Mandipropamid (231)

The first draft was prepared by Dr Farag Mahmoud Malhat, Central Agricultural pesticides Laboratory. Giza, Egypt

EXPLANATION

Mandipropamid was first evaluated by the JMPR in 2008 when an ADI of 0–0.2 mg/kg bw was established and it was not necessary to establish an ARfD. The 2008 JMPR recommended a residue definition of mandipropamid for plant and animal commodities for compliance with MRLs and for dietary intake purposes. The residue is not fat soluble. MRLs were recommended for a number of plant commodities by the 2008 JMPR. An additional use on hops was evaluated by the JMPR in 2013. Mandipropamid was listed by the Forty-ninth Session of the CCPR for the evaluation of additional uses. The Meeting received additional potato metabolism and hen metabolism data, registered labels, analytical method data, and residue trials data for snap beans, potato and cacao beans.

METABOLISM

The Meeting received additional metabolism studies on plants (potato), and animals (laying hens). The metabolism and distribution of mandipropamid in laying hens and potato were investigated using mandipropamid radiolabelled in either the chlorophenyl or the methoxyphenyl moieties.

[chlorophenyl-U-^{14}C]-mandipropamid

*=Position of Radiolabel

[methoxyphenyl-U-^{14}C]-mandipropamid

*=Position of Radiolabel

The following abbreviated names were used for the metabolites discussed below.

Compound Name/Code	Structure	Occurrence in metabolism studies
NOA458422 2-(4-Chlorophenyl)-N-[2-(4-hydroxy-3-methoxyphenyl)-ethyl]-2-prop-2-ynyloxy-acetamide		Plant, animal
CGA380778 2-(4-Chlorophenyl)-2-hydroxy-N-[2-(3-methoxy- 4-prop-2-ynyloxyphenyl)-ethyl]-acetamide		Plant, animal
CGA380775 2-(4-Chlorophenyl)-2-hydroxy-N-[2-(4-hydroxy- 3-methoxyphenyl)-ethyl]-acetamide		animal
SYN500003 (4-Chloro-phenyl)-prop-2-ynyloxy-acetic acid		plant

Compound Name/Code	Structure	Occurrence in metabolism studies
SYN521195 2-(4-Chlorophenyl)-N-[2-(3-hydroxy-4-prop-2-ynyloxyphenyl)-ethyl]-2-prop-2-ynyloxy-acetamide		animal
M186/1 [2-(4-chlorophenyl)-2-hydroxyacetic acid]		animal
M401/1		animal
M415/1		animal
M431/1		animal
M439/1		animal
M453/1		animal
SYN505503 2-(4-Chlorophenyl)-N-[2-(3,4-dihydroxyphenyl)-ethyl]-2-prop-2-ynyloxy-acetamide		animal

Plant metabolism

A new metabolism study on potatoes following seed piece treatment has been provided and is summarised below.

Potato

The metabolic fate and distribution of mandipropamid was studied outdoors in potatoes following seed piece treatment [Fleischmann, T., (2014), NOA446510_50201].

Two radiolabelled forms of the mandipropamid were used in the study, [chlorophenyl-U-^{14}C]-mandipropamid and [methoxyphenyl-U-^{14}C]- mandipropamid. Seed pieces were dosed with a known volume (100 µl) of ^{14}C radiolabelled material in acetonitrile. Application to individual seed pieces occurred at a treatment rate equivalent to 0.1 kg ai/t seed [6.07 mg per seed piece (chlorophenyl) and 6.28 mg per seed piece (methoxyphenyl)]. Treated seed pieces were planted outdoors in raised beds in Madera, CA. Tubers were harvested at maturity (183 days after planting). The total radioactive residue (TRR), mg ai equivalents per kg of commodity, was measured in mature tubers (peel and flesh intact).

A sub-sample of approximately 50 g of mature tubers was extracted sequentially with acetonitrile:water (4:1) and acetonitrile. Samples were extracted on a wrist action shaker for at least 30 minutes. Liquids and solids were separated by centrifugation. Extracts were weighed and radioassayed by LSC. Remaining solids were combusted then analysed by LSC.

Extracts were combined and concentrated prior to HPLC analysis. Specific [methoxyphenyl-^{14}C]-NOA446510 extracts were subjected to purification using C18 solid phase extraction (SPE) for subsequent analysis by 1D-TLC and mass spectrometry. Fraction collection in conjunction with C18 reverse phase HPLC analysis was utilised for characterisation of [chlorophenyl-^{14}C] mandipropamid extracts that were later analysed by LC-MS .

Exact mass in positive ion mode showed the distribution of ions at m/z 412.131, m/z 413.134 and m/z 414.127 to be the same for HPLC fraction and an authentic standard of parent compound. MS data confirmed that the component eluting at 27.25 by HPLC was parent compound (mandipropamid).

The levels of radioactivity in post-extraction solid fractions were ≤0.013 mg/kg eq. Therefore, unextracted residues in potato tuber PES fractions were not further characterised.

Total Radioactive Residues and Extractability

The total radioactive residues of mandipropamid in potatoes following seed treatment were 0.054 mg/kg eq in potato tubers treated with [chlorophenyl-^{14}C]-mandipropamid and 0.024 mg/kg eq in potato tubers treated with [methoxyphenyl-^{14}C]-mandipropamid.

Table 1 Total Radioactive Residues and Extractability in Potatoes Following Seed Treatment with [14C]-mandipropamid

Radiolabel	Crop Commodity	Extractable* Radioactivity		Non-extractable Radioactivity		TRR
		% TRR	mg/kg eq	% TRR	mg/kg eq	mg/kg eq
[chlorophenyl-U-^{14}C]-mandipropamid	Mature Tubers	76.4	0.041	23.6	0.013	0.054
[methoxyphenyl-U-^{14}C]-mandipropamid	Mature Tubers	49.5	0.012	50.5	0.012	0.024

*Extraction with acetonitrile/water (80/20, v/v) and acetonitrile

Characterization and Identification of Residues

The extracted radioactivity was analysed by chromatography. The identified components for each sample are summarised in Table for each experiment.

Table 2 Identification and Characterisation of Residues in Potato Tubers Following Seed Treatment [^{14}C]-mandipropamid

			[Chlorophenyl-^{14}C] mandipropamid		[Methoxyphenyl-^{14}C] mandipropamid	
TRR by summation mg/kg			0.054[a]		0.024[a]	
TRR by direct quantification mg/kg			0.054[b]		0.020[b]	
Percent of TRR for chromatography, %			71.6%		42.4%	
Origin of component	Component	RT (min)	TRR	Residue (mg/kg)	TRR	Residue (mg/kg)
Chromatographed[c]	parent	27.25	5.5%	0.003	10.9%	0.003
	NOA458442	24.75			1.4%	<0.001
	CGA380778	23.75	1.2%	0.001	2.9%	0.001
	SYN500003	22.75	40.1%	0.022	N/A	N/A
	Unassigned[d]		24.7%	0.014	27.1%	0.005
	Total		71.5	0.040	42.30	0.009
Unextracted[e]			23.6	0.013	50.5	0.012

N/D = Not detected

N/A = Not applicable to this radiolabel

[a] TRR determined by summation of radioactivity present in the extracts and debris following solvent extraction

[b] The radioactive residue determined by direct quantification employing combustion/LSC.

[c] The components of the TRR that were derived from chromatographic analysis.

[d] Unassigned radiocomponents which chromatographed away from the void volume in HPLC Method 1:

Chlorophenyl label: comprising at least 7 discrete components, no single one of which ≥6.6% TRR (≥0.004 mg/kg)
Methoxyphenyl label: comprising at least 13 discrete components, no single one of which ≥5.8% TRR (≥0.001 mg/kg)

[e] Radioactivity remaining in the debris after extraction with acetonitrile and aqueous acetonitrile. The nature of this residue was not further characterised.

The total extractability for tubers treated with [chlorophenyl-^{14}C]-mandipropamid was >76% TRR extracted which corresponds with a residue of 0.041 mg/kg. The total extractability for tubers treated with [methoxyphenyl-^{14}C] mandipropamid was lower at 50% TRR extracted which corresponds with a residue of 0.012 mg/kg. Non-extractable radioactivity levels corresponds

with low residues of 0.013 and 0.012 mg/kg respectively, thus, unextracted residues in potato tuber PES fractions were not further characterised.

Parent compound was detected at levels of 0.003 to 0.004 mg/kg in potato tuber extracts. The only major metabolite was SYN500003 with residue levels between 0.022 to 0.023 mg/kg in samples treated with [chlorophenyl-^{14}C]-mandipropamid only. Other minor components characterised included NOA458422 and CGA380778 at levels of ≤0.001 mg/kg.

The principal metabolite, SYN500003, was formed by cleavage of the amide bond in the parent molecule. Minor components formed by loss of one of the propargyl groups were characterised as NOA458422 and CGA380778.

Extracts with total radioactive residues ≥0.01 ppm were chromatographically characterised by reverse phase HPLC compared to authentic reference compounds. Specific [methoxyphenyl-^{14}C]-mandipropamid extracts were purified using C18 solid phase extraction (SPE). Purification via the SPE allowed for subsequent identification of parent (mandipropamid) by comparision with authentic reference standard by 1D-TLC and mass spectrometry.

Parent compound was isolated from extracts derived from potato tubers treated with [chlorophenyl-^{14}C]-mandipropamid using reverse phase HPLC with C18 stationary phase. A fraction collector was used to collect the peak of interest. LC-MS analysis using Q-Exactive high resolution mass spectrometry confirmed the collected fraction as mandipropamid and the radiochromatogram showed the retention time of the radiochemical component retention time was consistent with mandipropamid. Exact mass in positive ion mode showed the distribution of ions at m/z 412.131, m/z 413.134 and m/z 414.127 to be the same as that of the authentic standard of mandipropamid.

Identification of SYN500003 was confirmed by mass spectrometry as compared to authentic reference compound. SYN500003 was isolated from extracts derived from potato tubers treated with [chlorophenyl-^{14}C]-mandipropamid using preparative reverse phase HPLC with a C18 stationary phase. The chromatographic peak of interest was collected and compared to an authentic standard of SYN500003. LC-MS analysis using Exact Mass of the molecular ion from the collected fraction and SYN500003 showed a similar distribution of ions at m/z 223.016, m/z 224.019 and m/z 225.013. MS data confirmed that the peak eluting at 22.75 min in HPLC profiles was metabolite SYN500003. An overall metabolic pathway for mandipropamid in potatoes following seed piece treatment is given in **Error! Reference source not found.**.

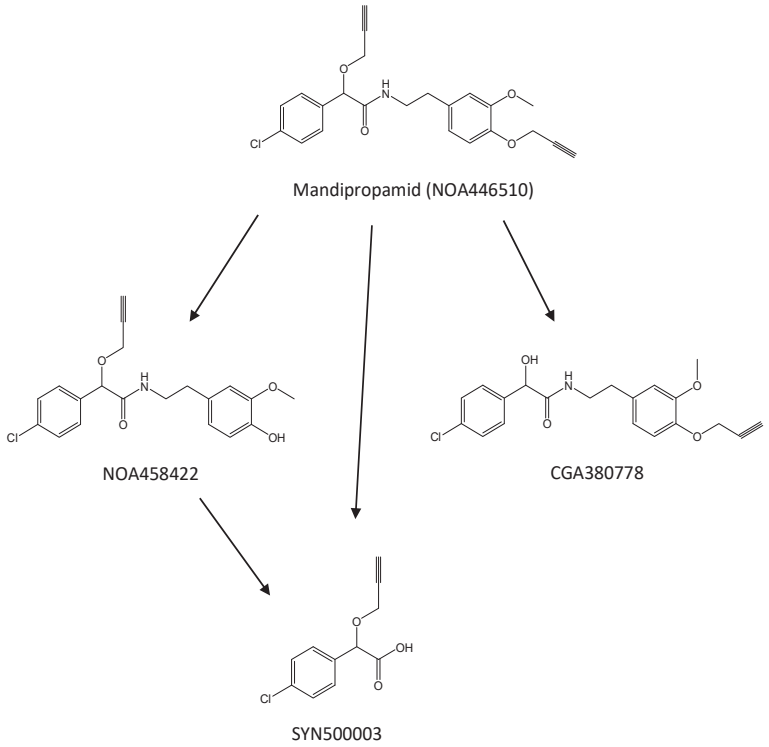

Figure 1 Metabolic pathway of mandipropamid in potatoes following seed piece treatment

Animal metabolism

Laying hens

The Meeting received information on the results of studies on laying hens which were fed isotope-labelled mandipropamid.

[Chlorophenyl-U-^{14}C]-mandipropamid and [Methoxyphenyl-U-^{14}C]-mandipropamid were administered orally in gelatine capsules to two separate groups of hens comprised of five birds each once daily for 14 consecutive days (Wang, p 2016. Report no. NOA446510_50364). The administered daily dose was 22–24 ppm dry feed per day. Eggs and excreta were collected daily. Hen were sacrificed approximately 12–14 hours after the last dose administration, and liver, muscle, fat and gastrointestinal tracts with contents were collected for analysis.

All tissues, eggs, and excreta samples were processed, sub-sampled, combusted, and counted for TRR determination by liquid scintillation counting (LSC). Further characterisation was carried out on samples where the radioactive residue was greater than 0.01 mg/kg eq. The results are shown in Table 3.

Table 3 Total radioactive residues (TRR) in egg and tissues of hens

Sample	Radioactive Residue									
	[chlorophenyl-U-^{14}C]-mandipropamid					[methyoxyphenyl-U-^{14}C]-mandipropamid*				
	Extractable Radioactivity		Non-extractable Radioactivity		TRR	Extractable Radioactivity		Non-extractable Radioactivity		TRR
	% TRR	(mg eq./kg)	% TRR	(mg eq./kg)	(mg eq./kg)	% TRR	(mg eq./kg)	% TRR	(mg eq./kg)	(mg eq./kg)
Egg White (Day 9)	95.1	0.044	4.9	0.002	0.046	93.7	0.047	6.4	0.003	0.05
Egg Yolk (Day 9)	38	0.031	62	0.051	0.083	30.8	0.038	69.2	0.084	0.122
Liver	34.7	0.107	65.3	0.199	0.306	29.4	0.095	70.5	0.228	0.323
Muscle	61.7	0.01	38.3	0.006	0.016	-	-	-	-	-
Fat	59	0.013	40.9	0.009	0.021	73.3	0.016	26.6	0.006	0.022

* Muscle was not analysed for this label because TRR upon initial combustion was <0.01 mg/kg

Table 4 Total radioactive residues (TRRs) in egg as function of time

Time point (days)	Egg white		Egg yolk	
	[chlorophenyl-U-^{14C}]-mandipropamid	[methoxyphenyl-U-^{14}C]-mandipropamid	[chlorophenyl-U-^{14}C]-mandipropamid	[methoxyphenyl-U-^{14}C]-mandipropamid
	Mean (mg eq./kg)	Mean (mg eq./kg)	Mean (mg eq./kg)	Mean (mg eq./kg)
1	0.0439	0.0471	0.0175	0.0181
2	0.0515	0.084	0.0355	0.0393
3	0.0353	0.0962	0.0539	0.0487
4	0.0505	0.0832	0.0675	0.0726
5	0.0503	0.0667	0.0774	0.0885
6	0.0564	0.0589	0.0906	0.0985
7	0.0464	0.0608	0.0926	0.1031
8	0.0616	0.0639	0.094	0.1089
9	0.0442	0.0503	0.0927	0.1082
10	0.0411	0.0478	0.0928	0.1106
11	0.0603	0.0485	0.0878	0.1019
12	0.0312	0.0407	0.0877	0.1105
13	0.043	0.0304	0.0953	0.0972

The radioactivity balance for the treated hens was greater than 85–90% with the majority (83–88%) of the radioactivity found in the excreta.

Following dosing of the laying hens, the highest radioactive residue was observed in the liver. Overall levels of TRR [chlorophenyl-U-^{14}C]-mandipropamid and [methoxyphenyl-U-^{14}C]-mandipropamid in liver, egg yolk (Day 9), egg white (Day 9), muscle, and fat were determined to be 0.306 and 0.323 mg/kg, 0.083 and 0.122 mg/kg, 0.046 and 0.050 mg/kg, 0.016 and <0.01 mg/kg, and 0.021 and 0.022 mg/kg, respectively.

Residues in the egg whites and yolks reached a plateau within 9 days for both radiolabels.

Characterisation and identification of residues

Sub-samples of liver, muscle, and egg white and yolk were extracted with acetonitrile, acetonitrile/water (8:2, v/v), then acetonitrile/water (3:7, v/v). Composite fat samples were extracted with hexane then hexane:diethyl ether (1:1,v/v). Excreta was extracted multiple times with acetonitrile then acetonitrile/water. Extracts were combined and concentrated prior to HPLC analysis.

Concentrated extracts from egg white, egg yolk, liver, muscle, and fat were evaporated to dryness under nitrogen then subjected to sulfatase hydrolysis for 24 hrs at 37 ºC. Samples were evaporated and reconstituted for analysis by HPLC and LSC.

Unextracted residues in the post extraction debris from the initial extraction of liver were subjected to sodium dodecylsulfate (SDS) and SDS/mercaptoethanol extractions. After solubilisation with SDS, remaining liver debris was subjected to protease digestion using Papain, a crystalline protease which hydrolyses a number of peptide and ester bonds. Resultant radioactivity was determined by HPLC, LSC, or combustion analysis.

