REGISTRATION REPORT

Part B

Section 7

Metabolism and Residues

Detailed summary of the risk assessment

Product code: ADM.06001.H.2.B

Product name(s): EDAPTIS

Chemical active substances:

Mesosulfuron-methyl, 12 g/L
Pinoxaden, 60 g/L

Safener:

Mefenpyr-diethyl, 35 g/L

Central Zone

Zonal Rapporteur Member State: Poland

CORE ASSESSMENT

(authorization)

Sponsor: ADAMA Agan Ltd.
Applicant: Country organisation / representative of ADAMA, as given in Part A

Submission date: June 2021

MS Finalisation date: April 2023 (initial Core Assessment)

August 2023, December 2023 (final Core Assessment)

Version history

When	What
June 2021	First version submitted by applicant
April 2023	Initial zRMS assessment The report in the dRR format has been prepared by the Applicant, therefore all comments, additional evaluations and conclusions of the zRMS are presented in grey commenting boxes. Minor changes are introduced directly in the text and highlighted in grey. Not agreed or not relevant information are ~~struck through and shaded for transparency~~.
August 2023	Final report (Core Assessment updated following the commenting period) Additional information/assessments included by the zRMS in the report in response to comments received from the cMS and the Applicant are highlighted in yellow. Information no longer relevant is ~~struck through and shaded~~.
December 2023	Final report (Core Assessment updated following the second commenting period) No additional information or assessments after the second commenting period.

DATA PROTECTION CLAIM

Under Article 59, Regulation 1107/2009/EC, on behalf of the Sponsor Company the applicant claims data protection for these studies. The data protection status and corresponding justification as valid for the respective country will be confirmed in the respective PART A

STATEMENT FOR OWNERSHIP

The summaries and evaluations contained in this document may be based on unpublished proprietary data submitted for the purpose of the assessment undertaken by the regulatory authority that prepared it. Other registration authorities should not grant, amend, or renew a registration on the basis of the summaries and evaluation of unpublished proprietary data contained in this document unless they have received the data on which the summaries and evaluation are based, either –

- from the owner of the data, or
- from a second party that has obtained permission from the owner of the data for this purpose or,
- following expiry of any period of exclusive use, by offering – in certain jurisdictions – mandatory compensation, unless the period of protection of the proprietary data concerned has expired.

Table of Contents

7 Metabolism and residue data (KCA section 6)

7.1 Summary and zRMS Conclusion

7.1.1 Critical GAP(s) and overall conclusion

Selection of critical uses and justification

The critical GAP with respect to consumer intake and risk assessment for the preparation ADM.06001.H.2.B in wheat, rye and triticale is presented in Table 7.1-1. A list of all intended uses within the Central Zone is given in Part B, Section 0.

Justification for the selection of the critical GAP

The critical GAP uses concern

- the highest single and yearly application rates (highest single application rate of 1 L product/ha in cereals),
- the maximum number of applications, (1/1) and
- the latest application growth stage in the crop (BBCH 39 in cereals).

Residue data from wheat can be used to support intended uses on rye and triticale according to SANTE/2019/12752. Therefore, data obtained from wheat can be used to support the intended uses on rye, and triticale.

Overall conclusion

The data available are considered sufficient for risk assessment. An exceedance of the current MRLs in wheat and rye of 0.01 mg/kg mesosulfuron-methyl and of ~~1.0~~ 0.7 mg/kg pinoxaden as laid down in Reg. (EU) 396/2005 is not expected. No MRL has been set for the safener mefenpyr-diethyl.

The chronic and the short-term intakes of residues of mesosulfuron-methyl, pinoxaden or mefenpyr-diethyl (safener) are unlikely to present a public health concern.

As far as consumer health protection is concerned, the zRMS agrees with the authorization of the intended use(s).

According to available data, no specific mitigation measures should apply.

Data gaps

Noticed data gaps are:

- none

Table 7.1-1: Acceptability of critical GAPs (and respective fall-back GAPs, if applicable)

1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
GAP number (see Part B.0)* [(e)]	**Member state(s)**	**Crop and/ or situation**** **(crop destination / purpose of crop)**	**F, Fn, Fpn G, Gn, Gpn or I*****	**Pests or Group of pests controlled** (additionally: developmental stages of the pest or pest group)	**Application**				**Application rate**			**PHI** (days)	**Remarks:** e.g. g safener/synergist per ha [(f)]	**Comments:**
					Method / Kind	Timing / Growth stage of crop & season	Max. number a) per use b) per crop/ season	Min. interval between applications (days)	kg or L product / ha a) max. rate per appl. b) max. total rate per crop/season	g or kg as/ha a) max. rate per appl. b) max. total rate per crop/season	Water L/ha min / max			

Zonal uses (field or outdoor uses, certain types of protected crops)														
2	AT, DE, BE, NL, CZ, PL, HU, IE	Winter wheat, rye, triticale	F	ALOMY, APESV, AVESS, BROSS, LOLMU, LOLPE, POAAN, POATR, Broad-leaved weeds	Foliar, spraying, overall	BBCH 20-39 (spring)	a) 1 b) 1	-	a) 1 L/ha b) 1 L/ha	a) 12 / 60 g/ha b) 12 / 60 g/ha	80 / 300	n.a.	Mefenpyr-diethyl applied as a safener at 35.0 g/ha In PL applied also in tank mix with adjuvat Insert : 0.5-1.0 + 0.2 l/ha (Insert) and with Camaro 306 SE: 0.5 + 0.5 l/ha (Camaro 306 SE)	A
3	AT, BE, NL, CZ, PL, HU, IE (DE****)	Spring wheat	F	ALOMY, APESV, AVESS, BROSS, LOLMU, LOLPE, POAAN, POATR, Broad-leaved weeds	Foliar, spraying, overall	BBCH 13-39 (spring)	a) 1 b) 1	-	a) 1 L/ha b) 1 L/ha	a) 12 / 60 g/ha b) 12 / 60 g/ha	80 / 300	n.a.	Mefenpyr-diethyl applied as a safener at 35.0 g/ha Doser range 0.75-1 L/ha	A
4	DE	Winter wheat, rye, triticale	F	APESV, AVESS, Broad-leaved weeds	Foliar, spraying, overall	BBCH 20-39 (spring)	a) 1 b) 1	-	a) 0.75 L/ha b) 0.75 L/ha	a) 9 / 45 g/ha b) 9 / 45 g/ha	80 / 300	n.a.	Mefenpyr-diethyl applied as a safener at 26.3 g/ha	A
5	DE	Spring wheat	F	ALOMY, APESV, AVESS, BROSS, POAAN, POATR, Broad-leaved weeds	Foliar, spraying, overall	BBCH 13-20 (spring)	a) 1 b) 1	-	a) 1 L/ha b) 1 L/ha	a) 12 / 60 g/ha b) 12 / 60 g/ha	80 / 300	n.a.	Mefenpyr-diethyl applied as a safener at 35.0 g/ha	A
6	DE	Spring wheat	F	ALOMY, APESV, AVESS, BROSS, POAAN, POATR, Broad-leaved weeds	Foliar, spraying, overall	BBCH 20-39 (spring)	a) 1 b) 1	-	a) 1 L/ha b) 1 L/ha	a) 12 / 60 g/ha b) 12 / 60 g/ha	80 / 300	n.a	Mefenpyr-diethyl applied as a safener at 35.0 g/ha	A
7	DE	Spring wheat	F	ALOMY, APESV, AVESS, BROSS, POAAN, POATR, Broad-leaved weeds	Foliar, spraying, overall	BBCH 13-20 (spring)	a) 1 b) 1	-	a) 0.75 L/ha b) 0.75 L/ha	a) 9 / 45 g/ha b) 9 / 45 g/ha	80 / 300	n.a.	Mefenpyr-diethyl applied as a safener at 26.3 g/ha	A
8	DE	Spring wheat	F	APESV, AVESS, Broad-leaved weeds	Foliar, spraying, overall	BBCH 20-39 (spring)	a) 1 b) 1	-	a) 0.75 L/ha b) 0.75 L/ha	a) 9 / 45 g/ha b) 9 / 45 g/ha	80 / 300	n.a.	Mefenpyr-diethyl applied as a safener at 26.3 g/ha	A

* Use number(s) in accordance with the list of all intended GAPs in Part B, Section 0 should be given in column 1
** Use also code numbers according to Annex I of Regulation (EU) No 396/2005
*** F: professional field use, Fn: non-professional field use, Fpn: professional and non-professional field use, G: professional greenhouse use, Gn: non-professional greenhouse use, Gpn: professional and non-professional greenhouse use, I: indoor application
**** The German GAP is split in use 5 and 6) i.e. before and after GS 20 due to mitigation required
n.a. – The PHI is covered by the conditions of use and/or the vegetation period remaining between the application of the plant protection product and the use of the product (e. g. harvest)

Explanation for Column 15 “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 ADM.06001.H.2.B is composed of mesosulfuron-methyl, pinoxaden and the safener mefenpyr-diethyl.

Table 7.1-2: Toxicological reference values for the dietary risk assessment of mesosulfuron-methyl, pinoxaden and mefenpyr-diethyl

Reference value	Source	Year	Value (mg/kg bw/d)	Study relied upon	Safety factor
Mesosulfuron-methyl					
ADI	EFSA	2016	1.0	18-months, mouse	100
ARfD	EFSA	2016	Not necessary		
Pinoxaden					
ADI	EFSA	2013, 2021	0.1	2-year study, rats supported by rat teratology	100
ARfD	EFSA	2013, 2021	0.1	Teratology study, rabbit	100
Mefenpyr-diethyl (safener)					
ADI	Austria & France	2011*	0.1	1-year dog study (supported by 2-year mouse oncogenicity study)	100
ARfD	Austria & France	2011*	0.4	Developmental toxicity in rabbit	100

* Proposed in Monograph, which has been voluntarily prepared by AGES and ANSES in the context of zonal authorisation of plant protection products containing mefenpyr-diethyl.

7.1.2.1 Summary for mesosulfuron-methyl

Table 7.1-3: Summary for mesosulfuron-methyl

Use-No.*	Crop	Plant metabolism covered?	Sufficient residue trials?	PHI sufficiently supported?	Sample storage covered by stability data?	MRL compliance	Chronic risk for consumers identified?	Acute risk for consumers identified?
2	Wheat	Yes	Yes (~~41~~ 8 residue trials)	Yes	Yes	Yes	No	Not applicable
2	Triticale	Yes	Yes (extrapolation from wheat)	Yes	Yes	Yes		Not applicable
2	Rye	Yes	Yes (extrapolation from wheat)	Yes	Yes	Yes		Not applicable

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

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

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

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

7.1.2.2 Summary for pinoxaden

Table 7.1-4: Summary for pinoxaden

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?
2	Wheat	Yes	Yes (~~30~~ 8 residue trials)	Yes	Yes	Yes	No	No
2	Triticale	Yes	Yes (extrapolation from wheat)	Yes	Yes	Yes		No
2	Rye	Yes	Yes (extrapolation from wheat)	Yes	Yes	Yes		No

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

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

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

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

7.1.2.3 Summary for mefenpyr-diethyl

Table 7.1-5: Summary for mefenpyr-diethyl

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?
2	Wheat	Yes	Yes (8 residue trials)	Yes	Yes	~~Yes~~ No MRLs set at EU level. Mefenpyr-diethyl is a safener and does not fall under the Regulation (EC) 396/2005.	No	No
2	Triticale	Yes	Yes (extrapolation from wheat)	Yes/No	Yes			No
2	Rye	Yes	Yes (extrapolation from wheat)	Yes/No	Yes			No

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

Mefenpyr-diethyl as safener is not considered as an active substance, consequently has not been subject to review on EU level for inclusion into Annex I of Directive 91/414/EEC or Regulation (EC) No 1107/2009 and at present MRLs are not set in the EU for safeners.

The Applicant provided the data for safener, for mefenpyr-diethyl, reviewed by Austria and France in 2011, but has not been assessed at EU level. Results and conclusion of this evaluation are reported in this section for the sake of completeness. According to Regulation 1107/2009, data for safener should be evaluated in line with requirements relevant for active substances and EU agreed and peer-reviewed endpoints should be generated. Such evaluation, however, is outside the scope of the product registration and should be carried out at the EU level in order to derive uniform endpoints that may be used in evaluation of various formulations. For this reason data provided for mefenpyr-diethyl were not validated by the zRMS.

Available residue data presented in point 7.4 are compliant with data presented in Monograph for mefenpyr-diethyl and are considered informative.

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

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

Considering dietary burden and based on the intended uses, no significant modification of the intake was calculated for livestock. Further investigation of residues is therefore not necessary. MRLs have not been set for mefenpyr-diethyl in animal commodities.

7.1.2.4 Summary for ADM.06001.H.2.B

Table 7.1-6: Information on ADM.06001.H.2.B (KCA 6.8)

Crop	PHI for ADM.06001.H.2.B proposed by applicant	PHI/ Withholding period* sufficiently supported for			PHI for ADM.06001.H.2.B proposed by zRMS	zRMS Comments (if different PHI proposed)
		Mesosulfuron-methyl	Pinoxaden	Mefenpy-diethyl (safener)		
Wheat	F**	NR	NR	NR	NR	-
Triticale	F**	NR	NR	NR	NR	-
Rye	F**	NR	NR	NR	NR	-

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

Table 7.1-7: Waiting periods before planting succeeding crops

Waiting period before planting succeeding crops				Overall waiting period proposed by zRMS for ADM.06001.H.2.B
Crop group	Led by mesosulfuron-methyl	Led by pinoxaden	Led by mefenpy-diethyl (safener)	
Leafy vegetables	None	None	None	None
Root vegetables	None	None	None	None
Cereal	None	None	None	None

NR: not relevant

In accordance with the EFSA Scientific Report on mesosulfuron-methyl (EFSA, 2016), the EFSA

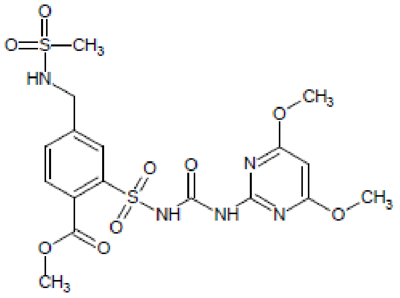
Scientific Report on pinoxaden (EFSA, 2013) and the DAR for mefenpyr-diethyl (France, 2011), no particular restriction related to rotational crops is needed.

Assessment

7.2 Mesosulfuron-methyl

General data on mesosulfuron-methyl are summarized in the table below (last updated 2020/10/19)

Table 7.2-1: General information on mesosulfuron-methyl

Active substance (ISO Common Name)	Mesosulfuron Mesosulfuron-methyl
IUPAC	Mesosulfuron: 2-[(4,6-dimethoxypyrimidin-2-ylcarbamoyl)sulfamoyl]-α-methanesulfonamido-*p*-toluic acid Mesosulfuron-methyl: Methyl-2-[(4,6-dimethoxypyrimidin-2-ylcarbamoyl)sulfamoyl]-α-(methanesulfonamido)-*p*-toluate
Chemical structure	
Molecular formula	$C_{17}H_{21}N_5O_9S_2$
Molar mass	503.51 g/mol
Chemical group	Sulfonyl-urea
Mode of action (if available)	Inhibiting the biosynthesis of essential amino acids in susceptible plants, through inhibition of acetolactate synthase (ALS)
Systemic	Yes
Company (ies)	Bayer CropScience AG
Rapporteur Member State (RMS)	France
Approval status	Approved (01/07/2017) Commission Implementing Regulation (EU) 2017/755 of 28 April 2017
Restriction (e.g. is restricted to use as "...")	The risk assessment for the renewal of the approval of mesosulfuron is based on a limited number of representative uses, which however do not restrict the uses for which plant protection products containing mesosulfuron may be authorised. It is therefore appropriate not to maintain the restriction for use only as a herbicide.
Review Report	SANTE/11827/2016 Rev 2 23 March 2017
Current MRL regulation	Commission Regulation (EU) No 289/2014 of 21 March 2014
Peer review of MRLs according to Article 12 of Reg No 396/2005 EC performed	Yes
EFSA Journal : Conclusion on the peer review	Yes: EFSA, 2016
EFSA Journal: conclusion on article 12	Yes: EFSA, 2012
Current MRL applications on intended uses	None

7.2.1 Stability of Residues (KCA 6.1)

7.2.1.1 Stability of residues during storage of samples

Available data

Reference: France, 2001

No new data submitted in the framework of this application.

Table 7.2-2: Summary of stability data achieved at ≤ - 18°C (unless stated otherwise)

Matrix	Characteristics of the matrix	Acceptable Maximum Storage duration	Reference
Data relied on in EU			
Plant products			
Wheat shoot	High water content	13 months	France, 2001
Wheat grain	High starch content	13 months	France, 2001
Wheat straw	Other	13 months	France, 2001
Animal Products			
Muscle		Not applicable	EFSA, 2016
Liver			
Milk			
Egg			
Other			

Conclusion on stability of residues during storage

The residue data are supported by validated analytical methods and by acceptable storage stability data where mesosulfuron-methyl was shown to be stable for up to 13 months in high starch content commodities, high water content commodities and in straw.

The storage stability periods cover the storage periods of samples in the residue trials presented in this submission.

zRMS comments:

In EFSA Journal 2012;10(11):2976 it is stated that *The potential degradation of residues during storage of the residues trials samples was also assessed. In the framework of the peer review, storage stability of mesosulfuron-methyl was demonstrated for a period of 13 months at –18°C in dry commodities (wheat) (France, 2001).*

The residue data are valid with regard to storage stability.

No additional study is required.

7.2.1.2 Stability of residues in sample extracts (KCA 6.1)

The relevant information on the stability in the final or any intermediate step can be derived from the fortification experiments performed during method validation. If the recoveries in the fortified samples are within the acceptable range of 70 - 120%, stability is sufficiently proven.

The procedural recoveries obtained fully support the residue data presented in this submission.

zRMS comments:

Information provided by Applicant is acceptable.

No additional study is required.

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

Reference: France 2001, France, 2015; EFSA, 2016

The metabolism of mesosulfuron-methyl was investigated in wheat matrices using 2-^{14}C-pyrimidyl and U-^{14}C-phenyl-labelled mesosulfuron-methyl.
No new data are submitted in the framework of this application.

Table 7.2-3: 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	Wheat (grain, straw)	[2-^{14}C-pyrimidyl]	Foliar	10 g a.s./ha	1-2	0, 35, 49, 95	C008761	France, 2001 France, 2015 EFSA, 2016
	Wheat (grain, straw)	[U-^{14}C-phenyl]	Foliar	30 g a.s./ha	1-2	0, 41/42, 57/58, 103/104	C009588	

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

Summary of plant metabolism studies reported in the EU

"The metabolism of mesosulfuron-methyl was investigated upon foliar application at the tillering stage (growth stages of mono- and dicotyledonous plants (BBCH) 29) in cereals (wheat) using, respectively, 2-^{14}C-pyrimidyl and U-^{14}C-phenyl labellings. The total radioactive residues (TRRs) accounted for 0.018 mg eq/kg in forage, 0.0112 mg eq/kg in hay, 0.0012–0.0014 mg eq/kg in grain and 0.019–0.045 mg eq/kg in straw for both labelling forms indicating a limited translocation of the radioactivity throughout the whole plant.
Metabolites' identification was not attempted in grain in view of the very low recovered residue levels. The parent compound was recovered at significant proportions in wheat forage and hay (23% TRR and 15% of TRR, respectively) and occurred only at a level of up to 3% TRR in straw. In wheat forage, hay and straw, mesosulfuron-methyl was shown to be degraded into metabolites identified as AE F160459 (3.7–14% TRR), AE F140584 (8.8–10% TRR) and AE F147447 (5–18% TRR). These metabolites accounted for a residue concentration < 0.01 mg eq/kg. The major part of the radioactivity in these plant parts was characterised as polar fractions that globally accounted for 22–34% TRR and were constituted of several components that did not exceed each 0.004 mg eq/kg. The identity of these compounds was not further investigated. [...]
Since all the identified and characterised metabolites were recovered at very low concentrations (< 0.01 mg eq/kg) in wheat forage, hay and straw and in rotational crops, the residue definition for monitoring and risk assessment is proposed as mesosulfuron-methyl for cereals following post-emergence foliar application." (*EFSA, 2016*)

Conclusion on metabolism in primary crops

The metabolism of mesosulfuron-methyl in cereal crops following foliar application is sufficiently addressed to support the proposed uses of product ADM.06001.H.2.B.

Evaluator comments:
Metabolism of mesosulfuron-methyl was investigated for foliar application on cereals (wheat), using 2-^{14}C-pyrimidyl and ^{14}C-phenyl labelled mesosulfuron-methyl (France, 2001) and evaluated in the renewal of the active substance (France 2015, EFSA 2016) and is sufficiently addressed to support the proposed uses of product ADM.06001.H.2.B.

The residue definition for monitoring and risk assessment is proposed as mesosulfuron-methyl for cereals following post-emergence foliar application. No additional data are required.

7.2.2.2 Nature of residue in rotational crops (KCA 6.6.1)

Available data

Reference: France 2001, France, 2015; EFSA, 2016

The metabolism of mesosulfuron-methyl was investigated in rotational crops spinach, carrot and wheat. No new data are submitted in the framework of this application.

Table 7.2-4: Summary of metabolism studies in rotational crops

Crop group	Crop	Label position	Application and sampling details					Reference
			Method, F or G *	Rate (g a.s./ha)	Sowing intervals (DAT)	Harvest Intervals (DAT)	Remarks	
EU data								
Leafy vegetables	Spinach	[2-^{14}C-pyrimidyl] and [U-^{14}C-phenyl]	Bare soil, F	15	32, 120, 365	162, 411	C008238 C008240 C008242 C008243 C008239 C008241	France, 2001 France, 2015 EFSA, 2016
Root and tuber vegetables	Carrot				32, 120, 365	139, 237, 487		
Cereals	Wheat				32, 120, 365	131, 238, 482		

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

Summary of plant metabolism studies reported in the EU

"A confined rotational crop metabolism study was conducted with a bare soil application of mesosulfuron-methyl labelled, respectively, on the pyrimidyl ring and on the phenyl ring at a dose rate of 15 g a.s./ha (1N rate). Spinach, carrot and wheat were sown at plant-back intervals (PBIs) of 30, 120 and 365 days. The total residues in all plant parts and at all PBIs were below 0.01 mg/kg, except in wheat straw where TRRs accounted for up to 0.022 mg eq/kg (30-day-PBI), 0.012 mg eq/kg (120-day-PBI) and 0.014 mg eq/kg (365-day-PBI) for both labelling forms. The radioactive residues in wheat straw at the 30-day-PBI were constituted of a major polar fraction (34% TRR) besides numerous minor polar fractions and a major metabolite identified as AE F147447 (31% TRR). Hence, the metabolic pathway in the rotational crops is deemed to be similar to that depicted in the primary crops and residues are not expected to be present in rotational crops (> 0.01 mg/kg), providing that mesosulfuron-methyl is applied according to the representative uses." (*EFSA, 2016*)

Conclusion on metabolism in rotational crops

The metabolism in primary and rotational crops was found to be similar and a specific residue definition for rotational crops is not deemed necessary. No residues of mesosulfuron-methyl >0.01 mg/kg are expected in rotational crops grown after the use ADM.06001.H.2.B according to the intended GAP.

Evaluator comments:
The metabolic pathway in the rotational crops is deemed to be similar to that depicted in the primary crops and residues are not expected to be present in rotational crops (> 0.01 mg/kg), providing that mesosulfuron-methyl is applied according to the representative uses (EFSA, 2012).
No additional study is required.

7.2.2.3 Nature of residues in processed commodities (KCA 6.5.1)

Available data

"The investigation of effects of processing on the nature and magnitude of residues was not triggered by the representative uses." (*EFSA, 2016*)
The representative uses included wheat and rye and cover the intended uses for ADM.06001.H.2.B.

Evaluator comments:
Information given by the Applicant is sufficient. As residues of mesosulfuron-methyl exceeding 0.1 mg/kg are not expected in the treated crops, there is no need to investigate the effect of industrial and/or household processing.

No further data are required.

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

Table 7.2-5: Summary of the nature of residues in commodities of plant origin

Endpoints	
Plant groups covered	Cereals (wheat)
Rotational crops covered	Spinach, carrot, wheat
Metabolism in rotational crops similar to metabolism in primary crops?	Yes
Processed commodities	Not triggered
Residue pattern in processed commodities similar to pattern in raw commodities?	Not applicable
Plant residue definition for monitoring	Mesosulfuron-methyl (Regulation (EU) No 289/2014)
Plant residue definition for risk assessment	Mesosulfuron-methyl (EFSA, 2016)
Conversion factor from enforcement to RA	Not applicable

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

Available data

Reference: France 2001; France, 2015; EFSA, 2016

Although not triggered according to the representative uses, poultry and ruminant metabolism studies conducted with [U-^{14}C-phenyl] mesosulfuron-methyl were submitted.

No new data submitted in the framework of this application.

Table 7.2-6: Summary of animal metabolism studies

Group	**Species**	**Label position**	**No of animal**	**Application details**		**Sample details**		**Comment**	**Reference**
				Rate (mg/kg bw/d)	**Duration (days)**	**Commodity**	**Time of samp-ling**		
EU data									
Lactating ruminants	Cow	[U-^{14}C-phenyl]	1	0.340	5	Milk	Twice daily	C005418	France 2001, France, 2015 EFSA; 2016
						Urine and faeces	Daily		
						Tissues	At sacrifice		
Laying poultry	Hen	[U-^{14}C-phenyl]	6	0.758	14	Eggs	Twice daily	C005417	France 2001, France, 2105 EFSA, 2016
						Excreta	Daily		
						Tissues	At sacrifice		

Summary of animal metabolism studies reported in the EU

"The parent compound was the predominant compound of the total residues in milk (23% TRR), liver (21–52% TRR), kidney (41% TRR) and in fat (20–70% TRR). Other compounds that occur at significant proportions, such as the alcohol metabolite AE F0195141 in fat (27% TRR), mesosulfuron-methyl or AE F140584 in poultry liver (18% TRR) and AE F140584 or AE F160459 in milk (17% TRR), accounted for a very low concentration (< 0.01 mg/kg) in all matrices at the calculated dietary burden. Metabolites' identification was not attempted in eggs and in the muscle because of the low recovered residue levels

(0.012 and 0.004 mg eq/kg, respectively). On the basis of the available metabolism studies in lactating ruminants and laying hens conducted with U-14C-phenyl labelled mesosulfuron-methyl only, the residue definition for both monitoring and risk assessment for animal commodities is proposed as mesosulfuron-methyl only.” (*EFSA, 2016*)

Conclusion on metabolism in livestock

The metabolism of mesosulfuron-methyl in livestock animals is sufficiently addressed to support the proposed uses of product ADM.06001.H.2.B.

Evaluator comments:

Information given by the Applicant is sufficient.

Metabolism of mesosulfuron-methyl was investigated for poultry and ruminant (France, 2001) and evaluated in the renewal of the active substance (France 2015, EFSA 2016) and is sufficiently addressed to support the proposed uses of product ADM.06001.H.2.B.

The residue definition for monitoring and risk assessment is proposed as mesosulfuron-methyl only.

No further data are required.

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

Table 7.2-7: Summary on the nature of residues in commodities of animal origin

Endpoints	
Animals covered	Lactating goats
	Laying hens
Time needed to reach a plateau concentration	5 days in milk (very low concentration, but 5 days experiment only)
	10 days in eggs
Animal residue definition for monitoring	Not required for intended uses – if required a default residue definition could be set as mesosulfuron-methyl only (EFSA, 2016)
Animal residue definition for risk assessment	Not required for intended uses (EFSA, 2016)
Conversion factor	Not applicable
Metabolism in rat and ruminant similar	Yes
Fat soluble residue	No

7.2.3 Magnitude of residues in plants (KCA 6.3)

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

Reference: France, 2015; France, 2016; EFSA, 2012; 2016
The intended cGAPs for ADM.06001.H.2.B in wheat, rye and triticale are comparable or less critical than the EU cGAPs as shown in the table below.
New studies on the magnitude of residue have been submitted by the applicant in the framework of this application. The detailed assessment of these studies is presented in Appendix 2 (KCP 8/01 – KCP 8/02).

Table 7.2-8: Comparison of intended and critical EU GAPs

Type of GAP	Region	Crop	Number of applications	Application rate per treatment (kg a.s./ha)	Interval between applications [min. days]	Growth stage at last application	PHI (days)	Remark
cGAP EU (France, 2015, EFSA, 2016)	EU	Wheat	1	0.015	-	32	n.a.	
	EU	Rye	1	0.006	-	32	n.a.	
cGAP EU (Art. 12, EFSA, 2012)	EU	Wheat	1	0.020	-	32	90	
	EU	Rye	1	0.020	-	32	90	
Intended cGAP (number 2)	C-EU	Wheat	1	0.012	-	39	n.a.	
Intended cGAP (number 2)	C-EU	Rye	1	0.012	-	39	n.a.	
Intended cGAP (number 2)	C-EU	Triticale	1	0.012	-	39	n.a.	

n.a.: not applicable, the PHI is covered by the time remaining between application and harvest

Table 7.2-9: Summary of EU reported and new data supporting the intended uses of ADM.06001.H.2.B and conformity to existing MRL

<table>
<tr><th>Commodity</th><th>Source</th><th>Residue zone (N-EU, S-EU, EU, outside EU)</th><th>Evaluation
GAP
Residue levels (mg/kg)
E = according to enforcement residue definition
RA = according to risk assessment residue definition</th><th>STMR (mg/kg)</th><th>HR (mg/kg)</th><th>Unrounded OECD calculator MRL (mg/kg)</th><th>Current EU MRL (mg/kg) (a)</th><th>MRL compliance</th></tr>
<tr><td rowspan="4">Wheat grain (extrapolated to rye and triticale)</td><td>EFSA, 2012</td><td>N-EU</td><td>GAP on which MRL/EU a.s. assessment is based: 1 x 20 g as/ha, BBCH 13-32 (39), PHI 90d, outdoor
E/RA(b): 18 x <0.01</td><td colspan="5" rowspan="3">N/A</td></tr>
<tr><td>France, 2015, France, 2016, EFSA, 2016</td><td>N-EU</td><td>GAP on which MRL/EU a.s. assessment is based: 1 x 15 g as/ha, BBCH 13-32, outdoor
E/RA(b): 15 x <0.01</td></tr>
<tr><td>New trials</td><td>N-EU</td><td>Trials GAP: 1 x 12 g as/ha, BBCH 39, outdoor
E/RA(b): 8 x <0.01</td></tr>
<tr><td>Overall supporting data for cGAP</td><td>N-EU</td><td>E/RA(b): 41 x <0.01</td><td>E: <0.01
RA: <0.01</td><td>E: <0.01
RA: <0.01</td><td>0.01</td><td>0.01</td><td>Y</td></tr>
<tr><td rowspan="4">Wheat straw (extrapolated to rye and triticale)</td><td>EFSA, 2012</td><td>N-EU</td><td>GAP on which MRL/EU a.s. assessment is based: 1 x 20 g as/ha, BBCH 13-32 (39), PHI 90d, outdoor
E/RA(b): 18 x <0.05</td><td colspan="5" rowspan="3">N/A</td></tr>
<tr><td>France, 2015, France, 2016, EFSA, 2016</td><td>N-EU</td><td>GAP on which MRL/EU a.s. assessment is based: 1 x 15 g as/ha, BBCH 13-32, outdoor
E/RA(b): 15 x <0.05</td></tr>
<tr><td>New trials</td><td>N-EU</td><td>Trials GAP: 1 x 12 g as/ha, BBCH 39, outdoor
E/RA(b): 7 x <0.01, 0.016</td></tr>
<tr><td>Overall supporting data for cGAP</td><td>N-EU</td><td>E/RA(b): 7 x <0.01, 0.016, 15 x <0.05</td><td>E: <0.05
RA: <0.05</td><td>E: <0.05
RA: <0.05</td><td>N/A</td><td>N/A</td><td>N/A</td></tr>
</table>

(a) Source of EU MRL: Commission Regulation (EU) No 289/2014 of 21 March 2014
(b) Residue definitions for enforcement and risk assessment are the same: mesosulfuron-methyl only
N/A Not applicable

7.2.3.2 Conclusion on the magnitude of residues in plants

Central Europe

Wheat is a major crop in Central Europe and 8 trials are required in the zone. Four trials per zone are sufficient if residues are below LOQ (0.01 mg/kg).

Fifteen valid trials in Central Europe have been evaluated by France (2015) and EFSA (2016) that are comparable to the intended cGAP for ADM.06001.H.2.B in Central Europe, since the application rate is slightly lower (12 g as/ha vs 15 g as/ha) but the application timing is later (up to BBCH 32 vs BBCH 39).

Eighteen valid trials in Central Europe have been evaluated by EFSA (2012) that are more critical than the intended cGAP for ADM.06001.H.2.B in Central Europe, since the application rate is lower (12 g as/ha vs 20 g as/ha). All trials are applicable as residues in wheat grain were always below LOQ.

Eight new trials were conducted with wheat in Central Europe that correspond to the intended cGAP for ADM.06001.H.2.B. Overall, there are 41 trials in Central Europe Europe that support the intended cGAP for ADM.06001.H.2.B on wheat.

As the last application according to the intended GAP for ADM.06001.H.2.B is done before edible parts are formed (i.e. before BBCH 51), data on wheat can be extrapolated to rye (SANTE/2019/12752), and are also valid for triticale.

Residues of mesosulfuron-methyl in wheat grain are below LOQ (0.01 mg/kg) in all trials.

Thus, according to the available data, the intended uses on wheat, triticale and rye are considered acceptable. The data submitted show that no exceedance of the current MRL will occur.

Evaluator comments:

<u>Wheat, rye, triticale</u>

Wheat and rye are the major crops in northern Europe (SANTE/2019/12752). A minimum of eight trials are required. Based on the SANTE/2019/12752, 8 residue trials on wheat can be used for extrapolation to rye and triticale before and after forming of the edible part.

Sufficient trials on wheat are available and presented in EFSA Journal 2016;14(10):4584. It should be noted that no LoA is available. Nevertheless new data submitted by the Applicant in the framework of this application are sufficient to support the intended uses in NEU.

Eight N-EU trials were conducted in accordance with the following GAP: 1 x 12 g a.s. /ha, application at BBCH 39, PHI - not applicable, the PHI is covered by the time remaining between application and harvest; outdoor.
For mesosulfuron-methyl, at harvest no residues were found in grain and straw (<0.01 mg/kg).

Available results show that the in force MRL of mesosulfuron-methyl on wheat and rye of 0.01 mg/kg (Reg. (EU) No 289/2014) will not be exceeded. The current EU MRL for mesosulfuron-methyl is sufficient to support the proposed uses.
The trials are supported by valid storage stability data and validated analytical methods.

The proposed uses on wheat, rye and triticale are considered acceptable.

7.2.4 Magnitude of residues in livestock

7.2.4.1 Dietary burden calculation

According to the OECD guidance document on residues in livestock (ENV/JM/MONO(2013)8), wheat, triticale and rye straw and grain, and wheat by-products (distiller's grain, wheat gluten meal, wheat milled by-products) are fed to livestock. Residues from rotational crops are expected to be below LOQ and therefore do not need to be considered. The dietary burdens were calculated for different groups of livestock using the EFSA calculator[1].

The dietary burden calculation made by EFSA (2012) in the framework of the Art. 12 evaluation is available for mesosulfuron-methyl, which considered cereal grain, bran and straw, but did not consider by-products. A new dietary burden calculation is therefore presented below.

[1] http://ec.europa.eu/food/plant/docs/pesticides_mrl_guidelines_animal_model_2017.xls

Table 7.2-10: Input values for the dietary burden calculation (considering the uses evaluated in Art. 12 procedure and the uses under consideration)

Feed Commodity	Median dietary burden		Maximum dietary burden	
	Input value (mg/kg)	Comment	Input value (mg/kg)	Comment
Risk assessment residue definition: mesosulfuron-methyl				
Rye straw	0.05	Extrapolated from wheat. Median residue (EFSA, 2012, 2016)	0.09	Extrapolated from wheat. Highest residue (EFSA, 2012, 2016)
Triticale straw	0.05	Extrapolated from wheat. Median residue (EFSA, 2012, 2016)	0.09	Extrapolated from wheat. Highest residue (EFSA, 2012, 2016)
Wheat straw	0.05	Median residue (EFSA, 2012, 2016)	0.09	Highest residue (EFSA, 2012, 2016)
Rye grain	0.01	Extrapolated from wheat. Median residue (EFSA, 2012, 2016)	0.01	Extrapolated from wheat. Median residue (EFSA, 2012, 2016)
Triticale grain	0.01	Extrapolated from wheat. Median residue (EFSA, 2012, 2016)	0.01	Extrapolated from wheat. Median residue (EFSA, 2012, 2016)
Wheat grain	0.01	Median residue (EFSA, 2012, 2016)	0.01	Median residue (EFSA, 2012, 2016)
Distiller’s grain, dried	0.03	Median residue x PF (0.01 x 3.3) (EFSA, 2012, 2016)	0.03	Median residue x PF (0.01 x 3.3) (EFSA, 2012, 2016)
Wheat gluten meal	0.02	Median residue x PF (0.01 x 1.8) (EFSA, 2012, 2016)	0.02	Median residue x PF (0.01 x 1.8) (EFSA, 2012, 2016)
Wheat milled by-products	0.07	Median residue x PF (0.01 x 7) (EFSA, 2012, 2016)	0.07	Median residue x PF (0.01 x 7) (EFSA, 2012, 2016)

Table 7.2-11: 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: mesosulfuron-methyl					
Beef cattle*	0.001	0.001	Rye straw	0.05	N
Dairy cattle*	0.002	0.002	Rye straw	0.05	N
Ram/ewe	0.002	0.003	Rye straw	0.08	N
Lamb	0.003	0.003	Rye straw	0.08	N
Breeding swine	0.001	0.001	Wheat milled by-products	0.05	N
Finishing swine*	0.001	0.001	Wheat milled by-products	0.05	N
Broiler poultry	0.002	0.002	Wheat milled by-products	0.02	N
Layer poultry*	0.002	0.002	Wheat milled by-products	0.03	N
Turkey	0.002	0.002	Wheat milled by-products	0.02	N

* These categories correspond to those (formerly) assessed at EU level.

Evaluator comments:
The calculated dietary burdens for all groups of livestock did not exceed the trigger value. No further data are required.

7.2.4.2 Livestock feeding studies (KCA 6.4.1-6.4.3)

As none of the animals considered in the dietary burden calculation are likely to be exposed to residues via feed above the trigger values according to Reg. (EC) No 1107/2009, livestock feeding studies are not required. Further investigation is not necessary.

Conclusion on feeding studies
The new mode of calculation modifies the theoretical maximum daily intake for animals, but regarding available feeding data, there is no requirement to set MRLs in commodities of animal origin. Residues of mesosulfuron-methyl in commodities of animal origin are not to be expected.

Evaluator comments:
Information given by the Applicant is sufficient.
Feeding study are not required.

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

“The investigation of effects of processing on the nature and magnitude of residues was not triggered by the representative uses.” (*EFSA, 2016*)
The representative uses included wheat and rye and cover the intended uses for ADM.06001.H.2.B.

7.2.5.1 Available data for all crops under consideration

Not applicable. Please refer to Point 7.2.5.

7.2.5.2 Conclusion on processing studies

Not applicable. Please refer to Point 7.2.5.

Evaluator comments:
Information given by the Applicant is sufficient. As residues of mesosulfuron-methyl exceeding 0.1 mg/kg are not expected in the treated crops, there is no need to investigate the effect of industrial and/or household processing.
No further data are required.

7.2.6 Magnitude of residues in representative succeeding crops

The crops under consideration can be grown in rotation.
Considering available data dealing with nature of residues (see Point 7.2.2.2), no study dealing with magnitude of residues in succeeding crops is needed. No residues of mesosulfuron-methyl >0.01 mg/kg are expected in rotational crops grown after the use ADM.06001.H.2.B according to the intended GAP.

7.2.6.1 Field rotational crop studies (KCA 6.6.2)

Not applicable. Please refer to Point 0.

Evaluator comments:
According to the EFSA Journal 2012;10(11):2976 *Based on the rotational confined crop studies and considering that the maximum application rate of mesosulfuron-methyl within the EU is 0.02 kg a.s./ha and the fact that mesosulfuron-methyl was applied to bare soil (interception of mesosulfuron-methyl by the plants is expected in practice), it can be concluded that mesosulfuron-methyl residue levels in rotational commodities are not expected to exceed 0.01 mg/kg, provided that mesosulfuron-methyl is applied in compliance with the GAPs reported in Appendix*

A.
No further data are required.

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

Wheat, triticale and rye have no melliferous capacity according to SANTE/11956/2016 rev. 9, therefore data on residues in honey are not required.
The available data for the active substance sufficiently address aspects of the residue situation that might arise from the use of ADM.06001.H.2.B. Other / special studies are not needed.

zRMS comments:
Information given by the Applicant is sufficient. According to the SANTE/11956/2016 rev. 9, 14 September 2018, wheat, triticale and rye have no melliferous capacity, so no further data are required.

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

Toxicological reference values relevant for dietary risk assessment are reported in the summary of the evaluation (see 7.1.2).
As an ARfD was not deemed necessary, acute risk assessment is not relevant.

7.2.8.1 Input values for the consumer risk assessment

The TMDI was calculated with MRL values for all crops and animal commodities. All MRLs for mesosulfuron-methyl are set at the LOQ.

Table 7.2-12: Input values for the consumer risk assessment

Code no	Commodity	Chronic risk assessment	
		Input value (mg/kg)	**Comment**
Risk assessment residue definition: mesosulfuron-methyl			
500070	Rye	0.01*	MRL (Reg. (EU) No 289/2014
500090	Wheat	0.01*	MRL (Reg. (EU) No 289/2014
-	All other crops	0.01*- 0.05*	MRL (Reg. (EU) No 289/2014
100000	All products of animal origin – terrestrial animals	0.02*	MRL (Reg. (EU) No 289/2014

* MRL at LOQ

7.2.8.2 Conclusion on consumer risk assessment

Extensive calculation sheets are presented in Appendix 3.

Table 7.2-13: Consumer risk assessment

TMDI (% ADI) according to EFSA PRIMo 3.1	0.0019 % (based on NL toddler)

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

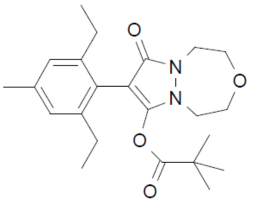
The proposed uses of mesosulfuron-methyl in the formulation ADM.06001.H.2.B do not represent unacceptable chronic risks for the consumer.

Evaluator comment:
Calculation presented by the Applicant is acceptable.
The data available are considered sufficient for risk assessment. The chronic intakes of mesosulfuron-methyl residues are unlikely to present a public health concern.
The intended uses of ADM.06001.H.2.B are accepted.

7.3 Pinoxaden

General data on pinoxaden are summarized in the table below (last updated 2020/10/26)

Table 7.3-1: General information on pinoxaden

Active substance (ISO Common Name)	pinoxaden
IUPAC	8-(2,6-diethyl-p-tolyl)-1,2,4,5-tetrahydro-7-oxo-7H-pyrazolo[1,2-d][1,4,5]oxadiazepin-9-yl 2,2-dimethylpropionate
Chemical structure	
Molecular formula	$C_{23}H_{32}N_2O_4$
Molar mass	400.5 g/mol
Chemical group	Phenylpyrazolin
Mode of action (if available)	Acetyle-CoA-carboxylase inhibition
Systemic	Yes
Company (ies)	Syngenta UK Ltd.
Rapporteur Member State (RMS)	United Kingdom
Approval status	Approved 01/07/2016 Commission Implementing Regulation (EU) 2016/370 of 15 March 2016
Restriction (e.g. is restricted to use as "…")	None
Review Report	SANCO/11794/2013 rev 3 29 January 2016
Current MRL regulation	Regulation (EC) No 839/2008 of 31 July 2008 Regulation (EU) No 2022/1346 of 1 August 2022
Peer review of MRLs according to Article 12 of Reg No 396/2005 EC performed	Yes: EFSA 2021
EFSA Journal : Conclusion on the peer review	Yes: EFSA 2013
EFSA Journal: conclusion on article 12	~~No~~ Yes, EFSA Journal 2021;19(3):6503
Current MRL applications on intended uses	EFSA-Q-2017-00280 (United Kingdom) Barley, oat, rye, wheat Status: Evaluation ongoing

7.3.1 Stability of Residues (KCA 6.1)

7.3.1.1 Stability of residues during storage of samples

Available data
Reference: EFSA, 2013
No new data submitted in the framework of this application.

