

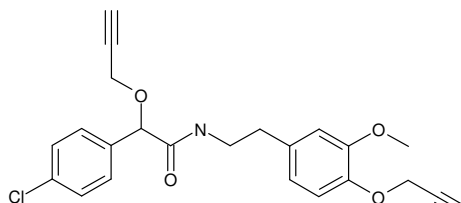
**MANDIPROPAMID (231)***First draft prepared by Dr. Yibing He,**Department of Science and Education, Ministry of Agriculture, China***EXPLANATION**

Mandipropamid was considered for the first time by the present Meeting. It belongs to the mandelamide chemical class of fungicides and is a synthetic fungicide intended for the control of Oomycete fungal pathogens in a range of crops.

At the 39<sup>th</sup> session of the CCPR (ALINORM 07/30/24), it was scheduled for evaluation as a new compound by 2008 JMPR. The Meeting received information on physical and chemical properties, animal and plant metabolism, environmental fate, analytical methods, storage stability, national registered use patterns, supervised residue trials and processing.

The 2008 JMPR established an ADI for mandipropamid of 0–0.2 mg/kg bw/day and concluded that an ARfD was unnecessary.

**IDENTITY**

ISO Common name	Mandipropamid
Chemical name	
IUPAC name	2-(4-chloro-phenyl)-N-[2-(3-methoxy-4-prop-2-ynyloxy-phenyl)-ethyl]-2-prop-2-ynyloxy-acetamide
CAS name	benzeneacetamide, 4-chloro-N-[2-[3-methoxy-4-(2-propynyl-oxy)phenyl]ethyl]- $\alpha$ -(2-propynyloxy)
CAS Registry Number	374726-62-2
CIPAC Number	
Synonyms and trade names	
Manufacturer's codes	NOA446510
Structural formula	
Molecular formula	C <sub>23</sub> H <sub>22</sub> ClNO <sub>4</sub>
Molecular weight	411.9 g/mol
Minimum content of ai	

**PHYSICAL AND CHEMICAL PROPERTIES*****Pure active ingredient***

Property	Description or results	Reference
Appearance	Light beige powder	Das, R, 2002, NOA446510/0025
		Das, R, 2005, NOA446510/0376
Odour	odourless	Das, R, 2002, NOA446510/0025
		Das, R, 2005, NOA446510/0376

Property	Description or results	Reference
Vapour pressure (purity 99.0%):	$9.4 \times 10^{-7}$ Pa at 20 °C $9.4 \times 10^{-7}$ Pa at 25 °C $9.4 \times 10^{-7}$ Pa at 50 °C	Geoffroy, A, 2003, NOA446510/0064
Henry's law constant	< $9.2 \times 10^{-5}$ Pa m <sup>3</sup> /mol at 25 °C (calculated)	Baker, SD, 2005, NOA446510/0445
Boiling point (purity 99.0%)	Thermal decomposition starts at about 200 °C	Das, R, 2003, NOA446510/0038
Melting point (purity 99.0%)	96.4 °C to 97.3 °C	Das, R, 2002, NOA446510/0024
Octanol-water partition coefficient:	Pow = 1600 (± 42), log Pow = 3.2 at pH 7.39 and 25 °C	Das, R, 2003, NOA446510/0027
Solubility in water at 25 °C (purity 99.0%):	pH 8.1: 4.2 mg/L	Das, R, 2003, NOA446510/0026
Solubility in organic solvents at 25 °C (purity 95.2%):	Acetone 300 g/L Dichloromethane 400 g/L Ethyl acetate 120 g/L Hexane 42 mg/L Methanol 66 g/L Octanol 4.8 g/L Toluene 29 g/L	Das, R, 2005, NOA446510/0375
Relative density (purity 99.0%)	1.24 g/cm <sup>3</sup> at 22 °C	Füldner, HH, 2003, NOA446510/0031
Dissociation constant in water	No pKa was found in the range of 1.0 to 12.0 for the pure active substance.	Martin, N, 2003, NOA446510/0029
Hydrolysis rate 14 <sup>C</sup> labelled mandipropamid, (98.9% radio-chemical purity)	<p>The hydrolysis study conducted with [ethyl-1-14<sup>C</sup>]mandipropamid at a concentration of 1 mg/L in sterile buffer solution at pH 4, 5, 7 and 9 at 50 °C for seven days and at pH 5, 7 and 9 at 25 °C for 32 days.</p> <p>The recovery for all samples was between 92.7% and 105.7% of the applied radioactivity. No degradation of the test substance was observed under all conditions.</p> <p>Mandipropamid is hydrolytically stable at pH 4, 5, 7 and 9.</p>	Hand, LH, Towers, J, 2003, NOA446510/0041  Hand, LH, 2004, NOA446510/0041-addendum

Property	Description or results	Reference
Photochemical degradation 14 <sup>C</sup> labelled NOA446510	<p>The photolytic degradation was evaluated in sterile buffer solution at pH 7 and 25 °C using methoxyphenyl label test substance at a concentration of 1 µg/mL. The samples were irradiated for periods up to the equivalent of 17 days summer sunlight. Duplicate “dark” control samples were also prepared and maintained at 25 °C and analysed at the same time as the irradiated samples.</p> <p>The estimated half-life DT<sub>50</sub> was 34 hours of continuous irradiation.</p> <p>At least 16 degradates were formed, none of which represented &gt; 5% of the applied radioactivity.</p> <p>The mean mass balance from irradiated samples was 102.9% of the applied radioactivity, of which up to 16.2% was characterised as 14CO<sub>2</sub>.</p>	Buckel, T, 2002, NOA446510/0018

### Formulations

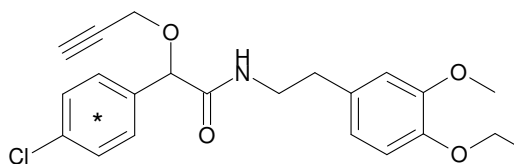
Mandipropamid is available in the following formulations:

Trade Names	Formulation		Member State or Country
	Type	Conc. (g ai/kg)	
Pergado	WG	Mandipropamid/Folpet (50/250 g/kg)	Austria
Revus	SC	250 g/L	Austria, UK, USA

### METABOLISM

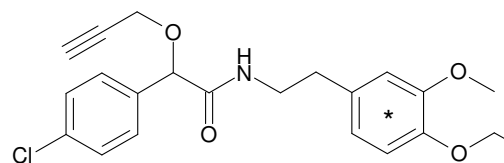
The Meeting received information on animal metabolism, plant metabolism and environmental fate studies using mandipropamid uniformly radiolabelled in either the chlorophenyl ring or the methoxyphenyl ring.

[Chlorophenyl-(U)-<sup>14</sup>C]-mandipropamid:



\* = Position of <sup>14</sup>C-label

[Methoxyphenyl-(U)-<sup>14</sup>C]-mandipropamid:

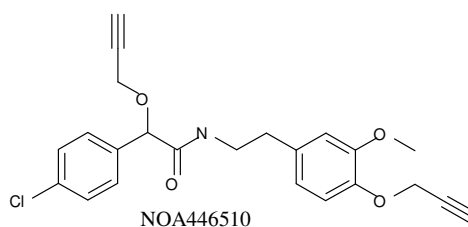


\* = Position of <sup>14</sup>C-label

Structures, names and codes for mandipropamid and its metabolites in metabolism and environmental fate studies are summarized below.

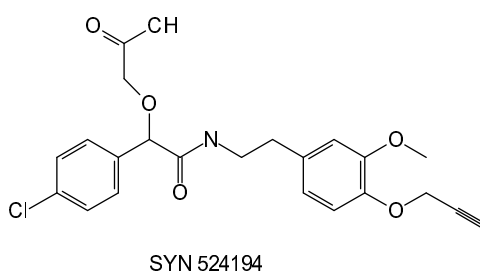
Mandipropamid (NOA446510)

2-(4-chloro-phenyl)-N-[2-(3-methoxy-4-prop-2-ynyloxy-phenyl)-ethyl]-2-prop-2-ynyloxy-acetamide



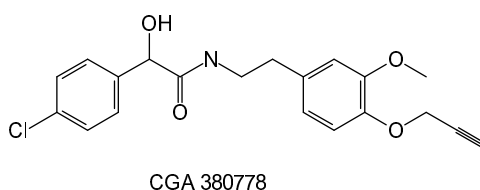
(SYN524194)

{(4-chloro-phenyl)-[2-(3-methoxy-4-prop-2-ynyloxy-phenyl)-ethylcarbamoyl]-methoxy}-acetic acid



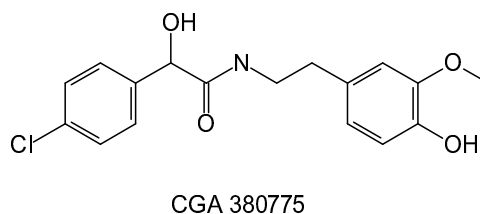
(CGA380778)

2-(4-Chlorophenyl)-2-hydroxy-N-[2-(3-methoxy-4-prop-2-ynyloxyphenyl)-ethyl]-acetamide



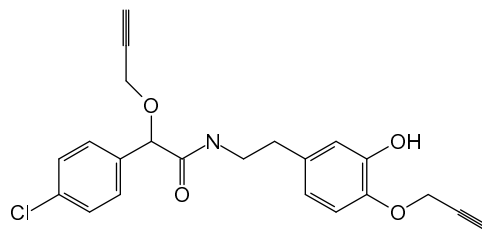
(CGA380775)

2-(4-Chlorophenyl)-2-hydroxy-N-[2-(4-hydroxy-3-methoxyphenyl)-ethyl]-acetamide



(SYN521195)

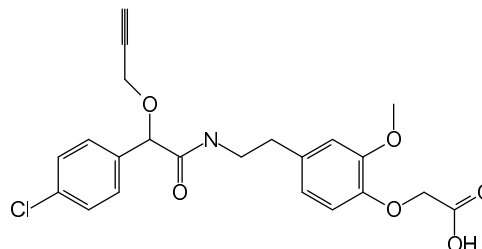
2-(4-Chlorophenyl)-N-[2-(3-hydroxy-4-prop-2-ynyloxyphenyl)-ethyl]-2-prop-2-ynyloxy-acetamide



SYN 521195

(SYN524193)

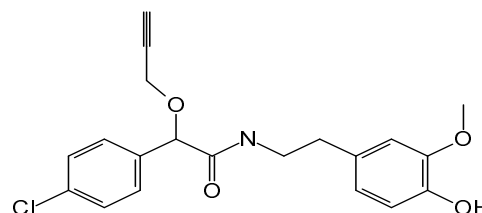
(4-{2-[2-(4-chloro-phenyl)-2-prop-2-ynyloxy-acetylamino]-ethyl}-2-methoxy-phenoxy)-acetic acid



SYN 524193

(NOA458422)

2-(4-Chlorophenyl)-N-[2-(4-hydroxy-3-methoxyphenyl)-ethyl]-2-prop-2-ynyloxy-acetamide

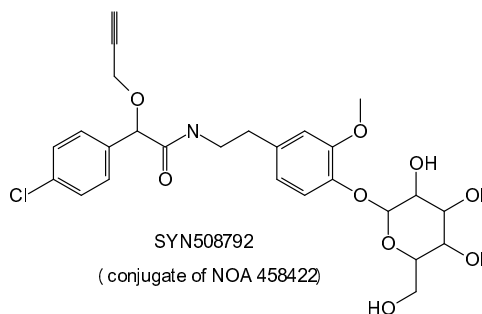


NOA 458422

(SYN508792)

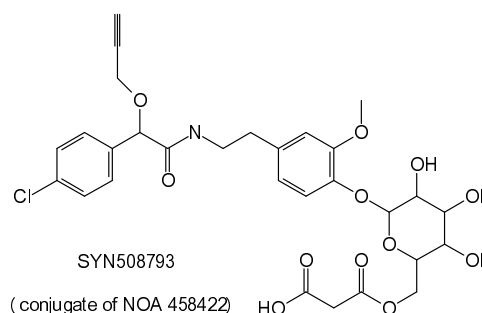
(conjugate of SYN458422)

2-(4-chloro-phenyl)-N-{2-[3-methoxy-4-(3,4,5-trihydroxy-6-hydroxymethyl-tetrahydro-pyran-2-yloxy)-phenyl]-ethyl}-2-prop-2-ynyloxy-acetamide

SYN 508792  
(conjugate of NOA 458422)

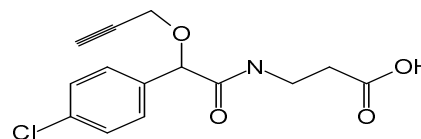
(SYN508793)

(conjugate of SYN458422)

SYN 508793  
(conjugate of NOA 458422)

(SYN524197)

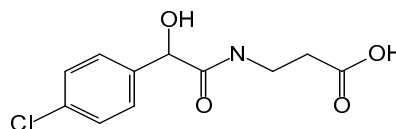
3-[2-(4-Chlorophenyl)-2-prop-2-ynyloxy-acetylamino]-propionic acid



SYN 524197

(SYN524198)

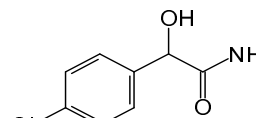
3-[2-(4-chloro-phenyl)-2-hydroxy-acetyl-amino]-propionic acid



SYN 524198

(SYN524195)

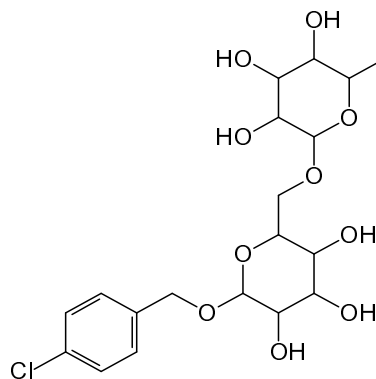
2-(4-chloro-phenyl)-2-hydroxy-acetamide



SYN 524195

(SYN524200)

2-(4-chloro-benzyloxy)-6-(3,4,5-trihydroxy-6-methyl-tetrahydro-pyran-2-yloxymethyl)-tetrahydro-pyran-3,4,5-triol

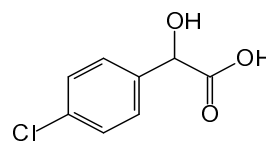


SYN 524200

(conjugate of 4-chlorobenzyl alcohol)

(SYN459119)

(4-Chlorophenyl)-hydroxy-acetic acid

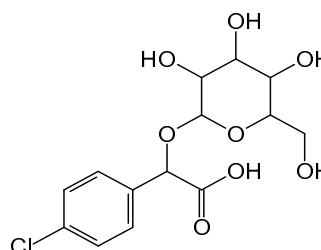


SYN 459119

(SYN524199)

(conjugate of SYN459119)

(4-chloro-phenyl)-(3,4,5-trihydroxy-6-hydroxymethyl-tetrahydro-pyran-2-yloxy)-acetic acid

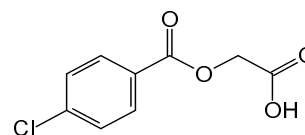


SYN 524119

(conjugate of SYN 459119)

(SYN524196)

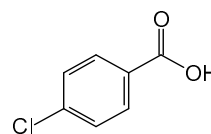
4-chloro-benzoic acid carboxymethyl ester



SYN 524196

(CGA155705)

4-chloro-benzoic acid

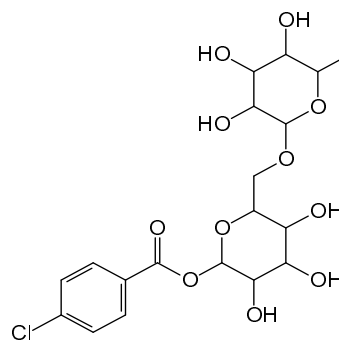


CGA 155705

(SYN524201)

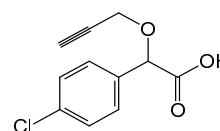
(conjugate of CGA155705)

4-chloro-benzoic acid 3,4,5-trihydroxy-6-(3,4,5-trihydroxy-6-methyl-tetrahydro-pyran-2-yloxymethyl)-tetrahydro-pyran-2-yl ester

SYN 524201  
(conjugate of CGA 155705)

(SYN500003)

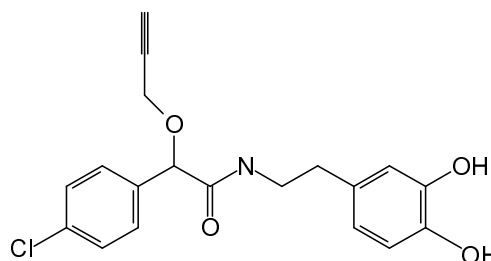
(4-Chlorophenyl)-prop-2-ynyloxy-acetic acid



SYN 500003

(SYN505503)

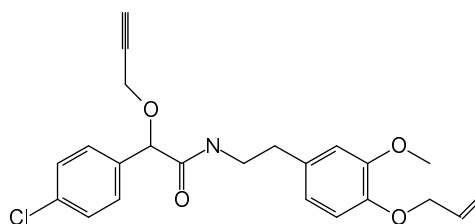
2-(4-Chlorophenyl)-N-[2-(3,4-dihydroxyphenyl)-ethyl]-2-prop-2-ynyloxy-acetamide



SYN 505503

(SYN536638)

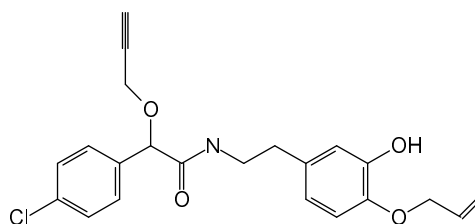
N-[2-(4-Allyloxy-3-methoxyphenyl)-ethyl]-2-(4-chlorophenyl)-2-prop-2-ynyloxy-acetamide



SYN 536638

(SYN539678)

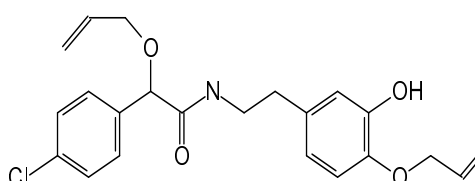
N-[2-(4-Allyloxy-3-hydroxyphenyl)-ethyl]-2-(4-chlorophenyl)-2-prop-2-ynyloxy-acetamide



SYN 539678

(SYN539679)

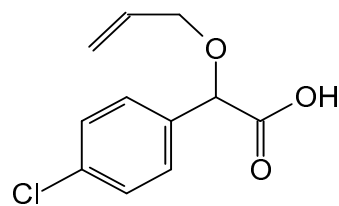
2-Allyloxy-N-[2-(4-allyloxy-3-hydroxyphenyl)-ethyl]-2-(4-chlorophenyl)-acetamide



SYN 539679

(SYN504851)

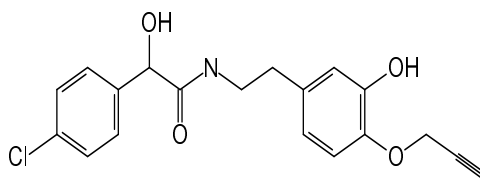
Allyloxy-(4-chlorophenyl)-acetic acid



SYN 504851

(SYN518495)

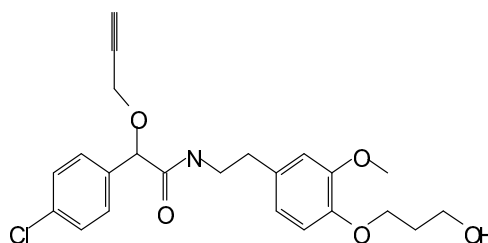
2-(4-Chlorophenyl)-2-hydroxy-N[2-(3-hydroxy-4-prop-2-nyloxyphenyl)-ethyl]-acetamide



SYN 518495

(U7 comp.2)

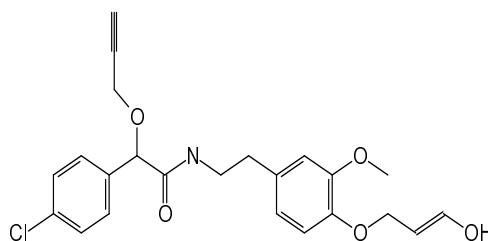
2-(4-Chlorophenyl)-N-{2-[4-(3-hydroxy-propoxy)-3-methoxyphenyl]-ethyl}-2-prop-2-nyloxy-acetamide



U7 or Component 2

(U8)

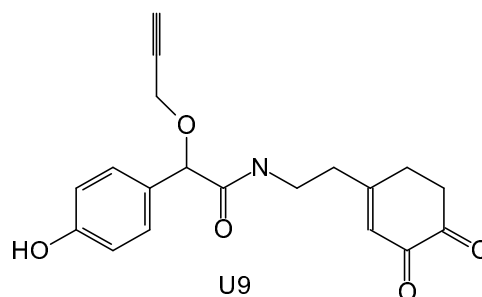
2-(4-Chlorophenyl)-N-{2-[4-((E)-3-hydroxy-allyloxy)-3-methoxyphenyl]-ethyl}-2-prop-2-nyloxy-acetamide



U8 or Component 3

(U9)

N-[2-(3,4-Dioxo-cyclohex-1-enyl)-ethyl]-2-(4-hydroxyphenyl)-2-prop-2-nyloxy-acetamide

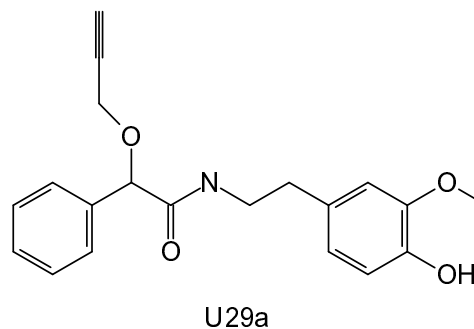


U9



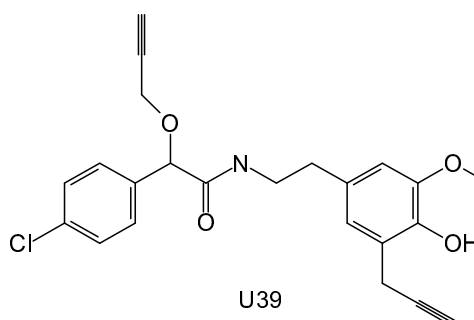
(U29a)

N-[2-(4-Hydroxy-3-methoxyphenyl)-ethyl]-2-phenyl-2-prop-2-ynyloxy-acetamide



(U39)

2-(4-Chlorophenyl)-N-[2-(4-hydroxy-3-methoxy-5-prop-2-ynyl-phenyl)-ethyl]-2-prop-2-ynyloxy-acetamide



### Animal metabolism

The Meeting received animal metabolism studies with mandipropamid in mice, rats, rabbits, dogs and lactating goats. Mouse, rat, rabbit and dog metabolism studies were evaluated by the WHO Core Assessment Group of the 2008 JMPR.

#### Rats

In a metabolism study, a single oral dose of [methoxyphenyl-U-<sup>14</sup>C]-mandipropamid, was administered by gavage to male and female rats (Alpk:AP<sub>1</sub>SD (Wistar derived)) at dose levels of 3 mg/kg and 300 mg/kg (Roberts, K, 2005, NOA446510/0533). At both dose levels, concentrations of radioactivity were much lower in rat tissues. The highest tissue concentrations were found in the liver for both sexes and at both dose levels. The values obtained at the 3 mg/kg dose level were 1.25 and 0.64 mg equivalents/kg mandipropamid for males and females respectively. For the higher dose level of 300 mg/kg, concentrations of 46.4 and 27.1 mg equivalents/kg were found for males and females respectively. The concentrations of radioactivity in fat and muscle orally dosed at a single oral dose level of 3 mg/kg are 0.016 and 0.014 equivalents mg/kg 8 h after administration, 0.010 and 0.012 mg equivalents/kg 24 h after administration, respectively. The concentrations of radioactivity in fat and muscle orally dosed at a single oral dose level of 300 mg/kg are 0.93 and 0.57 equivalents mg/kg 8 h after administration, 0.49 and 0.46 equivalents mg/kg 24 h after administration, respectively.

#### Lactating goats

Two pairs of lactating goats (*Capra hircus*, 2–3 years old, 52–71 kg) were orally dosed separately with [<sup>14</sup>C]mandipropamid, radiolabelled uniformly in either the chlorophenyl or methoxyphenyl ring, equivalent to 27–49 mg/kg in the total diet (on a dry basis) once daily via balling gun for seven consecutive days (Cary, CA and Aver, E, 2005, RJ3557B). Milk was collected twice daily during the dosing period, and the test goats were sacrificed 20 h after the last dose administration. Kidneys, liver, omental fat, renal fat and skeletal muscle (hind and fore quarters) were collect for analysis. The goat that was fed with methoxyphenyl label at 49 ppm in the feed became ill during dosing, and samples from this goat were not utilized.

The majority of the radioactivity was found in the faeces and urine. For the [<sup>14</sup>C]chlorophenyl treated goats, 46% of the administered dose was excreted in the faeces and 30% and 33% in the urine. For the remaining goat treated with [<sup>14</sup>C]methoxyphenyl mandipropamid, 49% of the administered radioactivity was excreted in the faeces and 33% in the urine.

The total radioactivity residues in milk plateaued after approximately 3 days of dosing for both radiolabels. The highest TRR expressed in mandipropamid equivalents were 0.006 mg/kg and 0.011 mg/kg in the afternoon milking of day 3. In the duration of metabolism study, no milk sample contained more than 0.05% of the administered dose.

Table 1 Summary of total radioactive residues in milk, tissue and excreta. (Cary, CA and Aver, E, 2005, RJ3557B)

Matrix	Chlorophenyl Label		Methoxyphenyl Label	
	%administered dose	TRR <sup>a</sup> (mg/kg)	%administered dose	TRR <sup>a</sup> (mg/kg)
Urine <sup>a</sup>	31	74	33	150
Faeces <sup>a</sup>	47	249	49	228
Milk <sup>a</sup>				
Day 1 pm	0.011	0.004		0.007
Day 1 am		0.004		0.007
Day 2 pm		0.004		0.009
Day 2 am		0.006		0.010
Day 3 pm		0.004		0.009
Day 3 am		0.006	0.048	0.011
Day 4 pm		0.004		0.008
Day 4 am		0.005		0.010
Day 5 pm		0.004		0.008
Day 5 am		0.005		0.010
Day 6 pm		0.004		0.008
Day 6 am		0.005		0.010
Day 7 pm		0.005		0.010
Day 7 am		0.005		0.010
Fat <sup>b</sup>		0.01	0.0174	0.01
Muscle <sup>a</sup>	0.03	0.0051	0.03	0.005
Liver <sup>b</sup>	0.12	0.480	0.09	0.472
Kidney <sup>b</sup>	0.01	0.136	0.01	0.121
Blood <sup>a</sup>	0.01	0.013/0.011	0.02	0.016
Bile (one goat) <sup>a</sup>	0.02	6.2	0.05	12.4
GI tract <sup>a</sup>	9.4/5.4	5.2/1.4	4.07	1.3
Cage wash <sup>a</sup>	0.28/0.54	0.35/0.64	0.93	1.2
Sum of administered dose	85.5/85.3		87.5	

<sup>a</sup> Quantification performed by direct quantification of sample.

<sup>b</sup> Quantification performed by summation of radioactivity in extracts and debris.

Characterization and identification of radioactive residue was carried out on tissues and milk where the total radioactive residue (TRR) determined at the biological phase locations was  $\geq 0.01$  mg/kg mandipropamid equivalents. For the goats treated with chlorophenyl-labelled mandipropamid these were liver, kidney and fat. For the goat treated with methoxyphenyl-labelled mandipropamid these were liver, kidney, fat and milk.

