha, BBCH 39** 0.14, 0.30, 0.93, 1.47	0.665	1.47	Not relevant for animal feed commodities		
Barley grain→ Oat grain	Witte, A. (2015) TRC14-059	NEU	Trials GAP: 1 x 0.663 - 0.708 kg a.s./ha, BBCH 39, outdoor 3x <LOD, <0.01	-				

	Overall supporting data for cGAP	NEU	**KINVARA cGAP: 1 x 0.699 kg a.s./ha, BBCH 39** 3x <LOD, <0.01	<0.01	<0.01	0.01*	0.2	Yes
Barley straw→ Oat straw	Witte, A. (2015) TRC14-059	NEU	Trials GAP: 1 x 0.663 - 0.708 kg a.s./ha, BBCH 39, outdoor 0.08, 0.26, 0.27, 0.28	-				
	Overall supporting data for cGAP	NEU	**KINVARA cGAP: 1 x 0.699 kg a.s./ha, BBCH 39** 0.08, 0.26, 0.27, 0.28	0.265	0.28	Not relevant for animal feed commodities		
Grassland	2015 dRR KINVARA (1) (Witte, 2015, TRC14-022)	NEU	Trials GAP: 1 x 0.700 kg a.s./ha, March to June, PHI 7 days 4.46, 5.53, 25.3, 32.1	-				
	New trials (Diebold, 2019, R B8208)	NEU	Trials GAP: 1 x 0.700 kg a.s./ha, March to September, PHI 7 days 12.94, 20.17, 24.08, 27.18	-				
	Overall supporting data for cGAP	NEU	**KINVARA cGAP: 1 x 0.699 kg a.s./ha, March up to the end of September, PHI = 7 days:** 4.46, 5.53, 12.94, 20.17, 24.08, 25.3, 27.18, 32.1	22.125	32.10	Not relevant for animal feed commodities		

* Source of EU MRL: Reg (EU) No 491/2014
(a) Definition of residue for enforcement and risk assessment are the same: MCPA and MCPB (MCPA, MCPB including their salts, esters and conjugates expressed as MCPA)
(1) CEU: Updated in Sep 2016, zRMS = UK, Annex point IIIA 8.3/03.

Additional information*
At the time studies TRC14-059, TRC14-045 and TRC14-022 were commissioned XXX incorrectly listed the formulation as an EW when in actual fact KINVARA was developed as, and remains, a micro-emulsion (ME) formulation. A signed statement from product/process development chemists is available. In addition, a final report amendment has been produced for residue field trials reports TRC14-059, TRC14-045 and TRC14-022.

7.2.3.2 Conclusion on the magnitude of residues in plants

Wheat, triticale, rye, barley and oat
A total of 4 trials, each, were performed on wheat and barley in Northern Europe according to the intended GAP to support the registration of KINVARA on wheat, triticale, rye, barley and oat. All residues in cereal grain were <LOQ. According to SANTE/2019/12752, since the application is performed before the edible part is formed, and as wheat data can be extrapolated to barley and *vice versa*, it can be concluded that the existing dataset of 8 trials (wheat/barley) in Northern Europe is sufficient to support the proposed uses of KINVARA on cereals.
Grassland
There is currently a degree of ambiguity on the numbers of supervised residue trials required for fodder crops, such as pasture grass, as this is not yet harmonized in Europe. SANTE/2019/12752 provides guidelines on comparability, extrapolation, group tolerances and data requirements for setting MRLs. However, MRLs are not currently established for crops used exclusively for animal feed and limited guidance is provided within the guidelines. Sufficient supervised residue trials are required to enable a robust estimate of animal intake of residues from feed items.
Typically, criteria such as cultivation area and production are used to guide trial requirements for fodder crops. Considering grass cultivation area and production[1], and intake by livestock in the EU[2], grass can be considered a major crop. For major crops, eight supervised residue trials are usually required per residue zone. However, a lower number of trials have been accepted on grasses in some circumstances[3].
Residue trials conducted at eight sites in northern Europe are available. Trials were conducted according to the proposed GAP of MCPA on KINVARA, with appropriate sampling of grass green matter to support a PHI of 7 days. A ninth trial (B8208 CZ1) has not been included in the analysis. Several deviations were recorded for this trial, therefore it is not considered to be reliable. Most notably, the application timing was outside the specified range (October, instead of March to September) and residues were detected in untreated specimens.
Whilst the application parameters are equivalent in all available studies, it is noted that the trials conducted in 2018 (Diebold, J.L., 2019, R B8208) were conducted at the slightly later seasonal timing (March to September). However, the MCPA residues obtained in both studies are statistically similar populations (Mann Whitney, α 0.05). Therefore, a combined dataset has been relied upon within this evaluation.
It is considered that sufficient trials (8 NEU) are available to support the intended use of MCPA in KINVARA on grassland and to allow a robust estimate of animal intake of MCPA residues from grass.
Conclusions
The data submitted show that no exceedance of current EU MRLs will occur. The proposed uses of KINVARA are considered acceptable.

zRMS agrees with the above consideration of the applicant.

[1] https://ec.europa.eu/eurostat/documents/2393397/8259002/Grassland_2014_Final+report.pdf/58aca1dd-de6f-4880-a48e-1331cafae297
[2] OECD ENV/JM/MONO(2013)8 04-Sep-2013 Guidance Document on Residues in Livestock.
[3] For example, 7 NEU and 4 SEU trials on grasses were considered sufficient within EFSA Journal 2017;15(3):4735.

7.2.4 Magnitude of residues in livestock

7.2.4.1 Dietary burden calculation

Livestock dietary burden calculations have been performed taking into account commodities from the proposed uses of KINVARA that might be used as animal feed.
Cereal grain, cereal straw, grass and wheat and barley processed commodities may form a part of livestock diets in the EU. The potential dietary exposure to MCPA has been calculated using the EFSA model (2017). The dietary inputs into the animal diet according to the EU model are summarised in Table 7-13.
The highest residues in supervised trials are used to calculate the maximum potential dietary intake except for feed commodities that are bulked or processed where the STMR is used. As residues in the RAC for wheat and barley are below the limit of quantification (< 0.01 mg/kg), the default processing factors are set at 1.

Table 7-13 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: *MCPA and MCPB (MCPA, MCPB including their salts, esters and conjugates expressed as MCPA)*				
Barley - straw	0.27	STMR Barley (this submission)	0.28	HR Barley (this submission)
Oat - straw	0.27	STMR Barley (this submission)	0.28	HR Barley (this submission)
Rye - straw	0.67	STMR Wheat (this submission)	1.47	HR Wheat (this submission)
Triticale - straw	0.67	STMR Wheat (this submission)	1.47	HR Wheat (this submission)
Wheat - straw	0.67	STMR Wheat (this submission)	1.47	HR Wheat (this submission)
Barley - grain	0.01	STMR Barley (this submission)	-	-
Oat - grain	0.01	STMR Barley (this submission)	-	-
Rye - grain	0.01	STMR Wheat (this submission)	-	-
Triticale - grain	0.01	STMR Wheat (this submission)	-	-
Wheat - grain	0.01	STMR Wheat (this submission)	-	-
Brewer’s grain - dried	0.01	STMR (Barley)	-	-
Distiller’s grain - dried	0.01	STMR (Wheat)	-	-
Wheat gluten - meal	0.01	STMR (Wheat)	-	-
Wheat - milled by-products	0.01	STMR (Wheat)	-	-

Feed Commodity	Median dietary burden		Maximum dietary burden	
	Input value (mg/kg)	Comment	Input value (mg/kg)	Comment
Grass - forage	22.125	STMR Grass (this submission)	32.10	HR Grass (this submission)
Grass - hay	77.44	STMR Grass (this submission) x default PF	112.35	HR Grass (this submission) x PF
Grass - silage	35.40	STMR Grass (this submission) x default PF	51.36	HR Grass (this submission) x PF

Table 7-14: Results of the dietary burden calculation

Animal species	Median dietary burden (mg/kg bw/d)	Maximum dietary burden (mg/kg bw/d)	Highest contributing commodity	Max dietary burden (mg/kg DM)	Trigger exceeded** (Y/N)
Risk assessment residue definition: *MCPA and MCPB (MCPA, MCPB including their salts, esters and conjugates expressed as MCPA)*					
Beef cattle*	2.043	2.963	Grass (silage)	77.05	Y
Dairy cattle*	2.043	2.963	Grass (silage)	77.05	Y
Ram/ewe	2.803	4.066	Grass (forage)	121.98	Y
Breeding swine	0.409	4.066	Grass (forage)	121.98	Y
Finishing swine*	0.409	0.593	Grass (forage)	25.69	Y
Broiler poultry	0.006	0.012	Wheat straw	0.18	Y
Layer poultry*	0.006	0.012	Wheat straw	0.18	Y

* These categories correspond to those (formerly) assessed at EU level.
** Although the most recent dietary burden calculator has been used, the old trigger value of 0.1 mg/kg DM remains valid, as the active substance falls under the old data requirements.

Use of the most recent EFSA dietary burden calculator (model 2017) modifies the theoretical maximum daily intake for animals, compared to those considered for Annex I inclusion. However, regarding available feeding data, there is no risk for current animal MRLs to be exceeded, as these are based on more critical GAPs considered for the Annex I inclusion of MCPA. Grass silage and forage (fresh) were identified as the most critical commodity in the ruminant diet. Wheat straw was identified as the most critical commodity in the poultry diet. The calculated dietary burdens were found to exceed the trigger value of 0.004 mg/kg bw. Therefore, further consideration of residues in livestock is provided below.

zRMS agrees with the above consideration of the applicant.

7.2.4.2 Livestock feeding studies (KCA 6.4.1-6.4.3)

No new data were submitted in the framework of this application.
Livestock feeding studies were reviewed during the evaluation for EU approval. The data was acceptable and is summarised in the EU Draft Assessment Reports (DAR) and is summarised below.

Poultry

Available data

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

Poultry feeding studies for MCPA were reviewed during the evaluation for EU approval. The data was acceptable and is summarised in the EU Draft Assessment Reports (DAR). These studies are presented below.

Annex Point	IIIA 8.4/02
Reference	MCPA DAR - Vol. 3, B.6, Oct 2003
Title	Nature of the residue study of ^{14}C-2-Methyl-4-chlorophenoxyacetic acid (^{14}C-MCPA) using egg-laying white Leghorn hens.
Author/Year	XXXX (1995)
Guideline	MCPA Task Force Internal method. EPA Pesticide assessment guidelines and EPA's Good Laboratory Practices regulations.

Annex Point	IIIA 8.4/03
Reference	MCPA DAR - Vol. 3, B.6, Oct 2003
Title	Supplemental Report to: Nature of the residue study of ^{14}C-MCPA using egg-laying white leghorn hens.
Author/Year	XXXX (1996)
Guideline	GLP

Method

^{14}C-MCPA (2-Methyl-4-chlorophenoxyacetic acid; ring (U)- ^{14}C-labeled) was administered orally to 15 egg-laying hens once daily for 7 consecutive days at a dose equivalent to 100 ppm dietary feed. Eggs and excreta were collected daily. The hens were sacrificed 22 hours ± 1 hour after the last dose. Liver, kidneys, light and dark muscle, fat, skin, and gastrointestinal tract contents were collected and analysed along with the extract and eggs for total radioactive residues (TRR).

Result

Approximately 99% of the administered radioactivity was eliminated in the excreta after 7 days. Eggs and tissues accounted for a mean of 0.04% of the dose; gastrointestinal tract and contents, 0.02%; cage rinse 0.10%; and excreta, 99.3%, giving a total recovery of 99.5%. MCPA or base-labile conjugates of MCPA were the principle labelled products found in eggs and tissues. Only egg yolk contained one of these metabolites at a concentration >0.01 ppm. No other single metabolite accounted for greater than 0.01 ppm (MCPA acid equivalents). The daily recovery of ^{14}C in the excreta indicated that each daily dose is almost completely eliminated within 24 hr. Residue levels were very low.

Conclusion

From the two animal studies submitted one in hen and one in goat, the MCPA administered to animals was completely excreted within 24 hours as parent compound. No poultry feeding studies were conducted, since MCPA products are applied early in the season to cereals and in all residues trials conducted, residues in grain at harvest were at or below the limit of determination of the analytical method used.

Conclusion on feeding studies

The proposed GAP for MCPA in 'KINVARA' on cereals and grassland (1 x 0.699 kg a.s./ha) is less critical than the EU GAP for MCPA on cereals and grassland (1 x 1.8 kg a.s./ha) supported at Annex I inclusion. Therefore, the use of 'KINVARA' will not result in higher livestock intakes of MCPA or MRLs higher than current values in animal commodities.

The current MRLs in poultry commodities will therefore not be exceeded following the use of 'KINVARA'.

Lactating ruminants

Available data

No new data were submitted in the framework of this application.
Ruminant feeding studies for MCPA were reviewed during the evaluation for EU approval. The data was acceptable and is summarised in the EU Draft Assessment Reports (DAR). These studies are presented below.

Annex Point	IIIA 8.4/01
Reference	MCPA DAR - Vol. 3, B.6, Oct 2003
Title	Nature of the residue study of ^{14}C-2-Methyl-4-chlorophenoxyacetic acid (^{14}C-MCPA) using lactating goats.
Author/Year	XXXX (1995)
Guideline	MCPA Task Force Internal method. EPA Pesticide assessment guidelines and EPA's Good Laboratory Practices regulations.

Method
^{14}C-MCPA (2-Methyl-4-chlorophenoxyacetic acid; ring (U)- ^{14}C-labeled) was administered orally to two lactating goats twice daily for 3 consecutive days at a target dose equivalent to 750 ppm dietary feed. Milk, urine, and faeces were collected daily. The goats were sacrificed 22.5 hours after the last dose. Liver, kidneys, muscle, fat, bile, and gastrointestinal tract contents were collected and analysed along with the excreta and milk for total radioactive residues (TRR).

Result
TRR levels in the milk and tissues of goats

	ppm	
	Animal No. 29	Animal No. 53
Milk (72 hr)	0.172	0.160
Muscle	0.070	0.099
Fat	0.159	0.140
Liver	0.455	0.480
Kidney	0.899	0.886
Bile	0.816	1.19
Urine	309	757
Feces	22.2	79.2

MCPA is rapidly excreted with 99.5% of the administered dose being excreted within 23 hr of the last dose. Milk and tissues collected in this study accounted for less than 0.1% of the dose. The small amount of MCPA that is not excreted is metabolized to the glycine conjugate of MCPA, which was only detected in milk. An unknown peak present in chromatograms from tissues and bile was identified as a glycine conjugate of MCPA.

Conclusion
In the study submitted for Annex I listing (XXXX, 1995), ^{14}C-MCPA (2-Methyl-4-chlorophenoxyacetic acid; ring (U)- ^{14}C-labeled) was administered orally to two lactating goats twice daily for 3 consecutive days at a target dose equivalent to 750 ppm dietary feed. Milk, urine, and faeces were collected daily. The goats were sacrificed 22.5 hours after the last dose. Liver, kidneys, muscle, fat, bile, and gastrointestinal tract contents were collected and analysed along with the excreta and milk for total radioactive residues (TRR). MCPA was rapidly excreted with 99.5% of the administered dose being excreted within 23 hr of the last dose. Milk and tissues collected in this study accounted for less than 0.1% of the dose. The small amount of MCPA that is not excreted is metabolized to the glycine conjugate of MCPA, which was only detected in milk. An unknown peak present in chromatograms from tissues and bile was identified as a glycine conjugate of MCPA.

Conclusion on feeding studies
The proposed GAP for MCPA in 'KINVARA' on cereals and grassland (1 x 0.699 kg a.s./ha) is less critical than the GAP for MCPA on cereals and grassland (1 x 1.8 kg a.s./ha) supported at Annex I inclusion. Therefore, the use of 'KINVARA' will not result in higher livestock intakes of MCPA or MRLs higher than current values in animal commodities.
The current MRLs in ruminant commodities will therefore not be exceeded following the use of 'KINVARA'.

Pigs
The proposed GAP for MCPA in 'KINVARA' on cereals and grassland (1 x 0.699 kg a.s./ha) is less critical than the EU GAP for MCPA on cereals and grassland (1 x 1.8 kg a.s./ha) supported at Annex I inclusion. Therefore, the use of 'KINVARA' will not result in higher livestock intakes of MCPA or MRLs higher than current values in animal commodities.

The current MRLs in swine commodities will therefore not be exceeded following the use of 'KINVARA'.

zRMS agrees with the above consideration of the applicant.

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

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

7.2.5.2 Conclusion on processing studies

Based on results from residue trials conducted to date, no MCPA residues in grain are expected at or above the limit of detection. It is therefore unlikely that MCPA residues will be detected in processed fractions such as flour or bread. Therefore, no study has been conducted regarding the effects of industrial processing and household preparation on the magnitude of MCPA residues.

Residues greater than 0.1 mg/kg are expected in cereal straw, but this is not a processed commodity.

zRMS agrees with the above consideration of the applicant.

7.2.6 Magnitude of residues in representative succeeding crops

The crops under consideration can be grown in rotation.

No new data submitted in the framework of this application. Data on the nature and magnitude of residues was reviewed during the EU approval of MCPA and was considered to be acceptable to support the respective representative uses.

MCPA was shown not to be persistent in soil degradation studies presented. Succeeding crops are planted after harvest of the previous crop at least 4 months after MCPA treatment, and it would be expected that MCPA would have totally broken down and therefore not available for translocation.

Nevertheless, a confined rotational crop study and a study investigating the long-term effect of repeated

applications of MCPA on succeeding crops were reviewed during the Annex I inclusion on MCPA and are discussed in the following section.

7.2.6.1 Field rotational crop studies (KCA 6.6.2)

Available data

No new data submitted in the framework of this application.

A confined rotational crop study and a study investigating the long-term effect of repeated applications of MCPA on succeeding crops were reviewed during the Annex I inclusion on MCPA. The studies are presented below.

Table 7-15: Summary of available studies in field rotational crops

Primary crop	Rate (kg a.s./ha) (GS at application or PHI)	Residue levels in succeeding crops			
		Succeeding crop group	Succeeding crop	Sowing intervals (DAT)	Reference / Remarks
EU data					
Bare ground treatment with ^{14}C-MCPA acid	0.84 kg MCPA/ha	Leafy vegetables	Lettuce	30 120 365	MCPA DAR, Vol. 3, B.6, Oct 2003
		Root and tuber vegetables	Turnip top	30 120 365	
			Turnip root	30 120 365	
		Cereals	Barley forage	30 120 365	
			Barley grain	30 120 365	
			Barley straw	30 120 365	

Annex Point	IIIA 8.6/01
Reference	MCPA DAR - Vol. 3, B.6, Oct 2003
Title	MCPA Confined Accumulation Study on Rotational Crops
Author/Year	Ewing D D (1988)
Guideline	EPA Guidelines. Subdivision N, Section 165-1. GLP

Method

Test material was ^{14}C-radiolabelled MCPA acid (position of labelling not specified) Batch No. CFQ 4528, radiochemical purity 98%. A study was conducted in the USA to determine the nature and amount of MCPA residue uptake in rotational crops planted in soil that was aged after bare ground treatment with ^{14}C-MCPA at 0.84 kg MCPA/ha. An untreated control plot was planted with rotational crops and harvested on the

same schedule as the treated plot. The rotational crops were as follows: lettuce tops; turnip tops and roots; barley grain; forage and straw.

Result

Total ^{14}C-residue in lettuce, turnip and barley (in mg/kg wet weight basis)

		Treatment to Planting Interval	Treatment to Sampling Interval	Mean ^{14}C-Residue Food (mg/kg)
Sample Type	**Sample Type**	**(day)**	**(day)**	
Lettuce	Foliage	30	114	0.026
Lettuce	Foliage	30	140	0.015
Lettuce	Foliage	30	185	<0.013
Turnip	Foliage	30	172	<0.013
Turnip	Root	30	172	<0.013
Barley	Forage	30	199	0.017
Barley	Grain	30	233	<0.013
Barley	Straw	30	233	0.017
Lettuce	Foliage	120	172	0.042
Lettuce	Foliage	120	199	0.015
Lettuce	Foliage	120	218	0.016
Lettuce	Foliage	120	247	0.013
Turnip	Foliage	120	233	<0.013
Turnip	Root	120	233	<0.013
Barley	Forage	120	218	<0.013
Barley	Grain	120	268	<0.013
Barley	Straw	120	268	0.025
Lettuce	Foliage	365	409	<0.013
Lettuce	Foliage	365	428	<0.013
Lettuce	Foliage	365	455	<0.013
Turnip	Foliage	365	455	<0.013
Turnip	Root	365	455	<0.013
Barley	Forage	365	409	<0.013
Barley	Grain	365	582	<0.013
Barley	Straw	365	582	<0.013

Soil ^{14}C-residue levels declined from 0.276 (Day 0) to 0.045 mg/kg (Day 582) over the duration of the study. A half-life value was calculated and found to be 63 days under the experimental conditions. All lettuce samples from the 365-day planting were below the limit of detection (limit of detection 0.013 mg/kg) and had a total residue level below 0.05 mg/kg. There were no residues detected in turnip samples at or above the limit of detection (< 0.013 mg/kg). Detectable residues were found in the barley forage and straw samples from the 30-day planting and the straw samples from the 120-day planting but all were less than 0.05 mg/kg. In all other samples no residues were detectable (< 0.013 mg/kg).

Conclusion

The levels of total ^{14}C-residues in the rotational crop samples were all less than 0.05 mg/kg. Due to the very low residue levels in the crop samples, metabolite identification work was not feasible. No detectable ^{14}C-residues were found in the rotational crop and soil samples from the untreated plot. In the literature (Fryer and Kirkland; 1970) some experiments had already confirmed that MCPA, when used at the recommended rate, is unlikely to have any injurious effect on the capacity of soil to product healthy crops. In this reference possible long-term effects of repeated applications of MCPA were examined on one soil type.

Annex Point	IIIA 8.6/02
Reference	MCPA DAR - Vol. 3, B.6, Oct 2003
Title	Field experiments to investigate long-term effect of repeated applications of MCPA, Tri-Allate, Simazine and Linuron. Report after 6 years.
Author/Year	Fryer J D, Kirkland K. (1970)
Guideline	WRO method, described in report published in Weed Research (1970) 10, pp 133-158. Guidelines not given. It was conducted prior to GLP requirements.

Method
Test material was MCPA acid. MCPA was applied to barley at the 5-leaf stage at a rate of 1.68 kg/ha over 6 years. MCPA was applied to bare soil twice a year (spring and autumn) at an abnormally high dose (about double the above dose).

Result
MCPA applied for 6 years did not affect barley yield.

Magnitude of MCPA residues in barley

Date of spraying	Day after spraying	Residues mg/kg
20.05.1965	0	0.45
	7	0.09
	14	<0.09
01.06.1966	0	0.50
	15	0.45
	19	<0.09
10.05.1967	0	0.63
	7	0.58
	15	<0.09
02.05.1968	0	0.76
	4	0.2
	15	<0.09

Conclusion
The results show that MCPA at 1.68 kg/ha disappears within 3 weeks of application. It is concluded that MCPA, when used repeatedly at the recommended rate, should not affect succeeding crops.

Conclusion on rotational crops studies

It is concluded that MCPA, when used repeatedly at the recommended rate, should not affect succeeding crops.

zRMS agrees with the above consideration of the applicant.

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 KINVARA. Therefore, other special studies are not needed.

zRMS agrees with the above consideration of the applicant.

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

Table 7-16: Input values for the consumer risk assessment

Commodity	Chronic risk assessment		Acute risk assessment	
	Input value (mg/kg)	Comment	Input value (mg/kg)	Comment
MCPA and MCPB (MCPA, MCPB including their salts, esters and conjugates expressed as MCPA)				
Barley	0.01	STMR (This submission)	0.01	HR (This submission)
Oat	0.01	STMR (This submission, extrapolated from barley)	0.01	HR (This submission, extrapolated from barley)
Rye	0.01	STMR (This submission, extrapolated from wheat)	0.01	HR (This submission, extrapolated from wheat)
Wheat	0.01	STMR (This submission)	0.01	HR (This submission)
Commodities of animal origin	Current EU MRL	Reg (EU) 491/2014	Current EU MRL	Reg (EU) 491/2014
All other commodities	Current EU MRL	Reg (EU) 491/2014	-	Only crops under consideration in this dRR are used in the acute risk assessment.

7.2.8.2 Conclusion on consumer risk assessment

Extensive calculation sheets are presented in Appendix 3.

Table 7-17: Consumer risk assessment

TMDI (% ADI) according to EFSA PRIMo (the report has to be repasted into the RR)	14% (based on NL Toddler)
IEDI (% ADI) according to EFSA PRIMo	14% (based on NL Toddler)
IESTI (% ARfD) according to EFSA PRIMo*	16% Bovine: Liver (children) Processed: Wheat/milling flour: 0.1 %
NTMDI (% ADI) **	N/A
NEDI (% ADI)**	N/A
NESTI (% ARfD) **	N/A

* include raw and processed commodities if both values are required for PRIMo
** if national model is available

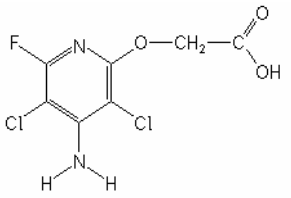
The proposed uses of MCPA in the formulation KINVARA do not represent unacceptable acute and chronic risks for the consumer.

zRMS agrees with the above consideration of the applicant.

7.3 Fluroxypyr

General data on fluroxypyr are summarized in the table below (last updated 2023/12/18)

Table 7-18: General information fluroxypyr

Active substance (ISO Common Name)	Fluroxypyr
IUPAC	4-amino-3,5-dichloro-6-fluoro-2-pyridyloxyacetic acid
Chemical structure	 Free acid
Molecular formula	$C_7H_5Cl_2FN_2O_3$
Molar mass	255.0 g/mol
Chemical group	Pyridine herbicides
Mode of action (if available)	By disrupting growth processes throughout the entire plant
Systemic	Yes
Company*	XXXX
Rapporteur Member State (RMS)	Ireland (Poland as co-RMS)
Approval status	Approved 1st January 2012 under Reg. (EU) 2017/856 and Reg. (EU) No 736/2011(00/10/EC 2007/21/EC Reg. (EU) No 540/2011)
Restriction	-
Review Report	SANCO/11019/2011 rev 5, 17 June 2011, 23 March 2017
Current MRL regulation	Reg. (EU) 2022/1363 Applicable from: 25/02/2023
Peer review of MRLs according to Article 12 of Reg No 396/2005 EC performed	No
EFSA Journal : Conclusion on the peer review	Yes EFSA Journal 2011;9(3):2091
EFSA Journal: Conclusion on article 12	Yes EFSA Journal 2013;11(12):3495
Current MRL applications on intended uses	-

* Notifier in the EU process to whom the a.s. belong(s)

7.3.1 Stability of Residues (KCA 6.1)

7.3.1.1 Stability of residues during storage of samples

Available data

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

Storage stability studies for residues of this active were reviewed during the evaluation for EU approval. The data was acceptable and is summarised in the EU Draft Assessment Reports (DAR).