Table 7.3-2: Summary of stability data achieved at ≤ - 18°C (unless stated otherwise)

Matrix	Characteristics of the matrix	Acceptable Maximum Storage duration		Reference
		SYN 505164 (M4)	SYN 502836 (M6)	
EU data				
Plant products				
Wheat grain	High ~~protein~~ starch content	28 months	28 months	EFSA, 2013
Wheat whole plant	High water content	28 months	28 months	EFSA, 2013
Wheat straw	No group	28 months	28 months	EFSA, 2013
Animal Products				
Beef liver	Liver	3 months(a)	3 months(a)	EFSA, 2013
Cow milk	Milk	3 months(a)	3 months(a)	EFSA, 2013
Chicken muscle	Muscle/meat	3 months(a)	3 months(a)	EFSA, 2013
Chicken eggs	Eggs	3 months(a)	3 months(a)	EFSA, 2013

(a) Storage at -20 ºC

Conclusion on stability of residues during storage

Residues of four metabolites of pinoxaden (NOA 407855): NOA 407854 (M2), SYN 505164 (M4), SYN 502836 (M6) and SYN 505887 (M10) in frozen samples of wheat grain, straw and whole plant have been shown to be stable for up to 28 months freezer storage (at -18 ºC).
The storage stability periods cover the storage periods of samples in the plant residue trials presented in this submission.
In animal products, (Chicken muscle, beef liver, cow milk and eggs), M4 and M6 are stable under frozen storage (- 20 ºC) for a period of 3 months.

zRMS comments:
In EFSA Journal 2021;19(3):6503 it is stated that *The storage stability of metabolites M2, M4, M6 and M10 in wheat whole plant, grain and straw was investigated in the framework of the peer review (United Kingdom, 2013; EFSA, 2013).*
In high water content, dry/high protein content commodities and no group (wheat straw), the available studies demonstrated the storage stability of metabolites M4 and M6 for a period of 28 months when stored at –18°C. The storage stability for M2 and M10 was the same as for M4 and M6 under the same conditions. This information on M2 and M10 is included here only for completeness. Additional storage stability studies are not needed for the current authorised uses.

The residue data are valid with regard to storage stability.

The stability of residues during storage of metabolites M4 and M6 (3 months) in animal products is sufficiently addressed to support the proposed uses of the product ADM.06001.H.2.B. No additional study is required.

7.3.1.2 Stability of residues in sample extracts (KCA 6.1)

The relevant information on the stability in the final or any intermediate step can be derived from the fortification experiments performed during method validation. If the recoveries in the fortified samples are within the acceptable range of 70 - 120%, stability is sufficiently proven.
The procedural recoveries obtained fully support the residue data presented in this submission.

zRMS comments:
Information provided by Applicant is acceptable.
No additional study is required.

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

Reference: United Kingdom, 2006; EFSA, 2013

The metabolism of pinoxaden was investigated in wheat matrices using ^{14}C-pyrazol-, ^{14}C-phenyl-, and ^{14}C-oxadiazepine-labelled pinoxaden.

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

Table 7.3-3: 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 (forage, grain, husks, straw)	[3,5-^{14}C-pyrazol]	Foliar, F	0.0685 (+ cloquintocet-mexyl)	1	0, 14, 42, 209, 264	99PSA55	UK, 2006 EFSA, 2013
	Winter wheat (grain)	[3,5-^{14}C-pyrazol]	Stem injection, Not indicated	50 µg a.s. into the stem	1	Not indicated		
	Winter wheat (forage, ears, grain, husks, straw)	[1-^{14}C-phenyl]	Foliar, F	0.064 (+ cloquintocet-mexyl)	1	0, 7, 14, 28, 55	00PSA58	
				0.318 (+ cloquintocet-mexyl)	1	0, 7, 14, 28, 55		
	Spring wheat (forage, grain, husks, straw)	[1-^{14}C-phenyl]	Foliar, F	0.062 (+ cloquintocet-mexyl)	1	0, 7, 14, 28, 67	01MK16	
		[3,6-^{14}C-oxadiazepine]	Foliar, F	0.066 (+ cloquintocet-mexyl)	1	0, 7, 14, 28, 67		
New data								
Cereals	Spring wheat (forage, hay, grain, straw)	[1-^{14}C-phenyl]	Foliar, G	0.067 (+ mefenpyr-diethyl)	1	6, 32, 47	Erk, T., 2021 Report No. S10-00664 (KCP 8/05)	ADAMA
	Wheat (forage, hay, grain, straw)	[1-^{14}C-phenyl]	Foliar, G	0.214 (+ mefenpyr-diethyl)	1	6, 32, 47		
Cereals	N/A[(b)]						Silcock, R., Gill, P., 2021 Report No. 1808368.UK0 - 0293 (KCP 8/05)	ADAMA

(a) Outdoor/field application (F) or glasshouse/protected/indoor application (G)
(b) Comparison of existing EU reviewed and new metabolism data of pinoxaden in wheat in the presence of different safeners

Summary of plant metabolism studies reported in the EU

"Following applications of [^{14}C]-phenyl and [^{14}C]-oxadiazepine labelled pinoxaden to wheat the major residues in grain at harvest were metabolites M6 and M4, while parent pinoxaden was not found. Acid hydrolysis of whole grain samples indicated a significant portion of metabolite M4 present as conjugated

residues. Whether metabolite M6 is present as conjugated residues is subject to some uncertainty, but if present as conjugated material, it is likely to be present at a much lower level than conjugated M4. Some other metabolites were identified but were not found in significant amounts and proportions in grain. Metabolite M4 (free and conjugated) was also the predominant residue in wheat forage and in the straw at harvest.
The residue definition for risk assessment for cereals is set as sum of M4 and M6 (both free and conjugated), expressed as pinoxaden. For monitoring, the same residue definition is provisionally proposed. During the peer review an alternative, simpler monitoring residue definition of free M6 alone was investigated. However, the latter could not be ultimately confirmed, since uncertainties arose as to whether free M6 would indeed be a reliable and universal marker. Consequently, ESFA suggest a global monitoring definition as free M6 alone to be reconsidered when a broader view on different crops and use scenarios will be available in future.” (*EFSA, 2013*).

Summary of new plant metabolism studies
The metabolism of the herbicide pinoxaden was investigated in wheat plants following a single application at BBCH 39 with [^{14}C]-pinoxaden (nominally 60 g a.s./ha) as an OD formulation also containing mesosulfuron-methyl and the safener mefenpyr-diethyl.
Raw agricultural commodities (RAC) were harvested at BBCH 47 (forage), 6 days after application, at BBCH 77 (hay), 32 days after application and at BBCH 92 (straw and grain), 47 days after application.
TRR values of forage, hay, straw and grain accounted for 2.686 mg eq/kg, 3.374 mg eq/kg, 4.987 mg eq/kg and 0.630 mg eq/kg, respectively.
The total recoveries following conventional solvent extraction of forage, hay, straw and grain accounted for 95.9%, 80.4%, 76.8% and 87.3% of TRR, respectively.
Identification rates of extracted residues from forage, hay, straw and grain, including the exhaustive extracts of the post-extraction solids, accounted for 79.9%, 66.1%, 47.8% and 63.7% of TRR, respectively.
Identification rates increased after sequential hydrolysis of the conventional solvent extracts of forage, hay, straw and grain and accounted for 82.6%, 69.1%, 55.8% and 92.0% of TRR, respectively, including the exhaustive extracts of the post-extraction solids.
Parent pinoxaden was not detected in any commodity.
SYN505164 (M4) and its hydrolysable conjugate Glc-SYN505164 (Glc-M4) were found as major metabolites (>10% TRR) in all RACs. In wheat grain, the hydrolysable conjugate SYN505164-Glc-HMG-2 (M4G2) was also detected as a major metabolite (>10% TRR).
M-X, SYN502836 (M6), NOA407854 (M2) and NOA447204 (M3) were additional metabolites detected in the conventional solvent extracts of all RACs. SYN505164-Glc-HMG-2 (M4G2) was also found in the conventional solvent extracts of hay and straw but was not detected in forage.
In wheat grain, the hydrolysable conjugate SYN505164-Glc-HMG-1 (M4G1) was also detected in the conventional solvent extract.
Extraction efficiency of the residue analytical method is sufficiently shown for the extraction of the metabolites SYN505164 (M4) and SYN502836 (M6) from wheat forage, hay, straw and grain.
Pinoxaden was metabolised in wheat after a single application. SYN505164 (M4) represented the major initial degradation product and was further conjugated with glucose and 3-hydroxy-3-methylglutaric acid to form Glc-SYN505164 (Glc-M4), SYN505164-Glc-HMG-1 (M4G1) and SYN505164-Glc-HMG-2 (M4G2). The metabolism of pinoxaden in wheat in the presence of the safener mefenpyr-diethyl has been sufficiently elucidated.

Comparison of plant metabolism in wheat in the presence of safeners
The metabolism of pinoxaden in wheat in the presence of the safener mefenpyr-diethyl has been qualitatively and quantitatively compared to the metabolism of pinoxaden in the presence of the safener cloquintocet-mexyl.
The main metabolic pathway observed for pinoxaden in wheat, with either cloquintocet-mexyl or mefenpyr-diethyl, was ester hydrolysis to M2, followed by hydroxylation to M4 and subsequent phase II glucoside conjugation. M4 can be further metabolised by oxidation to M6, and M6 was also found as a major metabolite in grain with both safeners.
Considering the plant residue definition, the sum of M4 and M6 (both free and conjugated) accounted for

65.3-83.9% TRR in mature grain and 46.4-50.2% TRR in mature straw from wheat treated with pinoxaden and cloquintocet-mexyl, and 88.0% TRR in mature grain and 47.9% TRR in mature straw from wheat treated with pinoxaden and mefenpyr-diethyl. This shows that in mature wheat the components of the residue definition are quantitatively similar when pinoxaden is applied with either safener.
Glycosidic conjugation of M4 was observed in all studies, with the glucose conjugate of M4 (M5, gluc-M4) being common to all studies and both safeners. Metabolites M10, M11 and M32 resulted from hydroxylation of M2 in two or more positions and were detected only in studies conducted with the safener cloquintocet-mexyl.
Metabolite M-X was found only in the study conducted with the safener mefenpyr-diethyl and was characterised by mass-spectrometry as a downstream metabolite of M2. M-X was detected at similarly low levels (3.8-5.0% TRR, including bound/conjugated material) in all commodities, and is therefore considered to be a minor metabolite.
As the main metabolic pathways of pinoxaden are the same with both safeners, it can be concluded that the safener does not substantially impact the metabolism of pinoxaden in wheat.

Conclusion on metabolism in primary crops
The metabolism of pinoxaden in cereal crops following foliar application is sufficiently addressed to support the proposed uses of product ADM.06001.H.2.B. As the main metabolic pathways of pinoxaden are the same with both safeners, it can be concluded that the safener does not substantially impact the metabolism of pinoxaden in wheat.

Evaluator comments:
The metabolism of pinoxaden was investigated after foliar treatment in cereals (wheat) (United Kingdom, 2005, 2013) and assessed in the framework of the peer review (EFSA, 2013).
Free and conjugated forms of metabolites M4 and M6 were the predominant species identified in cereals and therefore, the peer review set the residue definition for risk assessment for cereals as sum of M4 and M6 (both free and conjugated), expressed as pinoxaden. The residue definition for risk assessment set in the EFSA conclusion is still valid for this MRL review.
According to the EFSA Journal 2021;19(3):6503 two options for the residue definition for enforcement for cereals crop group are proposed,
RD-Mo option 1 – sum of M4 and M6 (both free and conjugated), expressed as pinoxaden,
RD-Mo option 2 – sum of M4 and M6 (both free only), expressed as pinoxaden.

According to the Reg. (EU) 2022/1346 applicable from 22/02/2023 the residue definition for monitoring is “Sum of M4 and M6 (both free and conjugated), expressed as pinoxaden (R) (A)” (superseded Pinoxaden on 22/02/2023).

Applicant submitted new metabolism study (Erk, T., 2021). **zRMS-PL is of the opinion that the new studies investigating the metabolism of residues should be assessed at the EU level. It can be considered as supporting data.**
The metabolism of the herbicide pinoxaden was investigated in wheat plants following a single application at BBCH 39 with [^{14}C]-pinoxaden (nominally 60 g a.s./ha) as an OD formulation also containing mesosulfuron-methyl and the safener mefenpyr-diethyl. Parent pinoxaden was not detected in any commodity. Major metabolites are M4 and M6.
Extraction efficiency of the residue analytical method is sufficiently shown for the extraction of the metabolites SYN505164 (M4) and SYN502836 (M6) from wheat forage, hay, straw and grain.
The study meets the requirements of the OECD 501 and SANTE 2017/10632 - Rev. 3, 22 November 2017.

Additionally Applicant submitted the document of Silcock, R., Gill, P., 2021. The purpose of the study was the comparison of the available metabolism studies (previously evaluated in DAR (UK, 2006) and DAR Addendum (UK, 2013) and new data (Erk, T., 2021) on pinoxaden in the presence of safeners cloquintocet-mexyl and mefenpyr diethyl in wheat.
Based on available data zRMS-PL agrees with the following conclusion of the analysis: *“As the main metabolic pathways of pinoxaden are the same with both safeners, it can be concluded that the safener does not substantially impact the metabolism of pinoxaden in wheat.”*

During the commenting period Applicant provided additional explanation:
The objective of the study was to demonstrate the primary plant metabolism of pinoxaden was not significantly altered when the proposed formulated product was applied to wheat. Since the product contained a different safener to that evaluated during the first EU review it was considered necessary to evaluate this product/safener specific

study as part of this Article 33 application to verify to cMS that according to the zRMS, the metabolism of pinoxaden had not significantly changed thereby allowing for the existing residue definitions set for pinoxaden during the EU review to be applied to this application.

No additional data are required.

7.3.2.2 Nature of residue in rotational crops (KCA 6.6.1)

Available data

Reference: United Kingdom, 2006; EFSA, 2013

The metabolism of pinoxaden was investigated in rotational crops lettuce, radish and spring and winter wheat using ^{14}C-phenyl-, and ^{14}C-oxadiazepine-labelled pinoxaden.
No new data submitted in the framework of this application.

Table 7.3-4: 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-phenyl]	Bare soil, F	0.0603 (+cloquintocet-mexyl)	30, 120	84, 170	00PSA57	UK, 2006 EFSA, 2013
	Lettuce	[^{14}C-oxadiazepine]	Bare soil, F	0.0655 (+cloquintocet-mexyl)	29, 120	70, 166	01PSA59	UK, 2006 EFSA, 2013
Root and tuber vegetables	Radish	[^{14}C-phenyl]	Soil, F	0.0603 (+cloquintocet-mexyl)	30, 120	84, 170	00PSA57	UK, 2006 EFSA, 2013
	Radish	[^{14}C-oxadiazepine]	Bare soil, F	0.0655 (+cloquintocet-mexyl)	29, 120	70, 166	01PSA59	UK, 2006 EFSA, 2013
Cereals	Spring wheat	[^{14}C-phenyl]	Bare soil, F	0.0603 (+cloquintocet-mexyl)	30, 120, 365	84, 141, 170, 240, 450, 496	00PSA57	UK, 2006 EFSA, 2013
	Winter wheat	[^{14}C-phenyl]	Bare soil, F	0.0603 (+cloquintocet-mexyl)	177	240, 430, 470	00PSA57	UK, 2006 EFSA, 2013
	Spring wheat	[^{14}C-oxadiazepine]	Bare soil, F	0.0655 (+cloquintocet-mexyl)	29, 120, 361	70, 139, 166, 249, 433, 473	01PSA59	UK, 2006 EFSA, 2013
	Winter wheat	[^{14}C-oxadiazepine]	Bare soil, F	0.0655 (+cloquintocet-mexyl)	168	249, 424, 447	01PSA59	UK, 2006 EFSA, 2013

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

Summary of metabolism studies in rotational crops reported in the EU

"The metabolism and distribution in rotational crops was investigated in lettuce, radish and wheat. Given the low total residues, metabolite identification and quantification was only carried out in lettuce, radish tops and in wheat straw and forage. Parent pinoxaden was not found in any sample, and of the detected metabolites only M3 slightly exceeded 0.01 mg/kg in wheat forage at the shortest plant back interval of 30 days. Significant residues in succeeding crops are not expected when the application is made to cereals according to the representative GAP, and therefore no residue trials data were required for succeeding or rotational crops." (*EFSA, 2013*).

Conclusion on metabolism in rotational crops

The metabolism in primary and rotational crops was found to be similar and a specific residue definition for rotational crops is not deemed necessary. No residues of pinoxaden >0.01 mg/kg are expected in rotational crops grown after the use ADM.06001.H.2.B according to the intended GAP.

Evaluator comments:
Residues are not significant in rotational crops for the current authorised uses, and the residue definition for plants does not require a particular consideration for rotational crops (EFSA, 2021).
No additional study is required.

7.3.2.3 Nature of residues in processed commodities (KCA 6.5.1)

Available data

Reference: EFSA, 2013; EFSA, 2021

Stability of pinoxaden and metabolite M2 was assessed under hydrolytic conditions of pasteurisation, baking, boiling and brewing, and sterilisation.
No new data submitted in the framework of this application.

Table 7.3-5: Nature of the residues in processed commodities

Conditions (Duration, Temperature, pH)	Identified compound(s) (%)	Reference
EU data		
Parent pinoxaden		
Pasteurisation (20 minutes, 90°C, pH 4)	Pinoxaden (86.3%), M2 (5.3%)	UK, 2006 EFSA, 2013 EFSA, 2021
Baking, boiling, brewing (60 minutes, 100°C, pH 5)	Pinoxaden (72.3%), M2 (20.2%)	
Sterilisation (20 minutes, 120°C, pH 6)	Pinoxaden (53.5%), M2 (39.7)	
Metabolitees M4 and M6		
Degradation under hydrolytic conditions not expected (EFSA, 2013)		

Conclusion on nature of residues in processed commodities

"A case was made based on validation data of the analytical method using acid hydrolysis at 100°C for 60 min, that M4 and M6 are also deemed stable under the standard hydrolysis conditions simulating food processing." (*EFSA, 2013*)
The relevant metabolites M4 and M6 are considered stable under standard hydrolysis conditions. A separate residue definition for processed commodities is not required.

Evaluator comments:
Information given by the Applicant is sufficient.
No further data are required.

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

Table 7.3-6: Summary of the nature of residues in commodities of plant origin

Endpoints	
Plant groups covered	Cereals (wheat)
Rotational crops covered	Lettuce, radish, spring wheat, winter wheat
Metabolism in rotational crops similar to metabolism in primary crops?	Yes
Processed commodities	Metabolites M4 and M6 are stable under standard hydrolysis conditions

Endpoints	
Residue pattern in processed commodities similar to pattern in raw commodities?	Yes
Plant residue definition for monitoring	(1) ~~Pinoxaden (Reg. (EC) No 839/2008)~~ Sum of M4 and M6 (both free and conjugated), expressed as pinoxaden (R),(A) (Reg. (EU) 2022/1346) superseded Pinoxaden on 22/02/2023 (2) Sum of M4 and M6 expressed as parent pinoxaden (to include free and conjugated residues of M4 and M6); provisionally (EFSA, 2013) M6 (free metabolite) only has been proposed as enforcement residue definition for plant products (cereals). However, the peer review did not come to a final agreement (EFSA, 2013) (3) Cereal crop group (option 1): sum of M4 and M6 (both free and conjugated), expressed as pinoxaden Cereal crop group (option 2): sum of M4 and M6 (both free only), expressed as pinoxaden (EFSA, 2021)
Plant residue definition for risk assessment	Sum of M4 and M6 expressed as parent pinoxaden (to include free and conjugated residues of M4 and M6) (EFSA, 2013)
Conversion factor from enforcement to RA	Not applicable (based on (2) and (3) option 1

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

Available data

Reference: United Kingdom, 2006; EFSA, 2013

The metabolism of pinoxaden has been investigated in goat and hens using ^{14}C-phenyl-labelled pinoxaden and in goats using ^{14}C-pyrazol-labelled metabolite M4.

No new data submitted in the framework of this application.

Table 7.3-7: Summary of animal metabolism studies

Group	Species	Label position	No of animal	Application details		Sample details		Comment	Reference
				Rate (mg/kg bw/d)	Duration (days)	Commodity	Time of sampling		
EU data									
Lactating ruminants	Goat	[1-^{14}C-phenyl]-pinoxaden	2	120.6 mg/kg	4	Milk	twice daily	046AM04 751-02	UK, 2006 EFSA, 2013
						Urine and faeces	daily		
						Tissues	at sacrifice		
	Goat	[3,5-^{14}C-pyrazol]-M4	2	10 mg/kg	4	Milk	twice daily	046AM04 751-02	UK, 2006 EFSA, 2013
						Urine and faeces	daily		
						Tissues	at sacrifice		
Laying poultry	Hens	[1-^{14}C-phenyl]-pinoxaden	5	96.7 mg/kg	4	Eggs	twice daily	046AM06	UK, 2006 EFSA, 2013
						Excreta	daily		
						Tissues	at sacrific		

Summary of animal metabolism studies reported in the EU

"Livestock metabolism of pinoxaden was studied in the goat and hen, and of metabolite M4 in the goat. For poultry, exposure estimates did not trigger any further assessments. In terms of the representative use, there is unlikely any significant exposure of ruminants to parent pinoxaden from the consumption of wheat and barley commodities, but to metabolites M4 and M6. Therefore, the goat study conducted with parent was less relevant for the peer review but was considered supportive to the assessment. In the goat metabolism study with radio labelled M4, unchanged M4 was the dominant residue identified in liver and kidney (41-55% TRR) and in urine and faeces (90-98% TRR), indicating that there was little metabolism of M4. Total residues in milk, fat and muscle were insignificant despite of the exaggerated dose administered. There was no evidence from the studies with ruminants that M4 was further metabolised into M6 by the animals, which, in contrary, appeared to be the case in poultry. Metabolism of M6 was not separately studied in ruminants, but based on the similarity of both M6 and M4 in terms of molecule structure and polarity, a similar behaviour of M6 compared to M4 can be assumed. Dietary exposure of ruminants to M6 residues is expected to be approximately three times lower than exposure to M4 residues, based on the findings from the residue trials in wheat and barley." (*EFSA, 2013*).

Conclusion on metabolism in livestock

The metabolism of pinoxaden in livestock animals is sufficiently addressed to support the proposed uses of product ADM.06001.H.2.B.

Evaluator comments:

The metabolism of pinoxaden residues in livestock was investigated in lactating goats and laying hens at dose rates covering the maximum dietary burdens calculated in this review (United Kingdom, 2005). These studies were assessed in the framework of the peer review (EFSA, 2013).

According to the EFSA Journal 2021;19(3):6503:

The peer review did not set residue definitions for livestock but indicated that M4 would be the most suitable component for ruminant matrices. From the residue trials in plants evaluated in this review, it is expected that dietary exposure of animals to M6 residues would be approximately from two to five times lower than that to M4. No exposure to M2 is expected, as pinoxaden is not present in the feed items, and M4 is not metabolised further to form M2. Bearing this in mind, the overdose rate of the animal metabolism studies compared to the maximum dietary burdens calculated in this review, and the results of the feeding studies (see below), the residue definitions for enforcement and risk assessment in livestock can be proposed as M4 (free and conjugated), expressed as pinoxaden. The residue is not fat soluble. Since residues are expected to remain far below the LOQ for enforcement, this residue definition could be simplified to M4 free only.

It is stressed that if additional uses are authorised in the future, the inclusion of metabolite M6 in the residue definition for risk assessment might be reconsidered, mostly for poultry.

Animal residue definition for monitoring:

- M4 (free and conjugated), expressed as pinoxaden (EFSA, 2021);
- Sum of M4 and M6 (both free and conjugated), expressed as pinoxaden (R),(A) (Reg. (EU) 2022/1346 superseded Pinoxaden on 22/02/2023);

Animal residue definition for risk assessment: M4 (free and conjugated), expressed as pinoxaden (EFSA, 2021).

No additional study is required.

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

Table 7.3-8: Summary on the nature of residues in commodities of animal origin

Endpoints	
Animals covered	Lactating goats
	Laying hens
Time needed to reach a plateau concentration	Not stated: The metabolism studies were dosed for 4 days and residues were low in eggs and milk. In feeding studies residues of M4 and M6 were below the LOQs for milk and eggs.

Endpoints	
Animal residue definition for monitoring	(1) ~~Pinoxaden (Reg. (EC) No 839/2008)~~ Sum of M4 and M6 (both free and conjugated), expressed as pinoxaden (R),(A) (Reg. (EU) 2022/1346) superseded Pinoxaden on 22/02/2023 (2) None necessary as a result of the representative use; however M4 would be the most suitable component for ruminant matrices based on exposure resulting from the representative use in cereals (EFSA, 2013) (3) M4 (free and conjugated), expressed as pinoxaden (EFSA, 2021)
Animal residue definition for risk assessment	(1) None necessary as a result of the representative use; however M4 would be the most suitable component for ruminant matrices based on exposure resulting from the representative use in cereals (EFSA, 2013) (2) M4 (free and conjugated), expressed as pinoxaden (EFSA, 2021) (3) M4 (free only), expressed as pinoxaden, if residues are below LOQ (0.01 mg/kg) (EFSA, 2021).
Conversion factor	Not applicable
Metabolism in rat and ruminant similar	Yes, when considering the main metabolites
Fat soluble residue	No

7.3.3 Magnitude of residues in plants (KCA 6.3)

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

Reference: United Kingdom, 2006; EFSA, 2013; EFSA, 2021

The intended cGAPs for ADM.06001.H.2.B in wheat, rye and triticale correspond to the respective EU cGAPs as shown in the table below.

New studies on the magnitude of residues of pinoxaden have been submitted by the applicant in the framework of this application. The detailed assessment of these studies is presented in Appendix 2 (KCP 8/01 – KCP 8/02).

Table 7.3-9: Comparison of intended and critical EU GAPs for pinoxaden

Type of GAP	Region	Crop	Number of applications	Application rate per treatment (kg a.s./ha)	Interval between applications [min. days]	Growth stage at last application	PHI (days)	Remark
cGAP EU (UK, 2006; EFSA, 2013, EFSA, 2021)	EU	Wheat	1	0.060	-	39	n.a.	
	EU	Rye	1	0.060	-	39	n.a.	FR: PHI of 60 days
	EU	Triticale	1	0.060	-	39	n.a.	
Intended cGAP (number 2)	C-EU	Wheat	1	0.060	-	39	n.a.	
Intended cGAP (number 2)	C-EU	Rye	1	0.060	-	39	n.a.	
Intended cGAP (number 2)	C-EU	Triticale	1	0.060	-	39	n.a.	

n.a.: not applicable, the PHI is covered by the time remaining between application and harvest

.

Table 7.3-10: Summary of EU reported and new data supporting the intended uses of ADM.06001.H.2.B and conformity to existing MRL

Commodity	**Source**	**Residue zone (N-EU, S-EU, EU, outside EU)**	**Evaluation GAP Residue levels (mg/kg) E = according to enforcement residue definition RA = according to risk assessment residue definition**	**STMR (mg/kg)**	**HR (mg/kg)**	**Unrounded OECD calculator MRL (mg/kg)**	**Current EU MRL (mg/kg) (a)**	**MRL compliance**
Wheat grain (extrapolated to rye and triticale)	EFSA, 2021	N-EU[c]	GAP on which MRL/EU a.s. assessment is based: 1 x 60 g as/ha, BBCH 39, outdoor E/RA[b]: <0.03, 3 x 0.04, 3 x 0.05, 3 x 0.06, 4 x 0.08, 3 x 0.09, 2 x 0.10, 0.11, 0.14, 0.20	0.08	0.20	0.232	~~1.0~~ 0.7	Yes
	New trials	N-EU	Trials GAP: 1 x 60 g as/ha, BBCH 39, outdoor E/RA[b]: 0.031, 0.037, 0.038, 0.039, 0.040, 0.053, 0.065, 0.071	0.040	0.071	0.149	~~1.0~~ 0.7	Yes
	Overall supporting data for cGAP	N-EU	E/RA[b]: <0.03, 0.031, 0.037, 0.038, 0.039, 4 x 0.04, 3 x 0.05, 0.053, 3 x 0.06, 0.065, 0.071, 4 x 0.08, 3 x 0.09, 2 x 0.10, 0.11, 0.14, 0.20	E: 0.06 RA: 0.06	E: 0.20 RA: 0.20	0.215	~~1.0~~ 0.7	Yes
Wheat straw (extrapolated to rye and triticale)	EFSA, 2021	N-EU[c]	GAP on which MRL/EU a.s. assessment is based: 1 x 60 g as/ha, BBCH 39, outdoor E/RA[b]: <0.05, 0.06, 0.08, 2 x 0.09, 3 x 0.10, 0.11, 0.14, 2 x 0.16, 0.17, 2 x 0.19, 0.20, 0.21, 0.22, 0.24, 2 x 0.29, 0.35	0.16	0.35	~~y~~ N/A	N/A	N/A
	New trials	N-EU	Trials GAP: 1 x 60 g as/ha, BBCH 39, outdoor E/RA[b]: 0.071, 0.145, 0.192, 0.222, 0.269, 0.33, 0.778, 0.958	0.226	0.958	N/A	N/A	N/A
	Overall supporting data for cGAP	N-EU	E/RA[b]: <0.05, 0.06, 0.071, 0.08, 2 x 0.09, 3 x 0.10, 0.11, 0.14, 0.145, 2 x 0.16, 0.17, 2 x 0.19, 0.192, 0.20, 0.21, 0.22, 0.222, 0.24, 0.269, 2 x 0.29, 0.33, 0.35, 0.778, 0.958	E: 0.18 RA: 0.18	E: 0.958 RA: 0.958	N/A	N/A	N/A

(a) Source of EU MRL: Commission Regulation (EU) No ~~839/2008 of 31 July 2008~~ Regulation (EU) No 2022/1346 of 1 August 2022
(b) Residue definitions for enforcement and risk assessment are the same (acc. to EFSA, 2013 and option 1 in EFSA, 2021): Sum of M4 and M6 expressed as parent pinoxaden (to include free and conjugated residues of M4 and M6)
(c) Combined data set with residue trials on wheat and barley compliant with GAP (EFSA, 2013)
N/A Not applicable

7.3.3.2 Conclusion on the magnitude of residues in plants

Central Zone

Wheat is a major crop in Central Europe and 8 trials are required in the zone. Four trials per zone are sufficient if residues are below LOQ (0.01 mg/kg).

Twenty-two valid trials with pinoxaden in Central Europe (10 trials on wheat and 12 trials on barley) have been evaluated by EFSA (2021) that correspond to the intended cGAP for ADM.06001.H.2.B in Central and Southern Europe. Data sets for wheat and barley were combined as GAPs are identical and the last application was done before BBCH 51.

Eight new trials were conducted with wheat in Central Europe that correspond to the intended cGAP for ADM.06001.H.2.B. Residues of pinoxaden in grain in the new trials were 0.031 – 0.071 mg/kg and therefore within the residue data available from EU reviewed trials (<0.03 – 0.20 mg/kg). Overall, there are 30 trials in Central Europe that support the intended cGAP for ADM.06001.H.2.B on wheat.

As the last application according to the intended GAP for ADM.06001.H.2.B is done before edible parts are formed (i.e. before BBCH 51), data on wheat can be extrapolated to rye (SANTE/2019/12752), and are also valid for triticale.

Residues of pinoxaden in wheat grain are up to 0.20 mg/kg in Central Europe.

Thus, according to the available data, the intended uses on wheat, triticale and rye are considered acceptable. The data submitted show that no exceedance of the current MRL will occur.

Evaluator comments:

<u>**Wheat, rye, triticale**</u>

Wheat and rye are the major crops in northern Europe (SANTE/2019/12752). A minimum of eight trials are required. Based on the SANTE/2019/12752, 8 residue trials on wheat can be used for extrapolation to rye and triticale before and after forming of the edible part.

Sufficient trials on wheat are available and presented in EFSA Journal 2021;19(3):6503. It should be noted that this is review of the existing maximum residue levels for pinoxaden according to Article 12 of Regulation (EC) No 396/2005 and no LoA for all studies is available. Nevertheless new data submitted by the Applicant in the framework of this application are sufficient to support the intended uses in NEU.

Eight N-EU trials were conducted in accordance with the following GAP: 1 x 60 g a.s. /ha, application at BBCH 39, PHI - not applicable, the PHI is covered by the time remaining between application and harvest; outdoor.

Residues of pinoxaden in grain in the new trials were 0.031 – 0.071 mg/kg (with the addition of an adjuvant, Adigor).

Available results show that the in force MRL of pinoxaden on wheat and rye of 0.7 mg/kg (Reg. (EU) 2022/1346) will not be exceeded. The current EU MRL for pinoxaden is sufficient to support the proposed uses.

The trials are supported by valid storage stability data and validated analytical methods.

The proposed uses on wheat, rye and triticale are considered acceptable.

7.3.4 Magnitude of residues in livestock

7.3.4.1 Dietary burden calculation

According to the OECD guidance document on residues in livestock (ENV/JM/MONO(2013)8), envisaged uses of ADM.06001.H.2.B on cereal crops may lead to residues in livestock, therefore the possible transfer of residues into animal commodities should be considered.

The dietary burdens were calculated for different groups of livestock using the EFSA calculator[2]. Livestock intake calculations are provided below.

The dietary burden calculation made by EFSA (2021) in the framework of the Art. 12 evaluation is available for pinoxaden, The calculation is applicable to the current uses, with one minor change

[2] http://ec.europa.eu/food/plant/docs/pesticides_mrl_guidelines_animal_model_2016.xls

regarding the STMR value for straw (based on new trials in Southern Europe), which, however, does not lead to a modification of the result.

Table 7.3-11: Input values for the dietary burden calculation (considering the uses evaluated in Art. 12 procedure and the uses under consideration)

Feed Commodity	Median dietary burden		Maximum dietary burden	
	Input value (mg/kg)	**Comment**	**Input value (mg/kg)**	**Comment**
Risk assessment residue definition: Sum of M4 and M6 expressed as parent pinoxaden (to include free and conjugated residues of M4 and M6)				
Barley straw	0.26	STMR (EFSA, 2021)	1.16	HR (EFSA, 2021)
Rye straw	0.26	STMR (EFSA, 2021)	1.16	HR (EFSA, 2021)
Triticale forage	0.13	STMR (EFSA, 2021)	0.54	HR (EFSA, 2021)
Triticale hay	0.38	STMR x default PF (2.9) (EFSA, 2021)	1.57	HR x default PF (2.9) (EFSA, 2021)
Triticale straw	0.26	STMR (EFSA, 2021)	1.16	HR (EFSA, 2021)
Wheat forage	0.13	STMR (EFSA, 2021)	0.54	HR (EFSA, 2021)
Wheat hay (fodder dry)	0.46	STMR x default PF (3.5) (EFSA, 2021)	1.89	HR x default PF (3.5) (EFSA, 2021)
Wheat straw	0.26	STMR (EFSA, 2021)	1.16	HR (EFSA, 2021)
Barley grain	0.09	STMR (EFSA, 2021)	0.09	STMR (EFSA, 2021)
Rye grain	0.09	STMR (EFSA, 2021)	0.09	STMR (EFSA, 2021)
Triticale grain	0.09	STMR (EFSA, 2021)	0.09	STMR (EFSA, 2021)
Wheat grain	0.09	STMR (EFSA, 2021)	0.09	STMR (EFSA, 2021)
Brewer’s grain dried	0.09	STMR x PF (1) (EFSA, 2021)	0.09	STMR x PF (1) (EFSA, 2021)
Distiller’s grain dried	0.08	STMR x PF (0.9) (EFSA, 2021)	0.08	STMR x PF (0.9) (EFSA, 2021)
Wheat gluten meal	0.16	STMR x default PF (1.8) (EFSA, 2021)	0.16	STMR x default PF (1.8) (EFSA, 2021)
Wheat milledby-pdts	0.39	STMR x PF (4.3) (EFSA, 2021)	0.39	STMR x PF (4.3) (EFSA, 2021)

The results of the calculations are reported in

Table 7.3-12. The calculated dietary burdens for ruminants, swine and poultry were found to exceed the trigger value of 0.004 mg/kg bw per day. Further investigation of residues is therefore required for all groups of livestock.

Table 7.3-12: Results of the dietary burden calculation (EFSA, 2021)

Animal species	Median dietary burden (mg/kg bw/d)	Maximum dietary burden (mg/kg bw/d)	Most critical subgroup	Highest contributing commodity	Max dietary burden (mg/kg DM)	Trigger exceeded (Y/N)
Risk assessment residue definition: Sum of M4 and M6 expressed as parent pinoxaden (to include free and conjugated residues of M4 and M6)						
Cattle (all)	0.011	0.023	Dairy cattle	Wheat forage	0.62	Y
Cattle (dairy	0.011	0.023	Dairy cattle	Wheat forage	0.60	Y

Animal species	Median dietary burden (mg/kg bw/d)	Maximum dietary burden (mg/kg bw/d)	Most critical subgroup	Highest contributing commodity	Max dietary burden (mg/kg DM)	Trigger exceeded (Y/N)
only)						
Sheep (all)	0.017	0.041	Lamb	Barley straw	1.06	Y
Sheep (ewe only)	0.013	0.035	Ram/Ewe	Wheat forage	1.06	Y
Swine (all)	0.008	0.016	Swine (breeding)	Wheat forage	0.68	Y
Poultry (all)	0.014	0.026	Poultry layer	Wheat forage	0.38	Y
Poultry (layer only)	0.014	0.026	Poultry layer	Wheat forage	0.38	Y
Fish	-	-	-	-	-	-

Evaluator comments:
The calculated dietary burdens for all groups of livestock were found to exceed the trigger value. Further investigation of residues should be performed in all relevant commodities of animal origin.

7.3.4.2 Livestock feeding studies (KCA 6.4.1-6.4.3)

The residue intake to livestock via feed exceeds the trigger values established in Reg. (EC) No 1107/2009, therefore livestock feeding studies are required.

Available data
Reference: EFSA, 2021
Feeding studies were submitted in the DAR (UK, 2006) on dairy cows and hen, but because the trigger was not exceeded these studies were not evaluated. However, EFSA (2021) evaluated the available feeding studies and calculated expected residues in animal matrices. As the results of the EFSA (2021) dietary burden calculation are not modified due to the intended uses, they also apply for ADM.06001.H.2.B. Results are shown in the table below.
No new data were submitted in the framework of this application.

Table 7.3-13: Overview of the values derived from livestock feeding studies (EFSA, 2021)

Animal commodity	Residues at the closest feeding level (mg/kg)		Estimated value at 1N		MRL proposal (mg/kg)
	Mean	Highest	STMRMo[a] (mg/kg)	HRMo[b] (mg/kg)	
Cattle (all) – Closest feeding level (0.04 mg/kg bw; 1.7 N rate)[c]					
Muscle	<0.02	<0.02	0.02	0.02	0.02* (tentative)[d]
Fat	<0.02	<0.02	0.02	0.02	0.02* (tentative)[d]
Liver	<0.02	<0.02	0.02	0.02	0.02* (tentative)[d]
Kidney	<0.02	<0.02	0.02	0.02	0.02* (tentative)[d]
Cattle (dairy only) – Closest feeding level (0.04 mg/kg bw; 1.7 N rate)[c]					
Milk[e]	< 0.01	n.a.	0.01	0.01	0.01* (tentative)[d]
Sheep (all) [f] – Closest feeding level (0.04 mg/kg bw; 1.0 N rate) [c]					
Muscle	<0.02	<0.02	0.02	0.02	0.02* (tentative)[d]
Fat	<0.02	<0.02	0.02	0.02	0.02* (tentative)[d]
Liver	<0.02	<0.02	0.02	0.02	0.02* (tentative)[d]
Kidney	<0.02	<0.02	0.02	0.02	0.02* (tentative)[d]
Sheep (ewe only)[f] – Closest feeding level (0.04 mg/kg bw; 1.1 N rate) [c]					
Milk[e]	< 0.01	n.a.	0.01	0.01	0.01* (tentative)[d]
Swine (all)[f] – Closest feeding level (0.04 mg/kg bw; 2.5 N rate)(c)					
Muscle	<0.02	<0.02	0.02	0.02	0.02* (tentative)[d]
Fat	<0.02	<0.02	0.02	0.02	0.02* (tentative)[d]
Liver	<0.02	<0.02	0.02	0.02	0.02* (tentative)[d]
Kidney	<0.02	<0.02	0.02	0.02	0.02* (tentative)[d]

Poultry (all) – Closest feeding level (0.04 mg/kg bw; 1.6 N rate) [c]					
Muscle	<0.02	<0.02	0.02	0.02	0.02* (tentative)[d]
Fat	<0.02	<0.02	0.02	0.02	0.02* (tentative)[d]
Liver	<0.02	<0.02	0.02	0.02	0.02* (tentative)[d]
Poultry (layer only) – Closest feeding level (0.04 mg/kg bw; 1.6 N rate) [c]					
Eggs[g]	<0.02	<0.02	0.02	0.02	0.02* (tentative)[d]

MRL: maximum residue level; STMR: supervised trials median residue; HR: highest residue; Mo: monitoring; bw: body weight;
*: Indicates that the MRL is proposed at the limit of quantification.n.a.: not applicable.
n.r.: not reported.
(a) Median residues expressed according to the residue definition for monitoring, recalculated at the 1N rate for the mediandietary burden.
(b) Highest residues expressed according to the residue definition for monitoring, recalculated at the 1N rate for the maximum dietary burden.
(c) Closest feeding level and N dose rate related to the maximum dietary burden.
(d) Tentative MRL in the absence of confirmatory method for all livestock commodities.
(e) For milk, mean was derived from samplings performed from day 2 to day 28 (daily mean of 3 cows).
(f) Since extrapolation from cattle to other ruminants and swine is acceptable, results of the livestock feeding study onruminants were relied upon to derive the MRL and risk assessment values in sheep and swine.
(g) For eggs, mean and highest residues were derived from samplings performed from day 1 to day 28 (daily mean or dailyhighest of 15 laying hens).

Conclusion on feeding studies

"The results of the feeding studies confirm the findings of the metabolism, and MRLs and risk assessment values are proposed at the enforcement LOQs for all livestock commodities. Considering that a confirmatory method is still required for enforcement purposes, MRLs in livestock are considered tentative."
(EFSA, 2021)

Evaluator comments:

"Pinoxaden is authorised for use on wheat, barley and rye that might be fed to livestock. Livestock dietary burden calculations were therefore performed for different groups of livestock according to OECD guidance (OECD, 2013), which has now also been agreed upon at European level. The animal intake of pinoxaden residues via this commodity is thus overestimated. Since wheat forage was found to be the major contributor in all diets, except in sheep (lamb), the calculated dietary burden represents a worst-case scenario.
No residues of M4 or M6 above the LOQ of 0.01 mg/kg for milk, and 0.02 mg/kg for animal tissues and eggs were found in any sample from the highest dosing level of 0.4 mg/kg bw per day.
Consequently, samples from the lower dose treatment groups were not analysed in the cow or hen study, and it is not required. Since extrapolation from ruminants to pigs is acceptable, results of the livestock feeding study on ruminants can be applied also to pigs.
The results of the feeding studies confirm the findings of the metabolism, and MRLs and risk assessment values are proposed at the enforcement LOQs for all livestock commodities. Considering that a confirmatory method is still required for enforcement purposes, MRLs in livestock are considered tentative." (EFSA, 2021)

The uses under consideration in the framework of this dossier does not modify the animal exposure due to uses already authorised. There is no risk for MRLs to be exceeded in animal commodities.