Table 2 Summary of characterization and identification of radioactive residues in goat matrices dosed with [Chlorophenyl-<sup>14</sup>C]mandipropamid at 27 or 45 ppm (composite samples from two goats) (Cary, CA and Aver, E, 2005, RJ3557B)

Compound	Fat		Kidney		Liver <sup>a</sup>	
	TRR= 0.0174 mg/kg		TRR= 0.136 mg/kg		TRR= 0.480 mg/kg	
	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg
Mandipropamid	75.1	0.0128	–	–	0.8	0.0038
CGA 380775	–	–	9.3	0.0126	1.0	0.0045
					2.6	0.0123
CGA 380778	–	–	5.6	0.0076	1.6	0.0080
SYN 505503	–	–	2.6	0.0035	–	–
NOA 458422	–	–	17.7	0.0240	4.1	0.0197
					1.2	0.0057
SYN 521195	–	–	4.3	0.0059	7.3	0.0351
SYN 518495	–	–	6.5	0.0088	1.2	0.0057
					0.4	0.0019
Unknowns	17.1	0.0029	27.5	0.0373	16.9	0.0817
					30.0	0.1438
Baseline	6.5	0.0011	11.2	0.0152	8.7	0.0415
					3.2	0.0154
Unassigned remainder	12.2	0.0021	2.7	0.0038	6.5	0.0303
					13.0	0.0631
Hexane phase	3.4	0.0006	–	–	–	–
Hexane/diethyl ether extract	2.2	0.0004	–	–	–	–
ACN/water (3:7) extract	–	–	1.4	0.002	3.3	0.016
SPE aqueous load	–	–	3.2	0.0043	0.7	0.0033
SPE water eluate	–	–	0.8	0.0011	0.3	0.0013
Microwave 2 <sup>nd</sup> aqueous	–	–	–	–	0.7	0.0033
Microwave Propanol/HCl	–	–	–	–	3.1	0.0149
Microwave Aqueous SPE retained	–	–	–	–	5.3	0.0253
Total identified	75.1	0.0128	46.0	0.0624	20.2	0.0967
Total characterized	41.1	0.0071	46.8	0.0637	91.7	0.4399
Total extractable	96.5	0.0164	85.3	0.116	113	0.543
Unextractable (PES) <sup>b</sup>	3.6	0.0010	14.7	0.020	0	0
Accountability <sup>c</sup>	109	0.0174	108	0.136	123	0.543

<sup>a</sup> When two values are reported, the second value represents that compound released from non-extractable residues with microwave extraction.

<sup>b</sup> Residues remaining after exhaustive extractions.

<sup>c</sup> Accountability = (Total extractable + Total unextractable)/(TRR from combustion analysis) × 100.

Table 3 Summary of characterization and identification of radioactive residues in goat matrices dosed with [methoxyphenyl-<sup>14</sup>C]mandipropamid at 30 ppm (Cary, CA and Aver, E, 2005, RJ3557B)

Compound	Milk, Day 4 am		Fat		Kidney		Liver <sup>a</sup>	
	TRR = 0.0095 mg/kg		TRR = 0.0244 mg/kg		TRR= 0.121 mg/kg		TRR= 0.472 mg/kg	
	%TRR	mg/kg	%TRR	mg/kg	%TRR	mg/kg	%TRR	mg/kg
Mandipropamid	7.9	0.0008	77.4	0.0187	–	–	1.4	0.0065
CGA 380775	–	–	–	–	5.8	0.0071	1.0	0.0047
							2.4	0.0113
CGA 380778	–	–	–	–	5.6	0.0068	0.2	0.0008
							0.8	0.0036
SYN 505503	–	–	–	–	1.4	0.0017	0.8	0.0037
NOA 458422	–	–	–	–	15.0	0.0183	4.4	0.0210
							1.4	0.0065
SYN 521195	–	–	–	–	2.0	0.0024	2.2	0.0108
SYN 518495	–	–	–	–	3.3	0.0041	0.9	0.0041
							0.4	0.0021
Unknowns	12.2	0.0012	5.5	0.0013	19.6	0.0239	11.5	0.0558
							8.5	0.0405
Baseline	13.0	0.0012	1.3	0.0003	13.4	0.0162	4.4	0.0208
							1.0	0.0050
Unassigned remainder	24.2	0.0022	7.6	0.0019	0.4	0.0003	1.4	0.0077
							4.8	0.0223
Hexane phase	–	–	1.6	0.0004	–	–	–	–
Hexane/diethyl ether extract	–	–	1.8	0.0004	–	–	–	–
ACN/water (3:7) extract	–	–	–	–	3.9	0.005	3.4	0.016
SPE aqueous load	–	–	–	–	8.4	0.0102	2.6	0.0126
SPE water eluate	–	–	–	–	0.9	0.0011	0.3	0.0015
Microwave Aqueous SPE retained	–	–	–	–	–	–	9.0	0.0426
Total identified	7.9	0.0008	77.4	0.0187	33.1	0.0404	15.9	0.0751
Total characterized	49.4	0.0046	17.8	0.0043	46.6	0.0567	46.9	0.2248
Total extractable	62.2	0.0059	97.2	0.0234	89.2	0.108	97.2	0.459
Unextractable (PES) <sup>b</sup>	37.8	0.0036	2.8	0.0010	10.8	0.013	0	0
Accountability <sup>c</sup>	95.0	0.0095	102	0.0244	106	0.121	105	0.459

<sup>a</sup> When two values are reported, the second value represents that compound released from non-extractable residues with microwave extraction.

<sup>b</sup> Residues remaining after exhaustive extractions.

<sup>c</sup> Accountability = (Total extractable + Total unextractable)/(TRR from combustion analysis) × 100.

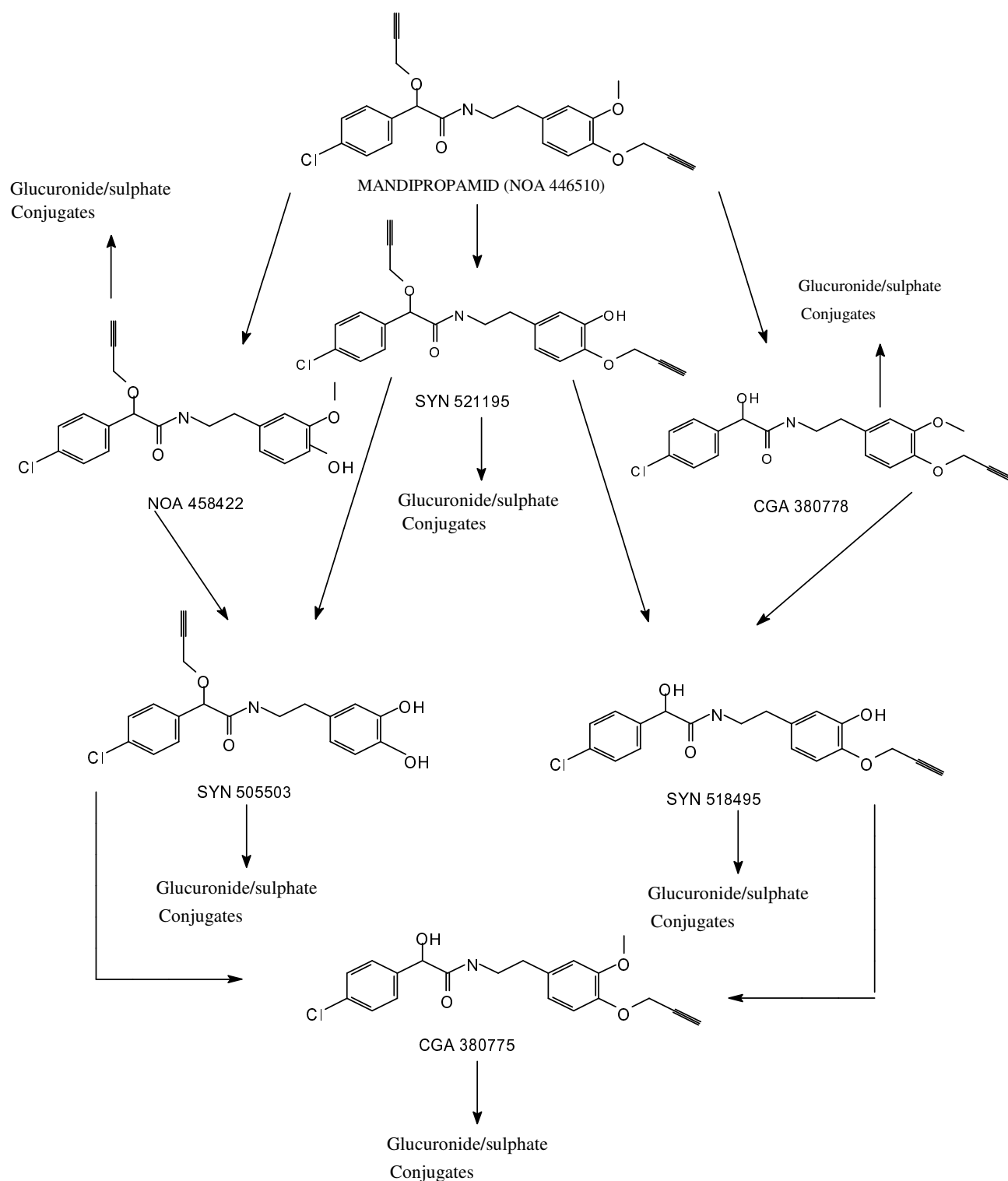


Figure 1 Proposed Metabolic Profile of Mandipropamid in Lactating Goat (Cary, CA and Aver, E, 2005, RJ3557B)

All tissue and milk samples with a TRR  $\geq 0.01$  ppm were extracted with organic solvents and analysed. Extractable residues were approximately 97% TRR in fat, approximately 85–89% TRR in kidney, approximately 62% TRR in milk, and approximately 39–55% TRR in liver. The remaining non-extractable residues in liver following solvent extractions were further investigated by employing

microwave and surfactant extraction procedures. The residue extraction and fractionation procedures employed in the study adequately released and characterized the majority of residues from goat milk and tissues; accountabilities were 95–123% based on TRR determined by LSC. Residues were quantitated by TLC, and identified using TLC, HPLC, and/or LC/MS.

The metabolite profiles were similar between the two labels with all the metabolites observed containing both phenyl rings. The parent mandipropamid was the major residue component identified in fat and accounted for 75.1–77.4% TRR (0.013–0.019 mg/kg). The parent, however, was a minor residue in methoxyphenyl-labelled milk at 7.9% TRR (0.013 mg/kg) and liver at 0.8–1.4% TRR (0.004–0.007 mg/kg). The parent was not detected in kidney samples.

The metabolite NOA 458422 was a significant residue in kidney at 15.0–17.7% TRR (0.018–0.024 mg/kg) but was a minor residue in liver at 5.3–5.8% TRR (0.025–0.028 mg/kg). Metabolites CGA 380775, CGA 380778, SYN 505503, SYN 521195, and SYN 518495 were identified as minor residues in kidney (each  $\leq$  9.3% TRR,  $<$  0.02 mg/kg) and liver (each  $\leq$  7.3% TRR,  $\leq$  0.04 mg/kg). The remaining residues in goat milk and tissues were characterized as:

(i) Unknowns totalling 12.2% TRR in milk, 5.5–17.1% TRR in fat, 19.6–27.5% TRR in kidney, and 20.0–46.9% TRR in liver with individual peaks accounting for  $<$  0.04 mg/kg;

(ii) Baseline material accounting for  $<$  0.03 mg/kg.

(iii) Unassigned (TLC) remainder accounting for  $\leq$  0.06 mg/kg.

Mandipropamid undergoes extensive metabolism to produce more polar metabolites in goats. Metabolism occurs primarily by:

(i) The demethylation of the methoxyphenyl functionality to generate the phenol moiety.

(ii) The removal of either or both of the propargyl side chain(s) yielding the corresponding alcohol or phenol functionalities.

All molecules, except the parent, have the potential to form polar conjugates.

### ***Plant metabolism***

The Meeting received plant metabolism studies with mandipropamid on grapes, lettuce, potatoes and tomatoes.

Metabolism studies of mandipropamid in three different crop groups (fruit–grapes, leafy vegetables–lettuce and root and tuber vegetables–potato) have demonstrated that the compound undergoes extensive metabolism to form a range of metabolites which are more polar than parent. The extent of metabolism is related to the length of time between application of mandipropamid and harvest of the crop. When this time period is short, as in lettuce, mandipropamid is the principal residue (up to 94% TRR). Levels of metabolites are very low and are structurally similar to the parent. In the case of the other two crops, (grape and potato), the multiple application regimes over a relatively long time period allowed more extensive metabolism to take place. Unchanged mandipropamid remained as the major component in all aerial crop parts (ranging from approximately 40% to 94% TRR) and metabolites structurally very similar to the parent were still evident; however, it was possible to identify more of the minor metabolites and to establish further steps in the biotransformation pathway. Overall, extensive degradation of the molecule was demonstrated, although individual metabolites were detected only at low levels and there was no evidence for accumulation of any specific compound. In lettuce, grapes and potato leaves no individual metabolite released by room temperature extraction accounted for  $>$  3.8% TRR mandipropamid equivalents. Although the major metabolite in potato tubers accounted for 12.7% TRR, this represented only 0.006 mg/kg mandipropamid equivalents.

### Grapes

An outdoor confined  $^{14}\text{C}$ -grape metabolism study was conducted in Switzerland during 2002 and 2003 (Sandmeier, P, 2003, NOA446510/0061). Mandipropamid, uniformly radiolabelled in either the chlorophenyl ring or the methoxyphenyl ring ([chlorophenyl-(U)- $^{14}\text{C}$ ]mandipropamid or [methoxyphenyl-(U)- $^{14}\text{C}$ ]mandipropamid) and formulated as a suspension concentrate (formulation code A12946C containing 250 g/L mandipropamid) was applied as a foliar spray to grape vines (Variety: Blauburgunder). Six applications were made, separated by intervals of 10–12 days, at calculated application rates of 143–151 g ai/ha for the 1× rate plots and 411–464 g ai/ha for the 3× rate plots. From the 1× rate plot samples of fruit and leaves were harvested on the day of the final application and also 14 and 28 days later. From the 3× rate plots, samples of fruit and leaves were harvested only at the 28 day interval.

Grapes were dipped twice in acetonitrile:water (80:20 v/v) to remove the surface radioactivity, after which the grapes were homogenized in the presence of liquid nitrogen. Radioactivity washed from the surface was determined directly by liquid scintillation counting (LSC) and the radioactivity remaining in the grapes was determined by direct combustion/LSC. The total radioactive residues (TRRs) in grapes were initially determined by the summation of the surface radioactivity and the radioactivity remaining in the fruit. The total radioactive residues in leaves were initially determined by direct combustion/LSC of homogenized samples. Surface washed fruits and leaves were extracted into acetonitrile:water (80:20 v/v) using an accelerated solvent extractor (ASE) and extracts were analysed by thin layer chromatography (TLC) and high performance liquid chromatography (HPLC). Following extraction of homogenised samples, TRRs in grapes and leaves were also determined by the summation of the radioactivity present in the extracts and the remaining debris. Microwave extraction was performed on the debris from all the fruit samples following ASE extraction. The samples were extracted into 1-propanol:1M HCl (85:15 v/v) for 15 minutes at 100 °C followed by 5 minutes at 150 °C. Resulting extracts were analysed by TLC.

Table 4 Summary of total radioactive residues in grapevine samples (Sandmeier, P, 2003, NOA446510/0061)

Radiolabel position	PHI [Days]	Plant Part	TRR [mg/kg]			
			By Direct Combustion and LSC Quantification <sup>a</sup>		By Summation of Extracted and Unextracted Radioactivity	
			1× Rate	3× Rate	1× Rate	3× Rate
Chlorophenyl	0	Fruits	1.32	–	1.32	–
		Leaves	59.3	–	74.9	–
	14	Fruits	1.33	–	1.32	–
		Leaves	48.6	–	50.4	–
	28	Fruits	0.91	7.32	0.91	7.38
		Leaves	29.5	126.7	45.5	122.5
Methoxyphenyl	0	Fruits	2.12	–	2.09	–
		Leaves	67.0	–	75.6	–
	14	Fruits	1.03	–	1.04	–
		Leaves	59.0	–	62.0	–
	28	Fruits	1.08	4.40	1.08	4.38
		Leaves	35.6	90.4	43.3	122.8

<sup>a</sup> For fruit this is the summation of the surface wash and direct combustion/LSC of the remaining fruit.

Table 5 Extractability of residues from grapevine samples (Sandmeier, P, 2003, NOA446510/0061)

Radiolabel Position	Plant Part	PHI [Days]	Surface Radioactivity		Extracted Radioactivity		Unextracted Radioactivity	
			[mg/kg]	[% TRR]	[mg/kg]	[% TRR]	[mg/kg]	[% TRR]
Chloro-phenyl	Fruit	0	1.17	88.6	0.100	7.6	0.050	3.8
	Leaves	0	–	–	66.7	89.1	8.20	10.9
	Fruit	14	1.08	81.5	0.18	13.4	0.067	5.1
	Leaves	14	–	–	41.8	83.0	8.56	17.0
	Fruit	28	0.72	79.0	0.12	13.0	0.073	8.0
	Leaves	28	–	–	35.5	83.7	6.94	16.3
Methoxy-phenyl	Fruit	0	1.83	87.3	0.17	8.1	0.096	4.6
	Leaves	0	–	–	69.1	91.3	6.59	8.7
	Fruit	14	0.82	79.1	0.14	13.3	0.079	7.6
	Leaves	14	–	–	52.1	84.1	9.87	15.9
	Fruit	28	0.85	79.1	0.13	12.0	0.096	8.9
	Fruit	28	–	–	36.1	83.4	7.18	16.6

Identification of the radioactive components in sample extracts was carried out either by co-chromatography with reference standards or by isolation and identification by LC-MS and LC-NMR. TRRs in the fruit following application at the 1×rate were 1.3–2.1 mg/kg in samples harvested immediately after the final application and had reduced to 0.9–1.1 mg/kg 28 days later. TRRs in the grape leaves following application at the 1×rate were much higher ranging from 59–76 mg/kg in samples with a 0 day PHI and 29–45 mg/kg in samples with a 28 day PHI. The TRR values for grapes determined from the summation of the radioactivity present in the extracts and the debris after initial extraction were in good agreement with those derived by direct quantification. TRR values determined by summation of the radioactivity present in the extracts and the debris after initial extraction are considered the most reliable, due to the large sample sizes taken for analysis, and will therefore be used to express residue levels from this point forwards.

The majority of the radioactivity in the fruit was present on the surface, accounting for 79–89% TRR. Of the remaining radioactivity 8–13% TRR was extractable using acetonitrile:water (80:20 v/v) leaving a maximum of 9% TRR unextracted. The majority of the radioactivity (83–91% TRR) in the leaves was extractable using acetonitrile:water (80:20 v/v) leaving a maximum of 17% unextracted. Parent mandipropamid was identified as the major component of the residue in all fruit samples from both labels, ranging from 79.0 to 80.2% TRR in the 0 day PHI samples and reducing to 53.6–59.2% TRR in the 28 day PHI samples. A large number of additional components were detected in the room temperature extracts of the fruit samples of which the largest fraction accounted for a maximum of only 3.8% TRR; 0.040 mg/kg.

Table 6 Summary of identification and characterization of residues in chlorophenyl treated fruit samples (Sandmeier, P, 2003, NOA446510/0061)

Components	Fruit					
	0 day PHI		14 day PHI		28 day PHI	
	[% TRR]	[mg/kg]	[% TRR]	[mg/kg]	[% TRR]	[mg/kg]
Mandipropamid (I21)	79.0	1.04	64.7	0.86	53.6	0.49
NOA458422 (I20)	2.7	0.036	2.7	0.036	3.8	0.035
SYN521195 (I20)						
SYN508792 (I14)	1.4	0.018	1.1	0.015	1.2	0.011
CGA380778 (I19)	1.4	0.019	2.9	0.038	2.8	0.025
CGA380775 (I18)	1.0	0.014	1.6	0.021	2.7	0.025



Components	Fruit					
	0 day PHI		14 day PHI		28 day PHI	
	[% TRR]	[mg/kg]	[% TRR]	[mg/kg]	[% TRR]	[mg/kg]
SYN524193 (I9)	0.4	0.005	0.8	0.011	0.8	0.008
SYN524194 (I9)						
SYN524196 (I9)						
CGA155705 (I16)	nd	nd	1.0	0.013	1.5	0.014
SYN524197 (I16)						
SYN524198 (I8)	0.3	0.004	1.1	0.015	1.3	0.012
NOA459119 (I8)						
SYN524195 (I15)	nd	nd	0.9	0.012	1.4	0.013
SYN524199 (I5a)	nd	nd	1.1	0.015	0.6	0.006
SYN524200 (I12)	0.6	0.008	2.0	0.026	1.4	0.013
SYN524201 (I12)						
Unresolved	3.9	0.051	3.8	0.050	8.0	0.073
Unidentified	5.6 <sup>a</sup>	0.073 <sup>a</sup>	11.2 <sup>b</sup>	0.148 <sup>b</sup>	12.9 <sup>c</sup>	0.116 <sup>c</sup>
Unextracted <sup>d</sup>	3.8	0.050	5.1	0.067	8.0	0.073
Total	100.0	1.321	100.0	1.320	100.0	0.911

<sup>a</sup> Comprised of at least 9 components none greater than 1.2% TRR; 0.016 mg/kg

<sup>b</sup> Comprised of at least 11 components none greater than 2.1% TRR; 0.027 mg/kg

<sup>c</sup> Comprised of at least 11 components none greater than 2.8% TRR; 0.026 mg/kg

<sup>d</sup> Results of further extraction are presented in Table 7

nd Not detected

Table 7 Summary of identification and characterization of residues in chlorophenyl treated leaf samples (Sandmeier, P, 2003, NOA446510/0061)

Components	Leaves					
	0 day PHI		14 day PHI		28 day PHI	
	[% TRR]	[mg/kg]	[% TRR]	[mg/kg]	[% TRR]	[mg/kg]
Mandipropamid (I21)	69.2	51.9	55.5	28.0	55.7	23.7
NOA458422 (I20)	1.5	1.10	2.0	1.03	2.5	1.07
SYN521195 (I20)						
SYN508792 (I14)	0.3	0.22	0.4	0.21	0.5	0.23
CGA380778 (I19)	1.7	1.26	2.6	1.30	2.6	1.09
CGA380775 (I18)	1.6	1.16	1.7	0.84	1.9	0.80
SYN524193 (I9)	0.5	0.39	0.6	0.29	0.6	0.24
SYN524194 (I9)						
SYN524196 (I9)						
CGA155705 (I16)	1.0	0.77	1.2	0.62	1.2	0.53
SYN524197 (I16)						
SYN524198 (I8)	0.8	0.57	1.4	0.71	1.3	0.55
NOA459119 (I8)						
SYN524195 (I15)	0.5	0.41	1.0	0.50	0.8	0.35
SYN524199 (I5a)	0.3	0.21	0.8	0.39	0.6	0.26
SYN524200 (I12)	0.3	0.21	0.7	0.37	0.7	0.29
SYN524201 (I12)						

Components	Leaves					
	0 day PHI		14 day PHI		28 day PHI	
	[% TRR]	[mg/kg]	[% TRR]	[mg/kg]	[% TRR]	[mg/kg]
Unresolved	4.6	3.46	2.5	1.24	4.4	1.88
Unidentified	6.9 <sup>a</sup>	5.14 <sup>a</sup>	12.7 <sup>b</sup>	6.37 <sup>b</sup>	10.7 <sup>c</sup>	4.60 <sup>c</sup>
Unextracted	10.9	8.20	17.0	8.56	16.3	6.94
Total	100.0	75.0	100.0	50.4	100.0	42.5

<sup>a</sup> Comprised of at least 11 components none greater than 1.0% TRR; 0.768 mg/kg

<sup>b</sup> Comprised of at least 11 components none greater than 2.4% TRR; 1.230 mg/kg

<sup>c</sup> Comprised of at least 11 components none greater than 2.5% TRR; 1.069 mg/kg

Table 8 Summary of identification and characterisation of residues in methoxyphenyl treated fruit samples (Sandmeier, P, 2003, NOA446510/0061)

Components	Fruit					
	0 day PHI		14 day PHI		28 day PHI	
	[% TRR]	[mg/kg]	[% TRR]	[mg/kg]	[% TRR]	[mg/kg]
Mandipropamid (I21)	80.2	1.68	68.7	0.71	59.2	0.64
NOA458422 (I20)	1.9	0.039	2.7	0.028	3.0	0.033
SYN521195 (I20)						
SYN508792 (I14)	1.0	0.021	1.4	0.015	1.3	0.014
CGA380778 (I19)	1.9	0.040	2.3	0.024	2.6	0.028
CGA380775 (I18)	1.2	0.024	1.1	0.012	1.8	0.020
SYN524193 (I9)	0.4	0.009	0.6	0.007	0.6	0.006
SYN524194 (I9)						
SYN524197 (I16)	0.6	0.012	0.4	0.004	0.6	0.007
SYN524198 (I8)	0.3	0.006	0.6	0.006	0.8	0.008
Unresolved	3.8	0.080	4.5	0.005	7.7	0.083
Unidentified	4.1 <sup>a</sup>	0.087 <sup>a</sup>	9.9 <sup>b</sup>	0.10 <sup>b</sup>	13.4 <sup>c</sup>	0.15 <sup>c</sup>
Unextracted <sup>d</sup>	4.6	0.096	7.6	0.079	8.9	0.096
Total	100.0	2.09	100.0	1.04	100.0	1.08

<sup>a</sup> Comprised of at least 10 components none greater than 0.7% TRR; 0.015 mg/kg

<sup>b</sup> Comprised of at least 12 components none greater than 1.9% TRR; 0.020 mg/kg

<sup>c</sup> Comprised of at least 12 components none greater than 3.5% TRR; 0.037 mg/kg

<sup>d</sup> Results of further extraction are presented in Table 8

Table 9 Summary of identification and characterisation of residues in methoxyphenyl treated leaf samples (Sandmeier, P, 2003, NOA446510/0061)

Components	Leaves					
	0 day PHI		14 day PHI		28 day PHI	
	[% TRR]	[mg/kg]	[% TRR]	[mg/kg]	[% TRR]	[mg/kg]
Mandipropamid (I21)	76.1	57.6	55.3	34.3	60.0	26.0
NOA458422 (I20)	1.0	0.73	1.1	0.70	1.2	0.52
SYN521195 (I20)						
SYN508792 (I14)	0.2	0.15	0.4	0.27	0.5	0.20
CGA380778 (I19)	1.7	1.29	3.1	1.91	2.6	1.11
CGA380775 (I18)	0.5	0.41	1.0	0.61	0.8	0.37
SYN524193 (I9)	0.4	0.30	0.6	0.35	0.5	0.22
SYN524194 (I9)						

Components	Leaves					
	0 day PHI		14 day PHI		28 day PHI	
	[% TRR]	[mg/kg]	[% TRR]	[mg/kg]	[% TRR]	[mg/kg]
SYN524197 (I16)	0.5	0.36	0.7	0.42	0.6	0.24
SYN524198 (I8)	0.4	0.34	1.0	0.62	0.9	0.41
Unresolved	4.7	3.54	6.8	4.24	6.6	2.84
Unidentified	5.8 <sup>a</sup>	4.35 <sup>a</sup>	14.0 <sup>b</sup>	8.75 <sup>b</sup>	9.9 <sup>c</sup>	4.25 <sup>c</sup>
Unextracted	8.7	6.59	15.9	9.87	16.6	7.18
Total	100.0	75.6	100.0	62.0	100.0	43.3

<sup>a</sup> Comprised of at least 11 components none greater than 1.3% TRR; 0.98 mg/kg

<sup>b</sup> Comprised of at least 11 components none greater than 4.0% TRR; 2.48 mg/kg

<sup>c</sup> Comprised of at least 11 components none greater than 2.2% TRR; 0.95 mg/kg

Sixteen of these metabolites were identified and can be classified into two groups:

- Metabolites that contained both the chlorophenyl and methoxyphenyl rings with metabolism having occurred on one or both of the propargyl groups and/or the methoxy functionality (SYN521195, SYN524193, SYN524194, NOA458422, CGA80775, CGA380778). SYN508792, a sugar conjugate of NOA458422, was also detected.
- Metabolites that contained only the chlorophenyl ring (SYN524195, SYN524196, SYN524197, SYN524198, NOA459119, CGA155705). SYN524199, a sugar conjugate of NOA459119, SYN524200, a sugar conjugate of 4-chlorobenzyl alcohol, and SYN524201, a sugar conjugate of CGA155705 (4-chlorobenzoic acid), were also detected.