Table 7-19: 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			
Cereal grain	High starch content	24 months	Fluroxypyr AR, Vol. 3, B.7, Oct 2009
Cereal straw	Dry matrix	24 months	
Immature plant	High water content	24 months	
Animal products			
Egg	-	202 days	
Poultry muscle	-	202 days	
Poultry liver	-	56 days	

The applicant points out that the fluroxypyr Renewal Assessment Report clarified that the report by Teasdale, R (1996) included storage stability for both cereals and pasture. Although not specified in the title of the report, the storage stability of fluroxypyr in pasture was determined as detailed in the results section. Therefore, data submitted by the notifier for the Annex I Inclusion of fluroxypyr in cereals and pasture was considered acceptable for the evaluation of storage stability and is sufficient to be used in the evaluation of the product KINVARA.

Brief details of the report by Teasdale, R (1996) are provided below.

Annex Point	IIIA 8.1/03
Reference	Fluroxypyr AR, Vol. 3, B.7, Oct 2009
Title	Frozen storage stability of fluroxypyr in winter wheat immature plant, grain and straw.
Author/Year	Teasdale, R (1996)
Guideline	GLP

Method
Samples of wheat immature plant and straw were fortified with fluroxypyr (99.2% purity) at a rate of 2.0 mg/kg and wheat grain at a rate of 0.5 mg/kg. Samples were then frozen and stored at < - 18°C for up to 24 months. Storage stability was also assessed for egg, chicken fat, muscle and liver. Samples of eggs, muscle and liver were prepared by spiking each type of tissue with fluroxypyr at the 1 mg/kg level.

Result
Fluroxypyr residues in wheat immature whole plant, grain and straw are stable for periods of storage at <-18ºC of up to 24 months (730 days). The longest frozen storage periods for samples used to generate residue data were 433 days for cereal matrices and 544 days for maize matrices and 463 days for pasture. Fluroxypyr was shown to be stable under frozen storage conditions in eggs and chicken muscle for up to 202 days, and in liver for up to 56 days.

Conclusion
The presented data is therefore considered acceptable for evaluation of storage stability of fluroxypyr.

Conclusion on stability of residues during storage

Sufficient storage stability data are available to support the intended uses.

Animal Matrices
The fluroxypyr Renewal Assessment Report clarified that the below report included storage stability on animal matrices for the active substance, fluroxypyr. Although not specified in the title of the report, the storage stability of fluroxypyr in animal matrices was determined as detailed in the results section. Therefore, data submitted by the notifier for the Annex I Inclusion of fluroxypyr in animal matrices was considered acceptable for the evaluation of storage stability and is sufficient to be used in the evaluation of the product KINVARA.

Annex Point	IIIA 8.1/04
Reference	Fluroxypyr AR, Vol. 3, B.7, Oct 2009
Title	Determination of residues of fluroxypyr in eggs, muscles, liver and fat from chickens administered Fluroxypyr herbicide.
Author/Year	XXXX (1990)
Guideline	GLP

Method
Samples of eggs, muscle and liver were prepared by spiking each type of tissue Fluroxypyr at the 1 mg/kg level.

Result
Fluroxypyr was shown to be stable under frozen storage conditions in eggs and chicken muscle for up to 202 days, and in liver for up to 56 days. These periods exceed those before analysis of animal tissues in animal feeding and metabolism studies.

Conclusion
The presented data is therefore considered acceptable for evaluation of storage stability of fluroxypyr.

The intended uses of KINVARA (cereals) are considered to be covered by the storage stability of fluroxypyr in wheat (grain and forage). Fluroxypyr residues were stable in water containing materials and dry commodities up to 24 months.
Although further information on the storage conditions of the samples from the livestock feeding study would be desirable this is not a data requirement for KINVARA but should be addressed as part of the renewal of the active ingredient fluroxypyr at EU level.

zRMS agrees with the above consideration of the applicant.

7.3.1.2 Stability of residues in sample extracts (KCA 6.1)

Please refer to Section 7.3.1.1 above.

Conclusion on stability of residues in sample extracts

Sufficient data are available to support the intended uses.

zRMS agrees with the above consideration of the applicant.

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.

Studies on the metabolism of this active substance in plants were reviewed during the evaluation for EU approval. The data was acceptable and is summarised in the EU Draft Assessment Reports (DAR). The studies are also summarised below.

Table 7-20: 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	Spring wheat	2,6-^{14}C ring labelled fluroxypyr-meptyl (MHE)	Foliar, F	0.3	1	Whole plant: 0 Stalk and leaves; heads: 28 Straw and grain: 62		Fluroxypyr DAR, Vol. 3, B.7, Oct 2009, Ireland, 2011 EFSA, 2013
	Spring wheat	2,6-^{14}C ring labelled fluroxypyr-meptyl (MHE)	Foliar, G	0.6	1	Wheat forage: 0, 13 Straw and grain: 62		
	Winter wheat	2,6-^{14}C ring labelled fluroxypyr-meptyl	Foliar, F @BBCH 31	0.2	1	Whole plant: 0, 3, 7, 14, 28 Straw and grain: 104		Ireland, 2011 EFSA, 2013
		2,6-^{14}C ring labelled fluroxypyr-butoxypropyl ester (BPE)	Foliar, F @BBCH 31	0.2	1			

Crop Group	Crop	Label position	Application and sampling details					Reference
			Method, F or G (a)	Rate (kg a.s./ha)	No	Sampling (DAT)	Remarks	
Broadleaved weeds	Weed	Not specified	Foliar	0.15	1	7	Indicative information only.	DAR, Germany, 1996 EFSA, 2013
	Weed	2,6-^{14}C ring labelled fluroxypyr-meptyl	Foliar, G	0.075	1	1, 7		

Summary of plant metabolism studies reported in the EU

Residue Definition: "*fluroxypyr, its esters, salts and its conjugates expressed as fluroxypyr*"

Annex Point	IIIA 8.2/12
Reference	Fluroxypyr DAR, Vol. 3, B.7, Oct 2009
Title	The metabolism of ^{14}C-DOWCO MHE in spring wheat and soil after field application
Author/Year	Hawkins DR, Kirkpatrick D, Conway B, Finn CM, Powell GP (1981)
Guideline	Non GLP

Annex Point	IIIA 8.2/13
Reference	Fluroxypyr DAR, Vol. 3, B.7, Oct 2009
Title	Metabolism of ^{14}C-Fluroxypr in wheat
Author/Year	Puvanesarajah V, Stewart RC (1991)
Guideline	GLP

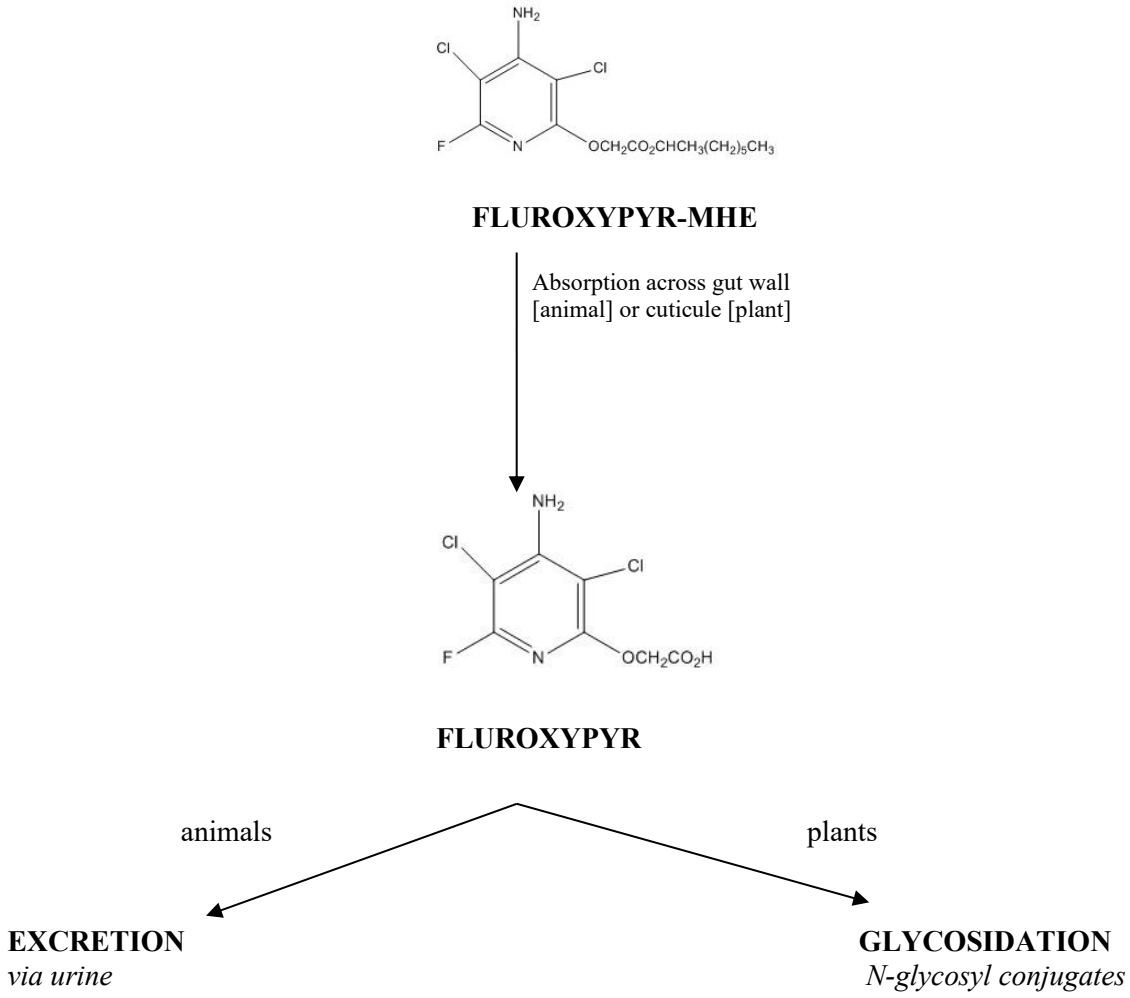
Annex Point	IIIA 8.2/14
Reference	Fluroxypyr DAR, Vol. 3, B.7, Oct 2009
Title	Comparative Metabolism of [^{14}C]-Fluroxypyr butoxypropyl ester and [^{14}C]-Fluroxypyr methylheptyl ester in winter wheat
Author/Year	Caley CY, O' Boyle F (1995)
Guideline	GLP

Two wheat metabolism studies *(Hawkins, 1981 and Puvanesarajah, 1991)* were submitted and accepted for the foliar application of fluroxypyr under the original EU evaluation. The studies were conducted with [^{14}C-fluroxypyr-MHE (4-amino-3,5-dichloro-6-fluoro-2,6-[^{14}C]-2-pyridinyloxyacetic acid 1-methylheptylester) applied at exaggerated rates. Both studies demonstrated that fluroxypyr-MHE was shown to be partially absorbed from a foliar application. Fluroxypyr-MHE appeared to be mainly residuent on the plant surface where it was either lost by "weathering" or absorbed and translocated into the cuticula where hydrolysis took place to form the parent acid. These residues are translocated within the plant to the vegetation tips. At harvest levels were generally low in grain (<0.1 mg/kg) form applications up to 150% the maximum recommended rate, whilst in straw a range of 3.0-79 mg/kg were present. The bulk of the residue was shown to be either fluroxypyr acid or a fluroxypyr conjugate and was readily extractable with a methanolic alkali procedure. Two further metabolism studies were accepted under the original EU evaluation.

The two studies conducted on broad leaved weeds were designed primarily to investigate the herbicidal mode of action of fluroxypyr 1-methylheptyl ester. Studies undertaken to measure uptake and behaviour within broad-leaved weed species indicated a similar fate to that in grass species. These results confirm the findings of the studies in the wheat metabolism studies in that following hydrolysis of the applied ester no other degradative step occurs in plants, with conjugation believed to be the route of detoxification. The metabolic pathway in plants is shown below.

It was concluded that on the basis of the studies presented that the most appropriate residue definition for fluroxypyr is "fluroxypyr and its ester fluroxypyr 1-MHE expressed as fluroxypyr'. It should also be noted that the notifier provided an additional wheat metabolism study (Caley, 1995) as part of the re-review process. The additional wheat metabolism study merely provides additional data and does not alter any of the End Points from the original plant metabolism evaluation. A full evaluation of the additional wheat metabolism study has not been reported here because plant metabolism has been adequately addressed under the original EU evaluation.

Proposed metabolic pathway for fluroxypyr in plants.



Conclusion on metabolism in primary crops

The requested uses in the GAP table are accommodated by the plant metabolism data previously reviewed at EU level, therefore the existing residue definitions apply.

7.3.2.2 Nature of residue in rotational crops (KCA 6.6.1)

Available data

No new data submitted in the framework of this application.

Data on the nature of residues was reviewed during the EU evaluation of fluroxypyr and was considered to be acceptable to support the respective representative uses.

Table 7-21: 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	^{14}C-pyridinyl fluroxypyr-MHE	Bare soil, F	0.6 & 0.7	30, 120 366	86, 113, 128 156, 200, 225 422, 443 & 77, 168 418	-	EFSA, 2013
Root and tuber vegetables	Turnip		Bare soil, F	0.6 & 0.7	30, 120 366	98, 183 438 & 91, 215 428	Roots and tops	
Pulses and oilseeds	Broad beans		Bare soil, F	0.6	30, 120 366	94, 119 441, 451	whole plant, beans	
	soya beans		Bare soil, F	0.6	120	226	Beans, trash	
Cereals	Wheat		Bare soil, F	0.6 & 0.7	30, 120 366 & 30, 120 365	128, 232 458 & 83, 156 202, 289 414, 467	Grains and straw & Immature plant, grain, chaff and straw	
	Corn		Bare soil, F	0.7	365	467	Fodder and grain	

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

Summary of plant metabolism studies reported in the EU

Under the original EU evaluation, rotational crop studies conducted with radiolabelled fluroxypyr on lettuce, turnips, broad beans, soya beans and wheat were evaluated and accepted. The analyses of succeeding crops indicated that all residues were below the LOD (0.02 mg/kg).

The notifier also provided an additional rotational crop study (Yaskovich, P.R., 1996) as part of the re-review process. The additional rotational crop study was conducted on wheat, lettuce and turnip. The highest residues were found in the crops 30 day after the last application (DAA) and ranged from 0.02 mg/kg in turnip foliage to 0.59 mg/kg in wheat straw. The 120 DAA and 365 DAA crops contained lower radioactive residues with the highest residue level being approx. 0.06 mg/kg in 120 DAA wheat straw.

Residues in edible crop parts were always below 0.10 mg/kg despite the fact that an exaggerated dose rate was used in the study.

Annex Point	IIIA 8.6/03
Reference	Fluroxypyr AR, Vol. 3, B.7, Oct 2009
Title	^{14}C Fluroxypyr-MHE: Confined accumulation study on rotational crops planted at 30, 120 and 366 days after soil treatment.
Author/Year	Lickly LS, Lardie TS, Miller JH, Baldwin WS (1990)
Guideline	GLP

A new confined rotational crop study (Lickly, L.S., 1990) was conducted to determine residues in crops grown in soil previously treated with fluroxypyr-MHE, either in the normal rotation or after crop failure the study used an application rate of 0.594 kg a.s./ha. The rotational crops were planted 30, 120 and 360 days after application (DAA) to soil. The rotational crop study results from the new study are in agreement with residue results from each older rotational crop study. It was not considered necessary to provide a full report for the new study considering the new rotational crop study is viewed as additional data. The new rotational crop study does not change the End points from the original EU evaluation.

Conclusion on metabolism in rotational crops

Data on the nature of residues reviewed during the EU evaluation of fluroxypyr is acceptable to support the proposed uses. It was concluded that the metabolism in rotational crops is similar to primary crops and that significant residues are not expected to be present in rotational crops (EFSA, 2011).

zRMS agrees with the above consideration of the applicant.

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.

It was concluded in the EU evaluation of fluroxypyr that processing studies were not required (EFSA, 2011). Furthermore, the MRL review (EFSA, 2013) concluded that residues exceeding 0.1 mg/kg are not expected (except for leek) and the chronic exposure does not exceed 10 % of the ADI, therefore investigation of processing on the nature and magnitude of the residues is desirable only.

Conclusion on nature of residues in processed commodities

It was concluded in the EU evaluation of fluroxypyr that processing studies were not required (EFSA, 2011). No further information is submitted or required.

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

Table 7-22: Summary of the nature of residues in commodities of plant origin

Endpoints (Fluroxypyr)	
Plant groups covered	Cereals (Wheat)
Rotational crops covered	Wheat, lettuce, turnip and broad beans (30, 120 and 360 day crop rotation), soya beans (120 day crop rotation).

Metabolism in rotational crops similar to metabolism in primary crops?	Yes
Processed commodities	Not provided and not required
Residue pattern in processed commodities similar to pattern in raw commodities?	Not applicable
Plant residue definition for monitoring	Fluroxypyr, its esters, salts and its conjugates expressed as fluroxypyr ~~(Reg. (EU) 2015/1040)~~ Reg. (EU) 2022/1363
Plant residue definition for risk assessment	Fluroxypyr, its esters, salts and its conjugates expressed as fluroxypyr (EFSA Conclusion on Article 12, 2013)
Conversion factor from enforcement to RA	None

zRMS agrees with the above consideration of the applicant.

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.

Studies on the metabolism of this active substance in livestock were reviewed during the evaluation for EU approval. The data was acceptable and is summarised in the EU Draft Assessment Reports (DAR) and the EFSA Conclusion for this active substance. The studies are also presented below.

Table 7-23: 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	^{14}C-2,6-ring labelled fluroxypyr acid	3 (1 control)	100 mg/kg feed (2 goats) 344 mg/kg feed (1 goat)	4	Milk	twice daily	Fluroxypyr DAR, Vol. 3, B.7, Oct 2009 EFSA, 2013
						Excreta	daily	
						Tissues	at sacrifice	
	Cow	^{14}C-fluroxypyr acid	1	20 g, single dose	-	-	-	
Laying poultry	Hens	^{14}C-fluroxypyr acid	15 (5 control)	0.663	10	Eggs	daily	
						Excreta	daily	
						Tissues	at sacrifice	

Summary of animal metabolism studies reported in the EU

Residue Definition: "*fluroxypyr and its salts expressed as fluroxypyr*"

Annex Point	IIIA 8.2/15
Reference	Fluroxypyr DAR, Vol. 3, B.7, Oct 2009
Title	The fate of ^{14}C labelled Fluroxypyr fed to laying hens
Author/Year	XXXX (1989)
Guideline	GLP

Annex Point	IIIA 8.2/16
Reference	Fluroxypyr DAR, Vol. 3, B.7, Oct 2009
Title	The excretion and tissue levels of radioactivity in a dairy cow after oral administration of ^{14}C DOWCO 433 acid
Author/Year	XXXX (1985)
Guideline	GLP

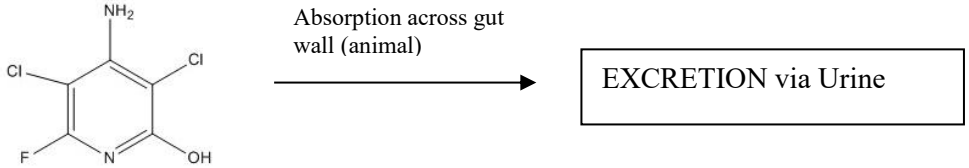
Annex Point	IIIA 8.2/17
Reference	Fluroxypyr DAR, Vol. 3, B.7, Oct 2009
Title	The fate of ^{14}C labelled fluroxypyr fed to lactating goats
Author/Year	XXXX (1990)
Guideline	GLP

Three animal metabolism studies (hen, cow and goat) were evaluated under the original EU evaluation. The test material in these experiments was fluroxypyr acid. Administration of fluroxypyr acid is justified because this is the most relevant residue in plants used for animal nutrition. In addition, investigations in rats have shown that the ester (Fluroxypyr 1-MHE) is metabolised to the acid and that both are pharmacokinetically equivalent. Laying hens were exposed orally to ^{14}C -Fluroxypyr acid (9.77 mg/kg in the diet or 0.663 mg/kg bw/day) for 10 days. In a dairy cow, the excretion of radioactivity was studied after a single oral dose of ^{14}C-Fluroxypyr acid (approx. 20 g). In a goat metabolism study, two lactating goats received orally administered ^{14}C-Fluroxypyr acid at a level equivalent to 100mg/kg in feed for four consecutive days. A third goat was similarly dosed at the equivalent of 344 mg/kg in feed. A fourth goat was given placebo doses containing no chemical and served as a control.

It was accepted under the original EU evaluation that the three metabolism studies indicated that fluroxypyr acid was the major residue detected in all animal matrices tested. The three metabolism studies also noted that unchanged fluroxypyr acid is rapidly excreted. The highest residue level of fluroxypyr found in poultry was in the liver with an average level of 0.005 mg/kg and gizzard with an average level of 0.01mg/kg. Residues were below 0.01mg/kg in all other poultry tissues. No measurable level of fluroxypyr appeared in eggs. In the ruminant metabolism studies the vast majority of the recovered activity was found in the urine and faeces, while only 0.05% was found in tissues or milk. Fluroxypyr was the major residue detected in urine, faeces, milk, liver and kidney tissue samples.

On the basis of the information provided, it was agreed that the animal residue definition should be "fluroxypyr acid" only. No additional animal metabolism studies were provided for the re-review.

The proposed metabolic pathway for fluroxypyr-MHE in animals is presented below.



Fluroxypyr acid

Under the original evaluation, a comparison of the animal and rat metabolism studies indicated that both animal and rats provide the same metabolic profile. On the basis of this information it was decided that it was not necessary to conduct a metabolism study for pigs.

Confirmatory data submitted to the RMS, Ireland, confirmed the fate of the fluroxypyr esters in animal matrices; described below.

Fluroxypyr Confirmatory Data - Fate of the fluroxypyr esters in animal matrices

It should be noted that plant metabolism studies have demonstrated that fluroxypyr esters are typically converted to the acid in plant matrices, however these same studies have also shown that fluroxypyr esters will be present, but to a lesser extent than their acid counter parts in forage, straw and grain 1,2.

It has been estimated that cattle ruminate for approximately 6-10 hours a day food passes from the rumen and reticulum (slightly acidic to neutral pH) through the abomasums (acidic pH) to the small intestines (basic pH, due to bile) 3. Food passage in dairy cattle is very dependent on type of feed 4 but estimated time in reticulo-rumen is 60-80 hours for digestible feed or up to 10 days for straw. From the omasum through abomasum to duodenum digestion is from 11 hours to 60 hours depending on digestibility of feed. Feed in the small intestines takes 2.2 to 4.5 hours and 10-26 hours in the large intestine. Studies on passage of ingesta through the GI tract as a whole indicate that the first part of an ingested diet can start appearing within 12-24 hours with 80% passed in 70-90 hours and 7-10 days before the entire meal (*ca.* 100%) is passed. The pH of the rumen varies with the type of feedstuff eaten-roughage diets cause higher pH's (estimated 6.9 to 6.5) and concentrate type diets cause lower pH's (estimated 6.2 to 5.7). Rumen pH reaches a low 2-6 hours after feeding. Rumen acidosis occurs at approximately a pH of 5.5 in cattle. The abomasum has a pH similar to people (2 to 4). The small intestine has a pH of 7 to 9.

Fluroxypyr butoxyethyl ester (BPE) and fluroxypyr methylheptyl ester (MHE) are stable to hydrolysis at acidic pH, and degrade to fluroxypyr-acid with half-lives of 3.6 and 4.8 days at neutral pH, respectively, and DT50 of approximately 2 hours at pH 9 5,6. Therefore, during the time required for digestion, especially the time spent in the basic small intestine, the esters of fluroxypyr would be converted to fluroxypyr-acid.

Limited data in rats indicate that fluroxypyr MHE undergoes hydrolysis to the acid 7. The data suggests that fluroxypyr and its 1-methylheptyl ester (MHE) are absorbed rapidly across the gut following oral ingestion. The ester undergoes hydrolysis to the parent acid which is then virtually eliminated, unchanged, in the urine within 24 hours. No significant levels of metabolite are detectable in urine or other tissues including milk. The study indicated that the absence of bile depressed intestinal absorption of fluroxypyr MHE. Since bile is basic, it is likely that fluroxypyr MHE is hydrolysed to fluroxypyr-acid before absorption. Therefore, the metabolism of fluroxypyr MHE would be identical to the metabolism of fluroxypyr-acid. In other words, a combination of hydrolysis to the acid, and absorption and metabolism of fluroxypyr-acid occurs in the intestines. Fluroxypyr esters would be converted to fluroxypyr-acid before being distributed throughout the animal, and therefore no different residues would be expected in the edible tissues from consumption of either fluroxypyr esters or fluroxypyr-acid.

Annex Point	IIIA 8.2/13
Author	Hamburg, A. W., Puvanesarajah, V. (1991)
Reference	LLC GH-C 2650
Title	Metabolism of [14C]Fluroxypyr MHE in Wheat, unpublished
GLP	Not stated

Annex Point	IIIA 8.2/14
Author	O"Boyle, F. and Caley, C. Y. (1995)
Reference	LLS GHE-P-4236

Title	Comparative Metabolism of [14C]-Fluroxypyr Butoxypropyl Ester and [14C]-Fluroxypyr Methylheptyl Ester in Winter Wheat, unpublished
GLP	Not stated

Annex Point	IIIA 8.2/18
Author	John Moran (2005)
Reference	LLS GHE-P-4236
Title	Tropical dairy farming: feeding management for small holder dairy farmers in the humid tropics, Lanilinks Press
GLP	No

Annex Point	IIIA 8.2/19
Author	D. C. Church (1988)
Reference	LLS GHE-P-4236
Title	The Ruminant Animal: Digestive Physiology and Nutrition
GLP	No

Annex Point	IIIA 8.2/20
Author	Reeves, G. L. (1995)
Reference	LLS GHE-P-4191
Title	The Hydrolysis of [14C]-Fluroxypyr-1-Butoxypropyl Ester, unpublished
GLP	No

Annex Point	IIIA 8.2/21
Author	Knowles, S. J. and Cowlyn, T. C. (1991)
Reference	LLS GHE-P-2542
Title	Fluroxypyr Methyl Ester (Technical) : Determination of Hydrolysis as a Function of pH, unpublished
GLP	No

Annex Point	IIIA 8.2/22
Author	Not Stated (1990)
Reference	NA
Title	STARANE* Herbicides (FLUROXYPYR) Pharmacokinetic and Metabolic Behaviour in Mammals
GLP	No

Conclusion on metabolism in livestock

The requested uses in the GAP table are accommodated by the livestock metabolism data previously re-viewed at EU level, therefore the existing residue definitions apply.

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

Table 7-24: Summary on the nature of residues in commodities of animal origin

	Endpoints (Fluroxypyr)
Animals covered	Lactating goats (using fluroxypyr)
	(Poultry and cow studies informative only; no characterisation of the nature of the residues)
Time needed to reach a plateau concentration	3 days in milk
	Not mentioned in EFSA Conclusion

Animal residue definition for monitoring	Fluroxypyr and its salts expressed as fluroxypyr (EFSA Conclusion on Article 12, 2013) Reg. (EU) 2022/1363
Animal residue definition for risk assessment	Fluroxypyr, its esters, salts and its conjugates expressed as fluroxypyr (EFSA Conclusion on Article 12, 2013)
Conversion factor	None
Metabolism in rat and ruminant similar	Yes
Fat soluble residue	Fluroxypyr-MHE – Yes Fluroxypyr - No

zRMS agrees with the above consideration of the applicant.