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

7.3.5.1 Available data for all crops under consideration

Reference: United Kingdom, 2006; EFSA, 2013; EFSA, 2013
Processing studies on wheat and barley have been submitted and were considered acceptable.
No new data were submitted in the framework of this application.

Table 7.3-14: Overview of the available processing studies

Processed commodity	Number of studies	Median PF *	Median CF **	Comments	Reference
EU data					
Enforcement residue definition (option 1): Sum of M4 and M6 (both free and conjugated), expressed as pinoxadenRD-RA: sum of M4 and M6 (both free and conjugated), expressed as pinoxaden					
Barley, brewing malt	4	1.3			United Kingdom, 2006 EFSA, 2013 EFSA, 2021
Barley, beer	4	0.2			
Barley, pot/pearl	4	0.5			
Barley, dry brewer's grain	4	1			
Wheat, whole-meal flour	4	1.1			
Wheat, whole-meal bread	4	0.6			
Wheat, white flour	4	<0.3			
Wheat, dry milled by-products (incl. bran)	4	4.3			
Wheat, dry distiller's grain	4	0.9		-	
Enforcement residue definition (option 2): Sum of M4 and M6 (both free only), expressed as pinoxadenRD-RA: sum of M4 and M6 (both free and conjugated), expressed as pinoxaden					
-	-	-			No data available and not required[(a)]

* The median processing factor is obtained by calculating the median of the individual processing factors of each processing study.

** The median conversion factor for enforcement to risk assessment is obtained by calculating the median of the individual conversion factors of each processing study.

(a) No processing studies available analysing free forms (only) of metabolites M6 and M4. However, they are not required as residues in raw commodity were below 0.1 mg/kg according to RD-Mo option 2 (EFSA, 2021)

7.3.5.2 Conclusion on processing studies

Robust processing factors could be obtained for the sum of the metabolites M4 and M6 (free and conjugated) in processed wheat and barley, covering the intended uses for ADM.06001.H.2.B. No further data are required.

Evaluator comments:
The effect of industrial processing and/or household preparation on the levels of metabolites M4 and M6 was assessed on studies conducted on barley and wheat (United Kingdom, 2013; EFSA, 2013).
No additional study is required.

7.3.6 Magnitude of residues in representative succeeding crops

Metabolism studies on confined representative crops were conducted showing that residues of pinoxaden in rotational crops are not to be expected, "therefore no residue trials data were required for succeeding or rotational crops." (*EFSA, 2013*)
Likewise, EFSA (2021) stated that "based on the confined rotational crop study and considering the fact that pinoxaden was applied to a bare soil (interception of active substance by the plants is expected in practice), it can be concluded that pinoxaden residue levels in rotational commodities are not expected to exceed 0.01 mg/kg, provided that pinoxaden is applied in compliance with the GAPs reported".

Evaluator comments:
Information given by the Applicant is sufficient. Based on the available information, it was concluded that significant residue levels are unlikely to occur in rotational crops, provided that the compound is used according to the proposed good agricultural practice (GAP).
The crops under consideration can be grown in rotation.
No further data are required.

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

Wheat, triticale and rye have no melliferous capacity according to SANTE/11956/2016 rev. 9, therefore data on residues in honey are not required.
The available data for the active substance sufficiently address aspects of the residue situation that might arise from the use of ADM.06001.H.2.B. Other special studies are not needed.

zRMS comments:
According to the SANTE/11956/2016 rev. 9, 14 September 2018, wheat, triticale and rye have no melliferous capacity, so no further data are required.

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

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

7.3.8.1 Input values for the consumer risk assessment

The TMDI was calculated with current EU MRL values for all crops. MRLs above the LOQ are detailed in the table below. MRLs for all other crops are set at the LOQ. No MRLs have been set for animal commodities.
The IESTI was calculated using current EU MRLs for the crops under consideration.

Table 7.3-15: Input values for the consumer risk assessment

~~Code no~~	~~Commodity~~	~~Chronic risk assessment~~		~~Acute risk assessment~~	
		~~Input value (mg/kg)~~	~~Comment~~	~~Input value (mg/kg)~~	~~Comment~~
~~Risk assessment residue definition: Sum of M4 and M6 expressed as parent pinoxaden (to include free and conjugated residues of M4 and M6)~~					
~~500010~~	~~Barley~~	~~1.0~~	~~MRL (Reg. (EU) No No 839/2008~~	~~--~~	~~Not relevant for this submission~~
~~500060~~	~~Rice~~	~~0.05~~	~~MRL (Reg. (EU) No No 839/2008~~	~~--~~	~~Not relevant for this submission~~
~~500070~~	~~Rye~~	~~1.0~~	~~MRL (Reg. (EU) No No 839/2008~~	~~1.0~~	~~MRL (Reg. (EU) No No 839/2008~~
~~500090~~	~~Wheat~~	~~1.0~~	~~MRL (Reg. (EU) No No 839/2008~~	~~1.0~~	~~MRL (Reg. (EU) No No 839/2008~~
	~~All other crops~~	~~0.02* 0.05*~~	~~MRL at LOQ (Reg. (EU) No No 839/2008~~	~~--~~	~~Not relevant for this submission~~

* MRL at LOQ

Code no	Commodity	Chronic risk assessment		Acute risk assessment	
		Input value (mg/kg)	Comment	Input value (mg/kg)	Comment
Risk assessment residue definition: Sum of M4 and M6 expressed as parent pinoxaden (to include free and conjugated residues of M4 and M6)					
500010	Barley	0.7	MRL (Reg. (EU) No 2022/1346	--	Not relevant for this submission
500060	Rice	0.03*	MRL (Reg. (EU) No 2022/1346	--	Not relevant for this submission

Code no	Commodity	Chronic risk assessment		Acute risk assessment	
		Input value (mg/kg)	Comment	Input value (mg/kg)	Comment
500070	Rye	0.7	MRL (Reg. (EU) No 2022/1346	0.7	MRL (Reg. (EU) No 2022/1346
500090	Wheat	0.7	MRL (Reg. (EU) No 2022/1346	0.7	MRL (Reg. (EU) No 2022/1346
	All other crops and animal commodities	MRL	MRL (Reg. (EU) No 2022/1346	--	Not relevant for this submission

7.3.8.2 Conclusion on consumer risk assessment

Extensive calculation sheets are presented in Appendix 3.

Table 7.3-16: Consumer risk assessment

~~TMDI (% ADI) according to EFSA PRIMo 3.1~~	~~10% (based on DK child)~~
~~IESTI (% ARfD) according to EFSA PRIMo 3.1~~	~~Wheat: 14% (based on UK 4-6 years old)~~ ~~Rye: 6% (based on UK infant)~~ ~~Processed commodities:~~ ~~Wheat (milling flour): 12% (DE child)~~ ~~Wheat (milling, wholemeal): 6% (NL child)~~ ~~Rye (boiled): 4% (NL child)~~

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

TMDI (% ADI) according to EFSA PRIMo 3.1	8% (based on DK child)
IESTI (% ARfD) according to EFSA PRIMo 3.1	Wheat: 10% for children and 6% for adults Rye: 4% for children and 3% for adults Processed commodities: Wheat (milling flour): 8% for children Wheat (milling, wholemeal): 4% for children Rye (boiled): 3% for children

The proposed uses of pinoxaden in the formulation ADM.06001.H.2.B do not represent unacceptable chronic or acute risks for the consumer.

zRMS comments:
Due to the fact that the MRLs for pinoxaden have changed, the calculations using EFSA model (PRIMo ver. 3.1) and MRLs according to Regulation (EU) 2022/1346 have been performed and updated by the zRMS-PL.
The intended uses will not result in a consumer chronic and acute exposure exceeding the ADI and ARfD for pinoxaden, respectively.
No further data are required to support the proposed uses.

7.4 Mefenpyr-diethyl (safener)

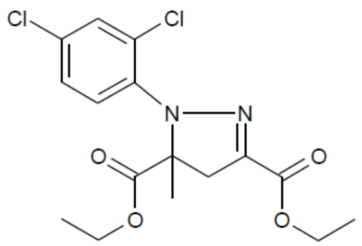
zRMS comments:
Formulation ADM.06001.H.2.B contains two active substances: mesosulfuron-methyl, pinoxaden and safener: mefenpyr-diethyl.
It should be noted that mefenpyr-diethyl as safener is not considered as an active substance, consequently has not been subject to review on EU level for inclusion into Annex I of Directive 91/414/EEC or Regulation (EC) No 1107/2009 and at present MRLs are not set in the EU for safeners.

The Applicant provided the data for safener, for mefenpyr-diethyl, reviewed by Austria and France in 2011, but has not been assessed at EU level. Results and conclusion of this evaluation are reported in this section for the sake of completeness. According to Regulation 1107/2009, data for safener should be evaluated in line with requirements relevant for active substances and EU agreed and peer-reviewed endpoints should be generated. Such evaluation, however, is outside the scope of the product registration and should be carried out at the EU level in order to derive uniform endpoints that may be used in evaluation of various formulations. For this reason data provided for mefenpyr-diethyl were not validated by the zRMS.

Available residue data presented in point 7.4 are compliant with data presented in Monograph for mefenpyr-diethyl and are considered informative.

General data on mefenpyr-diethyl are summarized in the table below (last updated 2021/01/29).

Table 7.4-1: General information on mefenpyr-diethyl

Active substance (ISO Common Name)	Mefenpyr-diethyl
IUPAC	Diethyl 1-(2,4-dichlorophenyl)-5-methyl-2-pyrazoline-3,5-dicarboxylate
Chemical structure	
Molecular formula	$C_{16}H_{18}Cl_2N_2O_4$
Molar mass	373.26
Chemical group	Unclassified
Mode of action (if available)	Mefenpyr-diethyl is a safener for cereal herbicides. It enhances the metabolism of mesosulfuron-methyl and iodosulfuron-methyl. There are no harmful organisms against which protection can be achieved with mefenpyr-diethyl alone. Selective action of the safener is related to its property to trigger enhanced detoxification in cereal crops.
Systemic	N/A
Company (ies)	Bayer CropScience*
Rapporteur Member State (RMS)	Austria
Approval status	Not yet assessed at EU level
Restriction	N/A
Review Report	N/A
Current MRL regulation	N/A
Peer review of MRLs according to Article 12 of Reg No 396/2005 EC performed	N/A

Active substance (ISO Common Name)	Mefenpyr-diethyl
EFSA Journal : Conclusion on the peer review	N/A
EFSA Journal: conclusion on article 12	N/A
Current MRL applications on intended uses	N/A

* Notifier in the EU process
N/A Not applicable

7.4.1 Stability of Residues (KCA 6.1)

7.4.1.1 Stability of residues during storage of samples

Available data
Reference: Austria, 2011, Austria & France, 2011
New studies on the stability of mefenpyr-diethyl and its metabolite AE F094270 have been submitted by the applicant in the framework of this application. The detailed assessment of this study is presented in Appendix 2.

Table 7.4-2: Summary of stability data achieved at ≤- 18°C)

Matrix	Characteristics of the matrix	Acceptable Maximum Storage duration (months)				Reference
		Mefenpyr-diethyl	AE F094270	AE F113225	AE F109453	
Data relied on in EU*						
Plant products						
Barley, grain	High starch content	30	30	30		Austria & France, 2011
Barley, shoot	High water content				30	Austria & France, 2011
Barley, straw	No group	30	30	30	30	Austria & France, 2011
New data						
Plant products						
Wheat, grain	High starch content	12	12			Lefresne, S., 2021 Report No. B19S-A4-M-04 (KCP 8/06)
Wheat, whole plant	High water content	12	12			
Wheat, straw	No group	12	12			

* Not assessed at EU level. Proposed in Monograph, which has been voluntarily prepared by AGES and ANSES in the context of zonal authorisation of plant protection products containing mefenpyr-diethyl.

Conclusion on stability of residues during storage
The residue data are supported by validated analytical methods and by acceptable storage stability data where mefenpyr-diethyl, and its metabolites AE F094270 and AE F113225 have been shown to be stable for 30 months in high starch content commodities and in straw. Metabolite AE F092370 has been shown to be stable for at least 12 months in high water content commodities. Metabolite AE F109453 has been shown to be stable for 30 months in high water content commodities and in straw.
The storage stability periods cover the storage periods of samples in the residue trials presented in this submission.

7.4.1.2 Stability of residues in sample extracts (KCA 6.1)

Available data
Reference: Austria, 2011, Austria & France, 2011
No new data submitted in the framework of this application.

Table 7.4-3: Summary of extract stability data achieved at 4º C ± 3º C

Matrix	Characteristics of the matrix	Acceptable Maximum Storage duration				Reference
		Mefenpyr-diethyl	AE F094270	AE F113225	AE F109453	
Data relied on in EU*						
Plant products						
Wheat, grain	High starch content	4 weeks				Austria & France, 2011
Wheat, green material	High water content	4 weeks				Austria & France, 2011
Wheat, straw	No group	4 weeks				Austria & France, 2011
Rape, seed	High oil content	29/30 days	29/30 days			Austria & France, 2011
Tomato, fruit	High water content	29/30 days	29/30 days			Austria & France, 2011
Orange, fruit	High acid content	29/30 days	29/30 days			Austria & France, 2011
Animal Products						
Cattle, liver	Liver	11 days	11 days	11 days		Austria & France, 2011
Cattle, kidney	Kidney	11 days	11 days	11 days		Austria & France, 2011
Cattle, meat	Muscle	11 days	11 days	11 days		Austria & France, 2011
Cattle, milk	Milk	11 days	11 days	11 days		Austria & France, 2011
Cattle, fat	Fat	11 days	11 days	11 days		Austria & France, 2011

* Not assessed at EU level. Proposed in Monograph, which has been voluntarily prepared by AGES and ANSES in the context of zonal authorisation of plant protection products containing mefenpyr-diethyl.

Conclusion on stability of residues in sample extracts

Mefenpyr-diethyl has been shown to be stable for about 4 weeks under refrigerator conditions in extracts of representative plant matrices, including high water, high starch, high oil, high acid content commodities and straw, obtained using enforcement method 00814.

Metabolite AE F094270 has been shown to be stable for about 4 weeks under refrigerator conditions in extracts of representative plant matrices, including high water, high starch and straw, obtained using enforcement method 00814.

Mefenpyr-diethyl and metabolites AE F904270 and AE F113225 have been shown to be stable for about 11 days under refrigerator conditions in extracts of representative animal matrices, including liver, kidney, muscle, milk and fat, obtained using enforcement method 00814.

The data obtained obtained fully support the residue data presented in this submission.

7.4.2 Nature of residues in plants, livestock and processed commodities

7.4.2.1 Nature of residue in primary crops (KCA 6.2.1)

Available data

Reference: Austria, 2011, Austria & France, 2011

The metabolism of mefenpyr-diethyl was investigated in barley, using ^{14}C-phenyl-labelled mefenpyr-diethyl. No new data submitted in the framework of this application.

Table 7.4-4: 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	
Data relied on in EU*								
Cereals	Barley	[U-^{14}C-phenyl]	Semi-field	87	1	Green material: 0,	CM90/069	Austria & France, 2011

Crop Group	Crop	Label position	Application and sampling details					Reference
			Method, F or G (a)	Rate (kg a.s./ha)	No	Sampling (DAT)	Remarks	
						2, 9, 16, 29, 43 Grain, husks, straw: 85		

* Not assessed at EU level. Proposed in Monograph, which has been voluntarily prepared by AGES and ANSES in the context of zonal authorisation of plant protection products containing mefenpyr-diethyl.
(a) Outdoor/field application (F) or glasshouse/protected/indoor application (G)

Summary of plant metabolism studies reported
"Approximately two thirds to three quarters of the total radioactive residues in grain and straw could be liberated and identified. All losses of radioactivity which occurred were spread evenly over the many extraction and concentration steps and can thus not be attributed to distinct unknown compounds. It can thus be concluded that the metabolism of mefenpyr-diethyl in barley has been elucidated and involves the following steps:
• successive hydrolysis of the two carboxylic acid ester groups
• decarboxylation of one of the carboxylic acid groups resulting in
• the aromatisation of the heterocyclic ring.
Since the structure of the substance remained unchanged (no cleavage of the phenyl-pyrazole linkage) a metabolism study with pyrazole-labelled mefenpyr-diethyl is not requested.[...]
Based on these results relevant metabolites in crops are proposed to be AE F094270 in grain and AE F113225, AE F109543 and AE F094270 in straw. All metabolites identified in samples from barley were also observed in rat metabolism study" (*Austria, 2011*)

Conclusion on metabolism in primary crops
The metabolism of mefenpyr-diethyl in cereal crops following foliar application is sufficiently addressed to support the proposed uses of product ADM.06001.H.2.B.

7.4.2.2 Nature of residue in rotational crops (KCA 6.6.1)

Available data
Reference: Austria, 2011, Austria & France, 2011
The metabolism of mefenpyr-diethyl was investigated in rotational crops spinach, radish, carrots and wheat, using ^{14}C-phenyl-labelled mefenpyr-diethyl.
No new data submitted in the framework of this application.

Table 7.4-5: Summary of metabolism studies in rotational crops

Crop group	Crop	Label position	Application and sampling details					Reference
			Method, F or G (a)	Rate (kg a.s./ha)	Sowing intervals (DAT)	Harvest Intervals (DAT)	Remarks	
Data relied on in EU*								
Leafy vegetables	Spinach	[U-^{14}C-phenyl]	F	90	29	Leaves: 67	CM91/023	Austria & France, 2011
Root and tuber vegetables	Carrot	[U-^{14}C-phenyl]	F	90	29	Roots: 132		
	Small radish	[U-^{14}C-phenyl]	F	90	29	Tubers: 67		
Cereals	Wheat	[U-^{14}C-phenyl]	F	90	29	Grain, straw: 147		
Leafy vegetables	Spinach	[U-^{14}C-	F	90	1 year	Leaves: 420	CM91/024	Austria &

Crop group	Crop	Label position	Application and sampling details					Reference
			Method, F or G [(a)]	Rate (kg a.s./ha)	Sowing intervals (DAT)	Harvest Intervals (DAT)	Remarks	
		phenyl]						France, 2011
Root and tuber vegetables	Carrot	[U-^{14}C-phenyl]	F	90	1 year	Roots: 496		
Cereals	Wheat	[U-^{14}C-phenyl]	F	90	1 year	Grain, straw: 512		

* Not assessed at EU level. Proposed in Monograph, which has been voluntarily prepared by AGES and ANSES in the context of zonal authorisation of plant protection products containing mefenpyr-diethyl.

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

Summary of plant metabolism studies reported

“Since the total residues were in general extremely low, they could not be identified. However, the residue composition in rotated crops is assumed to be similar to that in soil and plants, since the degradation of the test substance in plants and in soil is identical.

The data show that residues taken up by crops rotated after an interval of 1 year were below the analytical limit of quantification (LOQ) of the residue analytical methods of 0.01 mg/kg in the edible parts of all crops examined.

The test substance was practically not taken up by crops rotated early, 1 year after treatment of the soil at a field rate of 90 g a.s./ha. Residues of mefenpyr-diethyl or its metabolites in succeeding crops after a plant back interval of 1 year are expected to be very low and therefore they do not pose any risk to the consumer.

Comment of RMS: No information is available about a possible uptake in oily crop (sunflower, rapeseed, etc.). Log Pow for the parent is 3.83 (defined at pH 6.3 and 21°C). However, regarding the metabolic pathway in soil, the metabolites identified are considered to be of increasing polarity compared to the parent. The higher polarity is due to hydrolytic processes (i.e. mainly ester hydrolysis) to form carboxylic acids and their readily water-soluble salts. The same metabolites identified in soil have been detected in livestock metabolism studies. Considering the comparably low total radioactivity in fat tissues, it is not expected that oily plants will take up or accumulate soil metabolites. Additionally, polar metabolites might be available for the plant but will usually not accumulate in the oily parts of the crop.” (*Austria, 2011*)

Conclusion on metabolism in rotational crops

Residues of mefenpyr-diethyl or metabolites in rotational crops were extremely low and a specific residue definition for rotational crops is not deemed necessary. No residues of mefenpyr-diethyl >0.01 mg/kg are expected in rotational crops grown after the use ADM.06001.H.2.B according to the intended GAP.

7.4.2.3 Nature of residues in processed commodities (KCA 6.5.1)

Available data

Reference: Austria, 2011, Austria & France, 2011

“No studies on the effects of industrial processing and/or household preparation have been submitted: Residues of mefenpyr-diethyl in the raw agricultural commodity cereal grain were found to be at or below the LOQ. Based on the demonstrated residue situation, a very low acute toxicity and an adequate high ADI, studies on the effects of industrial/household processing on nature or level of the residue are not required.” (*Austria, 2011*)

No new data submitted in the framework of this application.

Conclusion on nature of residues in processed commodities

As residues in cereal grain from the use of ADM.06001.H.2.B are expected to be below LOQ, studies on the nature of residues in processed commodities are not required.

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

Table 7.4-6: Summary of the nature of residues in commodities of plant origin

Endpoints	
Plant groups covered	Cereals (wheat)
Rotational crops covered	Spinach, carrot, small radish, wheat
Metabolism in rotational crops similar to metabolism in primary crops?	Yes
Processed commodities	Not triggered
Residue pattern in processed commodities similar to pattern in raw commodities?	Not applicable
Plant residue definition for monitoring	Mefenpyr-diethyl (AE F107892) and metabolite AE F094270 (pyrazole carboxylic acid) expressed as mefenpyr-diethyl In Mefenpyr-diethyl_LoEP (October 2011) is states: Please refer to the Vol.3 Annex B7 Addendum 1 (October 2011) where the following residue definitions are proposed for different plant matrices: Cereal grain: Mefenpyr-diethyl (AE F107892) and metabolite AE F094270 (pyrazole carboxylic acid) expressed as mefenpyr-diethyl. Cereal shoot and straw: Mefenpyr-diethyl (AE F107892) and metabolites AE F113225 (pyrazoline ester carboxylic acid), AE F109453 (pyrazoline dicarboxylic acid) and AE F094270 (pyrazole carboxylic acid) expressed as mefenpyr-diethyl (Austria & France, 2011)*
Plant residue definition for risk assessment	Mefenpyr-diethyl (AE F107892) and metabolite AE F094270 (pyrazole carboxylic acid) expressed as mefenpyr-diethyl In Mefenpyr-diethyl_LoEP (October 2011) is states: Please refer to the Vol.3 Annex B7 Addendum 1 (October 2011) where the following residue definitions are proposed for different plant matrices: Cereal grain: Mefenpyr-diethyl (AE F107892) and metabolite AE F094270 expressed as mefenpyr-diethyl. Cereal shoot and straw: Mefenpyr-diethyl (AE F107892) and metabolites AE F113225, AE F109453 and AE F094270 expressed as mefenpyr-diethyl (Austria & France, 2011)*
Conversion factor from enforcement to RA	Not applicable

* Proposed in Monograph, which has been voluntarily prepared by AGES and ANSES in the context of zonal authorisation of plant protection products containing mefenpyr-diethyl.

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

Available data

Reference: Austria, 2011, Austria & France, 2011

The metabolism of mefenpyr-diethyl was investigated in lactating goat and laying hen, using ^{14}C-phenyl-labelled mefenpyr-diethyl.

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

Table 7.4-7: Summary of animal metabolism studies

Group	Species	Label position	No of animal	Application details		Sample details		Comment	Reference
				Rate (mg/kg bw/d)	Duration (days)	Commodity	Time of sampling		
Data relied on in EU*									
Lactating ruminants	Goat	[U-^{14}C-phenyl]	1	0.32	7	Milk	Twice daily	TOX95287	Austria & France, 2011
						Urine and faeces	Daily		
						Tissues	At sacrifice		
Laying poultry	Hen	[U-^{14}C-phenyl]	4	0.76	14	Eggs	Twice daily	TOX95289	Austria & France, 2011
						Excreta	Daily		
						Tissues	At sacrifice		

* Not assessed at EU level. Proposed in Monograph, which has been voluntarily prepared by AGES and ANSES in the context of zonal authorisation of plant protection products containing mefenpyr-diethyl.

Summary of animal metabolism studies reported

"The metabolism of AE F107892 in the goat showed successive de-ethylation of the parent molecule to form AE F113225 followed by AE F109453, and finally decarboxylation of one carboxylic acid group with aromatisation of the heterocyclic ring to form AE F094270. The major metabolite present in milk, urine and all tissues except subcutaneous fat was the mono carboxylic acid AE F113225. Trace levels of parent mefenpyr diethyl were detected in kidney, liver, heart and milk.

The major route of excretion was via the urine (63% ±15%) with faecal elimination accounting for 12.5% (mean of daily dose ±7%).

All metabolites identified in milk and tissues of goat were also observed in rat metabolism (see Point B.6.1.2).

Since the structure of the substance remained unchanged (no cleavage of the phenyl-pyrazole linkage) a metabolism study with pyrazole-labelled mefenpyr-diethyl is not requested." (*Austria, 2011*)

"The metabolism of AE F107892 in laying hen results in the successive de-ethylation of the parent molecule to form AE F113225 followed by AE F109453, and finally decarboxylation of one carboxylic acid group with aromatisation of the heterocyclic ring to form AE F094270. Mass spectrometric analysis of excreta has confirmed the identity of the three known metabolites and has also resulted in the tentative identification of an additional metabolite which may be formed by alternative de-ethylation of AE F107892 at position 5 of the pyrazoline ring (AE F114952) prior to formation of AE F109453.

Since the structure of the substance remained unchanged (no cleavage of the phenyl-pyrazole linkage) a metabolism study with pyrazole-labelled mefenpyr-diethyl is not requested." (*Austria, 2011*)

"Livestock metabolism was investigated in goat and poultry. The metabolites already discovered in plants and rat also appeared in both species. In fat, liver and egg-yolk additional unknown metabolites were detected, each of them at a level below 0.01 mg-equiv./kg. The metabolism studies in rats, ruminants and poultry did not indicate significant differences in the nature and distribution of residues in the three species examined. Therefore studies on metabolism, distribution and expression of residues in pigs were not triggered.

Residue levels in milk and eggs were very low, in general, and reached a plateau by day 3 (milk) and day 7 (eggs), respectively. The excretion was rapid in all cases (> 80% of the TRR within 24h) indicating that there is no potential for bioaccumulation. Based on low transfer factors (please see point B.7.8 Livestock feeding studies) and on the used high dose levels (administered in the livestock metabolism studies), compared to the low residues in grain and straw (up to BBCH32) detected in field trials, no residues are to be expected in food of animal origin." (*Austria, 2011*)

Conclusion on metabolism in livestock

The metabolism of mefenpyr-diethyl in livestock is sufficiently addressed to support the proposed uses of product ADM.06001.H.2.B.

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

Table 7.4-8: Summary on the nature of residues in commodities of animal origin

Endpoints	
Animals covered	Lactating goats
	Laying hens
Time needed to reach a plateau concentration	3 days in milk
	7 days in eggs
Animal residue definition for monitoring	Mefenpyr diethyl (AE F107892) and metabolite AE F113225 (pyrazoline ester carboxylic acid) expressed as mefenpyr diethyl (Austria & France, 2011)*
Animal residue definition for risk assessment	Mefenpyr diethyl (AE F107892) and metabolite AE F113225 expressed as mefenpyr diethyl (Austria & France, 2011)*
Conversion factor	No applicable
Metabolism in rat and ruminant similar	Yes
Fat soluble residue	Yes/No

* Not assessed at EU level. Proposed in Monograph, which has been voluntarily prepared by AGES and ANSES in the context of zonal authorisation of plant protection products containing mefenpyr-diethyl.

7.4.3 Magnitude of residues in plants (KCA 6.3)

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

Reference: Austria, 2011, Austria & France, 2011

The intended cGAPs for ADM.06001.H.2.B in wheat, rye and triticale are more critical than the respective cGAPs as reviewed by the RMS Austria and France (2011), as shown in the table below.

New studies on the magnitude of residue have been submitted by the applicant in the framework of this application. The detailed assessment of these studies is presented in Appendix 2 (KCP 8/01 – KCP 8/02).

Table 7.4-9: Comparison of intended and critical EU GAPs

Type of GAP	Region	Crop	Number of applications	Application rate per treatment (kg a.s./ha)	Interval between applications [min. days]	Growth stage at last application	PHI (days)	Remark
cGAP EU (Austria, 2011; France, 2011)	EU	Wheat	1	0.090	-	39	n.a.	
	EU	Rye	1	0.090	-	39	n.a.	
	EU	Trititcale	1	0.090	-	39	n.a.	
Intended cGAP (number 2)	C-EU	Wheat	1	0.035	-	39	n.a.	
Intended cGAP (number 2)	C-EU	Rye	1	0.035	-	39	n.a.	
Intended cGAP (number 2)	C-EU	Triticale	1	0.035	-	39	n.a.	

n.a.: not applicable, the PHI is covered by the time remaining between application and harvest

.

Table 7.4-10: Summary of EU reported and new data supporting the intended uses of ADM.06001.H.2.B and conformity to existing MRL

Commodity	Source	Residue zone (N-EU, S-EU, EU, outside EU)	Evaluation GAP Residue levels (mg/kg) E = according to enforcement residue definition RA = according to risk assessment residue definition	STMR (mg/kg)	HR (mg/kg)	Unrounded OECD calculator MRL (mg/kg)	Current EU MRL (mg/kg) (a)	MRL compliance
Wheat grain (extrapolated to rye and triticale)	Austria & France, 2011[(b)]	N-EU	GAP on which RMS a.s. assessment is based: 1 x 90 g as/ha, BBCH 39, outdoor E/RA[(c)]: 8 x <0.02, 0.02, 0.03	N/A				
	New trials	N-EU	Trials GAP: 1 x 35 g as/ha, BBCH 39, outdoor E/RA[(c))]: 8 x <0.02					
	Overall supporting data for intended GAP	N-EU	E/RA[(c)]: 8 x 0.02	E: <0.02 RA: <0.02	E: 0.02 RA: 0.02	0.02	N/A	N/A
Wheat straw (extrapolated to rye and triticale)	Austria & France, 2011[(b)]	N-EU	GAP on which RMS a.s. assessment is based: 1 x 90 g as/ha, BBCH 39, outdoor E/RA[(c)]: 0.26 0.32 0.33 0.39 0.41 0.42 0.43 0.44 0.48 0.53 Adjusted using correction factor 4 to account for extraction efficiency of method: E/RA[(c)]: 1.04, 1.28, 1.32, 1.56, 1.64, 1.68, 1.72, 1.76, 1.92, 2.12	N/A				
	New trials	N-EU	Trials GAP: 1 x 35 g as/ha, BBCH 39, outdoor E/RA[(c)]: 0.035, 0.052, 0.059, 0.064, 0.071, 0.073, 0.079, 0.089[(d)]					
	Overall supporting data for intended GAP	N-EU	E/RA[(c)]: 0.26 0.32 0.33 0.39 0.41 0.42 0.43 0.44 0.48 0.53 Adjusted using correction factor 4 to take account of low method extraction efficiency[(e)]: 1.04, 1.28, 1.32, 1.56, 1.64, 1.68, 1.72, 1.76, 1.92, 2.12	E: 1.66[(e)] RA: 1.66[(e)]	E: 2.12[(e)] RA: 2.12[(e)]	N/A	N/A	N/A

(a) No MRL has been set at EU level
(b) Not assessed at EU level. Proposed in Monograph, which has been voluntarily prepared by AGES and ANSES in the context of zonal authorisation of plant protection products containing mefenpyr-diethyl.
(c) Residue definitions for enforcement and risk assessment are the same: Cereal grain: Mefenpyr-diethyl (AE F107892) and metabolite AE F094270 expressed as mefenpyr-diethyl.
Cereal straw: Mefenpyr-diethyl (AE F107892) and metabolites AE F113225, AE F109453 and AE F094270 expressed as mefenpyr-diethyl (Austria, 2011)
(d) Only mefenpyr-diethyl (AE F107892) and metabolite AE F094270 were analysed in straw. As metabolites AE F113225 and AE F109453 were not analysed, there are no data available that correspond to the proposed residue definition. Data were not taken into account for calculation of STMR and HR.
(e) In addition to mefenpyr-diethyl (AE F107892) and metabolite AE F094270, analysis for straw does include also AE F109453 and AE F113225in addition to AE F107892, all together determined as AE F109453. Residue data correspond to the residue definition for enforcement and risk assessment.
N/A Not applicable

7.4.3.2 Conclusion on the magnitude of residues in plants

Central Zone
Wheat is a major crop in Central Southern Europe and eight trials are required in the zone. Four trials per zone are sufficient if all residues are below LOQ (0.01 mg/kg).
Ten trials in Central Europe were considered acceptable by the RMS (Austria, 2011; France, 2011), which were carried out to a more critical GAP than the cGAP intended for ADM.06001.H.2.B in Central and Southern Europe (90 g as/ha vs 35 g as/ha). As residues in grain above LOQ were detected in Central European trials, data obtained were not used to support the cGAP for ADM.06001.H.2.B in Central Europe.
Eight new trials were conducted with wheat in Central Europe that correspond to the intended cGAP for ADM.06001.H.2.B. Overall, there are therefore eight trials in Central Europe that support the intended cGAP for ADM.06001.H.2.B on wheat.
As the last application according to the intended GAP for ADM.06001.H.2.B is done before edible parts are formed (i.e. before BBCH 51), data on wheat can be extrapolated to rye (SANTE/2019/12752), and are also valid for triticale.
Residues of mefenpyr-diethyl in wheat grain were always below LOQ (0.02 mg/kg) in Central Europe, the calculated MRL_{OECD} is 0.02 mg/kg.
No MRL has been set at EU level. An MRL of 0.05 mg/kg in cereals has been set in France[3] and in Germany[4] of 0.05 mg/kg. Based on the available residue data for mefenpyr-diethyl, these MRLs are unlikely to be exceeded.
Thus, according to the available data, the intended uses on wheat, triticale and rye are considered acceptable.

7.4.4 Magnitude of residues in livestock

7.4.4.1 Dietary burden calculation

According to the OECD guidance document on residues in livestock (ENV/JM/MONO(2013)8), envisaged uses of ADM.06001.H.2.B on cereal crops may lead to residues in livestock, therefore the possible transfer of residues into animal commodities should be considered.
The dietary burdens were calculated for different groups of livestock using the EFSA calculator[5]. Livestock intake calculations are provided below.

Table 7.4-11: Input values for the dietary burden calculation (considering the uses authorized within the zone and the uses under consideration)

Feed Commodity	Median dietary burden		Maximum dietary burden	
	Input value (mg/kg)	Comment	Input value (mg/kg)	Comment
Risk assessment residue definition: Cereal grain: Mefenpyr-diethyl (AE F107892) and metabolite AE F094270 expressed as mefenpyr-diethyl. Cereal shoot and straw: Mefenpyr-diethyl (AE F107892) and metabolites AE F113225, AE F109453 and AE F094270 expressed as mefenpyr-diethyl				
Rye straw	1.66	Extrapolated from wheat. Median residue (see Table 7.4-10)	2.12	Extrapolated from wheat. Highest residue (see Table 7.4-10)

[3] “Journal Officiel de la République Française” (JORF) 8th May 2008
[4] German Maximum Residue Ordinance (RHmV): http://www.lexsoft.de/cgi-bin/lexsoft/justizportal_nrw.cgi?t=160577515993764111&sessionID=14743857381029654366&templateID=document&source=lawnavi&chosenIndex=Dummy_nv_68&xid=139469,11
Residue definition in Germany is mefenpyr-diethyl only.
[5] http://ec.europa.eu/food/plant/docs/pesticides_mrl_guidelines_animal_model_2016.xls

Feed Commodity	Median dietary burden		Maximum dietary burden	
	Input value (mg/kg)	Comment	Input value (mg/kg)	Comment
Triticale straw	1.66	Extrapolated from wheat. Median residue (see Table 7.4-10)	2.12	Extrapolated from wheat. Highest residue (see Table 7.4-10)
Wheat straw	1.66	Median residue (see Table 7.4-10)	2.12	Highest residue (see Table 7.4-10)
Rye grain	0.02	Extrapolated from wheat. Median residue (see Table 7.4-10)	0.02	Extrapolated from wheat. Median residue (see Table 7.4-10)
Triticale grain	0.02	Extrapolated from wheat. Median residue (see Table 7.4-10)	0.02	Extrapolated from wheat. Median residue (see Table 7.4-10)
Wheat grain	0.02	Median residue (see Table 7.4-10)	0.02	Median residue (see Table 7.4-10)
Distiller's grain, dried	0.07	Median residue x PF (0.02 x 3.3) (see Table 7.4-10)	0.07	Median residue x PF (0.02 x 3.3) (see Table 7.4-10)
Wheat gluten meal	0.04	Median residue x PF (0.02 x 1.8) (see Table 7.4-10)	0.04	Median residue x PF (0.02 x 1.8) (see Table 7.4-10)
Wheat milled by-products	0.14	Median residue x PF (0.02 x 7) (see Table 7.4-10)	0.14	Median residue x PF (0.02 x 7) (see Table 7.4-10)

The results of the calculations are reported in Table 7.4-12. The calculated dietary burdens for dairy cattle, ram/ewe, lamb and layer poultry were found to exceed the trigger value of 0.004 mg/kg bw per day. Further investigation of residues is therefore required for these groups of livestock.

Table 7.4-12: 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: Mefenpyr diethyl and metabolite AE F113225 expressed as mefenpyr diethyl					
Beef cattle*	0.0104	0.013	Rye straw	0.54	N
Dairy cattle*	0.0167	0.021	Rye straw	0.54	Y
Ram/ewe	0.0274	0.034	Rye straw	1.03	Y
Lamb	0.0355	0.044	Rye straw	1.05	Y
Breeding swine	0.002	0.002	Wheat milled byproducts	0.09	N
Finishing swine*	0.003	0.003	Wheat milled byproducts	0.09	N
Broiler poultry	0.003	0.003	Wheat milled byproducts	0.05	N
Layer poultry*	0.016	0.029	Wheat straw	0.29	Y
Turkey	0.003	0.003	Wheat milled byproducts	0.05	N

* These categories correspond to those (formerly) assessed at EU level.

7.4.4.2 Livestock feeding studies (KCA 6.4.1-6.4.3)

Available data

Reference: Austria, 2011, Austria & France, 2011

A feeding study on dairy cows and a metabolism study on poultry have been evaluated by the RMS.
No new data were submitted in the framework of this application.

Table 7.4-13: Overview of the values derived from livestock feeding studies

Commodity	Dietary burden		Results of the livestock feeding study						Median residue (mg/kg)[a]	Highest residue (mg/kg)[b]	Calculated MRL (mg/kg)	CF for RA©
	Med. (mg/kg bw/d)	Max. (mg/kg bw/d)	Dose Level (mg/kg bw/d)	No	Result for enforcement		Result for RA					
					Mean (mg/kg)	Max. (mg/kg)	Mean (mg/kg)	Max. (mg/kg)				
EU data (Austria & France, 2011)*												
Enforcement and risk assessment residue definition: Mefenpyr diethyl and metabolite AE F113225 expressed as mefenpyr diethyl												
Pig meat	0.003	0.003	0.017	3	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	N/A	N/A
			0.082	3	<0.01	<0.01	<0.01	<0.01				
			0.21	3	<0.01	<0.01	<0.01	<0.01				
			0.72	3	<0.01	<0.01	<0.01	<0.01				
Pig fat	0.003	0.003	0.017	3	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	N/A	N/A
			0.082	3	<0.01	<0.01	<0.01	<0.01				
			0.21	3	<0.01	<0.01	<0.01	<0.01				
			0.72	3	<0.01	<0.01	<0.01	<0.01				
Pig liver	0.003	0.003	0.017	3	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	N/A	N/A
			0.082	3	<0.01	<0.01	<0.01	<0.01				
			0.21	3	<0.01	<0.01	<0.01	<0.01				
			0.72	3	<0.01	<0.01	<0.01	<0.01				
Pig kidney	0.003	0.003	0.017	3	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	N/A	N/A
			0.082	3	<0.01	<0.01	<0.01	<0.01				
			0.21	3	<0.01	<0.01	<0.01	<0.01				
			0.72	3	<0.01	<0.01	<0.01	<0.01				
Ruminant meat	0.0355	0.044	0.017	3	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	N/A	N/A
			0.082	3	<0.01	<0.01	<0.01	<0.01				
			0.21	3	<0.01	<0.01	<0.01	<0.01				
			0.72	3	<0.01	<0.01	<0.01	<0.01				
Ruminant fat	0.0355	0.044	0.017	3	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	N/A	N/A

Commodity	Dietary burden		Results of the livestock feeding study						Median residue (mg/kg)[(a)]	Highest residue (mg/kg)[(b)]	Calculated MRL (mg/kg)	CF for RA[©]
	Med. (mg/kg bw/d)	Max. (mg/kg bw/d)	Dose Level (mg/kg bw/d)	No	Result for enforcement		Result for RA					
					Mean (mg/kg)	Max. (mg/kg)	Mean (mg/kg)	Max. (mg/kg)				
			0.082	3	<0.01	<0.01	<0.01	<0.01				
			0.21	3	<0.01	<0.01	<0.01	<0.01				
			0.72	3	0.025	0.052	0.025	0.052				
Ruminant liver	0.0355	0.044	0.017	3	<0.01	<0.01	<0.01	<0.01	<0.01	0.01	N/A	N/A
			0.082	3	0.017	0.019	0.017	0.019				
			0.21	3	0.074	0.089	0.074	0.089				
			0.72	3	0.189	0.193	0.189	0.193				
Ruminant kidney	0.0355	0.044	0.017	3	0.011	0.016	0.011	0.016	0.026	0.03	N/A	N/A
			0.082	3	0.060	0.061	0.060	0.061				
			0.21	3	0.192	0.207	0.192	0.207				
			0.72	3	0.594	0.723	0.594	0.723				
Poultry meat	0.016	0.020	0.76[(d)]	4	-	<0.002	-	<0.002	<0.01	<0.01	N/A	N/A
			N/A									
Poultry fat	0.016	0.020	0.76[(d)]	4	-	0.005	-	0.005	<0.01	<0.01	N/A	N/A
			N/A									
Poultry liver	0.016	0.020	0.76[(d)]	4	-	0.0024	-	0.0024	<0.01	<0.01	N/A	N/A
			N/A									
Milk	0.0167	0.021	0.017	3	<0.002	<0.002	<0.002	<0.002	<0.01	<0.01	N/A	N/A
			0.082	3	<0.002	<0.002	<0.002	<0.002				
			0.21	3	<0.002	<0.002	<0.002	<0.002				
			0.72	3	<0.002	<0.002	<0.002	<0.002				
			0.77	3	<0.002	<0.002	<0.002	<0.002				
Eggs	0.016	0.020	0.76[(d)]	4	-	0.003	-	0.003	<0.01	<0.01	N/A	N/A

Commodity	Dietary burden		Results of the livestock feeding study						Median residue (mg/kg)[(a)]	Highest residue (mg/kg)[(b)]	Calculated MRL (mg/kg)	CF for RA©
	Med. (mg/kg bw/d)	Max. (mg/kg bw/d)	Dose Level (mg/kg bw/d)	No	Result for enforcement		Result for RA					
					Mean (mg/kg)	Max. (mg/kg)	Mean (mg/kg)	Max. (mg/kg)				
			N/A									

* Not assessed at EU level. Proposed in Monograph, which has been voluntarily prepared by AGES and ANSES in the context of zonal authorisation of plant protection products containing mefenpyr-diethyl.

N/A: Not applicable – only the mean values are considered for calculating MRLs in milk.

n.r.: Not reported

(F): MRL is expressed as mg/kg of fat contained in the whole product.

(a): Median residue value according to the enforcement residue definition, derived by interpolation/extrapolation from the feeding study for the median dietary burden (FAO, 2009).

(b): Highest residue value (tissues, eggs) or mean residue value (milk) according to the enforcement residue definition, derived by interpolation/extrapolation of the maximum dietary burden between the relevant feeding groups of the study (FAO, 2009).

(c): The median conversion factor for enforcement to risk assessment.