The post extraction debris of liver and egg yolks from the initial extraction was also subjected to microwave extraction using an array of mild extraction solvents at different conditions to facilitate the release of strongly bound metabolites from their conjugated forms. The post extraction debris following microwave extraction was subjected to further microwave extraction with mineral acid (IPA:1 N HCl (1:1, v/v)) to facilitate the release of strongly bound metabolites from their conjugated forms. Resultant radioactivity was determined by LSC. All samples were analysed within 6 month

Table 5 Characterisation and Identification of Components in Egg White Acetonitrile/Water Extract Prior to and Post Enzyme Hydrolysis from Laying Hens Treated with [^{14}C]-mandipropamid

		[chlorophenyl-U-^{14}C]-mandipropamid		[methoxyphenyl-U-^{14}C]-mandipropamid	
TRR by summation mg/kg		0.046 [a]		0.050 [a]	
TRR by direct quantification mg/kg		0.045 [b]		0.055 [b]	
Percentage of TRR for chromatography, %		83.0 [83.8]		85.4 [80.0]	
	Component	% TRR	Residue	% TRR	Residue
			(mg/kg)		(mg/kg)
Chromatographed [c]	M186/1	8.1 [3.5]	0.004 [0.002]		
	CGA380778	15.3 [14.4]	0.007 [0.007]	16.9 [16.2]	0.008 [0.008]
	NOA458422	3.3 [3.5]	0.002 [0.002]	4.0 [4.4]	0.002 [0.002]
	SYN521195	1.1 [1.0]	0.001 [<0.001]	1.7 [1.8]	0.001 [0.001]
	Mandipropamid	33.7 [32.9]	0.016 [0.015]	36.9 [29.9]	0.018 [0.015]
	Unassigned	12.1 [18.0]	0.007 [0.010]	13.8 [15.5]	0.007 [0.008]
	Remainder [d]	9.3 [10.3]	0.004 [0.005]	12.0 [12.2]	0.006 [0.006]
	Unextracted [e]	4.9	0.002	6.4	0.003
	Total	87.8 [88.5]	0.043 [0.043]	91.7 [86.4]	0.045 [0.043]

xxx [xxx]: numbers prior to enzyme hydrolysis [numbers post enzyme hydrolysis]

[a] TRR determined by summation of radioactivity present in the extracts and debris following solvent extraction

[b] The radioactive residue determined by direct quantification employing combustion/LSC.

[c] The components of the TRR that were derived from chromatographic analysis. Final % TRR is presented in one decimal. % TRR = %HPLC × % TRR of the fraction/100.

[d] The remainder comprises diffuse areas of radioactivity within the chromatogram accounting for <1% of radioactivity in HPLC which cannot be assigned to discrete radioactive components.

[e] Radioactivity remaining in the debris after extraction with acetonitrile and water.

Table 6 Characterisation and Identification of Components in Egg yolk Acetonitrile/Water Extract Prior to and Post Enzyme Hydrolysis from Laying Hens Treated with [^{14}C]-mandipropamid

		[chlorophenyl-U-^{14}C]-mandipropamid		[methoxyphenyl-U-^{14}C]-mandipropamid	
TRR by summation mg/kg		0.083 [a]		0.122 [a]	
TRR by direct quantification mg/kg		0.096 [b]		0.110 [b]	
Percentage of TRR for chromatography, %		32.8 [32.2]		28.7 [25.1]	
	Component	% TRR	Residue	% TRR	Residue
			(mg/kg)		(mg/kg)
Chromatographed [c]	M186/1	7.4 [5.1]	0.006 [0.004]		
	CGA380775			2.0 [1.9]	0.002 [0.002]

		[chlorophenyl-U-^{14}C]-mandipropamid		[methoxyphenyl-U-^{14}C]-mandipropamid	
	SYN505503			0 [0.5]	0 [0.001]
	CGA380778	1.4 [3.3]	0.001 [0.003]	3.8 [3.8]	0.005 [0.005]
	NOA458422	2.5 [3.2]	0.002 [0.003]	0.4 [3.0]	<0.001 [0.004]
	SYN521195	0.5 [3.6]	<0.001 [0.003]		
	Mandipropamid	2.6 [2.2]	0.002 [0.002]	2.8 [2.5]	0.003 [0.003]
	Unassigned	12.6 [9.2]	0.011 [0.007]	14.1 [9.1]	0.017 [0.011]
	Remainder [d]	4.9 [5.5]	0.005 [0.005]	5.4 [4.3]	0.007 [0.005]
	Unextracted [e]	62	0.051	69.2	0.084
	Total	93.9 [94.0]	0.078 [0.078]	97.6 [94.2]	0.118 [0.115]

xxx [xxx]: numbers prior to enzyme hydrolysis [numbers post enzyme hydrolysis]

[a] TRR determined by summation of radioactivity present in the extracts and debris following solvent extraction

[b] The radioactive residue determined by direct quantification employing combustion/LSC

[c] The components of the TRR that were derived from chromatographic analysis. Final % TRR is presented in one decimal. % TRR = %HPLC × % TRR of the fraction/100.

[d] The remainder comprises diffuse areas of radioactivity within the chromatogram accounting for <1% of radioactivity in HPLC which cannot be assigned to discrete radioactive components.

[e] Radioactivity remaining in the debris after extraction with acetonitrile and water

Table 7 Characterisation and identification of residues released from the debris of egg yolk from hens treated with [^{14}C]-mandipropamid

		[chlorophenyl-U-^{14}C]-Mandipropamid		[methoxyphenyl-U-^{14}C]-Mandipropamid	
TRR by summation mg/kg		0.083 [a]		0.122 [a]	
TRR by direct quantification mg/kg		0.096 [b]		0.110 [b]	
Percentage of TRR for chromatography, %		47.7		39.9	
	Component	% TRR [c]	Residue (mg/kg)	% TRR [c]	Residue (mg/kg)
Chromatographed [c]	M186/1	8.2	0.007		
	CGA380775	4.7	0.004	2.8	0.003
	SYN505503	1	0.001	1.3	0.002
	CGA380778	3.1	0.003	3.4	0.004
	NOA458422	3.4	0.003	4.2	0.005
	Mandipropamid	2	0.002	2.2	0.003
	Unassigned (14 peaks)	22	0.018	18.6	0.02
	Remainder [d]	3.3	0.003	7.3	0.009
	Extract VII [e]	6.3	0.005	5.3	0.01
	Extract VIII [e]	3.4	0.003	5.3	0.01
	Extract IX [f]	11.1	0.009	18.5	0.02
	Unextracted (PES-2) [g]	1.3	0.001	1.8	0
	Gain or loss [h]	7.8		1.6	
	Total	69.8	0.059	70.7	0.08

[a] TRR determined by summation of radioactivity present in the extracts and debris following solvent extraction

[b] The radioactive residue determined by direct quantification employing combustion/LSC.

[c] The components of the TRR that were derived from chromatographic analysis. Final % TRR is presented in one decimal. % TRR = %HPLC × % TRR of the fraction/100.

[d] The remainder comprises diffuse areas of radioactivity within the chromatogram accounting for <1% of radioactivity in HPLC which cannot be assigned to discrete radioactive components.

[e] Fractions obtained from a series of microwave extractions with a mixture of acetonitrile and water. The fraction was not further analysed.

[f] Fractions obtained from a series of microwave extractions with a mixture of 1 N HCl and IPA. The fraction was not further.

[g] Radioactivity remaining in the debris after the microwave extractions. No further work was conducted

[h] The net cumulative incremental losses or gains during analysis.

Table 8 Characterisation and identification of components in liver in acetonitrile/water extract prior to and post enzyme hydrolysis from laying hens treated with [^{14}C]-mandipropamid

		[chlorophenyl-U-^{14}C]-mandipropamid		[methoxyphenyl-U-^{14}C]-mandipropamid	
TRR by summation mg/kg		0.306 [a]		0.323 [a]	
TRR by direct quantification mg/kg		0.278 [b]		0.288 [b]	
Percentage of TRR for chromatography, %		40.5 [39.4]		26.5 [24.1]	
	Component	% TRR [c]	Residue (mg/kg)	% TRR [c]	Residue (mg/kg)
	M186/1	1.9 [2.0]	0.006 [0.006]		
Chromatographed [c]	CGA380775	1.4 [3.5]	0.004 [0.011]	2.6 [2.0]	0.008 [0.006]
	SYN505503	0.1 [1.4]	<0.001 [0.004]	0.1 [0.8]	<0.001 [0.003]
	NOA458422	0.9 [14.8]	0.003 [0.045]	0.4 [6.3]	0.001 [0.020]
	Unassigned [d]	30.4 [12.9]	0.095 [0.039]	18.0 [10.1]	0.059 [0.034]
	Remainder [e]	5.5 [4.8]	0.017 [0.015]	5.3 [4.9]	0.017 [0.016]
	Unextracted [f]	65.3	0.199	70.5	0.228
	Total	105.3 [104.5]	0.324 [0.319]	97.0 [94.9]	0.313 [0.307]

xxx [xxx]: numbers prior to enzyme hydrolysis [numbers post enzyme hydrolysis]

[a] TRR determined by summation of radioactivity present in the extracts and debris following solvent extraction

[b] The radioactive residue determined by direct quantification employing combustion/LSC

[c] The components of the TRR that were derived from chromatographic analysis. Final % TRR is presented in one decimal. % TRR = %HPLC × % TRR of the fraction/100.

[d] None of the component was greater than 0.01 mg/kg

[e] The remainder comprises diffuse areas of radioactivity within the chromatogram accounting for <1% of radioactivity in HPLC which cannot be assigned to discrete radioactive components.

[f] Radioactivity remaining in the debris after extraction with acetonitrile and water. The nature of this residue was characterised further by extraction with an array of solvent mixtures at different parameters in a microwave accelerated reaction system.

Table 9 Characterisation and identification of components in liver debris in 80:20 acetonitrile/water fraction from laying hens treated with [^{14}C]-mandipropamid

		[chlorophenyl-U-^{14}C]-Mandipropamid		[methoxyphenyl-U-14C]-Mandipropamid	
TRR by summation mg/kg		0.306 [a]		0.306 [a]	
TRR by direct quantification mg/kg		0.278 [b]		0.278 [b]	
Percentage of TRR for chromatography, %		20.8		12	
	Component	% TRR [c]	Residue (mg/kg)	% TRR [c]	Residue (mg/kg)
	M186/1	3.3	0.01		
Chromatographed [c]	CGA380775	2.9	0.009	0.8	0.003
	SYN505503	0.3	0.001	0.3	0.001
	NOA458422	1.1	0.003	0.5	0.002
	Unassigned (16 peaks)	9.9	0.031	6.5	0.025
	Remainder [d]	3.7	0.011	4.1	0.013
	Extract VII [e]	2.9	0.009	2.5	0.008
	Extract VIII [e]	1.8	0.006	1.5	0.005
	Extract IX [f]	7.9	0.024	9.7	0.031
	Unextracted (PES-2) [g]	26.5	0.081	33.8	0.109
	Gain or loss [h]	-4.8		-10.9	
	Total	60.3	0.185	59.7	0.197

[a] TRR determined by summation of radioactivity present in the extracts and debris following solvent extraction

[b] The radioactive residue determined by direct quantification employing combustion/LSC

[c] The components of the TRR that were derived from chromatographic analysis. Final % TRR is presented in one decimal. % TRR = %HPLC × % TRR of the fraction/100.

[d] The remainder comprises diffuse areas of radioactivity within the chromatogram accounting for <1.5% of radioactivity in HPLC which cannot

be assigned to discrete radioactive components.

[e] Fractions obtained from a series of microwave extractions with a mixture of acetonitrile and water. The fraction was not further analysed.

[f] Fractions obtained from a series of microwave extractions with a mixture of 1 N HCl and IPA. The fraction was further analysed by HPLC.

[g] Radioactivity remaining in the debris after the microwave extractions. The debris was further extracted with SDS and mercaptoethanol.

[h] The net cumulative incremental losses or gains during analysis.

Table 10 Characterisation and identification of components in muscle in acetonitrile/water extract prior to and post enzyme hydrolysis from laying hens treated with [chlorophenyl-U-^{14}C]-mandipropamid

TRR by summation mg/kg	0.016 [a]		
TRR by direct quantification mg/kg	0.015 [b]		
Percentage of TRR for chromatography, %	58.9 [51.4]		
Chromatographed [c]	Component	% TRR [c]	Residue (mg/kg)
	M186/1	3.0 [14.5]	0.001 [0.002]
	CGA380775	1.1 [0.8]	<0.001 [<0.001]
	NOA458422	0 [1.9]	0 [<0.001]
	Mandipropamid	3.2 [2.3]	0.001 [<0.001]
	Unassigned	31.8 [17.9]	0.005 [0.003]
	Remainder [d]	19.9 [16.3]	0.003 [0.003]
	Unextracted [e]	38.3	0.006
	Total	97.3 [92.0]	0.013 [0.014]

xxx [xxx]: numbers prior to enzyme hydrolysis [numbers post enzyme hydrolysis]

[a] TRR determined by summation of radioactivity present in the extracts and debris following solvent extraction

[b] The radioactive residue determined by direct quantification employing combustion/LSC.

[c] The components of the TRR that were derived from chromatographic analysis. Final % TRR is presented in one decimal. % TRR = %HPLC × % TRR of the fraction/100.

[d] The remainder comprises diffuse areas of radioactivity within the chromatogram accounting for <1% of radioactivity in HPLC which cannot be assigned to discrete radioactive components

[e] Radioactivity remaining in the debris after extraction with acetonitrile and water. This debris was not analyzed further.

Table 11 Characterisation and identification of components in fat acetonitrile phases of hexane/diethyl ether extracts from laying hens treated with [^{14}C]-mandipropamid

		[chlorophenyl-U-^{14}C]-Mandipropamid		[methoxyphenyl-U-^{14}C]-Mandipropamid	
TRR by summation mg/kg		0.021 [a]		0.022 [a]	
TRR by direct quantification mg/kg		0.019 [b]		0.020 [b]	
Percentage of TRR for chromatography, %		46.3		68.5	
Chromatographed [c]	Component	% TRR [c]	Residue (mg/kg)	% TRR [c]	Residue (mg/kg)
	M186/1	6.2	0.001		
	CGA380775	0.8	<0.001	0.7	<0.001
	NOA458422	1.4	<0.001	1.7	<0.001
	Mandipropamid	28.3	0.006	36.8	0.008
	Unassigned (2 peaks)	1.2	<0.001	4.6	0.001
	Remainder [d]	8.4	0.002	24.7	0.005
	Acetonitrile [e]	13.6	0.003	9.4	0.002
	Unextracted [f]	40.9	0.009	26.6	0.006
	Total	100.8		104.5	0.021

[a] TRR determined by summation of radioactivity present in the extracts and debris following solvent extraction.

[b] The radioactive residue determined by direct quantification employing combustion/LSC.

[c] The components of the TRR that were derived from chromatographic analysis. Final % TRR is presented in one decimal. % TRR = %HPLC × % TRR of the fraction/100.

[d] The remainder comprises diffuse areas of radioactivity within the chromatogram accounting for <1% of radioactivity in HPLC which cannot be assigned to discrete radioactive components.

[e] Extractable residues in acetonitrile fraction.

[f] Radioactivity remaining in the debris after extraction with acetonitrile and water. No further analysis was performed.

Table 12 Characterisation and identification of components in fat acetonitrile extracts prior to and post enzyme hydrolysis from laying hens treated with [^{14}C]-mandipropamid

	[chlorophenyl-U-^{14}C]-Mandipropamid			[methoxyphenyl-U-^{14}C]-Mandipropamid		
TRR by summation mg/kg	0.021 [a]			0.022 [a]		
TRR by direct quantification mg/kg	0.019 [b]			0.020 [b]		
Percentage of TRR for chromatography, %	13.7 [15.3]			10.0 [10.4]		
	Component	% TRR	Residue (mg/kg)	Component	% TRR	Residue (mg/kg)
	M186/1	0.8 [0.1]	<0.001 [<0.001]			
Chromatographed [c]	CGA380775	1.0 [1.4]	<0.001 [<0.001]	CGA380775	0.1 [0.8]	<0.001 [<0.001]
	NOA458422	0.3 [3.1]	<0.001 [0.001]	NOA458422	0.3 [1.7]	<0.001 [<0.001]
	Mandipropamid	0.2 [0.2]	<0.001 [<0.001]	Mandipropamid	0.1 [0]	<0.001 [0]
	Unassigned	9.4 [9.1]	0.002 [0.002]	Unassigned	7.1 [3.7]	0.002 [0.001]
	Remainder [d]	2.1 [1.5]	<0.001 [<0.001]	Remainder [4]	2.2 [4.3]	<0.001 [0.001]
	Total	13.8 [15.4]	0.003 [0.003]	Total	9.2 [9.4]	0.002 [0.002]

xxx [xxx]: numbers prior to enzyme hydrolysis [numbers post enzyme hydrolysis]

[a] TRR determined by summation of radioactivity present in the extracts and debris following solvent extraction.

[b] The radioactive residue determined by direct quantification employing combustion/LSC.

[c] The components of the TRR that were derived from chromatographic analysis. Final % TRR is presented in one decimal. % TRR = %HPLC × % TRR of the fraction/100.

[d] The remainder comprises diffuse areas of radioactivity within the chromatogram accounting for <1% of radioactivity in HPLC which cannot be assigned to discrete radioactive components.