No metabolites containing only the methoxyphenyl ring were identified. Radioactivity remaining in the fruit debris after initial extraction was further investigated and was shown to contain small amounts of parent mandipropamid and also five of the previously identified metabolites, all of which contained both the chlorophenyl and methoxyphenyl rings (SYN508792, SYN521195, NOA458422, CGA380775, CGA380778).

Table 10 Summary of identification and characterisation of residues in chlorophenyl treated fruit debris after microwave extraction (Sandmeier, P, 2003, NOA446510/0061)

Components	Fruit					
	0 day PHI		14 day PHI		28 day PHI	
	[% TRR]	[mg/kg]	[% TRR]	[mg/kg]	[% TRR]	[mg/kg]
Mandipropamid (I21)	0.22	0.003	0.99	0.013	2.09	0.019
NOA458422 (I20)	0.23	0.003	0.33	0.004	0.67	0.006
SYN521195 (I20)						
CGA380778 (I19)						
SYN508792 (I14)	0.05	< 0.001	0.17	0.002	0.26	0.002
CGA380775 (I18)	0.11	0.001	0.21	0.003	0.48	0.004
Unresolved	0.14	0.002	0.22	0.003	1.30	0.012
Unidentified	0.05	< 0.001	0.07	< 0.001	–	–
Unextracted	2.90	0.038	3.3	0.044	5.30	0.048
Total <sup>a</sup>	3.70	0.049	5.29	0.070	10.1	0.091

<sup>a</sup> May vary slightly from those figures in Table 3 due to rounding errors

Table 11 Summary of identification and characterisation of residues in methoxyphenyl treated fruit debris after microwave extraction (Sandmeier, P, 2003, NOA446510/0061)

Components	Fruit					
	0 day PHI		14 day PHI		28 day PHI	
	[% TRR]	[mg/kg]	[% TRR]	[mg/kg]	[% TRR]	[mg/kg]
Mandipropamid (I21)	0.71	0.015	1.59	0.016	1.83	0.020
NOA458422 (I20)	0.98	0.021	1.76	0.018	2.02	0.022
SYN521195 (I20)						
CGA380778 (I19)						
SYN508792 (I14)	0.32	0.007	0.57	0.006	0.79	0.009
CGA380775 (I18)	0.56	0.012	0.90	0.009	1.11	0.012
Unresolved	0.18	0.004	0.47	0.005	0.85	0.009
Unidentified	0.16	0.003	0.41	0.004	–	–
Unextracted	1.70	0.036	2.50	0.026	4.10	0.044
Total <sup>a</sup>	4.61	0.098	8.20	0.084	10.70	0.116

<sup>a</sup> May vary slightly from those figures in Table 5 due to rounding errors

The profile of radioactivity present in leaves was very similar to that in the fruit; no additional metabolites were identified in leaves that were not identified in the fruits. These results demonstrate that unchanged parent mandipropamid comprises the majority of the residue in grapes. The principal metabolic steps are cleavage of the methyl ether functionality and the removal or modification of either or both of the propargyl side chains to generate the corresponding alcohol, phenol or carboxylic acid functionalities. Cleavage of the amide bond between the two aromatic rings and breakdown of the methoxyphenyl ring occurred to a limited extent resulting in several metabolites which were exclusive to the chlorophenyl label. Some of these compounds, which contained either an alcohol or carboxylic acid functionality, formed sugar conjugates. A metabolic pathway for mandipropamid in grapes is proposed in Figure 2.

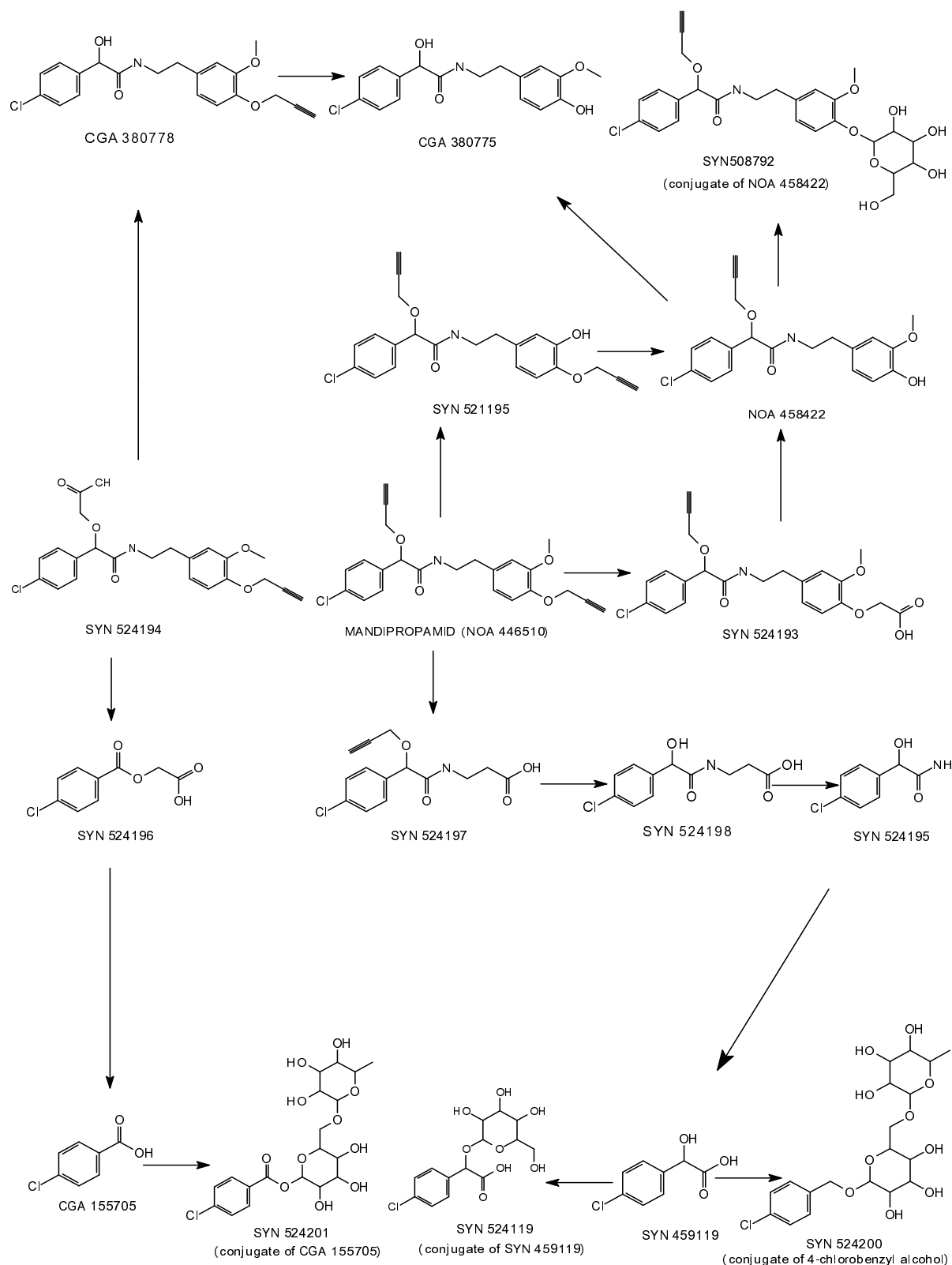


Figure 2 Proposed metabolic pathway of mandipropamid in grapevines (Sandmeier, P, 2003, NOA446510/0061)

### Lettuce

An outdoor confined mandipropamid metabolism study on lettuce (Variety: Little Gem) was conducted in the UK during 2003 and 2004 (Chen, L, Evans, J, 2005, NOA446510/0237).

[Chlorophenyl-(U)-<sup>14</sup>C]-mandipropamid or [methoxyphenyl-(U)-<sup>14</sup>C]-mandipropamid, formulated as suspension concentrates (formulation code A12946C containing 250 g/L mandipropamid) were applied as a foliar spray to lettuce plants. Two applications were made, separated by an interval of 7 days at calculated application rates of 136–138 g ai/ha for the chlorophenyl label and 156–160 g ai/ha for the methoxyphenyl label. The containers were located outdoors allowing full exposure of the lettuce plants to direct sunlight. Lettuce plants were harvested 3 and 14 days after the second application and were homogenised in the presence of solid carbon dioxide without further preparation.

Total radioactive residues (TRRs) were initially determined in all samples by direct combustion/LSC. Each sample was extracted into acetonitrile:water (80:20 v/v) and the extracts analysed by thin layer chromatography (TLC). Following extraction of homogenised samples, TRRs in lettuce were also determined by the summation of the radioactivity present in the extracts and the remaining debris. The initial extract from the 14 day PHI chlorophenyl sample was further investigated using a liquid–liquid partition with diethyl ether:water (5:1 v/v). The organic and aqueous extracts were analysed by TLC and the aqueous phase was then subjected to enzyme hydrolysis using driselase in a sodium acetate buffer (pH 5) at 37 °C for 24 h. Following a further liquid–liquid partition with diethyl ether, the organic and aqueous extracts were analysed by TLC. Identification of the radioactive components in sample extracts was carried out by co-chromatography with reference standards. LC–MS/MS was used to confirm the identity of mandipropamid, NOA458422 and CGA380778.

Lettuce samples with a 3 day PHI contained TRRs of 3.0 mg/kg (chlorophenyl) and 4.4 mg/kg (methoxyphenyl) and reduced to 1.3 mg/kg and 2.7 mg/kg respectively at the 14 day PHI time point. The TRR values were determined from the summation of the radioactivity present in the extracts and the debris after initial extraction were in good agreement with those derived from direct quantification. TRR values determined by summation of the radioactivity present in the extracts and the debris after initial extraction are considered the most reliable, due to the large sample sizes taken for analysis, and will therefore be used to express residue levels from this point forwards. The total radioactive residues (TRRs) found in the lettuce plants are summarised in Table 12.

Table 12 Summary of total radioactive residues in lettuce samples (Chen, L, Evans, J, 2005, NOA446510/0237)

Radiolabel position	PHI [Days]	TRR [mg/kg]	
		By Direct Combustion and LSC Quantification	By Summation of Extracted and Unextracted Radioactivity
Chlorophenyl	3	3.04	3.09
	14	1.32	1.39
Methoxyphenyl	3	4.41	4.44
	14	2.64	2.70

The percentages of the TRRs that were extractable using acetonitrile:water (80:20 v/v) were very high for all samples (> 97% TRR) and therefore no further work was conducted on the debris. Table 13 summarises the extractability of radioactive residues from the lettuce samples using acetonitrile:water (80:20 v/v).

Table 13 Extractability of residues from lettuce samples (Chen, L, Evans, J, 2005, NOA446510/0237)

Radiolabel Position	PHI [Days]	Extracted Radioactivity		Unextracted Radioactivity		TRR [mg/kg]
		[mg/kg]	[% TRR]	[mg/kg]	[% TRR]	
Chlorophenyl	3	3.06	99.1	0.029	0.9	3.09
	14	1.35	97.3	0.038	2.7	1.39
Methoxyphenyl	3	4.41	99.2	0.036	0.8	4.44
	14	2.64	97.8	0.059	2.2	2.70

No significant difference was found between the profiles of lettuce samples derived from the two radiolabelled experiments. In all lettuce samples, parent mandipropamid was the largest component of the residue accounting for 82.4–93.5% TRR. Four metabolites were identified, all of which contained both the chlorophenyl and methoxyphenyl rings. NOA458422 and CGA380778 were present both as free metabolites at maximum levels of 1.1% TRR, 0.018 mg/kg and also as conjugated metabolites at maximum levels of 0.4% TRR, 0.005 mg/kg. SYN521195 and CGA380775 were only present as conjugated metabolites at maximum levels of 0.2% TRR; 0.003 mg/kg.

Table 14 Summary of identification and characterisation of residues in 3 day PHI lettuce samples (Chen, L, Evans, J, 2005, NOA446510/0237)

Components	[Chlorophenyl- <sup>14</sup> C]-		[Methoxyphenyl- <sup>14</sup> C]-	
	[% TRR]	[mg/kg]	[% TRR]	[mg/kg]
Mandipropamid	92.5	2.86	93.5	4.16
NOA458422	0.6	0.018	0.3	0.013
CGA380778	0.6	0.018	0.3	0.013
Unknown <sup>a</sup> (Non-baseline)	0.3	0.009	0.2	0.009
Baseline	2.3	0.071	2.2	0.096
Remainder <sup>b</sup>	3.1	0.095	1.9	0.083
Unextracted	0.9	0.029	0.8	0.036
Gain / Losses on analysis	-0.3	-0.010	0.9	0.039
Total	100.0	3.09	100.1	4.44

<sup>a</sup> Area of radioactivity not aligned with standard reference markers on TLC.

<sup>b</sup> A complex mixture of minor diffuse unassigned radio components with varying polarity.

Table 15 Summary of identification and characterisation of residues in 14 day PHI lettuce samples (Chen, L, Evans, J, 2005, NOA446510/0237)

Components	[Chlorophenyl- <sup>14</sup> C]-		[Methoxyphenyl- <sup>14</sup> C]-	
	[% TRR]	[mg/kg]	[% TRR]	[mg/kg]
Mandipropamid	82.4	1.15	89.3	2.41
NOA458422	1.0	0.015	0.4	0.010
CGA380778	1.1	0.016	0.6	0.016
Unknown <sup>a</sup> (Non-baseline)	0.9	0.012 <sup>c</sup>	0.6	0.016
Baseline	4.7 <sup>c</sup>	0.065 <sup>c</sup>	3.3	0.089
Remainder <sup>b</sup>	5.0	0.070	2.6	0.071
Unextracted	2.7	0.038	2.2	0.059
Gain / Losses on analysis	2.2	0.031	1.1	0.029
Total	100.0	1.39	100.1	2.70

<sup>a</sup> Area of radioactivity not aligned with standard reference markers on TLC.

<sup>b</sup> A complex mixture of minor diffuse unassigned radio components with varying polarity.

<sup>c</sup> Further investigated by enzyme hydrolysis.

Table 16 Summary of identification of polar residues following enzyme hydrolysis of 14 day PHI chlorophenyl-<sup>14</sup>C sample (Chen, L, Evans, J, 2005, NOA446510/0237)

Components	[% TRR]	[mg/kg]
NOA458422	0.4	0.005
SYN521195	0.1	0.001

Components	[% TRR]	[mg/kg]
CGA380778	0.2	0.003
CGA380775	0.2	0.003

These results demonstrate that unchanged parent mandipropamid comprises the majority of the residue in lettuce. The principal metabolism steps are cleavage of the methyl ether functionality and the removal of either or both of the propargyl side chains to generate the corresponding alcohol or phenol functionalities. The hydroxyl functionalities showed the potential to form sugar conjugates. No cleavage of the amide bond between the two aromatic rings was observed. A metabolic pathway for mandipropamid in lettuce is proposed in Figure 3.

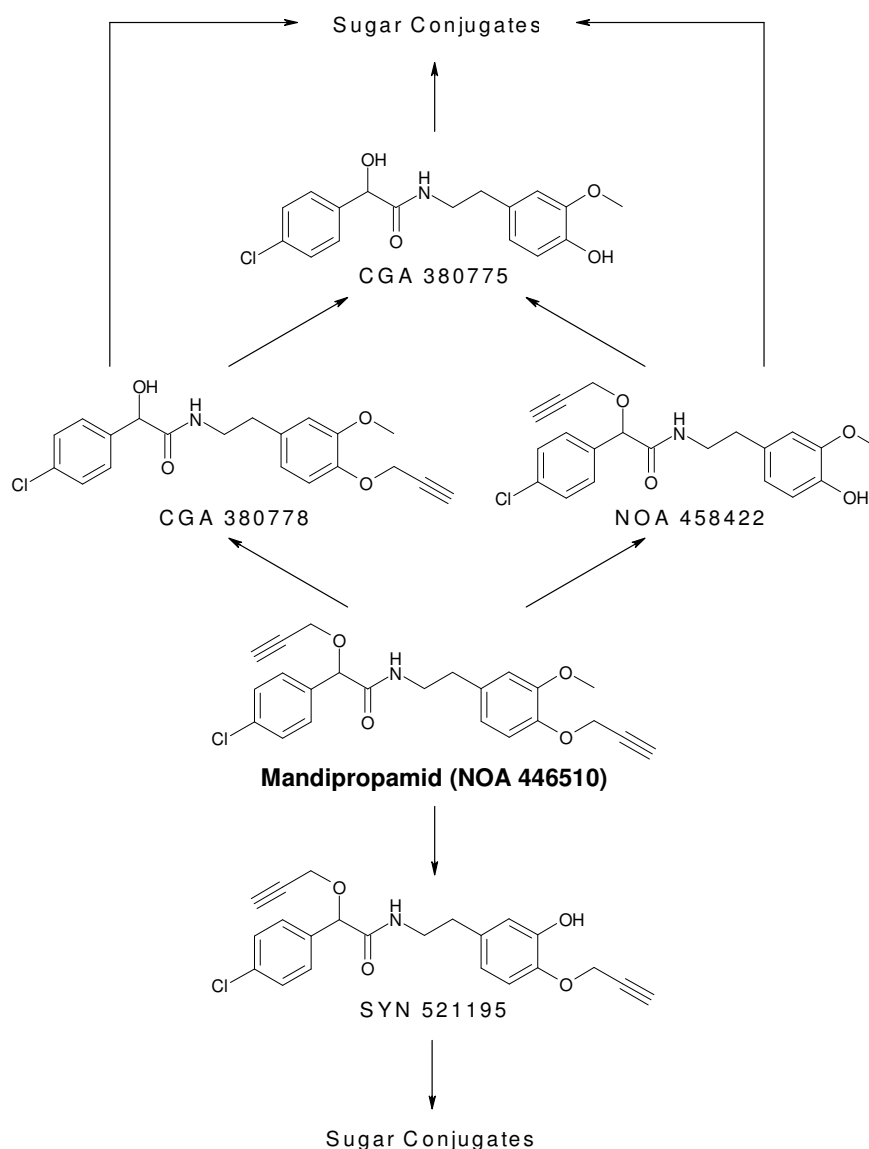


Figure 3 Proposed metabolic pathway of mandipropamid in lettuce (Chen, L, Evans, J, 2005, NOA446510/0237)

#### Potato

An outdoor confined mandipropamid metabolism study on potato (Variety: Appell) was conducted in Switzerland during 2002 (Sandmeier, P, 2003, NOA446510/0046; Hamlet, J, 2005,



NOA446510/0255). [Chlorophenyl-(U)-<sup>14</sup>C]-mandipropamid or [methoxyphenyl-(U)-<sup>14</sup>C]mandipropamid, formulated as suspension concentrates (formulation code A12946C containing 250 g/L mandipropamid) were applied as a foliar spray to potato plants. Six applications were made, separated by intervals of 10–12 days, at calculated application rates of 146–158 g ai/ha for the 1 × rate plots and 418–458 g ai/ha for the 3× rate plots. Potato tubers and leaves were harvested 7 and 21 days after the final application from the plots treated at the 1× rate and at 21 days after the final application from the plots treated at the 3× rate. Potato tubers and leaves were harvested 7 and 21 days after the final application from the plots treated at the 1× rate and at 21 days after the final application from the plots treated at the 3× rate. The tubers were separated into peel and flesh before being separately homogenised in the presence of liquid nitrogen. The leaves were homogenised in the presence of liquid nitrogen without further preparation.

Total radioactive residues (TRRs) were initially determined in all samples by direct combustion/LSC. Each sample was extracted into acetonitrile:water (80:20 v/v) and the extracts analysed by thin layer chromatography (TLC). TRRs in peel, flesh and leaves were also determined by the summation of the radioactivity present in the extracts and the remaining debris. The total radioactive residues (TRRs) found in the potato commodities are summarised in Table 17.

Table 17 Summary of total radioactive residues in potato samples (Sandmeier, P, 2003, NOA446510/0046; Hamlet, J, 2005, NOA446510/0255)

Radiolabel Position	PHI [Days]	Plant Part	TRR [mg/kg]		
			By Direct Combustion and LSC Quantification	By Summation of Extracted and Unextracted Radioactivity Analytical Phase 1	By Summation of Extracted and Unextracted Radioactivity Analytical Phase 2
Chlorophenyl	7 (1× rate)	Leaves	6.31	6.24	na
		Flesh	0.042	0.042	0.046
		Peel	0.043	0.044	0.044
	21 (1× rate)	Leaves	4.24	4.16	na
		Flesh	0.049	0.049	na
		Peel	0.058	0.059	na
	21 (3× rate)	Leaves	13.80	13.4	na
		Flesh	0.12	0.11	na
		Peel	0.14	0.14	na
Methoxyphenyl	7 (1× rate)	Leaves	5.05	4.81	na
		Flesh	0.056	0.055	0.055
		Peel	0.047	0.048	0.048
	21 (1× rate)	Leaves	2.74	2.71	na
		Flesh	0.045	0.043	na
		Peel	0.040	0.040	na
	21 (3× rate)	Leaves	10.8	10.73	na
		Flesh	0.13	0.12	na
		Peel	0.11	0.11	na

na : not analysed

Table 18 Extractability of residues from potato samples (Sandmeier, P, 2003, NOA446510/0046; Hamlet, J, 2005, NOA446510/0255)

Radiolabel Position	Commodity	PHI [days]	Extracted Radioactivity		Unextracted Radioactivity		TRR [mg/kg]
			[mg/kg]	[% TRR]	[mg/kg ]	[% TRR]	
Chlorophenyl	Leaves	7	5.16	82.6	1.08	17.4	6.24
	Leaves	21	3.15	75.7	1.01	24.3	4.16
	Peel	7	0.025	57.7	0.019	42.3	0.044
	Flesh	7	0.026	57.1	0.020	42.9	0.046
Methoxyphenyl	Leaves	7	3.54	73.6	1.27	26.4	4.81
	Leaves	21	1.74	64.1	0.97	35.9	2.71
	Peel	7	0.016	33.5	0.032	66.5	0.048
	Flesh	7	0.014	25.9	0.041	74.1	0.055

Results for leaves are taken from NOA446510/0046.

Results for peel and flesh are taken from NOA446510/0255.

Microwave extraction into acetonitrile:water and subsequently isopropanol/1M HCl was performed on the 7 day PHI peel and flesh debris samples following room temperature extraction. The isopropanol:1M HCl extracts were cleaned-up by solid phase extraction and the resulting solutions analysed by TLC.

Table 19 Summary of identification and characterisation of residues in chlorophenyl tuber debris after microwave extraction (Sandmeier, P, 2003, NOA446510/0046; Hamlet, J, 2005, NOA446510/0255)

Components	Peel		Flesh	
	[% TRR]	[mg/kg]	[% TRR]	[mg/kg]
Glucose	10.0	0.004	12.7	0.006
Unknown <sup>a</sup>	9.3	0.004	6.7	0.003
Baseline	0.0	0.000	0.1	< 0.001
Remainder <sup>b</sup>	3.6	0.001	7.9	0.004
Unextracted	5.6	0.002	1.3	0.001
Not analysed	11.7	0.005	9.1	0.004
Total	40.2	0.016	37.8	0.019

<sup>a</sup> One unknown that is proposed to be an intermediate breakdown product formed during the acid hydrolysis of starch.

<sup>b</sup> Corresponding to diffuse and streaked areas of radioactivity.

Table 20 Summary of identification and characterisation of residues in methoxyphenyl tuber debris after microwave extraction (Sandmeier, P, 2003, NOA446510/0046; Hamlet, J, 2005, NOA446510/0255)

Components	Peel		Flesh	
	[% TRR]	[mg/kg]	[% TRR]	[mg/kg]
Glucose	18.1	0.009	30.4	0.017
Unknown <sup>a</sup>	11.0	0.005	15.8	0.009
Baseline	0.6	< 0.001	0.4	< 0.001
Remainder <sup>b</sup>	10.3	0.005	10.2	0.005
Unextracted	9.7	0.005	3.9	0.002
Not analysed	10.7	0.006	9.6	0.005

Components	Peel		Flesh	
	[% TRR]	[mg/kg]	[% TRR]	[mg/kg]
Total	60.4	0.031	70.3	0.039

<sup>a</sup> One unknown that is proposed to be an intermediate breakdown product formed during the acid hydrolysis of starch.

<sup>b</sup> Corresponding to diffuse and streaked areas of radioactivity.

Identification of the radioactive components in extracts from the tuber samples was carried out by co-chromatography with reference standards. LC-MS/MS was used to confirm the identity of mandipropamid, SYN524199, SYN500003 and CGA155705. TRRs in potato peel and flesh following application at the 1×rate were 0.040–0.059 mg/kg and were consistent from both labels and at both PHIs. TRRs in potato leaves following application at the 1× rate were much higher, ranging from 4.8–6.3 mg/kg in samples with a 7 day PHI and 2.7–4.2 mg/kg in samples with a 21 day PHI. Residues in samples from the 3×rate treatments showed a broadly linear relationship with residues in samples from the 1×rate treatments. The TRR values determined from the summation of the radioactivity present in the extracts and the debris after initial extraction were in good agreement with those derived from direct quantification. TRR values determined by summation of the radioactivity present in the extracts and the debris after initial extraction are considered the most reliable, due to the large sample sizes taken for analysis, and will therefore be used to express residue levels from this point forwards.

The percentage of the TRRs that were extracted from leaf samples using acetonitrile:water (80:20 v/v) were reasonably high and were similar for both labels (64–83% TRR). The percentage of the TRRs that were extracted from peel and flesh samples using acetonitrile:water (80:20 v/v) were lower and differed significantly for the chlorophenyl-label samples (57–58% TRR) and the methoxyphenyl-label samples (26–34% TRR). No significant difference was found between the profiles of the leaf samples derived from the two radiolabelled experiments. Parent mandipropamid was identified as the largest component of the residue in the leaves accounting for 39.9–60.6% TRR. Three other metabolites all containing the chlorophenyl and methoxyphenyl rings (NOA458422, CGA380775 and CGA380778) were identified at much lower levels than parent ranging from 0.4–1.8% TRR (0.011–0.114 mg/kg).