(d) Results from metabolism study on poultry (Report no. TOX/96/268-2)

Summary of animal feeding studies

"Residue transfer of mefenpyr-diethyl in cattle tissues and milk is generally very low. The active substance and its metabolite AE F094270 could not be found in any of the samples even not in the highest dose group. For the metabolite AE F113225 residues in milk of dose group 4 (174X dietary burden for beef cattle, 22.6 mg/kg feed or 0.77 mg/kg bw/day, respectively) reached a plateau at 0.0014 mg/kg between day 7 and day 9 of the study. In dose group 2 (17X dietary burden for beef cattle, 2.21 mg/kg feed or 0.082 mg/kg bw/day, respectively), only residues in liver (0.0171 mg/kg) and kidney (0.0598 mg/kg) could be found. Residues found showed a linear dose response. During the depuration phase residues rapidly declined within 3 days to values close to (kidney) or below the LOQ. No bioaccumulation has been observed; the results are in line with the results of goat metabolism study." (*Austria, 2011*)

Based on the results of the metabolism study on poultry, residues in poultry commodities above the LOQ of 0.01 mg/kg are not to be expected.

Conclusion on feeding studies

The requested uses modify the theoretical maximum daily intake for animals, but intakes are expected to be low. MRLs on animal commodities have not been set, however, MRLs of 0.03 mg/kg in bovine kidney and 0.02 mg/kg in bovine liver have been proposed in EFSA (2011). These results are not exceeded by the data presented here for the proposed uses of the product ADM.06001.H.2.B and are therefore considered acceptable.

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

The investigation of effects of processing on the magnitude of residues is not triggered by the intended uses for ADM.06001.H.2.B as residues in cereal grain are not expected to be ≥0.1 mg/kg and contribute to less than 10% of the ADI or ARfD.

7.4.5.1 Available data for all crops under consideration

Not applicable. Please refer to Point 7.4.5.

7.4.5.2 Conclusion on processing studies

Not applicable. Please refer to Point 7.4.5.

7.4.6 Magnitude of residues in representative succeeding crops

The crops under consideration can be grown in rotation.

Considering available data dealing with nature of residues (see Point 7.4.2.2), no study dealing with magnitude of residues in succeeding crops is needed. No residues of mefenpyr-diethyl >0.01 mg/kg are expected in rotational crops grown after the use ADM.06001.H.2.B according to the intended GAP.

7.4.6.1 Field rotational crop studies (KCA 6.6.2)

Not applicable. Please refer to Point 7.4.6.

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

Wheat, triticale and rye have no melliferous capacity according to SANTE/11956/2016 rev. 9, therefore data on residues in honey are not required.

The available data for the active substance sufficiently address aspects of the residue situation that might arise from the use of ADM.06001.H.2.B. Other special studies 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 Point 7.1.2).

7.4.8.1 Input values for the consumer risk assessment

As MRLs for mefenpyr-diethyl have not been set, TMDI and IESTI were calculated using median values for all crops under consideration and for animal commodities.

Table 7.4-14: Input values for the consumer risk assessment

Code no	Commodity	Chronic risk assessment		Acute risk assessment	
		Input value (mg/kg)	Comment	Input value (mg/kg)	Comment
Risk assessment residue definition: Cereal grain: Mefenpyr-diethyl (AE F107892) and metabolite AE F094270 expressed as mefenpyr-diethyl					
500070	Rye	0.02	Extrapolated from wheat Median value (see Table 7.4-10)	0.02	Extrapolated from wheat Median value (see Table 7.4-10)
500090	Wheat	0.02	Median value (see Table 7.4-10)	0.02	Median value (see Table 7.4-10)
100000	Products of animal origin	0.01	Median value (see Table 7.4-13)	0.01	Median value (see Table 7.4-13)

7.4.8.2 Conclusion on consumer risk assessment

Extensive calculation sheets are presented in Appendix 3.

Table 7.4-15: Consumer risk assessment

TMDI (% ADI) according to EFSA PRIMo 3.1	0.7 % (based on NL toddler)
IESTI (% ArfD) according to EFSA PRIMo 3.1	Wheat: 0.07 % (based on UK 4-6 years old) Rye: 0.03% (based on UK infant) Processed commodities: Processed commodities: Wheat (milling flour): 0.06% (DE child) Wheat (milling, wholemeal): 0.03% (NL child) Rye (boiled): 0.02% (NL child)

The proposed uses of mefenpyr-diethyl in the formulation ADM.06001.H.2.B do not represent unacceptable chronic or acute risks for the consumer.

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 two active substances and a safener and for 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 dRR that are acutely toxic by performing deterministic IESTI/NESTI calculations with the calculation models EFSA PRIMO (rev.3.1) and dividing the individual exposure levels by the respective ArfD. Addition of the individual HQs irrespective of any considerations on phenomenological effects or mode(s)/mechanisms of action results in the HI. The results of the HQ/HI calculations are summarized in the following table.

Table 7.5-1: Acute consumer risk assessment from combined exposure

Crop	**Active Ingredient**	**HQ (based on IESTI according to EFSA PRIMo 3.1)**
Wheat	Pinoxaden	0.14
	Mefenpyr-diethyl	0.0007
	Cumulative risk wheat (HI)	**0.1407**
Rye	Pinoxaden	0.06
	Mefenpyr-diethyl	0.0003
	Cumulative risk wheat (HI)	**0.0603**

* if national model wanted, otherwise to be deleted

The Hazard Index is <1. Thus combined exposure to all active substances in ADM.06001.H.2.B is not expected to present an acute 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.

zRMS comment:
Information presented by Applicant in point 7.5 has been accepted.

7.6 References

Mesosulfuron-methyl

EFSA (European Food Safety Authority), 2012. Reasoned opinion on the review of the existing maximum residue levels (MRLs) for mesosulfuron according to Article 12 of Regulation (EC) No 396/2005. EFSA Journal 2012;10(11):2976. [27 pp.] doi:10.2903/j.efsa.2012.2976.

EFSA (European Food Safety Authority), 2016. Conclusion on the peer review of the pesticide risk assessment of the active substance mesosulfuron (variant evaluated mesosulfuron-methyl). EFSA Journal 2016;14(10):4584, 26 pp. doi:10.2903/j.efsa.2016.4584

France, 2001. Draft Assessment Report on the active substance mesosulfuron-methyl prepared by the rapporteur Member State France in the framework of Council Directive 91/414/EEC, July 2001.
France, 2015. Draft Renewal Assessment Report prepared according to the Commission Regulation (EU) No. 1107/2009. Mesosulfuron, August 2015.
France, 2016. Revised Draft Renewal Assessment Report prepared according to the Commission Regulation (EU) No. 1107/2009. Mesosulfuron, May, 2016.

Pinoxaden

EFSA (European Food Safety Authority), 2013. Conclusion on the peer review of the pesticide risk assessment of the active substance pinoxaden. EFSA Journal 2013;11(8):3269, 112 pp. doi:10.2903/j.efsa.2013.3269

EFSA (European Food Safety Authority), 2017. Scientific Report of EFSA on scientific support for preparing an EU position in the 49th Session of the Codex Committee on Pesticide Residues (CCPR). EFSA Journal 2017;15(7):4929, 162 pp. https://doi.org/10.2903/j.efsa.2017.4929

EFSA (European Food Safety Authority), 2021. Reasoned opinion on the review of the existing maximum residue levels for pinoxaden according to Article 12 of Regulation (EC) No 396/2005. EFSA Journal 2021;19(3):6503, 41 pp. https://doi.org/10.2903/j.efsa.2021.6503

United Kingdom, 2006. Draft assessment report (DAR) Initial risk assessment provided by the rapporteur Member State the United Kingdom for the new active substance pinoxaden of the re-view programme referred to in Article 8(1) of Council Directive 91/414/EEC, July 2006

United Kingdom, 2013. Final Addendum to Draft Assessment Report on pinoxaden, compiled by EFSA, May 2013.

Mefenpyr-diethyl

Austria, 2011. Addendum to the evaluation prepared by AT and FR 2011. Volume 3, Annex B.7. Addendum 1. Mefenpyr-diethyl, October 2011

Austria & France, 2011. Monograph prepared in the context of zonal authorisation of plant protection products containing safener mefenpyr-diethyl, April 2017

Appendix 1 Lists of data considered in support of the evaluation

List of data submitted by the applicant and relied on

Data point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Vertebrate study Y/N	Owner
KCP 8/01	Bahnhardt, A.	2020	Magnitude of the residue of pinoxaden metabolites, mesosulfuron-methyl, mefenpyr-diethyl and its metabolite following one application of AG-PM1-72 OD in winter wheat in 6 trials (4 DCS + 2 HS), Northern Europe (Poland, Germany and France) – 2019, Staphyt GmbH, 74572 Blaufelden, Germany Report no. AB2-19-38159; ADAMA reference 000102607 GLP Not published	N	ADAMA
KCP 8/02	Meric, D.	2021a	Magnitude of the residue of pinoxaden metabolites, mesosulfuron-methyl, mefenpyr-diethyl and its metabolite following one application of ADM.06001.H.2.B in winter wheat in 2 trials (2 HS, one with process), Northern Europe (France and Poland) – 2020 Staphyt GmbH, 74572 Blaufelden, Germany Report no. DMC-20-42727; ADAMA reference 000105437 GLP Not published	N	ADAMA
KCP 8/03	Erk, T.	2021	Metabolism of [^{14}C]-pinoxaden in wheat, Report no. S19-00664, ADAMA reference 000102129 GLP Not published	N	ADAMA
KCP 8/04	Silcock, R., Gill, P.	2021	Comparison of the metabolism of pinoxaden in wheat in the presence of different safeners Report no. 1808368.UK0 - 0293, ADAMA reference 000108349 Non GLP Not published	N	ADAMA
KCP 8/05	Lefresne, S.	2021	Interim Report (12 Months). Freezing storage stability of mefenpyr-diethyl and its metabolite in wheat (whole plant, grain, straw) at/below -18°C during 18 months (0, 1, 3, 6, 9, 12, 15 and 18 months). Polleniz/Girpa, 49071 Beaucouze Cedex, France Report no. B19S-A4-M-04; ADAMA reference 000102682 GLP Not published	N	ADAMA

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

Data point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Vertebrate study Y/N	Owner
KCA 6.1/01	Wrede, A.	2000	Stability of AE F130060 in wheat grain during deep freeze storage Code: AE F130060 Interim report Aventis CropScience GmbH, Frankfurt am Main, Germany Bayer CropScience, Report No.: C015808, Edition Number: M-198607-03-1 Date: 2000-08-29 ...Amended: 2001-09-24 GLP, unpublished	N	BCS
KCA 6.1/02	Wrede, A.	2000	Stability of AE F130060 in wheat straw during deep freeze storage Mesosulfuron-methyl Code: AE F130060 Aventis CropScience GmbH, Frankfurt am Main, Germany Bayer CropScience, Report No.: C028927, Edition Number: M-198612-03-1 EPA MRID No.: 46229003 Date: 2000-08-29 ...Amended: 2003-01-27 GLP, unpublished	N	BCS
KCA 6.1/03	Wrede, A.	2000	Stability of AE F130060 in wheat shoot during deep freeze storage Mesosulfuron-methyl Code: AE F130060 Aventis CropScience GmbH, Frankfurt am Main, Germany Bayer CropScience, Report No.: C028928, Edition Number: M-198617-03-1 EPA MRID No.: 46229002 GLP, unpublished	N	BCS
KCA 6.1/04	Wrede, A.	2000	Stability of AE F130060 in soil during deep freeze storage of 24 months Code: AE F130060 Aventis CropScience GmbH, Frankfurt am Main, Germany Bayer CropScience, Report No.: C009366, Edition Number: M-198407-01-1 Date: 2000-08-21 GLP, unpublished	N	BCS
KCA 6.1/05	Wrede, A.	2003	Stability of AE F130060 in wheat grain during deep freeze storage Mesosulfuron-methyl Code: AE F130060 Bayer CropScience GmbH, Frankfurt am Main, Germany Bayer CropScience, Report No.: C028926, Edition Number: M-216176-01-1 EPA MRID No.: 46229004	N	BCS

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
			Date: 2003-01-27 GLP, unpublished		
KCA 6.2.1/01	Braun, P. J.; Koehn, D. M.; Buerkle, L. W.; Buerkle, L.	2000	Metabolism in wheat (Triticum aestivum) following single and double treatment at a nominal application rate of 10 g a.s./ha each Code: (2-^{14}C-pyrimidyl)-AE F130060 Aventis CropScience GmbH, Frankfurt am Main, Germany Bayer CropScience, Report No.: C008761, Edition Number: M-197766-02-1 Date: 2000-08-14 ...Amended: 2001-10-26 GLP, unpublished	N	BCS
KCA 6.2.1/02	Koehn, D. M.; Selzer, J.; Buerkle, L. W.	2000	Metabolism in wheat (Triticum aestivum) following single and double treatment at a nominal application rate of 30 g a.s./ha Each Code: (U-^{14}C-phenyl)-AE F130060 Aventis CropScience GmbH, Frankfurt am Main, Germany Bayer CropScience, Report No.: C009588, Edition Number: M-198861-01-1 Date: 2000-09-12 GLP, unpublished	N	BCS
KCA 6.2.2/01	[redacted]	1999	Poultry - Metabolism, distribution and nature of the residues in eggs and edible tissues Code: AE F130060 [redacted] Report No.: C005417, Edition Number: M-192019-01-1 Date: 1999-09-16 GLP, unpublished	Y	BCS
KCA 6.2.3/ 01	[redacted]	1999	Ruminant – Metabolism, distribution and nature of the residues in milk and edible tissues. Code: AE F130060 [redacted] Report No.: C005418 Edition Number: M-192023-01-1 Date: 1999-09-16 GLP, unpublished	Y	BCS
KCA 6.3.1/01	Helgers, A.; Wrede, A.; Neuss, B.	2000	Decline of residues in cereals European Union (northern zone) 1997 AE F130060 and AE F107892 (mefenpyr-diethyl) oil flowable 30 and 90 g/L Code: AE F130060 01 1K12 A201 Hoechst Schering AgrEvo GmbH, Frankfurt am Main, Germany Bayer CropScience, Report No.: C006208, Edition Number: M-193491-01-1	N	BCS

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
			Date: 2000-01-24 GLP, unpublished		
KCA 6.3.1/02	Davies, P.	2000	Residues at harvest in wheat European Union (northern zone) 1998 AE F130060 and mefenpyr- diethyl oil flowable 30 + 90 g/L Code: AE F130060 01 1K12 A701 Aventis CropScience GmbH, Frankfurt am Main, Germany Bayer CropScience, Report No.: C007152, Edition Number: M-195315-01-1 Date: 2000-08-18 GLP, unpublished	N	BCS
KCA 6.3.1/03	Helgers, A.; Wrede, A.; Neuss, B.	2000	Decline of residues in cereals European Union (southern zone) 1997 AE F130060 and AE F107892 (mefenpyr-diethyl) oil flowable 30 and 90 g/L Code: AE F13 0060 01 1K12 A201 Hoechst Schering AgrEvo GmbH, Frankfurt am Main, Germany Bayer CropScience, Report No.: C006209, Edition Number: M-193494-01-1 Date: 2000-01-27 GLP, unpublished	N	BCS
KCA 6.3.1/04	Davies, P., Wrede, A.	2000	Residues at harvest in cereals European Union (southern zone) 1998 AE F130060 + mefenpyr-diethyl oil flowable 30 + 90 g/L Code: AE F130060 01 1K12 A701 Aventis CropScience GmbH, Frankfurt am Main, Germany Bayer CropScience, Report No.: C008074, Edition Number: M-197167-01-1 Date: 2000-08-18 GLP, unpublished	N	BCS
KCA 6.3.1/05	Barreau, C.	2014	Residue trial tables - Mesosulfuron-methyl - Annex I Renewal Bayer CropScience Bayer CropScience, Report No.: M-475643-01-1, Edition Number: M-475643-01-1 Date: 2014-01-16 GLP, unpublished	N	BCS
KCA 6.3.1/06	Davies, P.	2000	Decline of residues in wheat European Union Northern Zone and Southern France 1999 Iodosulfuron-methyl-sodium + mesosulfuron-methyl + mefenpyr-diethyl water dispersible granule 1% + 3 % + 9 % Code: AE	N	BCS

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
			F130060 02 WG13 A202 Aventis CropScience GmbH, Frankfurt am Main, Germany Bayer CropScience, Report No.: C009932, Edition Number: M-199542-01-1 Date: 2000-12-15 GLP, unpublished		
KCA 6.3.1/07	Freitag, T.	2004	Determination of residues of iodosulfuron-methyl-sodium, mesosulfuron-methyl-sodium and mefenpyr-diethyl in / on wheat following spray application of AE F115008 06 OD04 A1 (042 OD) in the field in Germany, Sweden, Great Britain, and Northern France Bayer CropScience, Report No.: RA-2677/03, Edition Number: M-227133-02-1 Date: 2004-01-30 ...Amended: 2007-01-16 GLP, unpublished	N	BCS
KCA 6.3.1/08	Freitag, T.	2004	Determination of residues of iodosulfuron-methyl-sodium, mesosulfuron-methyl-sodium and mefenpyr-diethyl in / on wheat following spray application of AE F115008 06 OD04 A1 (042 OD) in the field in Italy and Southern France Bayer CropScience, Report No.: RA-2690/03, Edition Number: M-227096-02-1 Date: 2004-01-30 ...Amended: 2007-01-16 GLP, unpublished	N	BCS
KCA 6.6.2/01	Frey, J. A.; Harrison, C. L.; Buerkle, L. W.	2000	Residues in rotated crops sown 31 days after application to bare soil at a rate of 15 g a.s./ha (2-^{14}C-pyrimidyl)-AE F130060 Aventis CropScience GmbH, Frankfurt am Main, Germany Bayer CropScience, Report No.: C008238, Edition Number: M-197310-01-1 Date: 2000-08-09 GLP, unpublished	N	BCS
KCA 6.6.2/02	Frey, J.A.; Harrison, C. L.; Buerkle, L. W.	2000	Residues in rotated crops sown 32 days after application to bare soil at a rate of 15 g a.s./ha (U-^{14}C- phenyl)-AE F130060 Aventis CropScience GmbH, Frankfurt am Main, Germany	N	BCS

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
			Bayer CropScience, Report No.: C008240, Edition Number: M-197312-01-1 Date: 2000-08-09 GLP, unpublished		
KCA 6.6.2/03	Frey, J.A.; Harrison, C. L.;	2000	Residues in rotated crops sown 4 months after application to bare soil at a rate of 15 g a.s./ha Code: (2-^{14}C-pyrimidyl)-AE F130060 Aventis CropScience GmbH, Frankfurt am Main, Germany Bayer CropScience, Report No.: C008242, Edition Number: M-197314-01-1 EPA MRID No.: 45386506 Date: 2000-09-13 GLP, unpublished	N	BCS
KCA 6.6.2/04	Frey, J.A.; Harrison, C. L.;	2000	Residues in rotated crops sown 4 months after application to bare soil at a rate of 15 g a.s./ha Code: (U-^{14}C-phenyl)-AE F130060 Aventis CropScience GmbH, Frankfurt am Main, Germany Bayer CropScience, Report No.: C008243, Edition Number: M-197315-01-1 Date: 2000-09-13 GLP, unpublished	N	BCS
KCA 6.6.2/05	Frey, J.A.; Harrison, C. L.;	2000	Residues in rotated crops sown 1 year after application to bare soil at a rate of 15 g a.s./ha Code: (2-^{14}C-pyrimidyl)-AE F130060 Aventis CropScience GmbH, Frankfurt am Main, Germany Bayer CropScience, Report No.: C008239, Edition Number: M-197311-01-1 Date: 2000-09-13 GLP, unpublished	N	BCS
KCA 6.6.2/06	Frey, J.A.; Harrison, C. L.;	2000	Residues in rotated crops sown 1 year after application to bare soil at a rate of 15 g a.s./ha Code: (U-^{14}C-phenyl)-AE F130060 Aventis CropScience GmbH, Frankfurt am Main, Germany Bayer CropScience, Report No.: C008241, Edition Number: M-197313-01-1 Date: 2000-09-13 GLP, unpublished	N	BCS

Pinoxaden

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
KIIA 6.0.1.1/01	Kwiatkowski, A.	2003a	Stability of residues of NOA 407854, SYN 505164, SYN 502836 and SYN 505887 in deep freeze stored analytical specimens of wheat (whole plant, straw, grains) Syngenta Crop Protection AG, Basel, Switzerland Syngenta, Jealott's Hill, United Kingdom, Report No 02-S305/1 (Interim), Syngenta File No. NOA 407854/0041 GLP, unpublished	N	SYN
KIIA 6.0.1.3/01	Lin, K.	2003	Stability of SYN 505164 (M4) and SYN 502836 (M6) metabolites of NOA 407855 in animal tissues under freezer storage conditions Syngenta Crop Protection AG, Basel, Switzerland Syngenta, Jealott's Hill, United Kingdom, Report NoT001241-03 Syngenta File No. NOA407855/0259 GLP, unpublished	N	SYN
KIIA 6.0.1.2/01 KIIA 6.1.1/01	Sandmeier, P.	2001a	Metabolism of NOA 407855 in field grown winter wheat after fall application of [pyrazol-3,5-^{14}C]labelled material Syngenta Crop Protection AG, Basel, Switzerland Report No. 99PSA55 Syngenta File No. NOA 407855/0035 GLP, unpublished	N	SYN
KIlA 6.0.1.2/02 KIIA 6.1.1/02	Sandmeier, P.	2003a	Metabolism of NOA 407855 in field grown winter wheat after spring application of [phenyl-1-^{14}C]labelled material Syngenta Crop Protection AG, Basel, Switzerland Report No. 00PSA58 Syngenta File No. NOA 407855/0088 GLP, unpublished	N	SYN
KIIA 6.1.1/03	Stingelin, J.	2002a	Metabolism of [Phenyl-1-^{14}C] and [Oxadiazepin-3,6-^{14}C] NOA 407855 in field grown spring wheat Syngenta Crop Protection AG, Basel, Switzerland, Report No 01MK16, Syngenta File N° NOA407855/0071 GLP, unpublished	N	SYN
KIIA 6.2.1/01	[redacted]	2002a	The metabolism of [phenyl-1-^{14}C] NOA 407855 after multiple oral administration to lactating goats Report No. 046AM04 [redacted] GLP, unpublished	Y	SYN

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
KIIA 6.2.1/02	[redacted]	2003	[7-^{14}C]-SYN-505164: Nature of the residue in lactating goat. Report No. 751-02 [redacted] GLP, unpublished	Y	SYN
KIIA 6.2.2/01	[redacted]	2002b	The metabolism of [phenyl-1-^{14}C] NOA 407855 after multiple oral administration to laying hens Report No. 046AM06 [redacted] GLP, unpublished	Y	SYN
KIIA 6.3.1/01	Gasser, A.	2003a	Residue study with cloquintocet-mexyl (CGA 185072) and NOA 407855 in or on winter wheat in France (North) Syngenta Crop Protection AG, Basel, Switzerland, Report No 3004/01, Syngenta File N° NOA407855/0179 GLP, unpublished	N	SYN
KIIA 6.3.1/02	Stolze, K.	2003a	Determination of residues of NOA 407855 and CGA 185072 in winter wheat after application of A 12303 C in Germany, 2001 Syngenta Crop Protection AG, Basel, Switzerland Syngenta Agro GmbH, Maintal, Germany, Report No gr 03101, Syngenta File N° NOA407855/0123 GLP, unpublished	N	SYN
KIIA 6.3.1/03	Stolze, K.	2003b	Determination of residues of NOA 407855 and CGA 185072 in winter wheat after application of A 12303 C in Germany, 2001 Syngenta Crop Protection AG, Basel, Switzerland Syngenta Agro GmbH, Maintal, Germany, Report No gr 03201, Syngenta File N° NOA407855/0120 GLP, unpublished	N	SYN
KIIA 6.3.1/04	Gill, J.P.	2003a	Residue study with cloquintocet-mexyl (CGA 185072) and NOA 407855 in or on winter wheat in France (North) Syngenta Crop Protection AG, Basel, Switzerland Syngenta - Jealott's Hill International, Bracknell, Berkshire, United Kingdom, Report No 3021/01, Syngenta File N° NOA407855/0223 GLP, unpublished	N	SYN
KIIA 6.3.1/05	Stolze, K.	2003c	Determination of residues of NOA 407855 and CGA 185072 in winter wheat after application of A 12303 C in Germany, 2001	N	SYN

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
			Syngenta Crop Protection AG, Basel, Switzerland Syngenta Agro GmbH, Maintal, Germany, Report No gwh10601, Syngenta File N° NOA407855/0121 GLP, unpublished		
KIIA 6.3.1/06	Stolze, K.	2003d	Determination of residues of NOA 407855 and CGA 185072 in winter wheat after application of A12303 C in Germany, 2001 Syngenta Crop Protection AG, Basel, Switzerland Syngenta Agro GmbH, Maintal, Germany, Report No gwh40601, Syngenta File N° NOA407855/0122 GLP, unpublished	N	SYN
KIIA 6.3.1/07	Clarke, D.	2003	Residue study with cloquitocet-metaxyl (CGA 185072) and NOA 407855 in or on winter wheat in France (North) Syngenta Crop Protection AG, Basel, Switzerland Syngenta Jealott’s Hill Internationa, Bracknell, Berkshire, United Kingdom Report No. 3089/01 Syngenta File No. NOA 407855/0246 GLP, unpublished	N	SYN
KIIA 6.3.1/08	Stolze, K.	2003e	Determination of residues of NOA 407855 and CGA 185072 in winter wheat after application of A 12303 C in Germany, 2002 Syngenta Crop Protection AG, Basel, Switzerland Syngenta Agro GmbH, Maintal, Germany, Report No gwh021002, Syngenta File N° NOA407855/0248 GLP, unpublished	N	SYN
KIIA 6.3.1/09	Stolze, K.	2003f	Determination of a decline curve for residues of NOA 407855 and CGA 185072 in winter wheat after application of A 12303 C in Germany, 2002 Syngenta Crop Protection AG, Basel, Switzerland Syngenta Agro GmbH, Maintal, Germany, Report No gwh029002, Syngenta File N° NOA407855/0133 GLP, unpublished	N	SYN
KIIA 6.3.1/10	Gasser, A.	2003b	Residue study with cloquintocet-mexyl (CGA 185072) and NOA 407855 in or on durum wheat in Italy Syngenta Crop Protection AG, Basel, Switzerland, Report No 3014/01, Syngenta File N° NOA407855/0126	N	SYN

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
			GLP, unpublished		
KIIA 6.3.1/11	Gasser, A.	2003d	Residue study with cloquintocet-mexyl (CGA 185072) and NOA 407855 in or on durum wheat in Italy Syngenta Crop Protection AG, Basel, Switzerland, Report No 3015/01, Syngenta File N° NOA407855/0127 GLP, unpublished	N	SYN
KIIA 6.3.1/12	Richards, S.	2003a	Residue study with cloquintocet-mexyl (CGA 185072) and NOA 407855 in or on durum wheat in Italy Syngenta Crop Protection AG, Basel, Switzerland, Report No 02-3007, Syngenta File N° NOA407855/0181 GLP, unpublished	N	SYN
KIIA 6.3.1/13	Richards, S.	2003b	Residue study with cloquintocet-mexyl (CGA 185072) and NOA 407855 in or on durum wheat in Italy Syngenta Crop Protection AG, Basel, Switzerland, Report No 02-3006, Syngenta File N° NOA407855/0255 GLP, unpublished	N	SYN
KIIA 6.3.1/14	Gill, J.P.	2003b	Residue study with cloquintocet-mexyl (CGA 185072) and NOA 407855 in or on winter wheat in France (South) Syngenta Crop Protection AG, Basel, Switzerland Syngenta - Jealott's Hill International, Bracknell, Berkshire, United Kingdom, Report No 3022/01, Syngenta File N° NOA407855/0240 GLP, unpublished	N	SYN
KIIA 6.3.1/15	Gasser, A.	2003e	Residue study with cloquintocet-mexyl (CGA 185072) and NOA 407855 in or on winter wheat in France (South) Syngenta Crop Protection AG, Basel, Switzerland, Report No 3023/01, Syngenta File N° NOA407855/0170 GLP, unpublished	N	SYN
KIIA 6.3.1/16	Kwiatkowski, A.,	2003b	Residue study with cloquintocet-mexyl (CGA 185072) and NOA 40785 or on winter wheat in Spain Syngenta Crop Protection, Basel, Switzerland Syngenta- Jealott's Hill International, Bracknell, Berkshire, United Kingdom. Report No 02-3002 Syngenta File OA407855/0245 GLP, unpublished	N	SYN
KIIA 6.4.1/01	[redacted]	2003	SYN 505164 (M4) and SYN 502836 (M6), metabolites of NOA 407855 – Magnitude of residues in meat and milk resulting from the feeding of three levels of SYN 505 164 to dairy cattle	~~N~~ Y	SYN

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
			Report No. 746-02 [redacted] GLP, unpublished		
KIIA 6.4.2/01	[redacted]	2003	SYN 505164 (M4) and SYN 502836 (M6), metabolites of NOA 407855 – Magnitude of residues in meat and eggs resulting from the feeding of three levels of SYN 505 164 to laying hens Report No. 747-02 [redacted] GLP, unpublished	~~N~~ Y	SYN
KIIA 6.5.1/01	Stingelin, J	2002b	Hydrolysis of [phenyl-1-^{14}C] labelled NOA407855 under processing conditions Syngenta Crop Protection AG, Basel, Switzerland, Report No 02JS34, Syngenta File N° NOA407855/0064 GLP, unpublished	N	SYN
KIIA6.5.3.1/01	Stolze, K.	2004a	Amended : Determination of residues of NOA 407855 and CGA 185072 in winter wheat and processing products after application of A 12303 C in Germany, 2002 Syngenta Crop Protection AG, Basel, Switzerland Syngenta Agro GmbH, Maintal, Germany, Report No gwh043102, Syngenta File N° NOA407855/0466 GLP, unpublished	N	SYN
KIIA6.5.3.1/02	Stolze, K	2003m	Determination of Residues of NOA 407855 and CGA 185072 in winter wheat and processing products after application of A12303C in Germany, 2002 Syngenta Agro GmbH, Maintal, Germany Report Nogwh049002 Syngenta File N° NOA407855/0309 GLP, unpublished	N	SYN
KIIA 6.5.3.2/01	Stolze, K	2003n	Determination of residues of NOA 407855 and CGA 185072 in spring barley and processing products after application of A12303C in Germany, 2002 Syngenta Crop Protection AG, Basel, Switzerland Syngenta Agro GmbH, Maintal, Germany, Report No gba033102, Syngenta File N° NOA407855/0287 GLP, unpublished	N	SYN
KIIA 6.5.3.2/02	Stolze, K	2004b	Determination of residues of NOA 407855 and CGA 185072 in spring barley and processing products after	N	SYN

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
			application of A12303C in Germany, 2002 Syngenta Crop Protection AG, Basel, Switzerland Syngenta Agro GmbH, Maintal, Germany, Report No gba039002, Syngenta File N° NOA407855/0465 GLP, unpublished		
KIIA 6.6/01	Sandmeier, P.	2002	Outdoor confined accumulation study on rotational crops after bareground application of [phenyl-1-^{14}C] NOA 407855 Syngenta Crop Protection AG, Basel, Switzerland, Report No 00PSA57, Syngenta File N° NOA407855/0056 GLP, unpublished	N	SYN
KIIA 6.6/01	Sandmeier, P.	2003b	Outdoor confined accumulation study on rotational crops after bareground application of [oxadiazepin-3,6-^{14}C1] NOA 407855 Syngenta Crop Protection AG, Basel, Switzerland, Report No 01PSA59, Syngenta File N° NOA407855/0146 GLP, unpublished	N	SYN

Mefenpyr-diethyl

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
KIIA 6.1.1 /01	Tillkes, M.	1996	Storage stability of Hoe 107892 and its metabolite Hoe 094270 in barley (grain) Dr. Specht und Partner Chem Lab. GmbH; Bayer CropScience, Report No.: A56514 Edition Number: M-191088-01-1 Method Report No.: Az.93866/92 Date: 1996-03-28 GLP, unpublished	N	BCS
KIIA 6.1.1 /02	Schmidt, F.; Tillkes, M.	1997	Storage stability of AE F107892 and its metabolites AE F113225 and AE F094270 in barley (shoot and straw) Dr. Specht und Partner Chem Lab. GmbH; Bayer CropScience, Report No.: A58613 Edition Number: M-142345-01-1	N	BCS

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
			Date: 1997-03-20 GLP, unpublished		
KIIA 6.1.1 /03	Junker, H.; Ullenberger, S.	1997	Code: AE F109453 Storage stability of AE F109453 (metabolite of Mefenpyr-diethyl) in barley straw and shoot over a storage period of 30 months Hoechst Schering AgrEvo GmbH, Frankfurt am Main, Germany Bayer CropScience, Report No.: A58218 Edition Number: M-141921-01-1 Date: 1997-04-10 GLP, unpublished	N	BCS
KIIA 6.2.1 /01	Buerkle, W. L.	1994	Code: Hoe 107892 00 ZE99 0001 Hoe 107892-^{14}C, Metabolism in Barley (Hordeum vulgare) After Application of the Test Substance at a Rate of 90 g/ha in the Presence of Fenoxaprop-P-ethyl (Hoe 046360) Hoechst Schering AgrEvo GmbH, Frankfurt am Main, Germany Bayer CropScience, Report No.: CM90/069, Ref. No. A53202, Edition Number: M-133950-01-1 Date: 1994-10-27 GLP, unpublished	N	BCS
KIIA 6.6.1 /01	Buerkle, W. L.	1994	Code: Hoe 107892 00 ZE99 0001 Residues in Rotational Crops Sown 29 Days after Treatment of the ^{14}C-labelled Test Substance to Bare Soil at a Rate of 90 g a.i./ha in the Presence of Fenoxaprop-P- ethyl Hoechst Schering AgrEvo GmbH, Frankfurt am Main, Germany Bayer CropScience, Report No.: CM91/023, Ref. No. A53373, Edition Number: M-134100-01-1 Date: 1994-12-05 GLP, unpublished	N	BCS

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
KIIA 6.6.1 /02	Buerkle, W. L.	1995	Code: Hoe 107892 00 ZE99 0001 Residues in Rotational Crops Sown 1 Year affer Treatment of the ^{14}C-Labelled Test Substance to Bare Soil at a Rate of 90 g a.i./ha in the Presence of Fenoxaprop-P- ethyl Hoechst Schering AgrEvo GmbH, Frankfurt am Main, Germany Bayer CropScience, Report No.: CM91/024, Ref. No. A53435, Edition Number: M-134153-01-1 Date: 1995-01-03 GLP, unpublished	N	BCS
KIIA 6.2.2 /01	[redacted]	1996	HOE 107 892 Code: HOE 107892 Poultry - Metabolism, distribution and nature of the residues in the eggs and edible tissues [redacted] Report No.: TOX/96/268-2, ref. No. A57659, Report includes Trial Nos.: TOX95289 Edition Number: M-141343-01-1 Date: 1996-10-21 GLP, unpublished	Y	BCS
KIIA 6.2.3 /01	[redacted]	1996a	HOE 107892 Code : HOE 107892 Goat: Metabolism, distribution and nature of the residues in the milk and edible tissues [redacted] Report No.: TOX/96/268-1, Ref. No. A57957, Report includes Trial Nos.: TOX95287 Edition Number: M-141683-01-1 Date: 1996-11-12 GLP, unpublished	Y	BCS

List of data submitted by the applicant and not relied on

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

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

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

Appendix 2 Detailed evaluation of the additional studies relied upon

A 2.1 Mesosulfuron-methyl

A 2.1.1 Stability of residues

A 2.1.1.1 Stability of residues during storage of samples

No new data submitted.

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

A 2.1.2.1 Nature of residue in plants

No new data submitted.

A 2.1.2.2 Nature of residues in livestock

No new data submitted.

A 2.1.3 Magnitude of residues in plants

A 2.1.3.1 Winter wheat

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)
cGAP EU (France, 2015, EFSA, 2016)	1	0.015 kg a.s./ha	--	32	n.a.
cGAP EU (Art. 12, EFSA, 2012)	1	0.020 kg a.s./ha	--	32	90
Intended cGAP (number 2)	1	0.012 kg a.s./ha	--	39	n.a.

* Use number(s) in accordance with the list of all intended GAPs in Part B, Section 0
n.a. not applicable, the PHI is covered by the time remaining between application and harvest

A 2.1.3.1.1 Study AB2-19-38159 (wheat, NEU)

Comments of zRMS:	Six residue trials were conducted in Northern Europe to determine the magnitude of residues of pinoxaden metabolites (M4 and M6), expressed separately and their sum as pinoxaden, mesosulfuron-methyl (parent only), mefenpyr-diethyl and metabolite 1-(2,4-dichlorophenyl)-5-methyl-pyrazole-3-carboxylic acid (AE F094270) expressed as mefenpyr-diethyl in raw agricultural commodity specimens of winter wheat (RAC whole plant, grain and straw) after one application of AG-PM1-72 OD. Target application rate was 1.0 L/ha, representing 60 g/ha pinoxaden, 12 g/ha mesosulfuron-methyl and 35 g/ha mefenpyr-diethyl. Applications were placed at BBCH 39 (flag leaf stage). Three different analytical methods for pinoxaden, mesosulfuron-methyl and mefenpyr-diethyl were fully validated according to SANTE/2020/12830, rev. 1. Limit of quantification (LOQ) achieved was 0.01 mg/kg for grain and 0.02 mg/kg for whole plant and straw for pinoxaden metabolite M4, 0.01 mg/kg for grain and straw and 0.02 mg/kg for whole plant for pinoxaden metabolite M6 and 0.02 mg/kg for grain, 0.03 mg/kg for straw and 0.04 mg/kg for whole plant for the sum of M4 and M6 expressed as pinoxaden. The results are given as M4 or M6 and as their sum expressed as pinoxaden. Limit of quantification (LOQ) for mesosulfuron-methyl achieved was 0.01 mg/kg for all matrices. The results are given as mesosulfuron-methyl. Limit of quantification (LOQ) for mefenpyr-diethyl achieved was 0.01 mg/kg for all matrices. The results are expressed as mefenpyr-diethyl. The mean recoveries at each fortification level comply with the standard acceptance criteria of the guidance document SANTE/2020/12830, rev. 1. No residue of all analytes were found above LOQ in any untreated specimen. <u>Results:</u> For the sum of pinoxaden metabolites M4 and M6 expressed as pinoxaden, at harvest residues found in grain were between 0.031 and 0.065 mg/kg and between 0.145 and 0.958 mg/kg in straw. For mesosulfuron-methyl, at harvest no residues were found in grain and straw. For mefenpyr-diethyl, the residues found in whole plant were between 0.36 and 0.78 mg/kg just after application. No residues were found in whole plant, grain and straw for the other samplings. For metabolite 1-(2,4-dichlorophenyl)-5-methyl-pyrazole-3-carboxylic acid expressed as mefenpyrdiethyl, at harvest no residues were found in grain and the residues in straw were between 0.025 to 0.079 mg/kg. The storage of samples is covered by the storage stability data in wheat grain and straw. The study is acceptable.