7.3.3 Magnitude of Fluroxypyr residues in plants (KCA 6.3)

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

New studies on the magnitude of residue have been submitted by the applicant in the framework of this application. These studies are summarized in the table below. The detailed assessment of these studies is presented in Appendix 2. Unprotected trials data to cover the magnitude of residues in grassland (pasture) were evaluated as part of the EU Peer Review of the pesticide risk assessment of the active substance fluroxypyr (EFSA Journal 2011;9(3):2091) and are relied upon in support of the proposed uses of KINVARA on grassland.

Table 7-25: Summary of EU reported and new data supporting the intended uses of KINVARA and conformity to existing MRL (Fluroxypyr)

Commodity	Source	Residue zone (N-EU, S-EU, EU, outside EU)	Evaluation GAP Residue levels (mg/kg) [a]	STMR (mg/kg)	HR (mg/kg)	Unrounded OECD calculator MRL (mg/kg)	Current EU MRL (mg/kg) *	MRL compliance
Wheat grain→ Triticale, rye grain	Witte, A. (2015) TRC14-045	NEU	Trials GAP: 1 x 0.161 kg a.s./ha, BBCH 39, outdoor <0.01, 0.01, 0.02, 0.04	-				
	Overall supporting data for cGAP	NEU	**KINVARA cGAP: 1 x 0.150 kg a.s./ha, BBCH 39, outdoor** <0.01, 0.01, 0.02, 0.04	0.015	0.04	0.077	0.1	Yes
Wheat straw→ Triticale, rye straw	Witte, A. (2015) TRC14-045	NEU	Trials GAP: 1 x 0.161 kg a.s./ha, BBCH 39, outdoor 0.80, 1.09, 1.45, 3.22	-				
	Overall supporting data for cGAP	NEU	**KINVARA cGAP: 1 x 0.150 kg a.s./ha, BBCH 39, outdoor** 0.80, 1.09, 1.45, 3.22	1.27	3.22	Not relevant for animal feed commodities		
Barley grain→ Oat grain	Witte, A. (2015) TRC14-059	NEU	Trials GAP: 1 x 0.161 kg a.s./ha, BBCH 39, outdoor <0.01, 0.02, 0.03, 0.10	-				

	DAR trials (EFSA, 2011)	NEU	Trials GAP: 1 x 0.150-0.200 kg a.s./ha, BBCH 37-45, outdoor 11x <0.05					
	Overall supporting data for cGAP	NEU	**KINVARA cGAP: 1 x 0.150 kg a.s./ha, BBCH 39, outdoor** <0.01, 0.019, 0.028, 11x<0.05, 0.093	0.05	0.093	0.12**	0.1	Yes**
Barley straw→ Oat straw	Witte, A. (2015) TRC14-059	NEU	Trials GAP: 1 x 0.161 kg a.s./ha, BBCH 39, outdoor 0.74, 0.99, 1.48, 1.99	-				
	Overall supporting data for cGAP	NEU	**KINVARA cGAP: 1 x 0.150 kg a.s./ha, BBCH 39, outdoor** 0.74, 0.99, 1.48, 1.99	1.235	1.99	Not relevant for animal feed commodities		
Grassland (pasture)	DAR trials (EFSA, 2011)	NEU	EU cGAP: 1 x 0.200 kg a.s./ha, PHI = 7 days 0.95, 2.77, 6.41, 6.97, 8.26	-				
	Overall supporting data for cGAP	NEU	**KINVARA cGAP: 1 x 0.150 kg a.s./ha, March - September, PHI = 7 days** 0.95, 2.77, 6.41, 6.97, 8.26	6.41	8.26	Not relevant for animal feed commodities		

* Source of EU MRL: Reg (EU) No 2022/1363
(a) Definition of residue for enforcement and risk assessment are the same: Fluroxypyr, its esters, salts and its conjugates expressed as fluroxypyr
** Proportionality approach (values in brackets) has been applied. Considering the individual scaled residues the current MRL is not exceeded. The dataset demonstrates that when KINVARA is applied in accordance with the intended GAP, residues within the current MRL are expected. See also additional information below this table.

Additional information

The current fluroxypyr EU MRL in wheat, barley, rye and oats (0.1 mg/kg, ~~Reg. (EU) 2021/1098~~ Reg (EU) No 2022/1363) was established using the old EU MRL calculator. Subsequently, the EU MRL calculator has been updated and when inputting the residue data from the DAR (Ireland 2009), gives a rounded EU MRL value of 0.15 mg/kg. Similarly, when inputting either the new residue data from the KINVARA dRR section 7 alone, or a combination of the residue data from both the DAR and the dRR, the new EU MRL calculator also gives a rounded MRL value of 0.15 mg/kg. The apparent exceedance of the EU MRL is not therefore related to the data set supporting KINVARA, but an issue with the current fluroxypyr EU MRL in wheat, barley, rye and oats itself, which should be addressed outside the scope of this product submission.

In addition, the use proposed for KINVARA on cereals (wheat, barley, rye, triticale) will not result in residues of fluroxypyr at levels exceeding the current EU MRL in wheat, barley, rye and oats (0.1 mg/kg, ~~Reg. (EU) 2021/1098~~ Reg (EU) No 2022/1363). The EU MRL calculator builds in a number of contingencies which have resulted in an apparent exceedance of the current EU MRL when using the new residue trials data provided in the dRR.

It is noted that the residue data evaluated at Annex I listing and subsequently considered during fluroxypyr active substance renewal were conducted at a more critical GAP compared with the representative use proposed for this product application (1 x 0.4-0.5 kg a.e./ha, up to BBCH 45, compared with 1 x 0.2 kg a.e./ha, up to BBCH 39), however these trials were sufficient to support the proposed critical GAP and did not result in fluroxypyr residues in grain exceeding the current EU MRL of 0.1 mg/kg (residue trials results ranging from <0.05 – 0.09 mg/kg in cereal grain). The data considered during the renewal for fluroxypyr was also considered during the review of existing EU MRLs for fluroxypyr and was sufficient to support the current EU MRL.

In addition, the plant metabolism data for fluroxypyr in cereals, evaluated during Annex I listing and considered during active substance renewal were also considered in support of this product submission and demonstrated that at application rates of up to 2.7N (1 x 0.6 kg a.e./ha), fluroxypyr residues in grain were ≤ 0.02 mg/kg (less than the current EU MRL of 0.1 mg.kg).

There is sufficient evidence to demonstrate that the uses proposed of KINVARA on cereals will not result in fluroxypyr residues in grain exceeding the current EU MRL of 0.1 mg/kg.

zRMS definitely agrees with the above consideration of the applicant.

7.3.3.2 Conclusion on the magnitude of residues in plants

A total of 4 trials, each, were performed in wheat and barley in Northern Europe. Trials were performed according to the intended GAP to support the registration of KINVARA on wheat, triticale, rye, barley and oat in the Northern European residues zone.
According to SANTE/2019/12752, since the application is performed before the edible part is formed, and as wheat data can be extrapolated to barley and *vice versa*, it can be concluded that the existing dataset of eight trials (wheat/barley) in Northern Europe is sufficient to extrapolate to triticale, oats and rye.
According to the available data, the intended uses on wheat, triticale, barley, rye and oats are considered acceptable. The data submitted show that no exceedance of the MRL will occur.
Unprotected trials data in grassland previously evaluated at EU level (EFSA, 2011) cover a more critical GAP than that proposed for KINVARA (0.200 vs 0.150 kg a.s./ha), therefore are considered acceptable in support of the proposed uses of KINVARA on grassland.

Accepted. zRMS agrees with the above consideration of the applicant.

7.3.4 Magnitude of residues in livestock

7.3.4.1 Dietary burden calculation

Cereal grain, cereal straw, grass and wheat and barley processed commodities may form a part of livestock diets in the EU. Livestock dietary burden calculations have been performed taking into account commodities from the proposed uses of KINVARA that might be used as animal feed, alongside the inputs used in the Article 12 MRL review of fluroxypyr (EFSA, 2013).
The potential dietary exposure to fluroxypyr has been calculated using the EFSA model (2017). The dietary inputs into the animal diet according to the EU model are summarised in Table 7-26.
The highest residues in supervised trials are used to calculate the maximum potential dietary intake except for feed commodities that are bulked or processed where the STMR is used.

Table 7-26: 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: *Fluroxypyr, its esters, salts and its conjugates expressed as fluroxypyr*				
Barley - straw	1.24	STMR Barley (this submission)	1.99	HR Barley (this submission)
Oat - straw	1.24	STMR Barley (this submission)	1.99	HR Barley (this submission)
Rye - straw	1.27	STMR Wheat (this submission)	3.22	HR Wheat (this submission)
Triticale - straw	1.27	STMR Wheat (this submission)	3.22	HR Wheat (this submission)
Wheat - straw	1.27	STMR Wheat (this submission)	3.22	HR Wheat (this submission)
Barley - grain	0.05	STMR Barley (this submission)	-	-
Oat - grain	0.05	STMR Barley (this submission)	-	-
Rye - grain	0.015	STMR Wheat (this submission)	-	-
Triticale - grain	0.015	STMR Wheat (this submission)	-	-
Wheat - grain	0.015	STMR Wheat (this submission)	-	-
Brewer's grain - dried	0.08	STMR (Barley) x default PF	-	-
Distiller's grain - dried	0.05	STMR (Wheat) x default PF	-	-
Wheat gluten - meal	0.03	STMR (Wheat) x default PF	-	-
Wheat - milled by-products	0.11	STMR (Wheat) x default PF	-	-

Feed Commodity	Median dietary burden		Maximum dietary burden	
	Input value (mg/kg)	Comment	Input value (mg/kg)	Comment
Grass (fresh)	6.41	STMR Grass	8.26	HR Grass x default PF
Grass, silage	10.26	STMR Grass x default PF	13.22	HR Grass x default PF
Grass, hay	22.44	STMR Grass x default PF	28.91	HR Grass x default PF
Apple pomace	0.05	EFSA, 2013	0.05	EFSA, 2013

Table 7-27: Results of the dietary burden calculation

Animal species	Median dietary burden (mg/kg bw/d)	Maximum dietary burden (mg/kg bw/d)	Highest contributing commodity	Max dietary burden (mg/kg DM)	Trigger exceeded (Y/N)	Article 12 Max DB (mg/kg DM)
Risk assessment residue definition: *Fluroxypyr, its esters, salts and its conjugates expressed as fluroxypyr*						
Beef cattle*	0.593	0.764	Grass, silage	19.86	Y	85.19
Dairy cattle*	0.593	0.764	Grass, silage	19.86	Y	86.34
Ram/ewe	0.812	1.046	Grass, forage	31.39	Y	-
Lamb	0.812	1.046	Grass, forage	31.39	Y	-
Breeding swine	0.120	0.154	Grass, forage	6.68	Y	-
Finishing swine*	0.120	0.154	Grass, forage	6.68	Y	12.91
Broiler poultry	0.013	0.028	Wheat, straw	0.41	Y	-
Layer poultry*	0.013	0.028	Wheat straw	0.41	Y	0.068

* These categories correspond to those (formerly) assessed at EU level.
** Although the most recent dietary burden calculator has been used, the old trigger value of 0.1 mg/kg DM remains valid, as the active substance falls under the old data requirements.

Use of the most recent EFSA dietary burden calculator (model 2017) along with the data presented in this submission, modifies the theoretical maximum daily intake for animals. However, the maximum dietary intakes for the species formerly assessed at EU level are within those considered in the Article 12 review of MRLs, with the exception of layer poultry. The poultry metabolism study was conducted at 0.663 mg/kg bw/d (17N the calculated maximum poultry dietary burden) and no residues above 0.01 mg eq./kg were detected in muscle, eggs, liver and fat (EFSA, 2013). It can therefore be concluded that residues in poultry commodities arising from the use of KINVARA will be <0.01 mg/kg and fall within the current EU MRL (0.01* mg/kg).
The current animal MRLs are therefore sufficient to accommodate the use of KINVARA in accordance with the intended GAP.

7.3.4.2 Livestock feeding studies (KCA 6.4.1-6.4.3)

Available data

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

Livestock feeding studies with the active substance fluroxypyr were reviewed and evaluated in the original EU evaluation and are considered sufficient to describe the behaviour of the formulated product, which is comparable in its proposed uses to the representative uses considered during EU evaluation. Therefore, no new studies are being submitted. Please refer to out of protection data from the original dossier submission.

Summary of animal metabolism studies reported in the EU

The following livestock feeding studies in ruminants and poultry were submitted and evaluated during the Annex I inclusion of fluroxypyr.

Annex Point	IIIA 8.4/05
Reference	Fluroxypyr DAR, Vol. 3, B.7, Oct 2009
Title	The fate of ^{14}C labelled Fluroxypyr fed to laying hens
Author/Year	XXXX (1989)
Guideline	GLP
Annex Point	IIIA 8.4/06
Reference	Fluroxypyr DAR, Vol. 3, B.7, Oct 2009
Title	The excretion and tissue levels of radioactivity in a dairy cow after oral administration of ^{14}C DOWCO 433 acid
Author/Year	XXXX (1985)
Guideline	GLP

Annex Point	IIIA 8.4/07
Reference	Fluroxypyr DAR, Vol. 3, B.7, Oct 2009
Title	The fate of ^{14}C labelled fluroxypyr fed to lactating goats
Author/Year	XXXX (1990)
Guideline	GLP
Annex Point	IIIA 8.4/08
Reference	Fluroxypyr DAR, Vol. 3, B.7, Oct 2009
Title	DOWCO 433 (fluroxypyr) residues in milk and tissue
Author/Year	XXXX (1986)
Guideline	GLP
Annex Point	IIIA 8.4/09
Reference	Fluroxypyr DAR, Vol. 3, B.7, Oct 2009
Title	Determination of residues of fluroxypyr in eggs, muscle, liver and fat tissues from chickens administered fluroxypyr herbicide
Author/Year	XXXX (1990)
Guideline	GLP

Overall Conclusion
The results from the livestock feeding studies in ruminant and poultry submitted and evaluated as part of Annex I inclusion were deemed acceptable.

Conclusion on feeding studies

The requested uses modify the theoretical maximum daily intake for animals, but in general they fall within the risk envelope considered in the Article 12 MRL review (EFSA, 2013), therefore the current animal MRLs accommodate the use of KINVARA. Regarding poultry intakes, reference to the poultry metabolism data demonstrates that there is no risk for the current poultry MRL to be exceeded.

zRMS: Acceptable.

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

No new data submitted in the framework of this application.

It was concluded in the EU evaluation of fluroxypyr that processing studies were not required (EFSA, 2011). Furthermore, the MRL review (EFSA, 2013) concluded that residues exceeding 0.1 mg/kg are not expected (except for leek) and the chronic exposure does not exceed 10 % of the ADI, therefore investigation of processing on the nature and magnitude of the residues is desirable only. No further consideration is required.

Accepted. zRMS agrees with the above consideration of the applicant.

7.3.6 Magnitude of residues in representative succeeding crops

See 7.3.2.2.
Data not submitted or required.

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 KINVARA. Therefore, other special studies are not 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). As ARfD was not deemed necessary, acute risk assessment is not relevant.

7.3.8.1 Input values for the consumer risk assessment

Table 7-28: Input values for the consumer risk assessment

Commodity	Chronic risk assessment		Acute risk assessment	
	Input value (mg/kg)	Comment	Input value (mg/kg)	Comment
Fluroxypyr (sum of fluroxypyr, its salts, its esters, and its conjugates, expressed as fluroxypyr)				
Barley	0.05	STMR (This submission)	An ARfD was not deemed necessary – an acute risk assessment is not relevant.	
Oat	0.05	STMR (This submission, extrapolated from barley)		
Rye	0.015	STMR (This submission, extrapolated from wheat)		
Wheat	0.015	STMR (This submission)		
Commodities of animal origin	Current EU MRL	Reg (EU) 2022/1363		
All other commodities	Current EU MRL	Reg (EU) 2022/1363		

7.3.8.2 Conclusion on consumer risk assessment

Extensive calculation sheets are presented in Appendix 3.

Table 7-29: Consumer risk assessment

TMDI (% ADI) according to EFSA PRIMo (the report has to be repasted into the RR)	0.7 % (based on NL toddler)
IEDI (% ADI) according to EFSA PRIMo	0.6 % (based on NL toddler)
IESTI (% ARfD) according to EFSA PRIMo*	N/A
NTMDI (% ADI) **	N/A
NEDI (% ADI)**	N/A
NESTI (% ARfD) **	N/A

* include raw and processed commodities if both values are required for PRIMo
** if national model is available
N/A Not applicable, as no ARfD is defined.

The proposed uses of fluroxypyr in the formulation KINVARA do not represent unacceptable chronic risks for the consumer. No acute risk assessment is necessary, as no ARfD is proposed.

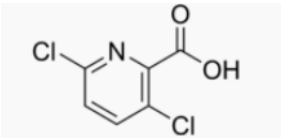
zRMS agrees with the above text.

7.4 Clopyralid

XXXX have access to the Dow AgroSciences S.A.S. data evaluated for the renewal of clopyralid (EFSA Journal 2018;16(8):5389).

General data on clopyralid are summarised in the table below (last updated 2021/12/18)

Table 7-30: General information on clopyralid

Active substance (ISO Common Name)	Clopyralid
IUPAC	3,6-dichloropyridine-2-carboxylic acid or 3,6-dichloropicolinic acid
Chemical structure	
Molecular formula	$C_6H_3Cl_2NO_2$
Molar mass	191.96 g/mol
Chemical group	picolinic acid herbicides, pyridine herbicides
Mode of action (if available)	By disrupting plant growth processes
Systemic	Yes
Company*	Dow AgroSciences S.A.S.
Rapporteur Member State (RMS)	FI (PL as co-RMS)
Approval status	Approved 01/10/2021 - Reg. (EU) No 540/2011 (Reg. (EU) No 2021/1191 -19th July 2021)
Restriction	-
Review Report	SANTE/10206/2021 Rev 1 20 May 2021
Current MRL regulation	Reg. (EU) 2021/1807 Applicable from: 03/11/2021
Peer review of MRLs according to Article 12 of Reg No 396/2005 EC performed	No
EFSA Journal: Conclusion on the peer review	Yes EFSA Journal 2018;16(7):5389
EFSA Journal: conclusion on Article 12	No
Current MRL applications on intended uses	No

* Notifier in the EU process to whom the a.s. belong(s)

7.4.1 Stability of Residues (KCA 6.1)

7.4.1.1 Stability of residues during storage of samples

Available data

No new data submitted in the framework of this application.

Storage stability studies for residues of this active were reviewed during the evaluation for EU approval

(EFSA, 2006) and renewal (EFSA, 2018). The data was acceptable and is summarised in the EU Draft Assessment Report (DAR) and Renewal Assessment Report (RAR).

Table 7-31: 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			
Maize grain	High starch content	13 months	Clopyralid RAR, 2017 EFSA, 2018
Maize fodder	Dry commodity	13 months	
Maize forage	High water content	13 months	
Pasture	High water content	17 months	
Rapeseed	High oil content	24 months	
Animal products			
Bovine muscle	-	19 months	Clopyralid RAR, 2017 EFSA, 2018
Bovine kidney	-	19 months	
Bovine liver	-	19 months	
Bovine fat	-	24 months	
Milk	-	19 months	
Eggs	-	19 months	

Summary of plant storage stability data reported in the EU

In the clopyralid DAR storage stability studies indicated that clopyralid was stable for at least 12 months (382 days) in maize grain, forage and fodder and 17.3 months in pasture (520 days). These studies cover starch and water containing commodities. Although no data is available for freezer storage stability of clopyralid in oil containing commodities, this did not obstruct the Annex I inclusion of clopyralid nor was it detailed as a confirmatory data requirement. This was based on the case that clopyralid is relatively stable within plant tissues and the studies in plant metabolism have indicated that radioactivity labelled residues of clopyralid are mainly distributed in straw than in seed of oilseed rape. Furthermore, oilseed rape is not a use for which KINVARA will be applied.

The storage stability data presented on maize covers the high starch content category, while pasture covers the high water content category. In accordance with OECD 506 cereal grain (wheat, barley, rye and oats) comes under the high starch content commodity category and its storage stability profile is therefore covered by that presented on maize.

Additional storage stability data have been evaluated in the RAR (Finland, 2017) for high acid and high oil content commodities that are not considered relevant to the proposed uses of KINVARA.

In conclusion the Annex II data submitted by the notifier for the Annex I Inclusion of clopyralid in maize and pasture was considered acceptable for the evaluation of storage stability and is sufficient to be used in the evaluation of the product KINVARA.

Summary of animal storage stability data reported in the EU

In the clopyralid RAR (Finland, 2017) residues of clopyralid were confirmed as being stable in bovine muscle, liver, kidney, milk and poultry eggs for up to 19 months when stored at -20 ±10 °C. XXXX have a letter of access (LoA) from the notifier (Dow AgroSciences) for these data.

Conclusion on stability of residues during storage

Sufficient storage stability data are available to support the intended uses.

7.4.1.2 Stability of residues in sample extracts (KCA 6.1)

Please refer to Section 7.4.1.1 above.

Conclusion on stability of residues in sample extracts

Sufficient data are available to support the intended uses.

Accepted. zRMS agrees with the above consideration of the applicant.

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)

No new data submitted in the framework of this application.

Studies on the metabolism of this active substance in plants were reviewed during the evaluation for EU approval (EFSA, 2006) and renewal (EFSA, 2018). The data was acceptable and is summarised in the EU DAR and RAR. The studies are also summarised below.

Table 7-32: Summary of plant metabolism studies

Crop Group	Crop	Label position	Application and sampling details					Reference
			Method, F or G	Rate (kg a.s./ha)	No	Sampling (DAT)	Remarks	
EU data								
Leafy vegetables	Cabbage	[^{14}C]-Clopyralid	Foliar, Protected	0.42 @BBCH 31 (8-10 leaf stage or 46 days after planting)	1	0, 5, 38 (maturity)	-	Clopyralid DAR, 2005 EFSA, 2006
Root and tuber	Sugar beet	[^{14}C]-Clopyralid	Foliar, F	0.3 @BBCH 36	1	0, 28, 105 (maturity, BBCH 49)	-	Clopyralid RAR, 2017 EFSA, 2018
Pulses and oilseeds	Rapeseed	[^{14}C]-Clopyralid	Foliar, F	0.3 @BBCH 36	1	0, 28, 77 (maturity)	-	

Crop Group	Crop	Label position	Application and sampling details					Reference
			Method, F or G	Rate (kg a.s./ha)	No	Sampling (DAT)	Remarks	
Other	Pasture Grass	[^{14}C]-Clopyralid	Foliar, F	1.121	1	7, 14, 28, 56, 126	Limited insight as extraction was with caustic methanol, only parent detected. Does not meet GLP requirements.	

Conclusion on metabolism in primary crops

Overall, the metabolism of clopyralid was studied in four different crops: sugar beet, oilseed rape, cabbage and pasture. The metabolism of clopyralid was similar in all studied crop groups, thus the metabolic behaviour of clopyralid in plants can be regarded sufficiently studied. Clopyralid was found to be the major component of the residue.

The requested uses for KINVARA are accommodated by the plant metabolism data previously reviewed at EU level, therefore the existing residue definitions apply.

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.

Summary of plant metabolism studies reported in the EU

Studies on the metabolism of clopyralid in rotational crops were reviewed during the evaluation for EU renewal. The data were considered acceptable and are summarised in the EU RAR and the EFSA Conclusion:

'Three nature of residues studies in three rotational crops covering the plant-back interval (PBI) of ca 30, 120 and 365 days are available. Only in the most recent study covering PBI of 30 days, identification of residues was performed and besides the parent only conjugated clopyralid is found in wheat, cabbage and radish. As residues in rotational crops cannot be excluded based on the available data, rotational crop field trials according to current guidelines should be submitted (data gap).'

An overview of the studies are also presented below.

Table 7-33: 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	Cabbage	3,6-dichloro-2-6-^{14}C-2-pyridine-carboxylic acid	Bare soil, F	1x 0.30	30	78, 128	30 DAT cabbage was not fully grown to maturity. Heads were collected before fully grown. The residues indicate similar results.	Clopyralid RAR, 2017 EFSA, 2018
Root and tuber vegetables	Turnip		Bare soil, F	1x 0.28	319	Maturity	-	
	Radish		Bare soil, F	1x 0.30	30	Maturity	-	
Other	Soybean (green plant and beans)		Bare soil, F	1x 0.28	125, 319	Not stated	-	
Cereals	Wheat		Bare soil, F	1x 0.30 (30 days) 1x 0.28 (125 and 319 days)	30, 125, 319	62, 78, 107	-	

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

The magnitude of clopyralid residues in rotational crops was not assessed in the framework of the peer review under Directive 91/414/EEC (Finland, 2005). On the basis of soil dissipation studies (below) clopyralid is rapidly degraded in soil. At 28-56 days, which is considered to be the minimum time from application to planting the succeeding crop, residues were in soil at 0.02-0.001 mg/kg of dry soil. However, clopyralid is relatively stable within plant tissue. Leguminous and solanaceous crops are sensitive to clopyralid in soil and therefore, all residues of the treated crop have to be completely decayed before planting such a crop.

Annex Point	IIIA 8.6/04
Reference	Clopyralid DAR, Vol. 3 B.7, Feb 2005
Title	The dissipation of clopyralid in soil following a single application of LONTREL (EF-1136), Denmark and the UK
Author/Year	Rawle N, Yon D (2002)
Guideline	GLP

Annex Point	IIIA 8.6/05
Reference	Clopyralid DAR, Vol. 3 B.7, Feb 2005
Title	The dissipation of clopyralid in soil following a single application of LONTREL (EF-1136), Germany and Northern France
Author/Year	Rawle N, Yon D (2002)
Guideline	GLP

The conclusions regarding a data gap for crop field studies remain valid in the more recent modification of clopyralid MRLs (EFSA Journal 2021;19(1):6389):

'EFSA re-iterates the data gap from the EU pesticides peer review to request rotational crop field studies to address this data requirement. Until these studies become available EFSA suggests to risk managers as risk mitigation measure to label clopyralid containing products with the restriction not to use clopyralid on the same field for 125 days after the initial application regardless of the crop grown.'

Data to demonstrate that no residue of clopyralid above 0.01 mg/kg would occur in case of crop failure, for crops grown less than 125 days after application of clopyralid is required at EU level at the review of the active substance. This is not a data requirement for KINVARA but should be addressed as part of the renewal of the active ingredient clopyralid at EU level, with the clopyralid renewal report (SANTE/10206/2021 Rev 1, 20 May 2021) stating that:

'In its conclusion in 2018, EFSA indicated that the consumer risk assessment could not be performed as it was awaiting the outcome of the evaluation of the residue trial data for grass and cereals, which would affect the animal dietary burden calculation, and the exposure assessment for consumers. However, on 16 December 2020, EFSA adopted a reasoned opinion on the modification of the existing maximum residue levels for clopyralid in various commodities, in which it considered certain risk mitigation measures to avoid the presence of clopyralid residues in rotational crops (e.g. not to use clopyralid on the same field for 125 days after the initial application regardless of the crop grown). Taking into account these measures, EFSA concluded that the proposed uses of clopyralid on wheat, oat and grass will not result in a consumer exposure exceeding the toxicological reference value and therefore are unlikely to pose a risk to consumers' health.'

In accordance with the Central Zone Steering Committee guidance on data gaps in EFSA Conclusions (CZSC February 2021) the data gap is not identified as (eco)toxicologically relevant in the review report and therefore is not considered relevant at PPP level.