Table 13 Summary of characterisation and identification of radioactivity in hen eggs and tissues

[chlorophenyl-U-^{14}C] -mandipropamid						
Components	Egg White		Egg Yolk		Fat	
	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg
Mandipropamid	33.7 [32.9]	0.016 [0.015]	2.6 [4.2] (2.0)	0.002 [0.004] (0.002)	28.5 [0.2]	0.006 [<0.001]
M186/1	8.1 [3.5]	0.004 [0.002]	7.4 [13.3] (8.2)	0.006 [0.011] (0.007)	7.0 [0.1]	0.001 [<0.001]
CGA380775	ND	ND	1.4 [8.0] (4.7)	0.001 [0.007] (0.004)	1.8 [1.4]	<0.001 [<0.001]
SYN505503	ND	ND	0 [1.0] (1.0)	0 [0.001] (0.001)	ND	ND
CGA380778 [1]	15.3 [14.4]	0.007 [0.007]	2.5 [6.3] (4.7)	0.002 [0.006] (0.003)	ND	ND
NOA458422	3.3 [3.5]	0.002 [0.002]	0.5 [7.0] (3.4)	<0.001 [0.006] (0.003)	1.7 [3.1]	<0.001 [0.001]
SYN521195	1.1 [1.0]	0.001 [<0.001]	ND	ND	ND	ND
Components	Liver			Muscle		
	% TRR	mg/kg		% TRR	mg/kg	

[chlorophenyl-U-^{14}C] -mandipropamid								
Components	Egg White		Egg Yolk		Fat			
	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg		
Mandipropamid	ND		ND		3.2 [2.3]		0.001 [<0.001]	
M186/1	1.9 [5.3] (3.3)		0.006 [0.016] (0.010)		3.0 [14.5]		0.001 [0.002]	
CGA380775	1.4 [6.4] (2.9)		0.004 [0.020] (0.009)		1.1 [0.8]		<0.001 [<0.001]	
SYN505503	0.1 [1.7] (0.3)		<0.001 [0.005] (0.001)		ND		ND	
NOA458422	0.9 [15.9] (1.1)		0.003 [0.048] (0.003)		0 [1.9]		0 [<0.001]	
[methoxyphenyl-U-^{14}C] -mandipropamid								
Components	Egg White		Egg Yolk		Fat		Liver	
	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg
Mandipropamid	36.9 [29.9]	0.018 [0.015]	2.8[4.7] (2.2)	0.003[0.006] (0.003)	36.9	0.008	ND	ND
CGA380775	ND	ND	2.0[4.7] (2.8)	0.002 [0.005] (0.003)	0.8 [0.8]	<0.001 [<0.001]	2.6[2.8] (0.8)	0.008 [0.009] (0.003)
SYN505503	ND	ND	0 [1.8] (1.3)	0 [0.003] (0.002)	ND	ND	0.1[1.3] (0.3)	<0.001[0.004] (0.001)
CGA380778 [a]	16.9 [16.2]	0.008 [0.008]	3.8[7.2] (3.4)	0.005 [0.009] (0.004)	ND	ND	ND	ND
NOA458422	4.0 [4.4]	0.002 [0.002]	0.4[7.2] (4.2)	<0.001 [0.009] (0.005)	2.0 [1.7]	<0.001 [<0.001]	0.5[8.3] (0.6)	0.001 [0.022] (0.002)
SYN521195	1.7 [1.8]	0.001 [0.001]	ND	ND	ND	ND	ND	ND

xxx [xxx] (xxx): proportion of the total extracted residue prior to enzyme hydrolysis [proportion of the total extracted residue attributable to the sulfate conjugated form + microwave extraction, if any] (proportion attributable to microwave extraction). ND: non-detectable.

[a] CGA380778 detectable in egg white and yolk was not detected in fat, liver, and muscle tissues.

No tissue specific metabolites were detected and no significant differences between the two radiolabels with the exception of formation of M186/1 following amide cleavage in the chlorophenyl labelled eggs and tissues.

Unchanged parent compound was detected in egg whites but was minor in all other tissues and excreta. Mandipropamid was either excreted or extensively metabolised by hens following oral dosing for 14 days.

The principle biotransformation occurred through O-demethylation and O-depropylation) to form CGA380775, CGA380778, SYN505503, NOA458422, SYN521195 and by cleavage of the amide bond to form the half molecule M186/1.

Sulfate conjugates M401/1, M415/1, M431/1, M439/1, and M453/1 were confirmed to be present in excreta by LC/MS and may well be present in egg yolk, liver, muscle and fat but this was not confirmed. The differences in residue levels prior to and post sulfatase hydrolysis also suggested the presence of sulfate conjugates in egg and tissue.

CGA380778 (mono-depropynyloxy mandipropamid) was detected as a prominent metabolite in egg whites. NOA458422 was detected as major component in liver.

All egg and homogenised tissue samples were stored frozen to minimize potential decomposition during storage. Initial analysis of all the sample fractions took place within 6 months after egg sampling or necropsy. Therefore, no additional extraction was performed to evaluate the storage stability.

Table 14 Characterisation and identification of components in day 12 excreta from laying hens treated with ^{14}C-mandipropamid

A [chlorophenyl-U-^{14}C]-mandipropamid

Compound Code	Assignment	ROI (min)	Peak as % in Day 12 Excreta from Hens
M186/1	2-(4-chlorophenyl)-2-hydroxyacetic acid	24.13	1.63
M431/1	Sulfate of mono-oxidative CGA380775	25.63	6.36
M415/1	Sulfate of CGA380775	30.13	10.6
M401/1	Sulfate of dimethyl and di-depropynyloxy mandipropamid	31.13	4.55
CGA380775	Di-depropynyloxy mandipropamid	37.38	11.3
M453/1	Sulfate of NOA458422	39.13	6.87
M439/1	Sulfate of SYN505503	39.88	6.10

Compound Code	Assignment	ROI (min)	Peak as % in Day 12 Excreta from Hens
SYN505503	Mono-depropynyloxy mandipropamid	43.88	3.89
NOA458422	Mono-depropynyloxy mandipropamid	48.38	17.3
Mandipropamid	Test substance	55.88	1.09

B [methoxyphenyl-U-^{14}C]-mandipropamid

Compound Code	Assignment	ROI (min)	Peak as % in Day 12 Excreta from Hens
M431/1	Sulfate of mono-oxidative CGA380775	26.13	3.85
M415/1	Sulfate of CGA380775	30.13	11.6
M401/1	Sulfate of dimethyl and di-depropynyloxy mandipropamid	31.13	3.80
CGA380775	Di-depropynyloxy mandipropamid	37.38	10.0
M453/1	Sulfate of NOA458422	39.13	8.23
M439/1	Sulfate of SYN505503	39.63	4.31
SYN505503	Mono-depropynyloxy mandipropamid	43.88	4.14
NOA458422	Mono-depropynyloxy mandipropamid	48.38	19.8
Mandipropamid	Test substance	55.88	1.47

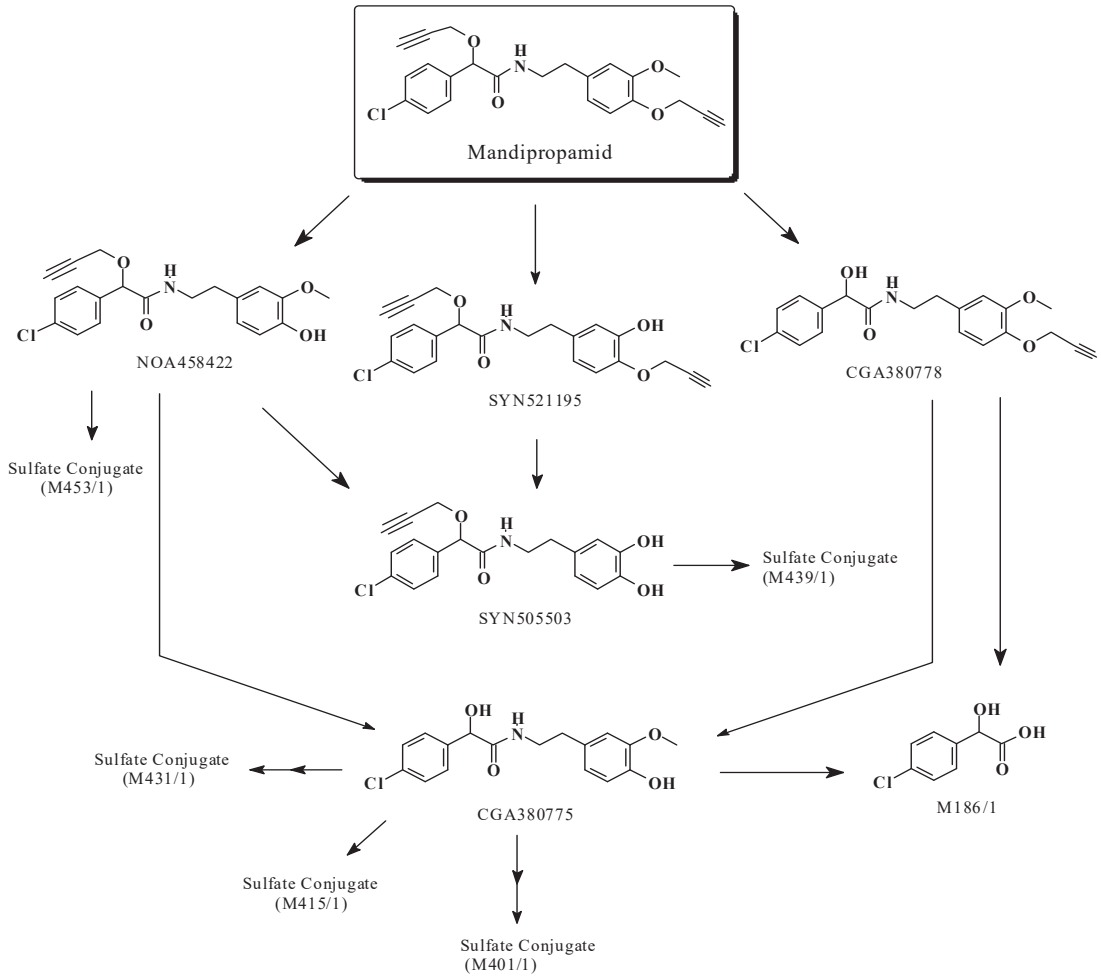

Figure 2 Proposed metabolic pathways for mandipropamid in the laying hen

RESIDUE ANALYTICAL METHODS

Analytical methods for food and feedstuffs of plant origin

Analytical methods for the determination of residues of mandipropamid in food and feedstuffs of plant origin were evaluated by the 2008 and 2015 JMPR. The methods previously submitted (RAM 415/01 and RAM 415/02) are suitable for measuring residues of mandipropamid with a LOQ of 0.01 mg/kg in high water, high acid, high starch and high oil matrices. The method was also validated on processed fractions of tomatoes and grapes.

The Meeting received additional or extended analytical methods and validation data for mandipropamid, and SYN500003 in plant matrices, and these are summarised below

Method PWO 9.154, v.3

This method (Le-onard, R., 2012)was used in the residues studies on beans (whole plant with pods and bean pods with seeds) and is based on reference method "N0A446510: Validation of Residue Analytical Method RAM 415/01 for the Determination of Residue in Crops", by J.P. Gill, 2004., which was previously evaluated by the 2008 JMPR. Minor modifications were made in order to improve method performance and these are described below. Additional validation data were generated to support the minor modifications.

Residues of mandipropamid were extracted from the sample by homogenising with acetonitrile:water (80:20, v/v). The resulting extract was diluted to 10 mL with acetonitrile:water (20:80, v/v) to produce a solution of acetonitrile:water (1:1, v/v). Further dilutions were conducted with acetonitrile:water (1:1, v/v). Mandipropamid residues were determined by LC-LC/MS/MS with on-line cleanup (two different C18 columns).

Method WO 9.154, v.3 has been validated for the determination of mandipropamid residues in beans (snap/common).

Acceptable mean recoveries (70–110%) were obtained for each matrix at each fortification levels. The overall relative standard deviation (RSD) for each matrix at each fortification level was ≤20%, thereby demonstrating satisfactory analytical precision. A validated LOQ of 0.01 mg/kg has been established for the determination of mandipropamid residues in beans (plants with pods and pods with seeds).

Table 15 Recovery of mandipropamid residues from beans using method WO 9.154, v.3

Commodity (Category)	Fortification level (mg/kg)	No. of analyses (n)	Recovery (%)	Mean recovery (%)	RSD (%)
Beans (snap) pods with seeds	0.01	6	98 - 110	102	5
	0.1	4	99 - 106	102	3
	1.0	3	99 - 105	101	3
Beans (snap) plants with pods	0.01	6	97 - 107	101	4
	0.1	3	97 - 102	99	3
	1.0	3	93 - 95	94	1
	20	3	98 - 105	101	4

Method GRM001.01A

This LC-MS/MS methods for measuring residues of mandipropamid in potato tubers and processed potato commodities were reported by Hill SE and Lin K (2006, SYN500003/0031) and Hill SE (2006, SYN500003/0030).

The method has been validated for the determination of SYN500003 residues in potato tubers and processed commodities (wet peel, crisps and dry granules). The modifications to the method are minor and do not affect the validity of the method for determining SYN500003 residues in potato matrices.

Samples are extracted by homogenisation with acetonitrile:water (80:20, v/v). Extracts are centrifuged and 5 mL aliquots are concentrated to 1 mL using clean dry air in a heating block. Samples are then diluted to 10 mL with water (7mL) and acetonitrile (2mL). Final determination is by LC-MS/MS using electrospray ionisation in the negative mode. An optional C18 solid phase extractions clean up can be used if interferences or unacceptable matrix effects are encountered during analysis.

The following is a description of the minor modifications of the method for potato: Extracts were filtered with a 0.45-µm PTFE filter. Filtered sample extracts were diluted with 50:50 (acetonitrile: water) and submitted for analysis, omitting solid phase extraction clean-up. A different analytical column was used for this study as were different mobile phases. Mandipropamid and SYN500003 were analysed in one analytical run for each sample.

Residues in the control samples were well < 30% of the LOQ. Linearity of the detector response was demonstrated in the range 0.0001– 0.01 µg/mL (n = 7) with a correlation coefficient of 0.999. Acceptable mean recoveries (70-110%) were obtained for each matrix at each fortification levels.

The overall relative standard deviation (RSD) for each matrix at each fortification level was ≤20%, thereby demonstrating satisfactory analytical precision. A validated LOQ of 0.005 mg/kg has been established for the determination of SYN500003 residues in potato tubers and processed commodities.

Table 16 Recovery of SYN500003 residues from potatoes using method GRM001.01A

Commodity (Category)	Fortification level (mg/kg)	No. of analyses (n)	Recovery (%)	Mean recovery (%)	RSD (%)	Recovery (%)	Mean recovery (%)	RSD (%)
			Multi-point calibration			Single point calibration		
Primary transition m/z 223→139								
Potato tubers (No SPE clean-up)	0.005	5	82 - 93	87	5	84 - 101	90	7
	0.05	5	96 - 111	103	5	101 - 106	104	2
	Overall	10	82 - 111	95	10	84 - 106	97	9
Potato tubers (Including SPE clean-up)	0.005	5	84 - 108	96	10	94 - 105	97	5
	0.05	5	94 - 103	99	4	95 - 99	97	1
	Overall	10	84 - 108	98	7	94 - 105	97	3
Potato peel, wet (No SPE clean-up)	0.005	5	76 - 93	84	7	84 - 94	89	5
	0.05	5	96 - 105	101	3	88 - 106	98	7
	Overall	10	76 - 105	93	11	84 - 106	93	8
Potato crisps (No SPE clean-up)	0.005	5	83 - 99	93	7	88 - 104	98	7
	0.05	5	104 - 111	107	4	103 - 110	106	3
	Overall	10	83 - 111	100	8	88 - 110	102	6
Potato granules (dry) (No SPE clean-up)	0.005	5	77 - 97	84	9	84 - 109	98	10
	0.05	5	104 - 110	108	2	102 - 115	108	5
	Overall	10	77 - 110	96	14	84 - 115	103	9
Confirmatory transition m/z 225→141								
Potato tubers (No SPE clean-up)	0.005	5	83 - 107	93	10	85 - 116	100	14
	0.05	5	96 - 107	103	4	97 - 111	101	6
	Overall	10	83 - 107	98	9	85 - 116	100	10
Potato tubers (Including SPE clean-up)	0.005	5	70 - 91	8	12	79 - 124	99	17
	0.05	5	96 - 108	102	4	91 - 103	96	5
	Overall	10	70 - 108	92	14	79 - 124	98	12
Potato peel, wet (No SPE clean-up)	0.005	5	81 - 112	92	14	89 - 114	101	10
	0.05	5	96 - 105	101	4	103 - 117	109	5
	Overall	10	81 - 105	97	11	89 - 117	105	8
Potato crisps (No SPE clean-up)	0.005	5	95 - 109	102	6	91 - 106	97	6
	0.05	5	105 - 111	107	2	100 - 106	104	3
	Overall	10	95 - 111	104	5	91 - 106	100	6
Potato granules (dry) (No SPE clean-up)	0.005	5	85 - 96	91	5	96 - 109	102	6
	0.05	5	100 - 112	106	4	102 - 111	107	4
	Overall	10	85 - 112	99	9	96 - 111	104	5

GRM001.01B (Potato)

This is LC-MS/MS method used to determine SYN500003 residues in potato tubers and processed commodities was reported by Francis P, Joseph T and Lin K (2017, SYN500003_50003).