Reference:	KCP 8/01 (KCA 6.3.1)
Report	Magnitude of the residue of pinoxaden metabolites, mesosulfuron-methyl, mefenpyr-diethyl and its metabolite following one application of AG-PM1-72 OD in winter wheat in 6 trials (4 DCS + 2 HS), Northern Europe (Poland, Germany and France) – 2019, Bahnhardt, A., 2020 Report no. AB2-19-38159; ADAMA reference 000102607
Guideline(s):	General Recommendations for the Design, Preparation and Realization of Residue Trials (SANCO 7029/VI/95 rev.5, 22 July 1997). OECD Guideline for the Testing of Chemicals on Crop Field Trial (TG 509 published on 7 September 2009). Guidance for Generating and Reporting Methods of Analysis in Support of Pre-Registration Data Requirements (SANCO/3029/99 rev.4, 11 July 2000). OECD (2007): Guidance Document on Pesticide Residue Analytical Methods ENV/JM/MONO(2007)17.
Deviations:	No
GLP:	Yes
Acceptability:	Yes

Table A 2: Summary of the study AB2-19-38159 trials

Active Substance:	Mesosulfuron-methyl	**Commercial Product:**	AG-PM1-72 OD
Crop:	Winter wheat	**Producer:**	ADAMA AGAN Ltd., Ashod, Israel
Responsible for reporting:	STAPHYT GmbH – 74572 Blaufelden, Germany		
Country:	Poland, Germany, Northern France	**Indoor/glasshouse/outdoor:**	Outdoor
Content of as (actual):	11.7 g/L	**Other a.s. in formulation:**	pinoxaden, mefenpyr-diethyl
Formulation:	OD	**Residue calculated as:**	mesosulfuron-methyl

1	2	3	4	5			6	7	8	9	10	11
Location	**Commodity Variety**	**Date of 1-Sowing 2-Flowering 3-Harvest**	**Method of Treatment**	**Application Rate per Treatment**			**Date of Treatment**	**BBCH Crop Growth Stage at Treatment**	**Portions analysed**	**Residues (mg/kg)**	**PHI (days)**	**Remarks**
				kg as/ha	**Water (L/ha)**	**kg (as/hl)**				**Mesosulfuron-methyl**		
Poland Łódzkie 99-440 Wiskienica Dolna Trial number AB2-19- 38159 PL01	Winter wheat Arkadia	1- 04.10.2018 2- 28.05.2019 to 12.06.2019 3- 27.07.2019	Foliar broadcast application	T1 0.012	T1 205	T1 0.006	T1 13.05.2019	T1 39	T1 Whole plant Whole plant Whole plant Whole plant Grain Straw	T1 0.16 <LOQ <LOQ (nd) <LOQ (nd) <LOQ (nd) <LOQ (nd)	T1 0 14 30 60 74 74	Analytical method involved extraction of mesosulfuron-methyl from homogenised laboratory samples by maceration in an acetonitrile/0.02 M triethylamine (80/20 v/v) mixture. Then, extracts were purified by solid/liquid partitions, before quantification with LC-MS/MS. Method fully validated in a separate report (Sponsor reference: 000102681). LOQ: 0.01 mg/kg Untreated specimens were all <LOQ (nd) Max. Storage Interval between sampling and analysis: 164 days Max. Storage Interval between extraction and analysis: 1 day
				T2* 0.012	T2* 202	T2* 0.006	T2* 13.05.2019	T2* 39	T2* Whole plant Whole plant Whole plant Whole plant Grain Straw	T2* 0.21 <LOQ (nd) <LOQ (nd) <LOQ (nd) <LOQ (nd) <LOQ (nd)	T2* 0 14 30 60 74 74	

Germany Thuringia 04617 Dobraschütz Trial number AB2-19- 38159 DE02	Winter wheat Patras	1- 10.10.2018 2- 11.06.2019 to 19.06.2019 3- 24.07.2019	Foliar broadcast application	T1 0.012	T1 201	T1 0.006	T1 24.05.2019	T1 39	T1 Whole plant Whole plant Whole plant Grain Straw	T1 0.17 <LOQ (nd) <LOQ (nd) <LOQ (nd) <LOQ (nd)	T1 0 14 31 60 60	Analytical method involved extraction of mesosulfuron-methyl from homogenised laboratory samples by maceration in an acetonitrile/0.02 M triethylamine (80/20 v/v) mixture. Then, extracts were purified by solid/liquid partitions, before quantification with LC-MS/MS. Method fully validated in a separate report (Sponsor reference: 000102681). LOQ: 0.01 mg/kg
				T2* 0.012	T2* 203	T2* 0.006	T2* 24.05.2019	T2* 39	T2* Whole plant Whole plant Whole plant Grain Straw	T2* 0.23 <LOQ <LOQ (nd) <LOQ (nd) <LOQ (nd)	T2* 0 14 31 60 60	Untreated specimens were all <LOQ (nd) Max. Storage Interval between sampling and analysis: 195 days Max. Storage Interval between extraction and analysis: 1 day
Northern France Grand Est 08360 Saint Fergeux Trial number AB2-19- 38159 FR03	Winter wheat Syllon	1- 15.10.2018 2- 31.05.2019 to 07.06.2019 3- 21.07.2019	Foliar broadcast application	T1 0.012	T1 205	T1 0.006	T1 14.05.2019	T1 39	T1 Whole plant Whole plant Whole plant Whole plant Grain Straw	T1 0.22 0.041 <LOQ <LOQ (nd) <LOQ (nd) 0.016**	T1 0 14 30 59 70 70	Analytical method involved extraction of mesosulfuron-methyl from homogenised laboratory samples by maceration in an acetonitrile/0.02 M triethylamine (80/20 v/v) mixture. Then, extracts were purified by solid/liquid partitions, before quantification with LC-MS/MS. Method fully validated in a separate report (Sponsor reference: 000102681). LOQ: 0.01 mg/kg
				T2* 0.012	T2* 205	T2* 0.006	T2* 14.05.2019	T2* 39	T2* Whole plant Whole plant Whole plant Whole plant Grain Straw	T2* 0.26 0.023 <LOQ <LOQ (nd) <LOQ (nd) <LOQ	T2* 0 14 30 59 70 70	Untreated specimens were all <LOQ (nd) Max. Storage Interval between sampling and analysis: 241 days Max. Storage Interval between extraction and analysis: 1 day

Poland Wielkopolska 62-105 Werkowo Trial number AB2-19- 38159 PL04	Winter wheat Arkadia	1- 25.09.2018 2- 04.06.2019 to 17.06.2019 3- 24.07.2019	Foliar broadcast application	T1 0.011	T1 189	T1 0.006	T1 20.05.2019	T1 39	T1 Whole plant Whole plant Whole plant Whole plant Grain Straw	T1 0.18 <LOQ (nd) <LOQ (nd) <LOQ (nd) <LOQ (nd) <LOQ (nd)	T1 0 14 30 58 65 65	Analytical method involved extraction of mesosulfuron-methyl from homogenised laboratory samples by maceration in an acetonitrile/0.02 M triethylamine (80/20 v/v) mixture. Then, extracts were purified by solid/liquid partitions, before quantification with LC-MS/MS. Method fully validated in a separate report (Sponsor reference: 000102681). LOQ: 0.01 mg/kg Untreated specimens were all <LOQ (nd) Max. Storage Interval between sampling and analysis: 240 days Max. Storage Interval between extraction and analysis: 1 day
				T2* 0.012	T2* 207	T2* 0.006	T2* 20.05.2019	T2* 39	T2* Whole plant Whole plant Whole plant Whole plant Grain Straw	T2* 0.31 <LOQ (nd) <LOQ (nd) <LOQ (nd) <LOQ (nd) <LOQ (nd)	T2* 0 14 30 58 65 65	

Germany Schleswig-Holstein 24364 Holzdorf Trial number AB2-19-38159 DE05	Winter wheat Colonia	1- 11.10.2018 2- 02.07.2019 to 16.07.2019 3- 12.08.2019	Foliar broadcast application	T1 0.013	T1 217	T1 0.006	T1 20.05.2019	T1 39	T1 Grain Straw	T1 <ins><LOQ (nd)</ins> <ins><LOQ (nd)</ins>	T1 87 87	Analytical method involved extraction of mesosulfuron-methyl from homogenised laboratory samples by maceration in an acetonitrile/0.02 M triethylamine (80/20 v/v) mixture. Then, extracts were purified by solid/liquid partitions, before quantification with LC-MS/MS. Method fully validated in a separate report (Sponsor reference: 000102681). LOQ: 0.01 mg/kg Untreated specimens were all <LOQ (nd) Max. Storage Interval between sampling and analysis: 68 days Max. Storage Interval between extraction and analysis: 1 day
				T2* 0.012	T2* 207	T2* 0.006	T2* 20.05.2019	T2* 39	T2* Grain Straw	T2* <ins><LOQ (nd)</ins> <ins><LOQ (nd)</ins>	T2* 87 87	

Northern France Pays de la Loire 49260 Vaudelnay Trial number AB2-19-38159 FR06	Winter wheat Apache	1- 05.10.2018 2- 05.05.2019 to 17.05.2019 3- 14.07.2019	Foliar broadcast application	T1 0.012	T1 203	T1 0.006	T1 29.04.2019	T1 39	T1 Grain Straw	T1 <LOQ (nd) <LOQ (nd)	T1 70 70	Analytical method involved extraction of mesosulfuron-methyl from homogenised laboratory samples by maceration in an acetonitrile/0.02 M triethylamine (80/20 v/v) mixture. Then, extracts were purified by solid/liquid partitions, before quantification with LC-MS/MS. Method fully validated in a separate report (Sponsor reference: 000102681). LOQ: 0.01 mg/kg Untreated specimens were all <LOQ (nd) Max. Storage Interval between sampling and analysis: 106 days Max. Storage Interval between extraction and analysis: 1 day
				T2* 0.012	T2* 207	T2* 0.006	T2* 29.04.2019	T2* 39	T2* Grain Straw	T2* <LOQ (nd) <LOQ (nd)	T2* 70 70	

*On plot T2, the adjuvant Adigor was added at the rate of 1% of the spray volume (representing 2 L/ha)

A 2.1.3.1.1 Study DMC-20-42727 (wheat, NEU)

Comments of zRMS:	Two residue trials were conducted in Northern Europe to determine the magnitude of residues of pinoxaden metabolites (M4 and M6), expressed separately and their sum as pinoxaden, mesosulfuron-methyl (parent only), mefenpyr-diethyl and its metabolite 1-(2,4-dichlorophenyl)-5-methyl-pyrazole-3-carboxylic acid expressed as mefenpyr-diethyl in raw agricultural commodity specimens of winter wheat (RAC grain and straw) after one application of ADM.06001.H.2.B. Application was done on two plots with one treatment involving the use of an adjuvant, Adigor. Target application rate was 1.0 L/ha, representing 60 g/ha pinoxaden, 12 g/ha mesosulfuronmethyl and 35 g/ha mefenpyr-diethyl. Applications were placed at BBCH 39 (flag leaf stage). Three different analytical methods for pinoxaden, mesosulfuron-methyl and efenpyr-diethyl were fully validated according to SANTE/2020/12830, rev. 1. For pinoxaden metabolite M4 the limit of quantification (LOQ) achieved was 0.01 mg/kg for grain and 0.02 mg/kg for straw. For pinoxaden metabolite M6, the LOQ was 0.01 mg/kg for grain and straw. For the sum of M4 and M6 expressed as pinoxaden, the LOQ was 0.024 mg/kg for grain, 0.036 mg/kg for straw. The results are given as M4 or M6 and as their sum expressed as pinoxaden. Limit of quantification (LOQ) for mesosulfuron-methyl achieved was 0.01 mg/kg for all matrices. The results are given as mesosulfuron-methyl. Limit of quantification (LOQ) for mefenpyr-diethyl achieved was 0.01 mg/kg for all matrices. The results are expressed as mefenpyr-diethyl. No residue of all analytes were found above LOQ in any untreated specimen. The mean recoveries at each fortification level comply with the standard acceptance criteria of the guidance document SANTE/2020/12830, rev. 1. <u>Results:</u> - for pinoxaden metabolites, the sum of M4 and M6 residues expressed as pinoxaden found at harvest were between below LOQ and 0.071 mg/kg in grain and between 0.068 and 0.33 mg/kg in straw. - for mesosulfuron-methyl, no residues were found in grain and the residues in straw were found below LOQ (0.01 mg/kg). - for mefenpyr-diethyl, no residues were found in grain and straw. - for metabolite 1-(2,4-dichlorophenyl)-5-methyl-pyrazole-3-carboxylic acid expressed as mefenpyr-diethyl, the residues found in grain specimens were below LOQ (0.01 mg/kg) and the residues in straw specimens were between 0.018 and 0.064 mg/kg. The storage of samples is covered by the storage stability data in wheat grain and straw. The study is acceptable.

Reference: KCP 8/02 (KCA 6.3.1)

Report: Magnitude of the residue of pinoxaden metabolites, mesosulfuron-methyl, mefenpyr-diethyl and its metabolite following one application of ADM.06001.H.2.B in winter wheat in 2 trials (2 HS, one with process), Northern Europe (France and Poland) – 2020
Meric, D., 2021
Report no. DMC-20-42727; ADAMA reference 000105437

Guideline(s): General Recommendations for the Design, Preparation and Realization of Residue Trials (SANCO 7029/VI/95 rev.5, 22 July 1997).
OECD Guideline for the Testing of Chemicals on Crop Field Trial (TG 509 published on 7 September 2009).
Guidance for Generating and Reporting Methods of Analysis in Support of Pre-Registration Data Requirements (SANCO/3029/99 rev.4, 11 July 2000).

	OECD (2007): Guidance Document on Pesticide Residue Analytical Methods ENV/JM/MONO(2007)17.
Deviations:	No
GLP:	Yes
Acceptability:	Yes

Table A 3: Summary of the study DMC-20-42727 trials

Active Substance:	Mesosulfuron-methyl	**Commercial Product:**	ADM.06001.H.2.B
Crop:	Winter wheat	**Producer:**	ADAMA AGAN Ltd., Ashod, Israel
Responsible for reporting:	STAPHYT GmbH – 74572 Blaufelden, Germany		
Country:	Poland, Northern France	**Indoor/glasshouse/outdoor:**	Outdoor
Content of as (actual):	12.1 g/L	**Other a.s. in formulation:**	pinoxaden, mefenpyr-diethyl
Formulation:	OD	**Residue calculated as:**	mesosulfuron-methyl

1	2	3	4	5			6	7	8	9	10	11
Location	**Commodity Variety**	**Date of 1-Sowing 2-Flowering 3-Harvest**	**Method of Treatment**	**Application Rate per Treatment**			**Date of Treatment**	**BBCH Crop Growth Stage at Treatment**	**Portions analysed**	**Residues (mg/kg)**	**PHI (days)**	**Remarks**
				kg as/ha	**Water (L/ha)**	**kg (as/hl)**				**Mesosulfuron-methyl**		
Northern France Grand Est 08360 Saint Fergeux Trial number DMC-20-42747 FR01	Winter wheat Mutic	1- 05.11.2019 2- 20.05.2020 to 05.06.2020 3- 24.07.2020	Foliar broadcast application	T1 0.013	T1 160	T1 0.008	T1 06.05.2020	T1 39	T1 Grain Straw	T1 <LOQ (nd) <LOQ	T1 82 82	Analytical method involved extraction of mesosulfuron-methyl from homogenised laboratory samples by maceration in an acetonitrile/0.02 M triethylamine (80/20 v/v) mixture. Then, extracts were purified by solid/liquid partitions, before quantification with LC-MS/MS. Method fully validated in a separate report (Sponsor reference: 000102680) and in this study. LOQ: 0.01 mg/kg Untreated specimens were all <LOQ (nd) Max. Storage Interval between sampling and analysis: 31 days Max. Storage Interval between extraction and analysis: 0 day
				T2* 0.013	T2* 160	T2* 0.008	T2* 06.05.2020	T2* 39	T2* Grain Straw	T2* <LOQ (nd) <LOQ	T2* 82 82	

Poland Wielkopolska 63-233 Lukaszewo Trial number DMC-20- 42747 PL01	Winter wheat Sailor	1- 27.0.2019 2- 03.06.2020 to 12.06.2020 3- 30.07.2020	Foliar broadcast application	T1 0.012	T1 153	T1 0.008	T1 14.05.2020	T1 39	T1 Grain Straw	T1 <u><LOQ (nd)</u> <u><LOQ (nd)</u>	T1 77 77	Analytical method involved extraction of mesosulfuron-methyl from homogenised laboratory samples by maceration in an acetonitrile/0.02 M triethylamine (80/20 v/v) mixture. Then, extracts were purified by solid/liquid partitions, before quantification with LC-MS/MS. Method fully validated in a separate report (Sponsor reference: 000102680) and in this study. LOQ: 0.01 mg/kg Untreated specimens were all <LOQ (nd) Max. Storage Interval between sampling and analysis: 28 days Max. Storage Interval between extraction and analysis: 0 day
				T2* 0.012	T2* 150	T2* 0.008	T2* 14.05.2020	T2* 39	T2* Grain Straw	T2* <LOQ (nd) <LOQ (nd)	T2* 77 77	

*On plot T2, the adjuvant Adigor was added at the rate of 1% of the spray volume (representing 1 L/ha)

A 2.2 Pinoxaden

A 2.2.1 Stability of residues

A 2.2.1.1 Stability of residues during storage of samples

No new data submitted.

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

A 2.2.2.1 Nature of residue in plants

A 2.2.2.1.1 Study S19-00664

Comments of zRMS:	The metabolism of the herbicide pinoxaden was investigated in wheat plants following a single application at BBCH 39 with [^{14}C]-pinoxaden (nominally 60 g a.s./ha) as an OD formulation also containing mesosulfuron-methyl and the safener mefenpyr-diethyl. Parent pinoxaden was not detected in any commodity and major metabolites are M4 and M6. Extraction efficiency of the residue analytical method is sufficiently shown for the extraction of the metabolites SYN505164 (M4) and SYN502836 (M6) from wheat forage, hay, straw and grain. The study meets the requirements of the OECD 501 and SANTE 2017/10632 - Rev. 3, 22 November 2017. The study is acceptable. Remark: zRMS-PL is of the opinion that this new study should be assessed at the EU level, since it investigates metabolism of residues.

Reference: KCP 8/03 (KCA 6.2.1/01)

Report: Metabolism of [^{14}C]-pinoxaden in wheat,
Erk, T., 2021
Report no. S19-00664, ADAMA reference 000102129

Guideline(s): Yes
OECD Guidelines for the Testing of Chemicals – Metabolism in Crops, No. 501, OECD, Paris 2007
Residue Chemistry Test Guidelines OPPTS 860.1300 Nature of the Residues in Plants, Livestock, EPA 712-C-96-172, August 1996.
Ministry of Agriculture, Forestry and Fisheries of Japan, 2000. The guidelines related to the study reports for the registration application of pesticide. 12-Nousan No 8147, 24 November 2000.
EC (European Commission), 2017. Technical Guideline on the Evaluation of Extraction Efficiency of Residue Analytical Methods. SANTE 2017/10632 - Rev. 3, 22 November 2017

Deviations: No

GLP: Yes

Acceptability: Yes

Materials and methods
Foliar application to spring wheat was done using test item [phenyl-1-^{14}C]-NOA407855 formulated as an OD formulation ADM.06001.H.2.B containing also unlabelled mesosulfuron-methyl and the safener mefenpyr-diethyl. The formulation was applied at a nominal application rate for pinoxaden of 60 g a.s./ha (A application) and a second separate trial at an exaggerated nominal application rate of 180 g a.s./ha (B

application), corresponding to 6.0 or 18.0 mg a.s./m^2.
The applications were performed at growth stage BBCH 39. The actual application rates for pinoxaden corresponded to 67 g a.s./ha (A application) and 214 g a.s./ha for the exaggerated rate (B application). Mefenpyr safener was applied at the actual rate of 51 g a.s./ha (A application) and 153 g a.s./ha (B application).
A total of two planting containers of spring wheat, with one planting container per application rate, were used for the study. Seeds of wheat plants (variety: Kadrilj) were sown before application at a seed density of 5,000,000 plants per hectare, corresponding to 500 wheat plants/m^2. The surface area of each container was 1 m^2 and each container was filled with a sandy loam soil.
For A and B application plots, wheat forage was harvested at BBCH 47, corresponding to a PHI of 6 days after application. Hay was harvested at BBCH 77, corresponding to a PHI of 32 days after application. Straw and grain were harvested at BBCH 92, corresponding to a PHI of 47 days after application.
The total radioactive residues (TRR) in the raw agricultural commodities (RACs) of wheat forage, hay, straw and grain samples were determined by summing up the extractable and unextractable radioactivity for the 60 g a.s./ha application. TRRs in wheat forage, hay, straw and grain samples from the 180 g a.s./ha application were determined by combustion of homogenised plant material. These samples were not extracted and were not further subjected to the investigation of the metabolism of pinoxaden in this study.
Post-extraction solids (PES) from the conventional extraction of wheat forage, hay, straw and grain from application A were subjected to sequential exhaustive extraction. Samples were extracted with HCl (1 M), NaOH (1 M), HCl (6 M), NaOH (6 M) and enzyme digestion (cellulase).
Residues in the conventional and exhaustive extracts were analysed and quantified by HPLC. The metabolites of pinoxaden were assigned and identified according to the following methodology:

- Comparison of metabolic profiles of all RACs, as analysed by HPLC
- Comparison of retention times of metabolite fractions by HPLC analysis with retention times of reference items using the same analytical method
- Isolation of major metabolite fractions from conventional extracts and further HPLC co-chromatography of the isolated fractions
- Structural elucidation of isolated fractions of conventional extract of wheat grain by the use of reference items and LC-MS/MS
- Confirmation of the identity of metabolites using LC-MS

To determine whether more conjugates were present among the characterised unknown metabolites in the chromatograms, conventional extracts were subjected to sequential hydrolysis. Samples were incubated with HCl (1 M), NaOH (1 M), HCl (6 M), NaOH (6 M) and enzyme digestion (cellulase) in order to analyse for hydrolysable conjugates.
The efficiency of extraction was tested by using samples containing incurred residues (wheat forage, hay, straw and grain). These samples were extracted following the extraction scheme from an analytical residue method, using a solvent system of acetonitrile/water (1/1, v/v). The efficiency of this method of extraction compared to the efficiency of extraction obtained by conventional metabolism extraction was 87, 101, 89 and 86% for metabolite M4 in forage, hay, straw and grain. For metabolite M6 the extraction efficiency was 147, 74, 100 and 80% in forage, hay, straw and grain.
All conventional solvent extractions of the raw agricultural commodities and the first HPLC analyses were performed within 6 months after harvest of the crop samples. Storage stability of wheat forage, hay, straw and grain were demonstrated for 548, 530, 510 and 515 days, respectively.

Results and discussion
Total radioactive residues (TRR) in the raw agricultural commodities (RACs) of wheat forage, hay, straw and grain samples were determined by summing up the extractable and unextractable radioactivity for the 60 g a.s./ha application and accounted for 2.686 mg eq/kg, 3.374 mg eq/kg, 4.987 mg eq/kg and 0.630 mg eq/kg, respectively (Table A 1).
TRRs in wheat forage, hay, straw and grain samples from the 180 g a.s./ha application were determined by combustion of homogenised plant material and accounted for 8.194 mg eq/kg, 13.25 mg eq/kg, 20.54 mg eq/kg and 1.669 mg eq/kg (Table A 1)

Table A 4: Total Radioactive Residues (TRRs) in matrices

Application rate	Matrix	PHI (days)	TRR (mg eq/kg)
60 g a.s./ha	Forage	6	2.686
	Hay	32	3.374
	Straw	47	4.987
	Grain	47	0.630
180 g a.s./ha	Forage	6	8.194
	Hay	32	13.25
	Straw	47	20.54
	Grain	47	1.669

The parent substance pinoxaden was not present in any RAC.
Metabolite M4 and its conjugates represented the most prominent residue components in all RACs, including residues in conventional solvent extracts and exhaustive extracts (Table A 5).

Table A 6: Summary of characterization and identification of radioactive residues in plant matrices following application of radiolabeled pinoxaden

Compound	Fraction	Conventional solvent extracts plus exhaustive extracts of PES							
		Forage		Hay		Straw		Grain	
		% TRR	mg eq/kg	% TRR	mg eq/kg	% TRR	mg eq/kg	% TRR	mg eq/kg
SYN505164 (M4)	Total	70.4	1.892	54.7	1.847	42.7	2.130	77.5	0.488
	Free	30.0	0.807	8.2	0.278	26.7	1.330	17.3	0.109
	Bound/conjugate1	40.4	1.084	46.5	1.569	16.0	0.800	60.2	0.379
SYN502836 (M6)	Total	7.0	0.188	9.3	0.313	5.2	0.262	10.5	0.066
	Free	4.8	0.129	8.88	0.2968	1.2	0.061	7.8	0.049
	Bound/conjugated2	2.2	0.059	0.5	0.017	4.0	0.200	2.7	0.017
NOA407854 (M2)	Total	5.0	0.134	3.8	0.127	4.1	0.206	0.6	0.004
	Free	1.7	0.045	1.0	0.034	0.7	0.034	<0.1	<0.001
	Bound/conjugated3	3.3	0.089	2.8	0.094	3.4	0.172	0.6	0.004
NOA447204 (M3)	Total	6.8	0.183	2.4	0.082	1.6	0.081	0.8	0.005
	Free	6.8	0.182	2.3	0.077	1.5	0.075	<0.1	<0.001
	Bound/conjugated4	<0.1	0.001	0.1	0.005	0.1	0.006	0.8	0.005
M-X	Total	3.8	0.101	4.1	0.140	4.9	0.244	5.0	0.031
	Free	3.6	0.096	2.6	0.089	3.3	0.163	2.3	0.014
	Bound/conjugated5	0.2	0.005	1.5	0.051	1.6	0.080	2.7	0.017
Total identified6		79.9	2.147	66.1	2.231	47.8	2.382	63.7	0.401
Total characterised7		18.7	0.503	30.0	1.012	47.1	2.351	34.9	0.220
Analysed extract		98.6	2.649	96.1	3.243	94.9	4.733	98.7	0.621
Not analysed / Losses		0.5	0.013	0.6	0.021	0.4	0.018	<0.1	<0.001
Total extracted		99.1	2.662	96.8	3.264	95.3	4.751	98.7	0.621
Unextractable (PES)		0.9	0.023	3.3	0.110	4.7	0.236	1.3	0.008
Accountability		100	2.685	100	3.374	100	4.986	100	0.630

PES = post extraction solid after exhaustive extraction
[1]Value includes Glc-SYN505164 (Glc-M4), SYN505164-Glc-HMG-1 (M4G1), SYN505164-Glc-HMG-2 (M4G2) and other unidentified conjugates in conventional solvent extracts and PES which converted to M4 after acid, base and cellulase hydrolysis
[2]Value includes unidentified conjugates in conventional solvent extracts which converted to M6 in the final hydrolysed extract, and M6 released from the PES after acid, base and cellulase hydrolysis
[3]Value includes unidentified conjugates in conventional solvent extracts which converted to M2 in the final hydrolysed extract, and M2 released from the PES after acid, base and cellulase hydrolysis
[4]Value includes M3 released from the PES after acid, base and cellulase hydrolysis
[5]Value includes M-X released from the PES after acid, base and cellulase hydrolysis
[6]Total identified in the conventional solvent extracts (unhydrolysed) and the exhaustive extracts of PES
[7]Total characterised in the conventional solvent extracts (unhydrolysed) and the exhaustive extracts of PES
[8]The amount of M6 in the solvent extract reduced from 8.8% TRR, 0.296 mg/kg before the hydrolysis procedures to 7.0% TRR, 0.235 mg/kg at the end of the hydrolysis procedures.

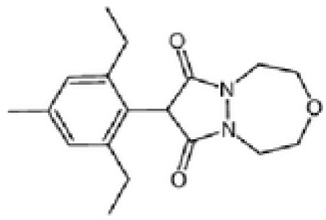
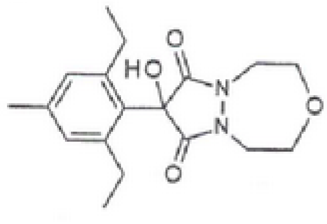
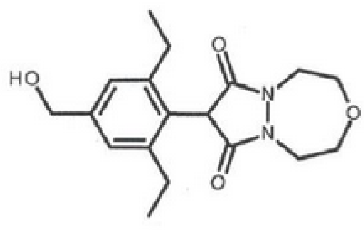
In forage, hay, straw and grain SYN505164 (M4) accounted for 30.7, 10.8, 28.9 and 17.3% of TRR (0.824, 0.363, 1.440 and 0.109 mg eq/kg), Glc-SYN505164 (Glc-M4) accounted for 31.6, 34.8, 8.1 and

8.3% of TRR (0.850, 1.175, 0.405 and 0.052 mg eq/kg), SYN505164-Glc-HMG-1 (M4G1) was only detected in grain and accounted for 6.2% of TRR (0.039 mg eq/kg), SYN505164-Glc-HMG-2 (M4G2) was below the limit of detection in forage extracts and accounted for 2.8, 0.6 and 17.9% of TRR (0.094, 0.032 and 0.112 mg eq/kg) in wheat hay, straw and grain extracts, respectively.
The minor metabolites in extracts of forage, hay, straw and grain were M-X with 3.8, 4.1, 4.9 and 5.0% of TRR (0.101, 0.140, 0.244 and 0.031 mg eq/kg), SYN502836 (M6) with 4.8, 9.3, 1.6 and 7.8% (0.130, 0.313, 0.078 and 0.049 mg eq/kg), NOA407854 (M2) with 2.2, 1.9, 2.1 and 0.6% of TRR (0.059, 0.065, 0.103 and 0.004 mg eq/kg) and NOA447204 (M3) with 6.8, 2.4, 1.6 and 0.8% of TRR (0.183, 0.082, 0.081 and 0.005 mg eq/kg).
The major hydrolysis products detected in the final hydrolysates were SYN505164 (M4) and SYN502836 (M6), with smaller amounts of M-X, NOA407854 (M2) and NOA447204 (M3).
Overall, identification rates in conventional solvent extracts and exhaustive extracts amounted to 79.9% of TRR for forage, 66.1% of TRR for hay, 47.8% of TRR for straw and 63.7% of TRR for grain.
In wheat forage, hay, straw and grain 60, 53, 73 and 39 unknown metabolites were characterised in the extracts by their chromatographic behaviour, individually accounting for less than 6.8, 3.3, 5.9 and 3.7% of the TRR and 0.184, 0.113, 0.293 and 0.023 mg eq/kg, respectively.
The main metabolic reactions observed were:

- Hydrolysis of the ester bond in pinoxaden to form NOA407854 (M2)
- Oxidation of NOA407854 (M2) to NOA447204 (M3) and SYN505164 (M4)
- Oxidation of SYN505164 (M4) to SYN502836 (M6)
- Glucoside Conjugation of SYN505164 (M4) to Glucose-SYN505164 (Glc-SYN505164 = Glc-M4)
- Conjugation of Glc-SYN505164 with 3-hydroxy-3-methylglutaric acid to SYN505164-Glc-HMG-1 (M4G1) and SYN505164-Glc-HMG-2 (M4G2)
- Oxidation and hydrolysis of NOA407854 (M2) to M-X

Based on the results, the metabolism of pinoxaden in wheat plant in the presence of mefenpyr is adequately understood.

Table A 7: Identification of compounds from metabolism study

Common name/code	Chemical name	Chemical structure
NOA407854 (M2)	8-(2,6-diethyl-4-methyl-phenyl)-tetrahydro-pyrazolo[1,2-d][1,4,5] oxadiazepine-7,9-dione	
NOA447204 (M3)	8-(2,6-diethyl-4-methyl-phenyl)-8-hydroxy-tetrahydro-pyrazolo[1,2-d][1,4,5] oxadiazepine-7,9-dione	
SYN505164 (M4)	8-(2,6-diethyl-4-hydroxymethyl-phenyl)-tetrahydro-pyrazolo[1,2-d][1,4,5]oxadiazepine-7,9-dione	

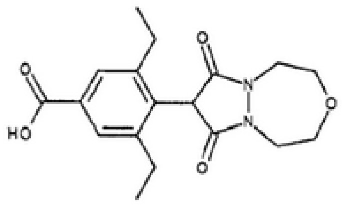
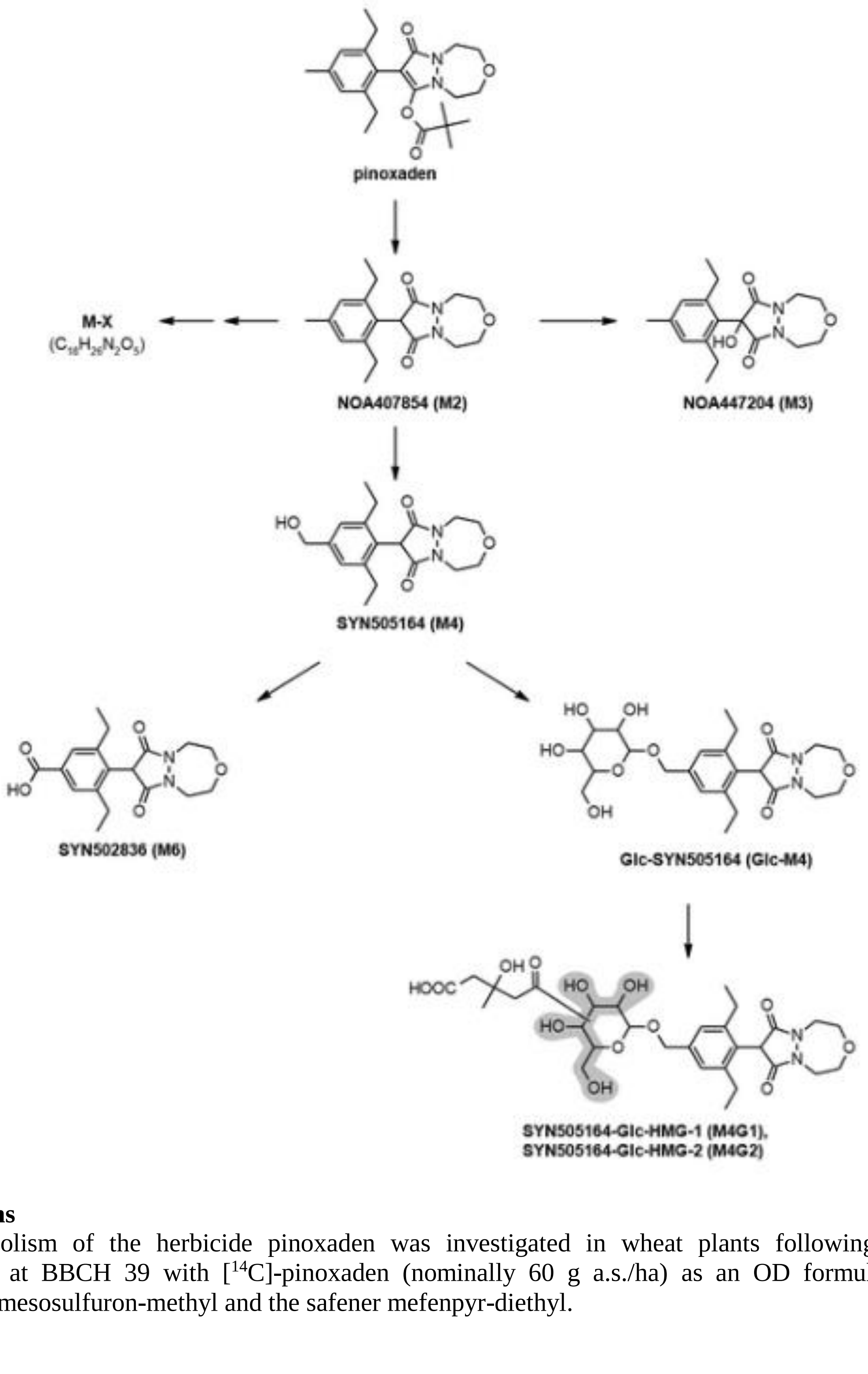
Common name/code	Chemical name	Chemical structure
SYN502836 (M6)	4-(7,9-dioxo-hexahydro-pyrazolo[1,2-d][1,4,5] oxadiazepin-8-yl)-3,5-diethyl-benzoic acid	

Figure A 1: **Proposed metabolic profile of pinoxaden in wheat**



Conclusions

The metabolism of the herbicide pinoxaden was investigated in wheat plants following a single application at BBCH 39 with [^{14}C]-pinoxaden (nominally 60 g a.s./ha) as an OD formulation also containing mesosulfuron-methyl and the safener mefenpyr-diethyl.

Raw agricultural commodities (RAC) were harvested at BBCH 47 (forage), 6 days after application, at BBCH 77 (hay), 32 days after application and at BBCH 92 (straw and grain), 47 days after application.
TRR values of forage, hay, straw and grain accounted for 2.686 mg eq/kg, 3.374 mg eq/kg, 4.987 mg eq/kg and 0.630 mg eq/kg, respectively.
The total recoveries following conventional solvent extraction of forage, hay, straw and grain accounted for 95.9%, 80.4%, 76.8% and 87.3% of TRR, respectively.
Identification rates of extracted residues from forage, hay, straw and grain, including the exhaustive extracts of the post-extraction solids, accounted for 79.9%, 66.1%, 47.8% and 63.7% of TRR, respectively.
Identification rates increased after sequential hydrolysis of the conventional solvent extracts of forage, hay, straw and grain and accounted for 82.6%, 69.1%, 55.8% and 92.0% of TRR, respectively, including the exhaustive extracts of the post-extraction solids.
Parent pinoxaden was not detected in any commodity.
SYN505164 (M4) and its hydrolysable conjugate Glc-SYN505164 (Glc-M4) were found as major metabolites (>10% TRR) in all RACs. In wheat grain, the hydrolysable conjugate SYN505164-Glc-HMG-2 (M4G2) was also detected as a major metabolite (>10% TRR).
M-X, SYN502836 (M6), NOA407854 (M2) and NOA447204 (M3) were additional metabolites detected in the conventional solvent extracts of all RACs. SYN505164-Glc-HMG-2 (M4G2) was also found in the conventional solvent extracts of hay and straw, but was not detected in forage.
In wheat grain, the hydrolysable conjugate SYN505164-Glc-HMG-1 (M4G1) was also detected in the conventional solvent extract.
Extraction efficiency of the residue analytical method is sufficiently shown for the extraction of the metabolites SYN505164 (M4) and SYN502836 (M6) from wheat forage, hay, straw and grain.
Pinoxaden was metabolised in wheat after a single application. SYN505164 (M4) represented the major initial degradation product and was further conjugated with glucose and 3-hydroxy-3-methylglutaric acid to form Glc-SYN505164 (Glc-M4), SYN505164-Glc-HMG-1 (M4G1) and SYN505164-Glc-HMG-2 (M4G2).

A 2.2.2.1.2 Study 1808368.UK0 – 0293

Comments of zRMS:	The purpose of the study was the comparison of the available metabolism studies (previously evaluated in DAR (UK, 2006) and DAR Addendum (UK, 2013) and new data (Erk, T., 2021) on pinoxaden in the presence of safeners cloquintocet-mexyl and mefenpyr diethyl in wheat. Based on available data zRMS-PL agrees with the following conclusion of the study: *"As the main metabolic pathways of pinoxaden are the same with both safeners, it can be concluded that the safener does not substantially impact the metabolism of pinoxaden in wheat."* It can be considered as supporting data.

Reference:	KCP 8/04 (KCA 6.2.1/02)
Report	Comparison of the metabolism of pinoxaden in wheat in the presence of different safeners Silcock, R., Gill, P., 2021 Report no. 1808368.UK0 - 0293, ADAMA reference 000108349
Guideline(s):	No Not applicable
Deviations:	Not applicable
GLP:	No
Acceptability:	Yes

Background
Three metabolism studies were previously evaluated in the DAR (UK, 2006) and DAR Addendum (UK,

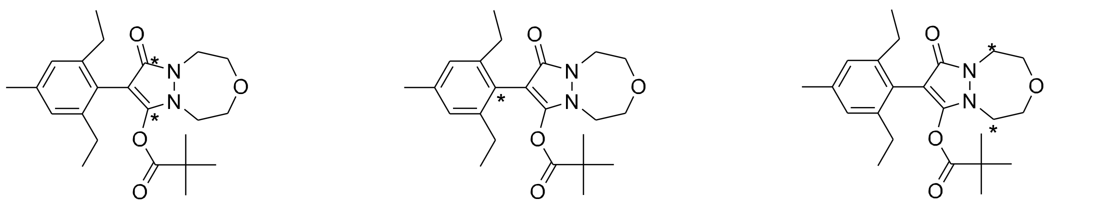
2013) in which winter or spring wheat was treated with pinoxaden formulated with the safener cloquintocet-mexyl (CGA 185072). A new metabolism study has been conducted on spring wheat using pinoxaden formulated with the safener mefenpyr- diethyl (Erk, T., 2021). The key features of these studies are presented below in Table A 8.

Table A 8: Pinoxaden wheat metabolism studies

Radiolabel	Crop	Application timing and growth stage	Application rate	Safener	Reference
[^{14}C-Pyrazol]-pinoxaden	Winter wheat, outdoor	Autumn application BBCH 13	1 x 68.5 g/ha	Cloquintocet-mexyl	Sandmeier, P., 2001a
[^{14}C-Phenyl]-pinoxaden	Winter wheat, outdoor	Spring application BBCH 49	1 x 64 g/ha	Cloquintocet-mexyl	Sandmeier, P., 2003a
[^{14}C-Phenyl]-pinoxaden	Spring wheat, outdoor	Spring application BBCH 37-39	1 x 62 g/ha	Cloquintocet-mexyl	Stingelin, J., 2002a
[^{14}C-Oxadiazepine]-pinoxaden	Spring wheat, outdoor	Spring application BBCH 37-39	1 x 66 g/ha	Cloquintocet-mexyl	Stingelin, J., 2002a
[^{14}C-Phenyl]-pinoxaden	Spring wheat, indoor	Spring application BBCH 39	1 x 67 g/ha	Mefenpyr-diethyl	Erk, T., 2021

The three different radiolabelling positions used in these studies are shown below.

Figure A 2: Radiolabelling of pinoxaden



* = position of radiolabel [Pyrazol-3,5-$^{14}C_1$]-pinoxaden

* = position of radiolabel [Phenyl-1-^{14}C]-pinoxaden

* = position of radiolabel [Oxadiazepin-3,6-$^{14}C_1$]-pinoxaden

The study conducted with the safener mefenpyr-diethyl (Erk, T., 2021) is most directly comparable to the study conducted with the safener cloquintocet-mexyl with application at BBCH 37-39 (Stingelin, J., 2002a) as the studies were performed at similar application rates and application timings.

Metabolic pathway of pinoxaden in wheat

The metabolic pathway of pinoxaden in wheat can be broken down into several key steps, which are described below. An overall metabolic pathway for pinoxaden in wheat is given in Figure A 3.

Summary tables are provided in the tables below which compare the profiles in the solvent extracts of early harvest/forage (PHI 7-14 days, Table A 9), forage/hay (PHI 28-42 days, Table A 10), mature grain (PHI 48-67 days, Table A 11) and straw (PHI 48-264 days, Table A 13).

In two studies with the safener cloquintocet-mexyl (Sandmeier, P., 2003a, and Stingelin, J., 2002a), grain samples were extracted using 1M HCl reflux hydrolysis, and these data are provided in an additional table (Table A 12).

In the study with the safener mefenpyr-diethyl (Erk, T., 2021), the solvent extract of each commodity was subjected to a sequential hydrolysis procedure with 1M HCl, 1M NaOH, 6M HCl, 6M NaOH and cellulase, and the post-extraction solids were also subjected to stepwise exhaustive extraction using the same hydrolysis procedures. This characterised additional material as being bound or conjugated metabolites, and the total amount of each metabolite after the hydrolysis procedures is also provided in the summary tables. The amount of each free metabolite is taken from the quantitation of the unhydrolysed solvent extract.

i) Ester hydrolysis of pinoxaden to M2

The metabolism of pinoxaden in wheat proceeds *via* ester hydrolysis to form M2. The initial ester hydrolysis step is very rapid and parent pinoxaden was found at low levels only in early forage samples (PHIs of 0-14 days) in the studies conducted with the safener cloquintocet- mexyl. Parent pinoxaden was not detected in later forage/hay samples or in mature grain, husks or straw in any study. This initial rapid hydrolysis of pinoxaden is seen with both cloquintocet-mexyl and mefenpyr-diethyl safeners.

ii) Hydroxylation of M2 to M4 and phase II conjugation

The major metabolic pathway seen in all studies was hydrolysis of pinoxaden to M2 followed by hydroxylation at the 4-methyl group of the phenyl moiety to form M4, and then phase II metabolism to M4 conjugates. This metabolic pathway is seen with both cloquintocet-mexyl and mefenpyr-diethyl safeners.

Conjugation of M4 with glucose formed M5 (gluc-M4), and this conjugate was found as a major metabolite in all studies and with both safeners.

Conjugation of M4 with a pentose sugar formed M14, which was found as a minor metabolite in forage, straw and husks in two studies with the safener cloquintocet-mexyl.

Further conjugation of M5 (gluc-M4) was observed with either malonic acid to form the malonyl-glucose conjugate M7, or with glutaric acid to form the 3-hydroxymethylglutaryl- glucose (HMG-glucose) conjugates M4G1 and M4G2. M7 was found as a minor metabolite in studies with the safener cloquintocet-mexyl, whereas M4G1 and M4G2 were found only in the study with the safener mefenpyr-diethyl.

iii) Oxidation of M4 to M31 and M6

This metabolic pathway is seen with both safeners. Oxidation of the hydroxymethyl group in M4 results initially in the formation of M31, and then further oxidation forms the carboxylic acid metabolite M6, which was found in all studies and with both safeners. M31 must have occurred transiently in all studies, but it was detected as a minor metabolite in straw in only one study with the safener cloquintocet-mexyl.

iv) Hydroxylation of M2 to M3

This is a minor metabolic pathway seen with both safeners. A second site of hydroxylation of M2 is on the pyrazole ring to form M3. M3 was found at low levels in forage, hay and straw in all studies and with both safeners. M3 was not found in the solvent extracts of grain from any study but was detected at very low levels in the exhaustive extracts of the grain post- extraction solids in the study with the safener mefenpyr-diethyl.

v) Hydroxylation of M6 to M11 and/or oxidation of M10 to M11

Hydroxylation on the pyrazole ring of M6 is a route of formation of M11. Oxidation of the hydroxymethyl group in M10 is another possible route for formation of M11. However, these are considered to be very minor pathways as M11 was only found at low levels in forage and/or straw in studies with the safener cloquintocet-mexyl.

vi) Hydroxylation of M3 and/or M4 to M10 and phase II conjugation

Hydroxylation on both the 4-methyl group of the phenyl moiety and the pyrazole ring forms M10, and therefore M10 can be formed from either M3 or M4. M10 is further conjugated with glucose to form M8 followed by malonylation to form M9. M10 (free and conjugated) was found in all the studies with the safener cloquintocet-mexyl but was not found in any commodity in the study with the safener mefenpyr-diethyl.

vii) Hydroxylation of M4 and/or M10 and cyclisation to M32

A third site of hydroxylation is on the 4-ethyl group of the phenyl moiety in M4 or M10. Hydroxylation on the 4-ethyl group and the pyrazole ring, followed by cyclisation, leads to the formation of M32. This is a very minor metabolic pathway seen in straw in only one study with the safener cloquintocet-mexyl.

viii) Conversion of M2 to M-X

Metabolite M-X was detected in the study conducted with the safener mefenpyr-diethyl and was characterised by mass spectrometry as having the molecular formula $C_{18}H_{26}N_2O_5$, which is equivalent to M2 with the addition of 2O + 2H. It is therefore a downstream metabolite of M2. It was found as a minor metabolite at similar levels in all matrices, accounting for 2.3-3.6% TRR in free form in the solvent extracts, and 3.8-5.0% TRR in total (free + bound/conjugated).

Quantitative comparison of metabolites of pinoxaden in wheat commodities

Early harvest forage (PHI 7-14 days)

The profiles in early harvest forage are presented in Table A 9.

The major metabolite (>10% TRR and >0.01 mg/kg) found in early harvest forage in all studies was M4, in both free and conjugated form. In the studies conducted with application at BBCH 37-39 (Stingelin, J., 2002a) or BBCH 39 (Erk, T., 2021), free M4 accounted for 30.5-52.2% TRR after treatment with pinoxaden and the safener cloquintocet-mexyl, and 30.0% TRR after treatment with pinoxaden and the safener mefenpyr-diethyl. The total amount of M4 (free + conjugated) was 74.1-78.9% TRR with the safener cloquintocet-mexyl, and 70.4% TRR with the safener mefenpyr-diethyl.

All other metabolites in early harvest forage were minor (<10% TRR). The metabolites M2, M3 and M6 were found in all studies with both safeners. M10 (free and/or conjugated) and M11 were found only in studies with the safener cloquintocet-mexyl, whilst metabolite M-X was found only in the study with the safener mefenpyr-diethyl.

Considering the plant residue definition (EFSA, 2013, EFSA, 2021), the sum of M4 and M6 (both free and conjugated) in early harvest forage amounted to 82.3-85.5% TRR after treatment with pinoxaden and the safener cloquintocet-mexyl at BBCH 37-39, and 77.4% TRR after treatment with pinoxaden and the safener mefenpyr-diethyl at BBCH 39.