Conclusion on metabolism in rotational crops

The crops under consideration are cereals, which are not sensitive to clopyralid in soil. Furthermore, following use of KINVARA on cereals there is a 4-month period before the next rotational crop would planted, therefore residues in rotational crops arising from the use of KINVARA are not expected.

7.4.2.3 Nature of residues in processed commodities (KCA 6.5.1)

Available data

No new data submitted in the framework of this application.
New data were submitted as part of the renewal of clopyralid (Finland, 2017), for which XXXX have a

LoA, with the EFSA Conclusion (EFSA, 2018) stating that:
"Clopyralid proved to be stable under pasteurisation, baking, brewing, boiling and sterilisation conditions. Processing factors have been established. Validity is pending the evaluation of the underlying residue field trials."

Conclusion on nature of residues in processed commodities

The hydrolysis study evaluated within the RAR (Finland, 2017) confirms that clopyralid is stable under representative processing conditions. No further information is considered necessary.

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

Table 7-34: Summary of the nature of residues in commodities of plant origin

Endpoints (Clopyralid)	
Plant groups covered	Rapeseed (P/O), sugar beet (R), cabbage (L), pasture The metabolism of clopyralid was similar in all studied crop groups, thus the metabolic behaviour of clopyralid in plants can be regarded sufficiently studied.
Rotational crops covered	Root/tuber, leafy, cereal (small grain) and other (soybean green plant and beans) (EFSA, 2018)
Metabolism in rotational crops similar to metabolism in primary crops?	Yes (EFSA, 2018)
Processed commodities	Clopyralid common moiety (sum of clopyralid, its salts and conjugates expressed as clopyralid) – pending the outstanding clarification on the nature of "polar clopyralid" (EFSA, 2018)
Residue pattern in processed commodities similar to pattern in raw commodities?	No changes proposed in residue definition on basis of hydrolysis test. Only parent has been tested. Clopyralid conjugates are also major residue and included in the proposed residue definitions.
Plant residue definition for monitoring	**Existing:** Clopyralid (~~Reg. (EU) No 322/2012~~; Reg. (EU) 2021/1807) **Proposed:** Clopyralid common moiety (sum of clopyralid, its salts and conjugates expressed as clopyralid) – pending the outstanding clarification on the nature of "polar clopyralid" (EFSA, 2018)
Plant residue definition for risk assessment	Clopyralid common moiety (sum of clopyralid, its salts and conjugates expressed as clopyralid) – pending the outstanding clarification on the nature of "polar clopyralid" (EFSA, 2018)
Conversion factor from enforcement to RA	None

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.

Summary of animal metabolism studies reported in the EU

Studies on the metabolism of this active substance in livestock were reviewed during the evaluation for EU approval. The data were considered acceptable and are summarised in the EU DAR, RAR and the EFSA Conclusion for this active substance. An overview of the studies are also presented below.

Table 7-35: 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								
Ruminants	Goat	^{14}C-ring labelled 3,6-dichloropicolinic acid, labelled in the 2,6-position	2	230 and 69 mg/kg feed	7	Milk	Twice daily	Clopyralid DAR, Vol. 3 B.7, Feb 2005 EFSA, 2005 EFSA, 2018
						Excreta	Daily	
						Tissues	At sacrifice	
	Lamb	unlabelled	4	100 mg/kg feed	8 weeks	Excreta	-	
Poultry	Laying hens	^{14}C-ring labelled 3,6-dichloropicolinic acid, labelled in the 2,6-position	2	100 mg/kg feed	5-6	Eggs	daily	
						Excreta	daily	
						Tissues	At sacrifice	
	Broiler chickens	^{14}C-DOWCO 290 (3,6 dichloropicolinic acid)	6	100 mg/kg feed	single dose	Droppings	Throughout the 24 hrs after dosing	
						Tissues	At sacrifice	

Conclusion on metabolism in livestock

The requested uses in the GAP table are accommodated by the livestock metabolism data previously reviewed at EU level, therefore the existing residue definitions apply.

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

Table 7-36: Summary on the nature of residues in commodities of animal origin

	Endpoints
Animals covered	Lactating goats
	Laying hens
	Sheep
Time needed to reach a plateau concentration	1 day (milk)
	7 days (egg)

Animal residue definition for monitoring	**Existing:** Clopyralid (~~**Reg. (EU) No 322/2012**~~; Reg. (EU) 2021/1807) **Proposed:** Clopyralid, its salts and conjugates, expressed as clopyralid (EFSA, 2018)
Animal residue definition for risk assessment	Clopyralid common moiety (sum of clopyralid, its salts and glycine conjugates expressed as clopyralid) (EFSA, 2018)
Conversion factor	The conversion factor monitoring / risk assessment is only relevant for milk and is based on the new ruminant metabolism study as 1.3.
Metabolism in rat and ruminant similar	Yes
Fat soluble residue	No (EFSA, 2018)

Accepted. zRMS agrees with the above consideration of the applicant on nature of the residues.

7.4.3 Magnitude of Clopyralid residues in plants (KCA 6.3)

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

New studies on the magnitude of residue have been submitted by the applicant in the framework of this application. In addition, the grassland (pasture) trials data evaluated for the renewal of clopyralid (EFSA, 2018) are relied upon. These studies are summarized in the table below, with detailed assessment of the new studies presented in Appendix 2. In accordance with SANTE/2019/12752, trials on barley, oat, rye and/or wheat with applications performed before the formation of the edible part (before growth stage BBCH 51 for cereals) may be extrapolated to cereal crops (barley, oat, rye and wheat).

Table 7-37: Summary of EU reported and new data supporting the intended uses of KINVARA and conformity to existing MRL (Clopyralid)

Commodity	Source	Residue zone (NEU, SEU, non-EU)	Evaluation GAP Residue levels (mg/kg) [a]	STMR (mg/kg)	HR (mg/kg)	Unrounded OECD calculator MRL (mg/kg)	Current EU MRL (mg/kg)*	MRL compliance
Wheat grain → Cereal grain (rye, triticale)	Witte, A. (2015) TRC14-045	NEU	Trial GAP: 1 x 0.090 kg a.s./ha, BBCH 39, outdoor 0.23, 0.27, 0.39, 0.58	0.33	0.58	1.103	2.0	Yes
Barley grain → Cereal grain (oat)	Witte, A. (2015) TRC14-059	NEU	Trial GAP: 1 x 0.090 kg a.s./ha, BBCH 39, outdoor 0.09, 0.10, 0.15, 0.17	0.125	0.17	0.383	2.0	Yes
Combined cereal grain dataset	**Overall supporting data for KINVARA cGAP**	**NEU**	**cGAP 1 x 0.084 kg a.s./ha, BBCH 39, outdoor 0.09, 0.10, 0.15, 0.17, 0.23, 0.27, 0.39, 0.58**	**0.20**	**0.58**	**0.913**	**2.0**	**Yes**
Wheat straw → Cereal Straw	Witte, A. (2015) TRC14-045	NEU	Trial GAP: 1 x 0.090 kg a.s./ha, BBCH 39, outdoor 0.19, 0.45, 0.88, 1.48	0.665	1.48	Not relevant for animal feed commodities		
Barley straw → Cereal Straw	Witte, A. (2015) TRC14-059	NEU	Trial GAP: 1 x 0.090 kg a.s./ha, BBCH 39, outdoor 0.15, 0.75, 1.02, 1.43	0.885	1.43	Not relevant for animal feed commodities		

Combined cereal straw dataset	**Overall supporting data for KINVARA cGAP**	**NEU**	**cGAP 1 x 0.084 kg a.s./ha, BBCH 39, outdoor 0.15, 0.19 0.45, 0.75, 0.88, 1.02, 1.43, 1.48**	**0.815**	**1.48**	**Not relevant for animal feed commodities**
Grassland (pasture)	RAR (Finland, 2017)	NEU	GAP: 1 x 0.201-218 kg a.s./ha, February to September, PHI = 7 days 2.49, 2.6, 2.8, 3.0, 3.48, 3.73, 4.4, 5.0, 5.4, 6.95	3.61	6.95	Not relevant for animal feed commodities
	Overall supporting data(1) for KINVARA cGAP	**NEU**	**cGAP: 1 x 0.084 kg a.s./ha, March to September, PHI = 7 days 1.00, 1.03, 1.12, 1.20, 1.39, 1.49, 1.76, 2.00, 2.16, 2.78**	**1.44**	**2.78**	**Not relevant for animal feed commodities**

***** Source of EU MRL: ~~Reg (EU) No 322/2012~~ Reg. (EU) 2021/1807:

The lowest current EU MRL (Barley) is used for a worst-case consideration: Barley (2.0 mg/kg), Oat (3.0 mg/kg), Rye (5.0 mg/kg), Wheat (3.0 mg/kg).

(a) Definition of residue for enforcement and risk assessment are the same: *Clopyralid common moiety (sum of clopyralid, its salts and conjugates expressed as clopyralid) – pending the outstanding clarification on the nature of "polar clopyralid"*

(1) As the RAR GAP uses an application rate >25% higher than the KINVARA cGAP, residues data were scaled to the cGAP target rate of 0.084 kg a.s./ha.

7.4.3.2 Conclusion on the magnitude of residues in plants

A total of 4 trials, each, were performed in wheat and barley in Northern Europe according to the intended GAP to support the registration of KINVARA on wheat, triticale, rye, barley and oat in the Northern and Central European zones. According to SANTE/2019/12752, since the application is performed before the edible part is formed, it can be concluded that the existing dataset of 8 trials (wheat/barley) is sufficient to extrapolate to oats and rye.

A total of 10 trials in grassland (pasture) in Northern Europe were evaluated in the RAR (Finland, 2017) and are relied upon in support of the proposed use of KINVARA on grassland.

According to the available data, the intended uses on wheat, triticale, barley, rye, oats and grassland are considered acceptable. The available data confirm that no exceedance of the MRL will occur.

Accepted. zRMS agrees with the above consideration of the applicant.

7.4.4 Magnitude of residues in livestock

7.4.4.1 Dietary burden calculation

Cereal grain, cereal straw, grass, and wheat and barley processed commodities may form a part of livestock diets in the EU. Livestock dietary burden calculations have been performed taking into account commodities from the proposed uses of KINVARA that might be used as animal feed, alongside the inputs used in the EFSA Reasoned Opinion on the modification of the existing MRLs of clopyralid (EFSA, 2021).

The potential dietary exposure to clopyralid has been calculated using the EFSA model (2017). The dietary inputs into the animal diet according to the EU model are summarised in Table 7-38.

The highest residues in supervised trials are used to calculate the maximum potential dietary intake except for feed commodities that are bulked or processed where the STMR is used. In line with inputs from the EFSA Reasoned Opinion, MRLs are used for certain commodities, which represent a significantly worst case residue.

Table 7-38: 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: *Clopyralid common moiety (sum of clopyralid, its salts and conjugates expressed as clopyralid) pending the outstanding clarification on the nature of "polar clopyralid"*				
Barley - straw	0.815	STMR Cereals (this submission)	1.48	HR Cereals (this submission)
Oat - straw	0.815	STMR Cereals (this submission)	1.48	HR Cereals (this submission)
Rye - straw	0.815	STMR Cereals (this submission)	1.48	HR Cereals (this submission)
Triticale - straw	0.815	STMR Cereals (this submission)	1.48	HR Cereals (this submission)
Wheat - straw	0.815	STMR Cereals (this submission)	1.48	HR Cereals (this submission)
Barley - grain	0.20	STMR Cereals (this submission)	-	-
Oat - grain	0.20	STMR Cereals (this submission)	-	-
Rye - grain	0.20	STMR Cereals (this submission)	-	-
Triticale - grain	0.20	STMR Cereals (this submission)	-	-
Wheat - grain	0.20	STMR Cereals (this submission)	-	-
Grass - forage	1.44	STMR Grass (this submission)	2.78	HR Grass (this submission)
Grass - hay	5.04	STMR Grass (this submission) x default PF	9.73	HR Grass (this submission) x default PF
Grass - silage	2.30	STMR Grass (this submission) x default PF	4.45	HR Grass (this submission) x default PF
Brewer's grain - dried	0.66	STMR (Barley, this submission) x default PF	-	-
Distiller's grain - dried	0.66	STMR (Wheat, this submission) x default PF	-	-
Wheat gluten - meal	0.36	STMR (Wheat, this submission) x default PF	-	-
Wheat - milled by-products	1.40	STMR (Wheat, this submission) x default PF	-	-
Feed items related to the previous evaluations (EFSA, 2021)				
Beet mangel, fodder	0.47	STMR	1.05	HR
Beet, sugar (tops)	0.47	STMR	1.05	HR
Cabbage, heads (leaves)	0.23	STMR	1.52	HR
Corn, field (stover)	0.46	STMR	0.88	HR

Feed Commodity	Median dietary burden		Maximum dietary burden	
	Input value (mg/kg)	Comment	Input value (mg/kg)	Comment
Corn, pop (stover)	0.46	STMR	0.88	HR
Kale	1	MRL	1	MRL
Turnip, tops (leaves)	0.47	STMR	1.05	HR
Swede, roots	0.35	STMR	0.80	HR
Turnip, roots	0.35	STMR	0.80	HR
Maize, field (grain)	0.06	STMR	-	-
Maize, pop (grain)	0.06	STMR	-	-
Cotton	0.5	MRL	-	-
Pea, seed (dry)	0.5	MRL	-	-
Soybean seed	0.5	MRL	-	-
Apple, pomace (wet)	0.25	STMR x default PF	-	-
Beet, sugar (dried pulp)	6.30	STMR x default PF	-	-
Beet, sugar (ensiled pulp)	1.05	STMR x default PF	-	-
Beet, sugar (molasses)	9.80	STMR x default PF	-	-
Canola (rapeseed), meal	0.06	STMR x default PF	-	-
Citrus, dried pulp	5	MRL x default PF	-	-
Corn, field (milled by-products)	0.06	STMR x default PF	-	-
Corn, field (hominy meal)	0.36	STMR x default PF	-	-
Corn, field (gluten feed)	0.15	STMR x default PF	-	-
Corn, field (gluten meal)	0.06	STMR x default PF	-	-
Cotton, meal	0.65	MRL x default PF	-	-
Flaxseed/Linseed, meal	8.92	STMR x default PF	-	-
Peanut, meal	1	MRL x default PF	-	-
Rape meal	0.06	MRL x default PF	-	-
Soybean, meal	0.65	MRL x default PF	-	-
Soybean, hulls	6.50	MRL x default PF	-	-
Sunflower meal	1	MRL x default PF	-	-

Table 7-39: Results of the dietary burden calculation

Relevant groups	Dietary burden expressed in				Most critical diet[a]	Most critical commodity[b]		Trigger exceeded (Yes/No)	Previous assessment[c]
	mg/kg bw per day		mg/kg DM						Max burden
	Median	Maximum	Median	Maximum					(mg/kg DM)
Risk assessment residue definition: *Clopyralid common moiety (sum of clopyralid, its salts and conjugates expressed as clopyralid) pending the outstanding clarification on the nature of "polar clopyralid"*									
Cattle (all diets)	0.241	0.378	6.26	10.07	Dairy cattle	Grass	forage (fresh)	Yes	39.55
Cattle (dairy only)	0.241	0.378	6.26	10.07	Dairy cattle	Grass	forage (fresh)	Yes	39.55
Sheep (all diets)	0.259	0.400	6.64	10.96	Ram/Ewe	Grass	forage (fresh)	Yes	58.01
Sheep (ewe only)	0.221	0.365	6.64	10.96	Ram/Ewe	Grass	forage (fresh)	Yes	58.01
Swine (all diets)	0.108	0.175	4.69	7.56	Swine (breeding)	Grass	forage (fresh)	Yes	17.62
Poultry (all diets)	0.112	0.170	1.64	2.49	Poultry layer	Flax/linseed	meal	Yes	2.98
Poultry (layer only)	0.112	0.170	1.64	2.49	Poultry layer	Flax/linseed	meal	Yes	2.98

bw: body weight; DM: dry matter.
(a): When one group of livestock includes several subgroups (e.g. poultry 'all' including broiler, layer and turkey), the result of the most critical subgroup 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'
(c): EFSA Journal 2021;19(1):6389

Use of the most recent EFSA dietary burden calculator (2017 model) along with the data presented in this submission, confirms that the theoretical maximum daily intakes for all animals are less critical than those calculated in the EFSA Reasoned Opinion (EFSA, 2021). It can therefore be concluded that residues in animal commodities arising from the use of KINVARA will fall within the current EU MRLs.

Accepted by zRMs.

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.

Livestock feeding studies for clopyralid were reviewed during the evaluation for EU renewal of approval. The data was acceptable and is summarised in the EU Renewal Assessment Reports (RAR) and EFSA Conclusion (EFSA, 2018). A summary of these data is presented within the EFSA Reasoned Opinion on the Modification of the existing maximum residue levels for clopyralid in various commodities (EFSA, 2021), for which the theoretical animal dietary burden has been demonstrated to be more critical than that calculated for the proposed uses of KINVARA (see Section 7.4.4.1):

"The feeding studies with lactating cows and laying hens were assessed in the framework of the EU pesticides peer review (EFSA, 2018d). The analytical method used in the two studies was sufficiently validated. It employs a hydrolysis step with sodium hydroxide converting all eventually present conjugates into clopyralid. Higher values are not expected as conjugates are only found in milk.

Hens were dosed orally with clopyralid at 0, 4.90 (19), 10.26 (29) 19.82 (49) and 50.5 (109) mg/ kg DM feed/day for 28 or 29 consecutive days, corresponding to approximately 0, 0.280, 0.571, 1.086 and 2.779 mg/kg bw per day, respectively. Plateau in eggs was reached after 7 days.
Residues of clopyralid in muscle, liver and eggs increased from the lowest to highest dose groups, with residues in the liver present above LOQ in all treatment groups. No residues of clopyralid above the LOQ were found in the fat in any treatment group. Residues of clopyralid in the tissues and eggs of the depuration animals fell to below the LOQ 3 days after withdrawal of the test item from the hens' diet.
Lactating cows were dosed orally with clopyralid at 0, 16.70, 56.60, 309.80 and 1,019.5 mg ai/kg DM feed/day for 28 or 29 consecutive days, corresponding to approximately 0, 0.451, 1.670, 8.517 and 30.538 mg/kg bw per day, respectively. Residues above the LOQ were found in liver and kidney at the lowest dose group, in milk, fat and muscle from the second dose group onwards. A plateau was reached in milk within 1 day. Residues of clopyralid declined rapidly following withdrawal of the test item from the cows' diet.

The dietary burdens calculated in the framework of the current assessment were compared with the feeding levels of available feeding studies in order to estimate whether the existing animal commodity MRLs would need to be modified.
Although the applicant requested only increases of MRLs for fat, liver and kidney of bovine, sheep and goat and swine kidney, EFSA agrees with the proposal of the EMS to recommend new MRLs for all animal commodities based on the latest valid feeding studies.

The data indicate that the proposed use in grass, wheat and oat will lead to higher MRLs in all animal commodities due to a new analytical method (see below) and the more recent guideline compliant feeding studies. EFSA agrees with the proposal of the EMS and applicant to maintain the MRLs at the value of 0.05 mg/kg (LOQ of the previous analytical method) for certain commodities (swine fat, liver, muscle, fat of bovine, sheep, goat and all poultry commodities) because the new analytical method cannot be regarded as fully validated in the absence of data on extraction efficiency. Once this outstanding data gap has been addressed, the MRL proposals should be reconsidered on the basis of the achievable LOQ of 0.01 mg/kg of the new analytical method. A discrepancy is observed in the EMS proposal of 0.15 mg/kg for sheep and goat fat in contrast to the value of 0.2 mg/kg requested by applicant and calculated by EFSA. This might be due to slightly different input values in the dietary burden calculator.

An analytical method for enforcement based on LC-MS/MS for all products of animal origin and a method based on QuEChERs for milk and fat, both with LOQ of 0.01 mg/kg, have been assessed during the EU pesticides peer review and was considered as not fully validated since the extraction efficiency was not demonstrated and a data gap was identified in the peer review (EFSA, 2018d).
The storage stability of clopyralid in commodities of animal origin was investigated in the framework of the EU pesticides peer review. The stability of conjugates has not been tested separately; it is assumed that conjugated clopyralid will be also stable (EFSA, 2018d)."

Conclusion on feeding studies

The requested uses result in calculated theoretical maximum daily intakes for animals within those considered in the 2021 Reasoned Opinion, therefore there is no risk for animal MRLs to be exceeded.

Accepted by zRMs.

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

Available data

No new data submitted in the framework of this application.

EU data

The following summary of the processing studies evaluated as part of the EU peer review (EFSA, 2018) is presented within the EFSA Reasoned Opinion on the Modification of the existing maximum residue levels for clopyralid in various commodities (EFSA, 2021):

"Studies investigating the effect of processing on the magnitude of clopyralid residues in wheat and barley were evaluated in the context of the EU pesticides peer review and used to propose processing factors (EFSA, 2018d). The studies demonstrate that clopyralid residues concentrate in wheat bran and germ whereas a reduction is observed in other processed commodities of wheat and barley. EFSA concluded that the reporting of the respective residue field trials with wheat and barley in the RAR was insufficient to decide on their validity and a data gap was identified to re-evaluate and report the results in a transparent manner. Provided evidence on the validity of the residue field studies is given, the number and quality of the processing studies would be sufficient to derive robust processing factors."

A summary of the tentative processing factors derived is presented in the table below:

Table 7-40: Processing factors

Processed commodity	Number of studies[a]	Processing Factor (PF)		Conversion factor (CF_P) for RA[b]
		Individual values	Median PF	
Wheat/bran	4	3.5, 4.3, 6.1, 10.4	5.7	n/a
Wheat/white flour	4	0.1, 0.2, 0.3, 0.6	0.25	
Wheat/wholemeal flour	2	0.8, 1.2	1	
Wheat/germ	2	2.3, 4.3	3.3	
Wheat/white bread	2	0.1, 0.1	0.1	
Wheat/wholemeal bread	2	0.5, 0.6	0.6	
Barley/malt sprouts	2	0.2, 0.2	0.2	
Barley/brewing malt	2	0.6, 0.7	0.7	
Barley/spelt grains and flocs	2	0.1, 0.2	0.2	
Barley/brewer's yeast	2	0.1, 0.1	0.1	
Barley/beer	2	0.1, 0.1	0.1	

(a): Studies with residues in the RAC at or close to the LOQ were disregarded (unless concentration may occur)
(b): When the residue definition for risk assessment differs from the residue definition for monitoring

7.4.5.2 Conclusion on processing studies

No further information is required.

Accepted by zRMs.

7.4.6 Magnitude of residues in representative succeeding crops

The crops under consideration can be grown in rotation.

Data to demonstrate that no residue of clopyralid above 0.01 mg/kg would occur in case of crop failure, for crops grown less than 125 days after application of clopyralid is required at EU level at the review of the active substance. This is not a data requirement for KINVARA but should be addressed as part of the renewal of the active ingredient clopyralid at EU level, with the clopyralid renewal report (SANTE/10206/2021 Rev 1, 20 May 2021) stating that:

"In its conclusion in 2018, EFSA indicated that the consumer risk assessment could not be performed as it was awaiting the outcome of the evaluation of the residue trial data for grass and cereals, which would affect the animal dietary burden calculation, and the exposure assessment for consumers. However, on 16 December 2020, EFSA adopted a reasoned opinion on the modification of the existing maximum residue levels for clopyralid in various commodities, in which it considered certain risk mitigation measures to avoid the presence of clopyralid residues in rotational crops (e.g. not to use clopyralid on the same field for 125 days after the initial application regardless of the crop grown). Taking into account these measures, EFSA concluded that the proposed uses of clopyralid on wheat, oat and grass will not result in a consumer exposure exceeding the toxicological reference value and therefore are unlikely to pose a risk to consumers' health."

In accordance with the Central Zone Steering Committee guidance on data gaps in EFSA Conclusions (CZSC February 2021) the data gap is not identified as (eco)toxicologically relevant in the review report and therefore is not considered relevant at PPP level.

The crops under consideration are cereals, which are not sensitive to clopyralid in soil. Furthermore, following use of KINVARA on cereals there is a 4 month period before the next rotational crop would be planted, therefore residues in rotational crops arising from the proposed uses of KINVARA are not expected.

Accepted by zRMs.
DE: As outlined in the dRR, in EFSA's conclusion on the peer review certain risk mitigation measures were proposed to avoid the presence of clopyralid residues in rotational crops (e.g. not to use clopyralid on the same field for 125 days after the initial application regardless of the crop grown). For the intended use on cereals under the intended application conditions such a waiting period before planting/seeding rotational crops is not relevant. However, such a waiting period can become relevant in case of crop failure. It is therefore proposed to set a waiting period of 125 days for succeeding crops.
As zRMS agrees with DE a waiting period of 125 days for succeeding crops was set.

7.4.6.1 Conclusion on succeeding crops

No further information is required.
A waiting period of 125 days for succeeding crops was set.

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 KINVARA. Applications are made prior to flowering, and the proposed uses are on non-melliferous crops only. Studies to investigate the potential for residues in honey are not 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

Table 7-41: Input values for the consumer risk assessment

Commodity	Chronic risk assessment		Acute risk assessment	
	Input value (mg/kg)	Comment	Input value (mg/kg)	Comment
Risk assessment residue definition: *Clopyralid common moiety (sum of clopyralid, its salts and conjugates expressed as clopyralid) pending the outstanding clarification on the nature of "polar clopyralid"*				
Barley	0.20	STMR (this submission)	0.58	HR (this submission)
Oat	0.20	STMR (this submission)	0.58	HR (this submission)
Rye	0.20	STMR (this submission)	0.58	HR (this submission)
Wheat	0.20	STMR (this submission)	0.58	HR (this submission)
Commodities of animal origin	Current EU MRL	Reg. (EU) 2021/1807	Current EU MRL	Reg. (EU) 2021/1807
All other commodities	Current EU MRL	Reg. (EU) 2021/1807	n/a	n/a

n/a - The acute risk assessment is only performed for crops under consideration.

7.4.8.2 Conclusion on consumer risk assessment

Extensive calculation sheets are presented in Appendix 3.

Table 7-42: Consumer risk assessment

TMDI (% ADI) according to EFSA PRIMo (the report has to be repasted into the RR)	42 % (based on NL toddler)
IEDI (% ADI) according to EFSA PRIMo	33 % (based on NL toddler)
IESTI (% ARfD) according to EFSA PRIMo*	4 % - Milk: Cattle (unprocessed, children) 1 % - Wheat / milling (flour, children)
NTMDI (% ADI) **	n/a
NEDI (% ADI)**	n/a
NESTI (% ARfD) **	n/a

* include raw and processed commodities if both values are required for PRIMo
** if national model is available

The proposed uses of clopyralid in the formulation KINVARA do not represent unacceptable chronic or acute risks for the consumer.

Accepted by zRMs.

7.5 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 and for at least two of them an acute reference dose has been allocated. Therefore, combined acute exposure can be considered.

7.5.1 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 within 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 summarised in the following table. Fluroxypyr is not considered acutely toxic and therefore only contribution of MCPA and clopyalid has been considered.