The method is a modification of GRM001.01A, omitting the optional SPE clean-up step and using simple sample dilution. Minor changes were also made to instrument parameters and only the primary transition (m/z 222.9→138.7) was monitored.

Samples are extracted by homogenisation with acetonitrile:water (80:20, v/v). Extracts are centrifuged and 5 mL aliquots are added to 5 mL water. If further dilution is necessary extracts are diluted to a final volume using acetonitrile:water (35:65, v/v).

Final determination is by LC-MS/MS using a C18 column and gradient separation with 0.2% formic acid aqueous solution and acetonitrile. MS/MS detection is accomplished by monitoring the transition m/z 223 to m/z 139 using electrospray ionisation in the negative mode.

Linearity of the detector response was demonstrated in the range 0.0001–0.005 µg/mL (n = 6) with a correlation coefficient of 0.9999484. Acceptable mean recoveries (70–110%) were obtained for each matrix at each fortification levels. The

overall relative standard deviation (RSD) for each matrix at each fortification level was ≤20%, thereby demonstrating satisfactory analytical precision. A validated LOQ of 0.005 mg/kg has been established for the determination of SYN500003 residues in potato tubers and processed commodities.

Table 17 Recovery of SYN500003 residues from potatoes and processed commodities using method GRM001.01B

Commodity (Category)	Fortification level (mg/kg)	No. of analyses (n)	Recovery (%)	Mean recovery (%)	RSD (%)
Potato tubers	0.005	17	74 - 115	92	14
	0.01	9	73 - 87	80	6
	0.02	9	71 - 98	77	13
	Overall	35	71 - 115	85	15
Granules/flakes	0.005	1	76	-	-
	0.01	1	70	-	-
	Overall	2	70 - 76	73	6
Chips	0.005	1	74	-	-
Wet peel	0.01	1	80	-	-

RAM 415/02 (cocoa beans and processed commodities)

This method was previously evaluated by the JMPR for various crop matrices, including high oil commodities. Method RAM 415/02 has been validated for the determination of mandipropamid residues in cocoa beans and processed cocoa commodities (roasted nibs, chocolate, cocoa powder and cocoa butter).

Linearity of the detector response was demonstrated in the range 0.1–50 ng/mL (n = 5) with a correlation coefficient of ≥0.99. Acceptable mean recoveries (70–110%) were obtained for each matrix at each fortification level. A validated LOQ of 0.01 mg/kg has been established for the determination of mandipropamid residues in processed cocoa commodities.

Table 18 Recovery of mandipropamid residues from cocoa beans and processed cocoa commodities using method RAM 415/02

Commodity	Fortification level	No. of analyses	Recovery (%)	Mean recovery	RSD
(Category)	(mg/kg)	(n)		(%)	(%)
Pimary transition (m/z 412→328)					
Cocoa beans	0.01	5	89 - 111	100	9
	0.1	5	78 - 110	97	13
Chocolate	0.01	3	78 - 91	84	8
	0.1	3	76 - 90	81	9
	Overall	6	76 - 91	83	7.9
Roasted nibs	0.01	3	76 - 92	83	10
	0.1	3	70 - 89	82	13
	Overall	6	70 - 92	83	10
Cocoa powder	0.01	3	85 - 92	88	4
	0.1	3	72 - 85	79	8
	Overall	6	72 - 92	83	8
Cocoa butter	0.01	3	98 - 110	104	6
	0.1	3	87 - 103	97	9
	Overall	6	87-110	101	8
Confirmatory transition (m/z 412→125)					
Chocolate	0.01	3	80 - 88	85	5
	0.1	3	77 - 90	82	9
	Overall	6	77 - 90	83	7
Roasted nibs	0.01	3	72 - 88	88	10
	0.1	3	66 - 85	78	13
	Overall	6	66 – 88	79	11
Cocoa powder	0.01	3	83 - 88	86	3
	0.1	3	71 - 82	77	7
	Overall	6	71 – 88	82	7
Cocoa butter	0.01	3	97 - 110	104	6

Commodity	Fortification level	No. of analyses	Recovery (%)	Mean recovery	RSD
	0.1	3	88 - 105	99	10
	Overall	6	88 – 110	101	8

Analytical methods for food and feed stuffs of animal origin

No methods for the determination of residues of mandipropamid in food and feedstuffs of animal origin were evaluated by the 2008 or 2013 JMPR. No methods have been provided.

Applicability of multi residue methods

Multi-residue method DFG S19 was evaluated by the 2008 JMPR. The JMPR concluded that the multi-residue method DFG S19 is suitable for monitoring residues of mandipropamid in plant commodities with a LOQ of 0.01 mg/kg. No additional multi-residue methods are provided.

Stability of residues in stored analytical samples

The Meeting received information on the stability of residues of mandipropamid and its metabolite in fortified samples of agricultural commodities: tomatoes (fruit and paste), grapes (fruit and juice), potatoes (tubers and granules/flakes), lettuce, cucumbers, wheat (forage, grain and straw), and soya beans (beans, hulls, meal and oil)stored at freezer temperatures of -20±5°C for up to 24 months.

In a study reported by Hamilton L, Joseph T (2006, NOA446510/0921), separate representative crop samples (10 g) were fortified with mandipropamid at 0.5 mg/kg. Immediately after fortification, sample sets were stored in a freezer at approximately -20 °C until analysed. At the desired storage intervals of approximately zero, three, six, twelve and twenty-four months a sample set of each substrate, consisting of a control sample, two freshly fortified samples and two freezer stored fortified samples, were analysed for residues of mandipropamid using the following method: RAM 415/01. Analysis of the soya bean oil samples required a modification of this method, using hexane in the homogenization process instead of acetonitrile/water and replacing the solid phase extraction clean-up with a liquid-liquid partition.

There was no significant change in the mandipropamid residue levels in any commodity during the 24 months of storage with any apparent losses being <30%. This is with the exception of wheat grain where the samples stored for 3 months appeared to contain only 59% of the expected mandipropamid concentration. However, the samples stored for 6, 12 and 24 months contained the expected mandipropamid concentrations, thus, demonstrating that the results after 3 months were anomalous. Therefore, residues of mandipropamid are expected to be stable in all crop commodities when stored at -20 °C for at least two years.

Table 19 Stability of mandipropamid residues in crop commodities following storage at -20 °C

Commodity	Storage Period (Months)	Mandipropamid Concentration – Uncorrected (mg/kg)[a]	Mean Procedural Recovery (%)[b]	Mandipropamid Concentration – Corrected (mg/kg)[c]	Percentage Recovery[d]
Tomatoes – Fruit	0	0.44	91	0.48	100
	3	0.46	97	0.47	98
	6	0.47	103	0.46	96
	12	0.42	99	0.42	88
	24	0.54	97	0.56	111
Tomatoes – Paste	0	0.45	87	0.51	100
	3	0.48	90	0.53	105
	6	0.49	104	0.49	97
	12	0.46	95	0.48	94
	24	0.48	108	0.45	88
Grapes – Fruit	0	0.48	95	0.50	100
	3	0.48	96	0.49	98
	6	0.47	94	0.49	98
	12	0.42	92	0.45	89
	24	0.50	84	0.60	120
Grapes – Juice	0	0.46	90	0.51	100

Commodity	Storage Period (Months)	Mandipropamid Concentration – Uncorrected (mg/kg)[a]	Mean Procedural Recovery (%)[b]	Mandipropamid Concentration – Corrected (mg/kg)[c]	Percentage Recovery[d]
	3	0.47	88	0.53	104
	6	0.36	85	0.41	81
	12	0.46	88	0.52	103
	24	0.52	98	0.53	103
Potatoes – Tubers	0	0.51	100	0.51	100
	3	0.55	98	0.56	109
	6	0.57	108	0.56	110
	12	0.47	89	0.53	104
	24	0.49	104	0.47	91
Potatoes – Granules/Flakes	0	0.47	90	0.52	100
	3	0.50	97	0.51	99
	6	0.48	102	0.48	93
	12	0.52	97	0.53	103
	24	0.49	108	0.45	87
Lettuce – Head	0	0.45	94	0.48	100
	3	0.44	81	0.55	114
	6	0.48	80	0.59	122
	12	0.41	102	0.40	83
	24	0.52	101	0.51	107
Cucumbers – Fruit	0	0.44	90	0.49	100
	3	0.49	104	0.48	98
	6	0.47	103*	0.47	95
	12	0.48	89	0.53	108
	24	0.59	114	0.52	106
Wheat – Forage	0	0.49	95	0.52	100
	3	0.46	88	0.52	100
	6	0.41	99	0.41	80
	12	0.41	90	0.45	87
	24	0.44	89	0.49	95
Wheat – Straw	0	0.37	82	0.45	100
	3	0.49	121	0.49	108
	6	0.58	113	0.58	127
	12	0.57	114	0.50	110
	24	0.42	80	0.52	115
Wheat – Grain	0	0.35	71*	0.49	100
	3	0.27	92	0.29	59
	6	0.48	100	0.48	99
	12	0.51	83	0.61	127
	24	0.52	97	0.53	109
Soya bean – Beans	0	0.45	91	0.50	100
	3	0.44	96	0.46	92
	6	0.46	88	0.48	96
	12	0.42	83	0.51	102
	24	0.44	109	0.40	81
Soya bean – Meal	0	0.46	93	0.49	100
	3	0.42	92	0.45	92
	6	0.46	99	0.45	93

Commodity	Storage Period (Months)	Mandipropamid Concentration – Uncorrected (mg/kg)[a]	Mean Procedural Recovery (%)[b]	Mandipropamid Concentration – Corrected (mg/kg)[c]	Percentage Recovery[d]
	12	0.41	100	0.41	84
	24	0.55	93	0.59	120
Soya bean – Hulls	0	0.44	87	0.50	100
	3	0.47	89	0.52	105
	6	0.45	104	0.45	90
	12	0.41	94	0.44	87
	24	0.55	112	0.49	98
Soya bean – Oil	0	0.48	94	0.50	100
	3	0.47	94	0.50	100
	6	0.51	91	0.56	112
	12	0.41	100	0.40	80
	24	0.53	104	0.50	100

[a] Mean of two samples, not corrected for procedural recovery

[b] Mean of two recoveries

[c] Mean of two samples, corrected for procedural recovery

[d] Percentage of 0 day = (residue concentration / zero month residue concentration using corrected residues)

* – one recovery sample only

Storage stability of mandipropamid in beans (snap/common) was investigated by Leonard, R. (2012, NOA446510_50170, IR-4 PR No.10324). Samples were spiked at 0.1 mg/kg and stored frozen for 357 days.

Table 20 Summary of storage stability of mandipropamid residues in beans (snap)

Commodity	Level (mg/kg)	Storage interval (days/months)	Individual values (mg/kg)	Mean Recovery (%)
Beans, pods with seeds	0.10	357 / 12	0.0939, 0.0926, 0.0977	92
Beans, whole plants with pods	0.10	357 / 12	0.0968, 0.0954, 0.0995	94

The storage stability of SYN500003 the major metabolitie of mandipropamid was investigated in potato commodities up to 32 months by Manuli M (2008, NOA446510_50000).

Samples were fortified with SYN500003 at 0.50 ppm concentration and were immediately stored frozen under conditions identical to those used to store residue samples prior to analysis. The stored samples were analysed at storage intervals of approximately 0, 3, 7, 12, 18, 21, 26 and 32 months.

Analytical Method GRM 001.01B with slight modifications was used to determine residues of SYN500003 in the potato tubers and processed fractions (granules/flakes, chips and wet peel). Results demonstrated that residues of SYN500003 were stable in potato tubers, potato granules/flakes, potato chips and potato wet peel when stored under freezer storage conditions for up to 32 months.

Table 21 Stability of SYN500003 residues in crop commodities following storage at -20 °C

Commodity	Storage Interval (Months)	SYN500003 Fortification Level (mg/kg)	SYN500003 Uncorrected residues found (ppm)[a]	SYN500003 Corrected residues found (ppm)[b]	SYN500003 Mean Conc. (ppm)	SYN500003 Percent of 0 Day[c]
Potatoes – Tubers	0	0.50	0.485, 0.450, 0.467	0.505, 0.469, 0.486	0.49	100
	3	0.50	0.490, 0.540	0.549, 0.605	0.58	118

Commodity	Storage Interval (Months)	SYN500003 Fortification Level (mg/kg)	SYN500003 Uncorrected residues found (ppm)[a]	SYN500003 Corrected residues found (ppm)[b]	SYN500003 Mean Conc. (ppm)	SYN500003 Percent of 0 Day[c]
	7	0.50	0.534, 0.517	0.534, 0.517	0.53	108
	12	0.50	0.472, 0.530	0.498, 0.559	0.53	108
	18	0.50	0.534, 0.549	0.541, 0.556	0.55	112
	21	0.50	0.409, 0.405	0.512, 0.506	0.51	104
	26	0.50	0.444, 0.440	0.515, 0.510	0.51	104
	32	0.50	0.471, 0.475	0.541, 0.546	0.54	110
Potatoes – Granules/Flakes	0	0.50	0.441, 0.481, 0.459	0.472, 0.516, 0.492	0.49	100
	3	0.50	0.489, 0.485	0.529, 0.524	0.53	108
	7	0.50	0.483, 0.518	0.489, 0.525	0.51	104
	12	0.50	0.461, 0.460	0.504, 0.502	0.50	102
	18	0.50	0.473, 0.519	0.481, 0.528	0.50	102
	21	0.50	0.374, 0.375	0.508, 0.510	0.51	104
	26	0.50	0.435, 0.441	0.519, 0.526	0.52	106
	32	0.50	*, 0.451	*, 0.538	0.54	110
Potato – Chips	0	0.50	0.455, 0.460, 0.433	0.462, 0.467, 0.440	0.46	100
	3	0.50	0.484, 0.483	0.484, 0.483	0.48	104
	7	0.50	0.535, 0.492	0.535, 0.492	0.51	111
	12	0.50	0.421, 0.449	0.488, 0.520	0.50	109
	18	0.50	0.520, 0.502	0.546, 0.527	0.54	117
	21	0.50	0.379, 0.377	0.510, 0.508	0.51	111
	26	0.50	0.418, 0.412	0.521, 0.514	0.52	113
	32	0.50	0.388, 0.374	0.467, 0.451	0.46	100
Potato – Wet Peel	0	0.50	0.453, 0.429, 0.465	0.517, 0.489, 0.530	0.51	100
	3	0.50	0.511, 0.425,	0.564, 0.469	0.52	102
	7	0.50	0.489, 0.532	0.493, 0.537	0.52	102
	12	0.50	0.465, 0.457	0.505, 0.495	0.50	98
	18	0.50	0.493, 0.501	0.507, 0.516	0.51	100
	21	0.50	0.404, 0.407	0.514, 0.518	0.52	102
	26	0.50	0.436, 0.421	0.487, 0.470	0.48	94
	32	0.50	0.472, 0.493	0.508, 0.530	0.52	102

[a] Uncorrected residues: Freezer storage sample results were not corrected control background or mean procedural recovery.

[b] Corrected residues: Freezer storage sample results were not corrected for control background but were corrected for the mean procedural recovery <100%.

[c] Storage stability % recovered = (interval mean conc/0 day mean conc) × 100.

* The 32 month potato flakes/granules rep A sample was not available for extraction. The sample was a replacement sample for the 18 month potato flakes/granules rep A sample which was lost in work up.

USE PATTERNS

Information on GAP in Cameroon, Canada and the USA was available to the Meeting on the use of mandipropamid. The authorised uses relevant to the supervised trial data submitted to the current Meeting are summarised in the following Table.

Crop/Commodity	Country	Formulation			Application					PHI (days)
		Active substance content	Type	Method	No	Rate	Spray volume	Interval (days)	Seasonal max.	
Beans, snap	USA.	250 g/L	SC	Foliar	4	146 g ai/ha	-	7 - 10	ca. 583 g ai/ha	1

Crop/Commodity	Country	Formulation			Application					PHI (days)
		Active substance content	Type	Method	No	Rate	Spray volume	Interval (days)	Seasonal max.	
Edible-podded beans [a]	Canada	250 g/L	SC	Foliar	4	150 g ai/ha	min. 100 L/ha (ground) min. 45 L/ha (aerial)	7 - 10	600 g ai/ha	1
Potato	USA.	250 g/L	SC	Foliar	-	101 - 146 g ai/ha	-	7 - 10	583 g ai/ha	14
				Seed treatment	-	3.25 - 10 g ai/100 kg seed	-	-	583 g ai/ha	-
				Seed treat + foliar	1 seed treatment + 3 foliar	1. 3.25 - 10 g ai/100 kg seed 2. 101 - 146 g ai/ha	-	7 - 10	583 g ai/ha	14
	Canada	250 g/L	SC	Foliar	-	100 - 150 g ai/ha	-	7 - 10	600 g ai/ha	14
				Seed treatment	-	3.25 - 6.5 g ai/100 kg seed	-	-	600 g ai/ha	-
				Seed treatment + foliar	1 seed treatment + 2 - 4 foliar	1. 3.25 - 6.5 g ai/100 kg seed 2. 100 - 150 g ai/ha	-	7 - 10	600 g ai/ha	14
Cocoa	Cameroon	125 g/kg	WG	Foliar	4 - 6	90 g ai/ha	360 L/ha‡	21	6 applications	14

[a] Complete list of succulent cultivar of edible-podded bean included on label: edible-podded runner beans, edible-podded snap beans, edible-podded wax beans, edible-podded moth beans, edible-podded yard long beans, edible-podded jack beans and edible-podded sword beans.