Forage and hay (PHI 28-42 days)

The profiles in forage and hay are presented in Table A 10.

M5 (gluc-M4), the glucose conjugate of M4, was the major metabolite (>10% TRR and >0.01 mg/kg) found in forage or hay in all studies. In the studies conducted with application at BBCH 37-39 (Stingelin, J., 2002a) or BBCH 39 (Erk, T., 2021), the total amount of M4 (free + conjugated) was 75.8% TRR in forage with the safener cloquintocet-mexyl, and 54.7% TRR in hay with the safener mefenpyr-diethyl. Of this, free M4 accounted for 5.6% TRR in forage with cloquintocet-mexyl and 8.2% TRR in hay with mefenpyr-diethyl.

In forage treated at BBCH 13 with pinoxaden and the safener cloquintocet-mexyl, the total amount of M10 (as the sum of the glucose conjugate M8 and the malonyl-glucose conjugate M9) exceeded 10% TRR, but M10 (free and conjugated) was a minor metabolite in studies treated with pinoxaden and the safener cloquintocet-mexyl at BBCH 37-39 or BBCH 49. M10 was not found in the study with the safener mefenpyr-diethyl.

All other metabolites in forage and hay were minor (<10% TRR). The metabolites M2, M3 and M6 were found in studies with both safeners. M11 was found only in one study with the safener cloquintocet-mexyl, whilst metabolite M-X was found only in the study with the safener mefenpyr-diethyl.

Considering the plant residue definition, the sum of M4 and M6 (both free and conjugated) in forage or hay harvested at a PHI of 28 days amounted to 83.2% TRR after treatment with pinoxaden and the safener cloquintocet-mexyl at BBCH 37-39, and 64.0% TRR after treatment with pinoxaden and the safener mefenpyr-diethyl at BBCH 39.

Grain (PHI 48-67 days)

The grain from the winter wheat study treated at BBCH 13 and harvested at a PHI of 264 days contained a TRR of 0.004 mg/kg and therefore was not extracted or profiled. The grain from studies treated at later growth stages was extracted, and the profiles are presented in Table A 11 (solvent extracts) and Table A 12 (after extraction by 1M HCl hydrolysis).

M4, in free and conjugated form, was a major metabolite (>10% TRR and >0.01 mg/kg) in grain in all studies. In the studies conducted with application at BBCH 37-39 (Stingelin, J., 2002a) or BBCH 39

(Erk, T., 2021), free M4 accounted for 7.7-9.4% TRR after treatment with pinoxaden and the safener cloquintocet-mexyl, and 17.3% TRR after treatment with pinoxaden and the safener mefenpyr-diethyl. The total amount of M4 (free + conjugated) in solvent extracts was 27.7-28.7% TRR with the safener cloquintocet-mexyl, and 49.1% TRR with the safener mefenpyr-diethyl.
Grain from the study treated with pinoxaden and the safener cloquintocet-mexy1 at BBCH 37-39 was extracted using 1M HCl reflux to hydrolyse conjugates, which released a total of 58.5-72.4% TRR as M4. Similarly, the grain from the study treated with pinoxaden and the safener mefenpyr-diethyl contained a total of 77.5% TRR as M4 after the hydrolysis procedures.
M6, in free and conjugated form, was also a major metabolite (>10% TRR and >0.01 mg/kg) in grain in studies with both safeners. In the studies conducted with application at BBCH 37-39 (Stingelin, J., 2002a) or BBCH 39 (Erk, T., 2021), free M6 in solvent extracts accounted for 12.0-13.6% TRR after treatment with pinoxaden and the safener cloquintocet-mexyl, and 7.8% TRR after treatment with pinoxaden and the safener mefenpyr-diethyl. The total amount of M6 (free + conjugated) in grain treated with pinoxaden and the safener mefenpyr-diethyl was 10.5% TRR.
All other metabolites in grain were minor (<10% TRR). Free M2 and M3 were not detected in solvent extracts of grain from any study, but very small amounts were detected after the hydrolysis procedure in the study with the safener mefenpyr-diethyl. M10 was found at very low levels (0.7% TRR) in one study with the safener cloquintocet-mexyl, whilst metabolite M-X was found at low levels (maximum 5.0% TRR including exhaustive extracts) only in the study with the safener mefenpyr-diethyl.
Considering the plant residue definition, the sum of M4 and M6 (both free and conjugated) in grain amounted to 65.3-83.9% TRR (after 1M HCl hydrolysis extraction) after treatment with pinoxaden and the safener cloquintocet-mexyl at BBCH 37-39, and 88.0% TRR after treatment with pinoxaden and the safener mefenpyr-diethyl at BBCH 39, respectively.

Straw (PHI 48-264 days)
The profiles in straw are presented in Table A 13.
In the wheat studies treated at later growth stages (BBCH 37 to BBCH 49), M4 was a major metabolite in straw (>10% TRR and >0.01 mg/kg), whereas in the winter wheat study treated at BBCH 13 and harvested at a PHI of 264 days, M4 was a minor metabolite.
In the studies conducted with application at BBCH 37-39 (Stingelin, J., 2002a) or BBCH 39 (Erk, T., 2021), free M4 accounted for 34.0-36.5% TRR after treatment with pinoxaden and the safener cloquintocet-mexyl, and 26.7% TRR after treatment with pinoxaden and the safener mefenpyr-diethyl. The total amount of M4 (free + conjugated) was 37.2-41.5% TRR with the safener cloquintocet-mexyl, and 42.7% TRR with the safener mefenpyr-diethyl.
M10 was a major metabolite (>10% TRR and >0.01 mg/kg) in straw treated at BBCH 49 with pinoxaden and the safener cloquintocet-mexyl, but a minor metabolite in the other studies treated with pinoxaden and the safener cloquintocet-mexyl. M10 was not found in the study with the safener mefenpyr-diethyl.
All other metabolites in straw were minor (<10% TRR or <0.01 mg/kg). M3 and M6 were found in studies with both safeners. In the studies conducted with application at BBCH 37-39 or BBCH 39, free M6 in solvent extracts accounted for 8.7-9.2% TRR after treatment with pinoxaden and the safener cloquintocet-mexyl, and 1.2% TRR after treatment with pinoxaden and the safener mefenpyr-diethyl. The total amount of M6 (free + conjugated) in straw treated with pinoxaden and the safener mefenpyr-diethyl was 5.2% TRR. M11, M31 and M32 were found at low levels in studies with the safener cloquintocet-mexyl, whilst metabolites M2 and M-X were found only in the study with the safener mefenpyr-diethyl.
Considering the plant residue definition, the sum of M4 and M6 (both free and conjugated) in straw amounted to 46.4-50.2% TRR after treatment with pinoxaden and the safener cloquintocet-mexyl at BBCH 37-39, and 47.9% after treatment with pinoxaden and the safener mefenpyr-diethyl at BBCH 39.

Conclusions
Pinoxaden in wheat undergoes the same types of metabolic transformations irrespective of the safener used, namely ester hydrolysis followed by hydroxylation and then oxidation or glucoside conjugation.
The main metabolic pathway observed for pinoxaden in wheat, with either cloquintocet-mexyl or mefenpyr-diethyl, was ester hydrolysis to M2, followed by hydroxylation to M4 and subsequent phase II conjugation. M4 (free and bound/conjugated) was the main component of the residue in all wheat commodities and with both safeners, except for straw from winter wheat treated in the autumn at BBCH

13.
Further metabolism of M4 by oxidation to M6 was seen in all wheat commodities, and M6 (free and bound/conjugated) was also found as a major metabolite in grain with both safeners, although at lower levels than M4 (free and bound/conjugated).
The residue definition of pinoxaden in plants is set as the “sum of M4 and M6 expressed as parent pinoxaden (to include free and conjugated residues of M4 and M6)” (EFSA, 2013, EFSA, 2021). In mature wheat, the sum of M4 and M6 (both free and conjugated) accounted for 65.3-83.9% TRR in grain and 46.4-50.2% TRR in straw from wheat treated with pinoxaden and cloquintocet-mexyl, and 88.0% TRR in grain 47.9% TRR in straw from wheat treated with pinoxaden and mefenpyr-diethyl. As the components of the residue definition are present at similar levels with either safener, it can be concluded that the safener does not substantially impact the metabolism of pinoxaden in wheat.
Metabolites resulting from hydroxylation of M2 in two or more positions (M10, M11 and M32) were detected only in studies conducted with the safener cloquintocet-mexyl. M11 and M32 were minor metabolites in forage and straw and were not found in grain. M10 (free and/or conjugated) was found at more significant levels in some forage and straw samples but was found only at very low levels or was non-detectable in grain. In the study conducted with the safener cloquintocet-mexyl with application at BBCH 37-39, which is directly comparable to the study conducted with mefenpyr-diethyl, M10 was found only as a minor metabolite in forage and straw, and was not found in grain.
Metabolite M-X was found as a minor metabolite in the study conducted with the safener mefenpyr-diethyl, but it was not detected in the studies with the safener cloquintocet-mexyl. Although metabolite M-X was not definitively identified, it was characterised by mass- spectrometry as a downstream metabolite of M2. Based on the low % TRR levels in each commodity (≤5% TRR including bound/conjugated material), it can be concluded that the route of formation of M-X is a minor metabolic pathway.
As the main metabolic pathways of pinoxaden are the same with both safeners, it can be concluded that the safener does not substantially impact the metabolism of pinoxaden in wheat.

Figure A 3: Metabolic pathway of pinoxaden in wheat

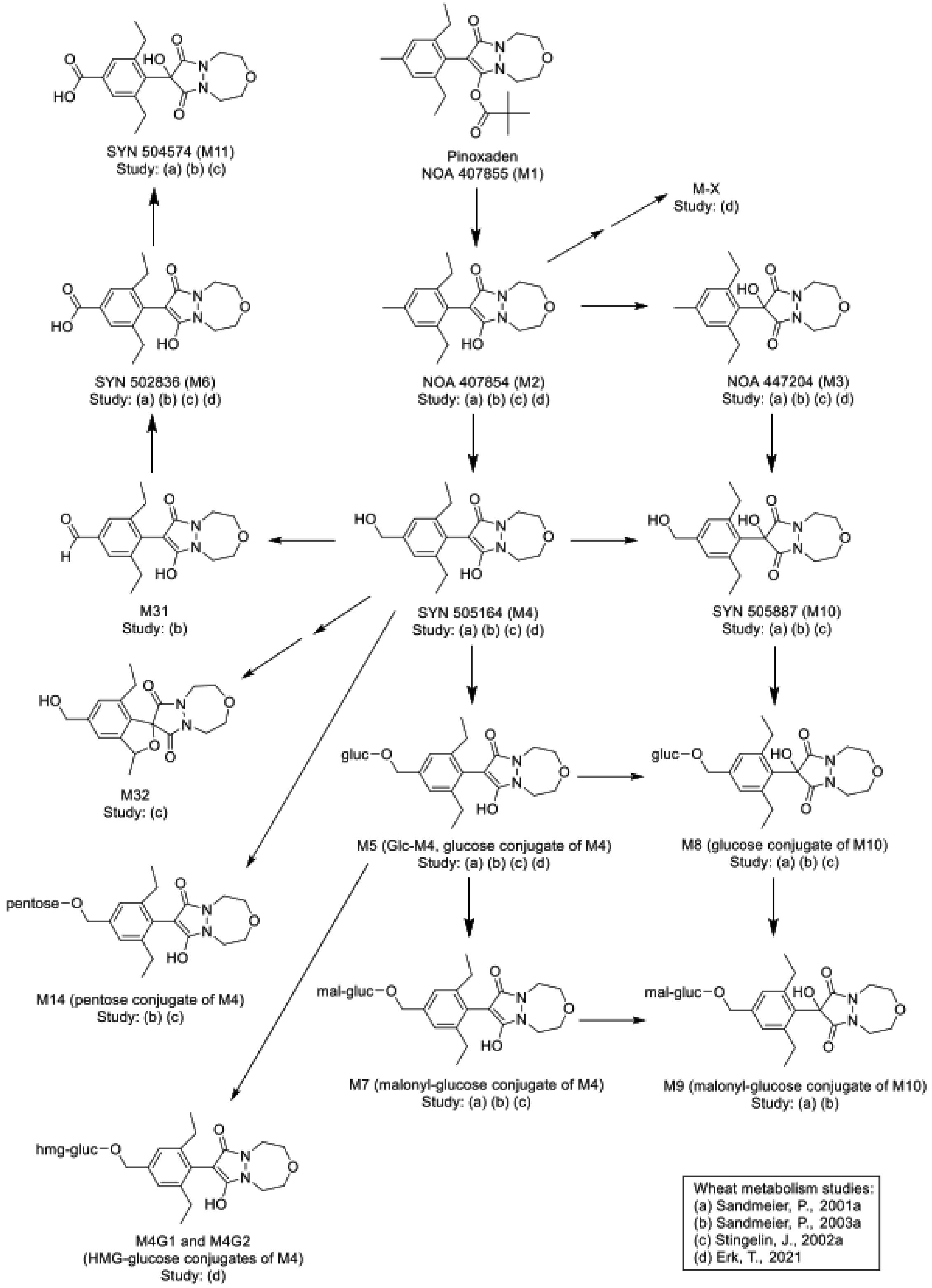


Table A 9: Comparison of metabolite profiles in forage (PHI 7-14 days) after application of pinoxaden to wheat

Study reference		**Sandmeier, P., 2001a**		**Sandmeier, P., 2003a**		**Stingelin, J., 2002a**		**Stingelin, J., 2002a**		**Erk, T., 2021**		**Erk, T., 2021**	
Radiolabel position		**[14C-pyrazol]**		**[14C-phenyl]**		**[14C-phenyl]**		**[14C-oxadiazepine]**		**[14C-phenyl]**		**[14C-phenyl]**	
Safener		**Cloquintocet-mexyl**		**Cloquintocet-mexyl**		**Cloquintocet-mexyl**		**Cloquintocet-mexyl**		**Mefenpyr-diethyl**		**Mefenpyr-diethyl**	
Treatment timing		**BBCH 13**		**BBCH 49**		**BBCH 37-39**		**BBCH 37-39**		**BBCH 39**		**BBCH 39**	
Sample/timing		**Forage, PHI 14 d – solvent extracts**		**Forage, – solvent**	**PHI 7 d extracts**	**– solvent**	**extracts**	**Forage, PHI 7 d – solvent extracts**		**Forage, – solvent**	**PHI 7 d extracts**	**Forage, PHI 7 d – after hydrolysis**	
Compound		**% TRR**	**mg/kg**	**% TRR**	**mg/kg**	**% TRR**	**mg/kg**	**% TRR**	**mg/kg**	**% TRR**	**mg/kg**	**% TRR**	**mg/kg**
Pinoxaden (M1)	Free	4.0	0.0123	1.0	0.019	0.4	0.004	1.7	0.033	n.d.	n.d.	n.d.	n.d.
NOA407854 (M2)	Free	5.4	0.0165	1.8	0.035	0.8	0.008	1.8	0.035	1.7	0.045	1.7	0.045
	Bound/conjugated	-	-	-	-	-	-	-	-	-	-	3.3(7)	0.089(7)
	Total	*5.4*	*0.0165*	*1.8*	*0.035*	*0.8*	*0.008*	*1.8*	*0.035*	*1.7*	*0.045*	*5.0*	*0.134*
NOA447204 (M3)	Free	5.7	0.0173	1.3	0.026	1.7	0.017	3.7	0.072	6.8	0.182	6.8	0.182
	Bound/conjugated	-	-	-	-	-	-	-	-	-	-	<0.1(8)	0.001(8)
	Total	*5.7*	*0.0173*	*1.3*	*0.026*	*1.7*	*0.017*	*3.7*	*0.072*	*6.8*	*0.182*	*6.8*	*0.183*
SYN505164 (M4)	Free	**25.6**	**0.0779**	**43.4**	**0.847**	**30.5**	**0.311**	**52.2**	**1.017**	**30.0**	**0.807**	**30.0**	**0.807**
	Bound/conjugated	**20.9(1)**	**0.0636(1)**	**33.1(1)**	**0.645(1)**	**43.6(4)**	**0.446(4)**	**26.7(5)**	**0.520(5)**	**31.5(6)**	**0.846(6)**	**40.4(9)**	**1.084(9)**
	Total	***46.5***	***0.1415***	***76.5***	***1.492***	***74.1***	***0.757***	***78.9***	***1.537***	***61.5***	***1.653***	***70.4***	***1.892***
SYN502836 (M6)	Free	3.4	0.0105	7.5	0.147	8.2	0.084	6.6	0.129	4.8	0.129	4.8	0.129
	Bound/conjugated	-	-	-	-	-	-	-	-	-	-	2.2(10)	0.059(10)
	Total	*3.4*	*0.0105*	*7.5*	*0.147*	*8.2*	*0.084*	*6.6*	*0.129*	*4.8*	*0.129*	*7.0*	*0.188*
SYN505887 (M10)	Free	n.d.	n.d.	0.6	0.011	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
	Conjugated	4.7(2)	0.0143(2)	0.9(3)	0.017(3)	-	-	2.2(3)	0.043(3)	-	-	-	-
	Total	*4.7*	*0.0143*	*1.5*	*0.028*	*n.d.*	*n.d.*	*2.2*	*0.043*	*n.d.*	*n.d.*	*n.d.*	*n.d.*
SYN504574 (M11)	Free	0.9	0.0027	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
M-X	Free	-	-	-	-	-	-	-	-	3.6	0.096	3.6	0.096
	Bound/conjugated	-	-	-	-	-	-	-	-	-	-	0.2(11)	0.005(11)
	Total	-	-	-	-	-	-	-	-	*3.6*	*0.096*	*3.8*	*0.101*
Unextractable (PES)		11.1	0.0337	2.2	0.042	5.9	0.061	4.3	0.084	4.1	0.109	0.9(12)	0.023(12)
TRR			**0.304**		**1.950**		**1.021**		**1.948**		**2.686**		**2.686**

n.d. not detected

(1) Value includes M5 (glucose conjugate of M4) and M7 (malonyl-glucose conjugate of M4)

(2) Value includes M8 (glucose conjugate of M10) and M9 (malonyl-glucose conjugate of M10)

(3) Value includes M8 (glucose conjugate of M10)

(4) Value includes M5 (glucose conjugate of M4), M7 (malonyl-glucose conjugate of M4) and M14 (pentose conjugate of M4)

(5) Value includes M5 (glucose conjugate of M4) and M14 (pentose conjugate of M4)

(6) Value includes M5 (Glc-M4, glucose conjugate of M4)

(7) Value includes unidentified conjugates in conventional solvent extracts which converted to M2 in the final hydrolysed extract, and M2 released from the PES after acid, base and cellulase hydrolysis

(8) Value includes M3 released from the PES after acid, base and cellulase hydrolysis

(9) Value includes M5 (Glc-M4, glucose conjugate of M4), M4G1 (HMG-glucose conjugate of M4), M4G2 (HMG-glucose conjugate of M4) and other unidentified conjugates in conventional solvent extracts and PES which converted to M4 after acid, base and cellulase hydrolysis

(10) Value includes unidentified conjugates in conventional solvent extracts which converted to M6 in the final hydrolysed extract, and M6 released from the PES after acid, base and cellulase hydrolysis

(11) Value includes M-X released from the PES after acid, base and cellulase hydrolysis

(12) Post extraction solids remaining after exhaustive extraction

Table A 10: Comparison of metabolite profiles in forage or hay (PHI 28-42 days) after application of pinoxaden to wheat

Study reference		**(a) Sandmeier, P., 2001a**		**(b) Sandmeier, P., 2003a**		**(c) Stingelin, J., 2002a**		**(d) Erk, T., 2021**		**(d) Erk, T., 2021**	
Radiolabel position		**[^{14}C-pyrazol]**		**[^{14}C-phenyl]**		**[^{14}C-oxadiazepine]**		**[^{14}C-phenyl]**		**[^{14}C-phenyl]**	
Safener		**Cloquintocet-mexyl**		**Cloquintocet-mexyl**		**Cloquintocet-mexyl**		**Mefenpyr-diethyl**		**Mefenpyr-diethyl**	
Treatment timing		**BBCH 13**		**BBCH 49**		**BBCH 37-39**		**BBCH 39**		**BBCH 39**	
Sample/timing		**Forage, PHI 42 d – solvent extracts**		**Forage, PHI 28 d – solvent extracts**		**Forage, PHI 28 d – solvent extracts**		**Hay, PHI 28 d – solvent extracts**		**Hay, PHI 28 d – after hydrolysis**	
Compound		**% TRR**	**mg/kg**	**% TRR**	**mg/kg**	**% TRR**	**mg/kg**	**% TRR**	**mg/kg**	**% TRR**	**mg/kg**
Pinoxaden (M1)	Free	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
NOA407854 (M2)	Free	1.4	0.0015	n.d.	n.d.	n.d.	n.d.	1.0	0.034	1.0	0.034
	Bound/conjugated	-	-	-	-	-	-	-	-	2.8[6]	0.094[6]
	Total	*1.4*	*0.0015*	*n.d.*	*n.d.*	*n.d.*	*n.d.*	*1.0*	*0.034*	*3.8*	*0.127*
NOA447204 (M3)	Free	3.0	0.0033	0.2	0.005	0.7	0.008	2.3	0.077	2.3	0.077
	Bound/conjugated	-	-	-	-	-	-	-	-	0.1[7]	0.005[7]
	Total	*3.0*	*0.0033*	*0.2*	*0.005*	*0.7*	*0.008*	*2.3*	*0.077*	*2.4*	*0.082*
SYN505164 (M4)	Free	9.3	0.0101	7.3	0.176	5.6	0.068	8.2	0.278	8.2	0.278
	Bound/conjugated	**40.0[1]**	**0.0437[1]**	**60.2[1]**	**1.443[1]**	**70.2[4]**	**0.851[4]**	**36.4[5]**	**1.228[5]**	**46.5[8]**	**1.569[8]**
	Total	***49.3***	***0.0538***	***67.5***	***1.619***	***75.8***	***0.919***	***44.6***	***1.506***	***54.7***	***1.847***
SYN502836 (M6)	Free	4.5	0.0049	8.4	0.201	7.4	0.090	8.8	0.296	8.8	0.296
	Bound/conjugated	-	-	-	-	-	-	-	-	0.5[9]	0.017[9]
	Total	*4.5*	*0.0049*	*8.4*	*0.201*	*7.4*	*0.090*	*8.8*	*0.296*	*9.3*	*0.313*
SYN505887 (M10)	Free	n.d.	n.d.	0.4	0.010	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
	Conjugated	**18.4[2]**	**0.0201[2]**	1.6[2]	0.039[2]	2.4[3]	0.029[3]	-	-	-	-
	Total	***18.4***	***0.0201***	*2.0*	*0.049*	*2.4*	*0.029*	*n.d.*	*n.d.*	*n.d.*	*n.d.*
SYN504574 (M11)	Free	0.5	0.0005	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
M-X	Free	-	-	-	-	-	-	2.6	0.089	2.6	0.089
	Bound/conjugated	-	-	-	-	-	-	-	-	1.5[10]	0.051[10]
	Total	-	-	-	-	-	-	*2.6*	*0.089*	*4.1*	*0.140*
Unextractable (PES)		12.8	0.0140	7.1	0.170	5.2	0.063	19.6	0.662	3.3[11]	0.110[11]
TRR			**0.109**		**2.396**		**1.211**		**3.374**		**3.374**

n.d. not detected

[1] Value includes M5 (glucose conjugate of M4) and M7 (malonyl-glucose conjugate of M4)

[2] Value includes M8 (glucose conjugate of M10) and M9 (malonyl-glucose conjugate of M10)

[3] Value includes M8 (glucose conjugate of M10)

(4) Value includes M5 (glucose conjugate of M4), M7 (malonyl-glucose conjugate of M4) and M14 (pentose conjugate of M4)

(5) Value includes M5 (Glc-M4, glucose conjugate of M4) and M4G2 (HMG-glucose conjugate of M4)

(6) Value includes unidentified conjugates in conventional solvent extracts which converted to M2 in the final hydrolysed extract, and M2 released from the PES after acid, base and cellulase hydrolysis

(7) Value includes M3 released from the PES after acid, base and cellulase hydrolysis

(8) Value includes M5 (Glc-M4, glucose conjugate of M4), M4G1 (HMG-glucose conjugate of M4), M4G2 (HMG-glucose conjugate of M4) and other unidentified conjugates in conventional solvent extracts and PES which converted to M4 after acid, base and cellulase hydrolysis

(9) Value includes unidentified conjugates in conventional solvent extracts which converted to M6 in the final hydrolysed extract, and M6 released from the PES after acid, base and cellulase hydrolysis

(10) Value includes M-X released from the PES after acid, base and cellulase hydrolysis

(11) Post extraction solids remaining after exhaustive extraction

Table A 11: Comparison of metabolite profiles in mature grain (PHI 48-67 days) after application of pinoxaden to wheat

Study reference		**(b) Sandmeier, P., 2003a**		**(c) Stingelin, J., 2002a**		**(c) Stingelin, J., 2002a**		**(d) Erk, T., 2021**		**(d) Erk, T., 2021**	
Radiolabel position		**[^{14}C-phenyl]**		**[^{14}C-phenyl]**		**[^{14}C-oxadiazepine]**		**[^{14}C-phenyl]**		**[^{14}C-phenyl]**	
Safener		**Cloquintocet-mexyl**		**Cloquintocet-mexyl**		**Cloquintocet-mexyl**		**Mefenpyr-diethyl**		**Mefenpyr-diethyl**	
Treatment timing		**BBCH 49**		**BBCH 37-39**		**BBCH 37-39**		**BBCH 39**		**BBCH 39**	
Sample/timing		**Grain, PHI 55 d – solvent extracts**		**Grain, PHI 67 d – solvent extracts**		**Grain, PHI 67 – solvent extracts**		**Grain, PHI 48 d – solvent extracts**		**Grain, PHI 48 d – after hydrolysis**	
Compound		**% TRR**	**mg/kg**	**% TRR**	**mg/kg**	**% TRR**	**mg/kg**	**% TRR**	**mg/kg**	**% TRR**	**mg/kg**
Pinoxaden (M1)	Free	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
NOA407854 (M2)	Free	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	<0.1	<0.001
	Bound/conjugated	-	-	-	-	-	-	-	-	0.6[3]	0.004[3]
	Total	*n.d.*	*n.d.*	*n.d.*	*n.d.*	*n.d.*	*n.d.*	*n.d.*	*n.d.*	*0.6*	*0.004*
NOA447204 (M3)	Free	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	<0.1	<0.001
	Bound/conjugated	-	-	-	-	-	-	-	-	0.8[4]	0.005[4]
	Total	*n.d.*	*n.d.*	*n.d.*	*n.d.*	*n.d.*	*n.d.*	*n.d.*	*n.d.*	*0.8*	*0.005*
SYN505164 (M4)	Free	**19.7**	**0.048**	9.4	0.013	7.7	0.013	**17.3**	**0.109**	**17.3**	**0.109**
	Bound/conjugated	9.4[1]	0.024[1]	**19.3[1]**	**0.027[1]**	**20.0[1]**	**0.033[1]**	**31.8[2]**	**0.199[2]**	**60.2[5]**	**0.379[5]**
	Total	***29.1***	***0.072***	***28.7***	***0.040***	***27.7***	***0.046***	***49.1***	***0.308***	***77.5***	***0.488***
SYN502836 (M6)	Free	9.6	0.024	**12.0**	**0.017**	**13.6**	**0.022**	7.8	0.049	7.8	0.049
	Bound/conjugated	-	-	-	-	-	-	-	-	2.7[6]	0.017[6]
	Total	*9.6*	*0.024*	***12.0***	***0.017***	***13.6***	***0.022***	*7.8*	*0.049*	***10.5***	***0.066***
SYN505887 (M10)	Free	0.7	0.002	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
	Conjugated	-	-	-	-	-	-	-	-	-	-
	Total	*0.7*	*0.002*	*n.d.*	*n.d.*	*n.d.*	*n.d.*	*n.d.*	*n.d.*	*n.d.*	*n.d.*
M-X	Free	-	-	-	-	-	-	2.3	0.014	2.3	0.014
	Bound/conjugated	-	-	-	-	-	-	-	-	2.7[7]	0.017[7]
	Total	-	-	-	-	-	-	*2.3*	*0.014*	*5.0*	*0.031*
Unextractable (PES)		45.9	0.113	21.8	0.031	18.7	0.031	12.7	0.080	1.3[8]	0.008[8]
TRR			**0.246**		**0.142**		**0.165**		**0.630**		**0.630**

n.d. not detected

(1) Value includes M5 (glucose conjugate of M4) and M7 (malonyl-glucose conjugate of M4)

(2) Value includes M5 (Glc-M4, glucose conjugate of M4), M4G1 (HMG-glucose conjugate of M4) and M4G2 (HMG-glucose conjugate of M4)

(3) Value includes unidentified conjugates in conventional solvent extracts which converted to M2 in the final hydrolysed extract, and M2 released from the PES after acid, base and cellulase hydrolysis

(4) Value includes M3 released from the PES after acid, base and cellulase hydrolysis

(5) Value includes M5 (Glc-M4, glucose conjugate of M4), M4G1 (HMG-glucose conjugate of M4), M4G2 (HMG-glucose conjugate of M4) and other unidentified conjugates in conventional solvent extracts and PES which converted to M4 after acid, base and cellulase hydrolysis

(6) Value includes unidentified conjugates in conventional solvent extracts which converted to M6 in the final hydrolysed extract, and M6 released from the PES after acid, base and cellulase hydrolysis

(7) Value includes M-X released from the PES after acid, base and cellulase hydrolysis

(8) Post extraction solids remaining after exhaustive extraction

Table A 12: Comparison of metabolite profiles after acid hydrolysis of mature grain (PHI 55-67 days) after application of pinoxaden to wheat

	Study reference	**(b) Sandmeier, P., 2003a**		**(c) Stingelin, J., 2002a**		**(c) Stingelin, J., 2002a**	
	Radiolabel position	**[^{14}C-phenyl]**		**[^{14}C-phenyl]**		**[^{14}C-oxadiazepine]**	
	Safener	**Cloquintocet-mexyl**		**Cloquintocet-mexyl**		**Cloquintocet-mexyl**	
	Treatment timing	**BBCH 49**		**BBCH 37-39**		**BBCH 37-39**	
	Sample/timing	**Grain, PHI 55 d - 1M HCl reflux hydrolysis**		**Grain, PHI 67 d - 1M HCl reflux hydrolysis**		**Grain, PHI 67 d - 1M HCl reflux hydrolysis**	
Compound		**% TRR**	**mg/kg**	**% TRR**	**mg/kg**	**% TRR**	**mg/kg**
Pinoxaden (M1)	Free						
SYN505164 (M4)	Free	**79.3**	**0.195**	**58.5**	**0.083**	**65.0**	**0.107**
	Bound/conjugated	1.9(1)	0.005(1)	-	-	7.4(1)	0.012(1)
	Total	***81.2***	***0.200***	***58.5***	***0.083***	***72.4***	***0.119***
SYN502836 (M6)	Free	**10.6**	**0.026**	6.8	0.010	**11.5**	**0.019**
	Bound/conjugated	-	-	-	-	-	-
	Total	***10.6***	***0.026***	*6.8*	*0.010*	***11.5***	***0.019***
SYN505887 (M10)	Free	n.d.	n.d.				
	Conjugated	-	-				
	Total	*n.d.*	*n.d.*				
Unextractable (PES)		n.d.	n.d.	7.6	0.011	5.1	0.008
TRR			**0.246**		**0.142**		**0.165**

n.d. not detected
(1) M5 (glucose conjugate of M4) remaining after 1M HCl reflux hydrolysis

Table A 13: Comparison of metabolite profiles in mature straw (PHI 48-264 days) after application of pinoxaden to wheat

	Study reference	(a) Sandmeier, P., 2001a		(b) Sandmeier, P., 2003a		(c) Stingelin, J., 2002a		(c) Stingelin, J., 2002a		(d) Erk, T., 2021		(d) Erk, T., 2021	
	Radiolabel position	**[^{14}C-pyrazol]**		**[^{14}C-phenyl]**		**[^{14}C-phenyl]**		**[^{14}C-oxadiazepine]**		**[^{14}C-phenyl]**		**[^{14}C-phenyl]**	
	Safener	**Cloquintocet-mexyl**		**Cloquintocet-mexyl**		**Cloquintocet-mexyl**		**Cloquintocet-mexyl**		**Mefenpyr-diethyl**		**Mefenpyr-diethyl**	
	Treatment timing	**BBCH 13**		**BBCH 49**		**BBCH 37-39**		**BBCH 37-39**		**BBCH 39**		**BBCH 39**	
	Sample/timing	**Straw, PHI 264 d – solvent extracts**		**Straw PHI 55 d – solvent extracts**		**Straw, PHI 67 d – solvent extracts**		**Straw, PHI 67 d – solvent extracts**		**Straw PHI 48 d – solvent extracts**		**Straw PHI 48 d – after hydrolysis**	
Compound		**% TRR**	**mg/kg**	**% TRR**	**mg/kg**	**% TRR**	**mg/kg**	**% TRR**	**mg/kg**	**% TRR**	**mg/kg**	**% TRR**	**mg/kg**
Pinoxaden (M1)	Free	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
NOA407854 (M2)	Free	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	0.7	0.034	0.7	0.034
	Bound/conjugated	-	-	-	-	-	-	-	-	-	-	3.4(6)	0.172(6)
	Total	*n.d.*	*n.d.*	*n.d.*	*n.d.*	*n.d.*	*n.d.*	*n.d.*	*n.d.*	*0.7*	*0.034*	*4.1*	*0.206*
NOA447204 (M3)	Free	11.1	0.0040	1.5	0.083	7.9	0.072	4.4	0.057	1.5	0.075	1.5	0.075
	Bound/conjugated	-	-	-	-	-	-	-	-	-	-	0.1(7)	0.006(7)
	Total	*11.1*	*0.0040*	*1.5*	*0.083*	*7.9*	*0.072*	*4.4*	*0.057*	*1.5*	*0.075*	*1.6*	*0.081*
SYN505164 (M4)	Free	3.4	0.0012	**36.8**	**2.021**	**36.5**	**0.331**	**34.0**	**0.441**	**26.7**	**1.330**	**26.7**	**1.330**
	Bound/conjugated	-	-	6.6(2)	0.363(2)	5.0(4)	0.046(4)	3.2(4)	0.042(4)	**7.5(5)**	**0.374(5)**	**16.0(8)**	**0.800(8)**
	Total	*3.4*	*0.0012*	***43.4***	***2.384***	***41.5***	***0.377***	***37.2***	***0.483***	***34.2***	***1.704***	***42.7***	***2.130***
SYN502836 (M6)	Free	n.d.	n.d.	3.2	0.173	8.7	0.079	9.2	0.119	1.2	0.061	1.2	0.061
	Bound/conjugated	-	-	-	-	-	-	-	-	-	-	4.0(9)	0.200(9)
	Total	*n.d.*	*n.d.*	*3.2*	*0.173*	*8.7*	*0.079*	*9.2*	*0.119*	*1.2*	*0.061*	*5.2*	*0.262*
SYN505887 (M10)	Free	14.2	0.0051	**12.8**	**0.701**	2.4	0.022	1.5	0.019	n.d.	n.d.	n.d.	n.d.
	Conjugated	5.4(1)	0.0020(1)	2.3(3)	0.126(3)	-	-	-	-	-	-	-	-
	Total	*19.6*	*0.0071*	***15.1***	***0.827***	*2.4*	*0.022*	*1.5*	*0.019*	*n.d.*	*n.d.*	*n.d.*	*n.d.*
SYN504574 (M11)	Free	2.5	0.009	1.9	0.102	2.8	0.025	0.8	0.010	n.d.	n.d.	n.d.	n.d.
M31	Free	-	-	1.7	0.094	-	-	-	-	n.d.	n.d.	n.d.	n.d.
M32	Free	-	-	-	-	-	-	0.7	0.009	n.d.	n.d.	n.d.	n.d.
M-X	Free	-	-	-	-	-	-	-	-	3.3	0.163	3.3	0.163
	Bound/conjugated	-	-	-	-	-	-	-	-	-	-	1.6(10)	0.080(10)
	Total	-	-	-	-	-	-	-	-	*3.3*	*0.163*	*4.9*	*0.244*
Unextractable (PES)		35.1	0.0126	17.0	0.933	22.2	0.201	27.8	0.360	23.2	1.156	4.7(11)	0.236(11)
TRR			**0.036**		**5.491**		**0.908**		**1.296**		**5.177**		**4.986**

n.d. not detected

(1) Value includes M8 (glucose conjugate of M10) and M9 (malonyl-glucose conjugate of M10)

(2) Value includes M5 (glucose conjugate of M4), M7 (malonyl-glucose conjugate of M4) and M14 (pentose conjugate of M4)

(3) Value includes M8 (glucose conjugate of M10)

(4) Value includes M5 (glucose conjugate of M4) and M14 (pentose conjugate of M4)

(5) Value includes M5 (Glc-M4, glucose conjugate of M4) and M4G2 (HMG-glucose conjugate of M4)

(6) Value includes unidentified conjugates in conventional solvent extracts which converted to M2 in the final hydrolysed extract, and M2 released from the PES after acid, base and cellulase hydrolysis

(7) Value includes M3 released from the PES after acid, base and cellulase hydrolysis

(8) Value includes M5 (Glc-M4, glucose conjugate of M4), M4G1 (HMG-glucose conjugate of M4), M4G2 (HMG-glucose conjugate of M4) and other unidentified conjugates in conventional solvent extracts and PES which converted to M4 after acid, base and cellulase hydrolysis

(9) Value includes unidentified conjugates in conventional solvent extracts which converted to M6 in the final hydrolysed extract, and M6 released from the PES after acid, base and cellulase hydrolysis

(10) Value includes M-X released from the PES after acid, base and cellulase hydrolysis

(11) Post extraction solids remaining after exhaustive extraction

A 2.2.2.2 Nature of residues in livestock

No new data submitted.

A 2.2.3 Magnitude of residues in plants

A 2.2.3.1 Winter wheat

Table A 14: 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)
cGAP EU (UK, 2006; EFSA, 2013)	1	0.060 kg a.s./ha	-	39	n.a.
Intended cGAP (number 2)	1	0.060 kg a.s./ha	-	39	n.a.

* Use number(s) in accordance with the list of all intended GAPs in Part B, Section 0
n.a.: not applicable, the PHI is covered by the time remaining between application and harvest

A 2.2.3.2 Nature of residues in livestock

No new data submitted.

~~A 2.2.4 Magnitude of residues in plants~~

~~A 2.2.4.1 Winter wheat~~

~~Table A 15: 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)~~
~~cGAP EU (Austria, 2011; France, 2011)~~	~~1~~	~~0.090 kg a.s./ha~~	~~-~~	~~39~~	~~n.a.~~
~~Intended cGAP (number 2)~~	~~1~~	~~0.035 kg a.s./ha~~	~~-~~	~~39~~	~~n.a.~~

~~* Use number(s) in accordance with the list of all intended GAPs in Part B, Section 0~~
~~n.a.: not applicable, the PHI is covered by the time remaining between application and harvest~~

A 2.2.4.1.1 Study AB2-19-38159 (wheat, NEU)

Comments of zRMS:	Six residue trials were conducted in Northern Europe to determine the magnitude of residues of pinoxaden metabolites (M4 and M6), expressed separately and their sum as pinoxaden, mesosulfuron-methyl (parent only), mefenpyr-diethyl and metabolite 1-(2,4-dichlorophenyl)-5-methyl-pyrazole-3-carboxylic acid (AE F094270) expressed as mefenpyr-diethyl in raw agricultural commodity specimens of winter wheat (RAC whole plant, grain and straw) after one application of AG-PM1-72 OD. Target application rate was 1.0 L/ha, representing 60 g/ha pinoxaden, 12 g/ha mesosulfuronmethyl and 35 g/ha mefenpyr-diethyl. Applications were placed at BBCH 39 (flag leaf stage). Three different analytical methods for pinoxaden, mesosulfuron-methyl and mefenpyr-diethyl were fully validated according to SANTE/2020/12830, rev. 1. Limit of quantification (LOQ) achieved was 0.01 mg/kg for grain and 0.02 mg/kg for whole plant and straw for pinoxaden metabolite M4, 0.01 mg/kg for grain and straw and 0.02 mg/kg for whole plant for pinoxaden metabolite M6 and 0.02 mg/kg for grain, 0.03 mg/kg for straw and 0.04 mg/kg for whole plant for the sum of M4 and M6 expressed as pinoxaden. The results are given as M4 or M6 and as their sum expressed as pinoxaden. Limit of quantification (LOQ) for mesosulfuron-methyl achieved was 0.01 mg/kg for all matrices. The results are given as mesosulfuron-methyl. Limit of quantification (LOQ) for mefenpyr-diethyl achieved was 0.01 mg/kg for all matrices. The results are expressed as mefenpyr-diethyl. The mean recoveries at each fortification level comply with the standard acceptance criteria of the guidance document SANTE/2020/12830, rev. 1. No residue of all analytes were found above LOQ in any untreated specimen. <u>Results:</u> For the sum of pinoxaden metabolites M4 and M6 expressed as pinoxaden, at harvest residues found in grain were between 0.031 and 0.065 mg/kg and between 0.145 and 0.958 mg/kg in straw. For mesosulfuron-methyl, at harvest no residues were found in grain and straw. For mefenpyr-diethyl, the residues found in whole plant were between 0.36 and 0.78 mg/kg just after application. No residues were found in whole plant, grain and straw for the other samplings. For metabolite 1-(2,4-dichlorophenyl)-5-methyl-pyrazole-3-carboxylic acid expressed as mefenpyrdiethyl, at harvest no residues were found in grain and the residues in straw were between 0.025 to 0.079 mg/kg. The storage of samples is covered by the storage stability data in wheat grain and straw. The study is acceptable.