Table 21 Summary of identification and characterisation of residues in potato leaf samples (Sandmeier, P, 2003, NOA446510/0046; Hamlet, J, 2005, NOA446510/0255)

Components	Chlorophenyl				Methoxyphenyl			
	7 day PHI		21 day PHI		7 day PHI		21 day PHI	
	[% TRR]	[mg/kg]	[% TRR]	[mg/kg]	[% TRR]	[mg/kg]	[% TRR]	[mg/kg]
Mandipropamid	60.6	3.78	40.1	1.67	51.2	2.47	39.9	1.08
NOA458422	1.8	0.11	1.5	0.063	0.8	0.040	1.0	0.027
CGA380778	1.2	0.076	1.2	0.050	1.1	0.051	1.4	0.039
CGA380775	0.4	0.026	0.4	0.019	0.4	0.018	0.4	0.011
Unknowns	12.2 <sup>a</sup>	0.75 <sup>a</sup>	21.0 <sup>b</sup>	0.88 <sup>b</sup>	13.1 <sup>c</sup>	0.64 <sup>c</sup>	14.1 <sup>d</sup>	0.39 <sup>d</sup>
Baseline	0.8	0.051	0.9	0.039	1.2	0.056	1.1	0.029
Unresolved	5.7	0.36	10.3	0.43	5.7	0.27	6.0	0.16
Unextracted	17.4	1.09	24.3	1.01	26.4	1.27	35.9	0.97
Total	100.0	6.24	100.0	4.16	100.0	4.81	100.0	2.71

<sup>a</sup> Comprised of at least 28 components none of which exceeded 0.9% TRR; 0.058 mg/kg.

<sup>b</sup> Comprised of at least 28 components none of which exceeded 2.3% TRR; 0.097 mg/kg.

<sup>c</sup> Comprised of at least 22 components none of which exceeded 1.7% TRR; 0.081 mg/kg.

<sup>d</sup> Comprised of at least 22 components none of which exceeded 1.5% TRR; 0.041 mg/kg.

A significant difference was found between the profiles of the peel and flesh samples derived from the two radiolabel experiments; however, within each experiment the peel and flesh profiles were similar. Parent mandipropamid was identified in the peel samples at a maximum level of 4.2% TRR, 0.002 mg/kg but was not detected in the flesh. Three small acidic molecules, containing only the chlorophenyl ring, were identified in both the peel and flesh samples. These were SYN500003, SYN524199, CGA155705 and were detected at maximum levels of 12.7% TRR, 7.2% TRR and 2.1% TRR respectively (maximum individual residue level of only 0.006 mg/kg). No metabolites containing only the methoxyphenyl ring were identified. Radioactivity remaining in the peel and flesh debris after initial extraction was further investigated using an acidic microwave extraction. A significant proportion of the radioactivity was solubilised and was shown to comprise mainly of glucose (10.0–30.4% TRR) and a second component (6.7–15.8% TRR) which was eluted at a higher R<sub>f</sub> than glucose and is proposed to be an intermediate breakdown product formed during the acid hydrolysis of starch.

Table 22 Summary of identification and characterisation of residues in chlorophenyl treated tuber samples (Sandmeier, P, 2003, NOA446510/0046; Hamlet, J, 2005, NOA446510/0255)

Components	Peel		Flesh	
	[% TRR]	[mg/kg]	[% TRR]	[mg/kg]
Mandipropamid	4.2	0.002	nd	nd
SYN524199	6.2	0.003	7.2	0.003
SYN500003	12.7	0.006	10.5	0.005
CGA155705	1.6	0.001	2.1	0.001
Unknowns	15.4 <sup>a</sup>	0.006 <sup>a</sup>	16.8 <sup>b</sup>	0.009 <sup>b</sup>
Baseline	5.4	0.002	6.4	0.003
Remainder <sup>c</sup>	8.1 <sup>d</sup>	0.004 <sup>d</sup>	10.5 <sup>e</sup>	0.005 <sup>e</sup>
Unextracted <sup>f</sup>	42.3	0.019	42.9	0.020
Gain/Losses on analysis	4.2	0.002	3.8	0.002
Total	100.1	0.045	100.2	0.048

<sup>a</sup> Comprised of at least 3 components none of which exceeded 9.9% TRR; 0.004 mg/kg

<sup>b</sup> Comprised of at least 3 components none of which exceeded 12.0% TRR; 0.006 mg/kg

<sup>c</sup> Corresponding to diffuse and streaked areas of radioactivity

<sup>d</sup> Maximum individual area not exceeding 2.5% TRR; 0.001 mg/kg

<sup>e</sup> Maximum individual area not exceeding 3.5% TRR; 0.002 mg/kg

<sup>f</sup> Results of further extraction are presented in Table 16

nd : not detected

Note: SYN505504, SYN521195 and CGA380775 were also detected by LC-MS/MS at trace levels

Table 23 Summary of identification and characterisation of residues in methoxyphenyl treated tuber samples (Sandmeier, P, 2003, NOA446510/0046; Hamlet, J, 2005, NOA446510/0255)

Components	Peel		Flesh	
	[% TRR]	[mg/kg]	[% TRR]	[mg/kg]
Mandipropamid	0.8	< 0.001	nd	nd
Unknowns	2.6 <sup>a</sup>	0.001 <sup>a</sup>	2.5 <sup>b</sup>	0.002 <sup>b</sup>
Baseline	14.0	0.007	12.4	0.007
Remainder <sup>c</sup>	8.5 <sup>d</sup>	0.004 <sup>d</sup>	6.1 <sup>e</sup>	0.003 <sup>e</sup>
Unextracted <sup>f</sup>	66.5	0.032	74.1	0.041
Gain/Losses on analysis	6.1	0.003	3.8	0.002

Components	Peel		Flesh	
	[% TRR]	[mg/kg]	[% TRR]	[mg/kg]
Total	97.4	0.047	98.9	0.055

<sup>a</sup> No unknown exceeding 2.6% TRR; 0.001 mg/kg

<sup>b</sup> No unknown exceeding 1.6% TRR; 0.001 mg/kg

<sup>c</sup> Corresponding to diffuse and streaked areas of radioactivity

<sup>d</sup> Maximum individual area not exceeding 7.0% TRR; 0.003 mg/kg

<sup>e</sup> Maximum individual area not exceeding 5.3% TRR; 0.003 mg/kg

<sup>f</sup> Results of further extraction are presented in Table 17

nd : not detected

These results demonstrate that unchanged parent mandipropamid comprises the majority of the residue in potato leaves but is only found at very low levels in potato tubers. The principal metabolism steps are the removal of either or both of the propargyl side chains to generate the corresponding alcohol or phenol functionalities. Cleavage of the amide bond between the two aromatic rings was also observed with small amounts of resulting metabolites from the chlorophenyl part of the molecule being transported downwards into the tubers from the leaves. In addition <sup>14</sup>C was detected in the starch contained within the tubers. This natural incorporation resulted from extensive metabolism of mandipropamid to generate small carbon fragments or carbon dioxide either in the plant or soil.

A metabolic pathway for mandipropamid in potatoes is proposed (Figure 4) and demonstrates that mandipropamid undergoes metabolism to produce more polar metabolites. The principal metabolism steps are the removal of either or both of the propargyl side chains to generate the corresponding alcohol or phenol functionalities. Cleavage of the amide bond between the two aromatic rings was also observed with small amounts of resulting metabolites from the chlorophenyl part of the molecule being transported downwards into the tubers. In addition <sup>14</sup>C was detected in the starch contained within the tubers. This natural incorporation resulted from extensive metabolism of mandipropamid to generate small carbon fragments or carbon dioxide either in the plant or soil.

## Mandipropamid

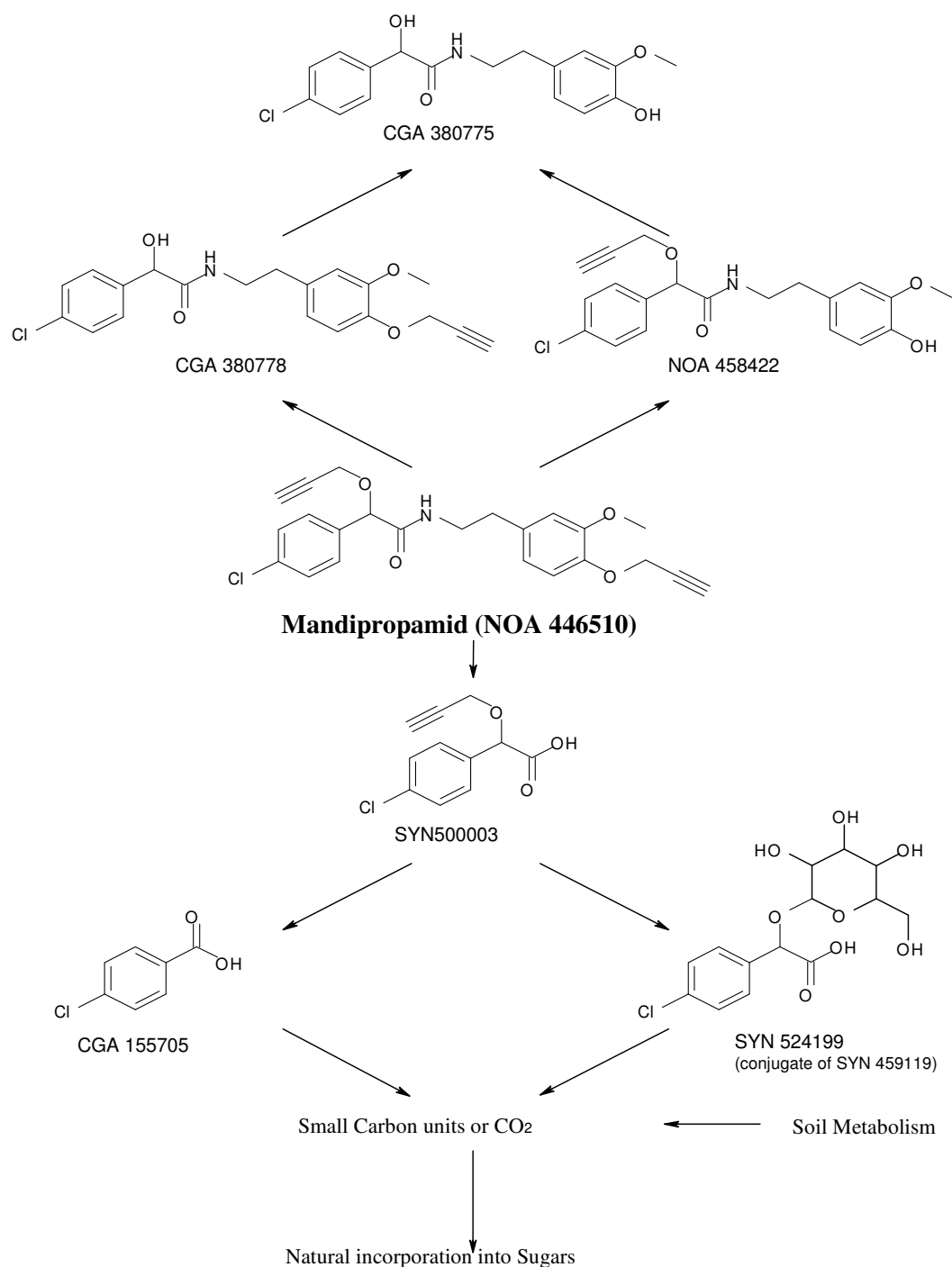


Figure 4 Proposed metabolic pathway of mandipropamid in potatoes (Sandmeier, P, 2003, NOA446510/0046; Hamlet, J, 2005, NOA446510/0255)

### Tomato

An outdoor confined mandipropamid metabolism study on tomato (Variety: Cristal F1) was conducted in Switzerland during 2001 (Vollmin, S., 2003, NOA446510/0049). [1-<sup>14</sup>C]mandipropamid was formulated as suspension concentrates. The tomato plants were treated to runoff at a rate of 276 g ai/ha and 295 g ai/ha in 2 week intervals, followed by two further treatments at a rate of 147 g ai/ha and 149 g ai/ha in weekly intervals. Total treatments resulted in an annual use rate of 867 g ai/ha. Tomato fruit and leaves/foilage were harvested at 5 intervals: 0, 3, 7, 14 and 28 DALA. At the fifth sampling all fruit were collected and separated into green and mature tomatoes.

In Study 1 tomato fruits were rinsed twice in acetonitrile:water (80:20 v/v) to remove the surface radioactivity, after which the rinsed fruits were homogenized with acetonitrile:water (80:20 v/v). Radioactivity washed from the surface was determined directly by liquid scintillation counting (LSC). The radioactivity remaining in the tomato fruits was determined by thin layer chromatography (TLC) and the extracted remainder was quantified by LSC. The total radioactive residues (TRRs) in tomato fruits were initially determined by the summation of the surface and extractable as well as the non-extractable residues. Leaves and foliage material was homogenized in the presence of liquid nitrogen. Total radioactive residues (TRRs) were initially determined in leaves and foliage material by direct combustion/LSC. Each sample was extracted into acetonitrile:water (80:20 v/v), and the extracts analysed by thin layer chromatography (TLC), and the extracted remainder was quantified by LSC. TRRs in tomato leaves were also determined by the summation of the surface and extractable as well as the non-extractable residues.

In Study 2 tomato leaves were rinsed in acetonitrile:water (80:20 v/v) to remove the surface radioactivity, after which the rinsed leaves were homogenized with acetonitrile:water (80:20 v/v). Radioactivity washed from the surface was determined directly by liquid scintillation counting (LSC). The radioactivity remaining in the tomato leaves was determined by thin layer chromatography (TLC) and the extracted remainder was quantified by LSC. The total radioactive residues (TRRs) in tomato leaves were initially determined by the summation of the surface and extractable as well as the non-extractable residues.

TRR in mature fruits amounted to 0.945 mg/kg just after the last application. Three days later TRR was 0.813 mg/kg. At 7, 14, and 28 DALA, TRR amounted to 0.608 mg/kg, 0.465 mg/kg, and 0.328 mg/kg, respectively. TRR consisted mainly of parent compound accounting for 0.760 mg/kg, 0.637 mg/kg, 0.455 mg/kg, 0.356 mg/kg, and 0.200 mg/kg at 0, 3, 7, 14 and 38 respectively. Green fruits, harvested 28 DALA were analysed separately. TRR was 0.033 mg/kg and parent compound amounted to 0.018 mg/kg. Surface radioactivity accounted for 87.0% of TRR at 0 DALA and decreased to 69.0% of TRR at 28 DALA. The penetrated radioactivity amounted to 13.0% of TRR (9.1% extractables and 3.9% non-extractables) at 0 DALA and increased to 31.0% of TRR (25.5% extractables and 5.5% non-extractables) at 28 DALA. In green fruits surface radioactivity accounted for 48.7% of TRR. Extractable radioactivity was 39.0% of TRR and non-extractables were 12.3% of TRR.

In leaves TRR accounted to 18.221 ppm just after the last application. Three days later TRR was 18.680 mg/kg. At 7, 14, and 28 DALA, TRR amounted to 22.976 mg/kg, 22.234 mg/kg, and 9.287 mg/kg, respectively. TRR consisted mainly of parent compound and accounted for 13.909 mg/kg, 13.881 mg/kg, 17.358 mg/kg, 17.427 mg/kg, and 6.080 mg/kg at 0, 3, 7, 14 and 28 DALA, respectively. The extractable radioactivity accounted for 84.6% of TRR at 0 DALA, and slightly decreased to 80.5% of TRR at 28 DALA. Non-extractable radioactivity accounted for 11.7% of TRR (0 DALA) and 18.4% of TRR (28 DALA).

Table 24 Distribution of radioactivity and residual [ $^{14}\text{C}$ ]mandipropamid (Vollmin, S, 2003, NOA446510/0049)

PHI (days)	Sample	TRR	Parent	Surface Radioactivity	Penetrated	Radioactivity
		[mg/kg] <sup>a</sup>	[mg/kg]	[% TRR]	Extractable [% TRR]	Non- extractable [% TRR]
0	fruits, ripe	0.95	0.76	87.0	9.1	3.9
	leaves	18.2	13.9	–	84.6	11.7
3	fruits, ripe	0.81	0.63	85.4	9.0	5.6
	leaves	18.7	13.9	–	85.6	13.6
7	fruits, ripe	0.61	0.45	80.4	14.7	4.9
	leaves	23.0	17.4	–	87.1	12.4

PHI (days)	Sample	TRR	Parent	Surface Radioactivity	Penetrated	Radioactivity
		[mg/kg] <sup>a</sup>	[mg/kg]	[% TRR]	Extractable [% TRR]	Non- extractable [% TRR]
14	fruits, ripe	0.47	0.35	80.2	15.7	4.1
	leaves	22.2	17.4	–	90.6	13.2
28	fruits, ripe	0.33	0.16	69.0	25.5	5.5
	fruits, green	0.034	0.017	48.7	39.0	12.3
	foliage	9.29	6.08	–	80.6	18.4

<sup>a</sup> in equivalents of mandipropamid.

From the results of this study it is concluded that mandipropamid showed a slow penetration/translocation of radioactivity into tomato plants. Most of the applied radioactivity remained on the surface of the fruits and leaves. The non-extractable in fruits and leaves were very low. In mature fruits, a maximum amount of 5.6% of TRR was found 3 days after the last treatment. In leaves the highest amount was 18.4% of TRR and was detected 28 days after the last treatment.

Mandipropamid is metabolized slowly to a number of metabolites, each of a small amount. Parent compound is the major residue in fruits and leaves. Five metabolites were identified by co-chromatography with reference standards or by LC-NMR and LC-MS as CGA 380775, CGA 380778, NOA 458422, SYN 508792 and SYN 508793. They were present in a range of 0.003 mg/kg and 0.013 mg/kg. The other metabolite fractions present in tomato fruits amounted to < 5% of TRR and ≤ 0.010 mg/kg, except the polar fractions I<sub>1</sub> and I<sub>2</sub> which amounted to 0.026 mg/kg and 0.015 mg/kg, respectively. Further analysis of these polar fractions showed that they consist of several compounds, each < 0.010 mg/kg. Based on the isomer ratios of residual NOA 446510 as well as of metabolite NOA 458422 and its conjugates SYN 508792 and SYN 508793, no indication for a stereo-selective metabolism was found. A metabolic pathway of mandipropamid in tomato plants was proposed (Figure 5).

Table 25 Quantification of metabolite fractions in mature tomato fruits (Vollmin, S, 2003, NOA446510/0049)

Components	Mature Fruits										Green Fruit	
	0 day PHI		3 day PHI		7 day PHI		14 day PHI		28 day PHI			
	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg
Mandipropamid	80.4	0.76	78.3	0.64	74.9	0.46	76.5	0.36	61.1	0.20	53.0	0.018
SYN 508793	0.4	0.004	0.8	0.006	1.0	0.006	1.6	0.007	3.8	0.013	2.8	0.001
SYN 508792	0.3	0.003	0.7	0.006	0.8	0.005	1.8	0.009	3.4	0.011	1.2	< 0.001
CGA 380775	0.6	0.005	0.6	0.005	1.0	0.006	0.6	0.003	0.9	0.003	0.3	< 0.001
CGA 380778	1.3	0.013	1.3	0.011	1.6	0.010	1.4	0.006	1.1	0.004	0.5	< 0.001
NOA 458422	1.2	0.012	1.2	0.010	2.1	0.013	1.5	0.007	1.5	0.005	1.4	< 0.001
I <sub>1</sub>	2.8	0.026	2.3	0.019	3.4	0.021	2.8	0.013	4.5	0.015	14.3	0.005
I <sub>2</sub>	1.6	0.015	1.4	0.012	2.3	0.014	1.8	0.008	3.8	0.013	4.1	0.001
Unidentified	7.5	0.070	7.8	0.061	8.0	0.048	7.9	0.037	14.4	0.046	10.1	0.005
Sub. Total	96.1	0.91	94.4	0.77	95.1	0.58	95.9	0.45	94.5	0.31	87.7	0.030
Non-extractable	3.9	0.037	5.6	0.046	4.9	0.030	4.1	0.019	5.5	0.018	12.3	0.004
Total <sup>a</sup>	100.0	0.95	100.0	0.81	100.0	0.61	100.0	0.47	100.0	0.33	100.0	0.034

<sup>a</sup> All other fractions of unidentified metabolites which were not included in this table were < 2.7%.



Table 26 Quantification of metabolite fractions in tomato leaves (Vollmin, S, 2003, NOA446510/0049)

Components	Leaves									
	0 day PHI		3 day PHI		7 day PHI		14 day PHI		28 day PHI	
	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg
Mandipropamid	76.3	13.9	74.3	13.9	75.6	17.4	78.4	17.4	65.5	6.08
SYN 508793	0.4	0.082	0.8	0.15	0.9	0.22	0.8	0.18	1.6	0.15
SYN 508792	0.2	0.031	0.3	0.048	0.2	0.040	0.2	0.036	0.4	0.035
CGA 380775	0.3	0.063	0.6	0.11	0.6	0.14	0.6	0.14	0.9	0.082
CGA 380778	0.6	0.102	0.8	0.15	0.8	0.18	1.0	0.21	0.9	0.086
NOA 458422	1.3	0.23	1.1	0.20	1.6	0.38	1.5	0.34	2.0	0.18
I <sub>1</sub>	0.3	0.046	0.4	0.083	0.3	0.062	0.4	0.095	0.3	0.029
I <sub>2</sub>	0.7	0.12	0.9	0.17	0.9	0.20	0.9	0.21	1.3	0.12
Unidentified	4.5	0.81	6.4	1.16	6.2	1.32	6.8	1.44	7.6	0.67
Sub. Total	84.6	15.4	85.6	15.9	87.1	19.9	90.6	20.1	80.5	7.43
Non- extractable	11.7	2.13	13.6	2.54	12.4	2.85	13.2	2.94	18.4	1.71
Total <sup>a</sup>	96.3	18.2	99.2	18.7	99.5	23.0	103.8	22.2	99.0	9.29

<sup>a</sup> All other fractions of unidentified metabolites which were not included in this table were < 2.7%.

## Mandipropamid

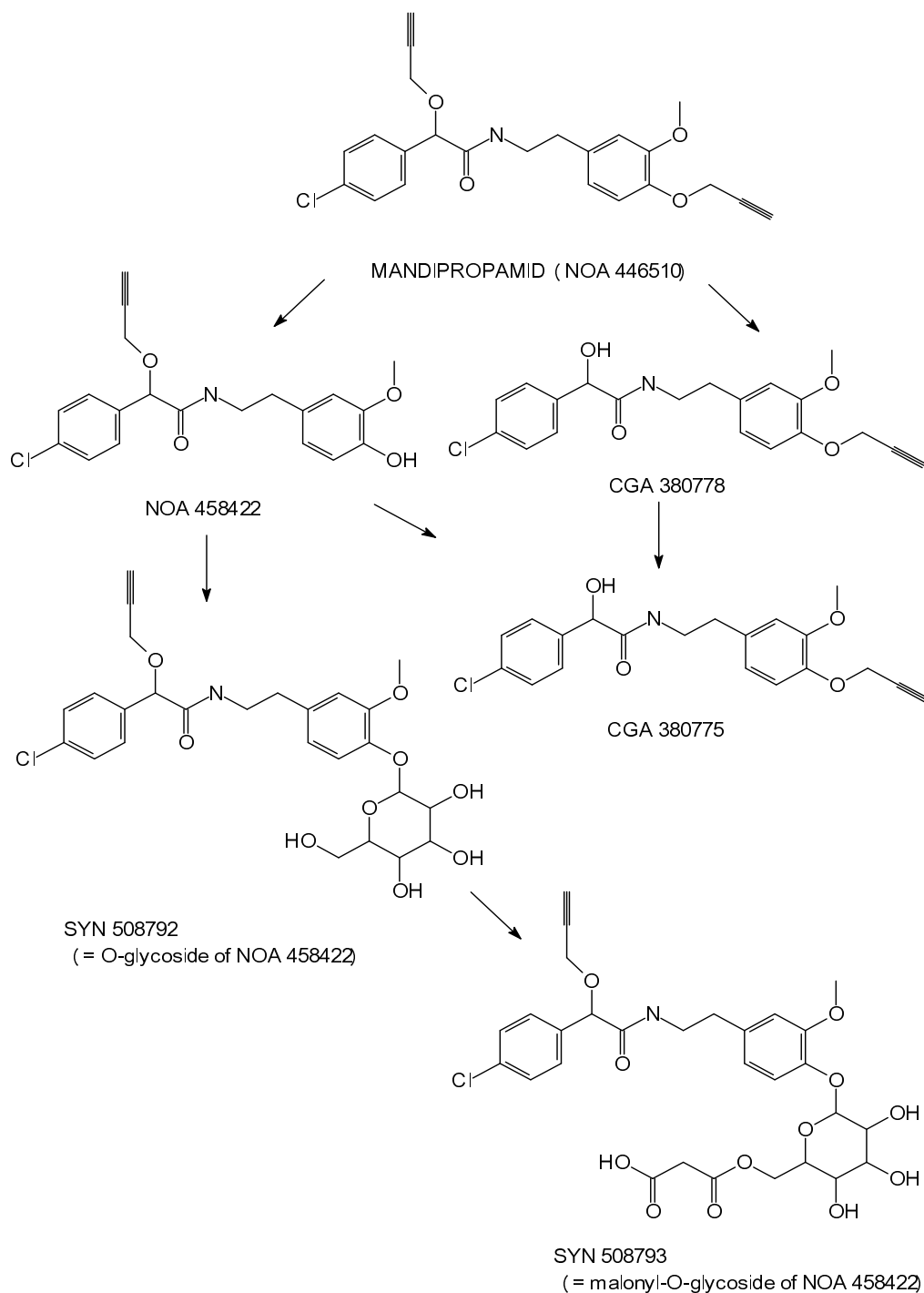


Figure 5 Proposed metabolic pathway of mandipropamid in tomatoes (Vollmin, S, 2003, NOA446510/0049)

### Environmental fate in soil

The Meeting received information on the environmental fate of mandipropamid in soil, including studies on aerobic soil metabolism, field dissipation and crop rotational studies. Because mandipropamid is used on onion and potato (edible portion in soil), studies on aerobic soil metabolism should be needed and studies on field dissipation are helpful.

*Soil metabolism*

A study on the aerobic soil metabolism of [<sup>14</sup>C]chlorophenyl-mandipropamid in a sandy loam soil showed that dealkylation of mandipropamid at the 2-nyloxy position led to formation of CGA-380778. Many other degradates including CGA-380775, SYN-500003 and NOA-458422 were found as minor parts of the residue (Clark, A, 2004, NOA446510/0152). Carbon dioxide was the terminal product, accumulating to 56.3% of the dose by day 371. After 371 days the majority of the radiocarbon was either in the fulvic acid and humin fractions or was trapped as carbon dioxide.