A spreading/penetrating type adjuvant such as a non-ionic surfactant, crop oil concentrate, silicone based, or blend must be added at the manufacturer's recommended rates. For other crop uses, an adjuvant is recommended.

Crops which are not registered for use with mandipropamid fungicide should be not planted for a period of 30 days after the last application.

RESIDUES RESULTING FROM SUPERVISED TRIALS ON CROPS

The Meeting received information on supervised trials conducted with mandipropamid used to the following crops.

Table 22 Overview of the crops considered in the framework of this submission

Type	Group / Subgroup	Group Letter Code	Commodity	Table No.
02 Vegetables	014 Legume vegetables	VP	Beans (except broad bean and soya bean)	24
	016 Root and tuber vegetables	VR	Potato	26, 27
04 Nuts and seeds	024 Seed for beverages and sweets	SB	Cocoa (cacao) beans	29
11 Primary feed commodities of plant origin	050 Legume animal feeds	AL	Bean forage (green)	30

Legume vegetables

Beans (fresh with pods))

The supported GAP for the use of mandipropamid on edible-podded beans is a foliar treatment. According to the labels in Canada and the USA, foliar applications may be made at 146–150 g ai/ha, up to a maximum of 600 g ai/ha per season (i.e. four applications), with a minimum 1-day PHI.

Table 23 Critical use pattern (cGAP) for mandipropamid on edible podded beans a

Region	Outdoor/Protected Crop	Method	Max No of Apps	App Interval (days)	App Rate (g a.s./ha)	Min PHI (days)
Canada	Outdoor	foliar	4	7	150	1

[a] Complete list of succulent cultivar of edible-podded bean included on label: edible-podded runner beans, edible-podded snap beans, edible-podded wax beans, edible-podded moth beans, edible-podded yard long beans, edible-podded jackbeans and edible-podded sword beans.

Ten supervised trials with mandipropamid on snap beans were conducted in the USA. Mandipropamid was applied four times at a nominal rate of 146 g ai/ha and sampled at a PHI of 1 day. Crop oil concentrates or non-ionic surfactants were included in the spray mixture, following label recommendations.

Samples at the indicated pre-harvest interval were collected at the normal commercial harvest date. Duplicate samples were collected at each sampling interval designated for collection from the treated plots. Each pod with seed sample weighed at least 1 kg and each sample of whole plants with pods consisted of a minimum of 12 plants.

Samples were frozen within approximately 2 hours of collection and maintained in frozen storage for periods of ≤ 359 days (ca. 12 months) prior to extraction. Residues of mandipropamid are stable in high water matrices for at least 12 months when stored at -20 °C.

Residues of mandipropamid in beans were determined using analytical method WO 9.154 v.3, with an LOQ of 0.01 mg/kg. The performance of the method was verified by mean procedural recoveries of mandipropamid in the acceptable range of 70–120%.

Table 24 Residues of mandipropamid on beans (snap/common) in USA (outdoor trials).

GLP and Trial Details	Crop (Variety)	Country (Region) (Postcode)	Application Rate (Additive Type, Rate)	Growth Stage at Application	PHI (days)	Crop Part	Residue Found (Uncorrected)
cGAP	Bean (snap)	USA	146 g ai/ha	n/a (cGAP based on PHI)	1		Mandipropamid (mg/kg)
Report: IR-4 PR No.10324 Study: 10324 Trial: 10-CA*85 - Study to GLP - Study carried out in 2010 (Field)	Bean (Provider)	United States (Salinas, CA)	147 145 145 149 (Activator 90)	25% flowering - 35% flowering flowering - pods at all levels on plant flowering - pods at all levels on plant mature pods	1	Pod with seeds	0.281; 0.227 (0.254)
Report: IR-4 PR No.10324 Study: 10324 Trial: 10-CA84 - Study to GLP - Study carried out in 2010 (Field)	Bean (Jade)	United States (Riverside, CA)	147 148 147 146 (R-11 Activator/ Spreader)	vegetative bloom 2 inch bean pod development - mature pods	1	Pod with seeds	0.526; 0.332 (0.429)
					3	Pod with seeds	0.411; 0.492 (0.451)
					7	Pod with seeds	0.374; 0.298 (0.336)
					10	Pod with seeds	0.119; 0.205 (0.162)
Report: IR-4 PR No.10324 Study: 10324 Trial: 10-FL24 - Study to GLP - Study carried out in 2010 (Field)	Bean (Dusky)	United States (Citra, FL)	151 155 151 146 (Agri Dex)	blooming blooming - fruiting blooming - fruiting blooming - fruiting	1	Pod with seeds	0.269; 0.227 (0.248)
Report: IR-4 PR No.10324 Study: 10324 Trial: 10-GA*06 - Study to GLP - Study carried out in 2010 (Field)	Bean (Contender Garden)	United States (Tifton, GA)	147 148 148 147 (UAP Surfactant 80/20)	vegetative blooming fruiting fruiting	1	Pod with seeds	0.117; 0.111 (0.114)

GLP and Trial Details	Crop (Variety)	Country (Region) (Postcode)	Application Rate (Additive Type, Rate)	Growth Stage at Application	PHI (days)	Crop Part	Residue Found (Uncorrected)
cGAP	Bean (snap)	USA	146 g ai/ha	n/a (cGAP based on PHI)	1		Mandipropamid (mg/kg)
Report: IR-4 PR No.10324 Study: 10324 Trial: 10-MD13 - Study to GLP - Study carried out in 2010 (Field)	Bean (Provider)	United States (Salisbury, MD)	147 148 106 146 (Reliable)	first bloom 2 inch bean - 3 inch bean mature beans mature beans	1	Pod with seeds	0.193; 0.189 (0.191)
Report: IR-4 PR No.10324 Study: 10324 Trial: 10-MI21 - Study to GLP - Study carried out in 2010 (Field)	Bean (Foremost)	United States (Holt, MI)	150 150 149 148 (Activator 90)	flowering fruiting fruiting fruiting	1	Pod with seeds	0.149; 0.110 (0.129)
Report: IR-4 PR No.10324 Study: 10324 Trial: 10-NY11 - Study to GLP - Study carried out in 2010 (Field)	Bean (California Early)	United States (Freeville, NY)	146 146 146 146 (Induce)	vegetative blooming blooming - fruiting blooming - fruiting	1	Pod with seeds	0.0858; 0.114 (0.100)
Report: IR-4 PR No.10324 Study: 10324 Trial: 10-OH*07 - Study to GLP - Study carried out in 2010 (Field)	Bean (Brio)	United States (Wooster, OH)	141 142 150 145 (Top Surf)	vegetative - 10% bloom blooming fruiting fruiting	1	Pod with seeds	0.329; 0.468 (0.399)
Report: IR-4 PR No.10324 Study: 10324 Trial: 10-WA*19 - Study to GLP - Study carried out in 2010 (Field)	Bean (Jade)	United States (Moxee, WA)	140 141 147 149 (90 Plus)	bloom - pods bloom - pod development bloom - pods pod maturation	1	Pod with seeds	0.761; 0.398 (0.580)

GLP and Trial Details	Crop (Variety)	Country (Region) (Postcode)	Application Rate (Additive Type, Rate)	Growth Stage at Application	PHI (days)	Crop Part	Residue Found (Uncorrected)
cGAP	Bean (snap)	USA	146 g ai/ha	n/a (cGAP based on PHI)	1		Mandipropamid (mg/kg)
Report: IR-4 PR No.10324 Study: 10324 Trial: 10-WI07 - Study to GLP - Study carried out in 2010 (Field)	Bean (Hercules)	United States (Arlington, WI)	149 147 146 148 (Activator 90)	bud - early bloom bloom - pods bloom - pods pods	1	Pod with seeds	0.135; 0.0918 (0.113)

Root and tuber vegetables

Potato

The current Meeting received information on supervised residue trials on potato in Canada and the USA. The supported GAP for the use of mandipropamid on potatoes is a seed treatment followed by multiple foliar applications. According to the labels in Canada and the USA, one seed potato treatment application may be made at 3.25–10 g ai/100 kg seed potato, followed by up to three foliar applications between 100–150 g ai/ha, with a minimum 14-day PHI. The cGAP is detailed in Table .

Table 25 Critical use pattern (cGAP) for mandipropamid on potato

Region	Outdoor/ Protected Crop	Method	Max No of Apps	App Interval (days)	App Rate	Min PHI (days)
Canada/USA	Outdoor	seed treatment + foliar	1 seed treatment + 3 × foliar	7 (foliar)	10 g ai/100 kg seed + 3 × 146 g ai/ha	14

Sixteen supervised trials with mandipropamid on potatoes were conducted in the USA in 2012. Mandipropamid was applied once as a seed treatment at a nominal rate of 10 g ai/100 kg seed potato followed by three foliar treatments at a nominal rate of 150 g ai/ha and sampled at a PHI of 14 days. Crop oil concentrates or non-ionic surfactants were included in the spray mixture, following label recommendations.

For magnitude of residue tests, specimens at the indicated pre-harvest interval were collected at the normal commercial harvest date. Duplicate specimens were collected at each sampling interval designated for collection from the treated plots. A single sample was collected from the control plot. A minimum of 24 tubers were collected.

Samples were frozen and maintained in frozen storage for periods of ≤373 days (ca. 12 months) prior to extraction. Residues of mandipropamid are stable in representative matrices for at least 12 months when stored at -20 °C. Extracts were stored frozen prior to analysis, which was conducted on the same or following day as extraction.

Residues of mandipropamid in potato tubers were determined using analytical method RAM 415/02, modified with an LOQ of 0.01 mg/kg. Residues of SYN500003 in potato tubers were determined using analytical method GRM001.01A, modified with an LOQ of 0.005 mg/kg. Only very minor modifications were made and the performance of the method was verified by mean procedural recoveries of mandipropamid in the acceptable range of 70–120%.

The results of the trials are summarised in Table , where residues relevant to the setting of an MRL and for use in risk assessment are underlined.

Table 26 Residues of mandipropamid on potato in the USA (outdoor trials)

GLP and Trial Details	Crop (Variety)	Country (Region)	Application Rate (g ai/100 kg seed OR g ai/ha)	Growth Stage at Application (BBCH)	PHI (days)	Crop Part	Residue Found (Uncorrected) † (mg/kg)		
cGAP	Potato	USA	10 g ai/100 kg seed + 3 × 146 g ai/ha	n/a (cGAP based on PHI)	14		SYN500003	Mandipropamid	Total *
Report: TK0069119 Trial: TK0069119-01 Study to GLP - Study carried out in 2012	Potato / Red Norland	USA (North Rose, NY)	10 g ai/100 kg seed 125 127 126 (EXC1253, 0.25 % v/v)	BBCH 00 BBCH 44 - 45 BBCH 45 - 46 BBCH 47 - 48	14	Tuber	0.0058; 0.0061 (0.0059)	<0.01; <0.01 (< 0.01)	0.021
Report: TK0069119 Trial: TK0069119-02 Study to GLP - Study carried out in 2012	Potato / Superior	USA (Alton, NY)	10 g ai/100 kg seed 130 130 130 (EXC1252, 0.2% v/v)	BBCH 000 - 001 BBCH 44 - 45 BBCH 45 - 46 BBCH 46 - 47	14	Tuber	0.014; 0.011 (0.013)	0.032; < 0.01 (0.021)	0.045
Report: TK0069119 Trial: TK0069119-03 Study to GLP - Study carried out in 2012	Potato / Red Pontiac	USA (Seven Springs, NC)	10 g ai/100 kg seed 130 129 124 (EXC1252, 0.3 - 0.5 % v/v)	BBCH 00 BBCH 41 - 42 BBCH 42 - 43 BBCH 46 - 48	12	Tuber	0.012; 0.014 (0.013)	0.030; < 0.01 (0.020)	0.044
Report: TK0069119 Trial: TK0069119-04 Study to GLP - Study carried out in 2012	Potato / Red LaSoda	USA (Oviedo, FL)	11 g ai/100 kg seed 130 129 130 (EXC1252, 0.25 % v/v)	BBCH 00 BBCH 43 BBCH 45 BBCH 47	13	Tuber	0.0060; 0.0056 (0.0058)	0.017; 0.015 (0.016)	0.027
Report: TK0069119 Trial: TK0069119-05 Study to GLP - Study carried out in 2012	Potato / Cobbler	USA (Richland, IA)	11 g ai/100 kg seed 127 127 128 (EXC1252, 0.25 % v/v)	BBCH 01 - 02 BBCH 44 BBCH 46 BBCH 48	7 10 14 17 21	Tuber	0.014 0.011 0.0088; 0.0090 (0.0089) 0.0083 < 0.005	0.24 0.051 0.028; 0.043 (0.036) 0.073 0.038	0.089

GLP and Trial Details	Crop (Variety)	Country (Region)	Application Rate (g ai/100 kg seed OR g ai/ha)	Growth Stage at Application (BBCH)	PHI (days)	Crop Part	Residue Found (Uncorrected) † (mg/kg)		
Report: TK0069119 Trial: TK0069119-06 Study to GLP - Study carried out in 2012	Potato / Yukon Gold	USA (Gardner, ND)	10 g ai/100 kg seed 129 129 128 (EXC1252, 0.25 % v/v)	BBCH 00 BBCH 90 - 91 BBCH 90 - 91 BBCH 91 - 93	14	Tuber	< 0.005; < 0.005 (< 0.005)	0.052; < 0.01 (0.031)	0.036
Report: TK0069119 Trial: TK0069119-07 Study to GLP - Study carried out in 2012	Potato / Dark Red Norland	USA (Campbell, MN)	10 g ai/100 kg seed 128 128 128 (EXC1252, 0.25 % v/v)	BBCH 0 BBCH 68 - 69 BBCH 72 BBCH 45 - 46	14	Tuber	< 0.005; < 0.005 (< 0.005)	0.027; 0.019 (0.023)	0.028
Report: TK0069119 Trial: TK0069119-08 Study to GLP - Study carried out in 2012	Potato / Dakota Pearl	USA (Campbell, MN)	11 g ai/100 kg 128 128 129 (EXC1252, 0.25 % v/v)	BBCH 00 BBCH 65 - 66 BBCH 68 - 69 BBCH 41 - 42	14	Tuber	< 0.005; < 0.005 (< 0.005)	0.066; 0.047 (0.056)	0.061
Report: TK0069119 Trial: TK0069119-09 Study to GLP - Study carried out in 2012	Potato / Russet Burbnk	USA (Lewiston, UT)	8.7 g ai/100 kg seed 127 126 131 (EXC1253, 0.5 % v/v)	BBCH 00 BBCH 44 BBCH 45 BBCH 47	14	Tuber	< 0.005; < 0.005 (< 0.005)	< 0.01; < 0.01 (< 0.01)	<0.015
Report: TK0069119 Trial: TK0069119-10 Study to GLP - Study carried out in 2012	Potato / Cal White G5	USA (Madera, CA)	10 g ai/100 kg seed 129 130 125 (EXC1253, 0.4 % v/v)	BBCH 00 BBCH 45 - 46 BBCH 47 - 48 BBCH 47 - 48	14	Tuber	0.0089; 0.011 (0.01)	0.024; < 0.01 (0.017)	0.035
Report: TK0069119 Trial: TK0069119-11 Study to GLP - Study carried out in 2012	Potato / Ranger Russet	USA (American Falls, ID)	10 g ai/100 kg seed 133 131 132 (EXC1253, 1 % v/v)	BBCH 00 BBCH 45 - 46 BBCH 46 BBCH 46 - 47	15	Tuber	< 0.005; < 0.005 (< 0.005)	< 0.01; 0.011 (0.011)	0.016

GLP and Trial Details	Crop (Variety)	Country (Region)	Application Rate (g ai/100 kg seed OR g ai/ha)	Growth Stage at Application (BBCH)	PHI (days)	Crop Part	Residue Found (Uncorrected) † (mg/kg)		
Report: TK0069119 Trial: TK0069119-12 Study to GLP - Study carried out in 2012	Potato / Ranger Russet	USA (Payette, ID)	10 g ai/100 kg seed 128 128 129 (EXC1253, 0.5 % v/v)	BBCH 00 - 01 BBCH 45 - 46 BBCH 46 - 47 BBCH 47 - 48	7 10 14 17 21	Tuber	< 0.005 < 0.005 < 0.005; < 0.005 (< 0.005) < 0.005 < 0.005	< 0.01 < 0.01 < 0.01; < 0.01 (< 0.01) < 0.01 < 0.01	<0.015
Report: TK0069119 Trial: TK0069119-13 Study to GLP - Study carried out in 2012	Potato / Russet Burbnk	USA (American Falls, ID)	10 g ai/100 kg seed 131 130 131 (EXC1253, 1 % v/v)	BBCH 00 BBCH 45 - 46 BBCH 46 BBCH 46 - 47	12	Tuber	< 0.005; < 0.005 (< 0.005)	0.050; 0.035 (0.043)	0.048
Report: TK0069119 Trial: TK0069119-14 Study to GLP - Study carried out in 2012	Potato / Dakota Pearl	USA (American Falls, ID)	10 g ai/100 kg seed 137 131 140 (EXC1253, 0.5 % v/v)	BBCH 00 BBCH 45 - 46 BBCH 46 BBCH 46 - 47	12	Tuber	< 0.005; < 0.005 (< 0.005)	< 0.01; 0.011 (0.011)	0.016
Report: TK0069119 Trial: TK0069119-15 Study to GLP - Study carried out in 2012	Potato / Russet Burbank	USA (Rupert, ID)	10 g ai/100 kg seed 127 123 125 (EXC1253, 0.5 % v/v)	BBCH 00 - 01 BBCH 46 - 47 BBCH 46 - 47 BBCH 47 - 48	14	Tuber	< 0.005; < 0.005 (< 0.005)	< 0.01; 0.025 (0.017)	0.022
Report: TK0069119 Trial: TK0069119-16 Study to GLP - Study carried out in 2012	Potato / Russet Burbank	USA (Rupert, ID)	11 g ai/100 kg seed 131 124 125 (EXC1252, 0.5 % v/v)	BBCH 00 - 01 BBCH 46 - 47 BBCH 46 - 47 BBCH 47 - 48	14	Tuber	< 0.005; < 0.005 (< 0.005)	0.022; 0.018 (0.020)	0.025

† Residues rounded to 2 significant figures, mean values in parentheses are based on un-rounded values,

*sum of mandipropamid and SYN500003 expressed as mandipropamid (conversion factor 1.847).