Reference:	KCP 8/01 (KCA 6.3.1)
Report	Magnitude of the residue of pinoxaden metabolites, mesosulfuron-methyl, mefenpyr-diethyl and its metabolite following one application of AG-PM1-72 OD in winter wheat in 6 trials (4 DCS + 2 HS), Northern Europe (Poland, Germany and France) – 2019, Bahnhardt, A., 2020 Report no. AB2-19-38159; ADAMA reference 000102607
Guideline(s):	General Recommendations for the Design, Preparation and Realization of Residue Trials (SANCO 7029/VI/95 rev.5, 22 July 1997). OECD Guideline for the Testing of Chemicals on Crop Field Trial (TG 509 published on 7 September 2009). Guidance for Generating and Reporting Methods of Analysis in Support of Pre-Registration Data Requirements (SANCO/3029/99 rev.4, 11 July 2000). OECD (2007): Guidance Document on Pesticide Residue Analytical Methods ENV/JM/MONO(2007)17.
Deviations:	No
GLP:	Yes
Acceptability:	Yes

Table A 16: Summary of the study AB2-19-38159 trials

Active Substance:	Pinoxaden	**Commercial Product:**	AG-PM1-72 OD
Crop:	Winter wheat	**Producer:**	ADAMA AGAN Ltd., Ashod, Israel
Responsible for reporting:	STAPHYT GmbH – 74572 Blaufelden, Germany		
Country:	Poland, Germany, Northern France	**Indoor/glasshouse/outdoor:**	Outdoor
Content of as (actual):	59.1 g/L	**Other a.s. in formulation:**	mesosulfuron-methyl, mefenpyr-diethyl
Formulation:	OD	**Residue calculated as:**	Pinoxaden metabolites M4 and M6 and sum expressed as pinoxaden

1	2	3	4	5			6	7	8	9			10	11
Location	**Commodity Variety**	**Date of 1-Sowing 2-Flowering 3-Harvest**	**Method of Treatment**	**Application Rate per Treatment**			**Date of Treatment**	**BBCH Crop Growth Stage at Treatment**	**Portions analysed**	**Residues (mg/kg)**			**PHI (days)**	**Remarks**
				kg as/ha	**Water (L/ha)**	**kg (as/hl)**				**M4**	**M6**	**Sum****		
Poland Łódzkie 99-440 Wiskienica Dolna Trial number AB2-19- 38159 PL01	Winter wheat Arkadia	1- 04.10.2018 2- 28.05.2019 to 12.06.2019 3- 27.07.2019	Foliar broadcast application	T1 0.061	T1 205	T1 0.030	T1 13.05.2019	T1 39	T1 Whole plant	T1 <LOQ (nd)	T1 <LOQ (nd)	T1 <LOQ (nd)	T1 0	Analytical method involved extraction of pinoxaden metabolites M4 and M6 free and conjugates together with a mix spiking from homogenised laboratory samples by hydrolysis with 1 N hydrochloric acid under reflux for two hours. Then, extracts were purified by solid/liquid purification, before quantification with LC-MS/MS. Method fully validated in a separate report (Sponsor reference: 000102680).
									Whole plant	0.020	<LOQ (nd)	<LOQ	14	
									Whole plant	0.029	<LOQ	0.058	30	
									Whole plant	<LOQ	<LOQ	0.047	60	
									Grain	<LOQ	<LOQ (nd)	<LOQ	74	
									Straw	0.031	<LOQ (nd)	0.037	74	
				T2* 0.060	T2* 202	T2* 0.030	T2* 13.05.2019	T2* 39	T2* Whole plant	T2* <LOQ (nd)	T2* <LOQ (nd)	T2* <LOQ (nd)	T2* 0	LOQ: 0.01 mg/kg (for grain (M4 and M6) and straw (M6) 0.02 mg/kg for straw (M4) , whole plant (M4 and M6) and sum of grain. 0.03 mg/kg for sum of straw 0.04 mg/kg for sum of whole plant
									Whole plant	0.22***	0.041	0.312	14	
									Whole plant	0.13	0.024	0.184	30	Untreated specimens were all <LOQ (nd)
									Whole plant	0.10	0.028	0.153	60	Max. Storage Interval between sampling and analysis: 217 days (M4), 216 days (M6)
									Grain	0.022	<LOQ	0.038	74	Max. Storage Interval between extraction and analysis: 3 days (M4), 2 days (M6)
									Straw	0.21***	0.014	0.269	74	

1	2	3	4	5			6	7	8	9			10	11
Location	**Commodity Variety**	**Date of 1-Sowing 2-Flowering 3-Harvest**	**Method of Treatment**	**Application Rate per Treatment**			**Date of Treatment**	**BBCH Crop Growth Stage at Treatment**	**Portions analysed**	**Residues (mg/kg)**			**PHI (days)**	**Remarks**
				kg as/ha	**Water (L/ha)**	**kg (as/hl)**				**M4**	**M6**	**Sum****		
Germany Thuringia 04617 Dobraschütz Trial number AB2-19- 38159 DE02	Winter wheat Patras	1- 10.10.2018 2- 11.06.2019 to 19.06.2019 3- 24.07.2019	Foliar broadcast application	T1 0.059	T1 201	T1 0.029	T1 24.05.2019	T1 39	T1 Whole plant	T1 0.021	T1 <LOQ (nd)	T1 <LOQ	T1 0	Analytical method involved extraction of pinoxaden metabolites M4 and M6 free and conjugates together with a mix spiking from homogenised laboratory samples by hydrolysis with 1 N hydrochloric acid under reflux for two hours. Then, extracts were purified by solid/liquid purification, before quantification with LC-MS/MS. Method fully validated in a separate report (Sponsor reference: 000102680). LOQ: 0.01 mg/kg (for grain (M4 and M6) and straw (M6) 0.02 mg/kg for straw (M4) , whole plant (M4 and M6) and sum of grain. 0.03 mg/kg for sum of straw 0.04 mg/kg for sum of whole plant Untreated specimens were all <LOQ (nd) Max. Storage Interval between sampling and analysis: 21720 days (M4), 219 days (M6) Max. Storage Interval between extraction and analysis: 3 days (M4), 2 days (M6)
									Whole plant	0.061	<LOQ	0.097	14	
									Whole plant	0.047	<LOQ	0.080	31	
									Grain	<LOQ	<LOQ (nd)	<LOQ	60	
									Straw	0.13***	<LOQ	0.168	60	
				T2* 0.060	T2* 203	T2* 0.030	T2* 24.05.2019	T2* 39	T2* Whole plant	T2* 0.12***	T2* <LOQ (nd)	T2* 0.145	T2* 0	
									Whole plant	0.49	0.060	0.660 0.369	14	
									Whole plant	0.27	0.038		31	
									Grain	0.044	<LOQ	0.065	60	
									Straw	0.61	0.037***	0.778	60	

1	2	3	4	5			6	7	8	9			10	11
Location	**Commodity Variety**	**Date of 1-Sowing 2-Flowering 3-Harvest**	**Method of Treatment**	**Application Rate per Treatment**			**Date of Treatment**	**BBCH Crop Growth Stage at Treatment**	**Portions analysed**	**Residues (mg/kg)**			**PHI (days)**	**Remarks**
				kg as/ha	**Water (L/ha)**	**kg (as/hl)**				**M4**	**M6**	**Sum****		
Northern France Grand Est 08360 Saint Fergeux Trial number AB2-19-38159 FR03	Winter wheat Syllon	1- 15.10.2018 2- 31.05.2019 to 07.06.2019 3- 21.07.2019	Foliar broadcast application	T1 0.061	T1 205	T1 0.030	T1 14.05.2019	T1 39	T1 Whole plant	T1 0.079***	T1 <LOQ (nd)	T1 0.095	T1 0	Analytical method involved extraction of pinoxaden metabolites M4 and M6 free and conjugates together with a mix spiking from homogenised laboratory samples by hydrolysis with 1 N hydrochloric acid under reflux for two hours. Then, extracts were purified by solid/liquid purification, before quantification with LC-MS/MS. Method fully validated in a separate report (Sponsor reference: 000102680). LOQ: 0.01 mg/kg (for grain (M4 and M6) and straw (M6) 0.02 mg/kg for straw (M4) , whole plant (M4 and M6) and sum of grain. 0.03 mg/kg for sum of straw 0.04 mg/kg for sum of whole plant Untreated specimens were all <LOQ (nd) Max. Storage Interval between sampling and analysis: 220 days (M4), 219 days (M6) Max. Storage Interval between extraction and analysis: 3 days (M4), 2 days (M6)
									Whole plant	0.10	<LOQ	0.144	14	
									Whole plant	0.073	<LOQ	0.111	30	
									Whole plant	0.060	<LOQ	0.095	59	
									Grain	<LOQ	<LOQ (nd)	<LOQ	70	
									Straw	0.22***	<LOQ	0.277	70	
				T2* 0.061	T2* 205	T2* 0.030	T2* 14.05.2019	T2* 39	T2* Whole plant	T2* 0.13***	T2* <LOQ (nd)	T2* 0.157	T2* 0	
									Whole plant	0.40	0.040	0.528	14	
									Whole plant	0.30	0.029	0.395	30	
									Whole plant	0.25	0.043	0.351	59	
									Grain	0.024	<LOQ	0.040	70	
									Straw	0.77	0.026	0.958	70	

1	2	3	4	5			6	7	8	9			10	11
Location	**Commodity Variety**	**Date of 1-Sowing 2-Flowering 3-Harvest**	**Method of Treatment**	**Application Rate per Treatment**			**Date of Treatment**	**BBCH Crop Growth Stage at Treatment**	**Portions analysed**	**Residues (mg/kg)**			**PHI (days)**	**Remarks**
				kg as/ha	**Water (L/ha)**	**kg (as/hl)**				**M4**	**M6**	**Sum****		
Poland Wielkopolska 62-105 Werkowo Trial number AB2-19- 38159 PL04	Winter wheat Arkadia	1- 25.09.2018 2- 04.06.2019 to 17.06.2019 3- 24.07.2019	Foliar broadcast application	T1 0.056	T1 189	T1 0.030	T1 20.05.2019	T1 39	T1 Whole plant Whole plant Whole plant Whole plant Grain Straw	T1 0.033 0.023 <LOQ <LOQ (nd) <LOQ 0.033	T1 <LOQ <LOQ <LOQ (nd) <LOQ <LOQ (nd) <LOQ	T1 0.063 0.051 <LOQ <LOQ <LOQ 0.051	T1 0 14 30 58 65 65	Analytical method involved extraction of pinoxaden metabolites M4 and M6 free and conjugates together with a mix spiking from homogenised laboratory samples by hydrolysis with 1 N hydrochloric acid under reflux for two hours. Then, extracts were purified by solid/liquid purification, before quantification with LC-MS/MS. Method fully validated in a separate report (Sponsor reference: 000102680). LOQ: 0.01 mg/kg (for grain (M4 and M6) and straw (M6) 0.02 mg/kg for straw (M4) , whole plant (M4 and M6) and sum of grain. 0.03 mg/kg for sum of straw 0.04 mg/kg for sum of whole plant Untreated specimens were all <LOQ (nd) Max. Storage Interval between sampling and analysis: 219 days (M4), 218 days (M6) Max. Storage Interval between extraction and analysis: 4 days (M4), 2 days (M6)
				T2* 0.061	T2* 207	T2* 0.029	T2* 20.05.2019	T2* 39	T2* Whole plant Whole plant Whole plant Whole plant Grain Straw	T2* 0.13*** 0.18 0.12 0.052 0.034 0.17***	T2* <LOQ 0.069*** 0.024 0.034 <LOQ 0.015	T2* 0.180 0.297 0.172 0.102 0.053 0.222	T2* 0 14 30 58 65 65	

1	2	3	4	5			6	7	8	9			10	11
Location	**Commodity Variety**	**Date of 1-Sowing 2-Flowering 3-Harvest**	**Method of Treatment**	**Application Rate per Treatment**			**Date of Treatment**	**BBCH Crop Growth Stage at Treatment**	**Portions analysed**	**Residues (mg/kg)**			**PHI (days)**	**Remarks**
				kg as/ha	**Water (L/ha)**	**kg (as/hl)**				**M4**	**M6**	**Sum****		
Germany Schleswig-Holstein 24364 Holzdorf Trial number AB2-19- 38159 DE05	Winter wheat Colonia	1- 11.10.2018 2- 02.07.2019 to 16.07.2019 3- 12.08.2019	Foliar broadcast application	T1 0.064	T1 217	T1 0.029	T1 20.05.2019	T1 39	T1 Grain Straw	T2** <LOQ 0.030	T2** <LOQ (nd) <LOQ	T2** <LOQ 0.048	T1 87 87	Analytical method involved extraction of pinoxaden metabolites M4 and M6 free and conjugates together with a mix spiking from homogenised laboratory samples by hydrolysis with 1 N hydrochloric acid under reflux for two hours. Then, extracts were purified by solid/liquid purification, before quantification with LC-MS/MS. Method fully validated in a separate report (Sponsor reference: 000102680). LOQ: 0.01 mg/kg (for grain (M4 and M6) and straw (M6) 0.02 mg/kg for straw (M4) , whole plant (M4 and M6) and sum of grain. 0.03 mg/kg for sum of straw 0.04 mg/kg for sum of whole plant Untreated specimens were all <LOQ (nd) Max. Storage Interval between sampling and analysis: 197 days (M4), 196 days (M6) Max. Storage Interval between extraction and analysis: 2 days (M4), 2 days (M6)
				T2* 0.061	T2* 207	T2* 0.029	T2* 20.05.2019	T2* 39	T2* Grain Straw	T2* 0.026 0.11***	T2* <LOQ (nd) 0.011	T2* 0.031 0.145	T2* 87 87	

1	2	3	4	5			6	7	8	9			10	11
Location	**Commodity Variety**	**Date of 1-Sowing 2-Flowering 3-Harvest**	**Method of Treatment**	**Application Rate per Treatment**			**Date of Treatment**	**BBCH Crop Growth Stage at Treatment**	**Portions analysed**	**Residues (mg/kg)**			**PHI (days)**	**Remarks**
				kg as/ha	**Water (L/ha)**	**kg (as/hl)**				**M4**	**M6**	**Sum****		
Northern France Pays de la Loire 49260 Vaudelnay Trial number AB2-19- 38159 FR06	Winter wheat Apache	1- 05.10.2018 2- 05.05.2019 to 17.05.2019 3- 14.07.2019	Foliar broadcast application	T1 0.060	T1 203	T1 0.030	T1 29.04.2019	T1 39	T1 Grain Straw	T1 <LOQ 0.047	T1 <LOQ (nd) <LOQ	T1 <LOQ 0.068	T1 70 70	Analytical method involved extraction of pinoxaden metabolites M4 and M6 free and conjugates together with a mix spiking from homogenised laboratory samples by hydrolysis with 1 N hydrochloric acid under reflux for two hours. Then, extracts were purified by solid/liquid purification, before quantification with LC-MS/MS. Method fully validated in a separate report (Sponsor reference: 000102680). LOQ: 0.01 mg/kg (for grain (M4 and M6) and straw (M6) 0.02 mg/kg for straw (M4) , whole plant (M4 and M6) and sum of grain. 0.03 mg/kg for sum of straw 0.04 mg/kg for sum of whole plant Untreated specimens were all <LOQ (nd) Max. Storage Interval between sampling and analysis: 235 days (M4), 234 days (M6) Max. Storage Interval between extraction and analysis: 2 days (M4), 1 day (M6)
				T2* 0.061	T2* 207	T2* 0.029	T2* 29.04.2019	T2* 39	T2* Grain Straw	T2* 0.021 0.15***	T2* <LOQ <LOQ	T2* 0.037 0.192	T2* 70 70	

*On plot T2, the adjuvant Adigor was added at the rate of 1% of the spray volume (representing 2 L/ha)
**Sum of metabolites is calculated as pinoxaden = Residue of M4 x 400.5 / 332.39 + Residues of M6 x 400.5 / 346.4
***Mean of two injections

A 2.2.4.1.1 Study DMC-20-42727 (wheat, NEU)

Comments of zRMS:	Two residue trials were conducted in Northern Europe to determine the magnitude of residues of pinoxaden metabolites (M4 and M6), expressed separately and their sum as pinoxaden, mesosulfuron-methyl (parent only), mefenpyr-diethyl and its metabolite 1-(2,4-dichlorophenyl)-5-methyl-pyrazole-3-carboxylic acid expressed as mefenpyr-diethyl in raw agricultural commodity specimens of winter wheat (RAC grain and straw) after one application of ADM.06001.H.2.B. Application was done on two plots with one treatment involving the use of an adjuvant, Adigor. Target application rate was 1.0 L/ha, representing 60 g/ha pinoxaden, 12 g/ha mesosulfuronmethyl and 35 g/ha mefenpyr-diethyl. Applications were placed at BBCH 39 (flag leaf stage). Three different analytical methods for pinoxaden, mesosulfuron-methyl and efenpyr-diethyl were fully validated according to SANTE/2020/12830, rev. 1. For pinoxaden metabolite M4 the limit of quantification (LOQ) achieved was 0.01 mg/kg for grain and 0.02 mg/kg for straw. For pinoxaden metabolite M6, the LOQ was 0.01 mg/kg for grain and straw. For the sum of M4 and M6 expressed as pinoxaden, the LOQ was 0.024 mg/kg for grain, 0.036 mg/kg for straw. The results are given as M4 or M6 and as their sum expressed as pinoxaden. Limit of quantification (LOQ) for mesosulfuron-methyl achieved was 0.01 mg/kg for all matrices. The results are given as mesosulfuron-methyl. Limit of quantification (LOQ) for mefenpyr-diethyl achieved was 0.01 mg/kg for all matrices. The results are expressed as mefenpyr-diethyl. No residue of all analytes were found above LOQ in any untreated specimen. The mean recoveries at each fortification level comply with the standard acceptance criteria of the guidance document SANTE/2020/12830, rev. 1. <u>Results:</u> - for pinoxaden metabolites, the sum of M4 and M6 residues expressed as pinoxaden found at harvest were between below LOQ and 0.071 mg/kg in grain and between 0.068 and 0.33 mg/kg in straw. - for mesosulfuron-methyl, no residues were found in grain and the residues in straw were found below LOQ (0.01 mg/kg). - for Mefenpyr-diethyl, no residues were found in grain and straw. - for metabolite 1-(2,4-dichlorophenyl)-5-methyl-pyrazole-3-carboxylic acid expressed as mefenpyr-diethyl, the residues found in grain specimens were below LOQ (0.01 mg/kg) and the residues in straw specimens were between 0.018 and 0.064 mg/kg. The storage of samples is covered by the storage stability data in wheat grain and straw. The study is acceptable.

Reference: KCP 8/02 (KCA 6.3.1)

Report: Magnitude of the residue of pinoxaden metabolites, mesosulfuron-methyl, mefenpyr-diethyl and its metabolite following one application of ADM.06001.H.2.B in winter wheat in 2 trials (2 HS, one with process), Northern Europe (France and Poland) – 2020
Meric, D., 2021
Report no. DMC-20-42727; ADAMA reference 000105437

Guideline(s): General Recommendations for the Design, Preparation and Realization of Residue Trials (SANCO 7029/VI/95 rev.5, 22 July 1997).
OECD Guideline for the Testing of Chemicals on Crop Field Trial (TG 509 published on 7 September 2009).
Guidance for Generating and Reporting Methods of Analysis in Support of Pre-Registration Data Requirements (SANCO/3029/99 rev.4, 11 July 2000).

	OECD (2007): Guidance Document on Pesticide Residue Analytical Methods ENV/JM/MONO(2007)17.
Deviations:	No
GLP:	Yes
Acceptability:	Yes

Table A 17: Summary of the study DMC-20-42727 trials

Active Substance:	Pinoxaden	**Commercial Product:**	ADM.06001.H.2.B
Crop:	Winter wheat	**Producer:**	ADAMA AGAN Ltd., Ashod, Israel
Responsible for reporting:	STAPHYT GmbH – 74572 Blaufelden, Germany		
Country:	Poland, Northern France	**Indoor/glasshouse/outdoor:**	Outdoor
Content of as (actual):	61.6 g/L	**Other a.s. in formulation:**	mesosulfuron-methyl, mefenpyr-diethyl
Formulation:	OD	**Residue calculated as:**	Pinoxaden metabolites M4 and M6 and sum expressed as pinoxaden

1	2	3	4	5			6	7	8	9			10	11
Location	**Commodity Variety**	**Date of 1-Sowing 2-Flowering 3-Harvest**	**Method of Treatment**	**Application Rate per Treatment**			**Date of Treatment**	**BBCH Crop Growth Stage at Treatment**	**Portions analysed**	**Residues (mg/kg)**			**PHI (days)**	**Remarks**
				kg as/ha	**Water (L/ha)**	**kg (as/hl)**				**M4**	**M6**	**Sum**		
Northern France Grand Est 08360 Saint Fergeux Trial number DMC-20-42747 FR01	Winter wheat Mutic	1- 05.11.2019 2- 20.05.2020 to 05.06.2020 3- 24.07.2020	Foliar broadcast application	T1 0.013	T1 160	T1 0.008	T1 06.05.2020	T1 39	T1 Grain Straw	T1 0.012 0.066	T1 <LOQ 0.012	T1 0.026 0.094	T1 82 82	Analytical method consisted in an extraction of pinoxaden metabolites M4 and M6 free and conjugates with a mix spiking from homogenised laboratory samples by hydrolysis with 1 N hydrochloric acid. Extracts purified by solid/liquid purification, before quantification with LC-MS/MS. Method fully validated in a separate report B19G-A4-P-05 (Sponsor reference: 000102680) and in this study.
				T2* 0.013	T2* 160	T2* 0.008	T2* 06.05.2020	T2* 39	T2* Grain Straw	T2* 0.012 0.23	T2* 0.012 0.041	T2* <u>0.071</u> <u>0.33</u>	T2* 82 82	LOQ: 0.01 mg/kg for grain (M4 & M6) and straw (M6), 0.02 mg/kg for straw (M4). Sum of M4 and M6 expressed as pinoxaden: 0.024 mg/kg for grain and 0.036 mg/kg for straw LOD: 0.003 mg/kg for grain (M4 & M6) and straw (M6), 0.006 mg/kg for straw (M4) Sum of M4 and M6 expressed as pinoxaden: 0.007 mg/kg for grain and 0.011 mg/kg for straw Untreated specimens were all <LOD Max. Storage Interval between sampling and analysis: 157 days (M4 and M6). Max. Storage Interval between extraction and analysis: 5 days (M4) and 7 days (M6).

1	2	3	4	5			6	7	8	9			10	11
Location	**Commodity Variety**	**Date of 1-Sowing 2-Flowering 3-Harvest**	**Method of Treatment**	**Application Rate per Treatment**			**Date of Treatment**	**BBCH Crop Growth Stage at Treatment**	**Portions analysed**	**Residues (mg/kg)**			**PHI (days)**	**Remarks**
				kg as/ha	**Water (L/ha)**	**kg (as/hl)**				**M4**	**M6**	**Sum**		
Poland Wielkopolska 63-233 Lukaszewo Trial number DMC-20-42747 PL01	Winter wheat Sailor	1- 27.0.2019 2- 03.06.2020 to 12.06.2020 3- 30.07.2020	Foliar broadcast application	T1 0.012	T1 153	T1 0.008	T1 14.05.2020	T1 39	T1 Grain Straw	T1 <LOQ 0.049	T1 <LOQ (nd) <LOQ	T1 <LOQ 0.071	T1 82 82	Analytical method consisted in an extraction of pinoxaden metabolites M4 and M6 free and conjugates with a mix spiking from homogenised laboratory samples by hydrolysis with 1 N hydrochloric acid. Extracts purified by solid/liquid purification, before quantification with LC-MS/MS. Method fully validated in a separate report B19G-A4-P-05 (Sponsor reference: 000102680) and in this study. LOQ: 0.01 mg/kg for grain (M4 & M6) and straw (M6), 0.02 mg/kg for straw (M4). Sum of M4 and M6 expressed as pinoxaden: 0.024 mg/kg for grain and 0.036 mg/kg for straw LOD: 0.003 mg/kg for grain (M4 & M6) and straw (M6), 0.006 mg/kg for straw (M4) Sum of M4 and M6 expressed as pinoxaden: 0.007 mg/kg for grain and 0.011 mg/kg for straw Untreated specimens were all <LOD Max. Storage Interval between sampling and analysis: 154 days (M4 and M6). Max. Storage Interval between extraction and analysis: 3 days (M4) and 14 days (M6).
				T2* 0.012	T2* 150	T2* 0.008	T2* 14.05.2020	T2* 39	T2* Grain Straw	T2* 0.023 0.027	T2* <LOQ 0.030	T2* 0.039 0.068	T2* 77 77	

*On plot T2, the adjuvant Adigor was added at the rate of 1% of the spray volume (representing 1 L/ha)

A 2.3 Mefenpyr-diethyl

A 2.3.1 Stability of residues

A 2.3.1.1 Stability of residues during storage of samples

A 2.3.1.1.1 Study B19S-A4-M-04

Comments of zRMS:	This is interim report. Mefenpyr-diethyl and metabolite AE F094270 are stable for 12 months at -18°C in wheat grain. The study is acceptable.

Reference:	KCP 8/05 (KCA 6.1/01)
Report	Interim Report (12 Months). Freezing storage stability of mefenpyr-diethyl and its metabolite in wheat (whole plant, grain, straw) at/below -18°C during 18 months (0, 1, 3, 6, 9, 12, 15 and 18 months)., Lefresne, S., 2021 Report no. B19S-A4-M-04; ADAMA reference 000102682
Guideline(s):	OECD Guideline for the Testing of Chemicals – Stability of Pesticide Residues in Stored Commodities (TG 506 published on 16 October 2007). Guidance Document on Pesticide Residue Analytical Methods, ENV/JM/MONO(2007)17 Guidance for Generating and Reporting Methods of Analysis in Support of Pre-Registration Data Requirements (SANCO/3029/99 rev.4, 11 July 2000).
Deviations:	No
GLP:	Yes
Acceptability:	Yes

Materials and methods

Storage stability of mefenpyr-diethyl and its metabolite AE F094270 (1-(2,4-dichlorophenyl)-5-methyl-pyrazole-3-carboxylic acid expressed as mefenpyr-diethyl) in wheat (whole plant, grain, straw) was tested under deep frozen conditions (at/below -18 ºC) over a storage period of 12 months.

For each matrix and each reference item, a minimum of 66 samples were prepared, 32 samples were kept as control sample with addition of 200 µL acetonitrile, the 34 remaining samples were fortified with mefenpyr-diethyl or metabolite 1 AE F094270 at 0.10 mg/kg with addition of 200 µL of a 1 mg/L standard solution of mefenpyr-diethyl or metabolite AE F094270. All sample containers were stored in a freezer at about -18°C.

For each reference item and each matrix, after a storage period of 0, 1, 3, 6, 9 and 12 months, two (or three in the case of day-0) samples fortified at 0.10 mg/kg and two control samples were removed from the freezer for analysis. One control sample was freshly fortified at 0.10 mg/kg and used as procedural recovery. This freshly fortified control was analysed together with the second control and with the two or three aged fortified samples. Control samples used for procedural recoveries were handled and stored in the same way and for the same time periods as the analytical sample extracts that were prepared within the same analytical set.

Samples were analysed using a QuEChERS-method (FREDON Pays de la Loire/GIRPA study code: B19S-A4-M-01 - Sponsor reference: 000102679). Residues of mefenpyr-diethyl and AE F094270 were extracted from homogenised specimens by maceration with acetonitrile acidified with 0.2M sulphuric acid and water. Then, extracts were purified by dispersive solid phase extraction. Quantification was performed by liquid chromatography with tandem mass spectrometry detection (LC-MS/MS). In order to ensure unambiguous identification, two mass transitions were monitored for each reference item. Full method validation is reported in Section B5 (KCP 5.1.2-03).

The LOQ was 0.01 mg/kg for both, mefenpyr-diethyl and its metabolite AE F094270 expressed as mefenpyr-diethyl.

Results and discussions

Residues in the control samples used for fortification were always below 30% of the LOQ.

After a deep-freezer storage period of about 12 months, the mean recovery rates of mefenpyr-diethyl and its metabolite AE F094270 from stored samples ranged between 75-78% and 76-80%, respectively, in whole plant, between 84-94% and 86%, respectively in grain, and between 66-73% and 75%, respectively, in straw.

Concurrent recoveries determined from freshly fortified samples were in the range of 70% - 110%.

Altogether, the study results demonstrate that residues of mefenpyr-diethyl and its metabolite AE F094270 are stable in the tested plant commodities for 12 months under deep-freezer storage conditions.

Table A 18: Summary of concurrent recoveries of mefenpyr-diethyl and its metabolite AE F094270 in wheat matrices

Matrix	Spike level (mg/kg)	Storage Interval (days)	Sample size (n)	Individual procedural recoveries (%)	Mean ± std dev
Mefenpyr-diethyl					
Wheat whole plant	0.10	0	4(1)	78, 82, 89, 86	84 ± 4.78
		32	1	75	75
		88	1	70	70
		178	1	85	85
		274	1	75	75
		364	1	75	75
Wheat grain	0.10	0	4(1)	70, 71, 74, 74	72 ± 2.06
		33	1	83	83
		91	1	102	102
		186	1	86	86
		271	1	98	98
		364	1	109	109
Wheat straw	0.10	0	4(1)	77, 81, 85, 85	82 ± 3.83
		33	1	71	71
		91	1	76	76
		186	1	79	79
		271	1	79	79
		364	1	81	81
AE F094270					
Wheat whole plant	0.10	0	4(1)	96, 100, 92, 95	95 ± 3.30
		28	1	79	79
		86	1	82	82
		177	1	70	70
		273	1	87	87
		364	1	84	84
Wheat grain	0.10	0	4(1)	103, 97, 96, 97	98 ± 3.20
		28	1	74	74
		86	1	78	78

Matrix	Spike level (mg/kg)	Storage Interval (days)	Sample size (n)	Individual procedural recoveries (%)	Mean ± std dev
		177	1	79	79
		273	1	87	87
		364	1	88	88
Wheat straw	0.10	0	4(1)	72, 72, 76, 81	75 ± 4.27
		28	1	71	71
		86	1	84	84
		177	1	74	74
		273	1	85	85
		364	1	81	81

(1) One procedural recovery sample plus three day-0 fortified samples

Table A 19: Stability of mefenpyr-diethyl and its metabolite AE F094270 in wheat matrices following storage at ≤18 C

Matrix	Spike level (mg/kg)	Storage interval (days)	Individual recovered residues (mg/kg) (range plus mean)	Individual recoveries (%) (range plus mean)
Mefenpyr-diethyl				
Wheat whole plant	0.10	0(1)	0.078, 0.082, 0.089, 0.086 (0.084)	78, 82, 89, 86 (84)
		32	0.089, 0.086 (0.088)	89, 86 (88)
		88	0.073, 0.072 (0.073)	73, 72 (73)
		178	0.086, 0.081 (0.083)	86, 81 (83)
		274	0.066, 0.063 (0.065)	66, 63 (65)
		364	0.075, 0.078 (0.076)	75, 78 (76)
Wheat grain	0.10	0(1)	0.070, 0.071, 0.074, 0.074 (0.072)	70, 71, 74, 74 (72)
		33	0.073, 0.079 (0.076)	73, 79 (76)
		91	0.107, 0.0107 (0.107)	107, 107 (107)
		186	0.084, 0.069 (0.076)	84, 69 (76)
		271	0.089, 0.093 (0.091)	89, 93 (91)
		364	0.084, 0.094 (0.089)	84, 94 (89)
Wheat straw	0.10	0(1)	0.077, 0.081, 0.085, 0.085 (0.082)	77, 81, 85, 85 (82)
		33	0.067, 0.067 (0.067)	67, 67 (67)
		91	0.062, 0.064 (0.063)	62, 64 (63)
		186	0.060, 0.069 (0.064)	60, 69 (64)
		271	0.072, 0.069 (0.071)	72, 69 (71)
		364	0.073, 0.066 (0.069)	73, 66 (69)

Matrix	Spike level (mg/kg)	Storage interval (days)	Individual recovered residues (mg/kg) (range plus mean)	Individual recoveries (%) (range plus mean)
AE F094270				
Wheat whole plant	0.10	0(1)	0.096, 0.100, 0.092, 0.095 (0.095)	96, 100, 92, 95 (95)
		28	0.085, 0.086 (0.085)	85, 86 (85)
		86	0.071, 0.086 (0.079)	71, 86 (79)
		177	0.079, 0.084 (0.082)	79, 84 (82)
		273	0.081, 0.085 (0.083)	81, 85 (83)
		364	0.076, 0.080 (0.078)	76, 80 (78)
Wheat grain	0.10	0(1)	0.103, 0.097, 0.096, 0.097 (0.098)	103, 97, 96, 97 (98)
		28	0.086, 0.080 (0.083)	86, 80 (83)
		86	0.075, 0.075 (0.075)	75, 75 (75)
		177	0.093, 0.092 (0.092)	93, 92 (92)
		273	0.093, 0.087 (0.090)	93, 87 (90)
		364	0.086, 0.086 (0.086)	86, 86 (86)
Wheat straw	0.10	0(1)	0.072, 0.072, 0.076, 0.081 (0.075)	72, 72, 76, 81 (75)
		28	0.070, 0.071 (0.071)	70, 71 (71)
		86	0.084, 0.094 (0.089)	84, 94 (89)
		177	0.090 : 0.086 (0.088)	90, 86 (88)
		273	0.083, 0.088 (0.086)	83, 88 (86)
		364	0.075, 0.075 (0.075)	75, 75 (75)

(1) One procedural recovery sample plus three day-0 fortified samples

Conclusion

After a deep-freezer storage period of about 12 months, the mean recovery rates of mefenpyr-diethyl and its metabolite AE F094270 from stored samples ranged between 75-78% and 76-80%, respectively, in whole plant, between 84-94% and 86%, respectively, in grain, and between 66-73% and 75%, respectively, in straw.

Concurrent recoveries determined from freshly fortified samples were in the range of 70% - 110%.

Altogether, the study results demonstrate that residues of mefenpyr-diethyl and its metabolite AE F094270 are stable in the tested plant commodities for 12 months under deep-freezer storage conditions.

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

A 2.3.2.1 Nature of residue in plants

A 2.3.2.1.1 Study AB2-19-38159 (wheat, NEU)

Comments of zRMS:	Six residue trials were conducted in Northern Europe to determine the magnitude of residues of pinoxaden metabolites (M4 and M6), expressed separately and their sum as pinoxaden, mesosulfuron-methyl (parent only), mefenpyr-diethyl and metabolite 1-(2,4-dichlorophenyl)-5-methyl-pyrazole-3-carboxylic acid (AE F094270) expressed as mefenpyr-diethyl in raw agricultural commodity specimens of winter wheat (RAC whole plant, grain and straw) after one application of AG-PM1-72 OD. Target application rate was 1.0 L/ha, representing 60 g/ha pinoxaden, 12 g/ha mesosulfuronmethyl and 35 g/ha mefenpyr-diethyl. Applications were placed at BBCH 39 (flag leaf stage). Three different analytical methods for pinoxaden, mesosulfuron-methyl and mefenpyr-diethyl were fully validated according to SANTE/2020/12830, rev. 1. Limit of quantification (LOQ) achieved was 0.01 mg/kg for grain and 0.02 mg/kg for whole plant and straw for pinoxaden metabolite M4, 0.01 mg/kg for grain and straw and 0.02 mg/kg for whole plant for pinoxaden metabolite M6 and 0.02 mg/kg for grain, 0.03 mg/kg for straw and 0.04 mg/kg for whole plant for the sum of M4 and M6 expressed as pinoxaden. The results are given as M4 or M6 and as their sum expressed as pinoxaden. Limit of quantification (LOQ) for mesosulfuron-methyl achieved was 0.01 mg/kg for all matrices. The results are given as mesosulfuron-methyl. Limit of quantification (LOQ) for mefenpyr-diethyl achieved was 0.01 mg/kg for all matrices. The results are expressed as mefenpyr-diethyl. The mean recoveries at each fortification level comply with the standard acceptance criteria of the guidance document SANTE/2020/12830, rev. 1. No residue of all analytes were found above LOQ in any untreated specimen. Results: For the sum of pinoxaden metabolites M4 and M6 expressed as pinoxaden, at harvest residues found in grain were between 0.031 and 0.065 mg/kg and between 0.145 and 0.958 mg/kg in straw. For mesosulfuron-methyl, at harvest no residues were found in grain and straw. For mefenpyr-diethyl, the residues found in whole plant were between 0.36 and 0.78 mg/kg just after application. No residues were found in whole plant, grain and straw for the other samplings. For metabolite 1-(2,4-dichlorophenyl)-5-methyl-pyrazole-3-carboxylic acid expressed as mefenpyrdiethyl, at harvest no residues were found in grain and the residues in straw were between 0.025 to 0.079 mg/kg. The study is acceptable.

Reference:	KCP 8/01 (KCA 6.3.1)
Report	Magnitude of the residue of pinoxaden metabolites, mesosulfuron-methyl, mefenpyr-diethyl and its metabolite following one application of AG-PM1-72 OD in winter wheat in 6 trials (4 DCS + 2 HS), Northern Europe (Poland, Germany and France) – 2019, Bahnhardt, A., 2020 Report no. AB2-19-38159; ADAMA reference 000102607
Guideline(s):	General Recommendations for the Design, Preparation and Realization of Residue Trials (SANCO 7029/VI/95 rev.5, 22 July 1997). OECD Guideline for the Testing of Chemicals on Crop Field Trial (TG 509 published on 7 September 2009). Guidance for Generating and Reporting Methods of Analysis in Support of Pre-Registration Data Requirements (SANCO/3029/99 rev.4, 11 July 2000). OECD (2007): Guidance Document on Pesticide Residue Analytical Methods ENV/JM/MONO(2007)17.
Deviations:	No

GLP: Yes

Acceptability: Yes

Table A 20: Summary of the study AB2-19-38159 trials

Active Substance:	Mefenpyr-diethyl	**Commercial Product:**	AG-PM1-72 OD
Crop:	Winter wheat	**Producer:**	ADAMA AGAN Ltd., Ashod, Israel
Responsible for reporting:	STAPHYT GmbH – 74572 Blaufelden, Germany		
Country:	Poland, Germany, Northern France	**Indoor/glasshouse/outdoor:**	Outdoor
Content of as (actual):	35.3 g/L	**Other a.s. in formulation:**	mesosulfuron-methyl, pinoxaden
Formulation:	OD	**Residue calculated as:**	Mefenpyr-diethyl and its metabolite 1-(2,4-dichlorophenyl)-5-methyl-pyrazole-3-carboxylic acid expressed as mefenpyr-diethyl (AE F094270)

1	2	3	4	5			6	7	8	9		10	11
Location	**Commodity Variety**	**Date of 1-Sowing 2-Flowering 3-Harvest**	**Method of Treatment**	**Application Rate per Treatment**			**Date of Treatment**	**BBCH Crop Growth Stage at Treatment**	**Portions analysed**	**Residues (mg/kg)**		**PHI (days)**	**Remarks**
				kg as/ha	**Water (L/ha)**	**kg (as/hl)**				**Mefenpyr-diethyl**	**Metabolite AE F094270 (expressed as mefenpyr-diethyl)**		
Poland Łódzkie 99-440 Wiskienica Dolna Trial number AB2-19- 38159 PL01	Winter wheat Arkadia	1- 04.10.2018 2- 28.05.2019 to 12.06.2019 3- 27.07.2019	Foliar broadcast application	T1 0.036	T1 205	T1 0.018	T1 13.05.2019	T1 39	T1 Whole plant	T1 0.54	T1 <LOQ (nd)**	T1 0	Analytical method involved extraction of mefenpyr-diethyl and metabolite 1-(2,4-dichlorophenyl)-5- methyl-pyrazole-3-carboxylic acid expressed as mefenpyr-diethyl from homogenised laboratory samples by maceration with acetonitrile acidified with 0.2M sulphuric acid and water. Then, extracts were purified by dispersive solid phase extraction, before quantification with LC-MS/MS. Method fully validated in a separate report (Sponsor reference: 000102679). LOQ: 0.01 mg/kg for each matrix and analyte Untreated specimens were all <LOQ (nd) Max. Storage Interval between sampling and analysis: 259 days (both analytes) Max. Storage Interval between extraction and analysis: 1 day (both analytes)
									Whole plant	<LOQ (nd)	<LOQ (nd)	14	
									Whole plant	<LOQ (nd)	<LOQ (nd)	30	
									Whole plant	<LOQ (nd)	<LOQ	60	
									Grain	<LOQ (nd)	<LOQ (nd)	74	
									Straw	<LOQ (nd)	0.012	74	
				T2* 0.036	T2* 202	T2* 0.018	T2* 13.05.2019	T2* 39	T2* Whole plant	T2* 0.78	T2* <LOQ (nd)**	T2* 0	
									Whole plant	<LOQ (nd)	<LOQ (nd)	14	
									Whole plant	<LOQ (nd)	<LOQ (nd)	30	
									Whole plant	<LOQ (nd)	0.017	60	
									Grain	<LOQ (nd)	<LOQ	74	
									Straw	<LOQ (nd)	0.063	74	

1	2	3	4	5			6	7	8	9		10	11
Location	**Commodity Variety**	**Date of 1-Sowing 2-Flowering 3-Harvest**	**Method of Treatment**	**Application Rate per Treatment**			**Date of Treatment**	**BBCH Crop Growth Stage at Treatment**	**Portions analysed**	**Residues (mg/kg)**		**PHI (days)**	**Remarks**
				kg as/ha	**Water (L/ha)**	**kg (as/hl)**				**Mefenpyr-diethyl**	**Metabolite AE F094270 (expressed as mefenpyr-diethyl)**		
Germany Thuringia 04617 Dobraschütz Trial number AB2-19- 38159 DE02	Winter wheat Patras	1- 10.10.2018 2- 11.06.2019 to 19.06.2019 3- 24.07.2019	Foliar broadcast application	T1 0.036	T1 201	T1 0.018	T1 24.05.2019	T1 39	T1 Whole plant	T1 0.35	T1 <LOQ (nd)	T1 0	Analytical method involved extraction of mefenpyr-diethyl and metabolite 1-(2,4-dichlorophenyl)-5- methyl-pyrazole-3-carboxylic acid expressed as mefenpyr-diethyl from homogenised laboratory samples by maceration with acetonitrile acidified with 0.2M sulphuric acid and water. Then, extracts were purified by dispersive solid phase extraction, before quantification with LC-MS/MS. Method fully validated in a separate report (Sponsor reference: 000102679). LOQ: 0.01 mg/kg for each matrix and analyte Untreated specimens were all <LOQ (nd) Max. Storage Interval between sampling and analysis: 199 days (both analytes) Max. Storage Interval between extraction and analysis: 3 days (both analytes)
									Whole plant	<LOQ (nd)	<LOQ (nd)	14	
									Whole plant	<LOQ (nd)	<LOQ (nd)	31	
									Grain	<LOQ (nd)	<LOQ (nd)	60	
									Straw	<LOQ (nd)	0.017	60	
				T2* 0.036	T2* 203	T2* 0.018	T2* 24.05.2019	T2* 39	T2* Whole plant	T2* 0.36	T2* <LOQ (nd)	T2* 0	
									Whole plant	<LOQ (nd)	<LOQ	14	
									Whole plant	<LOQ (nd)	<LOQ	31	
									Grain	<LOQ (nd)	<LOQ	60	
									Straw	<LOQ (nd)	0.069	60	

1	2	3	4	5			6	7	8	9		10	11
Location	**Commodity Variety**	**Date of 1-Sowing 2-Flowering 3-Harvest**	**Method of Treatment**	**Application Rate per Treatment**			**Date of Treatment**	**BBCH Crop Growth Stage at Treatment**	**Portions analysed**	**Residues (mg/kg)**		**PHI (days)**	**Remarks**
				kg as/ha	**Water (L/ha)**	**kg (as/hl)**				**Mefenpyr-diethyl**	**Metabolite AE F094270 (expressed as mefenpyr-diethyl)**		
Northern France Grand Est 08360 Saint Fergeux Trial number AB2-19- 38159 FR03	Winter wheat Syllon	1- 15.10.2018 2- 31.05.2019 to 07.06.2019 3- 21.07.2019	Foliar broadcast application	T1 0.036	T1 205	T1 0.018	T1 14.05.2019	T1 39	T1 Whole plant	T1 0.53	T1 <LOQ (nd)**	T1 0	Analytical method involved extraction of mefenpyr-diethyl and metabolite 1-(2,4-dichlorophenyl)-5- methyl-pyrazole-3-carboxylic acid expressed as mefenpyr-diethyl from homogenised laboratory samples by maceration with acetonitrile acidified with 0.2M sulphuric acid and water. Then, extracts were purified by dispersive solid phase extraction, before quantification with LC-MS/MS. Method fully validated in a separate report (Sponsor reference: 000102679). LOQ: 0.01 mg/kg for each matrix and analyte Untreated specimens were all <LOQ (nd) Max. Storage Interval between sampling and analysis: 192 days (both analytes) Max. Storage Interval between extraction and analysis: 1 day (both analytes)
									Whole plant	<LOQ (nd)	<LOQ (nd)	14	
									Whole plant	<LOQ (nd)	<LOQ (nd)	30	
									Whole plant	<LOQ (nd)	<LOQ (nd)	59	
									Grain	<LOQ (nd)	<LOQ (nd)	70	
									Straw	<LOQ (nd)	<LOQ	70	
				T2* 0.036	T2* 205	T2* 0.018	T2* 14.05.2019	T2* 39	T2* Whole plant	T2* 0.61	T2* <LOQ (nd)**	T2* 0	
									Whole plant	<LOQ (nd)	<LOQ	14	
									Whole plant	<LOQ (nd)	<LOQ	30	
									Whole plant	<LOQ (nd)	<LOQ	59	
									Grain	<LOQ (nd)	<LOQ (nd)	70	
									Straw	<LOQ (nd)	0.042	70	