*Aerobic soil metabolism*

Ref: Clark, A., 2004,  
NOA446510/0152

Test material: [ <sup>14</sup> C]mandipropamid, chlorophenyl-labelled	Dose rate: 0.23 mg/kg dry soil	
Sandy loam	pH: 6.6	Organic matter: 0.9%
Duration: 371 days	Temp: 25 °C	Field moisture capacity at 1/3 bar: 15.1%
Half-life of mandipropamid: 32 days		
% mandipropamid remaining, day 364 = 2.96%	% mineralization, day 371 = 56.3 %	
Metabolites	Max (% of dose)	Day
CGA 380778	4.25 %	30
Others	2.47 %	30
<sup>14</sup> CO <sub>2</sub>	56.3%	371
Non-extractable <sup>14</sup> C	16.6 %	59

A study on the aerobic soil metabolism of [<sup>14</sup>C]methoxyphenyl-mandipropamid in silt loam soil at different temperatures and soil moisture for 119 days showed that the degradation rate of mandipropamid was decreased markedly when the application rate was increased or the temperature or soil moisture content were reduced (Hand, LH, Howdle, M, 2004, NOA446510/0117). Two degradation products were observed, namely CGA 380778 and SYN 536638. NOA 458422 was also shown to present at levels below LOQ. No single product was observed at > 5 % of the applied radioactivity. Significant levels of radiolabelled carbon dioxide were produced during the incubation, indicating full mineralization of mandipropamid. Accumulated levels reached a maximum of 21.8 % of the applied dose experiment 1 (0.21mg/kg, 33.9 g/100 g soil, and 20 °C). The levels were reduced under the other conditions and ranged from 10.7 % to 19.7 % of the applied radioactivity. Unextractable residues increased throughout the incubation period with maximum levels ranging from 22.6 % to 30.9 % of the applied radioactivity.

*Aerobic soil metabolism*

Ref: Hand, LH, Howdle, M, 2004,  
NOA446510/0117

Test material: [ <sup>14</sup> C]mandipropamid, methoxyphenyl-labelled	Dose rate: 0.21 mg/kg dry soil	
Silt loam	pH: 7.3	Organic carbon: 4.0 %
Duration: 119 days	Temp: 20 °C	Soil Moisture Content: 33.9 g/100 g soil
Half-life of boscaild: 79 days		
% mandipropamid remaining, day 119 = 35.8 %	% mineralization, day 119 = 21.8 %	
Metabolites	Max (% of dose)	Day
CGA 380778	1.4 %	28 or 119
Others	2.4 %	91
<sup>14</sup> CO <sub>2</sub>	21.8 %	119
Non-extractable <sup>14</sup> C	30.9 %	119

**Mandipropamid**

Duration: 119 days                      Temp: 20 °C                      Dose rate: 1.04 mg/kg dry soil  
 Soil Moisture Content: 33.9 g/100 g soil

Half-life of mandipropamid: 103 days  
 % mandipropamid remaining, day 119 = 42.0 %                      % mineralization, day 119 = 19.7 %

Metabolites	Max (% of dose)	Day
CGA 380778	1.7 %	7
Others	3.1 %	119
<sup>14</sup> CO <sub>2</sub>	19.7 %	119
Non-extractable <sup>14</sup> C	27.1 %	119

Duration: 119 days                      Temp: 20 °C                      Dose rate: 0.21 mg/kg dry soil  
 Soil Moisture Content: 13.6 g/100 g soil

Half-life of mandipropamid: 150 days  
 % mandipropamid remaining, day 119 = 53.7 %                      % mineralization, day 119 = 10.7 %

Metabolites	Max (% of dose)	Day
CGA 380778	1.7 %	119
Others	0.8 %	56
<sup>14</sup> CO <sub>2</sub>	10.7 %	119
Non-extractable <sup>14</sup> C	22.6 %	119

Duration: 119 days                      Temp: 10 °C                      Dose rate: 0.22 mg/kg dry soil  
 Soil Moisture Content: 33.9 g/100 g soil

Half-life of mandipropamid: 159 days  
 % mandipropamid remaining, day 119 = 55.1 %                      % mineralization, day 119 = 13.7 %

Metabolites	Max (% of dose)	Day
CGA 380778	1.6 %	21
Others	0.9 %	91 or 119
<sup>14</sup> CO <sub>2</sub>	13.7 %	119
Non-extractable <sup>14</sup> C	24.5 %	119

The degradation of <sup>14</sup>C-chlorophenyl-mandipropamid has been investigated in three different soils: 18 Acres (sandy clay loam), Borstel (loamy sand) and Marsillargues (loam) incubated under aerobic conditions at 20 °C for up to 120 days (Kuet, SF, Dick, J, and Stapleton, CM, 2004, NOA446510/0119). Mandipropamid degraded relatively rapidly in 18 Acres but slower in the Borstel and Marsillargues soils under the conditions of the experiment. The major soil degradate of mandipropamid was found to be NOA 380778 reaching a steady state and remaining low in all soils. In addition, a number of discrete unknown metabolites were also observed, individually not exceeding 2.9% of applied activity according to the principal quantitative analytical techniques used. A number of very minor degradates (CGA 380775, NOA 458422 and SYN 505503) were qualitatively detected and identified by LC-MS-MS (MRM). Carbon dioxide was a major end point of metabolism in all soils reaching a maximum 21.1, 12.3 and 21.8 % of the applied doses by the end of the incubation, for 18 Acres, Borstel and Marsillargues soils respectively. Unextracted residues increased slowly throughout the incubation, reaching a maximum of 39.2 %, 31.0 % and 22.9 % of applied radioactivity by the end of the incubation, for 18 Acres, Borstel and Marsillargues soils respectively.

*Aerobic soil metabolism*

Ref: Kuet, SF, Dick, J, and Stapleton, CM, 2004, NOA446510/0119

Test material: [<sup>14</sup>C]mandipropamid, chlorophenyl-labelled

Dose rate: 0.21 mg/kg dry soil

Sandy Clay Loam (18 Acres)

pH: 6.2

Organic carbon: 6.0 %

Duration: 120 days

Temp: 20 °C

Soil Moisture Content: 38.7 %

Half-life of boscalid: 44 days

% mandipropamid remaining, day 120 = 16.3 %

% mineralization, day 120 = 21.1 %

Metabolites

	Max (% of dose)	Day
CGA 380778	4.0 %	21
Others	12.7 %	91
<sup>14</sup> CO <sub>2</sub>	21.1 %	120
Non-extractable <sup>14</sup> C	39.2 %	120

Loamy Sand (Borstel)

pH: 6.5

Dose rate: 0.21 mg/kg dry soil

Duration: 120 days

Temp: 20°C

Soil Moisture Content : 12.6 %

Half-life of mandipropamid: 81 days

% mandipropamid remaining, day 120 = 34.6 %

% mineralization, day 120 = 12.3 %

Metabolites

	Max (% of dose)	Day
CGA 380778	4.8 %	120
Others	10.9 %	120
<sup>14</sup> CO <sub>2</sub>	12.3 %	120
Non-extractable <sup>14</sup> C	31.0 %	120

Loam (Marsillargues)

pH: 8.5

Dose rate: 0.21 mg/kg dry soil

Duration: 120 days

Temp: 20 °C

Soil Moisture Content: 19.6 %

Half-life of mandipropamid: 86 days

% mandipropamid remaining, day 120 = 37.6 %

% mineralization, day 120 = 21.8 %

Metabolites

	Max (% of dose)	Day
CGA 380778	6.0 %	120
Others	8.1 %	61
<sup>14</sup> CO <sub>2</sub>	21.8 %	120
Non-extractable <sup>14</sup> C	22.9 %	120

The degradation of [<sup>14</sup>C]methoxyphenyl-mandipropamid has been investigated in one soil (silt loam) incubated under aerobic, aerobic/anaerobic and sterile aerobic conditions at about 20 °C for up to 120 days (Nicollier, G, 2003, NOA446510/0065). The soils were treated with mandipropamid at a concentration of 0.40 mg/kg dry weight of soil (equivalent to a field application rate of 0.3 kg ai/ha, two times the highest proposed field use rate). For the aerobic/anaerobic experiment the conversion to anaerobic conditions was established by water-logging the soil after 30 days of aerobic incubation. Mandipropamid was rapidly degraded in biologically active soil. Under aerobic conditions the half-life of the parent molecule was 19 days. As is common, most prominent end-products of the aerobic metabolism found were carbon dioxide and bound residues. In addition, numerous (up to 13) minor degradates were observed. The most prominent degradate was CGA 380778 amounting at its highest to 2.9%. Under anaerobic conditions mandipropamid was slowly degraded with a half life of 158 days. Up to 15 minor metabolites were found with CGA 380778 as the most prominent degradate. It amounted at its highest to 4.6%. Practically no degradation was observed under aerobic-sterile conditions.

*Aerobic soil metabolism*Ref: Nicollier, G, 2003,  
NOA446510/0065Test material: [<sup>14</sup>C]mandipropamid, methoxyphenyl –  
labelled

Dose rate: 0.40 mg/kg dry soil

Silt Loam

pH: 7.2

Organic carbon: 2.14 %

Duration: 120 days

Temp: 20 °C

Soil Moisture Content: 42.5 %

Half-life of mandipropamid: 19 days

% mandipropamid remaining, day 120 = 4.1 %

% mineralization, day 120 = 37.1 %

Metabolites

	Max (% of dose)	Day
CGA 380778	2.9 %	14
Others	2.4 %	30
<sup>14</sup> CO <sub>2</sub>	37.1 %	120
Non-extractable <sup>14</sup> C	46.3 %	90

*Aerobic/Anaerobic soil metabolism*

Half-life of mandipropamid: 158 days

% mandipropamid remaining, day 120 = 21.5 %

% mineralization, day 120 = 13.3 %

Metabolites

	Max (% of dose)	Day
CGA 380778	4.6 %	120
Others	9.8 %	120
<sup>14</sup> CO <sub>2</sub>	16.5 %	62
Non-extractable <sup>14</sup> C	37.1 %	120

*Aerobic-sterile soil metabolism*

Half-life of mandipropamid: stable

% mandipropamid remaining, day 120 = 92.7 %

% mineralization, day 120 = 0.02 %

Metabolites

	Max (% of dose)	Day
Others	0.7 %	7 or 120
<sup>14</sup> CO <sub>2</sub>	0.03 %	30
Non-extractable <sup>14</sup> C	2.57 %	120

The degradation of ethyl-1-<sup>14</sup>C-labelled-mandipropamid has been investigated in two soils (silt loam) incubated under aerobic, aerobic/anaerobic and sterile aerobic conditions at about 20°C for up to 120 days (Nicollier, G, 2003, NOA446510/0050). The soils were treated with mandipropamid at a concentration of 0.40 mg/kg dry weight of soil (equivalent to a field application rate of 0.3 kg ai/ha, two times the highest proposed field use rate). For the aerobic/anaerobic experiment the conversion to anaerobic conditions was established by water-logging the soil after 30 days of aerobic incubation. Mandipropamid was rapidly degraded in biologically active soil. Under aerobic conditions the half-life of the parent molecule was 26 days. The most prominent degradate was CGA 380778 amounting at its highest to 3.2%. In addition numerous (up to 10) minor degradates, mostly below LOQ, were observed. As end-products of the aerobic metabolism carbon dioxide from the mineralization of the phenyl-ring moiety and bound residues were found. Under anaerobic conditions mandipropamid was slowly degraded with a half life of 179 days. Up to 10 minor metabolites were found with CGA 380778 as the most prominent degradate. It amounted at its highest to 4.4%.

*Aerobic soil metabolism*Ref: Nicollier, G, 2003,  
NOA446510/0050Test material: [<sup>14</sup>C]mandipropamid, chlorophenyl –  
labelled

Dose rate: 0.40 mg/kg dry soil

Silt Loam

pH: 7.3

Organic carbon: 1.7 %

Duration: 120 days

Temp: 20 °C

Soil Moisture Content: 30.1 %

Half-life of mandipropamid: 26 days

% mandipropamid remaining, day 120 = 7.2 %

% mineralization, day 120 = 35.9 %

Metabolites	Max (% of dose)	Day
CGA 380778	3.2 %	14
Others	1.1 %	120
<sup>14</sup> CO <sub>2</sub>	35.9 %	120
Non-extractable <sup>14</sup> C	40.1 %	120

*Aerobic/Anaerobic soil metabolism*

Half-life of mandipropamid: 158 days

% mandipropamid remaining, day 120 = 28.4 %      % mineralization, day 120 = 17.4 %

Metabolites	Max (% of dose)	Day
CGA 380778	3.8 %	4
Others	1.8 %	120
<sup>14</sup> CO <sub>2</sub>	17.4 %	120
Non-extractable <sup>14</sup> C	34.6 %	120

The degradation of [<sup>14</sup>C]chlorophenyl-mandipropamid has been investigated in Gartenacker (silt loam) and Borstel (loamy sand) incubated under aerobic condition at about 20 °C for up to 120 days (Nicollier, G, Glänzel, A, 2002, NOA446510/0017). The soils were treated with mandipropamid at field rates of 0.2, 0.40, 0.60, 0.90, 1.2 and 1.5 mg/kg dry weight of soil. Under aerobic conditions the half-life of the parent molecule in Gartenacker soil were 13, 24, 25, 28, 34, and 37 days for the dose rates of 0.20, 0.40, 0.60, 0.90, 1.2 and 1.5 mg ai/kg, respectively. Based on chromatographic analysis besides mandipropamid, no major metabolite was found in the soil extracts. Few minor metabolites were formed in the course of the study with amounts ≤ 6.0% for all rates. The maximum amount of CGA 380778 was 3.7% and NOA 458422 1.7% at day 14 (0.20 mg ai/kg). Volatiles in the form of carbon dioxide steadily increased and reached a maximum of 44.2%, 38.9%, 38.1%, 38.1%, 37.7% and 30.3% at day 120, respectively. Organic volatiles were below limit of detection. The half-life of the parent molecule in Borstel soil were 39, 61, 80, 93, 107, and 131 days for the dose rates of 0.20, 0.40, 0.60, 0.90, 1.2 and 1.5 mg ai/kg, respectively. Based on chromatographic analysis besides mandipropamid, no major metabolite was found in the soil extracts. Few minor metabolites were formed in the course of the study with amounts ≤ 4.1% for all rates. The maximum amount of CGA 380778 was 4.1% at day 56 (0.40 mg ai/kg) and of NOA 458422 1.0% at day 120 (0.60 mg ai/kg). Volatiles in the form of carbon dioxide steadily increased and reached a maximum of 15.5%, 10.1%, 9.0%, 9.6%, 9.2% and 9.1% at day 120, respectively. Organic volatiles were below limit of detection. The degradation of mandipropamid was enantio-selective in both soils. The R-isomer was faster degraded than the S-isomer. The rate of degradation depended on the dose rate and slower for higher application rates of mandipropamid with a half-life of up to 131 days. Endpoint of the metabolic pathway under aerobic conditions was the mineralization to carbon dioxide accounting for up to 44.2% and the formation of bound residues.

*Aerobic soil metabolism*Ref: Nicollier, G, Glänzel, A, 2002,  
NOA446510/0017Test material: [<sup>14</sup>C]mandipropamid, ethyl-1-labelled

Dose rate: 0.20 mg/kg dry soil

Silt Loam

pH: 7.3

Organic carbon: 2.0 %

Duration: 120 days

Temp: 20 °C

Soil Moisture Content: 64.4 %

Half-life of mandipropamid: 13 days

% mandipropamid remaining, day 120 = 4.8 %

% mineralization, day 120 = 44.2 %

Metabolites	Max (% of dose)	Day
CGA 380778	3.7 %	14
NOA 458422	1.7 %	14
Others	4.7 %	14
<sup>14</sup> CO <sub>2</sub>	44.2 %	120
Non-extractable <sup>14</sup> C	43.6 %	120







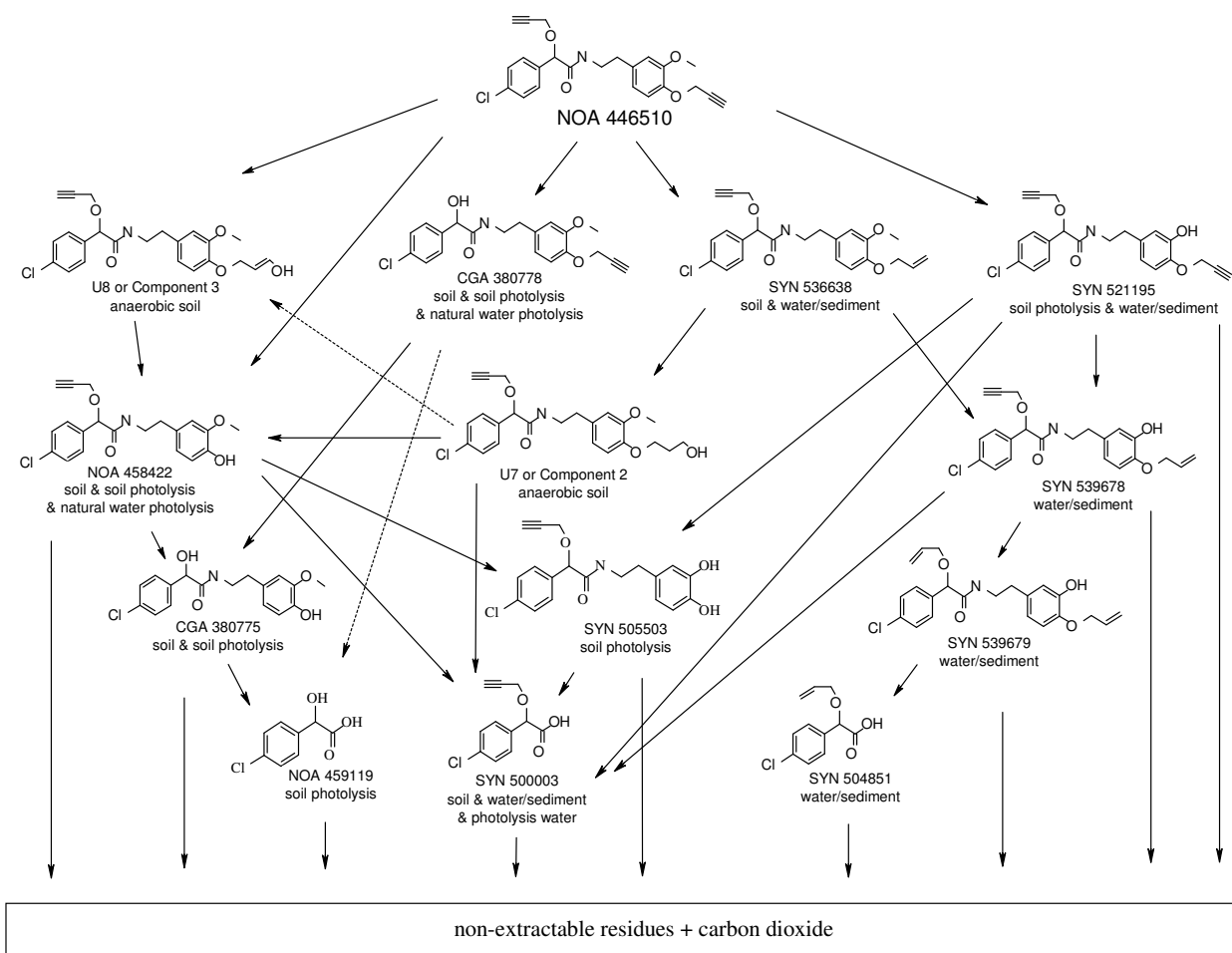


Figure 6 Proposed metabolic pathway for mandipropamid in soil and aquatic systems

### Field dissipation

Two trials were conducted at one site in Switzerland during 2002 and 2003 involving applications of mandipropamid as the SC formulation, A-12946 to the surface soil (Evans, P, 2003, NOA446510/0055; Evans, P, 2003, NOA446510/0054). A single application of mandipropamid was applied at the actual rates of 0.31 and 0.79 kg ai/ha, respectively. Soil samples were taken at 10 times up to 185 days after the last application and down to 30 cm. The highest amounts of mandipropamid were found in the top layer (0–10cm) of soil. Minor amounts were found in the 10 to 30 cm layers (Table 27). The residues detected at each depth have therefore been re-expressed as total residues in 0–10 cm to allow comparison of data from all the trials.

Table 27 Field dissipation of mandipropamid on bare soils at 1 site in Switzerland in 2002 (Evans, P, 2003, NOA446510/0055; Evans, P, 2003, NOA446510/0054)

Trial	Applic rate, kg/ha	Initial conc, mg/kg dry soil	Mandipropamid as % of original concentration in 0–10 cm soil.					
			2 days	7 days	21 days	56 days	128 days	185 days
Vouvry 2002 treat in June	Plot area 144 sq m. Sandy loam. Soil nature: pH 7.5, 1.4% organic matter.							
	0.79	0.54	113%	87%	37%	9.6%	1.3%	3.0%
			2 days	7 days	21 days	56 days	128 days	185 days
Vouvry 2002 treat in June	Plot area 144 sq m. Sandy loam. Soil nature: pH 7.5, 1.4% organic matter.							
	0.31	0.22	82%	95%	18%	4.1%	0.9%	0.9%

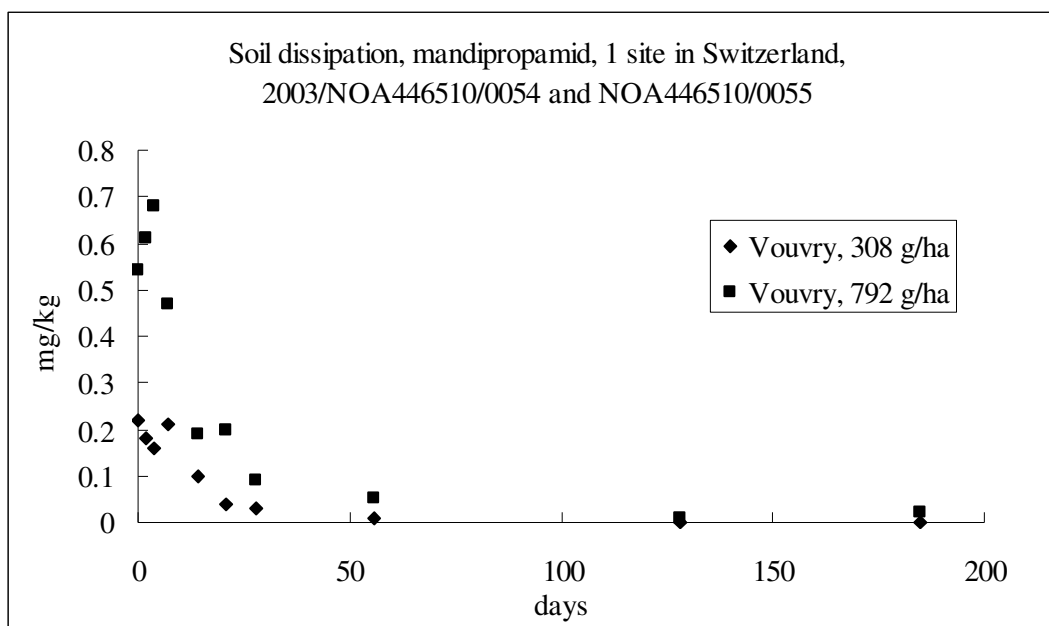


Figure 7 Field dissipation of mandipropamid on bare soils in 1 site in Switzerland in 2002 (Evans, P, 2003, NOA446510/0055; Evans, P, 2003, NOA446510/0054)

Two trials were conducted at one site in Spain in 2003 and 2004 involving applications of mandipropamid as the 50 SC formulation, A-12946 to the surface soil (Evans, P, 2005, NOA446510/0372; Evans, P, 2005, NOA446510/0373). A single application of mandipropamid was applied at the actual rates of 0.20 kg ai/ha. Soil samples were taken at 11 times up to 337 days after the last application and down to 30 cm. The highest amounts of mandipropamid were found in the top layer (0–10cm) of soil. Minor amounts were found in the 10 to 30 cm layers (Table 28). No measurable residues were present in samples below the 0–10 cm soil horizon after 28 days after application. The residues detected at each depth have therefore been re-expressed as total residues in 0–10 cm to allow comparison of data from all the trials.

Table 28 Field dissipation of mandipropamid on bare soils at 1 site in Spain in 2003 and 2004 (Evans, P, 2005, NOA446510/0372; Evans, P, 2005, NOA446510/0373)

Trial	Applic rate, kg/ha	Initial conc, mg/kg wet soil	mandipropamid as % of original concentration in 0–10 cm soil.					
			2 days	7 days	21 days	52 days	128 days	190 days
Seville 2003 treat in June	Plot area 144 sq m. Sandy loam. Soil nature: pH 7.9, 1.5% organic matter.							
	0.20	0.11	109%	73%	64%	27%	7.3%	4.5%
			2 days	7 days	21 days	56 days	126 days	192 days
Seville 2004 treat in May	Plot area 144 sq m. Loamy sand. Soil nature: pH 7.7, 0.5% organic carbon.							
	0.20	0.05	140%	100%	60%	20%	6.0%	4.0%

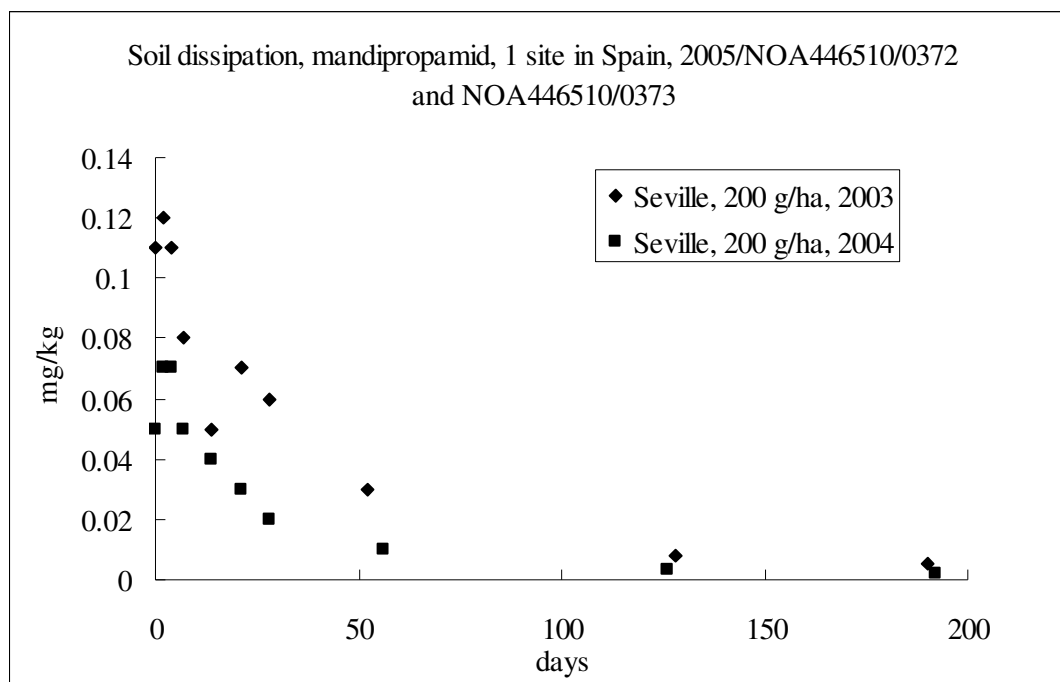


Figure 8 Field dissipation of mandipropamid on bare soils at 1 site in Spain in 2003 and 2004 (Evans, P, 2005, NOA446510/0372; Evans, P, 2005, NOA446510/0373)

Four trials were conducted in France in 2003 and 2004 involving applications of mandipropamid as the 50 SC formulation, A-12946 to the surface soil (Evans, P, 2005, NOA446510/0391; Evans, P, 2005, NOA446510/0392; Evans, P, 2005, NOA446510/0393; Evans, P, 2005, NOA446510/0394). A single application of mandipropamid was applied at the actual rates of 0.20 kg ai/ha. Soil samples were taken at 11 times up to 359 days after the last application and down to 30 cm. The highest amounts of mandipropamid were found in the top layer (0–10cm) of soil. Minor amounts were found in the 10 to 30 cm layers (Table 29). No measurable residues were present in samples below the 0–10 cm soil horizon after 133 days after application. The residues detected at each depth have therefore been re-expressed as total residues in 0–10 cm to allow comparison of data from all the trials.