Ten supervised trials with mandipropamid on potatoes were conducted in Canada in 2012. Mandipropamid was applied once as a seed treatment at a nominal rate of 10 g ai/100 kg seed followed by three foliar treatments at a nominal rate of 150 g ai/ha and sampled at a PHI of 14 days.

The trials included a talc treatment following application of the seed treatment. Crop oil concentrates or non-ionic surfactants were included in the spray mixture for the foliar applications, following label recommendations.

For magnitude of residue tests, specimens at the indicated pre-harvest interval were collected at the normal commercial harvest date. Duplicate specimens were collected at each sampling interval designated for collection from the treated plots. A single sample was collected from the control plot. A minimum of 12 tubers per sample were collected.

Samples were frozen on the day of sampling and maintained in frozen storage for periods of ≤ 329 days (ca. 11 months) prior to extraction. Residues of mandipropamid are stable in representative matrices for at least 12 months when stored at -20 °C (see Section 3.4). Extracts were stored frozen prior to analysis, which was conducted on the same or following day as extraction.

Residues of mandipropamid and SYN500003 in potato tubers were determined using an analytical method that combined method RAM 415/01 with an LOQ of 0.01 mg/kg for mandipropamid and method GRM001.01B, with an LOQ of 0.005 mg/kg for SYN500003. Method RAM 415/01 was previously evaluated by the 2008 JMPR and method GRM001.01B is described in section 3.1.3. The performance of the combined method was verified by mean procedural recoveries of mandipropamid in the acceptable range of 70–120%.

Table 27 Residues of mandipropamid on potato in Canada (outdoor trials)

GLP and Trial Details	Crop (Variety)	Country (Region)	Application Rate (g ai/100 kg seed OR g ai/ha)	Growth Stage at Application (BBCH)	PHI (days)	Crop Part	Residue Found (Uncorrected) (mg/kg)		Total Residue* (mg/kg)
cGAP	Potato	USA	10 g ai/100 kg seed + 3 × 146 g ai/ha	n/a (cGAP based on PHI)	14		SYN500003	Mandipropamid	mandipropamid +SYN
Report: TK0096294 Trial: T112 Study to GLP - Study carried out in 2012	Potato / Russet Burbank	Canada (New Glasgow, PE)	10 g ai/100 kg seed 151 152 149 (Talc, 500 g product/100 kg seed) (Agral 90, 0.25 % v/v)	BBCH 00 BBCH 33 - 34 BBCH 35 - 37 BBCH 35 - 36	8 10 15 18 22	Tuber	< 0.005 < 0.005 < 0.005; < 0.005 (< 0.005) < 0.005 < 0.005	< 0.01 < 0.01 < 0.01; < 0.01 (< 0.01) < 0.01 < 0.01	<0.01 <0.01 <0.01; <0.01 (<0.01) <0.01 <0.01
Report: TK0096294 Trial: T113 Study to GLP - Study carried out in 2012	Potato / Goldrush	Canada (New Glasgow, PE)	10 g ai/100 kg seed 158 157 158 (Talc, 500 g product/100 kg seed) (Agral 90, 0.25 % v/v)	BBCH 00 BBCH 32 - 33 BBCH 33 - 34 BBCH 90 - 91	15	Tuber	< 0.005; < 0.005 (< 0.005)	0.018; < 0.01 (0.014)	0.023; <0.01 (0.0165)
Report: TK0096294 Trial: T114 Study to GLP - Study carried out in 2012	Potato / Russet Burbank	Canada (Brackley Beach, PE)	10 g ai/100 kg seed 157 160 147 (Talc, 500 g product/100 kg seed) (Agral 90, 0.25 % v/v)	BBCH 00 BBCH 34 - 35 BBCH 35 - 36 BBCH 91 - 93	14	Tuber	< 0.005; < 0.005 (< 0.005)	0.019; < 0.01 (0.015)	0.024; 0.01 (0.017)
Report: TK0096294 Trial: T115 Study to GLP - Study carried out in	Potato / Irish Cobbler	Canada (Brackley Beach, PE)	10 g ai/100 kg seed 142 164 148	BBCH 00 BBCH 30 - 31 BBCH 30 - 32 BBCH 91 - 92	14	Tuber	0.0052; 0.0072 -0.0062	< 0.01; < 0.01 (< 0.01)	0.0196; 0.02329 0.0214

GLP and Trial Details	Crop (Variety)	Country (Region)	Application Rate (g ai/100 kg seed OR g ai/ha)	Growth Stage at Application (BBCH)	PHI (days)	Crop Part	Residue Found (Uncorrected) (mg/kg)		Total Residue* (mg/kg)
2012			(Talc, 500 g product/100 kg seed) (Agral 90, 0.25 % v/v)						
Report: TK0096294 Trial: T116 Study to GLP - Study carried out in 2012	Potato / Superior	Canada (New Glasgow, PE)	10 g ai/100 kg seed 164 161 151 (Talc, 500 g product/100 kg seed) (Agral 90, 0.25 % v/v)	BBCH 00 BBCH 60 - 65 BBCH 67 - 69 BBCH 45 - 50	13	Tuber	< 0.005; 0.0060; 0.0053; 0.0052 -0.0054	4x < 0.01 (< 0.01)	<0.01; 0.021; 0.0197; 0.0196 0.0199
Report: TK0096294 Trial: T117 Study to GLP - Study carried out in 2012	Potato / Superior	Canada (Branchton, ON)	10 g ai/100 kg seed 145 155 147 (Talc, 500 g product/100 kg seed) (Agral 90, 0.25 % v/v)	BBCH 00 BBCH 40 - 43 BBCH 42 - 45 BBCH 91 (tuber) / 43-45 (foliage)	14	Tuber	0.0096; 0.0099 -0.0098	0.064; 0.051 (0.058)	0.08173; 0.06928 0.0755
Report: TK0096294 Trial: T118 Study to GLP - Study carried out in 2012	Potato / Adora	Canada (Taber, AB)	10 g ai/100 kg seed 151 151 151 (Talc, 500 g product/100 kg seed) (Agral 90, 0.25 % v/v)	BBCH 00 BBCH 72-74 (tuber) /41-43 (foliage) BBCH 74-76 (foliage)/43-45 (tuber) BBCH 78-79 (foliage)/45-48 (tuber)	14	Tuber	< 0.005; < 0.005 (< 0.005)	< 0.01; < 0.01 (< 0.01)	<0.01; < 0.01 <0.01
Report: TK0096294 Trial: T119 Study to GLP - Study carried out in 2012	Potato / Norland	Canada (Taber, AB)	10 g ai/100 kg seed 152 151 151 (Talc, 500 g product/100 kg seed) (Agral 90, 0.25 % v/v)	BBCH 00 BBCH 72-74(foliage) /41-42(tuber) BBCH 74-76 (foliage)/43-45(tuber) BBCH 78-79(foliage)/45-48(tuber)	14	Tuber	0.0052; < 0.005 -0.0051	0.030; < 0.01 (0.02)	0.0396; <0.01 (0.0248)
Report: TK0096294 Trial: T120 Study to GLP - Study carried out in	Potato / Norland	Canada (Minto, MB Canada)	10 g ai/100 kg seed 154 156 154	BBCH 00 BBCH 40 - 41 BBCH 41 - 42 BBCH 47	15	Tuber	< 0.005; < 0.005 (< 0.005)	< 0.01; < 0.01 (< 0.01)	<0.01; <0.01 (<0.01)

GLP and Trial Details	Crop (Variety)	Country (Region)	Application Rate (g ai/100 kg seed OR g ai/ha)	Growth Stage at Application (BBCH)	PHI (days)	Crop Part	Residue Found (Uncorrected) (mg/kg)		Total Residue* (mg/kg)
2012			(Talc, 500 g product/100 kg seed) (Agral 90, 0.25 % v/v)						
Report: TK0096294 Trial: T121 Study to GLP - Study carried out in 2012	Potato / Russet Burbank	Canada (Minto, MB Canada)	10 g ai/100 kg seed 151 154 151 (Talc, 500 g product/100 kg seed) (Agral 90, 0.25 % v/v)	BBCH 00 BBCH 39 - 45 BBCH 48/91 BBCH 48/91	7 10 14 16 21	Tuber	< 0.005 < 0.005 < 0.005; < 0.005 (< 0.005) < 0.005 < 0.005	< 0.01 < 0.01 < 0.01; < 0.01 (< 0.01) < 0.01 < 0.01	<0.01 <0.01 <0.01; <0.01 (<0.01) <0.01 <0.01

Seed for beverages and sweets

Cocoa Bean

The supported GAP for the use of mandipropamid on cocoa is a foliar treatment. According to the label in Cameroon, six foliar applications may be made at 90 g ai/ha, with a minimum 14-day PHI. The cGAP is detailed in Table .

Table 28 Critical use pattern (cGAP) for mandipropamid on edible cocoa beans

Region	Outdoor/Protected Crop	Method	Max No of Apps	App Interval (days)	App Rate (g ai/ha)	Min PHI (days)
Cameroon	Outdoor	foliar	6	21	90	14

Eight supervised trials with mandipropamid on cocoa were conducted in West Africa (4 in Ghana and 4 in Ivory Coast) in 2016 to the following use pattern.

Formulation	Number of Appl	Rate per Appl (g ai/ha)	RTI[a] (days)	Spray Concentration (g ai/hL)	Water Volume	DALA[b]
A13747F 125 g/kg WG	6	90 g ai/ha	12 - 17	25 g ai/hL	360 L/ha	0, 1, 3, 6-7, 13-14
A13747F 125 g/kg WG	6	450 g ai/ha	12 - 17	125 g ai/hL	360 L/ha	3

[a] RTI = retreatment interval (days)

[a] DALA = Days After Last Application corresponding to sampling. "-0" indicates prior to last application.

No adjuvants or additives were included in the spray mixture.

Specimens at the indicated pre-harvest interval were collected at the normal commercial harvest date. At least two specimens were collected at each sampling interval from the treated and control plots. Pods were sampled from the tree and dropped onto the ground. Pods were opened directly in the field, the peel discarded and the pulp containing the fresh beans placed in plastic bags and buckets (separated for each sample) and transported under ambient conditions to the fermentation site. Fresh beans were wrapped in banana leaves and placed in wooden boxes for fermentation. After fermentation, the banana leaves were removed and discarded and the fermented beans were left in the framed boxes for air drying.

Samples were frozen once the drying process had finished and maintained in frozen storage for periods of ≤ 6 months prior to extraction. Residues of mandipropamid in cocoa beans and processed commodities were determined using analytical

method RAM 415/02, with an LOQ of 0.01 mg/kg. The performance of the method was demonstrated by mean procedural recoveries of mandipropamid in the acceptable range of 70–120%.

The results of the trials are summarised in Table Table , where residues relevant to the setting of an MRL and for use in risk assessment are underlined.

Table 29 Residues of mandipropamid on cocoa in West Africa (outdoor trials)

GLP and Trial Details	Crop (Variety)	Country (Region) (Postcode)	Application Rate (Additive Type, Rate)	Growth Stage at Application	PHI (days)	Crop Part	Residue Found (Uncorrected)
cGAP	Cocoa	Cameroon	6 × 90 g ai/ha	n/a (cGAP based on PHI)	14		Mandipropamid (mg/kg)
Report: S16-04493 Study: S16-04493 Trial: S16-04993-01 - Study to GLP - Study carried out in 2016 (Field)	Cocoa (Ghana)	Ivory Coast (Gobazra, Bouaflé)	86 92 88 101 90 91	BBCH 51-85 BBCH 51-85 BBCH 51-89 BBCH 51-87 BBCH 51-87 BBCH 51-89	0 1 3 6 12	Beans Beans Beans Beans Beans	0.02; 0.01 (0.02) 0.03; 0.02 (0.03) 0.02; 0.05 (0.04) 0.02; <0.01 (0.02) 0.01; <0.01 (<u>0.01</u>)
Report: S16-04493 Study: S16-04493 Trial: S16-04993-02 - Study to GLP - Study carried out in 2016 (Field)	Cocoa (Ghana)	Ivory Coast (Bouaflé)	87 99 97 102 89 94	BBCH 51-85 BBCH 51-85 BBCH 51-89 BBCH 51-89 BBCH 61-89 BBCH 61-89	0 1 3 7 13	Beans Beans Beans Beans Beans	0.07; 0.06 (0.07) 0.05; 0.03 (0.04) 0.03; 0.06 (0.05) 0.03; 0.02 (0.03) 0.03; 0.02 (<u>0.03</u>)
Report: S16-04493 Study: S16-04493 Trial: S16-04993-03 - Study to GLP - Study carried out in 2016 (Field)	Cocoa (Ghana)	Ivory Coast (Attiégounakro, Yamoussoukro)	94 82 96 82 96 94	BBCH 51-85 BBCH 51-85 BBCH 51-85 BBCH 51-87 BBCH 51-87 BBCH 61-89	0 1 3 6 14	Beans Beans Beans Beans Beans	0.08; 0.08 (0.08) 0.03; 0.05 (0.04) <0.01; 0.01 (0.01) <0.01; <0.01 (<0.01) 0.01; <0.01 (<u>0.01</u>)
Report: S16-04493 Study: S16-04493 Trial: S16-04993-04 - Study to GLP - Study carried out in 2016 (Field)	Cocoa (Ghana)	Ivory Coast (Agbouville)	95 79 94 94 94 94	BBCH 51-85 BBCH 51-85 BBCH 51-85 BBCH 51-89 BBCH 51-89 BBCH 51-89	0 1 3 6 14	Beans Beans Beans Beans Beans	0.06; 0.06 (0.06) 0.03; 0.02 (0.03) 0.01; <0.01 (0.01) <0.01; <0.01 (<0.01) <0.01; 0.01 (<u>0.01</u>)
Report: S16-04493 Study: S16-	Cocoa (Mixed Hybrid)	Ghana (Obugo)	87 87 87	BBCH 51-85 BBCH 51-89 BBCH 51-89	0 1 3	Beans Beans Beans	0.03; 0.03 (0.03) 0.06; 0.02 (0.04) 0.03, 0.05 (0.04)

GLP and Trial Details	Crop (Variety)	Country (Region) (Postcode)	Application Rate (Additive Type, Rate)	Growth Stage at Application	PHI (days)	Crop Part	Residue Found (Uncorrected)
cGAP	Cocoa	Cameroon	6 × 90 g ai/ha	n/a (cGAP based on PHI)	14		Mandipropamid (mg/kg)
04493 Trial: S16-04993-05 - Study to GLP - Study carried out in 2016 (Field)			88 91 91	BBCH 51-85 BBCH 51-89 BBCH 51-89	7	Beans	0.04; 0.03 (0.04)
					14	Beans	0.02; 0.04 (<u>0.03</u>)
Report: S16-04493 Study: S16-04493 Trial: S16-04993-06 - Study to GLP - Study carried out in 2016 (Field)	Cocoa (Mixed Hybrid)	Ghana (Nsutan)	96 98 93 88 94 95	BBCH 51-87 BBCH 51-89 BBCH 51-89 BBCH 51-85 BBCH 51-89 BBCH 51-89	0	Beans	0.01; 0.02 (0.02)
					1	Beans	0.03; 0.04 (0.04)
					3	Beans	<0.01; 0.02 (0.02)
					7	Beans	0.03; <0.01 (0.02)
					14	Beans	<0.01; <0.01 (<u><0.01</u>)
Report: S16-04493 Study: S16-04493 Trial: S16-04993-07 - Study to GLP - Study carried out in 2016 (Field)	Cocoa (Mixed Hybrid)	Ghana (Asare Kofi Villa)	92 96 100 86 88 90	BBCH 51-85 BBCH 51-89 BBCH 51-85 BBCH 51-85 BBCH 51-89 BBCH 51-89	0	Beans	0.03; 0.01 (0.02)
					1	Beans	0.04; 0.03 (0.04)
					3	Beans	0.05; 0.03 (0.04)
					7	Beans	0.02; 0.01 (0.02)
					14	Beans	<0.01; 0.02 (<u>0.02</u>)
Report: S16-04493 Study: S16-04493 Trial: S16-04993-08 - Study to GLP - Study carried out in 2016 (Field)	Cocoa (Mixed Hybrid)	Ghana (Pankese)	85 88 88 91 88 91	BBCH 51-89 BBCH 51-89 BBCH 51-85 BBCH 51-85 BBCH 51-89 BBCH 51-89	0	Beans	0.02; 0.03 (0.03)
					1	Beans	0.03; <0.01 (0.02)
					3	Beans	<0.01; 0.03 (0.02)
					7	Beans	0.02; 0.02 (0.02)
					14	Beans	0.01; <0.01 (<u>0.01</u>)

Animal feed commodities

Bean forage (green)

Ten trials were conducted in USA on <u>beans (snap/common)</u>, which support the USA label. Residues of mandipropamid in bean whole plants with pods at harvest were in the range mg/kg, when treated four times at a nominal rate of 146 g ai/ha and sampled at a PHI of 1. The residue values used in the calculations are underlined in Table .