1	2	3	4	5			6	7	8	9		10	11
Location	**Commodity Variety**	**Date of 1-Sowing 2-Flowering 3-Harvest**	**Method of Treatment**	**Application Rate per Treatment**			**Date of Treatment**	**BBCH Crop Growth Stage at Treatment**	**Portions analysed**	**Residues (mg/kg)**		**PHI (days)**	**Remarks**
				kg as/ha	**Water (L/ha)**	**kg (as/hl)**				**Mefenpyr-diethyl**	**Metabolite AE F094270 (expressed as mefenpyr-diethyl)**		
Poland Wielkopolska 62-105 Werkowo	Winter wheat	1- 25.09.2018	Foliar broadcast application	T1	T1	T1	T1	T1	T1	T1	T1	T1	Analytical method involved extraction of mefenpyr-diethyl and metabolite 1-(2,4-dichlorophenyl)-5- methyl-pyrazole-3-carboxylic acid expressed as mefenpyr-diethyl from homogenised laboratory samples by maceration with acetonitrile acidified with 0.2M sulphuric acid and water. Then, extracts were purified by dispersive solid phase extraction, before quantification with LC-MS/MS. Method fully validated in a separate report (Sponsor reference: 000102679).
	Arkadia	2- 04.06.2019 to 17.06.2019		0.033	189	0.017	20.05.2019	39	Whole plant	0.43	<LOQ (nd)**	0	
									Whole plant	<LOQ (nd)	<LOQ	14	
Trial number AB2-19- 38159 PL04		3- 24.07.2019							Whole plant	<LOQ (nd)	<LOQ	30	
									Whole plant	<LOQ (nd)	<LOQ	58	
									Grain	<LOQ (nd)	<LOQ (nd)	65	
									Straw	<LOQ (nd)	0.034	65	
				T2*	T2*	T2*	T2*	T2*	T2*	T2*	T2*	T2*	LOQ: 0.01 mg/kg for each matrix and analyte
				0.036	207	0.017	20.05.2019	39	Whole plant	0.43	<LOQ (nd)**	0	Untreated specimens were all <LOQ (nd)
									Whole plant	<LOQ (nd)	<LOQ	14	
									Whole plant	<LOQ (nd)	<LOQ	30	Max. Storage Interval between sampling and analysis:
									Whole plant	<LOQ (nd)	0.021	58	186 days (both analytes)
									Grain	<LOQ (nd)	<LOQ	65	Max. Storage Interval between extraction and analysis:
									Straw	<LOQ (nd)	0.079	65	1 day (both analytes)

1	2	3	4	5			6	7	8	9		10	11
Location	**Commodity Variety**	**Date of 1-Sowing 2-Flowering 3-Harvest**	**Method of Treatment**	**Application Rate per Treatment**			**Date of Treatment**	**BBCH Crop Growth Stage at Treatment**	**Portions analysed**	**Residues (mg/kg)**		**PHI (days)**	**Remarks**
				kg as/ha	**Water (L/ha)**	**kg (as/hl)**				**Mefenpyr-diethyl**	**Metabolite AE F094270 (expressed as mefenpyr-diethyl)**		
Germany Schleswig-Holstein 24364 Holzdorf Trial number AB2-19- 38159 DE05	Winter wheat Colonia	1- 11.10.2018 2- 02.07.2019 to 16.07.2019 3- 12.08.2019	Foliar broadcast application	T1 0.038	T1 217	T1 0.018	T1 20.05.2019	T1 39	T1 Grain Straw	T1 <LOQ (nd) <LOQ (nd)	T1 <LOQ (nd) 0.030	T1 87 87	Analytical method involved extraction of mefenpyr-diethyl and metabolite 1-(2,4-dichlorophenyl)-5- methyl-pyrazole-3-carboxylic acid expressed as mefenpyr-diethyl from homogenised laboratory samples by maceration with acetonitrile acidified with 0.2M sulphuric acid and water. Then, extracts were purified by dispersive solid phase extraction, before quantification with LC-MS/MS. Method fully validated in a separate report (Sponsor reference: 000102679). LOQ: 0.01 mg/kg for each matrix and analyte Untreated specimens were all <LOQ (nd) Max. Storage Interval between sampling and analysis: 77 days (both analytes) Max. Storage Interval between extraction and analysis: 1 day (both analytes)
				T2* 0.036	T2* 207	T2* 0.017	T2* 20.05.2019	T2* 39	T2* Grain Straw	T2* <LOQ (nd) <LOQ (nd)	T2* <LOQ 0.061	T2* 87 87	

1	2	3	4	5			6	7	8	9		10	11
Location	**Commodity Variety**	**Date of 1-Sowing 2-Flowering 3-Harvest**	**Method of Treatment**	**Application Rate per Treatment**			**Date of Treatment**	**BBCH Crop Growth Stage at Treatment**	**Portions analysed**	**Residues (mg/kg)**		**PHI (days)**	**Remarks**
				kg as/ha	**Water (L/ha)**	**kg (as/hl)**				**Mefenpyr-diethyl**	**Metabolite AE F094270 (expressed as mefenpyr-diethyl)**		
Northern France Pays de la Loire 49260 Vaudelnay Trial number AB2-19- 38159 FR06	Winter wheat Apache	1- 05.10.2018 2- 05.05.2019 to 17.05.2019 3- 14.07.2019	Foliar broadcast application	T1 0.036	T1 203	T1 0.018	T1 29.04.2019	T1 39	T1 Grain Straw	T1 <LOQ (nd) <LOQ (nd)	T1 <LOQ (nd) <LOQ	T1 70 70	Analytical method involved extraction of mefenpyr-diethyl and metabolite 1-(2,4-dichlorophenyl)-5- methyl-pyrazole-3-carboxylic acid expressed as mefenpyr-diethyl from homogenised laboratory samples by maceration with acetonitrile acidified with 0.2M sulphuric acid and water. Then, extracts were purified by dispersive solid phase extraction, before quantification with LC-MS/MS. Method fully validated in a separate report (Sponsor reference: 000102679). LOQ: 0.01 mg/kg for each matrix and analyte Untreated specimens were all <LOQ (nd) Max. Storage Interval between sampling and analysis: 115 days (both analytes) Max. Storage Interval between extraction and analysis: 1 day (both analytes)
				T2* 0.036	T2* 207	T2* 0.018	T2* 29.04.2019	T2* 39	T2* Grain Straw	T2* <u><LOQ (nd)</u> <u><LOQ (nd)</u>	T2* <u><LOQ (nd)</u> <u>0.025</u>	T2* 70 70	

*On T2 plot, the adjuvant Adigor was added at the rate of 1% of the spray volume (representing 2 L/ha)
**Mean of two extractions

A 2.3.2.1.1 Study DMC-20-42727 (wheat, NEU)

Comments of zRMS:	Two residue trials were conducted in Northern Europe to determine the magnitude of residues of pinoxaden metabolites (M4 and M6), expressed separately and their sum as pinoxaden, mesosulfuron-methyl (parent only), mefenpyr-diethyl and its metabolite 1-(2,4-dichlorophenyl)-5-methyl-pyrazole-3-carboxylic acid expressed as mefenpyr-diethyl in raw agricultural commodity specimens of winter wheat (RAC grain and straw) after one application of ADM.06001.H.2.B. Application was done on two plots with one treatment involving the use of an adjuvant, Adigor. Target application rate was 1.0 L/ha, representing 60 g/ha pinoxaden, 12 g/ha mesosulfuronmethyl and 35 g/ha mefenpyr-diethyl. Applications were placed at BBCH 39 (flag leaf stage). Three different analytical methods for pinoxaden, mesosulfuron-methyl and efenpyr-diethyl were fully validated according to SANTE/2020/12830, rev. 1. For pinoxaden metabolite M4 the limit of quantification (LOQ) achieved was 0.01 mg/kg for grain and 0.02 mg/kg for straw. For pinoxaden metabolite M6, the LOQ was 0.01 mg/kg for grain and straw. For the sum of M4 and M6 expressed as pinoxaden, the LOQ was 0.024 mg/kg for grain, 0.036 mg/kg for straw. The results are given as M4 or M6 and as their sum expressed as pinoxaden. Limit of quantification (LOQ) for mesosulfuron-methyl achieved was 0.01 mg/kg for all matrices. The results are given as mesosulfuron-methyl. Limit of quantification (LOQ) for mefenpyr-diethyl achieved was 0.01 mg/kg for all matrices. The results are expressed as mefenpyr-diethyl. No residue of all analytes were found above LOQ in any untreated specimen. The mean recoveries at each fortification level comply with the standard acceptance criteria of the guidance document SANTE/2020/12830, rev. 1. <u>Results:</u> - for pinoxaden metabolites, the sum of M4 and M6 residues expressed as pinoxaden found at harvest were between below LOQ and 0.071 mg/kg in grain and between 0.068 and 0.33 mg/kg in straw. - for mesosulfuron-methyl, no residues were found in grain and the residues in straw were found below LOQ (0.01 mg/kg). - for Mefenpyr-diethyl, no residues were found in grain and straw. - for metabolite 1-(2,4-dichlorophenyl)-5-methyl-pyrazole-3-carboxylic acid expressed as mefenpyr-diethyl, the residues found in grain specimens were below LOQ (0.01 mg/kg) and the residues in straw specimens were between 0.018 and 0.064 mg/kg. The study is acceptable.

Reference: KCP 8/02 (KCA 6.3.1)

Report: Magnitude of the residue of pinoxaden metabolites, mesosulfuron-methyl, mefenpyr-diethyl and its metabolite following one application of ADM.06001.H.2.B in winter wheat in 2 trials (2 HS, one with process), Northern Europe (France and Poland) – 2020
Meric, D., 2021
Report no. DMC-20-42727; ADAMA reference 000105437

Guideline(s): General Recommendations for the Design, Preparation and Realization of Residue Trials (SANCO 7029/VI/95 rev.5, 22 July 1997).
OECD Guideline for the Testing of Chemicals on Crop Field Trial (TG 509 published on 7 September 2009).
Guidance for Generating and Reporting Methods of Analysis in Support of Pre-Registration Data Requirements (SANCO/3029/99 rev.4, 11 July 2000).
OECD (2007): Guidance Document on Pesticide Residue Analytical Methods ENV/JM/MONO(2007)17.

Deviations:	No
GLP:	Yes
Acceptability:	Yes

Table A 21: Summary of the study DMC-20-42727 trials

Active Substance:	Mefenpyr-diethyl	**Commercial Product:**	ADM.06001.H.2.B
Crop:	Winter wheat	**Producer:**	ADAMA AGAN Ltd., Ashod, Israel
Responsible for reporting:	STAPHYT GmbH – 74572 Blaufelden, Germany		
Country:	Poland, Northern France	**Indoor/glasshouse/outdoor:**	Outdoor
Content of as (actual):	36.6 g/L	**Other a.s. in formulation:**	pinoxaden, mesosulfuron-methyl
Formulation:	OD	**Residue calculated as:**	mefenpyr-diethyl and its metabolite 1-(2,4-dichlorophenyl)-5-

1	2	3	4	5			6	7	8	9		10	11
Location	**Commodity Variety**	**Date of 1-Sowing 2-Flowering 3-Harvest**	**Method of Treatment**	**Application Rate per Treatment**			**Date of Treatment**	**BBCH Crop Growth Stage at Treatment**	**Portions analysed**	**Residues (mg/kg)**		**PHI (days)**	**Remarks**
				kg as/ha	**Water (L/ha)**	**kg (as/hl)**				**Mefenpyr-diethyl**	**Metabolite Metabolite AE F094270 (expressed as mefenpyr-diethyl)**		
Northern France Grand Est 08360 Saint Fergeux Trial number DMC-20-42747 FR01	Winter wheat Mutic	1- 05.11.2019 2- 20.05.2020 to 05.06.2020 3- 24.07.2020	Foliar broadcast application	T1 0.013	T1 160	T1 0.008	T1 06.05.2020	T1 39	T1 Grain Straw	T1 <LOQ (nd) <LOQ (nd)	T1 <LOQ (nd) 0.018	T1 82 82	Analytical method involved extraction of mefenpyr-diethyl and metabolite 1-(2,4-dichlorophenyl)-5- methyl-pyrazole-3-carboxylic acid expressed as mefenpyr-diethyl from homogenised laboratory samples by maceration with acetonitrile acidified with 0.2M sulphuric acid and water. Then, extracts were purified by dispersive solid phase extraction, before quantification with LC-MS/MS. Method fully validated in a separate report (Sponsor reference: 000102679). LOQ: 0.01 mg/kg for each matrix and analyte Untreated specimens were all <LOQ (nd) Max. Storage Interval between sampling and analysis: 33 days (both analytes) Max. Storage Interval between extraction and analysis: 1 day (both analytes)
				T2* 0.013	T2* 160	T2* 0.008	T2* 06.05.2020	T2* 39	T2* Grain Straw	T2* <LOQ (nd) <LOQ (nd)	T2* <LOQ (nd) 0.059	T2* 82 82	

1	2	3	4	5			6	7	8	9		10	11
Location	**Commodity Variety**	**Date of 1-Sowing 2-Flowering 3-Harvest**	**Method of Treatment**	**Application Rate per Treatment**			**Date of Treatment**	**BBCH Crop Growth Stage at Treatment**	**Portions analysed**	**Residues (mg/kg)**		**PHI (days)**	**Remarks**
				kg as/ha	**Water (L/ha)**	**kg (as/hl)**				**Mefenpyr-diethyl**	**Metabolite Metabolite AE F094270 (expressed as mefenpyr-diethyl)**		
Poland Wielkopolska 63-233 Lukaszewo Trial number DMC-20-42747 PL01	Winter wheat Sailor	1- 27.0.2019 2- 03.06.2020 to 12.06.2020 3- 30.07.2020	Foliar broadcast application	T1 0.012	T1 153	T1 0.008	T1 14.05.2020	T1 39	T1 Grain Straw	T1 <LOQ (nd) <LOQ (nd)	T1 <LOQ (nd) 0.018	T1 77 77	Analytical method involved extraction of mefenpyr-diethyl and metabolite 1-(2,4-dichlorophenyl)-5- methyl-pyrazole-3-carboxylic acid expressed as mefenpyr-diethyl from homogenised laboratory samples by maceration with acetonitrile acidified with 0.2M sulphuric acid and water. Then, extracts were purified by dispersive solid phase extraction, before quantification with LC-MS/MS. Method fully validated in a separate report (Sponsor reference: 000102679). LOQ: 0.01 mg/kg for each matrix and analyte Untreated specimens were all <LOQ (nd) Max. Storage Interval between sampling and analysis: 30 days (both analytes) Max. Storage Interval between extraction and analysis: 1 day (both analytes)
				T2* 0.012	T2* 150	T2* 0.008	T2* 14.05.2020	T2* 39	T2* Grain Straw	T2* <LOQ (nd) <LOQ (nd)	T2* <LOQ 0.064	T2* 77 77	

*On plot T2, the adjuvant Adigor was added at the rate of 1% of the spray volume (representing 1 L/ha)

Appendix 3 Pesticide Residue Intake Model (PRIMo rev. 3.1)

A 3.1 TMDI calculations

Mesosulfuron-methyl

European Food Safety Authority

EFSA PRIMo revision 3.1; 2019/03/19

Mesosulfuron-methyl

LOQs (mg/kg) range from:		to:	
Toxicological reference values			
ADI (mg/kg bw/day):	1	ARfD (mg/kg bw):	**calculation with ADI (no ARfD was inserted)**
Source of ADI:	EFSA	Source of ARfD:	
Year of evaluation:	2016	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)
0.0019	NL toddler	1.90	0.0012	Milk: Cattle	0.0001	Apples	0.0001	Maize/corn		
0.0010	UK infant	1.03	0.0008	Milk: Cattle	0.0000	Potatoes	0.0000	Eggs: Chicken		
0.0010	NL child	0.97	0.0005	Milk: Cattle	0.0001	Sugar beet roots	0.0001	Apples		
0.0009	FR toddler 2 3 yr	0.90	0.0006	Milk: Cattle	0.0000	Apples	0.0000	Wheat		
0.0009	DE child	0.87	0.0004	Milk: Cattle	0.0001	Apples	0.0000	Wheat		
0.0008	FR child 3 15 yr	0.84	0.0005	Milk: Cattle	0.0000	Wheat	0.0000	Sugar beet roots		
0.0007	UK toddler	0.68	0.0004	Milk: Cattle	0.0000	Wheat	0.0000	Potatoes		
0.0006	DK child	0.59	0.0003	Milk: Cattle	0.0001	Rye	0.0000	Swine: Muscle/meat		
0.0006	GEMS/Food G11	0.58	0.0002	Milk: Cattle	0.0001	Soyabeans	0.0000	Potatoes		
0.0006	ES child	0.56	0.0002	Milk: Cattle	0.0000	Wheat	0.0000	Bovine: Muscle/meat		
0.0006	SE general	0.55	0.0002	Milk: Cattle	0.0001	Bovine: Muscle/meat	0.0000	Potatoes		
0.0005	RO general	0.53	0.0002	Milk: Cattle	0.0001	Wheat	0.0000	Potatoes		
0.0005	GEMS/Food G07	0.52	0.0001	Milk: Cattle	0.0000	Wheat	0.0000	Potatoes		
0.0005	DE women 14-50 yr	0.52	0.0002	Milk: Cattle	0.0000	Sugar beet roots	0.0000	Apples		
0.0005	GEMS/Food G15	0.52	0.0001	Milk: Cattle	0.0000	Wheat	0.0000	Potatoes		
0.0005	DE general	0.51	0.0002	Milk: Cattle	0.0000	Sugar beet roots	0.0000	Apples		
0.0005	GEMS/Food G08	0.51	0.0001	Milk: Cattle	0.0000	Wheat	0.0000	Soyabeans		
0.0005	GEMS/Food G10	0.51	0.0001	Milk: Cattle	0.0001	Soyabeans	0.0000	Wheat		
0.0005	FR infant	0.47	0.0003	Milk: Cattle	0.0000	Potatoes	0.0000	Apples		
0.0004	GEMS/Food G06	0.45	0.0001	Wheat	0.0000	Milk: Cattle	0.0000	Tomatoes		
0.0004	NL general	0.43	0.0002	Milk: Cattle	0.0000	Sugar beet roots	0.0000	Potatoes		
0.0004	IE adult	0.41	0.0001	Milk: Cattle	0.0000	Sweet potatoes	0.0000	Wheat		
0.0004	FI adult	0.35	0.0003	Coffee beans	0.0000	Potatoes	0.0000	Rye		
0.0003	FR adult	0.29	0.0001	Milk: Cattle	0.0000	Wine grapes	0.0000	Wheat		
0.0003	ES adult	0.29	0.0001	Milk: Cattle	0.0000	Wheat	0.0000	Bovine: Muscle/meat		
0.0002	DK adult	0.24	0.0001	Milk: Cattle	0.0000	Swine: Muscle/meat	0.0000	Potatoes		
0.0002	LT adult	0.22	0.0001	Milk: Cattle	0.0000	Potatoes	0.0000	Swine: Muscle/meat		
0.0002	PT general	0.22	0.0001	Potatoes	0.0000	Wheat	0.0000	Wine grapes		
0.0002	UK vegetarian	0.18	0.0001	Milk: Cattle	0.0000	Wheat	0.0000	Potatoes		
0.0002	UK adult	0.18	0.0001	Milk: Cattle	0.0000	Wheat	0.0000	Potatoes		
0.0002	FI 3 yr	0.18	0.0000	Potatoes	0.0000	Bananas	0.0000	Wheat		
0.0002	IT toddler	0.17	0.0001	Wheat	0.0000	Other cereals	0.0000	Tomatoes		
0.0001	FI 6 yr	0.14	0.0000	Potatoes	0.0000	Cocoa beans	0.0000	Wheat		
0.0001	IE child	0.12	0.0001	Milk: Cattle	0.0000	Wheat	0.0000	Potatoes		
0.0001	IT adult	0.12	0.0000	Wheat	0.0000	Tomatoes	0.0000	Apples		
0.0001	PL general	0.10	0.0000	Potatoes	0.0000	Apples	0.0000	Tomatoes		

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

Pinoxaden

European Food Safety Authority

EFSA PRIMo revision 3.1; 2019/03/19

Pinoxaden

LOQs (mg/kg) range from:		to:	
Toxicological reference values			
ADI (mg/kg bw/day):	0.1	ARfD (mg/kg bw):	0.1
Source of ADI:	EFSA	Source of ARfD:	EFSA
Year of evaluation:	2013	Year of evaluation:	2013

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)
10%	DK child	10.20	6%	Rye	4%	Wheat	0.0005	Potatoes		
8%	GEMS/Food G06	7.92	7%	Wheat	0.0008	Rice	0.0007	Barley		
7%	IT toddler	6.86	7%	Wheat	0.0003	Other cereals	0.0003	Tomatoes		
6%	GEMS/Food G08	6.01	4%	Wheat	0.0089	Barley	0.0059	Rye		
6%	GEMS/Food G15	5.98	5%	Wheat	0.0078	Barley	0.0023	Rye		
6%	DE child	5.70	4%	Wheat	0.0080	Rye	0.0025	Apples		
6%	NL toddler	5.67	4%	Wheat	0.0042	Rye	0.0022	Apples		
5%	RO general	5.44	5%	Wheat	0.0007	Potatoes	0.0004	Tomatoes		
5%	GEMS/Food G07	5.33	4%	Wheat	0.0060	Barley	0.0008	Potatoes		
5%	GEMS/Food G10	5.10	4%	Wheat	0.0059	Barley	0.0011	Rye		
5%	FR child 3 15 yr	5.04	5%	Wheat	0.0007	Sugar beet roots	0.0007	Oranges		
5%	NL child	4.97	4%	Wheat	0.0017	Rye	0.0017	Sugar beet roots		
5%	GEMS/Food G11	4.91	4%	Wheat	0.0078	Barley	0.0008	Potatoes		
5%	ES child	4.73	4%	Wheat	0.0004	Oranges	0.0004	Potatoes		
4%	PT general	4.44	4%	Wheat	0.0014	Rye	0.0011	Potatoes		
4%	IT adult	4.31	4%	Wheat	0.0002	Tomatoes	0.0002	Apples		
4%	UK toddler	4.30	4%	Wheat	0.0007	Potatoes	0.0006	Sugar beet roots		
4%	SE general	3.83	3%	Wheat	0.0030	Rye	0.0008	Potatoes		
3%	FR toddler 2 3 yr	3.47	3%	Wheat	0.0006	Apples	0.0006	Sugar beet roots		
3%	DE general	3.31	2%	Wheat	0.0058	Rye	0.0051	Barley		
3%	DE women 14-50 yr	3.18	2%	Wheat	0.0048	Rye	0.0019	Barley		
3%	ES adult	3.04	2%	Wheat	0.0049	Barley	0.0003	Oranges		
3%	UK infant	2.96	3%	Wheat	0.0007	Potatoes	0.0003	Rice		
3%	IE adult	2.93	2%	Wheat	0.0015	Rye	0.0007	Sweet potatoes		
3%	NL general	2.61	2%	Wheat	0.0029	Barley	0.0007	Rye		
2%	FR adult	2.46	2%	Wheat	0.0005	Wine grapes	0.0002	Coffee beans		
2%	LT adult	2.36	1%	Rye	1%	Wheat	0.0006	Potatoes		
2%	UK vegetarian	2.27	2%	Wheat	0.0003	Potatoes	0.0002	Barley		
2%	FI 3 yr	2.23	1%	Wheat	0.0065	Rye	0.0009	Potatoes		
2%	FI 6 yr	1.89	0.0097	Wheat	0.0061	Rye	0.0008	Potatoes		
2%	UK adult	1.87	2%	Wheat	0.0003	Potatoes	0.0003	Barley		
2%	DK adult	1.79	1%	Wheat	0.0053	Rye	0.0003	Potatoes		
1%	FI adult	1.45	0.0070	Rye	0.0032	Wheat	0.0028	Coffee beans		
1%	IE child	1.22	1%	Wheat	0.0001	Rice	0.0001	Potatoes		
0.0099	FR infant	0.99	0.0079	Wheat	0.0004	Potatoes	0.0003	Apples		
0.0019	PL general	0.19	0.0007	Potatoes	0.0004	Apples	0.0002	Tomatoes		

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

European Food Safety Authority

EFSA PRIMo revision 3.1; 2019/03/19

Pinoxaden

LOQs (mg/kg) range from: to:

Toxicological reference values

ADI (mg/kg bw/day):	0,1	ARfD (mg/kg bw):	0,1
Source of ADI:	EFSA	Source of ARfD:	EFSA
Year of evaluation:	2013	Year of evaluation:	2013

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)
8%	DK child	7,57	4%	Rye	3%	Wheat	0,1%	Milk: Cattle		
6%	GEMS/Food G06	5,99	5%	Wheat	0,1%	Tomatoes	0,1%	Potatoes		
6%	NL toddler	5,52	3%	Wheat	0,6%	Milk: Cattle	0,3%	Apples		
5%	IT toddler	4,95	5%	Wheat	0,0%	Other cereals	0,0%	Tomatoes		
5%	DE child	4,80	3%	Wheat	0,6%	Rye	0,4%	Apples		
5%	GEMS/Food G08	4,70	3%	Wheat	0,6%	Barley	0,4%	Rye		
5%	GEMS/Food G15	4,67	3%	Wheat	0,5%	Barley	0,2%	Rye		
4%	NL child	4,33	3%	Wheat	0,3%	Sugar beet roots	0,2%	Milk: Cattle		
4%	RO general	4,26	4%	Wheat	0,1%	Milk: Cattle	0,1%	Potatoes		
4%	GEMS/Food G07	4,23	3%	Wheat	0,4%	Barley	0,1%	Potatoes		
4%	FR child 3 15 yr	4,21	3%	Wheat	0,2%	Milk: Cattle	0,1%	Sugar beet roots		
4%	GEMS/Food G10	4,04	3%	Wheat	0,4%	Barley	0,1%	Soyabeans		
4%	GEMS/Food G11	3,99	3%	Wheat	0,5%	Barley	0,1%	Potatoes		
4%	ES child	3,77	3%	Wheat	0,1%	Milk: Cattle	0,1%	Oranges		
4%	UK toddler	3,54	3%	Wheat	0,2%	Milk: Cattle	0,1%	Potatoes		
3%	PT general	3,36	3%	Wheat	0,2%	Potatoes	0,1%	Rye		
3%	SE general	3,16	2%	Wheat	0,2%	Rye	0,1%	Potatoes		
3%	IT adult	3,14	3%	Wheat	0,0%	Tomatoes	0,0%	Apples		
3%	FR toddler 2 3 yr	3,09	2%	Wheat	0,3%	Milk: Cattle	0,1%	Apples		
3%	DE general	2,77	1%	Wheat	0,4%	Rye	0,4%	Barley		
3%	UK infant	2,77	2%	Wheat	0,4%	Milk: Cattle	0,1%	Potatoes		
3%	DE women 14-50 yr	2,70	2%	Wheat	0,3%	Rye	0,1%	Sugar beet roots		
3%	IE adult	2,52	2%	Wheat	0,1%	Sweet potatoes	0,1%	Rye		
2%	ES adult	2,39	2%	Wheat	0,3%	Barley	0,0%	Milk: Cattle		
2%	NL general	2,22	1%	Wheat	0,2%	Barley	0,1%	Sugar beet roots		
2%	FR adult	2,00	2%	Wheat	0,1%	Wine grapes	0,0%	Milk: Cattle		
2%	LT adult	1,85	0,8%	Rye	0,7%	Wheat	0,1%	Potatoes		
2%	FI 3 yr	1,80	0,8%	Wheat	0,5%	Rye	0,1%	Potatoes		
2%	UK vegetarian	1,77	1%	Wheat	0,0%	Potatoes	0,0%	Milk: Cattle		
2%	FI 6 yr	1,52	0,7%	Wheat	0,4%	Rye	0,1%	Potatoes		
1%	UK adult	1,48	1%	Wheat	0,0%	Potatoes	0,0%	Wine grapes		
1%	FI adult	1,47	0,6%	Coffee beans	0,5%	Rye	0,2%	Wheat		
1%	DK adult	1,47	0,8%	Wheat	0,4%	Rye	0,1%	Milk: Cattle		
1%	FR infant	1,05	0,5%	Wheat	0,2%	Milk: Cattle	0,1%	Potatoes		
0,9%	IE child	0,94	0,8%	Wheat	0,0%	Milk: Cattle	0,0%	Potatoes		
0,3%	PL general	0,29	0,1%	Potatoes	0,1%	Apples	0,0%	Tomatoes		

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

Mefenpyr-diethyl

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

Mefenpyr-diethyl			
LOQs (mg/kg) range from:	0.01	to:	0.01
Toxicological reference values			
ADI (mg/kg bw/day):	0.1	ARfD (mg/kg bw):	0.4
Source of ADI:	Austria	Source of ARfD:	Austria
Year of evaluation:	2011	Year of evaluation:	2011

Input values | Details - chronic risk assessment | Supplementary results - chronic risk assessment | Details - acute risk | Details - acute risk

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)
0.7%	NL toddler	0.72	0.6%	Milk: Cattle	0.1%	Wheat	0.0%	Bovine: Muscle/meat	0.0%	0.1%
0.5%	UK infant	0.47	0.4%	Milk: Cattle	0.1%	Wheat	0.0%	Eggs: Chicken	0.0%	0.1%
0.4%	FR toddler 2 3 yr	0.40	0.3%	Milk: Cattle	0.1%	Wheat	0.0%	Bovine: Muscle/meat	0.0%	0.1%
0.4%	DK child	0.38	0.1%	Milk: Cattle	0.1%	Rye	0.1%	Wheat	0.1%	0.2%
0.4%	FR child 3 15 yr	0.38	0.2%	Milk: Cattle	0.1%	Wheat	0.0%	Bovine: Muscle/meat	0.1%	0.1%
0.4%	NL child	0.36	0.2%	Milk: Cattle	0.1%	Wheat	0.0%	Swine: Muscle/meat	0.0%	0.1%
0.3%	DE child	0.33	0.2%	Milk: Cattle	0.1%	Wheat	0.0%	Rye	0.0%	0.1%
0.3%	UK toddler	0.31	0.2%	Milk: Cattle	0.1%	Wheat	0.0%	Bovine: Muscle/meat	0.0%	0.1%
0.3%	ES child	0.26	0.1%	Milk: Cattle	0.1%	Wheat	0.0%	Bovine: Muscle/meat	0.1%	0.1%
0.2%	RO general	0.25	0.1%	Milk: Cattle	0.1%	Wheat	0.0%	Swine: Muscle/meat	0.0%	0.1%
0.2%	SE general	0.25	0.1%	Milk: Cattle	0.1%	Wheat	0.0%	Bovine: Muscle/meat	0.1%	0.1%
0.2%	GEMS/Food G15	0.20	0.1%	Wheat	0.1%	Milk: Cattle	0.0%	Swine: Muscle/meat	0.0%	0.1%
0.2%	DE women 14-50 yr	0.20	0.1%	Milk: Cattle	0.0%	Wheat	0.0%	Rye	0.0%	0.1%
0.2%	DE general	0.20	0.1%	Milk: Cattle	0.0%	Wheat	0.0%	Rye	0.0%	0.0%
0.2%	FR infant	0.20	0.2%	Milk: Cattle	0.0%	Wheat	0.0%	Swine: Muscle/meat	0.0%	0.0%
0.2%	GEMS/Food G07	0.19	0.1%	Wheat	0.1%	Milk: Cattle	0.0%	Poultry: Muscle/meat	0.0%	0.1%
0.2%	GEMS/Food G08	0.19	0.1%	Wheat	0.1%	Milk: Cattle	0.0%	Swine: Muscle/meat	0.0%	0.1%
0.2%	GEMS/Food G06	0.19	0.1%	Wheat	0.0%	Milk: Cattle	0.0%	Poultry: Muscle/meat	0.0%	0.1%
0.2%	GEMS/Food G11	0.18	0.1%	Milk: Cattle	0.1%	Wheat	0.0%	Swine: Muscle/meat	0.0%	0.1%
0.2%	GEMS/Food G10	0.17	0.1%	Wheat	0.1%	Milk: Cattle	0.0%	Poultry: Muscle/meat	0.0%	0.1%
0.1%	NL general	0.15	0.1%	Milk: Cattle	0.0%	Wheat	0.0%	Swine: Muscle/meat	0.0%	0.0%
0.1%	IT toddler	0.13	0.1%	Wheat		FRUIT AND TREE NUTS				0.1%
0.1%	ES adult	0.13	0.0%	Milk: Cattle	0.0%	Wheat	0.0%	Bovine: Muscle/meat	0.0%	0.0%
0.1%	IE adult	0.12	0.0%	Wheat	0.0%	Milk: Cattle	0.0%	Bovine: Muscle/meat	0.0%	0.0%
0.1%	FR adult	0.11	0.0%	Milk: Cattle	0.0%	Wheat	0.0%	Swine: Muscle/meat	0.0%	0.0%
0.1%	DK adult	0.11	0.1%	Milk: Cattle	0.0%	Wheat	0.0%	Rye	0.0%	0.0%
0.1%	LT adult	0.10	0.0%	Milk: Cattle	0.0%	Rye	0.0%	Wheat	0.0%	0.0%
0.1%	IT adult	0.08	0.1%	Wheat		FRUIT AND TREE NUTS				0.1%
0.1%	PT general	0.08	0.1%	Wheat	0.0%	Rye				0.1%
0.1%	UK adult	0.08	0.0%	Wheat	0.0%	Milk: Cattle	0.0%	Bovine: Muscle/meat	0.0%	0.0%
0.1%	UK vegetarian	0.08	0.0%	Wheat	0.0%	Milk: Cattle	0.0%	Eggs: Chicken	0.0%	0.0%
0.1%	IE child	0.07	0.0%	Milk: Cattle	0.0%	Wheat	0.0%	Swine: Muscle/meat	0.0%	0.0%
0.0%	FI 3 yr	0.04	0.0%	Wheat	0.0%	Rye				0.0%
0.0%	FI 6 yr	0.03	0.0%	Wheat	0.0%	Rye				0.0%
0.0%	FI adult	0.02	0.0%	Rye	0.0%	Wheat				0.0%
	Column7			FRUIT AND TREE NUTS		FRUIT AND TREE NUTS				

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

A 3.2 IEDI calculations

Not applicable.

A 3.3 IESTI calculations - Raw commodities

Pinoxaden

The acute risk assessment is based on the ARfD.
The calculation is based on the large portion of the most critical consumer group.

IESTI new calculations:
The calculation is performed with the MRL and the peeling/processing factor (PF), taking into account the residue in the edible portion and/or the conversion factor for the residue definition (CF). For case 2a, 2b and 3 calculations a variability factor of 3 is used. Since this methodology is not based on internationally agreed principles, the results are considered as indicative only.
Since this methodology is not based on internationally agreed principles, the results are considered as indicative only.

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)
14%	Wheat	1 / 1	14
6%	Rye	1 / 1	6.3

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%	Wheat	1 / 1	8.4
5%	Rye	1 / 1	4.9

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

IESTI new

Highest % of ARfD/ADI	Commodities	MRL / input for RA (mg/kg)	Exposure (µg/kg bw)
14%	Wheat	1 / 1	14
6%	Rye	1 / 1	6.3

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

IESTI new

Highest % of ARfD/ADI	Commodities	MRL / input for RA (mg/kg)	Exposure (µg/kg bw)
8%	Wheat	1 / 1	8.4
5%	Rye	1 / 1	4.9

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

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

	Acute risk assessment /children				Acute risk assessment / adults / general population				Acute risk assessment /children				Acute risk assessment / adults / general population			
	Details - acute risk assessment /children				Details - acute risk assessment/adults				Hide IESTI new calculations				Show IESTI new calculations			
	The acute risk assessment is based on the ARfD. The calculation is based on the large portion of the most critical consumer group.								**IESTI new calculations:** The calculation is performed with the MRL and the peeling/processing factor (PF), taking into account the residue in the edible portion and/or the conversion factor for the residue definition (CF). For case 2a, 2b and 3 calculations a variability factor of 3 is used. Since this methodology is not based on internationally agreed principles, the results are considered as indicative only. **Since this methodology is not based on internationally agreed principles, the results are considered as indicative only.**							
	Show results for all crops															
Unprocessed commodities	**Results for children** No. of commodities for which ARfD/ADI is exceeded (IESTI):			---	**Results for adults** No. of commodities for which ARfD/ADI is exceeded (IESTI):			---	**IESTI new** **Results for children** No. of commodities for which ARfD/ADI is exceeded (IESTI new):			---	**IESTI new** **Results for adults** No. of commodities for which ARfD/ADI is exceeded (IESTI new):			---
	IESTI				**IESTI**				IESTI new				IESTI new			
	Highest % of ARfD/ADI	Commodities	MRL / input for RA (mg/kg)	Exposure (µg/kg bw)	Highest % of ARfD/ADI	Commodities	MRL / input for RA (mg/kg)	Exposure (µg/kg bw)	Highest % of ARfD/ADI	Commodities	MRL / input for RA (mg/kg)	Exposure (µg/kg bw)	Highest % of ARfD/ADI	Commodities	MRL / input for RA (mg/kg)	Exposure (µg/kg bw)
	10%	Wheat	0,7 / 0,7	10	6%	Wheat	0,7 / 0,7	5,9	10%	Wheat	0,7 / 0,7	10	6%	Wheat	0,7 / 0,7	5,9
	4%	Rye	0,7 / 0,7	4,4	3%	Rye	0,7 / 0,7	3,4	4%	Rye	0,7 / 0,7	4,4	3%	Rye	0,7 / 0,7	3,4
	Expand/collapse list															
	Total number of commodities exceeding the ARfD/ADI in children and adult diets (IESTI calculation)								**Total number of commodities found exceeding the ARfD/ADI in children and adult diets (IESTI new calculation)**							

Mefenpyr-diethyl

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): ---				**Results for adults** No. of commodities for which ARfD/ADI is exceeded (IESTI): ---				**IESTI new** **Results for children** No. of commodities for which ARfD/ADI is exceeded (IESTI new): ---				**IESTI new** **Results for adults** No. of commodities for which ARfD/ADI is exceeded (IESTI new): ---			
IESTI				**IESTI**				IESTI new				IESTI new			
Highest % of ARfD/ADI	Commodities	MRL / input for RA (mg/kg)	Exposure (µg/kg bw)	Highest % of ARfD/ADI	Commodities	MRL / input for RA (mg/kg)	Exposure (µg/kg bw)	Highest % of ARfD/ADI	Commodities	MRL / input for RA (mg/kg)	Exposure (µg/kg bw)	Highest % of ARfD/ADI	Commodities	MRL / input for RA (mg/kg)	Exposure (µg/kg bw)
0.07%	Wheat	0.02 / 0.02	0.29	0.04%	Wheat	0.02 / 0.02	0.17	0.07%	Wheat	0.02 / 0.02	0.29	0.04%	Wheat	0.02 / 0.02	0.17
0.03%	Rye	0.02 / 0.02	0.13	0.02%	Rye	0.02 / 0.02	0.10	0.03%	Rye	0.02 / 0.02	0.13	0.02%	Rye	0.02 / 0.02	0.10
Expand/collapse list															
Total number of commodities exceeding the ARfD/ADI in children and adult diets (IESTI calculation)								**Total number of commodities found exceeding the ARfD/ADI in children and adult diets (IESTI new calculation)**							

A 3.4 IESTI calculations - Processed commodities

Pinoxaden

Processed commodities

Results for children No of processed commodities for which ARfD/ADI is exceeded (IESTI): ---				Results for adults No of processed commodities for which ARfD/ADI is exceeded (IESTI): ---				Results for children No of processed commodities for which ARfD/ADI is exceeded (IESTI new): ---				Results for adults No of processed commodities for which ARfD/ADI is exceeded (IESTI new): ---			
IESTI				**IESTI**				**IESTI new**				**IESTI new**			
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)	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)
12%	Wheat / milling (flour)	1 / 1	12	4%	Wheat / bread/pizza	1 / 1	4.4	12%	Wheat / milling (flour)	1 / 1	12	4%	Wheat / bread/pizza	1 / 1	4.4
6%	Wheat / milling (wholemea	1 / 1	5.5	4%	Wheat / pasta	1 / 1	3.8	6%	Wheat / milling	1 / 1	5.5	4%	Wheat / pasta	1 / 1	3.8
4%	Rye / boiled	1 / 1	3.6	3%	Wheat / bread	1 / 1	3.5	4%	Rye / boiled	1 / 1	3.6	3%	Wheat / bread (wholemeal)	1 / 1	3.5
4%	Rye / milling (wholemeal)-l	1 / 1	3.5	#ZAHL!	#ZAHL!	#ZAHL!	#ZAHL!	4%	Rye / milling (wholemeal)-	1 / 1	3.5	#ZAHL!	#ZAHL!	#ZAHL!	#ZAHL!
Expand/collapse list															

Conclusion:
No exceedance of the toxicological reference value was identified for any unprocessed commodity.
A short term intake of residues of Pinoxaden is unlikely to present a public health risk.
For processed commodities, no exceedance of the ARfD/ADI was identified.

Processed commodities

Results for children No of processed commodities for which ARfD/ADI is exceeded (IESTI): ---				Results for adults No of processed commodities for which ARfD/ADI is exceeded (IESTI): ---				Results for children No of processed commodities for which ARfD/ADI is exceeded (IESTI new): ---				Results for adults No of processed commodities for which ARfD/ADI is exceeded (IESTI new): ---			
IESTI				**IESTI**				**IESTI new**				**IESTI new**			
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)	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)
8%	Wheat / milling (flour)	0,7 / 0,7	8,5	3%	Wheat / bread/pizza	0,7 / 0,7	3,1	8%	Wheat / milling (flour)	0,7 / 0,7	8,5	3%	Wheat / bread/pizza	0,7 / 0,7	3,1
4%	Wheat / milling (wholemeal)-l	0,7 / 0,7	3,9	3%	Wheat / pasta	0,7 / 0,7	2,7	4%	Wheat / milling (wholemeal)-	0,7 / 0,7	3,9	3%	Wheat / pasta	0,7 / 0,7	2,7
3%	Rye / boiled	0,7 / 0,7	2,5	2%	Wheat / bread (wholemeal)	0,7 / 0,7	2,4	3%	Rye / boiled	0,7 / 0,7	2,5	2%	Wheat / bread (wholemeal)	0,7 / 0,7	2,4
2%	Rye / milling (wholemeal)-bal	0,7 / 0,7	2,5	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	2%	Rye / milling (wholemeal)-	0,7 / 0,7	2,5	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!
#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!
#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!
#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!
#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!
#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!
#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!
#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!
#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!
#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!
#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!
#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!	#LICZBA!
Expand/collapse list															

Conclusion:
No exceedance of the toxicological reference value was identified for any unprocessed commodity.
A short term intake of residues of Pinoxaden is unlikely to present a public health risk.
For processed commodities, no exceedance of the ARfD/ADI was identified.

Mefenpyr-diethyl

Processed commodities	Results for children				Results for adults				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):			---	No of processed commodities for which ARfD/ADI is exceeded (IESTI new):			---	No of processed commodities for which ARfD/ADI is exceeded (IESTI new):			---
	IESTI				**IESTI**				**IESTI new**				**IESTI new**			
	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)	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)
	0.06%	Wheat / milling (flour)	0.02 / 0.02	0.24	0.0%	Wheat / bread/pizza	0.02 / 0.02	0.09	0.06%	Wheat / milling (flour)	0.02 / 0.02	0.24	0.02%	Wheat / bread/pizza	0.02 / 0.02	0.09
	0.03%	Wheat / milling (wholemea	0.02 / 0.02	0.11	0.02%	Wheat / pasta	0.02 / 0.02	0.08	0.03%	Wheat / milling	0.02 / 0.02	0.11	0.02%	Wheat / pasta	0.02 / 0.02	0.08
	0.02%	Rye / boiled	0.02 / 0.02	0.07	0.02%	Wheat / bread	0.02 / 0.02	0.07	0.02%	Rye / boiled	0.02 / 0.02	0.07	0.02%	Wheat / bread (wholemeal)	0.02 / 0.02	0.07
	0.02%	Rye / milling (wholemeal)-l	0.02 / 0.02	0.07	#ZAHL!	#ZAHL!	#ZAHL!	#ZAHL!	0.02%	Rye / milling (wholemeal)-	0.02 / 0.02	0.07	#ZAHL!	#ZAHL!	#ZAHL!	#ZAHL!
	Expand/collapse list															

Conclusion:
No exceedance of the toxicological reference value was identified for any unprocessed commodity.
A short term intake of residues of Mefenpyr-diethyl is unlikely to present a public health risk.
For processed commodities, no exceedance of the ARfD/ADI was identified.