Table 7-43 Acute consumer risk assessment from combined exposure

Crop	Active Ingredient (ARfD)	HQ (based on IESTI according to EFSA PRIMo) [exposure]
Barley	MCPA (0.15 mg/kg bw)	0.0004 [0.06 µg/kg bw]
	Clopyralid (0.17 mg/kg bw)	0.0065 [1.1 µg/kg bw]
	Cumulative risk Barley (HI)	**0.0069**
Oat	MCPA (0.15 mg/kg bw)	0.00007 [0.01 µg/kg bw]
	Clopyralid (0.17 mg/kg bw)	0.0013 [0.22 µg/kg bw]
	Cumulative risk Oat (HI)	**0.0014**
Rye	MCPA (0.15 mg/kg bw)	0.0004 [0.06 µg/kg bw]
	Clopyralid (0.17 mg/kg bw)	0.0076 [1.3 µg/kg bw]
	Cumulative risk Rye (HI)	**0.0080**
Wheat	MCPA (0.15 mg/kg bw)	0.00093 [0.14 µg/kg bw]
	Clopyralid (0.17 mg/kg bw)	0.0171 [2.9 µg/kg bw]
	Cumulative risk Wheat (HI)	**0.0180**
Swine*	MCPA **(0.15 mg/kg bw)**	0.008 [1.2 µg/kg bw]

Crop	Active Ingredient (ARfD)	HQ (based on IESTI according to EFSA PRIMo) [exposure]
muscle/meat	Clopyralid (0.17 mg/kg bw)	0.0036 [0.61 µg/kg bw]
	Cumulative risk Swine muscle/meat (HI)	**0.0116**
Bovine* kidney	MCPA (0.15 mg/kg bw)	0.073 [11 µg/kg bw]
	Clopyralid (0.17 mg/kg bw)	0.033 [5.6 µg/kg bw]
	Cumulative risk Bovine kidney (HI)	**0.106**
Bovine* liver	MCPA (0.15 mg/kg bw)	0.16 [24 µg/kg bw]
	Clopyralid (0.17 mg/kg bw)	0.0071 [1.2 µg/kg bw]
	Cumulative risk Bovine liver (HI)	**0.17**
Bovine* edible offal	MCPA **(0.15 mg/kg bw)**	0.15 [22 µg/kg bw]
	Clopyralid (0.17 mg/kg bw)	0.0021 [0.36 µg/kg bw]
	Cumulative risk Bovine edible offal (HI)	**0.15**
Poultry muscle/meat	MCPA **(0.15 mg/kg bw)**	0.011 [1.7 µg/kg bw]
	Clopyralid (0.17 mg/kg bw)	0.005 [0.85 µg/kg bw]
	Cumulative risk Poultry muscle/meat (HI)	**0.016**
Milk: Cattle	MCPA **(0.15 mg/kg bw)**	0.041 [6.2 µg/kg bw]
	Clopyralid (0.17 mg/kg bw)	0.036 [6.2 µg/kg bw]
	Cumulative risk Milk: Cattle (HI)	**0.078**
Eggs: Poultry	MCPA **(0.15 mg/kg bw)**	0.0041 [0.62 µg/kg bw]
	Clopyralid (0.17 mg/kg bw)	0.0036 [0.62 µg/kg bw]
	Cumulative risk Eggs: Poultry (HI)	**0.0078**

*The HQ has been calculated for the worst-case ruminant group for each commodity.

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

7.5.2 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.

However, a provisional consideration of the combined chronic exposure has been made using the following methodology (akin to the proposed methodology for combined acute exposure):

In the first step, dose addition residues of the individual active substances are 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 chronically toxic by performing deterministic TMDI calculations with the EU PRIMo model

and dividing the individual exposure levels by the respective ADI. 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 HI calculations based on the critical consumer (NL toddler, IEDI calculations) are summarised in the following table.

Table 7-44 Chronic dietary risk assessment from combined exposure

Crops	% ADI (HQ)			
	MCPA	**Fluroxypyr**	**Clopyralid**	**Cumulative Risk (HI)**
All commodities as described in the tables of input values for the consumer risk assessment	14	0.6	33	47.6

The Hazard Index is <100 % for commodities relevant to the intended uses of KINVARA (47.6 % of the ADI). Therefore, the combined exposure to MCPA, fluroxypyr and clopyralid resulting from the proposed uses of KINVARA is not expected to present an unacceptable risk to the consumer.

Accepted by zRMs as supplemental supportive information.

7.6 References

MCPA

MCPA DAR, Vol. 3, B.6, Oct 2003.

EU COM, 2008. Review report for the active substance MCPA. Finalised in the Standing Committee on the Food Chain and Animal Health at its meeting on 15 April 2005; in view of the inclusion of MCPA in Annex I of Directive 91/414/EEC. SANCO/4062/2001-final, 11 July 2008

Fluroxypyr

EFSA (European Food Safety Authority), 2011. Conclusion on the peer review of the pesticide risk assessment of the active substance fluroxypyr (evaluated variant fluroxypyr-meptyl). EFSA Journal 2011; 9(3):2091.

EFSA (European Food Safety Authority), 2013. Reasoned opinion on the review of existing maximum residue levels (MRLs) for fluroxypyr according to Article 12 of Regulation (EC) No 396/2005. EFSA Journal 2013;11(12):3495.

Germany, 1996. Draft Assessment Report (DAR) on the active substance fluroxypyr prepared by the rapporteur Member State Germany in the framework of Directive 91/414/EEC, August 1996.

Ireland, 2009. Assessment Report on the active substance fluroxypyr prepared by the rapporteur Member State Ireland in consultation with Poland in the framework of Commission Regulation (EC) No 737/2007, October 2009.

Ireland, 2011. Final Addendum to Assessment Report on fluroxypyr prepared by the rapporteur Member State Ireland in consultation with Poland in the framework of Commission Regulation (EC) No 737/2007, compiled by EFSA, January 2011.

Clopyralid

Finland, 2003. Draft assessment report on the active substance clopyralid prepared by the rapporteur Member State Finland in the framework of Council Directive 91/414/EEC, November 2003.

Finland, 2005. Addendum 2 to the draft assessment report on the active substance clopyralid prepared by the rapporteur Member State Finland in the framework of Council Directive 91/414/EEC, August 2005.

Finland, 2017. Draft Renewal Assessment Report on the active substance clopyralid prepared by the rapporteur Member State Finland under Regulation (EC) 1107/2009, May 2017.

EFSA (European Food Safety Authority), 2005. Conclusion regarding the peer review of the pesticide risk assessment of the active substance clopyralid. Finalised 14 December 2005. EFSA Scientific Report (2005) 50, 1-65.

EFSA (European Food Safety Authority), 2018. Peer review of the pesticide risk assessment of the active substance clopyralid. EFSA Journal 2018;16(8):5389.

EFSA (European Food Safety Authority), 2021. Modification of the existing MRLs for clopyralid in various commodities. EFSA Journal 2021;19(1):6389.

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
KCA 6.3.1/01	Witte, A.	2015	Magnitude of Fluroxypyr, MCPA and Clopyralid Residues in wheat following one application with KINVARA (Fluroxypyr-meptyl 72 g/l + MCPA 233 g/l + Clopyralid 28 g/l, EW) in Southern and Northern Europe in 2014 TRIALCAMP Study No: TRC14-045 GLP Published	N	XXXX
KCA 6.3.1/02	Luna, F.	2018	Amendment to Magnitude of Fluroxypyr, MCPA and Clopyralid Residues in wheat following one application with KINVARA (Fluroxypyr-meptyl 72 g/l + MCPA 233 g/l + Clopyralid 28 g/l, EW) in Southern and Northern Europe in 2014 TRIALCAMP Study No: TRC14-045 GLP Published	N	XXXX
KCA 6.3.2/01	Witte, A.	2015	Magnitude of Fluroxypyr, MCPA and Clopyralid Residues in barley following one application with KINVARA (Fluroxypyr-meptyl 72 g/l + MCPA 233 g/l + Clopyralid 28 g/l, EW) in Southern and Northern Europe in 2014 TRIALCAMP Study No: TRC14-059 GLP Published	N	XXXX

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 6.3.2/02	Luna, F.	2018	Amendment to Magnitude of Fluroxypyr, MCPA and Clopyralid Residues in barley following one application with KINVARA (Fluroxypyr-meptyl 72 g/l + MCPA 233 g/l + Clopyralid 28 g/l, EW) in Southern and Northern Europe in 2014 TRIALCAMP Study No: TRC14-059 GLP Published	N	XXXX
KCP 6.3.3/01	Diebold, J-L	2018	Determination of MCPA Residues in Grass Following One Foliar application with KINVARA under Field Conditions in Northern Europe in 2018 R B8208 ANADIAG, 16, rue Ampère, 67500 HAGUENAU, France GLP Unpublished	N	XXXX
KCA 6.3.3/02	Witte, A.	2015	Magnitude of Fluroxypyr, MCPA and Clopyralid Residues in Grassland Following One Application with Kinvara (Fluroxypyr-meptyl 72 g/L + MCPA 233 g/L + Clopyralid 28 g/L, EW) in Northern Europe in 2014 + Amendment to the study. TRIALCAMP Study No: TRC14-022 GLP Published	N	XXXX

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

Annex 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
IIIA 8.1/01	Wasser C.	2002	Storage Stability of MCPA, MCPB and HMCPA residues in Cereals. MCPA DPWG Anadiag France 9123/AHMR99 144 GLP, Unpublished	N	Nufarm
IIIA 8.1/03	Teasdale, R.	1996	Frozen storage stability of fluroxypyr in winter wheat immature plant, grain and straw Dow Elanco, CEM Analytical Services, Oxon, UK GHE-P-4830 (O32C) 1996-06-19 GLP: yes Not published AR, Vol. 3, B.7, Oct 2009	N	DOW
IIIA 8.1/04 8.2/23	XXXX	1990	Determination of residues of Fluroxypyr in eggs, muscle, liver and fat tissues from chickens administered Fluroxypyr herbicide XXXX GH-C 2327 (N86) 1990-04-24 GLP: yes Not published DAR, Vol. 3, B.7, Oct 2009	Y	DOW
CA 6.1.1/1	Allen, L.	2013	Frozen Storage Stability of Residues of Clopyralid in Crop Matrices DAS Study No. 120939 CEM Analytical Services (CEMAS), North Ascot, Berkshire, UK GLP Not Published RAR, Vol. 3 B.7 May 2017	N	DAS
CA 6.1.2/1	-	2015	Frozen Storage Stability of Clopyralid in Bovine Fat XXXX Study No. 120602 GLP Not Published	Y	DAS

Annex 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
			RAR, Vol. 3 B.7 May 2017		
CA 6.1.2/2	-	2004	Frozen Storage Stability of Clopyralid in Beef Muscle, Liver, Kidney, Milk and Chicken Egg XXXX Study No. 020120.01 GLP Not Published RAR, Vol. 3 B.7 May 2017	Y	DAS
IIIA 8.1/05	Foster, DR, Blakeslee, BA, Rutherford, BS	1996	Frozen Storage Stability of Clopyralid, 2, 4 D on Corn grain, straw and fodder DowElanco, Indianapolis, Indiana, 46268, USA DAS Report No: GH-C-3779 Masterfile Number N136 GLP Not Published DAR, Vol. 3 B.7, Feb 2005	N	DAS
IIIA 8.1/06	Clements, B, Bolton, A	1996	Determination of the stability of clopyralid residues in pasture under frozen storage conditions DowElanco, Letcombe Laboratory DAS Report No: GHE-P-5350 Masterfile number N138 GLP Not Published DAR, Vol. 3 B.7, Feb 2005	N	DAS
IIIA 8.2/01	Keller W, Otto S	1979	Investigations into the Metabolism of MCPA in Winter Wheat. DAR - Vol. 3, B.6, Oct 2003).	N	Nufarm
IIIA 8.2/02	XXXX	1995	Nature of the residue of ^{14}C-2-Methyl-4-Chlorophenoxyacetic Acid (^{14}C-MCPA as the dimethylamine salt (^{14}C-MCPA DMA) and the 2-Ethylhexyl ester (^{14}C-MCPA 2-EHE) in wheat. MCPA, DPWG XXXX SC930053 GLP, Unpublished	N	Nufarm
IIIA 8.2/03	Achhireddy N, Kirkwood R ,C, Fletcher W W, *J. of*	1984	The Uptake, Metabolism and Phytotoxicity of MCPA in Plants. DAR - Vol. 3, B.6, Oct 2003).	N	Nufarm

Annex 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
	Pesticide Science 9; pp 617-622				
IIIA 8.2/05	XXXX	1995	Absorption, distribution, metabolism and excretion in the rat. XXXX GLP, Unpublished	Y	Nufarm
IIIA 8.2/06	XXXX	2000	MCPA: Interspecies Comparison of Metabolism XXX (no report number) Not GLP, Unpublished	Y	Nufarm
IIIA 8.2/08 & 8.4/02	XXXX	1995	Nature of the residue study of ^{14}C-2-Methyl-4-chlorophenoxyacetic acid (^{14}C-MCPA) using egg-laying white Leghorn hens. XXXX GLP, Unpublished DAR - Vol. 3, B.6, Oct 2003.	Y	Nufarm
IIIA 8.2/09 & 8.4/03	XXXX	1996	Supplemental Report to: Nature of the residue study of ^{14}C-MCPA using egg-laying white leghorn hens. XXXX GLP, Unpublished DAR - Vol. 3, B.6, Oct 2003	Y	Nufarm
IIIA 8.2/11 & 8.4/01	XXXX	1995	Nature of the residue study of ^{14}C-2-Methyl-4-chlorophenoxyacetic acid (^{14}C-MCPA) using lactating goats. XXXX GLP, Unpublished DAR - Vol. 3, B.6, Oct 2003	Y	Nufarm
IIIA 8.2/12	Hawkins D.R., Kirkpatrick, D., Conway, B., Finn, C.M., Powell, G.P.	1981	The metabolism of ^{14}C-DOWCO MHE in spring wheat and soil after field application Dow Chemical, Huntingdon Research Centre, Huntington, Cambridgeshire, UK GHE-P-895 (L1) 1982-01-07 GLP: no Not published DAR, Vol. 3, B.7, Oct 2009	N	DOW

Annex 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
IIIA 8.2/13	Puvanesarajah V., Stewart, R.C.	1991	Metabolism of ^{14}C-Fluroxypr in wheat Dow Elanco, ABC Lab., Inc., Columbia, Missouri, USA GHE-C-2650 (L2) 1991-10-25 GLP: yes Not published DAR, Vol. 3, B.7, Oct 2009	N	DOW
IIIA 8.2/14	Caley C. Y., O' Boyle, F.	1995	Comparative Metabolism of [^{14}C]-Fluroxypyr butoxypropyl ester and [^{14}C]-Fluroxypyr methylheptyl ester in winter wheat DowElanco, Inveresk Research International, Tranent, Scotland GHE-P-4236 1995-04-27 GLP: yes Not published DAR, Vol. 3, B.7, Oct 2009	N	DOW
IIIA 8.2/15 & 8.4/05	XXXX	1989	The fate of ^{14}C labelled Fluroxypyr fed to laying hens XXXX 1989-01-20 GLP: yes Not published DAR, Vol. 3, B.7, Oct 2009	Y	DOW
IIIA 8.2/16 & 8.4/06	XXXX	1985	The excretion and tissue levels of radioactivity in a dairy cow after oral administration of ^{14}C DOWCO 433 acid XXXX DET 602 (H3) 1985-06-27 GLP: yes Not published	Y	DOW

Annex 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
IIIA 8.2/17 & 8.4/07	XXXX	1990	The fate of ^{14}C labelled fluroxypyr fed to lactating goats XXXX GH-C-2297 1990-02-12 GLP: yes Not published Fluroxypyr DAR, Vol. 3, B.7, Oct 2009	Y	DOW
IIIA 8.2/18	Moran., J	2005	Tropical dairy farming: feeding management for small holder dairy farmers in the humid tropics, Lanilinks Press LLS GHE-P-4236 GLP – No	N	DAS
IIIA 8.2/19	Church, D. C	1988	The Ruminant Animal: Digestive Physiology and Nutrition LLS GHE-P-4236 GLP – No	N	DAS
IIIA 8.2/20	Reeves, G. L	1995	The Hydrolysis of [14C]-Fluroxypyr-1-Butoxypropyl Ester, Unpublished report LLS GHE-P-4191 GLP – No	N	DAS
IIIA 8.2/21	Knowles, S. J. and Cowlyn, T. C.	1991	Fluroxypyr Methyl Ester (Technical) : Determination of Hydrolysis as a Function of pH, Unpublished report LLS GHE-P-2542 GLP – No	N	DAS
IIIA 8.2/22	Not stated	1990	STARANE* Herbicides (FLUROXYPYR) Pharmacokinetic and Metabolic Behaviour in Mammals GLP – No	N	DAS
IIIA 8.2/24 & 8.4/08	XXXX	1986	DOWCO 433 (fluroxypyr) residues in milk and tissues of dairy cows, XXXX GLP: yes Not published DAR, Vol. 3, B.7, Oct 2009	Y	DOW

Annex 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
IIIA 8.2/25	Chapleo, S. and Caley, C.Y	2002	The metabolism of [^{14}C]-Clopyralid in Sugar Beet DAS Report No: GHE-P-9939 Masterfile No: L10 GLP Not published DAR, Vol. 3 B.7, Feb 2005	N	DAS
IIIA 8.2/26	Chapleo, S. and Caley, C.	2002	The metabolism of [^{14}C]-Clopyralid in Oilseed Rape DAS Report No: GHE-P-9938 Masterfile No: L09 GLP Not published DAR, Vol. 3 B.7, Feb 2005	N	DAS
IIIA 8.2/27	Guo, C.	1996	The metabolism of [^{14}C]-Clopyralid and Cabbage DowElanco, Indianapolis, Indiana, 46268, USA DAS Report No: GH-C-4289 Masterfile No: L06 GLP Not published DAR, Vol. 3 B.7, Feb 2005	N	DAS
IIIA 8.2/28	Bauriedel, WR and Miller, JH	1981	A field metabolism study of ^{14}C-labelled 3,6-dichloropicolinic acid applied to pasture grass Dow Chemical Company DAS Report No: GH-C-1424 Masterfile No: L03 Not GLP Not published DAR, Vol. 3 B.7, Feb 2005	N	DAS
CA 6.2.1/4	Gourlay, V.	2015	Plant uptake of 14C -labelled clopyralid in wheat and oilseed rape under greenhouse conditions DAS Study No. 150297 RLP AgroScience GmbH, 67435 Neustadt a.d. Weinstraße, Germany GLP RAR, Vol. 3 B.7, May 2017	N	DAS

Annex 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
IIIA 8.2/29	XXXX	1983	The metabolic fate of ^{14}C-3,6-dichloropicolinic acid fed to lactating goats XXXX Masterfile No: H03 Not GLP Not published DAR, Vol. 3 B.7, Feb 2005	Y	DAS
IIIA 8.2/30	XXXX	1974	The fate of ^{14}C-labelled DOWCO 290 Fed as a single oral dose to broiler chickens XXXX Masterfile No: H04 Not GLP Not Published DAR, Vol. 3 B.7, Feb 2005	Y	DAS
IIIA 8.2/31	XXXX	1974	The fate of ^{14}C-DOWCO 290 in laying hens XXXX Masterfile No: H05 Not GLP Not Published DAR, Vol. 3 B.7, Feb 2005	Y	DAS
IIIA 8.2/32	XXXX	1974	The fate of ^{14}C-DOWCO 290 in sheep XXXX Master file No: H02 Not GLP Not published DAR, Vol. 3 B.7, Feb 2005	Y	DAS
IIIA 8.4/08	XXXX	1986	DOWCO 433 (fluroxypyr) residues in milk and tissues of dairy cows, UK trial XXXX GLP: yes Not published DAR, Vol. 3, B.7, Oct 2009	Y	DOW

Annex 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
IIIA 8.4/09	XXXX	1990	Determination of residues of Fluroxypyr in eggs, muscle, liver and fat tissues from chickens administered Fluroxypyr herbicide XXXX 1990-04-24 GLP: yes Not published DAR, Vol. 3, B.7, Oct 2009	Y	DOW
IIIA 8.4/10	XXXX	1974	Residues of DOWCO 290 (3,6-dichloropicolinic acid) in milk and cream from cows fed the Herbicide XXXX MasterfileNo: N154 Not GLP Not published DAR, Vol. 3 B.7, Feb 2005	Y	DAS
IIIA 8.4/11	XXXX	1975	Residues of DOWCO 290(3,6-dichloropicolinic acid) in bovine tissues from calves fed the herbicide XXXX Masterifle no: N151 Not GLP Not Published DAR, Vol. 3 B.7, Feb 2005	Y	DAS
IIIA 8.4/12	XXXX	1975	Residues of DOWCO 290 (3,6-dichloropicolinic acid) in tissues of chickens fed the herbicide `XXXX Masterfile No: N156 Not GLP Not published DAR, Vol. 3 B.7, Feb 2005	Y	DAS
IIIA 8.4/13	XXXX	1975	Residues of DOWCO 290 (3,6-dichloropicolinic acid) in tissues of swine fed the herbicide XXXX Master file No: N161 Not GLP Not published DAR, Vol. 3 B.7, Feb 2005	Y	DAS

Annex 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
CA 6.2.2/1	-	2014	A Nature of the Residue Study in the Laying Hen with [14C]-Clopyralid XXXX GLP Not Published RAR, Vol. 3 B.7, May 2017	Y	DAS
CA 6.2.3/1	-	2015	A Nature of the Residue Study in the Ruminant with [14C]Clopyralid XXXX GLP Not Published RAR, Vol. 3 B.7, May 2017	Y	DAS
CA 6.3.1/1	Delmotte, R.	2015	Magnitude of the residues of clopyralid in grassland pasture (RAC fresh grass, hay and silage), following one application of GF-1966, Northern and Southern Europe – 2014 DAS Study No. 140653 Lab study No. CES-14-18931 STAPHYT, 23, Route de Moeuvres, 62860 Inchy en Artois, France GLP Not Published RAR, Vol. 3 B.7, May 2017	N	DAS
IIIA 8.6/01	Ewing D D.	1988	MCPA Confined Accumulation Study on Rotational Crops. MCPA DAR - Vol. 3, B.6, Oct 2003 EPA Guidelines. Subdivision N, Section 165-1. GLP DAR - Vol. 3, B.6, Oct 2003	N	Nufarm
IIIA 8.6/02	Fryer J D, Kirkland K.	1970	Field experiments to investigate long-term effect of repeated applications of MCPA, Tri-Allate, Simazine and Linuron. Report after 6 years. DAR - Vol. 3, B.6, Oct 2003	N	Nufarm

Annex 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
IIIA 8.6/03	Lickly, L.S., Lardie, T.s., Miller, J.H., Baldwin, W.S.	1990	^{14}C Fluroxypyr-MHE: Confined accumulation study on rotational crops planted at 30, 120 and 366 days after soil treatment Environemntal Chemistry Lab. DowElance, Midland, Michigan, USA GH-C-2410, (N38) 1990-09-17 GLP: yes Not published AR, Vol. 3, B.7, Oct 2009	N	DOW
IIIA 8.6/04	Rawle, N., Yon, D.	2002	The dissipation of clopyralid in soil following a single application of LONTREL (EF-1136), Denmark and the UK – 2000 CEMAS DAS Report No: GHE-P-9370 GLP Not Published DAR, Vol. 3 B.7, Feb 2005	N	DAS
IIIA 8.6/05	Rawle, N., Yon, D.	2002	The dissipation of clopyralid in soil following a single application of LONTREL (EF-113s6), Germany and Northern France – 2000 CEMAS DAS Report No: GHE-P-9371 GLP Not Published DAR, Vol. 3 B.7, Feb 2005	N	DAS
CA 6.4.1/1	-	1974	Dowco 290 and 2,4-D Chicken Feeding Study XXXX Not GLP Not Published RAR, Vol. 3 B.7, May 2017	Y	DAS

Annex 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
CA 6.4.1/2	-	1975	Residues of Dowco 290 (3,6-dichloropicolinic acid) in Tissues of Chickens Fed the Herbicide XXXX Not GLP Not Published RAR, Vol. 3 B.7, May 2017	Y	DAS
CA 6.4.1/3	-	2015	Summary of Clopyralid Livestock Feeding Study: Magnitude of Residue in Eggs, Muscle, Liver and Fat of Laying Hens XXXX GLP Not Published RAR, Vol. 3 B.7, May 2017	Y	DAS
CA 6.4.2/4	-	2015	Summary of Clopyralid Livestock Feeding Study: Magnitude of Residue in Milk, Muscle, Liver, Kidney and Fat of Lactating Dairy Cattle XXXX GLP Not Published RAR, Vol. 3 B.7, May 2017	Y	DAS
CA 6.5.1/1	Adusumilli, H.	2014	Processing Study to Determine the Nature of Residues of 14C -Clopyralid Following the Industrial or Household Preparation DAS Study No. 140574 Dow AgroSciences LLC, Indianapolis, Indiana, USA GLP Not Published RAR, Vol. 3 B.7, May 2017	N	DAS
CA 6.5.3/1	Garbay, M.	2005	Residue Study with Fluroxypyr and Clopyralid and 2,4-MCPA (Bofix = EF-1498) in or on Wheat in France (North And South); Analyse de Residus de Florasulam, Fluroxypyr, 2,4-MCPA et Clopyralid dans l'Orge,	N	DAS

Annex 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
			le Ble, la Farine et les Produits Transformes [Analysis of Residues of Florasulam, Fluroxypyr, 2,4-MCPA and Clopyralid in Barley, Corn, Flour and the Processed Products] DAS Study No. S03DAHBOFIX Solevi, Crest, France; IFBM, Vandoeuvre, France GLP Not Published RAR, Vol. 3 B.7, May 2017		
CA 6.5.3/2	Devine, H.C.	2006	Residues of clopyralid in wheat and process fractions at harvest following a single application of EF-1498, Northern France - 2005 DAS Study No. GHE-P-11274 CEM Analytical Services - UK GLP Not Published RAR, Vol. 3 B.7, May 2017	N	DAS
CA 6.5.33	Devine, H.C.	2006	Residues of clopyralid in spring barley and process fractions at harvest and at intervals following a single application of Lontrel 100 (EF-1136), Southern Europe 2006 DAS Study No. GHE-P-11684 CEM Analytical Services - UK GLP Not Published RAR, Vol. 3 B.7, May 2017	N	DAS
CA 6.6.1/1	Yackovich, P. R. ; Lardie, T. S. ; Brink, D. L.	1993	A 10-1/2 Month Rotational Crops Study With 14C -Labeled Clopyralid - MET90080 DAS Study No. GH-C 2992 Dow AgroSciences LLC, Indianapolis, Indiana, United States GLP Not Published RAR, Vol. 3 B.7, May 2017	N	DAS
CA 6.6.1/2	Yackovich, P. R. ; Lardie, T. S. ; Miller, J. H.	1989	A 125-Day Rotational Crops Study with 14C Labelled Clopyralid DAS Study No. GH-C 2277 DowElanco, Midland, Michigan, USA GLP Not Published	N	DAS

Annex 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
			RAR, Vol. 3 B.7, May 2017		
CA 6.6.1/3	Hall, L. R.	2015	14C -Clopyralid: Metabolism in Confined Rotational Crops with a 30-Day Plant-back Interval DAS Study No. 130733 ABC Laboratories, Inc., Columbia, Missouri 65202, USA GLP Not Published RAR, Vol. 3 B.7, May 2017	N	DAS

Appendix 2 Detailed evaluation of the additional studies relied upon

A 2.1 MCPA

A 2.1.1 Stability of residues

No data submitted in the framework of this application.

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

No data submitted in the framework of this application.