Table 30 Residues of mandipropamid on beans (snap/common) forage in USA (outdoor trials)

GLP and Trial Details	Crop (Variety)	Country (Region) (Postcode)	Application Rate (Additive Type, Rate)	Growth Stage at Application	PHI (days)	Crop Part	Residue Found (Uncorrected)
cGAP	Bean (snap)	USA	146 g ai/ha	n/a (cGAP based on PHI)	1		Mandipropamid (mg/kg)
Report: IR-4 PR No.10324 Study: 10324 Trial: 10-CA*85 - Study to GLP - Study carried out in 2010 (Field)	Bean (Provider)	United States (Salinas, CA)	147 145 145 149 (Activator 90)	25% flowering - 35% flowering flowering - pods at all levels on plant flowering - pods at all levels on plant mature pods	1	Plant + Pod with seeds	3.92; 5.15 (4.54)
Report: IR-4 PR No.10324 Study: 10324 Trial: 10-CA84 - Study to GLP - Study carried out in 2010 (Field)	Bean (Jade)	United States (Riverside, CA)	147 148 147 146 (R-11 Activator/ Spreader)	vegetative bloom 2 inch bean pod development - mature pods	1	Plant + Pod with seeds	5.35; 6.13 (5.74)
					3	Plant + Pod with seeds	7.19; 6.90 (7.05)
					7	Plant + Pod with seeds	5.41; 3.72 (4.57)
					10	Plant + Pod with seeds	3.79; 4.09 (3.94)
Report: IR-4 PR No.10324 Study: 10324 Trial: 10-FL24 - Study to GLP - Study carried out in 2010 (Field)	Bean (Dusky)	United States (Citra, FL)	151 155 151 146 (Agri Dex)	blooming blooming - fruiting blooming - fruiting blooming - fruiting	1	Plant + Pod with seeds	4.63; 4.34 (4.49)
Report: IR-4 PR No.10324 Study: 10324 Trial: 10-GA*06 - Study to GLP - Study carried out in 2010 (Field)	Bean (Contender Garden)	United States (Tifton, GA)	147 148 148 147 (UAP Surfactant 80/20)	vegetative blooming fruiting fruiting	1	Plant + Pod with seeds	4.70; 3.70 (4.20)
Report: IR-4 PR No.10324 Study: 10324 Trial: 10-MD13 - Study to GLP - Study carried out in 2010	Bean (Provider)	United States (Salisbury, MD)	147 148 106 146	first bloom 2 inch bean - 3 inch bean mature beans mature beans	1	Plant + Pod with seeds	2.68; 3.95 (3.32)

GLP and Trial Details	Crop (Variety)	Country (Region) (Postcode)	Application Rate (Additive Type, Rate)	Growth Stage at Application	PHI (days)	Crop Part	Residue Found (Uncorrected)
cGAP	Bean (snap)	USA	146 g ai/ha	n/a (cGAP based on PHI)	1		Mandipropamid (mg/kg)
(Field)			(Reliable)				
Report: IR-4 PR No.10324 Study: 10324 Trial: 10-MI21 - Study to GLP - Study carried out in 2010 (Field)	Bean (Foremost)	United States (Holt, MI)	150 150 149 148 (Activator 90)	flowering fruiting fruiting fruiting	1	Plant + Pod with seeds	235; 2.06 (2.21)
Report: IR-4 PR No.10324 Study: 10324 Trial: 10-NY11 - Study to GLP - Study carried out in 2010 (Field)	Bean (California Early)	United States (Freeville, NY)	146 146 146 146 (Induce)	vegetative blooming blooming - fruiting blooming - fruiting	1	Plant + Pod with seeds	1.42; 1.30 (1.36)
Report: IR-4 PR No.10324 Study: 10324 Trial: 10-OH*07 - Study to GLP - Study carried out in 2010 (Field)	Bean (Brio)	United States (Wooster, OH)	141 142 150 145 (Top Surf)	vegetative - 10% bloom blooming fruiting fruiting	1	Plant + Pod with seeds	9.84; 8.70 (9.27)
Report: IR-4 PR No.10324 Study: 10324 Trial: 10-WA*19 - Study to GLP - Study carried out in 2010 (Field)	Bean (Jade)	United States (Moxee, WA)	140 141 147 149 (90 Plus)	bloom - pods bloom - pod development bloom - pods pod maturation	1	Plant + Pod with seeds	4.91; 5.14 (5.03)
Report: IR-4 PR No.10324 Study: 10324 Trial: 10-WI07 - Study to GLP - Study carried out in 2010 (Field)	Bean (Hercules)	United States (Arlington, WI)	149 147 146 148 (Activator 90)	bud - early bloom bloom - pods bloom - pods pods	1	Plant + Pod with seeds	1.24; 1.29 (1.27)

FATE OF RESIDUES IN STORAGE AND PROCESSING

In stored products

Mandipropamid is not intended for use in stored products.

In processing

The Meeting received information on the fate of mandipropamid residues during the processing of potato and cocoa beans.

Potato processing

A processing study was conducted on potato in the USA to determine the potential for concentration of residues of mandipropamid in potato processed fractions (Smith, 2012, TK0069119).

One seed piece treatment at a nominal rate of 0.050 lb ai/100 lb seed (0.5 kg ai/ t seed pieces) followed by three foliar applications at a nominal rate of 650 g ai/ha with a 7 day interval were applied to the crop. Samples of tubers were taken for processing at harvest, 14 days after the final foliar application. Field samples for direct analysis were transported and stored deep-frozen prior to analysis. Samples for processing were transported at ambient temperature to the processing facility.

Upon receipt at the processing facility, the bulk potato samples were processed into flakes, chips (crisps in countries other than the United States), wet peel, and fries (chips in countries other than the United States) samples.

All processing samples were transported and stored under deep-frozen conditions prior to analysis. The potato tuber RAC and processed commodity samples were analysed for residues of mandipropamid and SYN500003. Residues of mandipropamid were determined by analytical method RAM 415/02, with an LOQ of 0.01 mg/kg. Residues of SYN500003 were determined by method GRM001.01A with an LOQ of 0.005 mg/kg.

The mandipropamid and SYN500003 residues in potato prior to processing and in flakes, chips, wet peel, and fries are presented in Table 30.

Table 31 Determination of mandipropamid processing factors for potatoes

Country (region) Year Crop (Variety)	Mandipropamid application			PHI (days)	Commodity/ Processed fraction	Mandipropamid residue (mg/kg)	Mandipropamid processing factor (PF)
	Formulation	Rate	No.				
Study TK0069119 Trial TK0069119-06 USA (Gardner, ND) 2012 Potato (Yukon Gold)	A12946B, 250 g/L, SC	0.5 kg ai/t seed 639 660 660	1 seed + 3x foliar	14	Pre-process tuber (RAC) Flakes Chip (crisp) Peel (wet) Fries (chips)	0.0876; 0.135; 0.0447 (0.0891) <0.01; <0.01 (<0.01) <0.01; <0.01 (<0.01) 0.249; 0.276 (0.263) <0.01; <0.01 (<0.01)	- <0.11 <0.11 3.0 <0.11
Study TK0069119 Trial TK0069119-13 USA (American Falls, ID) 2012 Potato (Russer Burbank)	A12946B, 250 g/L, SC	0.51 kg ai/t seed 633 663 630	1 seed + 3x foliar	12	Pre-process tuber (RAC) Flakes Chip (crisp) Peel (wet) Fries (chips)	0.655; 0.199; 0.266 (0.373) <0.01; <0.01 (<0.01) <0.01; <0.01 (<0.01) 0.375; 0.480 (0.428) 0.0147; 0.0190 (0.0169)	- <0.027 <0.027 1.1 0.045
Best estimate					Flakes Chip (crisp) Peel (wet) Fries (chips)		<0.027 <0.027 2.1 0.078

Table 32 Determination of SYN500003 processing factors for potatoes

Country (region) Year Crop (Variety)	Mandipropamid application			PHI (days)	Commodity/ Processed fraction	SYN500003 residue (mg/kg)	SYN500003 processing factor (PF)
	Formulation	Rate	No.				
Study TK0069119 Trial TK0069119-06 USA (Gardner, ND) 2012 Potato (Yukon Gold)	A12946B, 250 g/L, SC	0.50 kg ai/t seed 639 660 660	1 seed + 3x foliar	14	Pre-process tuber (RAC) Flakes Chip (crisp) Peel (wet) Fries (chips)	0.01; 0.0065; 0.0064 (0.00763) 0.0127; 0.0104 (0.0116) 0.0118; 0.013 (0.0124) <0.005; <0.005 (<0.005) 0.00559; 0.00551 (0.00555)	- 1.5 1.6 <0.70 <0.70
Study TK0069119 Trial TK0069119-13 USA (American Falls, ID)	A12946B, 250 g/L, SC	0.51 kg ai/t seed 633	1 seed + 3x	12	Pre-process tuber (RAC) Flakes	0.00839; 0.00764; <0.005 (0.00701) 0.0132; 0.0134 (0.0133)	- 1.9 1.1

Country (region) Year Crop (Variety)	Mandipropamid application			PHI (days)	Commodity/ Processed fraction	SYN500003 residue (mg/kg)	SYN500003 processing factor (PF)
	Formulation	Rate	No.				
2012 Potato (Russer Burbank)		663 630	foliar		Chip (crisp) Peel (wet) Fries (chips)	0.00852; 0.00694 (0.00773) <0.005; <0.005 (<0.005) <0.005; <0.005 (<0.005)	<0.70 <0.70
Best estimate					Flakes Chip (crisp) Peel (wet) Fries (chips)		1.7 1.4 <0.70 <0.70

Table 31 Overall summary of estimated processing factors

Raw	Processed	Individual Mandipropamid PF	Mean, Median or	Individual SYN500003 PF	Mean, Median or	Total PF* (parent + SYN)
Commodity	Commodity		Best Estimate		Best Estimate	
Potato	Flakes	<0.11, <0.027	<0.027	1.5, 1.9	1.7	3.2
	Chip (crisp)	<0.11, <0.027	<0.027	1.6, 1.1	1.4	2.6
	Peel (wet)	3.0, 1.1	2.1	<0.70, <0.70	<0.70	3.4
	Fries (chips)	<0.11, 0.045	0.078	<0.70, <0.70	<0.70	1.4

*Sum of PF of parent and SYN500003 expressed as parent (i.e. corrected for molecular weight).

Cocoa processing

A processing study was conducted on cocoa in West Africa to determine the potential for concentration of residues of mandipropamid in cocoa processed fractions (Petrova, 2017, S16-04993).

Six foliar treatments, each at a nominal rate of 450 g ai/ha with a 12–17 day interval were applied to the crop. Samples of mature cocoa beans were taken for processing 3 days after the final foliar application. Samples of cocoa beans were fermented and air dried, before being transported at ambient temperature to the processing facility.

Upon receipt at the processing facility, the cocoa beans were processed into roasted nibs, cocoa powder, cocoa butter and chocolate to simulate the common processes used by industry. All processing samples were stored under deep-frozen conditions prior to analysis.

Residues of mandipropamid were determined by analytical method RAM 415/02, with an LOQ of 0.01 mg/kg. Procedural recoveries were in the acceptable range 70–120%:

Residues of mandipropamid determined in fermented, dried, pre-processed cocoa beans (RAC) and the associated processed fractions (roasted nibs, cocoa powder, cocoa butter and chocolate) are shown in Table and an overall summary of the processing factors in Table .

The commodity mass balances (proportion of starting fermented dry cocoa beans material recovered) for all processes ranged from 93.4% to 98.2%.

Table 33 Determination of mandipropamid processing factors for cocoa

Country (region) Year Crop (Variety)	Mandipropamid application			PHI (days)	Commodity/ Processed fraction	Mandipropamid residue (mg/kg)	Mandipropamid processing factor (PF)
	Formulation	Rate	No.				
Study S16-04493 Trial S16-04993-01 Ivory Coast (Bouaflé) 2016 Cocoa (Ghana)	A13747F, 125 g/kg, WG	450 g ai/ha	6	3	Fermented dry bean (RAC) Roasted nib Cocoa powder Cocoa butter Chocolate	0.19; 0.21 (0.20) 0.06; 0.09 (0.08) 0.08; 0.08 (0.08) 0.08; 0.07 (0.08) 0.09; 0.11 (0.10)	- 0.4 0.4 0.4 0.5
Study S16-04493 Trial S16-04993-05	A13747F, 125 g/kg,	450 g ai/ha	6	3	Fermented dry bean (RAC)	0.31; 0.50 (0.41) 0.17; 0.29 (0.23)	- 0.56

Country (region) Year Crop (Variety)	Mandipropamid application			PHI (days)	Commodity/ Processed fraction	Mandipropamid residue (mg/kg)	Mandipropamid processing factor (PF)
	Formulation	Rate	No.				
Ghana (Obugo) 2016 Cocoa (Mixed Hybrid)	WG				Roasted nib Cocoa powder Cocoa butter Chocolate	0.22; 0.24 (0.23) 0.18; 0.36 (0.27) 0.23; 0.35 (0.29)	0.56 0.66 0.71
Best estimate					Roasted nib Cocoa powder Cocoa butter Chocolate		0.48 0.48 0.53 0.61

The mean calculated processing factors indicate that mandipropamid residues are reduced by processing into roasted nibs, cocoa butter, cocoa powder and chocolate. An overall summary of the cocoa processing data is given in Table .

Table 34 Overall summary of estimated processing factors

Raw Commodity	Processed Commodity	Individual Mandipropamid PF	Mean, Median or Best Estimate
Cocoa bean	Roasted nibs	0.4, 0.56	0.48
	Cocoa powder	0.4, 0.56	0.48
	Cocoa butter	0.4, 0.66	0.53
	Chocolate	0.5, 0.71	0.61

RESIDUES IN ANIMAL COMMODITIES

Farm animal feeding studies

Dairy cows

The Meeting did not receive a lactating dairy cow feeding study.

Poultry

The Meeting did not receive a laying hen feeding study.

APPRAISAL

Mandipropamid is a fungicide in the mandelamide class used for the control of foliar oomycete pathogens in a range of crops, including *Plasmopara viticola* in grapes, *Phytophthora infestans* in potatoes and tomatoes, and *Pseudoperonospora cubensis* in cucurbits. Mandipropamid was first evaluated by the JMPR in 2008 when an ADI of 0–0.2 mg/kg bw was established, and maximun residue levels were recommended for various crops. An ARfD was considered unnecessary. The 2008 JMPR agreed on the following residue definition for mandipropamid:

Definition of the residue for compliance with the MRL and dietary risk assessment for plant and animal commodities: *mandipropamid*.

The residue is not fat-soluble.

Mandipropamid was listed by the Forty-ninth Session of the CCPR for the evaluation of additional uses. The current Meeting received metabolism studies on potato (seed treatment) and on laying hens, registered labels, analytical method, sample storage stability data, and supervised residue trials for beans, potato and cacao beans.

The following abbreviated names are used for the metabolites discussed below.

Compound Name/Code	Structure	Occurrence in metabolism studies
NOA458422 2-(4-Chlorophenyl)-N-[2-(4-hydroxy-3- methoxyphenyl)-ethyl]-2-prop-2-ynyloxy-acetamide		Plant, animal
CGA380778 2-(4-Chlorophenyl)-2-hydroxy-N-[2-(3-methoxy- 4-prop-2-ynyloxyphenyl)-ethyl]-acetamide		Plant, animal
CGA380775 2-(4-Chlorophenyl)-2-hydroxy-N-[2-(4-hydroxy- 3-methoxyphenyl)-ethyl]-acetamide		Animal
SYN500003 (4-Chloro-phenyl)-prop-2-ynyloxy-acetic acid		Plant
SYN521195 2-(4-Chlorophenyl)-N-[2-(3-hydroxy-4-prop- 2-ynyloxyphenyl)-ethyl]-2-prop-2-ynyloxy-acetamide		Animal
M186/1 [2-(4- chlorophenyl)-2-hydroxyacetic acid]		Animal
M401/1		Animal
M415/1		Animal
M431/1		Animal
M439/1		Animal
M453/1		Animal

Compound Name/Code	Structure	Occurrence in metabolism studies
SYN505503 2-(4-Chlorophenyl)-N-[2-(3,4-dihydroxyphenyl)- ethyl]-2-prop-2-ynyloxy-acetamide		Animal

Plant metabolism

Potato

Potato seeds were treated with chlorophenyl- or methoxyphenyl-[^{14}C]mandipropamid at rates of 6.1 and 6.3 mg ai/seed piece, respectively. This application rate was equivalent to 0.1 kg ai/t potato seed pieces. Treated potato seed was planted in outdoor raised beds and harvested at maturity, 183 days after the application.

TRR levels in potato tuber ranged from 0.024 to 0.054 mg eq/kg for the methoxyphenyl- and chlorophenyl-[^{14}C]mandipropamid labelled experiments, respectively.