Table 29 Field dissipation of mandipropamid on bare soils in 4 sites in France in 2003 and 2004 (Evans, P, 2005, NOA446510/0391; Evans, P, 2005, NOA446510/0392; Evans, P, 2005, NOA446510/0393; Evans, P, 2005, NOA446510/0394)

Trial	Applic rate, kg/ha	Initial conc, mg/kg wet soil	Mandipropamid as % of original concentration in 0–10 cm soil.					
			2 days	8 days	21 days	57 days	129 days	203 days
Malpart, 2003 treat in July	Plot area 144 sq m. Silt loam. Soil nature: pH 7.8, 1.6%Organic C, 7% Sand.							
	0.20	0.10 $\underline{1}$ /	130%	110%	50%	30%	20%	8%
			2 days	7 days	21 days	58 days	129 days	199 days
Grisolles 2003 treat in June	Plot area 144 sq m. Sandy loam. Soil nature: pH 7.8, 0.4%Organic C, 69% Sand.							
	0.20	0.11 $\underline{1}$ /	73%	73%	27%	4.6%	2.7%	2.7%
			2 days	7 days	21 days	56 days	133 days	157 days
Grisolles 2004 treat in July	Plot area 156 sq m. Loam. Soil nature: pH 7.8, 0.7% Organic C, 46% Sand.							
	0.20	0.13 $\underline{1}$ /	85%	85%	54%	23%	3.1%	3.1%

Trial	Applic rate, kg/ha	Initial conc, mg/kg wet soil	Mandipropamid as % of original concentration in 0–10 cm soil.					
			2 days	8 days	21 days	57 days	129 days	203 days
Septoutre 2004 treat in July			2 days	7 days	22 days	56 days	128 days	157 days
	Plot area 144 sq m. Silt loam. Soil nature: pH 7.8, 1.4% Organic carbon, 16% Sand.							
	0.20	0.21 $\mu$	52%	48%	43%	19%	3.8%	3.3%

*Residue of the 0–10 cm soil horizon*

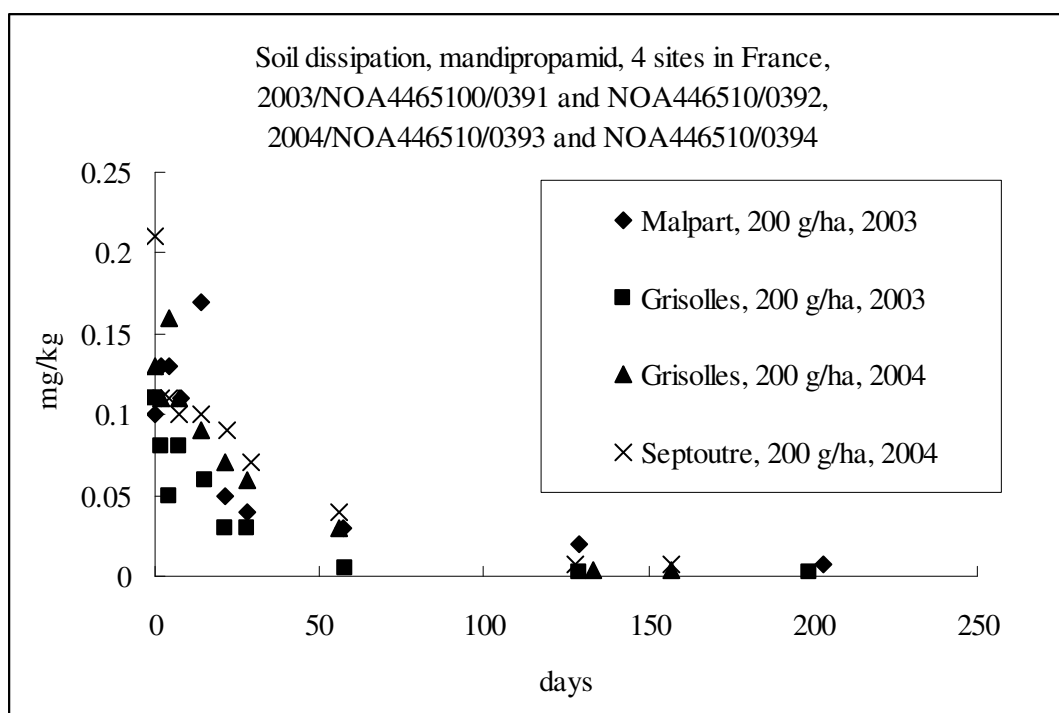


Figure 9 Field dissipation of mandipropamid on bare soils at 4 sites in France in 2003 and 2004 (Evans, P, 2005, NOA446510/0391; Evans, P, 2005, NOA446510/0392; Evans, P, 2005, NOA446510/0393; Evans, P, 2005, NOA446510/0394)

Two trials were conducted in Germany in 2003 and 2004 involving applications of mandipropamid as the 50 SC formulation, A-12946 to the surface soil (Simon, P, 2005, NOA446510/0358; Simon, P, 2005, NOA446510/0364). A single application of mandipropamid was applied at the actual rates of 0.20 kg ai/ha. Soil samples were taken at 11 times up to 359 days after the last application and down to 30 cm. The highest amounts of mandipropamid were found in the top layer (0–10cm) of soil. Minor amounts were found in the 10 to 30 cm layers (Table 30). No measurable residues were present in samples below the 0–10 cm soil horizon after 58 days after application. The residues detected at each depth have therefore been re-expressed as total residues in 0–10 cm to allow comparison of data from all the trials.

Table 30 Field dissipation of mandipropamid on bare soils at 2 sites in Germany in 2003 and 2004 (Simon, P, 2005, NOA446510/0358; Simon, P, 2005, NOA446510/0364)

Trial	Applic rate, kg/ha	Initial conc, mg/kg wet soil	Mandipropamid as % of original concentration in 0–10 cm soil.					
			2 days	8 days	21 days	53 days	112 days	189 days
Bavaria 2003 treat in June	Plot area 120 sq m. Silt loam. Soil nature: pH 7.0, 0.8% organic carbon, 8% Sand.							
	0.20	0.11	64%	45%	36%	27%	9.1%	3.6%

Trial	Applic	Initial conc,	Mandipropamid as % of original concentration in 0–10 cm soil.					
			2 days	7 days	21 days	58 days	119 days	178 days
Lower Saxony 2004 treat in May			Plot area 120 sq m. Loamy sand. Soil nature: pH 6.2, 0.7% organic carbon, 86% Sand.					
	0.20	0.11	55%	64%	55%	27%	27%	9.1%

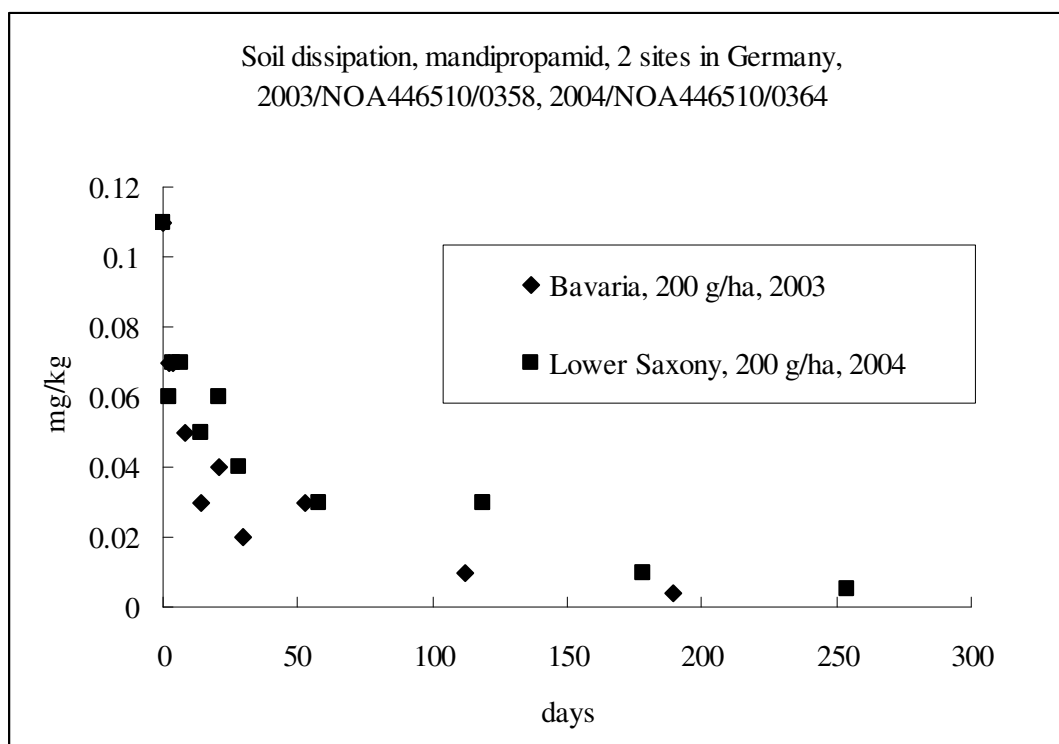


Figure 10 Field dissipation of mandipropamid on bare soils at 2 sites in Germany in 2003 and 2004 (Simon, P, 2005, NOA446510/0358; Simon, P, 2005, NOA446510/0364)

The dissipation of mandipropamid was consistent with degradation, since the decline of residue levels in the 0–10 cm increment was not associated with any significant increase in residue levels in the 10–20 and 20–30 cm depth increments and leaching did not contribute significantly to the dissipation. Only extremely low residues of the main metabolite CGA380778 were measured in the soil samples and these were within the top 0–10 cm horizon. Maximum residues of CGA380778 varied from 2.0 µg/kg to 9.2 µg/kg dry soil (1.5–7 g/ha) equivalent to 1.4% ± 0.6% of the nominal applied amount. For SYN536638, residues could not be detected in the 0–10 cm layer at or above the limit of quantification (LOQ = 0.0005 mg/kg) in any of the trials. No residues of CGA380778 or SYN536638 could be detected in the 10–20 cm or 20–30 cm layers.

### ***Crop rotation studies***

Information on the fate of mandipropamid in follow-on crop studies was made available to the meeting.

Two outdoor confined rotational crop studies in Switzerland between 2002 and 2003 (Stingelin J, 2004, NOA446510/0206; Stingelin J, 2004, NOA446510/0207) were conducted with [<sup>14</sup>C]mandipropamid (chlorophenyl- and methoxyphenyl-label), formulated as an emulsifiable concentrate (containing 100 g/L mandipropamid), with single application of 0.90 kg ai/ha to bare soil (silty clay loam, 1.9% organic carbon, pH 7.2, 19% sand). The calculated application rates for the [chlorophenyl-(U)-<sup>14</sup>C] and [methoxyphenyl-(U)-<sup>14</sup>C]mandipropamid were 903 g ai/ha and 932 g ai/ha respectively. Crops of lettuce, radish and spring wheat were sown into the treated soil at

intervals of 29, 58, 120 and 365 days after treatment. Crops were harvested at maturity or 50% maturity (spring wheat). Total radioactive residues (TRRs) were determined in all samples by direct combustion/LSC and samples with TRRs > 0.01 mg/kg were investigated further. These samples were extracted into acetonitrile:water (80:20 v/v) and the extracts analysed by thin layer chromatography (TLC). The content of  $^{14}\text{C}$  in soil and crop was analysed and the results were summarized in Tables 31 and 32.

Table 31 Total radioactive residues in soil samples after treatment with [ $^{14}\text{C}$ ]mandipropamid (chlorophenyl- and methoxyphenyl-label) (Stingelin J, 2004, NOA446510/0206; Stingelin J, 2004, NOA446510/0207)

Harvest (Plant back intervals)	Soil		Total Residues [mg/kg] <sup>b,c</sup>	Total Residues [mg/kg] <sup>b,c</sup>	Mandipro- pamid [mg/kg] <sup>b,d</sup>	Extractable radioactivity % TRR <sup>e</sup>	Non- Extractable Radioactivity % TRR <sup>e</sup>
	Layer	% TRR <sup>a</sup>					
[ $^{14}\text{C}$ ] chlorophenyl-mandipropamid							
Day 0	0–10 cm	100.0	0.89	0.95	0.85	91.4	8.6
Day 29	0–10 cm	98.7	0.66	0.69	0.50	78.6	21.4
	10–20 cm	0.7	0.005	n.a.	n.a.	n.a.	n.a.
	20–30 cm	0.6	0.003	n.a.	n.a.	n.a.	n.a.
	Total	100.0					
Day 58	0–10 cm	98.8	0.56	0.58	0.35	66.2	33.8
	10–20 cm	1.1	0.007	n.a.	n.a.	n.a.	n.a.
	20–30 cm	0.1	< 0.001	n.a.	n.a.	n.a.	n.a.
	Total	100.0					
Day 120	0–10 cm	98.0	0.61	0.59	0.24	48.6	51.4
	10–20 cm	0.9	0.006	n.a.	n.a.	n.a.	n.a.
	20–30 cm	1.1	0.006	n.a.	n.a.	n.a.	n.a.
	Total	100.0					
Day 365	0–10 cm	94.1	0.45	0.42	0.06	19.1	80.9
	10–20 cm	5.2	0.03	0.03	0.003	15.1	84.9
	20–30 cm	0.7	0.003	n.a.	n.a.	n.a.	n.a.
	Total	100.0					
[ $^{14}\text{C}$ ] methoxyphenyl-mandipropamid							
Day 0	0–10 cm	100.0	0.96	1.02	0.92	91.6	8.1
Day 29	0–10 cm	98.8	0.58	0.60	0.43	77.8	22.2
	10–20 cm	0.6	0.003	n.a.	n.a.	n.a.	n.a.
	20–30 cm	0.7	0.003	n.a.	n.a.	n.a.	n.a.
	Total	100.0					
Day 58	0–10 cm	99.0	0.38	0.39	0.22	64.4	35.6
	10–20 cm	0.9	0.004	n.a.	n.a.	n.a.	n.a.
	20–30 cm	< 0.1	< 0.001	n.a.	n.a.	n.a.	n.a.
	Total	100.0					
Day 120	0–10 cm	96.8	0.34	0.33	0.10	34.6	65.4
	10–20 cm	2.8	0.01	n.a.	n.a.	n.a.	n.a.
	20–30 cm	0.3	0.001	n.a.	n.a.	n.a.	n.a.
	Total	100.0					

Harvest (Plant back intervals)	Soil		Total Residues [mg/kg] <sup>b,c</sup>	Total Residues [mg/kg] <sup>b,c</sup>	Mandipro- pamid [mg/kg] <sup>b,d</sup>	Extractable radioactivity % TRR <sup>e</sup>	Non- Extractable Radioactivity % TRR <sup>e</sup>
	Layer	% TRR <sup>a</sup>					
Day 365	0–10 cm	94.3	0.51	0.49	0.06	19.2	80.8
	10–20 cm	4.4	0.03	0.03	0.002	136.6	86.4
	20–30 cm	1.3	0.005	n.a.	n.a.	n.a.	n.a.
	Total	100.0					

<sup>a</sup> in % of the total radioactivity found in the analysed soil core.

<sup>b</sup> in equivalents of NOA 446510.

<sup>c</sup> TRR determined by combustion.

<sup>d</sup> TRR determined by the sum of extractable + non-extractable radioactivity.

<sup>e</sup> in % of the total radioactivity found in the soil layer.

n.a. not analysed.

Table 32 Investigation of the nature of the residues in rotational crops after treatment with <sup>14</sup>C-mandipropamid (chlorophenyl- and methoxyphenyl-label) (Stingelin J, 2004, NOA446510/0206; Stingelin J, 2004, NOA446510/0207)

Commodity	TSI <sup>a</sup> days	THI <sup>b</sup> days	Mandipropamid		CGA380778		NOA458422		Unextracted Radioactivity		Total [mg/kg]
			[mg/kg]	[% TRR]	[mg/kg]	[% TRR]	[mg/kg]	[% TRR]	[mg/kg]	[% TRR]	
[ <sup>14</sup> C] chlorophenyl-mandipropamid											
Lettuce	29	64	0.001	9.5	nd	nd	nd	nd	0.005	45.7	0.011
	58	99	0.001	9.0	<0.001	0.7	nd	nd	0.006	47.6	0.013
	120	153	<0.001	1.5	0.001	6.1	nd	nd	0.005	45.7	0.012
	365	408	na	na	na	na	na	na	na	na	0.006 <sup>c</sup>
Radish Root	29	71	0.005	29.8	0.001	3.7	nd	nd	0.008	44.2	0.017
	58	99	0.002	21.9	<0.001	1.9	nd	nd	0.005	47.6	0.011
	120	167	na	na	na	na	na	na	na	na	0.007 <sup>c</sup>
Radish Top	29	71	0.003	8.8	0.001	3.1	nd	nd	0.010	31.3	0.031
	58	99	0.003	12.3	<0.001	1.7	nd	nd	0.010	40.2	0.025
	120	167	na	na	na	na	na	na	na	na	0.006 <sup>c</sup>
Wheat Forage	29	71	0.003	6.4	nd	nd	nd	nd	0.024	56.1	0.042
	58	99	0.002	12.1	<0.001	1.1	nd	nd	0.010	50.2	0.020
	120	167	0.001	5.6	0.001	2.9	nd	nd	0.015	59.5	0.026
	365	422	na	na	na	na	na	na	na	na	0.004 <sup>c</sup>
Wheat Grain	29	136	≤0.001	≤0.5	≤0.001	≤1.1	≤0.001	≤0.5	0.046	90.8	0.051
	58	170	≤0.001	≤3.5	≤0.001	≤3.5	≤0.001	≤3.5	0.026	86.2	0.030
	120	251	≤0.001	≤1.6	≤0.001	≤1.6	≤0.001	≤1.6	0.067	95.2	0.070
	365	464	na	na	na	na	na	na	na	na	0.009 <sup>c</sup>
Wheat Straw	29	136	0.020	6.0	0.009	2.7	0.016	4.8	0.200	60.0	0.334
	58	170	0.015	9.2	0.006	3.7	0.008	5.2	0.102	63.3	0.161
	120	251	0.002	2.1	≤0.002	≤2.6	≤0.002	≤2.6	0.061	69.8	0.087
	365	464	≤0.005	≤14.7	≤0.005	≤14.7	≤0.005	≤14.7	0.022	70.3	0.031



Commodity	TSI <sup>a</sup> days	THI <sup>b</sup> days	Mandipropamid		CGA380778		NOA458422		Unextracted Radioactivity		Total
			[mg/kg]	[% TRR]	[mg/kg]	[% TRR]	[mg/kg]	[% TRR]	[mg/kg]	[% TRR]	[mg/kg]
[ <sup>14</sup> C] methoxyphenyl-mandipropamid											
Lettuce	29	64	0.002	14.2	< 0.001	1.0	nd	nd	0.005	43.1	0.011
	58	99	0.001	6.2	< 0.001	0.6	nd	nd	0.006	51.3	0.011
	120	153	0.001	8.4	nd	nd	nd	nd	0.006	51.7	0.011
	365	408	na	na	na	na	na	na	na	na	0.006 <sup>a</sup>
Radish Root	29	71	0.005	21.1	< 0.001	1.8	nd	nd	0.011	49.6	0.022
	58	99	0.003	24.6	< 0.001	1.6	nd	nd	0.007	51.4	0.013
	120	167	na	na	na	na	na	na	na	na	0.007 <sup>a</sup>
Radish Top	29	71	0.004	9.5	0.002	6.5	nd	nd	0.013	35.8	0.037
	58	99	0.003	13.8	< 0.001	1.7	nd	nd	0.010	47.3	0.022
	120	167	na	na	na	na	na	na	na	na	0.008 <sup>a</sup>
Wheat Forage	29	71	0.003	7.3	0.001	1.2	nd	nd	0.023	50.0	0.045
	58	99	0.002	8.7	< 0.001	1.1	nd	nd	0.015	57.4	0.026
	120	167	0.001	7.1	< 0.001	1.6	nd	nd	0.011	55.6	0.019
	365	422	na	na	na	na	na	na	na	na	0.005 <sup>a</sup>
Wheat Grain	29	136	≤0.002	≤3.6	≤0.002	≤3.6	≤0.002	≤3.6	0.046	94.1	0.049
	58	170	≤0.001	≤3.8	≤0.001	≤3.8	≤0.001	≤3.8	0.036	93.2	0.039
	120	251	≤0.001	≤2.0	≤0.001	≤2.0	≤0.001	≤2.0	0.044	95.3	0.046
	365	464	≤0.001	≤3.4	≤0.001	≤3.4	≤0.001	≤3.4	0.011	91.3	0.012
Wheat Straw	29	136	0.021	5.8	0.005	1.4	0.016	4.3	0.249	67.1	0.371
	58	170	0.023	9.8	0.006	2.4	0.016	6.6	0.157	65.9	0.248
	120	251	0.001	2.2	≤0.001	≤2.2	≤0.001	≤2.2	0.048	73.9	0.065
	365	464	≤0.002	≤5.8	≤0.002	≤5.8	≤0.002	≤5.8	0.023	77.0	0.030

n.d. not detected. n.a. not analysed.

<sup>a</sup> TSI: interval between treatment on soil and sowing of rotation crop, days.

<sup>b</sup> THI: interval between treatment on soil and harvest of rotation crop (or sampling of soil), days.

<sup>c</sup> TRR determined by direct combustion and LSC quantification.

Metabolism of mandipropamid in three different succeeding crops (lettuce, radish and cereals) has been studied. Uptake of residues was quite limited with the only identified components being parent mandipropamid, CGA380778 and NOA458422 all of which were identified in the primary crop metabolism studies. In addition significant amounts of radioactivity were present in natural plant constituents. Levels of parent mandipropamid or any other metabolite in succeeding crops would not be expected to reach or exceed 0.01 mg/kg and therefore field studies on succeeding crops were not considered necessary. A metabolic pathway for mandipropamid in rotated crops is proposed in Figure 11.

## Mandipropamid

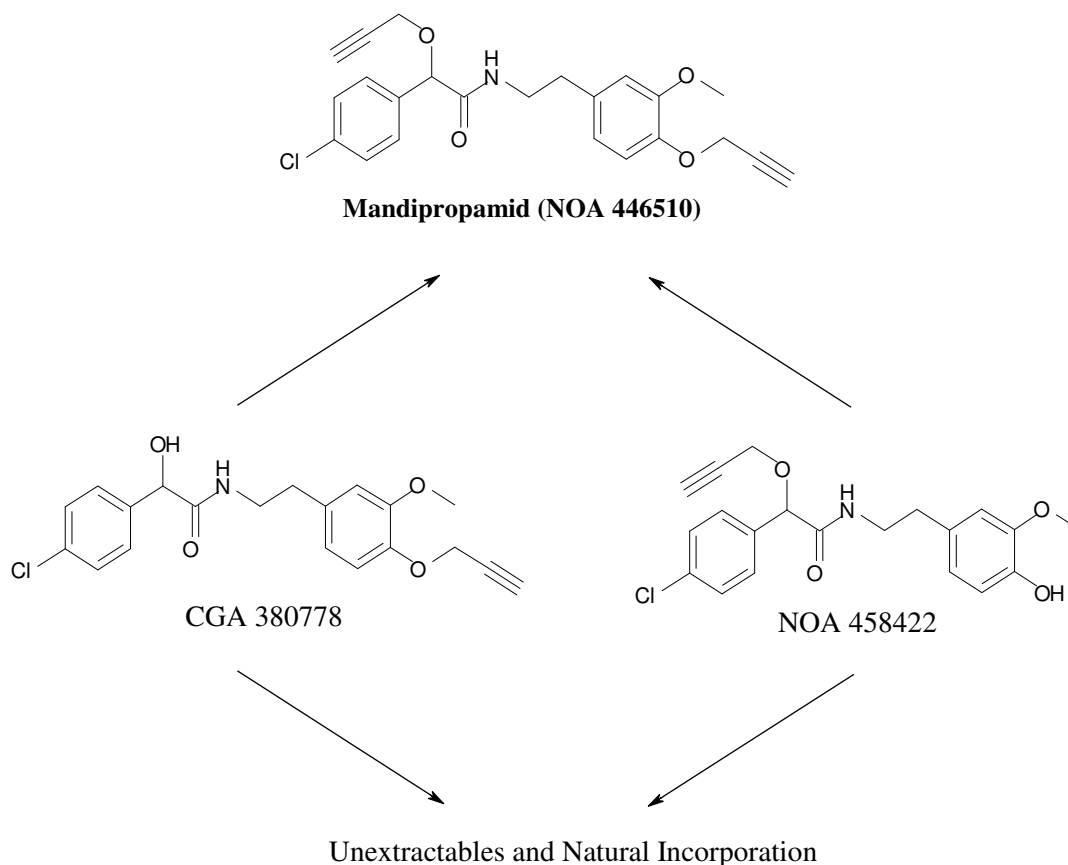


Figure 11 Proposed metabolic pathway of mandipropamid in rotated crops (Stingelin J, 2004, NOA446510/0206; Stingelin J, 2004, NOA446510/0207)

Rotational crops were planted at plant-back intervals of 30 and 60 days in the US during 2004 after mandipropamid was applied to cucumbers as a post foliar broadcast spray (Joseph T, Hamilton L S, 2005, NOA446510/0746). Four applications of a 250 SC formulation of mandipropamid were made with a seven-day interval between applications at an application rate of 38 g ai/ha for a total seasonal rate of 151 g ai/ha. Crops were harvested at typical agricultural intervals. Samples were extracted with acetonitrile/water and determined with triple quadrupole mass spectrometer detection (LC/MS/MS). The residues were summarized in Table 33. No residues (< 0.01 mg/kg) of mandipropamid were found in spinach, radishes, or wheat analysed at either the 30-day or 60-day plant back interval.

Table 33 Mandipropamid residues in rotational crops (Joseph T, Hamilton LS, 2005, NOA446510/0746)

Commodity	TSI <sup>a</sup> , days	THI <sup>b</sup> , days	Residues (mg/kg)	Trial ID
Spinach leaves	30	86	< 0.01	5A-FR-04-5690 Hudson, NY, 2004
	30	82	< 0.01	5A-FR-04-5692 Champaign, IL, 2004

Commodity	TSI <sup>a</sup> , days	THI <sup>b</sup> , days	Residues (mg/kg)	Trial ID
	30	120	< 0.01	5A-FR-04-5694 Champaign, IL, 2004
Radish tops	30	65	< 0.01	5A-FR-04-5690 Hudson, NY, 2004
	30	81	< 0.01	5A-FR-04-5692 Champaign, IL, 2004
	60	120	< 0.01	5A-FR-04-5694 Champaign, IL, 2004
Radish roots	30	65	< 0.01	5A-FR-04-5690 Hudson, NY, 2004
	30	81	< 0.01	5A-FR-04-5692 Champaign, IL, 2004
	60	120	< 0.01	5A-FR-04-5694 Champaign, IL, 2004
Wheat forage, fall	30	86	< 0.01	5A-FR-04-5690 Hudson, NY, 2004
	30	89	< 0.01	5A-FR-04-5692 Champaign, IL, 2004
	60	120	< 0.01	5A-FR-04-5694 Champaign, IL, 2004
Wheat forage, spring	30	285	< 0.01	5A-FR-04-5690 Hudson, NY, 2004
	30	230	< 0.01	5A-FR-04-5692 Champaign, IL, 2004
	60	269	< 0.01	5A-FR-04-5694 Champaign, IL, 2004
Wheat forage, hay	30	320	< 0.01	5A-FR-04-5690 Hudson, NY, 2004
	30	256	< 0.01	5A-FR-04-5692 Champaign, IL, 2004

Commodity	TSI <sup>a</sup> , days	THI <sup>b</sup> , days	Residues (mg/kg)	Trial ID
	60	295	< 0.01	5A-FR-04-5694 Champaign, IL, 2004
Wheat forage, straw	30	343	< 0.01	5A-FR-04-5690 Hudson, NY, 2004
	30	294	< 0.01	5A-FR-04-5692 Champaign, IL, 2004
	60	333	< 0.01	5A-FR-04-5694 Champaign, IL, 2004
Wheat forage, grain	30	343	< 0.01	5A-FR-04-5690 Hudson, NY, 2004
	30	294	< 0.01	5A-FR-04-5692 Champaign, IL, 2004
	60	333	< 0.01	5A-FR-04-5694 Champaign, IL, 2004

<sup>a</sup> TSI: Plant Back Interval, days.