A 2.1.3 Magnitude of residues in plants

The cereal studies provided are conducted with 'KINVARA' and analyse for all three actives substances, therefore the data for MCPA, fluroxypyr and clopyralid are presented together in the following sections.

A 2.1.3.1 Wheat

'KINVARA' contains 233 g MCPA/L, 50 g fluroxypyr/L and 28 g clopyralid/L. The cGAP in the EU (Annex I and MRL) and intended cGAP are summarised in the table below.

Table A 1: Comparison of intended and critical EU GAPs

Type of GAP	Number of applications	Application rate per treatment (precise unit)	Interval between application	Growth stage at last application	PHI (days)
MCPA cGAP EU, Cereals	1	3.6 litres product / ha (100-1000 L water/ha)	N/A	Spring, before first node detectable	-
Fluroxypyr cGAP EU, Cereals (winter & spring)	1	1 litre product / ha (200-400 L water/ha)	N/A	BBCH 12-39 (N-EU & S-EU) BBCH 13-39 (Winter cereals – DE) BBCH 13-29 (Spring cereals in DE)	-
Clopyralid cGAP EU, Cereals	1	1.3 litres product / ha (100-400 L water/ha)	N/A	BBCH 20-39 (N-EU) Mar-April BBCH 20-45 (S-EU) Mar-April	-
MCPA	**Wheat, barley, oats, rye, triticale**				

Type of GAP	Number of applications	Application rate per treatment (precise unit)	Interval between application	Growth stage at last application	PHI (days)
cGAP EU MRL	Not known. MRL of 0.2 mg/kg is established in Annex II of Regulation (EC) 396/2005 as part of Reg (EU) No 491/2014.				
Fluroxypyr cGAP EU MRL	**Wheat, barley, oats, rye, triticale** Not known. MRL of 0.1 mg/kg is established in Annex II of Regulation (EC) 396/2005 as part of ~~Reg (EU) No 822/2009~~ Reg. (EU) 2022/1363				
Clopyralid cGAP EU MRL	**Wheat, barley, oats, triticale** Not known. MRL of 2 mg/kg is established in Annex II of Regulation (EC) 396/2005 as part of Reg (EU) No 2021/1807				
	Rye Not known. MRL of 5 mg/kg is established in Annex II of Regulation (EC) 396/2005 as part of Reg (EU) No 2021/1807				
Intended cGAP (1,2*) Wheat (winter & spring) Barley Rye Triticale Oats	1	3 litres product / ha **or** ~~0.93 kg product~~ / ha (200-400 L water/ha) **MCPA:** 0.699 kg a.s./ha **Fluroxypyr:** 0.150 kg a.s./ha **Clopyralid:** 0.084 kg a.s./ha	N/A	BBCH 24-39	-

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

A 2.1.3.1.1 Study 1: Magnitude of Fluroxypyr, MCPA and Clopyralid Residues in wheat following one application with KINVARA (Fluroxypyr-meptyl 72 g/l + MCPA 233 g/l + Clopyralid 28 g/l, EW) in Southern and Northern Europe in 2014

Comments of zRMS:	The study has been accepted. A study was performed to determine the residues of Fluroxypyr (including Fluroxypyr meptyl ester), MCPA and Clopyralid in wheat following one application with Kinvara (Fluroxypyr-meptyl 72 g/L + MCPA 233 g/L + Clopyralid 28 g/L, EW) at a nominal rate of 3 L/ha. The study comprised four decline curve trials and four harvest trials. The study was carried out under GLP conditions. The field phase of the study was carried out in Northern Europe and in Southern Europe during 2014 under open field conditions. The trial sites chosen were representative areas of the test system (wheat: Triticum durum TRZDU and Tritium aestivum TRZAX); the crop was grown in a way typical of the producing regions. Trial sites in the same country were separated by at least 30 km and under different conditions of cultivation. The analytical methods for analysis of Fluroxypyr acid and Fluroxypyr-meptyl, Clopyralid and MCPA in cereal matrices (wheat whole plant, grain and straw) was validated according to SANCO/3029/99 rev. 4 in the current study. A full set of recoveries (5 recoveries at LOQ, 5 recoveries at least at one higher level, two blank samples) was prepared for each matrix under investigation. For Fluroxypyr-meptyl and Fluroxypyr acid, the analytical method was basically validated separately for

each analyte to check the efficiency of the hydrolysis step of the analytical method. Together with analysis of Fluroxypyr in field samples, procedural recoveries were analyzed for the Fluroxypyr meptyl ester to have a complete check (including hydrolysis step) on the validity of the analytical method at each analysis day.
Recovery results are summarized in the following tables.

Analyte	Fortification Level	Wheat whole plant				Wheat grain				Wheat straw			
		Recoveries		Overall recovery		Recoveries		Overall recovery		Recoveries		Overall recovery	
		Mean	RSD	Mean	RSD	Mean	RSD	Mean	RSD	Mean	RSD	Mean	RSD
	[mg/kg]	[%]	[%]	[%]	[%]	[%]	[%]	[%]	[%]	[%]	[%]	[%]	[%]
Fluroxypyr meptyl (as Fluroxypyr acid*)	0.01	102	6.1	98	6.7	95	8.5	95	9.0	98	8.0	100	7.0
	1.0	95	7.4			95	10.2			102	8.5		
	10	96	2.6			--	--			100	3.6		
Fluroxypyr acid	0.01	88	2.9	95	8.4	98	4.2	101	4.3	96	7.3	99	7.4
	1.0	102	3.9			103	3.6			101	7.2		
Clopyralid	0.01	83	6.7	79	8.8	70	8.2	72	8.3	91	5.9	91	5.2
	1.0	82	4.4			75	7.5			86	3.3		
	10	81	4.0			--	--			88	3.9		
	50	71	5.1			--	--			--	--		
MCPA	0.01	107	3.5	100	6.2	101	4.2	97	6.0	103	1.9	98	4.7
	1.0	101	1.2			92	2.0			94	2.0		
	10	99	4.9			--	--			95	3.2		
	50	92	2.6			--	--			--	--		

** concentrations/residues calculated as Fluroxypyr acid*
RSD: Relative Standard Deviation

Recovery values obtained by HPLC-MS/MS at all fortification levels comply with the standard acceptance criteria of SANCO/3029/99, which demands that the mean recovery at each fortification level should be in the range of 70 – 110 %. It is therefore concluded that the method has proven its applicability for the determination of residues of Fluroxypyr, Fluroxypyr meptyl ester, MCPA and Clopyralid residues in wheat (whole plant, straw and grain). The LOQ was defined as the lowest fortification level with mean recoveries ranging from 70 % to 110 % at RSD of ≤ 20 % and blanks not exceeding 30 % of the LOQ. These criteria were fulfilled for the 0.01 mg/kg fortification for all analytes. The LOD was defined as 30 % of the LOQ for residues in control samples (i.e. 0.003 mg/kg). Residues in the untreated specimens used for recovery experiments and blank samples were below the LOD.

The reference items of Fluroxypyr acid, Clopyralid and MCPA were used for preparing external matrix-matched standard solutions. An external standard calibration was carried out using the peak area in integrator units (counts) from injection of known standards versus standard concentrations in ng/mL. In the analytical sequence after every 2-5 sample extracts external standard solutions were injected. The found amount of the analyte was corrected with the average of the bracketing standards to compensate drifting detector response.

The linearity of the detector response was confirmed by injecting at least five matrix-matched standard solutions covering the following working ranges:
Fluroxypyr acid: 0.05 ng/mL to 50 ng/mL for whole plant and straw samples.
-0.2 ng/mL to 200 ng/mL for grain samples.
Clopyralid, MCPA: 1 ng/mL to 1000 ng/mL for whole plant and grain samples.
-0.75 ng/mL to 500 ng/mL for straw samples.
The correlation coefficients (r2) were ≥ 0.99. The lower margin of the linearity test was below 30 % of the LOQ. The concentration of the analytes in the final extracts was determined by high performance liquid chromatography with MS/MS detection, which is a highly specific detection method.

Residues of Fluroxypyr acid, MCPA and clopyralid in untreated wheat whole plant, grain and straw specimens were below the limit of quantification (i.e. bellow 0.01

mg/kg) and in most cases below the limit of detection (i.e. below 0.003 mg/kg). Residue results for the plot T (treated) samples are summarized in the following table:

Timing	Matrix	Trial TRC14-045							
		R1	R2	R3	R4	R5	R6	R7	R8
Fluroxypyr acid (sum)* (mg/kg)									
0 DAA	Whole plant	2.45	6.73	3.06	2.14	7.78	3.67	1.36	3.06
3 DAA	Whole plant	1.51	2.70	--	--	6.63	3.43	--	--
7±1 DAA	Whole plant	1.29	2.16	--	--	2.46	3.52	--	--
15±1 DAA	Whole plant	1.05	1.24	--	--	2.19	3.78	--	--
30±2 DAA	Whole plant	1.05	1.14	--	--	1.18	1.58	--	--
45±2 DAA	Whole plant	0.72	0.71	--	--	0.98	1.53	--	--
CH	Straw	0.80	1.09	3.22	1.45	1.32	2.80	4.25	4.87
CH	Grain	< LOQ	0.01	0.02	0.04	<LOD	< LOQ	0.01	< LOQ
MCPA (mg/kg)									
0 DAA	Whole plant	10.90	29.50	10.30	9.14	28.00	16.20	8.50	13.20
3 DAA	Whole plant	0.98	2.09	--	--	9.49	8.46	--	--
7±1 DAA	Whole plant	0.36	1.01	--	--	2.35	6.01	--	--
15±1 DAA	Whole plant	0.19	0.50	--	--	1.88	3.67	--	--
30±2 DAA	Whole plant	0.20	0.39	--	--	0.65	2.59	--	--
45±2 DAA	Whole plant	0.11	0.24	--	--	0.57	1.82	--	--
CH	Straw	0.14	0.30	1.47	0.93	0.71	3.66	2.88	2.93
CH	Grain	<LOD	<LOD	<LOD	< LOQ	<LOD	<LOD	<LOD	<LOD
Clopyralid (mg/kg)									
0 DAA	Whole plant	1.39	3.03	1.49	1.27	3.04	1.59	1.17	1.51
3 DAA	Whole plant	0.45	0.95	--	--	1.83	1.03	--	--
7±1 DAA	Whole plant	0.43	0.81	--	--	1.03	0.87	--	--
15±1 DAA	Whole plant	0.45	0.86	--	--	0.91	0.69	--	--
30±2 DAA	Whole plant	0.57	0.82	--	--	0.48	0.46	--	--
45±2 DAA	Whole plant	0.45	0.46	--	--	0.42	0.48	--	--
CH	Straw	0.19	0.88	1.48	0.45	0.73	0.61	1.52	1.08
CH	Grain	0.23	0.27	0.58	0.39	0.25	0.19	0.25	0.25

DAA: Days after application; CH: Commercial harvest
Limit of quantification (LOQ) = 0.01 mg/kg.
Limit of detection (LOD) = 0.003 mg/kg.
** Sum of Fluroxypyr acid and Fluroxypyr meptyl, expressed as Fluroxypyr acid*

Reference:	KCA 6.3.1/01 (previously IIIA 8.3/01)
Report	Magnitude of Fluroxypyr, MCPA and Clopyralid Residues in wheat following one application with KINVARA (Fluroxypyr-meptyl 72 g/l + MCPA 233 g/l + Clopyralid 28 g/l, EW) in Southern and Northern Europe in 2014. Witte, A., 2015, TRC14-045
Guideline(s):	Yes, EU Regulation 1107/2009 SANCO/3029/99 rev. 4 of 11/07/00 of the European Commission
Deviations:	9 - The reported deviations have no impact on the outcome of the study.
GLP:	Yes
Acceptability:	Yes

Executive Summary:
The objective of this study was to determine residue levels of MCPA, Fluroxypyr and Clopyralid in wheat. Eight residue trials were conducted on wheat during 2014. Trials were carried out in Belgium (TRC14-045R1), Germany (TRC14-045R2), Poland (TRC14-045R3), France (North) (TRC14-045 R4), Greece (TRC14-045R5), Spain (TRC14-045R6), Italy (TRC14-045R7) and France (South) (TRC14-045R8). One application of MCPA/Fluroxypyr/Clopyralid (MCPA 233 g/l; Fluroxypyr 50 g/l; Clopyralid 28 g/l) was applied at 1kg product/ha, diluted with water immediately prior to application to a spray volume of 200-400 L/ha, according to the proposed GAP.

Straw and whole plant samples were homogenized completely in a large scale mixer with addition of dry ice. Grain samples were homogenized completely by means of a laboratory mill. After mixing of the

homogenized field samples, laboratory samples were taken and stored deep frozen (≤ -18 °C) until analysis. Crop specimens were analysed for residues of MCPA, Fluroxypyr and Clopyralid using HPLC-MS/MS methods with an LOQ of 0.01 mg/kg for each analyte.

The analytical method for determination of residues of Fluroxypyr (as per the residue definition in plant matrices "fluroxypyr, its esters, salts and its conjugates expressed as fluroxypyr") was based on a slight modification an analytical method described in the DAR of Fluroxypyr (DOW method GRM 96.02, DOW Agrosciences, 1996)[4]. The method involves a hydrolysis step to hydrolyse esters of Fluroxypyr to its free acid. Final analysis is performed by HPLC-MS/MS.

Residues of Clopyralid and MCPA are analysed following a modification of the published QuEChERS method (DIN EN 15662), involving a hydrolysis step to ensure extraction of the acidic compounds during extraction.

The maximum sampling to analysis interval for this study was approx. 8 months. This is accommodated by storage stability data (18 months MCPA; 24 months fluroxypyr; 12 months clopyralid), it is therefore acceptable.

The results of the trials are summarised in Table A2.

[4] Method GRM 96.02 describes extraction with acidified acetone, a short alkaline hydrolysis (while the organic solvent evaporates) and again an acidic hydrolysis for 2 hours at 90^0C. This method was slightly modified by completing both an alkaline hydrolysis step and an acid hydrolysis step therefore it can be assumed that the glycosidic residues will be readily extracted and hydrolysed.

Table A 2: Summary of Study 1 trials in wheat

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 analysed	Residues (mg/kg)			PHI (days)	Details on trial
			g a.s./ ha	Water (l/ha)	g a.s./hl				Fluroxypyr acid (sum)[1]	MCPA	Clopyralid		
(a)		(b)				(c)						(d)	(e)
TRC14-045R1 6210, Villers-Perwin (Hainaut) NEU Belgium 2014	Wheat/ TRZDU Ozon	1) 18/10/13 2) - 3) 24/07/14	FXP: 221 MCPA: 703 CPD: 82	301	73.30	12/05/14	BBCH 39	Whole plant	2.45	10.90	1.39	0	
								Whole plant	1.51	0.98	0.45	3	
								Whole plant	1.29	0.36	0.43	7	
								Whole plant	1.05	0.19	0.45	15	
								Whole plant	1.05	0.20	0.57	30	
								Whole plant	0.72	0.11	0.45	45	
								Straw	0.80	0.14	0.19	NCH	
								Grain	<0.01	n.d*	0.23	NCH	
TRC14-045R2 31303, Burgdorf (Hannover) NEU Germany 2014	Wheat/ TRZDU Arezzo	1) 25/10/13 2) 3) 23/07/14	FXP: 197 MCPA: 631 CPD: 74	270	73.30	30/04/14	BBCH 39	Whole plant	6.73	29.5	3.03	0	
								Whole plant	2.70	2.09	0.95	3	
								Whole plant	2.16	1.01	0.81	7	
								Whole plant	1.24	0.50	0.86	15	
								Whole plant	1.14	0.39	0.82	30	
								Whole plant	0.71	0.24	0.46	44	
								Straw	1.09	0.30	0.88	NCH	
								Grain	0.01	n.d.	0.27	NCH	
TRC14-045R3 88-121, Witowice (Kujawskopomorskie) Poland 2014	Wheat/ TRZDU Zyta	1) 20/09/13 2) 3) 21/07/14	FXP: 229 MCPA: 731 CPD: 85	417	54.98	19/05/14	BBCH 39	Whole plant	3.06	10.30	1.49	0	
								Straw	3.22	1.47	1.48	NCH	
								Grain	0.02	n.d.	0.58	NCH	

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 analysed	Residues (mg/kg)			PHI (days)	Details on trial
			g a.s./ ha	Water (l/ha)	g a.s./hl				Fluroxypyr acid (sum)[1]	MCPA	Clopyralid		
	(a)	(b)				(c)						(d)	(e)
TRC14-045R4 France (North) NEU 2014	Wheat	1.- 2.- 3. 16.07.2014 (grain, straw)	FXP: 211 MCPA: 672 CPD: 79	288	73.31	13/05/14	BBCH 39	Whole plant	2.14	9.14	1.27	0	
								Straw	1.45	0.93	0.45	NCH	
								Grain	0.04	<0.01	0.39	NCH	
TRC14-045R5 Greece SEU 2014	Wheat	1.- 2.- 3. 12.06.2014 (grain, straw)	FXP: 220 MCPA: 702 CPD: 82	200	109.96	01/04/14	BBCH 39	Whole plant	7.78	28.0	3.04	0	
								Whole plant	6.63	9.49	1.83	3	
								Whole plant	2.46	2.35	1.03	7±1	
								Whole plant	2.19	1.88	0.91	15±1	
								Whole plant	1.18	0.65	0.48	30±2	
								Whole plant	0.98	0.57	0.42	45±2	
								Straw	1.32	0.71	0.73	NCH	
								Grain	<0.01	<0.01	0.25	NCH	
TRC14-045R6 Spain SEU 2014	Wheat	1.- 2.- 3. 28.07.2014 (grain, straw)	FXP: 230 MCPA: 733 CPD: 86	314	73.30	16/05/14	BBCH 39	Whole plant	3.67	16.2	1.59	0	Residue of 0.01 mg MCPA/kg in untreated straw sample
								Whole plant	3.43	8.46	1.03	3	
								Whole plant	3.52	6.01	0.87	7±1	
								Whole plant	3.78	3.67	0.69	15±1	
								Whole plant	1.58	2.59	0.46	30±2	
								Whole plant	1.53	1.82	0.48	45±2	
								Straw	2.80	3.66	0.61	NCH	
								Grain	<0.01	<0.01	0.19	NCH	
TRC14-045R7	Wheat	1.-	FXP: 230	314	73.30	22/04/14	BBCH 39	Whole plant	1.36	8.50	1.17	0	

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 analysed	Residues (mg/kg)			PHI (days)	Details on trial
			g a.s./ ha	Water (l/ha)	g a.s./hl				Fluroxypyr acid (sum)[1]	MCPA	Clopyralid		
	(a)	(b)				(c)						(d)	(e)
Italy SEU 2014		2.- 3. 03.07.2014 (grain, straw)	MCPA: 733 CPD: 86					Straw Grain	4.25 0.01	2.88 <0.01	1.52 0.25	NCH NCH	
TRC14-045R8 France (South) SEU 2014	Wheat	1.- 2.- 3. 01.07.2014 (grain, straw)	FXP: 196 MCPA: 626 CPD: 73	301	65.09	23/04/14	BBCH 39	Whole plant Straw Grain	3.06 4.87 <0.01	13.2 2.93 <0.01	1.51 1.08 0.25	0 NCH NCH	

NCH Normal commercial harvest

[1] Sum of Fluroxypyr acid and Fluroxypyr meptyl, expressed as Fluroxypyr acid

*n.d.= not detectable = <0.003 mg/kg

(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 2.1.3.2 Barley

Refer to Table A1 for comparison of the intended and critical EU GAPs.

A 2.1.3.2.1 Study 1: Magnitude of Fluroxypyr, MCPA and Clopyralid Residues in barley following one application with KINVARA (Fluroxypyr-meptyl 72 g/l + MCPA 233 g/l + Clopyralid 28 g/l, EW) in Southern and Northern Europe in 2014

Comments of zRMS:

The study has been accepted.
The analytical methods for analysis of Fluroxypyr acid and Fluroxypyr-meptyl, Clopyralid and MCPA in cereal matrices (wheat whole plant, grain and straw) were validated in study TRC14-045 (analytical part 14T05029-01-RACE). A full set of recoveries (5 recoveries at LOQ, 5 recoveries at least at one higher level, two blank samples) was prepared for each matrix under investigation.
In the current study, a reduced validation set (3 recoveries at LOQ, 3 recoveries at least at one higher level, two blank samples) was prepared for the similar barley matrices under investigation. For Fluroxypyr-meptyl and Fluroxypyr acid, the analytical method was basically validated separately for each analyte to check the efficiency of the hydrolysis step of the analytical method. Together with analysis of Fluroxypyr in field samples, procedural recoveries were analyzed for the Fluroxypyr meptyl ester to have a complete check (including hydrolysis step) on the validity of the analytical method at each analysis day.
Accuracy of the analytical method for barley whole plant, straw and grain samples was studied by means of recovery experiments with blank samples fortified at different concentration levels with Fluroxypyr acid, Fluroxypyr-meptyl, Clopyralid and MCPA, at the LOQ level and at a higher level. Precision and repeatability was also estimated from these experiments.
Recovery results are summarized in the following tables.

		Barley whole plant				Barley grain				Barley straw			
Analyte	Fortification Level	Recoveries		Overall recovery		Recoveries		Overall recovery		Recoveries		Overall recovery	
		Mean	RSD	Mean	RSD	Mean	RSD	Mean	RSD	Mean	RSD	Mean	RSD
	[mg/kg]	[%]	[%]	[%]	[%]	[%]	[%]	[%]	[%]	[%]	[%]	[%]	[%]
Fluroxypyr meptyl (as Fluroxypyr acid*)	0.01	95	12.9	92	11.7	86	6.3	89	7.3	100	2.2	97	3.6
	1.0	89	13.6			93	5.9			97	1.5		
	10	89	1.9			--	--			93	3.3		
Fluroxypyr acid	0.01	94	8.0	94	5.7	90	9.3	95	8.3	94	1.1	96	2.3
	1.0	93	3.9			100	1.2			98	1.2		
Clopyralid	0.01	87	4.7	85	4.0	77	8.4	74	7.5	92	5.6	85	12.8
	1.0	85	3.4			71	4.9			71	3.3		
	50	82	0.7			--	--			91	2.5		
MCPA	0.01	103	3.3	100	4.1	101	1.7	102	1.6	102	2.3	99	3.6
	1.0	100	2.6			103	1.1			98	1.2		
	50	95	1.8			--	--			98	2.2		

** concentrations/residues calculated as Fluroxypyr acid*
RSD: Relative Standard Deviation

Recovery values obtained by HPLC-MS/MS at all fortification levels comply with the standard acceptance criteria, which demands that the mean recovery at each fortification level should be in the range of 70 – 110 %. It is therefore concluded that the method has proven its applicability for the determination of residues of Fluroxypyr, Fluroxypyr meptyl ester, MCPA and Clopyralid residues in barley (whole plant, straw and grain).
The LOQ was defined as the lowest fortification level with mean recoveries ranging from 70 % to 110 % at RSD of ≤ 20 % and blanks not exceeding 30 % of the LOQ. These criteria were fulfilled for the 0.01 mg/kg fortification for all analytes. The LOD was defined as 30 % of the LOQ for residues in control samples (i.e. 0.003

mg/kg). Residues in the untreated specimens used for recovery experiments and blank samples were below of the LOD.
The reference items of Fluroxypyr acid, Clopyralid and MCPA were used for preparing external matrix-matched standard solutions. An external standard calibration was carried out using the peak area in integrator units (counts) from injection of known standards versus standard concentrations in ng/mL. In the analytical sequence after every 2-5 sample extracts external standard solutions were injected. The found amount of the analyte was corrected with the average of the bracketing standards to compensate drifting detector response.
The linearity of the detector response was confirmed by injecting at least five matrix-matched standard solutions covering the following working ranges:
Fluroxypyr acid: 0.05 ng/mL to 50 ng/mL for whole plant and straw samples.
-0.2 ng/mL to 200 ng/mL for grain samples.
Clopyralid, MCPA: 1 ng/mL to 1000 ng/mL for whole plant and grain samples.
-0.75 ng/mL to 500 ng/mL for straw samples.
The correlation coefficients (r2) were ≥ 0.99. The lower margin of the linearity test was below 30 % of the LOQ. The concentration of the analytes in the final extracts was determined by high performance liquid chromatography with MS/MS detection, which is considered to be a highly specific detection method. Residues of Fluroxypyr acid, MCPA and clopyralid in untreated barley whole plant, grain and straw specimens were below the LOQ (i.e. below 0.01 mg/kg), in most cases below the LOD (< 30 % of LOQ, i.e. 0.003 mg/kg), except in trial TRC14-059R3.
Residue results for the plot T (treated) samples are summarized in the following table:

Timing	Matrix	Trial TRC14-059							
		R1	R2	R3	R4	R5	R6	R7	R8
Fluroxypyr acid (sum)* (mg/kg)									
0 DAA	Whole plant	2.23	3.73	5.03	1.91	2.52	2.57	2.41	3.36
3 DAA	Whole plant	1.57	2.31	--	--	2.29	2.89	--	--
7±1 DAA	Whole plant	1.33	2.29	--	--	1.59	1.52	--	--
15±1 DAA	Whole plant	1.14	1.53	--	--	1.47	1.68	--	--
30±2 DAA	Whole plant	0.98	1.15	--	--	0.64	1.32	--	--
45±2 DAA	Whole plant	0.73	0.63	--	--	0.45	0.89	--	--
CH	Straw	1.48	0.99	1.99	0.74	1.07	2.07	1.53	1.75
CH	Grain	0.03	< LOQ	0.02	0.10	< LOQ	< LOQ	< LOQ	0.04
MCPA (mg/kg)									
0 DAA	Whole plant	11.7	18.8	11.2	9.02	20.0	11.9	11.8	14.7
3 DAA	Whole plant	0.67	0.90	--	--	8.83	7.60	--	--
7±1 DAA	Whole plant	0.30	0.68	--	--	1.36	3.45	--	--
15±1 DAA	Whole plant	0.19	0.32	--	--	0.86	0.98	--	--
30±2 DAA	Whole plant	0.15	0.28	--	--	0.43	0.43	--	--
45±2 DAA	Whole plant	0.10	0.15	--	--	0.29	0.28	--	--
CH	Straw	0.26	0.27	0.28	0.08	0.48	0.54	0.58	0.29
CH	Grain	<LOD	<LOD	<LOD	<LOD	<LOD	< LOQ	< LOQ	<LOD
Clopyralid (mg/kg)									
0 DAA	Whole plant	1.18	1.80	2.15	0.98	2.14	1.31	1.40	1.67
3 DAA	Whole plant	0.31	0.85	--	--	1.76	1.16	--	--
7±1 DAA	Whole plant	0.49	0.98	--	--	0.91	0.56	--	--
15±1 DAA	Whole plant	0.62	0.73	--	--	0.86	0.41	--	--
30±2 DAA	Whole plant	0.59	0.56	--	--	0.71	0.50	--	--
45±2 DAA	Whole plant	0.55	0.38	--	--	0.39	0.38	--	--
CH	Straw	1.02	0.75	1.43	0.15	0.68	0.68	0.75	0.83
CH	Grain	0.17	0.10	0.15	0.09	0.17	0.08	0.14	0.31

DAA: Days after application; CH: Commercial harvest
Limit of quantification (LOQ) = 0.01 mg/kg.
Limit of detection (LOD) = 0.003 mg/kg.
** Sum of Fluroxypyr acid and Fluroxypyr meptyl, expressed as Fluroxypyr acid*

Reference: KCA 6.3.2/01 (previously IIIA 8.3/02)

Report: Magnitude of Fluroxypyr, MCPA and Clopyralid Residues in barley following one application with KINVARA (Fluroxypyr-meptyl 72 g/l + MCPA 233 g/l + Clopyralid 28 g/l, EW) in Southern and Northern Europe in

	2014, Witte, A., 2015, TRC14-059
Guideline(s):	Yes, EU Regulation 1107/2009 SANCO/3029/99 rev. 4 of 11/07/00 of the European Commission
Deviations:	10 -The reported deviations have no impact on the outcome of the study.
GLP:	Yes
Acceptability:	Yes

Executive Summary:
The objective of this study was to determine residue levels of MCPA, Fluroxypyr and Clopyralid in barley. Eight residue trials were conducted on barley during 2014. Trials were carried out in Belgium (TRC14-059R1), Germany (TRC14-059R2), Poland (TRC14-059R3), France (North) (TRC14-059R4), Greece (TRC14-059R5), Spain (TRC14-059R6), Italy (TRC14-059R7) and France (South) (TRC14-059R8). One application of MCPA/Fluroxypyr/Clopyralid (MCPA 233 g/l; Fluroxypyr 50 g/l; Clopyralid 28 g/l) was applied at 1kg/ha, diluted with water immediately prior to application to a spray volume of 200-400 L/ha, according to the proposed GAP.