Tuber residues, extractable in acetonitrile: water (4:1) and acetonitrile, were 50% and > 76% TRR for the methoxyphenyl- and chlorophenyl-[14C]mandipropamid labels, respectively. Unextracted residues were not further characterised since residues were ≤ 0.013 mg eq/kg. The identification of the radioactive residues revealed the metabolite SYN500003 was the only major metabolite identified (40% TRR, up to 0.022 mg eq/kg), with parent being present at low proportions up to 11% TRR (0.003 mg eq/kg). Two other metabolites were found at very low levels ≤ 0.001 mg eq/kg).

In summary, residues of parent mandipropamid in potatoes following seed treatment were low. The major metabolite SYN500003 was formed by hydrolysis of the amide bond to the corresponding carboxylic acid.

At the 2008 JMPR, the metabolism of mandipropamid in plants (grapes, lettuce, potatoes and tomatoes) following foliar treatment was investigated. Unchanged mandipropamid was the major residue in all crops, except potato tubers, making up 40–94% TRR. The major metabolite in potato tubers after foliar treatment was SYN500003 accounting for up to 13% TRR however it was present at low levels (≤ 0.006 mg/kg).

Animal metabolism

Laying hens

The Meeting received information on a feeding study in which laying hens were orally dosed with chlorophenyl- or methoxyphenyl-[^{14}C]mandipropamid, at a dose equivalent to 22–24 ppm in dry feed for 14 consecutive days. The majority of the administered dose was recovered in excreta (83–88%) of both labels.

The highest TRR was observed in the liver. The TRR levels in liver were 0.31–0.32 mg eq/kg, in egg yolk (Day 9) 0.083–0.12 mg eq/kg, in egg white (Day 9) 0.046–0.05 mg eq/kg, in muscle < 0.01–0.016 mg eq/kg and in fat 0.021–0.022 mg eq/kg. Residues in the egg whites and yolks reached a plateau within 9 days for both radiolabels.

Eggs, liver and muscle were extracted with acetonitrile and acetonitrile:water (80:20, v/v and 30:70, v/v).

In egg white 94–95% TRR was extractable (0.044–0.047 mg eq/kg). In egg yolk 31–38% TRR was extracted (0.031–0.038 mg eq/kg). Parent mandipropamid was identified as the major component in egg white, accounting for 309–33% TRR (0.015 mg/kg). The metabolite CGA380778 was detected as a major metabolite in egg white, accounting for 14–16% TRR (0.007–0.008 mg/kg).

In liver 29–35% TRR was extractable (0.107 and 0.095 mg eq/kg). NOA458422 conjugated was the major component in liver, accounting for 6.3–14.8% TRR (0.02–0.045 mg eq/kg).

In muscle 62% TRR was extractable (0.010 mg/kg). Mandipropamid was a minor component, accounting for 2.3% TRR (< 0.001 mg/kg). M186/1, CGA380775 and NOA458422 were also detected, but at lower levels (≤ 0.002 mg/kg).

In fat residues extractable with hexane, hexane/diethyl ether (1:1, v/v) and acetonitrile were 45–64% TRR (0.01–0.014 mg eq/kg). Unchanged mandipropamid was a major component accounting for 28–37% TRR (0.006–0.008 mg eq/kg).

In summary, mandipropamid was detected in egg whites, but was minor in all other tissues. CGA380778 was detected at low level in egg whites and egg yolk. Conjugated NOA458422 was detected as the major component in liver.

Methods of analysis

The current Meeting received description and validation data for additional or extended analytical methods for mandipropamid and its metabolite SYN500003 in plant commodities (beans, potato tuber and processed and cacao bean and processed).

Crop samples were extracted with acetonitrile: water (80:20 v/v), cleaned-up using solid-phase extraction. Residues of mandipropamid and SYN500003 were quantified with HPLC-MS/MS. LOQ values are at 0.01 and 0.005 mg/kg for mandipropamid and SYN500003, respectively, in various plant matrices.

The methods are suitable for the analysis of mandipropamid and the metabolite SYN500003 in plants matrices.

Stability of pesticide residues in stored analytical samples

The current Meeting received information on the freezer storage stability of residues of mandipropamid in plant commodities. Residues were stable (at least 70% remaining) in various plant matrices and processed commodities: tomatoes, grapes, lettuce, cucumbers, wheat and soya bean for at least 24 months, in beans (with pod and forage) for at least 12 months and in potato for at least 32 months when stored frozen at -20 °C.

The Meeting received information on the freezer storage stability of residues of SYN500003 in potato tuber and processed potato commodities. Results demonstrated that residues of SYN500003 were stable in potato tubers, potato granules/flakes, potato chips and potato wet peel when stored under freezer storage conditions for up to 32 months.

Definition of the residue

The 2008 JMPR concluded that for plant, mandipropamid was the major component following foliar treatment with ^{14}C-mandipropamid in grapes, lettuce, potatoes and tomatoes, except potato tuber. The major metabolite (SYN500003) in potato tubers following foliar treatment accounted for up to 13% TRR but was present at very low levels (≤ 0.006 mg/kg).

In a potato metabolism study reviewed by the current Meeting (seed piece treatment), SYN500003 was the only major metabolite identified (40% TRR, up to 0.022 mg eq/kg), with parent being present at up to 11% TRR (0.003 mg eq/kg) in the tubers.

The Meeting concluded that the parent is an appropriate marker for the use of mandipropamid in potatoes after seed treatment, and confirms the previous residue definition for enforcement in plants as mandipropamid.

For dietary risk assessment, the Meeting noted that as no specific data were available on the toxicity of metabolite SYN500003, the TTC approach was applied[5]. The estimated exposure based on potatoes was up to 0.027 µg/kg bw, below the respective threshold of toxicological concern.

The Meeting concluded that dietary exposure to SYN500003 from the uses evaluated by the current Meeting is unlikely to present a public health concern, and confirms its previous residue definition for dietary intake assessment in plants as mandipropamid.

The 2008 JMPR concluded that mandipropamid comprised the majority of the residue in goat fat, and only a small proportion of the residue in goat milk and liver, and was not detected in kidney. The metabolite NOA 458422 was a significant residue in kidney but was a minor residue in liver.

In a hen metabolism study submitted to the current Meeting, mandipropamid was detected in egg whites, but was minor in egg yolk and tissues. CGA380778 was detected at low level (3–17% TRR, 0.002–0.008 mg eq/kg) in eggs and conjugated NOA458422 was detected in liver at low levels (6.3–14.8% TRR, 0.02–0.045 mg eq/kg).

The Meeting confirms its previous residue definition for compliance with the MRL and dietary risk assessment for animal commodities as mandipropamid.

Definition of the residue for compliance with the MRL and dietary risk assessment for plant and animal commodities: *mandipropamid.*

The residue is not fat-soluble.

Results of supervised residue trials on crops

The Meeting received supervised trials data for mandipropamid uses on beans, cacao beans and potatoes.

Beans with pod

The registered GAP in Canada for beans with pods allows 4 foliar applications at 150 g ai/ha, with a PHI of 1 day.

In 10 trials conducted in the USA on snap beans matching the critical GAP of Canada (4 × 146 g ai/ha; PHI: 1 day) residues of mandipropamid were (n = 10): 0.10, 0.11(2), 0.13, 0.19, 0.25(2), 0.40, 0.45 and 0.58 mg/kg.

The Meeting estimated a maximum residue level of 1 mg/kg and a STMR of 0.22 mg/kg for mandipropamid in the subgroup of beans with pods. The highest residue is 0.58 mg/kg.

[5] See toxicology section of the 2018 JMPR Report for further details

Potato

The critical GAP for potato is from Canada and the USA, which allows one seed treatment application at 100 g ai/t seed potato followed by up to three foliar applications at 146 g ai/ha with a PHI of 14 days.

In 18 field trials from Canada and the USA matching critical GAP (100 g ai/t seed potato + 3 × 146 g ai/ha, PHI 14-days) residues of mandipropamid in potato harvested at maturity were (n = 18): < 0.01 (5), 0.014, 0.015, 0.016, 0.017, 0.020 (3), 0.021, 0.031, 0.043, 0.056, 0.058 and 0.073 mg/kg.

Based on the trials on potato from Canada and the USA, the Meeting estimated a maximum residue level of 0.1 mg/kg and a STMR of 0.0185 mg/kg for mandipropamid in potato. This estimation replaces the previous recommendation of a maximum residue level of 0.01(*) mg/kg.

As noted the TTC approach was applied in relation to the metabolite SYN500003. In performing the TTC assessment of this compound, the following residue levels were identified in potato tubers (n = 18): < 0.005(10), 0.0051, 0.0058, 0.0059, 0.0089, 0.098, 0.01, 0.013 and 0.013 mg/kg.

The Meeting estimated a median residue of 0.005 mg/kg for (4-Chloro-phenyl)-prop-2-ynyloxy-acetic acid (SYN500003) in potato tubers to estimate exposure for TTC consideration.

Cacao Bean

The critical GAP in Cameroon for cacao beans is 6 × 90 g ai/ha, PHI 14 day.

In eight field trials from Ghana and the Ivory Coast matching critical GAP (6 × 90 g ai/ha with a PHI of 14 days) residues of mandipropamid in cacao beans were (n = 8): < 0.01, 0.01 (4), 0.02 and 0.03 (2) mg/kg.

The Meeting estimated a maximum residue level of 0.06 mg/kg and a STMR of 0.01 mg/kg in cacao beans.

Animal feedstuffs

Bean forage (green)

Data were available from supervised trials on bean forage (green) in the USA. In 10 field trials on beans from the USA matching critical GAP (4 × 146 g ai/ha; PHI: 1 day) the residues of mandipropamid in bean forage were (n = 10) 1.27, 1.36, 2.21, 3.32, 4.20, 4.49, 4.54, 5.03, 7.05 and 9.27 mg/kg.

Based on the residues in bean forage from trials in the USA, the Meeting estimated a median residue value of 4.35 mg/kg (as received) and a highest residue value of 9.27 mg/kg (as received) for mandipropamid in bean forage (green).

Fate of residues during processing

The current Meeting received information on the fate of mandipropamid residues during the processing of potato and cacao beans. Based on the results of processing studies in combination with the residues from supervised trials, the estimated processing factors and the derived STMR-Ps are summarised in the table below.

Mandipropamid processing factors, STMR-P and HR-P for food and feed

Crop	Residue value (mg/kg) in raw commodity		Processed Commodity	Calculated PF	PF (Mean or best estimated)*	Residue value (mg/kg) in processed commodity	
	MRL	STMR				MRL**	STMR-P
Potato	0.1	0.0185	Flakes	<0.11, < 0.027	< 0.027	-	-
			Chip (crisp)	<0.11, < 0.027	< 0.027	-	-
			Peel (wet)	3.0, 1.1	2.1	-	0.04
			Fries (chips)	<0.11, 0.045	0.045	-	-
Cocoa bean	0.06	0.01	Roasted nibs	0.4, 0.56	0.48	-	0.005
			Cocoa powder	0.4, 0.56	0.48	-	0.005
			Cocoa butter	0.4, 0.66	0.53	-	0.005
			Chocolate***	0.5, 0.71	0.61	-	0.006

*The factor is the ratio of the total residue in processed commodity divided by the total residue in the RAC.

** maximum residue levels in processed commodities are only proposed where they are higher than the maximum residue level in the RAC.

*** For 800 g cocoa liquor = 10 g of lecithin + 190 g of commercial sugar.

Residues in animal commodities

Farm animal dietary burden

Dietary burden calculation were calculated for beef cattle, dairy cattle, broilers and laying poultry based on feed items evaluated by the JMPR. The dietary burdens, estimated using the OECD diets listed in Appendix IX of the 2016 edition of the FAO manual, are presented in Annex 6 and summarised below. As mandipropamid is not registered for use on beans in Australia and Australia does not import any forage, the Meeting decided to refine the animal burden calculation (to exclude bean forage in Australia.

Region	Livestock dietary burden, mandipropamid, ppm of dry matter diet							
	USA-Canada		EU		Australia		Japan	
	Maximum	Mean	Maximum	Mean	Maximum	Mean	Maximum	Mean
Beef cattle	0.21	0.13	7.98	4.89	1.58	1.56	-	-
Dairy cattle	0.07	0.04	13.24[a,b]	7.34[c,d]	1.58	1.56	-	-
Broiler poultry			0.04	0.01	-	-	-	-
Laying poultry			1.97[e]	1.20[f]	-	-	-	-

[a] Highest maximum beef or dairy cattle dietary burden suitable for maximum residue level estimation for mammalian tissues

[b] Highest maximum dairy cattle dietary burden suitable for maximum residue level estimation for mammalian milk

[c] Highest mean beef or dairy cattle dietary burden suitable for STMR estimation for mammalian tissues.

[d] Highest mean dairy cattle dietary burden suitable for STMR estimation for milk.

[e] Highest maximum poultry dietary burden suitable for maximum residue level estimation for poultry tissues and eggs.

[f] Highest mean poultry dietary burden suitable for STMR estimation for poultry tissues and eggs.

Animal commodities maximum residue levels

The maximum and mean estimated dietary burden for dairy cattle was 13.2 and 7.3 ppm, respectively. No animal feeding studies on ruminants are available, and the lactating goat metabolism study submitted to the 2008 JMPR was used to estimate residues of mandipropamid in mammalian commodities, in line with the approach in 2008.

Lactating goats were fed for 7 days with [^{14}C] mandipropamid equivalent to 27–49 ppm in the diet. At 30 ppm, the highest residue of parent mandipropamid was found in fat (0.019 mg/kg), with residues being < 0.01 mg/kg in milk and other tissues. The Meeting agreed that no residues of mandipropramid are expected in ruminant commodities at the calculated dietary burden

The Meeting estimated a maximum residue level of 0.01(*) mg/kg and a STMR of 0 for mandipropamid in milks, edible offal (mammalian), mammalian fats (except milk fats) and meat (from mammals other than marine mammals).

The maximum and mean estimated dietary burdens for poultry were 2 and 1.2 ppm, respectively. No animal feeding studies on poultry are available, and the poultry metabolism study was used to estimate the residues of mandipropamid in poultry commodities.

Laying hens received [^{14}C] mandipropamid for 14 days at 22–24 ppm in the diet. The highest residue of parent mandipropamid was 0.018 mg/kg, found in egg white, and residues were < 0.01 mg/kg in egg yolk and in hen tissues. The Meeting agreed that no residues of mandipropramid are expected in poultry commodities at the calculated dietary burden

The Meeting estimated maximum residue levels of 0.01(*) mg/kg and a STMR of 0 for poultry meat, poultry fat, poultry edible offal and eggs.

RECOMMENDATION

On the basis of the data from supervised trials the Meeting concluded that the residue levels listed below are suitable for establishing maximum residue limits and for IEDI assessment.

Definition of the residue for compliance with the MRL and for dietary risk assessment for plant and animal commodities: *mandipropamid*

The residue is not fat-soluble.

CCN	Commodity	Recommended maximum residue level (mg/kg)		STMR or STMR-P (mg/kg)	HR or HR-P (mg/kg)
		New	Previous		
VP 2060	Beans with pods, subgroup of (includes all commodities in this subgroup)	1	-	0.22	
SB 0715	Cacao bean	0.06	-	0.01	
MO 0105	Edible offal (mammalian)	0.01*	-	0	
PE 0112	Eggs	0.01*	-	0	
MF 0100	Mammalian fats (except milk fats)	0.01*	-	0	
MM 0095	Meat (from mammals other than marine mammals)	0.01*	-	0	
ML0106	Milks	0.01*	-	0	
VR 0589	Potato	0.1	0.01*	0.0185	
PO 0111	Poultry edible offal	0.01*	-	0	
PF 0111	Poultry fats	0.01*	-	0	
PM 0110	Poultry meat	0.01*	-	0	
DM1215	Cocoa butter			0.005	
DM 0715	Cocoa powder			0.005	

For calculation of the livestock dietary burden

CCN	Commodity	New	Previous	Median, mg/kg	Highest residue, mg/kg
	Bean forage (green)			4.35	9.27
	Beans with pods			0.22	0.58

DIETARY RISK ASSESSMENT

Long-term dietary exposure

The ADI for mandipropamid is 0–0.2 mg/kg bw. The International Estimated Daily Intakes (IEDIs) for mandipropamid were estimated for the 17 GEMS/Food Consumption Cluster Diets using the STMR or STMR-P values estimated by the JMPR. The results are shown in Annex 3 of the 2018 JMPR Report. The IEDIs ranged from 0–6% of the maximum ADI.

The Meeting concluded that long-term dietary exposure to residues of mandipropamid from uses considered by the JMPR is unlikely to present a public health concern.

Acute dietary exposure

The 2008 JMPR decided that an ARfD for mandipropamid was unnecessary. Therefore, the Meeting concluded that the acute dietary exposure to residues of mandipropamid from the uses considered by the current JMPR is unlikely to present a public health concern.

REFERENCES

Reference Number	Author(s)	Year	Study Title
2397W	Fleischmann, T.	2014	[^{14}C]-Mandipropamid - Metabolism in Potatoes Following Seed Piece Treatment. Report No. 2397W GLP, Unpublished Syngenta File No. NOA446510_50201
RPT03107	Wang, P.	2016	^{14}C-Mandipropamid - Metabolism in the Laying Hen. Report No. RPT03107 GLP, Unpublished Syngenta File No. NOA446510_50364
PR No.10324	Leonard, R.	2012	Mandipropamid - Magnitude of the residue on Beans (Snap). Report No. IR-4 PR No.10324 GLP, Unpublished Syngenta File No. NOA446510_50170

Reference Number	Author(s)	Year	Study Title
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