<sup>b</sup> THI: interval between planting and sampling, days.

## METHODS OF RESIDUE ANALYSIS

### *Analytical methods*

The Meeting received descriptions and validation data for analytical methods for residues of mandipropamid in raw agricultural commodities and processed commodities. Methods rely on HPLC-MS-MS for analysis of mandipropamid in the various matrices.

### *Data collection method*

*Residue Analytical Method for the Determination of Residues of NOA 446510 in Crop Samples. Final Determination by LC-MS/MS.* (Crook, SJ ,2004, NOA446510/0160)

Analyte: mandipropamid LC-MS-MS Method RAM 415/01

LOQ: 0.01 mg/kg in crops

Description Samples are extracted by homogenisation with acetonitrile:water (80:20 v/v). Extracts are centrifuged and aliquots diluted with water. Clean-up is performed by solid-phase extraction cartridges. Residues of mandipropamid are quantified using high performance liquid chromatography with triple quadruple mass spectrometric detection (LC-MS/MS). The transition monitored for mandipropamid was 412.1 to 327.9.

*Validation of Residue Analytical Method RAM 415/01 for the Determination of Residues in Crops.* (Gill JP and Mound EL, 2004, NOA446510/0159)

Analyte: mandipropamid LC-MS-MS Method RAM 415/02  
 LOQ: 0.01 mg/kg in crops  
 Description Residues of mandipropamid were extracted from crop samples by homogenisation with acetonitrile:water (80:20 v/v). Extracts are centrifuged and aliquots diluted with water prior to being cleaned-up using polymeric solid-phase extraction cartridges. Residues of mandipropamid are quantified using high performance liquid chromatography with triple quadruple mass spectrometric detection (LC-MS/MS). The transition monitored for mandipropamid was 412.1 to 327.9.

#### *Enforcement methods*

*Analytical Method Development and Validation (S19) for the Determination of Residues of NOA 446510 in/on Plant Matrices.* (Klimmek, S, 2004, NOA446510/0095)

Analyte: mandipropamid LC-MS-MS Method DFSG S19  
 LOQ: 0.01 mg/kg in crops  
 Description Residues mandipropamid extracted from tomato and apple substrates is performed according to extraction Module E1 of DFG method S19. The extraction of mandipropamid residues from wheat grain and oilseed rape seed is performed according to Modules E2 and E7 of DFG method S19, respectively. Extracts are cleaned-up using gel permeation chromatography (GPC). Residues of mandipropamid are quantified using LC-MS/MS. The transition monitored for mandipropamid was 411.8 to 124.9.

Method RAM 415/002 was subjected to independent laboratory validation (ILV) where successful recoveries were obtained for various commodities tested (Gill JP and Mound EL, 2004, NOA446510/0159). An independent laboratory validation performed for the Method DFG S19 was carried out with numerous recoveries on tomato and wheat grain. (Lakaschus, S, 2005, NOA446510/0326).

Recovery data from the internal and independent laboratory validation (ILV) testing are summarised in Table 34.

Table 34 Validation data for analytical methods for the determination of mandipropamid residues in food

Sample Matrix	Fortification [mg/kg]	Number of Analyses	Mean Recovery [%]	RSD [%]	Recovery Range [%]	REF
Method RAM 415/001						
Tomatoes (Fruit)	0.01	5	95	2	93–98	Gill JP and Mound EL, 2004, NOA446510/0159
	0.1	5	92	2	89–94	
	Overall	10	93	3	89–98	
Tomatoes (Juice)	0.01	5	95	2	92–97	59
	0.1	5	93	1	92–94	

## Mandipropamid

Sample Matrix	Fortification [mg/kg]	Number of Analyses	Mean Recovery [%]	RSD [%]	Recovery Range [%]	REF
	Overall	10	94	2	92–97	Crook, SJ , 2004, NOA446510/01 60
Tomatoes (Puree)	0.01	5	94	4	90–99	
	0.1	5	102	3	97–106	
	Overall	10	98	6	90–106	
Cucumbers	0.01	5	80	4	76–84	
	0.1	5	87	1	85–89	
	Overall	10	83	5	76–89	
Grapes (Fruit)	0.01	5	84	4	79–88	
	1.0	5	85	4	80–88	
	Overall	10	85	4	79–88	
Grapes (Wine)	0.01	5	84	3	82–87	
	0.1	5	85	1	85–86	
	Overall	10	84	2	82–87	
Grapes (Raisins)	0.01	5	97	1	96–99	
	1.0	5	93	1	91–94	
	Overall	10	95	3	91–99	
Grapes (Dry pomace)	0.01	5	91	4	85–94	
	1.0	5	83	5	79–87	
	Overall	10	87	6	79–94	
Potatoes	0.01	5	84	2	82–87	
	0.1	5	86	2	85–88	
	Overall	10	85	2	82–88	
Spinach	0.01	5	94	2	91–96	
	5.0	5	99	1	97–101	
	Overall	10	97	3	91–101	
Melons (Peel)	0.01	5	86	4	82–90	
	0.5	5	83	3	79–85	
	Overall	10	85	4	79–90	
Melons (Flesh)	0.01	5	88	7	82–97	
	0.1	5	83	3	80–86	

Sample Matrix	Fortification [mg/kg]	Number of Analyses	Mean Recovery [%]	RSD [%]	Recovery Range [%]	REF
	Overall	10	85	6	80–97	
Onions	0.01	5	84	6	79–92	
	0.1	5	85	5	81–90	
	Overall	10	84	5	79–92	
Sweet Peppers	0.01	5	79	5	75–85	
	0.1	5	83	3	81–87	
	Overall	10	81	4	75–87	
Leeks	0.01	5	75	2	73–78	
	0.1	5	79	1	79–81	
	Overall	10	77	3	73–81	
Wheat (Straw)	0.01	5	90	5	84–95	
	5.0	5	89	2	87–92	
	Overall	10	90	3	84–95	
Oil Seed Rape (Seed)	0.01	5	83	9	76–91	
	0.1	5	95	4	91–100	
	Overall	10	90	9	76–100	
Oranges	0.01	5	80	6	73–84	
	0.1	5	79	3	76–82	
	Overall	10	79	4	73–84	
Method S19						
Wheat (Grain)	0.01	5	96	15	81–116	Klimmek, S, 2004, NOA446510/00
	0.1	5	87	18	69–105	
	Overall	10	91	16	69–116	
Oil Seed Rape (Seed)	0.01	5	89	14	75–103	95
	0.1	4*	80	2	79–82	
	Overall	9*	85	12	75–103	
Tomatoes	0.01	5	77	15	63–88	
	2	5	86	6	78–93	
	Overall	10	82	12	63–93	
Apples	0.01	5	90	9	85–101	
	2	5	82	8	75–89	

Sample Matrix	Fortification [mg/kg]	Number of Analyses	Mean Recovery [%]	RSD [%]	Recovery Range [%]	REF
	Overall	10	86	9	75–101	
ILV of method S19						
Wheat Grain	0.01	5	100	9	91–111	Lakaschus, S, 2005,
	0.1	5	111	6	102–117	
	Overall	10	106	9	91–117	NOA446510/03
Tomatoes	0.01	5	109	3	106–113	26
	2	5	109	9	94–121	
	Overall	10	109	6	94–121	

Method RAM 415/01 was successfully validated for the analysis of mandipropamid residues in a wide range of crops and an LOQ of 0.01 mg/kg was established, and is suitable to be used in support of pre-registration data requirements. Method S19 was successfully validated and independently validated for the analysis of mandipropamid residues in crops and an LOQ of 0.01 mg/kg was established, and could be used for post registration control and monitoring of mandipropamid residues in crop commodities.

#### *Stability of residues in stored analytical samples*

The Meeting received information on the stability of residues of mandipropamid in tomatoes, grapes, potatoes, lettuce, cucumbers, wheat, and soya beans.

A study on the stability of mandipropamid residues in crop commodities was conducted during 2004 and 2005 (Hamilton, LS, 2005, NOA446510/0423). Stability of mandipropamid residues was tested in both raw agricultural commodities and in processed commodities. Commodities used were 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).

Crop samples (10 g) were fortified with mandipropamid at 0.5 mg kg<sup>-1</sup>. 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 and twelve 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 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.

Table 35 Stability of mandipropamid residues in crop commodities following storage at –20 °C (Hamilton, LS, 2005, NOA446510/0423)

Commodity	Storage Period (months)	Fortification Level (mg/kg)	Recovered Residues (mg/kg) <sup>a</sup>	Mean Procedural Recovery (%) <sup>b</sup>
Tomatoes–Fruit	0	0.50	0.44	91
	3	0.50	0.46	97
	6	0.50	0.47	103
	12	0.50	0.42	99
Tomatoes – Paste	0	0.50	0.45	87
	3	0.50	0.48	90



Commodity	Storage Period (months)	Fortification Level (mg/kg)	Recovered Residues (mg/kg) <sup>a</sup>	Mean Procedural Recovery (%) <sup>b</sup>
	6	0.50	0.49	104
	12	0.50	0.46	95
Grapes – Fruit	0	0.50	0.48	95
	3	0.50	0.48	96
	6	0.50	0.47	94
	12	0.50	0.42	92
Grapes – Juice	0	0.50	0.46	90
	3	0.50	0.47	88
	6	0.50	0.36	86
	12	0.50	0.46	88
Potatoes – Tubers	0	0.50	0.51	100
	3	0.50	0.55	98
	6	0.50	0.57	108
	12	0.50	0.47	89
Potatoes – Granules/ Flakes	0	0.50	0.47	90
	3	0.50	0.50	97
	6	0.50	0.48	102
	12	0.50	0.52	97
Lettuce – Head	0	0.50	0.45	94
	3	0.50	0.44	81
	6	0.50	0.48	80
	12	0.50	0.41	102
Cucumbers – Fruit	0	0.50	0.44	90
	3	0.50	0.49	104
	6	0.50	0.47	103 <sup>c</sup>
	12	0.50	0.48	89
Wheat – Forage	0	0.50	0.49	95
	3	0.50	0.46	88
	6	0.50	0.41	99
	12	0.50	0.41	90
Wheat – Straw	0	0.50	0.37	82
	3	0.50	0.49	121
	6	0.50	0.58	113
	12	0.50	0.57	114
Wheat – Grain	0	0.50	0.35	71 <sup>c</sup>
	3	0.50	0.27	92
	6	0.50	0.48	100
	12	0.50	0.51	83

Commodity	Storage Period (months)	Fortification Level (mg/kg)	Recovered Residues (mg/kg) <sup>a</sup>	Mean Procedural Recovery (%) <sup>b</sup>
Soya bean – Beans	0	0.50	0.45	91
	3	0.50	0.44	96
	6	0.50	0.42	88
	12	0.50	0.42	83
Soya bean – Meal	0	0.50	0.46	93
	3	0.50	0.42	92
	6	0.50	0.46	99
	12	0.50	0.41	100
Soya bean – Hulls	0	0.50	0.44	87
	3	0.50	0.47	89
	6	0.50	0.45	104
	12	0.50	0.41	94
Soya bean – Oil	0	0.50	0.48	94
	3	0.50	0.47	94
	6	0.50	0.51	91
	12	0.50	0.41	100

<sup>a</sup> Mean of two samples, not corrected for procedural recovery

<sup>b</sup> Mean of two recoveries

<sup>c</sup> one recovery sample only

Residues of mandipropamid were found to be stable in a range of crop commodities when stored at  $-20^{\circ}\text{C}$  for 12 months. Residues of mandipropamid are expected to be stable in all crop commodities stored under these conditions for at least one year. No freezer storage stability studies were conducted with mandipropamid in/on animal matrices.

Lactating goats metabolism studies were conducted separately with [ $^{14}\text{C}$ ]mandipropamid, radiolabelled uniformly in either the chlorophenyl or methoxyphenyl ring, equivalent to 27–49 mg/kg in the total diet (on a dry basis) once daily via balling gun for seven consecutive days (Cary, CA and Aver, E, 2005, RJ3557B). Milk, liver, kidney and fat samples were extracted, fractionated, and initially chromatographed within 4–5 months of sampling; extraction dates and individual analysis dates were not provided. Further analyses were conducted after the 6 month storage interval including a stability check sample after the final analysis of each matrix. Comparison of the chromatographic profiles of the initial and stored extracts of liver and fat or the aqueous fraction from milk, demonstrated no significant changes during the storage periods.

## USE PATTERN

Mandipropamid is effective against most foliar Oomycete pathogens including *Plasmopara viticola* in grapes, *Phytophthora infestans* in potatoes and tomatoes and *Pseudoperonospora cubensis* in cucurbits. Labels and English translations were available for all the uses. Labels including the details of Good Agricultural Practices (GAP) are provided for the worst-case registered uses that are supported by relevant residue data. Information on registered uses included in this monograph is generally limited to countries where supervised trials had been conducted, and is summarized in Table 36.

Table 36 Registered field uses of mandipropamid in Austria, UK, and USA. Labels for the following uses were available to the Meeting

Crop	Country or Region	End use product	F/G/P <sup>a</sup>	Application					PHI [days]
				Method	No. per crop season min. max.	kg ai/hL <sup>b</sup> max.	Water L/ha per appl. Min. max.	kg ai/ha per applic. <sup>b</sup> min. max.	
Grapes	USA	250 SC	F	ground air	4			0.1–0.146	14
Onions, Garlic, Shallots	USA	250 SC	F	ground air chemigation	4			0.1–0.146	7
Leek Green Onions Welch Onions	USA	250 SC	F	ground air chemigation	3			0.1–0.146	7
Broccoli Cabbage Brussels Sprouts Cauliflower	USA	250 SC	F	foliar spray	4			0.1–0.146	1
Kale Collard Mustard greens	USA	250 SC	F	foliar spray	4			0.1–0.146	1
Cucumber Watermelon Musk-melon Honeydew Cantaloupe Pumpkin Squash Zucchini	USA	250 SC	F	ground air chemigation	4			0.1–0.146	0
Tomatoes	USA	250 SC	F	foliar spray	4			0.1–0.146	1
Pepper Eggplants	USA	250 SC	F	foliar spray	4			0.1–0.146	1
Okra Ground- cherry Pepino									
Lettuce Spinach Celery	USA	250 SC	F	foliar spray	4			0.1–0.146	1
Potatoes	Austria	250 SC	F	foliar spray	4		200–600	0.15	7

Crop	Country or Region	End use product	F/G/P <sup>a</sup>	Application					PHI [days]
				Method	No. per crop season min. max.	kg ai/hL <sup>b</sup> max.	Water L/ha per appl. Min. max.	kg ai/ha per applic. <sup>b</sup> min. max.	
Potatoes	Germany	250 SC	F	foliar spray	4	0.0375–0.075	200–400	0.15	7
Potatoes	Netherlands	250 SC	F	foliar spray	1–6			0.15	
Potatoes	UK	250 SC	F	foliar spray, tractor boom	4		200	0.15	3

<sup>a</sup> F = outdoor or field use, G = glasshouse, P = protected, I = indoor application

<sup>b</sup> Information given on active substance refers to mandipropamid only

### RESIDUES RESULTING FROM SUPERVISED TRIALS ON CROPS

The Meeting received information on supervised field trials for mandipropamid uses on the following crops.

Commodity	Country	Table No.
Grape	USA	Table 37
Onion	USA	Table 38
Broccoli	USA	Table 39
Cabbage	USA	Table 40
Mustard greens	USA	Table 41
Cucumber	USA	Table 42
Melon	USA	Table 43
Summer squash	USA	Table 44
Tomato	USA	Table 45
Pepper	USA	Table 46
Lettuce	USA	Table 47
Celery	USA	Table 48
Spinach	USA	Table 49
Potato	France, Germany, Italy, the Netherlands, Spain, Switzerland, the UK	Table 50

Where residues were not detected, they are reported as below the LOQ. Residue data, application rates and spray concentrations have generally been rounded to two significant figures or, for residues near the LOQ, to one significant figure. Residue data are recorded unadjusted for % recovery. Multiple results are recorded in the data tables where the trial design included replicate plots and where separate samples have been identified as being from these replicate plots. Results used to estimate STMRs are double underlined.

Trials were generally well documented with laboratory and field reports. Laboratory reports included method validation with procedural recoveries from spiking at residue levels similar to those occurring in samples from the supervised trials. Dates of analyses or duration of residue sample storage were also provided.

Conditions of the supervised residue trials were generally well reported in detailed field reports. Most field reports provided data on the sprayers used, plot size, residue sample size and sampling date. In multiple applications the application rate, spray concentration and water volume may not have been exactly the same for all applications; the recorded values in the supervised trials summary tables are for the final application.

All samples were frozen soon after harvest and kept frozen in storage until shipment to the residue analysis laboratory. Upon receipt, all samples were transferred to deep freeze storage ( $\leq 20\text{ }^{\circ}\text{C}$ ). Intervals between sampling and analysis were reported for all trials and were within the acceptable proven storage stability duration.

A total of 12 residue trials were carried out according to GAP ( $\pm 30\%$ ) in the United States in 2003 (Joseph, T, 2005, NOA/446510/0424). In all trials, mandipropamid was applied four times as an SC formulation containing 250 g ai/L at 6–7 days intervals at a nominal rate of 59.5 to 63.9 g ai/A (147–158 g ai/ha) as a foliar application to grapes. The water rate was between 59.5–63.9 L/ha. The PHI was 14 days. The residue data from the supervised trials is summarised in Table 37.

Table 37 Results of residue trials with mandipropamid conducted as a foliar application to grapes in US in 2003 (Joseph, T, 2005, NOA/446510/0424)

GRAPES Country, Year <i>Location</i> (variety)	Application					PHI days	Commodity	Residues, mg/kg mandipropamid	Ref. Reg.DocID. (Trail No.)
	Formulation	kg ai/ha	kg ai/hL	Water L/ha	No.				
2003 <i>Pennsylvania</i> (Concord)	250 SC	0.15	0.017	866	4	14 14 28 28	control whole fruit	< 0.01 0.17 <u>0.22</u> 0.11 0.17	EB-FR-002-03
2003 <i>New York</i> (DeChaunac)	250 SC	0.15	0.016	923	4	14 14 28 28	control whole fruit	< 0.01 0.58 <u>0.76</u> 0.54 0.55	EE-FR-001-03
2003 California ( <i>Chardonnay On SC Rootstock</i> )	250 SC	0.15	0.015	1000	4	14 14 28 28	control whole fruit	< 0.01 <u>0.43</u> 0.31 0.17 0.25	WC-FR-003-03
2003 California (Red Flames (Seedless))	250 SC	0.15	0.012	1227	4	14 14 14 14 28 28	control whole fruit	< 0.01 0.31 0.22 0.16 0.26 0.51 <u>0.59</u>	WC-FR-006-03
		0.76	0.062	1226	4	14 14 14 14		3.1 3.4 0.42 0.49	

## Mandipropamid

GRAPES Country, Year <i>Location</i> (variety)	Application					PHI days	Commodity	Residues, mg/kg mandipropamid	Ref. Reg.DocID. (Trail No.)
	Formulation	kg ai/ha	kg ai/hL	Water L/ha	No.				
2003 <i>California</i> (Thompson seedless)	250 SC	0.15	0.014	1073	4	14	control whole fruit	< 0.01 0.13 <u>0.38</u> 0.13 0.11 0.36	WC-FR-007-03
		0.77	0.072	1070	4	28		1.9 1.4 1.1	
2003 <i>California</i> (Crimson Seedless)	250 SC	0.15	0.013	1183	4	0	control whole fruit	< 0.01 0.32 0.29  0.31 0.39 0.65 1.3 0.50 1.5	WC-FR-008-03
						5		0.18 0.67 0.84 0.27 <u>0.85</u> 0.24 0.80 0.20	
						10		0.51 0.34	
						14		0.28 0.11	
2003 <i>California</i> (Thompson seedless)	250 SC	0.15	0.011	1435	4	14	control whole fruit	< 0.01 <u>0.62</u> 0.35	WC-FR-009-03
						28		0.43 0.42	
2003 <i>California</i> (Cabenet Sauvignon)	250 SC	0.15	0.010	1537	4	14	control whole fruit	< 0.01 0.65 <u>0.69</u> 0.57	WD-FR-001-03
						28		0.68	

GRAPES Country, Year <i>Location</i> (variety)	Application					PHI days	Commodity	Residues, mg/kg mandipropamid	Ref. Reg.DocID. (Trail No.)
	Formulation	kg ai/ha	kg ai/hL	Water L/ha	No.				
2003 <i>California</i> (Cabernet Sauvignon)	250 SC	0.15	0.016	935	4	14 28	control whole fruit	< 0.01 0.35 0.57 0.39 <u>0.63</u>	WD-FR-004-03
2003 <i>California</i> (Cabernet Sauvignon)	250 SC	0.15	0.032	474	4	7 14 21 28 35	control whole fruit	< 0.01 0.16 0.28 0.16 <u>0.21</u> 0.08 0.16 0.09 0.13 0.09 0.08	WD-FR-005-03
2003 <i>Washington</i> (Reisling)	250 SC	0.15	0.016	941	4	14 28	control whole fruit	< 0.01 0.26 <u>0.28</u> 0.26 0.27	WF-FR-004-03
2003 <i>Oregon</i> (Chardonnay)	250 SC	0.16	0.015	1090	4	14 28	control whole fruit	< 0.01 0.07 0.13 <u>0.20</u> 0.14	WF-FR-012-03

A total of 11 residue trials were carried out according to GAP ( $\pm 30\%$ ) in the United States in 2004 (Joseph, T, Hamilton, LS, 2005, NOA/446510/0425). In all trials, mandipropamid (A12946C SC 250 g/L) was applied three or four times at 6–8 days intervals at a nominal rate of 145–169 g ai/ha as a foliar application to onions. The water rate was between 28–394 L/ha. The PHI was 7 days. The residue data from the supervised trials is summarised in Table 38.

Table 38 Results of residue trials with mandipropamid conducted as a foliar application to green onions and dry bulb onions in US in 2004 (Joseph, T, Hamilton, LS, 2005, NOA/446510/0425)

BULB VEGETABLES Year <i>Location</i> (variety)	Application					PHI days	Commodity	Residues, mg/kg mandipropamid	Ref. Reg.DocID. (Trial and treatment No.)
	Formulation	kg ai/ha	kg ai/hL	Water L/ha	No.				
GREEN ONION									
2004 <i>Georgia</i>	250 SC	0.15	0.090	167	3	7	control whole plant	< 0.01 0.31	SL-FR-04-5360

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BULB VEGETABLES Year Location (variety)	Application					PHI days	Commodity	Residues, mg/kg mandipropamid	Ref. Reg.DocID. (Trial and treatment No.)
	Formulation	kg ai/ha	kg ai/hL	Water L/ha	No.				
(Yellow Granex Sweet Onions)								<u>0.48</u>	
2004 Texas (Texas Early White)	250 SC	0.15	0.090	168	3	7	control whole plant	< 0.01 <u>1.74</u> 1.15	SA-FR-04-5361
2004 California (Southport White 404)	250 SC	0.15	0.051	296	3	0	control whole plant	< 0.01 1.51 1.22 0.73 0.57 0.59 0.35 <u>0.25</u> 0.20 0.20 0.10	2A-FR-04-5362
BULB ONIONS, DRY									
2004 New York (White Sweet Spanish)	250 SC	0.15	0.039	379	4	0	control dry bulb onion	< 0.01 < 0.01 0.02 0.03 0.03 < 0.01 < 0.01 <u>≤ 0.01</u> < 0.01 < 0.01 < 0.01 < 0.01 < 0.01	5A-FR-04-5363
2004 Illinois (Yellow Sweet Spanish)	250 SC	0.16	0.56	28.7	4	7	control dry bulb onion	< 0.01 <u>≤ 0.01</u> < 0.01 < 0.01	4A-FR-04-5364
								< 0.01	
2004 Texas (Ebano)	250 SC	0.15	0.089	168	4	7	control dry bulb onion	< 0.01 0.02 <u>0.04</u> < 0.01 < 0.01	SA-FR-04-5365



BULB VEGETABLES Year Location (variety)	Application					PHI days	Commodity	Residues, mg/kg mandipropamid	Ref. Reg.DocID. (Trial and treatment No.)
	Formulation	kg ai/ha	kg ai/hL	Water L/ha	No.				
2004 <i>Colorado</i> (Candy)	250 SC	0.15	0.11	143	4	7	control	< 0.01	NM-FR-04-5366
							dry bulb	<u>≤ 0.01</u>	
							onion	< 0.01	
								< 0.01	
						14		< 0.01	
2004 <i>California</i> (Fresno White)	250 SC	0.15	0.054	282	4	7	control	< 0.01	WC-FR-04-5367
							dry bulb	<u>0.01</u>	
							onion	< 0.01	
								< 0.01	
								< 0.01	
								< 0.01	
						14		< 0.01	
2004 <i>Idaho</i> (Vaquero)	250 SC	0.15	0.064	235	4	7	control	< 0.01	WG-FR-04-5368
							dry bulb	<u>≤ 0.01</u>	
							onion	< 0.01	
								< 0.01	
						14		< 0.01	
2004 <i>Washington</i> (Walla Walla Sweet)	250 SC	0.15	0.10	149	4	7	control	< 0.01	WF-FR-04-5369
							dry bulb	< 0.01	
							onion	<u>0.02</u>	
								< 0.01	
						14		< 0.01	
2004 <i>California</i> (Stockton Early Red)	250 SC	0.152	0.065	235	4	7	control	< 0.01	WF-FR-04-5369
							dry bulb	<u>≤ 0.01</u>	
							onion	< 0.01	
								< 0.01	
						14		< 0.01	

A total of six residue trials were carried out according to GAP ( $\pm 30\%$ ) in the United States between 2004 and 2005 (Joseph, T, Hamilton, LS, 2005, NOA/446510/0626). In all trials, mandipropamid (A12946C SC 250 g/L) was applied four times at 5–10 days intervals at a nominal rate of 144–166 g ai/ha as a foliar application to broccoli. The water rate was between 19–600 L/ha. The PHI was 1 day. The residue data from the supervised trials is summarised in Table 39.