Straw and whole plant samples were homogenized completely in a large scale mixer with addition of dry ice. Grain samples were homogenized completely by means of a laboratory mill. After mixing of the homogenized field samples, laboratory samples were taken and stored deep frozen (≤ -18 °C) until analysis. Crop specimens were analysed for residues of MCPA, Fluroxypyr and Clopyralid using HPLC-MS/MS methods with an LOQ of 0.01 mg/kg for each analyte.

The analytical method for determination of residues of Fluroxypyr (as per the residue definition in plant matrices "fluroxypyr, its esters, salts and its conjugates expressed as fluroxypyr") was based on a slight modification an analytical method described in the DAR of Fluroxypyr (DOW method GRM 96.02, DOW Agrosciences, 1996)[5]. The method involves a hydrolysis step to hydrolyse esters of Fluroxypyr to its free acid. Final analysis is performed by HPLC-MS/MS.

Residues of Clopyralid and MCPA were analysed following a modification of the published QuEChERS method (DIN EN 15662), involving a hydrolysis step to ensure extraction of the acidic compounds during extraction.

The maximum sampling to analysis interval for this study was approx. 8 months. This is accommodated by storage stability data (18 months MCPA; 24 months fluroxypyr; 12 months clopyralid), it is therefore acceptable.

The results of the trials are summarised in Table A3.

[5] Method GRM 96.02 describes extraction with acidified acetone, a short alkaline hydrolysis (while the organic solvent evaporates) and again an acidic hydrolysis for 2 hours at 90^0C. This method was slightly modified by completing both an alkaline hydrolysis step and an acid hydrolysis step therefore it can be assumed that the glycosidic residues will be readily extracted and hydrolysed.

Table A 3: Summary of Study 1 trials in barley

Trial No./ Location/ EU zone/ Year (a)	Commodity/ Variety (a)	Date of 1.Sowing or planting 2.Flowering 3. Harvest (b)	Application rate per treatment: g a.s./ ha	Application rate per treatment: Water (l/ha)	Application rate per treatment: g a.s./hl	Dates of treatment or no. of treatments and last date (c)	Growth stage at last treatment or date	Portion analysed	Residues (mg/kg): Fluroxypyr acid (sum)[1]	Residues (mg/kg): MCPA	Residues (mg/kg): Clopyralid	PHI (days) (d)	Details on trial (e)
TRC14-059R1 B-1450, Cortil-Noirmont (Waloon-Brabant) NEU Belgium 2014	Barley/ HORVX Tenor + Meridian	1) 27/09/13 2) 3) 25/06/14	FXP: 218 MCPA: 696 CPD: 81	298	73.30	22/04/14	BBCH 39	Whole plant	2.23	11.7	1.18	0	
								Whole plant	1.57	0.67	0.31	3	
								Whole plant	1.33	0.30	0.49	7	
								Whole plant	1.14	0.19	0.62	15	
								Whole plant	0.98	0.15	0.59	30	
								Whole plant	0.73	0.1	0.55	45	
								Straw	1.48	0.26	1.02	NCH	
								Grain	0.03	n.d.*	0.17	NCH	
TRC14-059R2 31303, Burgdorf (Hannover) NEU Germany 2014	Barley/ HORVX Quench	1) 30/03/14 2) 3) 23/07/14	FXP: 208 MCPA: 663 CPD: 77.5	284	73.30	26/05/14	BBCH 37-39	Whole plant	3.73	18.8	1.80	0	
								Whole plant	2.31	0.9	0.85	3	
								Whole plant	2.29	0.68	0.98	7	
								Whole plant	1.53	0.32	0.73	15	
								Whole plant	1.15	0.28	0.56	30	
								Whole plant	0.63	0.15	0.38	45	
								Straw	0.99	0.27	0.75	NCH	
								Grain	<0.01	n.d.	0.10	NCH	
TRC14-059R3 88-306, Szczepanowo (Kujawskopomorskie) Poland 2014	Barley/ HORVX Antek	1) 18/04/14 2) 3) 21/07/14	FXP: 222 MCPA: 708 CPD: 83	404	73.30	31/05/14	BBCH 39	Whole plant	5.03	11.2	2.15	0	
								Straw	1.99	0.28	1.43	NCH	
								Grain	0.02	n.d.	0.15	NCH	
TRC14-059R4 France (North)	Barley	1.- 2.-	FXP: 214 MCPA: 682	292	73.39	23/04/14	BBCH 39	Whole plant	1.91	9.02	0.98	0	

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 analysed	Residues (mg/kg)			PHI (days)	Details on trial
			g a.s./ ha	Water (l/ha)	g a.s./hl				Fluroxypyr acid (sum)[1]	MCPA	Clopyralid		
(a)		(b)				(c)						(d)	(e)
NEU 2014		3. 26.06.2014 (grain, straw)	CPD: 80					Straw Grain	0.74 0.10	0.08 <0.01	0.15 0.09	NCH NCH	
TRC14-059R5 Greece SEU 2014	Barley	1.- 2.- 3. 29.05.2014 (grain, straw)	FXP: 220 MCPA: 701 CPD: 82	200	109.9	01/04/14	BBCH 39	Whole plant Whole plant Whole plant Whole plant Whole plant Whole plant Straw Grain	2.52 2.29 1.59 1.47 0.64 0.45 1.07 <0.01	20.0 8.83 1.36 0.86 0.43 0.29 0.48 <0.01	2.14 1.76 0.91 0.86 0.71 0.39 0.68 0.17	0 3 7±1 15±1 30±2 45±2 NCH NCH	
TRC14-059R6 Spain SEU 2014	Barley	1.- 2.- 3. 26.06.2014 (grain, straw)	FXP: 224 MCPA: 715 CPD: 83.5	306	73.3	14/04/14	BBCH 39	Whole plant Whole plant Whole plant Whole plant Whole plant Whole plant Straw Grain	2.57 2.89 1.52 1.68 1.32 0.89 2.07 <0.01	11.9 7.60 3.45 0.98 0.43 0.28 0.54 <0.01	1.31 1.16 0.56 0.41 0.50 0.38 0.68 0.08	0 3 7±1 15±1 30±2 45±2 NCH NCH	Residue of 0.01 mg MCPA/kg in untreated straw sample
TRC14-059R7 Italy	Barley	1.- 2.-	FXP: 217 MCPA: 691	296	73.3	16/04/14	BBCH 39	Whole plant	2.41	11.8	1.40	0	

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 analysed	Residues (mg/kg)			PHI (days)	Details on trial
			g a.s./ ha	Water (l/ha)	g a.s./hl				Fluroxypyr acid (sum)[1]	MCPA	Clopyralid		
	(a)	(b)				(c)						(d)	(e)
SEU 2014		3. 19.06.2014 (grain, straw)	CPD: 81					Straw Grain	1.53 <0.01	0.58 <0.01	0.75 0.14	NCH NCH	
TRC14-059R8 France (South) SEU 2014	Barley	1.- 2.- 3. 25.06.2014 (grain, straw)	FXP: 222 MCPA: 709 CPD: 83	303	73.31	15/04/14	BBCH 39	Whole plant Straw Grain	3.36 1.75 0.04	14.7 0.29 <0.01	1.67 0.83 0.31	0 NCH NCH	

NCH Normal commercial harvest

[1] Sum of Fluroxypyr acid and Fluroxypyr meptyl, expressed as Fluroxypyr acid

*n.d.= not detectable = <0.003 mg/kg

(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 2.1.3.3 Grassland

'KINVARA' contains 233 g MCPA/L, 50 g fluroxypyr/L and 28 g clopyralid/L. The cGAP in the EU (Annex I and MRL) and intended cGAP are summarised in the table below.

Table A 4: Comparison of intended and critical EU GAPs (MCPA-only)

Type of GAP	Number of applications	Application rate per treatment	Interval between application	Growth stage	PHI (days)
cGAP EU (DAR Addenda, Italy, 2003)	2	1800 g MCPA/ha	4 weeks	Spring to early summer	60
Intended cGAP	1	699 g MCPA/ha	n/a	March-Sept	7

Comments of zRMS:	The study has been accepted. The study summary: A study was performed to quantify residues of Fluroxypyr (including Fluroxypyr meptyl ester), MCPA and Clopyralid in Grassland following one application with Kinvara (Fluroxypyr-meptyl 72 g/L + MCPA 233 g/L + Clopyralid 28 g/L, EW) at a nominal rate of 3 L/ha under open field conditions in Northern Europe in 2014. The study comprised four decline curve trials and four harvest trials. The study was carried out under GLP conditions and according to OECD Good Laboratory Practice Standards. The field phase of the study was carried out in Northern Europe during 2014 under open field conditions. The trial sites chosen were representative areas of the test system (grassland); the crop was grown in a way typical of the producing regions. Trial sites in the same country were separated by at least 30 km and under different conditions of cultivation. The trials consisted of one untreated plot and one treated plot settled in the same field at enough distance to avoid any contamination. The plot size ranged from 30.0 m2 to 90.0 m2. One broadcast foliar spray application was performed 21 days before harvest time. Applications were performed according to the Good Agricultural Practices. The application equipment consisted of a motorized knapsack sprayer with a handheld boom, working at pressure of 200-400 kPa. The equipment was calibrated before each application. Calibration was performed at the trial site by using the volume/time method for liquid applications. The nominal application volume was fixed at 200-400 L/ha and the actual volume ranged from 218.00 to 318.33 L/ha. The actual application rate of formulated product ranged from 2886.64 to 3270.00 mL of commercial product per hectare (equivalent to 674.32 and 763.87 g of MCPA per hectare; 211.59 and 239.69 g of fluroxypyr per hectare and 78.81 and 89.27 g of clopyralid per hectare). In the decline curve trials, sampling was carried out three times in the control plots, where specimens were collected 0 days before the application, 21±2 and 28±2 days after the application. Sampling was carried out six times in the treated plots, where specimens were collected 0, 3, 7±1, 14±1, 21±2 and 28±2 days after the application. In the harvest trials, sampling was carried out once in both control and treated plots, where specimens were collected 21±2 days after the application (21±2 DAA). Additionally, 21±2 days after the application, green matter was cut and dried to obtain samples of hay in all trials. Two samples per plot were collected, one sample for shipping (S) and one spare sample (R). Each sample was representative of the whole plot. Samples were collected from the central area of each plot. The entire plants were collected from at least 12 short lengths from rows distributed over the plots. Plants were cut close to ground level avoiding soil contamination. Samples were frozen the same day of sampling, and they were maintained deep frozen (≤-18°C) during storage and shipment to the analytical laboratory. The storage period between sampling and extraction was 66-284 days. Samples were

analysed within 7 days after the extraction.
Specimens of grassland (green matter and hay) were analysed for Fluroxypyr (including Fluroxypyr meptyl ester), MCPA and Clopyralid. The analytical methods for analysis of Fluroxypyr acid and Fluroxypyr-meptyl, Clopyralid and MCPA in cereal matrices (wheat whole plant, grain and straw) were validated in study TRC14-045 (analytical part 14T05029-01-RACE). A full set of recoveries (5 recoveries at LOQ, 5 recoveries at least at one higher level, two blank samples) was prepared for each matrix. Accuracy of the analytical method for grassland green matter and hay samples was studied by means of recovery experiments with blank samples fortified at different concentration levels with Fluroxypyr acid, Fluroxypyr-meptyl, Clopyralid and MCPA, at the LOQ level and at higher levels. Precision and repeatability was also estimated from these experiments. In the current study, at least a reduced validation set (min. 3 recoveries at LOQ, min. 3 recoveries at least at one higher level, two blank samples) was prepared for the similar grass matrices under investigation. For Fluroxypyr-meptyl and Fluroxypyr acid, the analytical method was basically validated separately for each analyte to check the efficiency of the hydrolysis step of the analytical method. Together with analysis of Fluroxypyr in field samples, procedural recoveries were analyzed for the Fluroxypyr meptyl ester to have a complete check (including hydrolysis step) on the validity of the analytical method at each analysis day.
Recovery results are summarized in the following tables:

Analyte	Fortification Level	Grassland green matter				Grassland hay			
		Recoveries		Overall recovery		Recoveries		Overall recovery	
		Mean	RSD	Mean	RSD	Mean	RSD	Mean	RSD
	[mg/kg]	[%]	[%]	[%]	[%]	[%]	[%]	[%]	[%]
Fluroxypyr meptyl (as Fluroxypyr acid*)	0.01	88	7.0	88	6.5	94	8.0	93	6.4
	1.0	92	3.5			97	6.2		
	10	83	3.1			89	1.9		
Fluroxypyr acid	0.01	93	8.4	94	5.3	101	3.4	101	2.4
	1.0	95	1.1			102	1.5		
Clopyralid	0.01	86	6.3	78	9.9	78	6.8	78	13.5
	1.0	74	8.9			71	16.3		
	5.0	--	--			81	15.0		
	50	73	4.6			--	--		
MCPA	0.01	108	8.2	103	6.9	102	3.4	98	4.3
	1.0	105	3.5			98	3.1		
	5.0	--	--			96	4.5		
	50	97	2.7			96	4.6		

** concentrations/residues calculated as Fluroxypyr acid*
RSD: relative standard deviation

Recoveries for Clopyralid at 50 mg/kg in hay were not within guideline requirements (mean recovery was not between 70 - 110 %), therefore they were not used for further calculations. The lower level (5 mg/kg) was sufficient to cover the highest residues found in field samples; therefore the excluded recoveries at 50 mg/kg were not necessary for Clopyralid. Recovery values obtained by HPLC-MS/MS for all analytes at all other fortification levels comply with the standard acceptance criteria of SANCO/3029/99, which demands that the mean recovery at each fortification level should be in the range of 70 – 110 %. The limit of quantification (LOQ) was defined as the lowest fortification level with mean recoveries ranging from 70 % to 110 % at a relative standard deviation (RSD) of ≤ 20 % and blanks not exceeding 30 % of the LOQ. These criteria were fulfilled for the 0.01 mg/kg fortification for all analytes. The limit of detection (LOD) was defined as 30 % of the limit of quantification as required in the guideline SANCO/3029/99 rev.4 for residues in control samples (i.e. 0.003 mg/kg). Residues in the untreated specimens used for recovery experiments and blank samples were below 30 % of the LOQ, respectively below the limit of detection.
The reference items of Fluroxypyr acid, Clopyralid and MCPA were used for

preparing external matrix-matched standard solutions. An external standard calibration was carried out using the peak area in integrator units (counts) from injection of known standards versus standard concentrations in ng/mL. In the analytical sequence after every 2-5 sample extracts external standard solutions were injected. The found amount of the analyte was corrected with the average of the bracketing standards to compensate drifting detector response.
The linearity of the detector response was confirmed by injecting at least five matrix-matched standard solutions covering the following working ranges:
Fluroxypyr acid: 0.05 ng/mL to 50 ng/mL for grassland green matter and hay samples. Clopyralid, MCPA: 1 ng/mL to 1000 ng/mL for grassland green matter samples 0.50 ng/mL to 500 ng/mL for hay samples. The correlation coefficients (r2) were ≥ 0.99. The lower margin of the linearity test was below 30 % of the LOQ.
The concentration of the analytes in the final extracts was determined by high performance liquid chromatography with MS/MS detection, which is considered to be a highly specific detection method. Residues of all analytes in untreated specimens were below the limit of quantification (i.e. 0.01 mg/kg), in most cases below the limit of detection (< 30 % of LOQ, i.e. 0.003 mg/kg). Residue results for the plot T (treated) samples are summarized in the following table:

Timing	Matrix	Trial TRC14-022							
		R1	R2	R3	R4	R5	R6	R7	R8
Fluroxypyr acid (sum)* (mg/kg)									
0 DAA	Green matter	4.08	7.56	--	8.72	6.65	--	--	--
3 DAA	Green matter	2.86	7.25	--	5.91	2.60	--	--	--
7±1 DAA	Green matter	1.56	6.94	--	5.02	2.01	--	--	--
14±1 DAA	Green matter	1.35	3.84	--	3.46	4.60	--	--	--
21±2 DAA	Green matter	0.90	2.39	1.12	1.95	2.57	1.47	1.62	7.07
21±2 DAA	Hay	3.00	5.49	3.42	6.74	7.35	5.18	4.59	13.30
28±2 DAA	Green matter	0.54	3.05	--	1.76	0.85	--	--	--
MCPA (mg/kg)									
0 DAA	Green matter	19.4	41.10	--	52.30	33.90	--	--	--
3 DAA	Green matter	10.2	43.20	--	7.43	9.48	--	--	--
7±1 DAA	Green matter	4.46	32.10	--	5.53	6.81	--	--	--
14±1 DAA	Green matter	3.71	15.80	--	3.59	25.30	--	--	--
21±2 DAA	Green matter	2.61	10.80	1.59	2.21	9.61	3.75	9.10	8.22
21±2 DAA	Hay	9.00	16.60	3.89	4.57	28.00	9.16	14.90	8.33
28±2 DAA	Green matter	1.75	11.70	--	1.27	2.97	--	--	--
Clopyralid (mg/kg)									
0 DAA	Green matter	1.79	3.32	--	4.17	3.13	--	--	--
3 DAA	Green matter	0.98	1.25	--	1.78	1.62	--	--	--
7±1 DAA	Green matter	0.87	1.77	--	2.04	1.30	--	--	--
14±1 DAA	Green matter	0.79	1.11	--	1.71	1.40	--	--	--
21±2 DAA	Green matter	0.71	0.70	1.23	1.22	1.79	1.07	0.89	1.73
21±2 DAA	Hay	2.31	2.80	3.68	3.43	4.11	2.81	2.99	2.99
28±2 DAA	Green matter	0.52	0.91	--	1.29	0.90	--	--	--

DAA: Days after application
Limit of detection (LOQ) = 0.01 mg/kg .
Limit of detection (LOD) = 0.003 mg/kg .
** Sum of Fluroxypyr acid and Fluroxypyr meptyl, expressed as Fluroxypyr acid*

Reference:	KCA 6.3.3/02
Report	1. Magnitude of Fluroxypyr, MCPA and Clopyralid Residues in Grassland Following One Application with Kinvara (Fluroxypyr-meptyl 72 g/L + MCPA 233 g/L + Clopyralid 28 g/L, EW) in Northern Europe in 2014 Witte, A., 2015, study TRC14-022 2. Amendment 1 to the study
Guideline(s):	GLP Consensus Document, Regulation (EC) No 1107/2009, SANCO/3029 /99 rev. 4, 11/07/2000.
Deviations:	The following deviations occurred during the carrying out of the study: 1. Trial TRC14-022R3: Application was cancelled and performed again in a

	nearby plot 2. BBCH at sampling of immature samples ranged from 30 to 51; BBCH for mature samples ranged from 37 to 65. Nevertheless, main stage on each sampling occasion was within the range required in the study plan and samples were considered representative. 3. Trial TRC14-022R4: During storage of samples the temperature was punctually above -15ºC, with a maximum of -12.9ºC. 4. Trials TRC14-022R1 and TRC14-022R6: Crop destruction is not documented 5. Trial TRC14-022R5 and TRC14-022R8: Mean temperature records during the trial period are not available 6. Trial TRC14-022R4: Data were not filled in the Trial camp notebook but in the Test Site notebook. 7. The issue of the report was delayed. The reported deviations have no impact on the outcome of the study.
GLP:	Yes
Acceptability:	Yes

Comments of zRMS:

The study has been accepted.
Kinvara contains MCPA, clopyralid and fluroxypyr but only MCPA was the subject of the study.
The objective of the study was to determine the residue levels of MCPA in grass raw agricultural commodity after one foliar application of the formulated product Kinvara (233 g MCPA/L), at the rate of 3 L/ha.
The study consisted of two phases: the field phase and the analytical phase.
The study was conducted under field conditions at 5 sites in Northern Europe. All the trials were sampled frequently to monitor the decline of residues shortly after the treatment. In each trial one plot was treated once with Kinvara at the application rate of 3 L/ha (700 g MCPA/ha). The application was performed 64 (± 4) days before harvest (except for trial B8208 ND1, see deviation No. 181023). One plot remained untreated.
In all trials sampling was performed just before application in the untreated plot, just after application in the treated plot, then 1, 2, 3, 5 (±1), 7 (±1), 10 (±1) and 64 (± 4) (except for trial B8208 ND1, see deviation No. 181023) days after the application in both plots. MCPA residues were analysed in samples harvested during the field phase.
Some trials were not finished at the moment of writing this report, the missing data will be added in a further amended report.

SUMMARIZED RESULTS

MCPA residues in control samples were non-detectable or below the limit of quantification. The residue results for MCPA in the treated specimens are summarized below:

		MCPA residues (mg/kg)							
Trial No.	**Matrix**	**0 DAA**	**1 DAA**	**2 DAA**	**3 DAA**	**5 (± 1) DAA**	**7 (± 1) DAA**	**10 (± 1) DAA**	**64 (± 4) DAA**
B8208 MA1	Green matter	**91.61**	**106.14**	**35.18**	**23.02**	**25.38**	**24.08**	**17.53**	*
B8208 ND1	Green matter	**36.81**	**35.99**	**32.10**	**17.55**	**16.86**	**10.10**	**12.94**	*
B8208 BW1	Green matter	**65.69**	**53.45**	**28.16**	**29.53**	**24.04**	**27.18**	**19.26**	*
B8208 CZ1	Green matter	*	*	*	*	*	*	*	*
B8208 PL1	Green matter	**51.33**	**33.24**	**20.53**	**23.11**	**24.12**	**16.64**	**20.17**	**3.01**

DAA: Days after application
LOD = 0.002 mg/kg
LOQ = 0.01 mg/kg

* Data were not available at the moment of this report writing, the missing data will be added in a further amended report.

Residues are analysed following a modification of the QuEChERS method involving a hydrolysis step to ensure extraction of the acidic compounds during

extraction. The extract obtained is analyzed by liquid chromatography with MS/MS detection. Two transitions were monitored (for confirmation also).
Matrix effects (enhancement or suppression) on the instrument response were considered significant. Consequently, matrix-matched calibration solutions were used for calibration.

Summary of recoveries

Analyte	Matrix	Fortification level (mg/kg)	Mean recovery Percentage (%)	Standard deviation (SD) (%)	Relative standard deviation (RSD) (%)	Number of fortified samples (n)
MCPA	Grass (green matter)	0.01	86.3%	6.7%	7.7%	5
		0.10	90.3%	2.0%	2.2%	5
		All levels	88.3%	5.1%	5.8%	10

The accuracy of the method fulfils the requirements for residue analytical methods which demand that the mean recoveries per fortification level should be in the range 70-110% for samples spiked at 1 x LOQ and for samples spiked at 10 x LOQ.
RSD determined was less than 20% for samples spiked at 1 x LOQ and for samples spiked at 10 x LOQ, the method therefore fulfils the requirements for residue analytical methods.

Reference:	KCA 6.3.3/01
Report	Determination of MCPA Residues in Grass Following One Foliar application with KINVARA under Field Conditions in Northern Europe in 2018, Diebold, J-L., 2019, report No R B8208.
Guideline(s):	EU Regulation 1107/2009 OECD TG 509, 07/09/2009 SANCO 7525/VI/95 rev. 10.3, 13 June 2017 SANCO/825/00 rev.8.1, 16/11/2010 SANCO/3029/99 rev. 4, 11/07/2000 ENV/JM/MONO(2007)17, 13/08/2007
Deviations:	Yes – but considered to have no impact.
GLP:	Yes
Acceptability:	Yes

The study consisted of two phases: the field phase and the analytical phase. The study was conducted under field conditions at five sites in northern Europe. All the trials were sampled frequently to monitor the decline of residues shortly after the treatment. In each trial, one plot was treated once with KINVARA (formulation type ME) at the application rate of 3 L/ha (700 g MCPA/ha). The application was performed 64 (± 4) days before harvest (except for trial B8208 ND1, where the last sampling was performed 70 DAA). One plot remained untreated. In all trials sampling was performed just before application in the untreated plot, just after application in the treated plot, then 1, 2, 3, 5 (±1), 7 (±1), 10 (±1) and 64 (± 4) (except for trial B8208 ND1) DAA in both plots.

MCPA residues were analysed in samples harvested during the field phase. Samples were extracted according to the following method:

"*Magnitude of Fluroxypyr, MCPA and Clopyralid Residues in Grassland Following One Application with Kinvara (Fluroxypyr-meptyl 72 g/L + MCPA 233 g/L + Clopyralid 28 g/L, EW) in Northern Europe in 2014*"; CIP Chemisches Institut Pforzheim GmbH; CIP Phase ID: 14T05029-01-RAVE (ANADIAG reference No. MC 573).

ANADIAG References (French version) of the method are:

- for the preparation and extraction of the samples: SOP MP 612
- for the analysis of extracts and for the calibration: SOP MA 1431

Residues of MCPA were analysed following a modification of the QuEChERS method involving a hydrolysis step to ensure extraction of the acidic compounds during the extraction step. The extract obtained is analysed by liquid chromatography with MS/MS detection using a BEH C18 column (2.1 x 100 mm, 1.7 µm) monitoring the following ion transitions: 200.9→143.0 m/z and 198.9→141.0 m/z.

The method was fully validated in accordance with SANCO/3029/99 and SANCO/825/00 as part of the study. The LOQ was 0.01 mg/kg. The LOD was 0.002 mg/kg. The maximum storage time of treated samples was 123 days.

Table A 5: Summary of the study 1 trials in grassland

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 analysed	Residues (mg/kg)	PHI (days)	Details on trial
			g a.s./ ha	Water (l/ha)	g a.s./hl				MCPA		
	(a)	(b)				(c)				(d)	(e)
B8208 MA1 **Donnelay** **57810** **France (North)**	Grass	1) n/a 2) n/a 3) n/a	735	420	175	11/09/2018	BBCH 29-31	Green matter Green matter Green matter Green matter Green matter Green matter Green matter Green matter	91.61 106.14 35.18 23.02 25.38 24.08 17.53 9.30	0 1 2 3 6 7 10 64	None
B8208 ND1 **Steenbecque** **59189** **France (North)**	Grass	1) 26/04/2017 2) 20/07/2018-03/08/2018 3) 23/10/2018	723	310	233	14/08/2018	BBCH 30	Green matter Green matter Green matter Green matter Green matter Green matter Green matter Green matter	36.81 35.99 32.10 17.55 16.86 10.10 12.94 1.62	0 1 2 3 6 7 10 70	None
B8208 BW1 **Breisach** **79206** **Germany**	Grass	1) 2012-2014 2) n/a 3) n/a	739	422	175	24/07/2018	n.r.	Green matter Green matter Green matter Green matter Green matter Green matter Green matter Green matter	65.69 53.45 28.16 29.53 24.04 27.18 19.26 0.19	0 1 2 3 6 8 10 63	None
B8208 CZ1 **Prestaviky** **Borvnice** **51741** **Czech Republic**	Grass	1) n/a 2) n/a 3) n/a	684	293	233	10/10/2018	BBCH 29	Green matter Green matter Green matter Green matter Green matter Green matter Green matter Green matter	138.99 155.42 151.06 78.86 105.70 85.46 87.16 3.24	0 1 2 3 5 7 9 63	Several deviations were recorded for this trial. Notably, the application timing was outside the specified range (October, instead of March to September) and residues were detected in the untreated

											specimens.
B8208 PL1 **Gora Swietej Maigorzaty** **99-122** **Poland**	Grass	1) 27/03/2017 2) 02/08/2018-09/08/2018 3) n/a	688	393	175	30/07/2018	BBCH 59	Green matter Green matter Green matter Green matter Green matter Green matter Green matter Green matter	51.33 33.24 20.53 23.11 24.12 16.64 20.17 3.01	0 1 2 3 4 7 10 60	None

(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

No data submitted in the framework of this application.

A 2.1.5 Magnitude of residues in processed commodities (Industrial Processing and/or Household Preparation)

No data submitted in the framework of this application.

A 2.1.6 Magnitude of residues in representative succeeding crops

No data submitted in the framework of this application.

A 2.1.7 Other/Special Studies

No data submitted in the framework of this application.

A 2.2 Fluroxypyr

A 2.2.1 Stability of residues

No data submitted in the framework of this application.

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

No data submitted in the framework of this application.

A 2.2.2.1 Nature of residue in plants

A 2.2.3 Magnitude of residues in plants

See A 2.1.3.
Residue trials conducted with KINVARA on wheat and barley have been conducted. All three active substances (MCPA, fluroxypyr and clopyralid) are separately determined in the residues trials, but the results are displayed together in section A 2.1.3.

A 2.2.4 Magnitude of residues in livestock

No data submitted in the framework of this application.

A 2.2.5 Magnitude of residues in processed commodities (Industrial Processing and/or Household Preparation)

No data submitted in the framework of this application.

A 2.2.6 Magnitude of residues in representative succeeding crops

No data submitted in the framework of this application.

A 2.2.7 Other/Special Studies

No data submitted in the framework of this application.

A 2.3 Clopyralid

A 2.3.1 Stability of residues

No data submitted in the framework of this application.

A 2.3.2 Nature of residues in plants, livestock, rotational crops and processed commodities

No data submitted in the framework of this application.

A 2.3.2.1 Nature of residue in plants

A 2.3.3 Magnitude of residues in plants

See A 2.1.3.

Residue trials conducted with KINVARA on wheat and barley have been conducted. All three active substances (MCPA, fluroxypyr and clopyralid) are separately determined in the residues trials, but the results are displayed together in section A 2.1.3.

A 2.3.4 Magnitude of residues in livestock

No data submitted in the framework of this application.

A 2.3.5 Magnitude of residues in processed commodities (Industrial Processing and/or Household Preparation)

No data submitted in the framework of this application.

A 2.3.6 Magnitude of residues in representative succeeding crops

No data submitted in the framework of this application.

A 2.3.7 Other/Special Studies

No data submitted in the framework of this application.

Appendix 3 Pesticide Residue Intake Model (PRIMo)

A 3.1 TMDI calculations

IEDI estimations are sufficient therefore the TMDI reports of the applicant were removed by zRMS. These TMDI PRIMos were not relevant as reports without original headers with the active name in them. Such PRIMo reports without the original excel spreadsheet submitted, cannot be a scientific proof within the assessment in the registration report.
The applicant was asked to accordingly update them however the update of TMDI was not done.

The applicant is kindly requested once again to paste the TMDIs with the headers exactly as in IEDI reports on the next pages.

A 3.2 IEDI calculations

European Food Safety Authority
EFSA PRIMo revision 3.1; 2019/03/19

MCPA

LOQs (mg/kg) range from: to:

Toxicological reference values

ADI (mg/kg bw/day):	**0.05**	ARfD (mg/kg bw):	**0.15**
Source of ADI:		Source of ARfD:	
Year of evaluation:		Year of evaluation:	

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)
14%	NL toddler	7.21	6%	Milk: Cattle	1%	Apples	1%	Swine: Liver		9%
8%	UK infant	3.87	4%	Milk: Cattle	1.0%	Bovine: Edible offals (other than liver a	0.6%	Bovine: Liver		6%
8%	NL child	3.80	2%	Milk: Cattle	0.8%	Sugar beet roots	0.6%	Apples		4%
6%	FR toddler 2 3 yr	2.97	3%	Milk: Cattle	0.3%	Apples	0.3%	Sugar beet roots		4%
6%	FR child 3 15 yr	2.97	2%	Milk: Cattle	0.4%	Sugar beet roots	0.3%	Oranges		4%
6%	DE child	2.96	2%	Milk: Cattle	1%	Apples	0.4%	Oranges		3%
6%	GEMS/Food G07	2.78	0.8%	Bovine: Liver	0.6%	Milk: Cattle	0.5%	Swine: Liver		3%
5%	IE adult	2.66	1%	Sheep: Liver	0.6%	Sheep: Edible offals (other than liver a	0.4%	Milk: Cattle		3%
5%	GEMS/Food G15	2.47	0.7%	Milk: Cattle	0.6%	Swine: Liver	0.4%	Potatoes		3%
5%	UK toddler	2.43	2%	Milk: Cattle	0.3%	Potatoes	0.3%	Sugar beet roots		3%
5%	GEMS/Food G11	2.42	0.8%	Milk: Cattle	0.7%	Soyabeans	0.4%	Potatoes		2%
5%	GEMS/Food G10	2.36	0.7%	Soyabeans	0.5%	Milk: Cattle	0.3%	Bovine: Liver		2%
4%	GEMS/Food G08	2.24	0.6%	Milk: Cattle	0.4%	Soyabeans	0.4%	Swine: Muscle/meat		2%
4%	DK child	2.22	1%	Milk: Cattle	0.6%	Swine: Liver	0.4%	Swine: Muscle/meat		3%
4%	ES child	2.16	1%	Milk: Cattle	0.4%	Swine: Liver	0.3%	Bovine: Muscle/meat		3%
4%	GEMS/Food G06	2.01	0.4%	Tomatoes	0.3%	Bovine: Liver	0.2%	Milk: Cattle		1%
4%	SE general	1.96	1%	Milk: Cattle	0.9%	Bovine: Muscle/meat	0.4%	Potatoes		2%
4%	RO general	1.84	1%	Milk: Cattle	0.4%	Potatoes	0.2%	Swine: Muscle/meat		2%
4%	DE women 14-50 yr	1.79	1%	Milk: Cattle	0.5%	Sugar beet roots	0.3%	Apples		2%
4%	DE general	1.77	1%	Milk: Cattle	0.4%	Sugar beet roots	0.2%	Apples		2%
3%	NL general	1.66	0.8%	Milk: Cattle	0.3%	Sugar beet roots	0.2%	Potatoes		2%
3%	FR infant	1.53	2%	Milk: Cattle	0.2%	Potatoes	0.2%	Apples		2%
2%	FR adult	1.24	0.4%	Milk: Cattle	0.2%	Wine grapes	0.1%	Bovine: Edible offals (other than l		1%
2%	ES adult	1.16	0.5%	Milk: Cattle	0.1%	Bovine: Muscle/meat	0.1%	Swine: Muscle/meat		1%
2%	DK adult	1.04	0.5%	Milk: Cattle	0.2%	Swine: Liver	0.2%	Swine: Muscle/meat		1%
2%	PT general	0.94	0.5%	Potatoes	0.2%	Wine grapes	0.1%	Apples		0.1%
2%	LT adult	0.93	0.4%	Milk: Cattle	0.3%	Potatoes	0.2%	Swine: Muscle/meat		1%
2%	FI adult	0.87	1%	Coffee beans	0.1%	Potatoes	0.1%	Apples		0.0%
2%	FI 3 yr	0.77	0.5%	Potatoes	0.1%	Bananas	0.1%	Cucumbers		0.0%
1%	UK adult	0.73	0.3%	Milk: Cattle	0.1%	Potatoes	0.1%	Bovine: Muscle/meat		0.7%
1%	UK vegetarian	0.68	0.3%	Milk: Cattle	0.1%	Potatoes	0.1%	Oranges		0.4%
1%	FI 6 yr	0.61	0.4%	Potatoes	0.1%	Bananas	0.1%	Cucumbers		0.0%
1%	IT toddler	0.57	0.2%	Other cereals	0.1%	Tomatoes	0.1%	Wheat		0.1%
1.0%	PL general	0.49	0.3%	Potatoes	0.2%	Apples	0.1%	Tomatoes		
0.9%	IT adult	0.45	0.1%	Tomatoes	0.1%	Wheat	0.1%	Apples		0.1%
0.8%	IE child	0.40	0.4%	Milk: Cattle	0.1%	Potatoes	0.1%	Swine: Fat tissue		0.5%

Conclusion:
The estimated long-term dietary intake (TMDI/NEDI/IEDI) was below the ADI.
The long-term intake of residues of MCPA is unlikely to present a public health concern.

European Food Safety Authority

EFSA PRIMo revision 3.1; 2019/03/19

Fluroxypyr

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

Toxicological reference values

ADI (mg/kg bw/day):	0.8	ARfD (mg/kg bw):	not necessary
Source of ADI:	EFSA	Source of ARfD:	EFSA
Year of evaluation:	2011	Year of evaluation:	2011

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	Exposure (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)
0.6%	NL toddler	5.04	0.4%	Milk: Cattle	0.1%	Apples	0.0%	Maize/corn	0.0%	0.0%
0.3%	UK infant	2.74	0.3%	Milk: Cattle	0.0%	Apples	0.0%	Maize/corn	0.0%	0.0%
0.3%	FR toddler 2 3 yr	2.29	0.2%	Milk: Cattle	0.0%	Apples	0.0%	Leeks	0.0%	0.0%
0.3%	DE child	2.25	0.1%	Milk: Cattle	0.1%	Apples	0.0%	Wheat	0.0%	0.0%
0.3%	NL child	2.19	0.2%	Milk: Cattle	0.0%	Apples	0.0%	Sugar beet roots	0.0%	0.0%
0.2%	FR child 3 15 yr	1.89	0.2%	Milk: Cattle	0.0%	Apples	0.0%	Wheat	0.0%	0.0%
0.2%	UK toddler	1.61	0.2%	Milk: Cattle	0.0%	Apples	0.0%	Wheat	0.0%	0.0%
0.2%	FR infant	1.29	0.1%	Milk: Cattle	0.0%	Apples	0.0%	Leeks	0.0%	0.0%
0.2%	DK child	1.23	0.1%	Milk: Cattle	0.0%	Apples	0.0%	Rye	0.0%	0.0%
0.1%	DE women 14-50 yr	1.19	0.1%	Milk: Cattle	0.0%	Apples	0.0%	Sugar beet roots	0.0%	0.0%
0.1%	DE general	1.18	0.1%	Milk: Cattle	0.0%	Apples	0.0%	Sugar beet roots	0.0%	0.0%
0.1%	GEMS/Food G11	1.12	0.1%	Milk: Cattle	0.0%	Sugar canes	0.0%	Leeks	0.0%	0.0%
0.1%	RO general	1.11	0.1%	Milk: Cattle	0.0%	Wheat	0.0%	Apples	0.0%	0.0%
0.1%	ES child	1.11	0.1%	Milk: Cattle	0.0%	Wheat	0.0%	Apples	0.0%	0.0%
0.1%	SE general	1.09	0.1%	Milk: Cattle	0.0%	Apples	0.0%	Wheat	0.0%	0.0%
0.1%	GEMS/Food G15	0.98	0.1%	Milk: Cattle	0.0%	Wheat	0.0%	Sugar canes	0.0%	0.0%
0.1%	GEMS/Food G07	0.94	0.0%	Milk: Cattle	0.0%	Sugar canes	0.0%	Wheat	0.0%	0.0%
0.1%	GEMS/Food G08	0.92	0.0%	Milk: Cattle	0.0%	Sugar canes	0.0%	Wheat	0.0%	0.0%
0.1%	NL general	0.86	0.1%	Milk: Cattle	0.0%	Apples	0.0%	Leeks	0.0%	0.0%
0.1%	GEMS/Food G10	0.85	0.0%	Milk: Cattle	0.0%	Sugar canes	0.0%	Wheat	0.0%	0.0%
0.1%	GEMS/Food G06	0.79	0.0%	Milk: Cattle	0.0%	Wheat	0.0%	Sugar canes	0.0%	0.0%
0.1%	IE adult	0.70	0.0%	Milk: Cattle	0.0%	Apples	0.0%	Sweet potatoes	0.0%	0.0%
0.1%	FR adult	0.55	0.0%	Milk: Cattle	0.0%	Apples	0.0%	Leeks	0.0%	0.0%
0.1%	ES adult	0.54	0.0%	Milk: Cattle	0.0%	Apples	0.0%	Wheat	0.0%	0.0%
0.1%	DK adult	0.50	0.0%	Milk: Cattle	0.0%	Apples	0.0%	Wheat	0.0%	0.0%
0.1%	LT adult	0.46	0.0%	Milk: Cattle	0.0%	Apples	0.0%	Potatoes	0.0%	0.0%
0.0%	FI adult	0.40	0.0%	Coffee beans	0.0%	Apples	0.0%	Potatoes		0.0%
0.0%	UK vegetarian	0.37	0.0%	Milk: Cattle	0.0%	Wheat	0.0%	Apples	0.0%	0.0%
0.0%	UK adult	0.33	0.0%	Milk: Cattle	0.0%	Wheat	0.0%	Apples	0.0%	0.0%
0.0%	PT general	0.31	0.0%	Wheat	0.0%	Potatoes	0.0%	Apples		0.0%
0.0%	IE child	0.29	0.0%	Milk: Cattle	0.0%	Wheat	0.0%	Apples	0.0%	0.0%
0.0%	FI 3 yr	0.28	0.0%	Potatoes	0.0%	Apples	0.0%	Oat	0.0%	0.0%
0.0%	IT toddler	0.24	0.0%	Wheat	0.0%	Apples	0.0%	Other cereals		0.0%
0.0%	FI 6 yr	0.21	0.0%	Potatoes	0.0%	Apples	0.0%	Oat	0.0%	0.0%
0.0%	PL general	0.21	0.0%	Apples	0.0%	Potatoes	0.0%	Onions		
0.0%	IT adult	0.18	0.0%	Wheat	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 Fluroxypyr is unlikely to present a public health concern.

European Food Safety Authority

EFSA PRIMo revision 3.1; 2019/03/19

Clopyralid

LOQs (mg/kg) range from: 0.05 to: 0.05

Toxicological reference values

ADI (mg/kg bw/day):	0.15	ARfD (mg/kg bw):	0.17
Source of ADI:	EFSA	Source of ARfD:	EFSA
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	Exposure (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)
33%	NL toddler	49.50	9%	Maize/corn	4%	Apples	3%	Sugar beet roots	2%	3%
17%	NL child	24.78	6%	Sugar beet roots	2%	Apples	1%	Potatoes	0.9%	2%
14%	DE child	20.74	4%	Apples	1%	Oranges	0.9%	Potatoes	0.7%	1%
13%	GEMS/Food G06	20.04	2%	Rice	2%	Maize/corn	1%	Tomatoes	0.2%	1%
13%	IE adult	19.71	2%	Sweet potatoes	2%	Linseeds	0.8%	Potatoes	0.2%	0.6%
11%	RO general	16.94	3%	Head cabbages	1%	Maize/corn	1%	Potatoes	0.5%	1%
11%	FR child 3 15 yr	16.62	2%	Sugar beet roots	1%	Oranges	0.8%	Milk: Cattle	0.9%	2%
11%	GEMS/Food G10	16.50	2%	Rice	1%	Soyabeans	1.0%	Potatoes	0.3%	1.0%
10%	GEMS/Food G15	15.41	2%	Head cabbages	1%	Potatoes	0.9%	Maize/corn	0.4%	1%
10%	UK infant	14.84	1%	Maize/corn	1%	Milk: Cattle	1%	Potatoes	1%	2%
10%	FR toddler 2 3 yr	14.75	2%	Sugar beet roots	1%	Apples	1.0%	Milk: Cattle	1%	2%
10%	GEMS/Food G08	14.58	1%	Potatoes	0.9%	Head cabbages	0.7%	Soyabeans	0.3%	1%
9%	GEMS/Food G11	13.89	1%	Potatoes	1%	Soyabeans	0.5%	Apples	0.4%	1.0%
9%	GEMS/Food G07	13.76	1%	Potatoes	0.6%	Soyabeans	0.6%	Wheat	0.4%	1%
9%	UK toddler	13.71	2%	Sugar beet roots	1%	Potatoes	0.8%	Rice	0.7%	1%
9%	DE women 14-50 yr	13.16	3%	Sugar beet roots	0.9%	Apples	0.6%	Oranges	0.5%	0.9%
8%	SE general	12.70	1%	Potatoes	1%	Head cabbages	0.6%	Bananas	0.4%	1%
8%	DE general	12.47	3%	Sugar beet roots	0.8%	Apples	0.5%	Oranges	0.5%	0.9%
8%	NL general	11.51	2%	Sugar beet roots	0.8%	Potatoes	0.5%	Apples	0.3%	0.7%
8%	PT general	11.27	2%	Potatoes	1%	Rice	0.8%	Wine grapes		0.5%
7%	DK child	10.15	0.8%	Potatoes	0.8%	Apples	0.7%	Rye	0.5%	2%
7%	ES child	10.07	0.7%	Oranges	0.6%	Rice	0.6%	Potatoes	0.5%	1%
6%	FI 3 yr	9.17	2%	Potatoes	0.7%	Rice	0.4%	Bananas	0.0%	0.3%
6%	IT toddler	9.04	2%	Other cereals	0.9%	Wheat	0.5%	Tomatoes		0.9%
5%	FR infant	8.23	0.9%	Sugar beet roots	0.6%	Potatoes	0.6%	Milk: Cattle	0.6%	0.7%
5%	FR adult	7.29	0.8%	Wine grapes	0.5%	Sugar beet roots	0.3%	Wheat	0.2%	0.5%
5%	FI 6 yr	7.12	1%	Potatoes	0.6%	Rice	0.3%	Bananas	0.0%	0.3%
4%	FI adult	6.71	2%	Coffee beans	0.4%	Potatoes	0.2%	Head cabbages		0.2%
4%	ES adult	6.53	0.4%	Oranges	0.3%	Rice	0.3%	Wheat	0.2%	0.7%
4%	IT adult	6.53	0.9%	Other cereals	0.6%	Wheat	0.4%	Tomatoes		0.6%
4%	UK vegetarian	6.50	0.5%	Rice	0.5%	Potatoes	0.4%	Sugar beet roots	0.1%	0.4%
4%	LT adult	6.44	1%	Potatoes	0.8%	Head cabbages	0.6%	Apples	0.2%	0.5%
4%	PL general	6.17	1%	Potatoes	0.7%	Head cabbages	0.7%	Apples		
4%	UK adult	5.55	0.5%	Rice	0.5%	Potatoes	0.4%	Sugar beet roots	0.1%	0.4%
3%	DK adult	4.75	0.4%	Potatoes	0.3%	Apples	0.3%	Wine grapes	0.2%	0.5%
2%	IE child	2.35	0.4%	Rice	0.2%	Potatoes	0.2%	Wheat	0.1%	0.3%

Conclusion:
The estimated long-term dietary intake (TMDI/NEDI/IEDI) was below the ADI.
The long-term intake of residues of Clopyralid is unlikely to present a public health concern.

A 3.3 IESTI calculations - Raw commodities

MCPA

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
No. of commodities for which ARfD/ADI is exceeded (IESTI): ---

IESTI

Highest % of ARfD/ADI	Commodities	MRL / input for RA (mg/kg)	Exposure (µg/kg bw)
16%	Bovine: Liver	3 / 3	24
15%	Bovine: Edible offals	3 / 3	22
8%	Bovine: Kidney	3 / 3	11
6%	Swine: Edible offals	3 / 3	9.0
4%	Milk: Cattle	0.05 / 0.05	6.2
3%	Swine: Kidney	3 / 3	3.8
2%	Swine: Liver	3 / 3	3.7
1%	Poultry: Muscle/meat	0.1 / 0.1	1.7
0.8%	Swine: Muscle/meat	0.1 / 0.1	1.2
0.8%	Milk: Goat	0.05 / 0.05	1.2
0.5%	Bovine: Muscle/meat	0.1 / 0.1	0.72
0.5%	Other farmed animals:	0.1 / 0.1	0.69
0.4%	Eggs: Chicken	0.05 / 0.05	0.62
0.4%	Equine: Muscle/meat	0.1 / 0.1	0.60
0.4%	Sheep: Muscle/meat	0.1 / 0.1	0.54

Expand/collapse list

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

IESTI

Highest % of ARfD/ADI	Commodities	MRL / input for RA (mg/kg)	Exposure (µg/kg bw)
8%	Bovine: Liver	3 / 3	12
7%	Bovine: Edible offals	3 / 3	10.0
6%	Sheep: Liver	3 / 3	8.4
5%	Swine: Edible offals	3 / 3	7.8
4%	Swine: Kidney	3 / 3	6.6
4%	Bovine: Kidney	3 / 3	6.3
3%	Swine: Liver	3 / 3	4.2
1%	Sheep: Edible offals	3 / 3	2.1
1%	Milk: Cattle	0.05 / 0.05	1.9
0.8%	Poultry: Muscle	0.1 / 0.1	1.2
0.6%	Milk: Goat	0.05 / 0.05	0.92
0.5%	Milk: Sheep	0.05 / 0.05	0.76
0.4%	Bovine: Muscle	0.1 / 0.1	0.57
0.4%	Other farmed animals:	0.1 / 0.1	0.56
0.3%	Swine: Muscle/meat	0.1 / 0.1	0.48

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

Clopyralid

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
No. of commodities for which ARfD/ADI is exceeded (IESTI): ---

IESTI

Highest % of ARfD/ADI	Commodities	MRL / input for RA (mg/kg)	Exposure (µg/kg bw)
4%	Milk: Cattle	0.05 / 0.05	6.2
3%	Bovine: Kidney	1.5 / 1.5	5.6
2%	Wheat	3 / 0.2	2.9
0.7%	Rye	5 / 0.2	1.3
0.7%	Bovine: Liver	0.15 / 0.15	1.2
0.7%	Milk: Goat	0.05 / 0.05	1.2
0.7%	Barley	2 / 0.2	1.1
0.5%	Poultry: Muscle/meat	0.05 / 0.05	0.85
0.4%	Swine: Kidney	0.6 / 0.6	0.76
0.4%	Eggs: Chicken	0.05 / 0.05	0.62
0.4%	Swine: Muscle/meat	0.05 / 0.05	0.61
0.3%	Bovine: Muscle/meat	0.08 / 0.08	0.58
0.3%	Sheep: Muscle/meat	0.08 / 0.08	0.43
0.2%	Bovine: Edible offals	0.05 / 0.05	0.36
0.2%	Other farmed animals:	0.05 / 0.05	0.35

Expand/collapse list

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

IESTI

Highest % of ARfD/ADI	Commodities	MRL / input for RA (mg/kg)	Exposure (µg/kg bw)
2%	Bovine: Kidney	1.5 / 1.5	3.2
1%	Milk: Cattle	0.05 / 0.05	1.9
1.0%	Wheat	3 / 0.2	1.7
0.8%	Swine: Kidney	0.6 / 0.6	1.3
0.6%	Rye	5 / 0.2	0.97
0.6%	Barley	2 / 0.2	0.97
0.5%	Milk: Goat	0.05 / 0.05	0.92
0.4%	Milk: Sheep	0.05 / 0.05	0.76
0.4%	Bovine: Liver	0.15 / 0.15	0.60
0.3%	Poultry: Muscle	0.05 / 0.05	0.59
0.3%	Sheep: Liver	0.2 / 0.2	0.56
0.3%	Bovine: Muscle	0.08 / 0.08	0.46
0.2%	Sheep: Muscle/meat	0.08 / 0.08	0.38
0.2%	Other farmed animals:	0.05 / 0.05	0.28
0.1%	Swine: Muscle/meat	0.05 / 0.05	0.24

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

A 3.4 IESTI calculations - Processed commodities

MCPA

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%	Wheat / milling (flour)	0.01 / 0.01	0.12	0.0%	Barley / beer	0.01 / 0	0.07
0.0%	Wheat / milling (wholemea	0.01 / 0.01	0.06	0.0%	Wheat / bread/pizza	0.01 / 0.01	0.04
0.0%	Rye / boiled	0.01 / 0.01	0.04	0.0%	Wheat / pasta	0.01 / 0.01	0.04
0.0%	Oat / boiled	0.01 / 0.01	0.04	0.0%	Wheat / bread	0.01 / 0.01	0.02
0.0%	Barley / cooked	0.01 / 0.01	0.04				
0.0%	Rye / milling (wholemeal)-I	0.01 / 0.01	0.04				
0.0%	Oat / milling (flakes)	0.01 / 0.01	0.03				
0.0%	Barley / milling (flour)	0.01 / 0.01	0.02				
Expand/collapse list							

Conclusion:
No exceedance of the toxicological reference value was identified for any unprocessed commodity. A short term intake of residues of MCPA(F) is unlikely
For processed commodities, no exceedance of the ARfD/ADI was identified.

Clopyralid

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)
1%	Wheat / milling (flour)	3 / 0.2	2.4	0.8%	Barley / beer	2 / 0.04	1.4
0.7%	Wheat / milling (wholemea	3 / 0.2	1.1	0.5%	Wheat / bread/pizza	3 / 0.2	0.88
0.4%	Rye / boiled	5 / 0.2	0.73	0.4%	Wheat / pasta	3 / 0.2	0.76
0.4%	Oat / boiled	3 / 0.2	0.73	0.4%	Wheat / bread	3 / 0.2	0.70
0.4%	Barley / cooked	2 / 0.2	0.73	0.2%	Oat / boiled	3 / 0.2	0.30
0.4%	Rye / milling (wholemeal)-l	5 / 0.2	0.70	#NUM!	#NUM!	#NUM!	#NUM!
0.4%	Oat / milling (flakes)	3 / 0.2	0.60	#NUM!	#NUM!	#NUM!	#NUM!
0.2%	Barley / milling (flour)	2 / 0.2	0.36	#NUM!	#NUM!	#NUM!	#NUM!
#NUM!	#NUM!	#NUM!	#NUM!	#NUM!	#NUM!	#NUM!	#NUM!
#NUM!	#NUM!	#NUM!	#NUM!	#NUM!	#NUM!	#NUM!	#NUM!
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#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 Clopyralid is unlikely to present a public health risk.

For processed commodities, no exceedance of the ARfD/ADI was identified.

Appendix 4 Additional information provided by the applicant

None.