Table 39 Results of residue trials with mandipropamid conducted as a foliar application to broccoli in US in 2004 and 2005 (Joseph, T, Hamilton, LS, 2005, NOA/446510/0626)

BROCCOLI Year Location (variety)	Application					PHI days	Commodity	Residues, mg/kg mandipropamid	Ref. Reg.DocID. (Trial No.)
	Formulation	kg ai/ha	kg ai/hL	Water L/ha	No.				
2004 <i>Texas</i> (Arcadia)	250 SC	0.15	0.082	184	4	1	control	< 0.01	SA-FR-04-5315
							flower head	0.24	
							+ stem	<u>0.35</u>	

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BROCCOLI Year Location (variety)	Application					PHI days	Commodity	Residues, mg/kg mandipropamid	Ref. Reg.DocID. (Trial No.)	
	Formulation	kg ai/ha	kg ai/hL	Water L/ha	No.					
						7		< 0.01 < 0.01		
2004 <i>California</i> (Green Belt)	250 SC	0.15	0.082	185	4	0	control flower head + stem	< 0.01 0.16 0.12	WC-FR-04-5316	
						1		0.33 <u>0.44</u>		
						3		0.25 0.34		
						5		0.22 0.21		
						7		0.11 0.10		
						9		0.10 0.15		
2004 <i>California</i> (Marathan)	250 SC	0.16	0.81	19.5	4	1	control flower head + stem	< 0.01 <u>0.57</u> 0.35		WB-FR-04-5317
						7		0.09 0.16		
2004 <i>California</i> (Marathan)	250 SC	0.15	0.028	536	4	1	control flower head + stem	< 0.01 0.22 <u>0.43</u>		WB-FR-04-5318
						7		0.20 0.10		
2004 <i>Arizona</i> (Triathalon)	250 SC	0.15	0.096	157	4	1	control flower head + stem	< 0.01 0.28 <u>0.29</u>	WB-FR-04-5319	
						7		0.16 0.13		
2004 <i>Washington</i> (Laguna)	250 SC	0.15	0.065	237	4	1	control flower head + stem	< 0.01 <u>0.70</u> 0.47	WF-FR-04-5320	
						7		0.20 0.22		

A total of six residue trials were carried out according to GAP ( $\pm 30\%$ ) in the United States between 2004 and 2005 (Joseph, T, Hamilton, LS, 2005, NOA/446510/0626). In all trials, mandipropamid (A12946C SC 250 g/L) was applied four times at 7–10 days intervals at a nominal rate of 147–158 g ai/ha as a foliar application to cabbage. The water rate was between 19.1–194.5 L/ha. The PHI was 1 day. The residue data from the supervised trials is summarised in Table 40.

Table 40 Results of residue trials with mandipropamid conducted as a foliar application to cabbage in US in 2004 and 2005 (Joseph, T, Hamilton, LS, 2005, NOA/446510/0626)

CABBAGE Year Location (variety)	Application					PHI days	Commodity	Residues, mg/kg mandipropamid	Ref. Reg.DocID. (Trial No.)	
	Formulation	kg ai/ha	kg ai/hL	Water L/ha	No.					
2004 <i>New York</i> (Early Green)	250 SC	0.15	0.79	19.4	4	1	control	< 0.01	WF-FR-04-5321	
							Heads, w/wrapper	1.10		
								<u>1.30</u>		
							leaves	0.25		
								0.38		
							1	Head, w/o wrapper		<u>≤ 0.01</u>
										< 0.01
							7	leaves		< 0.01
										< 0.01
							1	wrapper leaves		3.70
										<u>5.80</u>
							7			1.50
1.80										
2004 <i>North Carolina</i> (Early J. Wakefield)	250 SC	0.15	0.10	147	4	1	control	< 0.01	WF-FR-04-5322	
							Heads, w/wrapper	<u>1.10</u>		
								1.00		
							7	leaves		0.09
										0.13
							1	Head, w/o wrapper		<u>≤ 0.01</u>
										< 0.01
							7	leaves		< 0.01
										< 0.01
							1	wrapper leaves		<u>1.90</u>
										1.90
							7			1.60
1.60										
2004 <i>Florida</i> (Bravo)	250 SC	0.15	0.077	195	4	0	control	< 0.01	VC-FR-04-5323	
							Heads, w/wrapper	2.60		
								1.50		
							1	leaves		<u>1.60</u>
										1.30
							3			0.93
										0.56
							5			0.29
										0.22
	0.22									
9		0.18								
		0.30								
0	Head, w/o wrapper	0.01								
		0.03								

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CABBAGE Year Location (variety)	Application					PHI days	Commodity	Residues, mg/kg mandipropamid	Ref. Reg.DocID. (Trial No.)
	Formulation	kg ai/ha	kg ai/hL	Water L/ha	No.				
						1	leaves	<u>0.05</u>	
								0.05	
						3		0.03	
								0.04	
						5		< 0.01	
								0.01	
						7		0.01	
								< 0.01	
						9		< 0.01	
								< 0.01	
						0	wrapper leaves	4.70	
								2.30	
						1		<u>2.90</u>	
								2.90	
						3		1.60	
								1.30	
						5		0.52	
								0.64	
						7		1.00	
								0.69	
9		0.60							
		0.64							
2004 Wisconsin (Vantage)	250 SC	0.15	0.083	181	4	1	control	< 0.01	NI-FR-04-5324
						1	Heads, w/wrapper	<u>1.80</u>	
								1.1	
						7	leaves	0.32	
								0.55	
						1	Head, w/o wrapper	0.19	
								<u>0.31</u>	
						7	leaves	< 0.01	
								< 0.01	
						1	wrapper leaves	3.55	
								<u>4.20</u>	
7		1.11							
		1.30							
2004 Texas (Solid Blue 780)	250 SC	0.15	0.083	184	4	1	control	< 0.01	SA-FR-04-5325
						1	Heads, w/wrapper	0.74	
								<u>1.11</u>	
						7	leaves	0.15	
								0.13	
						1	Head, w/o wrapper	<u>0.01</u>	
								< 0.01	
7	leaves	< 0.01							

CABBAGE Year Location (variety)	Application					PHI days	Commodity	Residues, mg/kg mandipropamid	Ref. Reg.DocID. (Trial No.)
	Formulation	kg ai/ha	kg ai/hL	Water L/ha	No.				
								< 0.01	
						1	wrapper leaves	2.20	
								<u>2.30</u>	
					7			0.41	
								0.32	
2004 <i>California</i> (Grenadier)	250 SC	0.151	0.081	187	4	1	control Heads, w/wrapper	< 0.01	WC-FR-04-5326
								0.41	
							<u>0.90</u>		
						7	leaves	0.23	
							0.21		
						1	Head, w/o wrapper	<u>≤ 0.01</u>	
							< 0.01		
						7	leaves	< 0.01	
							< 0.01		
						1	wrapper	<u>5.50</u>	
	leaves	4.40							
	2.50								
	3.10								

Cabbage w = Cabbage with wrapper leaves.

Cabbage w/o = Cabbage without wrapper leaves.

A total of five residue trials were carried out according to GAP ( $\pm 30\%$ ) in the United States between 2004 and 2005 (Joseph, T, Hamilton, LS, 2005, NOA/446510/0626). In all trials, mandipropamid (A12946C SC 250 g/L) was applied four times at 7–10 days intervals at a nominal rate of 142–180 g ai/ha as a foliar application to mustard greens. The water rate was between 22.7–303 L/ha. The PHI was 1 day. The residue data from the supervised trials is summarised in Table 41.

Table 41 Results of residue trials with mandipropamid conducted as a foliar application to mustard greens in US in 2004 and 2005 (Joseph, T, Hamilton, LS, 2005, NOA/446510/0626)

MUSTARD GREENS Year Location (variety)	Application					PHI days	Commodity	Residues, mg/kg mandipropamid	Ref. Reg.DocID. (Trial No.)
	Formulation	kg ai/ha	kg ai/hL	Water L/ha	No.				
2004 <i>Georgia</i> (Broadleaf)	250 SC	0.152	0.12	124	4	1	control Mustard Greens	< 0.01	SI-FR-04-5327
								3.80	
							<u>4.00</u>		
						7		0.37	
		0.90							
2004 <i>Illinois</i> (Southern Giant Curled)	250 SC	0.157	0.56	28.1	4	1	control Mustard Greens	< 0.01	4A-FR-04-5329
								<u>1.20</u>	
							0.99		
						7		0.23	
		0.39							

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MUSTARD GREENS Year Location (variety)	Application					PHI days	Commodity	Residues, mg/kg mandipropamid	Ref. Reg.DocID. (Trial No.)
	Formulation	kg ai/ha	kg ai/hL	Water L/ha	No.				
2004 <i>Texas</i> (Florida Broadleaf)	250 SC	0.15	0.082	184	4	0	control	< 0.01	SA-FR-04-5330
							Mustard	10.0	
							Greens	8.90	
								<u>4.50</u>	
								2.60	
								1.20	
								0.76	
								0.54	
								0.38	
								0.31	
								0.20	
	0.38								
	0.12								
2004 <i>California</i> (Florida Broad Leaf)	250 SC	0.151	0.051	298	4	1	control	< 0.01	2A-FR-04-5331
							Mustard	2.60	
							Greens	2.50	
								<u>4.50</u>	
	2.60								
2004 Louisiana (Florida Broadleaf)	250 SC	0.152	0.092	166	4	1	control	< 0.01	SD-FR-04-5332
							Mustard	<u>11.5</u>	
							Greens	11.0	
								5.70	
	5.40								

A total of seven residue trials were carried out according to GAP ( $\pm 30\%$ ) in the United States between 2004 (Joseph, T, Hamilton, LS, 2005, NOA/446510/0569). In all trials, mandipropamid (A12946C SC 250 g/L) was applied four times at 6–9 days intervals at a nominal rate of 148–158 g ai/ha as a foliar application to cucumbers. The water rate was between 18.7–287.4 L/ha. The PHI was 0 days. A summary of the residue data from the trials is given in Table 42.

Table 42 Results of residue trials with mandipropamid conducted as a foliar application to cucumbers in US in 2004 (Joseph, T, Hamilton, LS, 2005, NOA/446510/0569)

CUCUMBERS Year Location (variety)	Application					PHI days	Commodity	Residues, mg/kg mandipropamid	Ref. Reg.DocID. (Trial No.)
	Formulation	kg ai/ha	kg ai/hL	Water L/ha	No.				
2004 <i>Georgia</i> (Straight 8)	250 SC	0.15	0.13	121	4	0	control	< 0.01	S1-FR-04-5335
							fruit	<u>0.05</u>	
								0.02	
								0.01	
	0.02								
						7			

CUCUMBERS Year Location (variety)	Application					PHI days	Commodity	Residues, mg/kg mandipropamid	Ref. Reg.DocID. (Trial No.)
	Formulation	kg ai/ha	kg ai/hL	Water L/ha	No.				
2004 <i>North Carolina</i> (Poinsett 76)	250 SC	0.15	0.087	173	4	0	control	< 0.01	SJ-FR-04- 5336
							fruit	0.01	
								<u>0.02</u>	
								< 0.01	
						7		< 0.01	
2004 <i>Florida</i> (Straight)	250 SC	0.15	0.053	285	4	0	control	< 0.01	VC-FR-04- 5337
							fruit	<u>0.07</u>	
								0.07	
								< 0.01	
						7		< 0.01	
2004 <i>Michigan</i> (Marketmore 76)	250 SC	0.15	0.80	18.8	4	0	control	< 0.01	NL-FR-04- 5338
							fruit	<u>0.02</u>	
								< 0.01	
								0.01	
						7		0.01	
2004 <i>Wisconsin</i> (Marketmore 76)	250 SC	0.15	0.072	212	4	0	control	< 0.01	NI-FR-04- 5339
							fruit	<u>0.01</u>	
								< 0.01	
								< 0.01	
						7		< 0.01	
2004 <i>Texas</i> (Turbo)	250 SC	0.15	0.089	169	4	0	control	< 0.01	SA-FR-04- 5340
							fruit	<u>0.02</u>	
								< 0.01	
								< 0.01	
						7		< 0.01	
2004 <i>California</i> (Armenian Tard Long)	250 SC	0.15	0.053	283	4	0	control	< 0.01	WC-FR-04- 5341
							fruit	0.04	
								<u>0.05</u>	
								0.03	
								0.02	
								0.02	
						3		0.03	
						5		0.02	
						7		< 0.01	
						9		< 0.01	
								0.01	
								0.01	

A total of six residue trials were carried out according to GAP ( $\pm 30\%$ ) in the United States in 2004 (Joseph, T, Hamilton, LS, 2005, NOA/446510/0569). In all trials, mandipropamid (A12946C SC

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250 g/L) was applied four times at 6–8 days intervals at a rate of 138.6–156.8 g ai/ha as a foliar application to cantaloupe. The water rate was between 108.1–269.2 L/ha. The PHI was 0 day. A summary of the residue data from the trials is given in Table 43.

Table 43 Results of residue trials with mandipropamid conducted as a foliar application to cantaloupe in US in 2004 (Joseph, T, Hamilton, LS, 2005, NOA/446510/0569)

CANTALOUPE Year Location (variety)	Application					PHI days	Commodity	Residues, mg/kg mandipropamid	Ref. Reg.DocID. (Trial No.)
	Formulation	kg ai/ha	kg ai/hL	Water L/ha	No.				
2004 <i>Georgia</i> (Athena)	250 SC	0.15	0.057	264	4	0	control fruit	< 0.01	SI-FR-04-5342
								0.02	
								<u>0.07</u>	
								0.02	
2004 <i>Illinois</i> (Eclipse)	250 SC	0.15	0.11	135	4	0	control fruit	< 0.01	4A-FR-04-5343
								0.16	
								<u>0.19</u>	
								0.07	
2004 <i>Texas</i> (Caravelle)	250 SC	0.15	0.77	197	4	0	control fruit	< 0.01	SA-FR-04-5344
								<u>0.11</u>	
								0.08	
								0.06	
2004 <i>California</i> (Hale's Best Jumbo)	250 SC	0.15	0.11	133	4	0	control fruit	< 0.01	WC-FR-04-5345
								<u>0.12</u>	
								0.10	
						3		0.10	
								0.03	
								0.03	
						5		0.03	
								0.03	
								0.03	
7	0.05								
	0.03								
	0.04								
9	0.04								
	0.03								
	0.03								
2004 <i>California</i> (Durango)	250 SC	0.15	0.11	142	4	0	control fruit	< 0.01	WD-FR-04-5346
								0.05	
								0.03	
								0.05	
2004 <i>California</i> (Top Mark)	250 SC	0.15	0.11	141	4	0	control fruit	< 0.01	WD-FR-04-5347
								0.20	
								<u>0.26</u>	
								0.07	
7	0.07								
	0.02								



A total of five residue trials were carried out according to GAP ( $\pm 30\%$ ) in the United States in 2004 (Joseph, T, Hamilton, LS, 2005, NOA/446510/0569). In all trials, mandipropamid (A12946C SC 250 g/L) was applied four times at 5–9 days intervals at a rate of 145.7–158.0 g ai/ha as a foliar application to summer squash. The water rate was between 22.7–391.0 L/ha. The PHI was 0 day. A summary of the residue data from the trials is given in Table 44.

Table 44 Results of residue trials with mandipropamid conducted as a foliar application to summer squash in US in 2004 (Joseph, T, Hamilton, LS, 2005, NOA/446510/0569)

SQUASH Year Location (variety)	Application					PHI days	Commodity	Residues, mg/kg mandipropamid	Ref. Reg.DocID. (Trial No.)
	Formulation	kg ai/ha	kg ai/hL	Water L/ha	No.				
2004 <i>New York</i> (Yellow Straight)	250 SC	0.15	0.039	382	4	0	control fruit	< 0.01 0.02 <u>0.04</u> < 0.01 < 0.01	5E-FR-04- 5348
2004 <i>South Carolina</i> (Lemondrop L)	250 SC	0.15	0.050	301	4	0	control fruit	< 0.01 0.06 <u>0.08</u> 0.01 < 0.01	SJ-FR-04- 5349
2004 <i>Florida</i> (Early Yellow Crookneck)	250 SC	0.15	0.055	281	4	0	control fruit	< 0.01 0.05 <u>0.07</u> < 0.01 < 0.01	VC-FR-04- 5350
2004 <i>Illinois</i> (Ambassador)	250 SC	0.15	0.65	23.3	4	0	control fruit	< 0.01 0.02 <u>0.03</u> < 0.01 < 0.01	4A-FR-04- 5351
2004 <i>California</i> (Yellow Crookneck)	250 SC	0.15	0.064	234	4	0	control fruit	< 0.01 < 0.01 <u>0.02</u> < 0.01 0.02 < 0.01 < 0.01 < 0.01 < 0.01 < 0.01 < 0.01	WC-FR-04- 5352

A total of 11 residue trials were carried out according to GAP ( $\pm 30\%$ ) in the United States between 2003 and 2004 (Joseph, T, Hamilton, LS, 2005, NOA/446510/0566). In all trials,

mandipropamid (A12946C SC 250 g/L) was applied four times at 6–8 days intervals at a nominal rate of 135–158 g ai/ha as a foliar application to tomatoes. The water rate was between 157.1–699.7 L/ha. The PHI was 1 day. A summary of the residue data from the trials is given in Table 45

Table 45 Results of residue trials with mandipropamid conducted as a foliar application to tomatoes in US in 2003 and 2004 (Joseph, T, Hamilton, LS, 2005, NOA/446510/0566)

TOMATOES Year Location (variety)	Application					PHI days	Commodity	Residues, mg/kg mandipropamid	Ref. Reg.DocID. (Trial No.)
	Formulation	kg ai/ha	kg ai/hL	Water L/ha	No.				
2003 <i>New York</i> (Sebring)	250 SC	0.15	0.053	283	4	1  3	control fruit	< 0.01 0.02 <u>0.02</u> < 0.01 0.01	E5-FR-002-03
2003 <i>Illinois</i> (Roma)	250 SC	0.16	0.096	163	4	1  3	control fruit	< 0.01 0.06 <u>0.06</u> 0.02 0.02	N4-FR-006-03
2003 <i>South Carolina</i> (Celebrity)	250 SC	0.15	0.046	329	4	0  1	control fruit	< 0.01 0.10 0.10 <u>0.12</u>	SJ-FR-002-03
						2  3  4		0.08 0.02 0.07 0.05 0.05 0.02 0.06	
2004 <i>Florida</i> (Grande)	250 SC	0.15	0.035	429	4	1  3	control fruit	< 0.01 <u>0.20</u> 0.16 0.06 0.09	VB-FR-001-04
2003 <i>Florida</i> (Florida 47)	250 SC	0.15	0.043	347	4	1  3	control fruit	< 0.01 <u>0.09</u> 0.07 0.01 0.02	VB-FR-202-03
2003 <i>California</i> (Mountain Fresh)	250 SC	0.15	0.080	187	4	1  3	control fruit	< 0.01 0.03 <u>0.03</u> 0.02 0.03	WA-FR-001-03
2003 <i>California</i> (Bobcat)	250 SC	0.15	0.081	187	4	1	control fruit	< 0.01 0.03 <u>0.06</u>	WC-FR-002-03

TOMATOES Year Location (variety)	Application					PHI days	Commodity	Residues, mg/kg mandipropamid	Ref. Reg.DocID. (Trial No.)
	Formulation	kg ai/ha	kg ai/hL	Water L/ha	No.				
						3		0.04 0.02	
2003 <i>California</i> (830 (Roma))	250 SC	0.15	0.075	202	4	1	control fruit	< 0.01 0.02 0.03 0.03 <u>0.05</u> <u>0.06</u> 0.08 0.09 0.38	WC-FR-003-03
2003 <i>California</i> (U-941)	250 SC	0.15	0.022	666	4	1 3	control fruit	< 0.01 <u>0.06</u> 0.04 0.05 0.04	WC-FR-004-03
2003 <i>California</i> (9888)	250 SC	0.15	0.081	187	4	1	control fruit	< 0.01 0.04 0.06	WD-FR-002-03
		0.75	0.40	187		3 3		0.05 <u>0.08</u> 0.02 0.26 0.32 0.24 0.28	
2003 <i>California</i> (9888)	250 SC	0.15	0.081	186	4	0 1 2 3 4	control fruit	< 0.01 0.03 <u>0.03</u> 0.03 0.03 0.02 0.02 0.02 0.02 < 0.01 < 0.01	WD-FR-003-03

A total of nine residue trials were carried out according to GAP ( $\pm 30\%$ ) in the United States in 2003 (Joseph, T, Hamilton, LS, 2005, NOA/446510/0566). In all trials, mandipropamid (A12946C SC 250 g/L) was applied four times at 6–8 days intervals at a nominal rate of 133.6–157.3 g ai/ha as a foliar application to peppers. The water rate was between 18.6–369.1 L/ha. The PHI was 1 day. A summary of the residue data from the trials is given in Table 46.

Table 46 Results of residue trials with mandipropamid conducted as a foliar application to peppers in US in 2003 (Joseph, T, Hamilton, LS, 2005, NOA/446510/0566)

PEPPERS Year <i>Location</i> (variety)	Application					PHI days	Commodity	Residues, mg/kg mandipropamid	Ref. Reg.DocID.
	Formulation	kg ai/ha	kg ai/hL	Water L/ha	No.				
2003 <i>Illinois</i> (Capistrano) Pepper, Bell	250 SC	0.14	0.097	148	4	1 3	control fruit	< 0.01 <u>0.04</u> 0.04 0.03 0.03	<i>N4-FR-005-03</i>
2003 <i>Texas</i> (Taurus) Pepper, Bell	250 SC	0.15	0.097	156	4	1 3	control fruit	< 0.01 0.04 <u>0.07</u> 0.05 0.05	<i>SA-FR-001-03</i>
2003 <i>Texas</i> (Jalapeno M) Pepper, Hot	250 SC	0.15	0.079	192	4	1 3	control fruit	< 0.01 <u>0.38</u> 0.37 0.22 0.26	<i>SA-FR-002-03</i>
2003 <i>New Mexico</i> (Big Jim) Pepper, Hot	250 SC	0.15	0.070	218	4	1 3	control fruit	< 0.01 <u>0.11</u> 0.06 0.07 0.05	<i>SC-FR-001-03</i>
2003 <i>North Carolina</i> (HMX 1640 F1 (Heritage)) Pepper, Bell	250 SC	0.15	0.80	18.7	4	1 3	control fruit	< 0.01 <u>0.17</u> 0.09 0.08 0.06	<i>SJ-FR-003-03</i>
2004 <i>Florida</i> (Brigadier) Pepper, Bell	250 SC	0.15	0.043	352	4	1 3	control fruit	< 0.01 0.32 <u>0.34</u> 0.26 0.29	<i>VB-FR-203-03</i>
2004 <i>California</i> (Habanero) Pepper, Hot	250 SC	0.15	0.050	301	4	1 3	control fruit	< 0.01 0.11 <u>0.22</u> 0.08 0.14	<i>2A-FR-04-5621</i>



## Mandipropamid

LETTUCE Year Location (variety)	Application					PHI days	Commodity	Residues, mg/kg	Ref. Reg.DocID.
	Formulation	kg ai/ha	kg ai/hL	Water L/ha	No.				
2005  <i>Florida</i> (Ideal)	250 SC	0.15	0.77	19.4	4	1 7	control  leaves	< 0.01  3.10 <u>4.50</u> 1.10 1.30	VF-FR-05- 6031
2005  <i>Arizona</i> (Bergam Green)	250 SC	0.15	0.054	282	4	1 7	control  leaves	< 0.01  5.10 <u>5.30</u> 3.10 4.20	WA-FR-05- 6032
2005  <i>California</i> (Hacienda)	250 SC	0.15	0.050	301	4	1 7	control  leaves	< 0.01  5.70 <u>7.80</u> 2.10 3.70	2A-FR-05- 6033
2005  <i>California</i> (Pacheo)	250 SC	0.15	0.046	325	4	1 7	control  leaves	< 0.01  1.10 <u>1.90</u> 0.18 0.28	WC-FR-05- 6034
2005  <i>California</i> (Weston)	250 SC	0.15	0.072	212	4	1 7	control  leaves	< 0.01  <u>5.70</u> 4.50 1.70 1.80	WC-FR-05- 6054
HEAD LETTUCE									
2005  <i>New York</i> (Ithaca)	250 SC	0.15	0.096	155	4	1 7 1 7 1 7	control  heads, w/wrapper  leaves  head, w/o wrapper  leaves  wrapper  leaves	< 0.01  <u>2.70</u> 2.50 0.58 0.76 0.76 1.10 0.02 0.09 8.90 7.80 0.87 1.30	5E-FR-05- 6036

LETTUCE Year Location (variety)	Application					PHI days	Commodity	Residues, mg/kg	Ref. Reg.DocID.
	Formulation	kg ai/ha	kg ai/hL	Water L/ha	No.				
2005 <i>Arizona</i> (Sahara)	250 SC	0.15	0.054	280	4		control	< 0.01	WA-FR-05- 6038
						1	heads, w/wrapper	7.00 <u>9.60</u>	
						7	leaves	0.44 0.37	
						1	head, w/o wrapper	0.12 0.20	
						7	leaves	0.02 < 0.01	
						1	wrapper leaves	7.40 3.30	
						7		6.00 6.80	
2005 <i>California</i> (Sun Devil)	250 SC	0.15	0.050	300	4		control	< 0.01	2A-FR-05- 6039
						0	heads, w/wrapper	2.10 1.50	
						1	leaves	4.10 <u>6.10</u>	
						3		1.70 4.2	
						5		0.96 3.90	
						7		1.20 0.75	
						9		1.90 1.70	
						0	head, w/o wrapper	0.04 0.05	
						1	leaves	0.04 0.12	
						3		0.01 < 0.01	
						5		0.04 0.02	
						7		< 0.01 < 0.01	
						9		< 0.01 < 0.01	
						0	wrapper leaves	12.0 9.80	
						1		12.8	

## Mandipropamid

LETTUCE Year Location (variety)	Application					PHI days	Commodity	Residues, mg/kg	Ref. Reg.DocID.
	Formulation	kg ai/ha	kg ai/hL	Water L/ha	No.				
						3		10.7 10.6 7.30	
						5		10.2 7.80	
						7		7.00 5.10	
						9		3.80 5.50	
2005 <i>California</i> (Grand Slam)	250 SC	0.16	0.044	335	4		control	< 0.01	WC-FR-05- 6040
						1	heads, w/wrapper	<u>1.60</u> 0.98	
						7	leaves	0.68 0.64	
						1	head, w/o	0.06	
						7	wrapper leaves	0.07 < 0.01	
						1	wrapper leaves	0.02 6.90	
						7		6.00 3.10 3.40	
2005 <i>California</i> (Jupiter)	250 SC	0.15	0.040	387	4		control	< 0.01	WA-FR-05- 6041
						1	heads, w/wrapper	2.70 2.00	
						7	leaves	<u>3.50</u> 1.70	
						1	head, w/o wrapper	0.07 0.02	
						7	leaves	< 0.01 0.02	
						1	wrapper leaves	7.40 8.60	
						7		7.10 10.4	

A total of six residue trials were carried out according to GAP ( $\pm 30\%$ ) in the United States in 2005 (Joseph, T, Hamilton, LS, 2007, NOA/446510/1075). In all trials, mandipropamid (NOA-446510 SC 250 g/L) was applied four times at 7 days intervals at a rate of 151.2 g ai/ha as a foliar application to celery. The water rate was between 19–468 L/ha. The PHI was 1 days. A summary of the residue data from the trials is given in Table 48.



Table 48 Results of residue trials with mandipropamid conducted as a foliar application to celery in US in 2005 (Joseph, T, Hamilton, LS, 2007, NOA/446510/1075)

CELERY Year Location (variety)	Application					PHI days	Commodity	Residues, mg/kg mandipropamid	Ref. Reg.DocID. (Trial No.)
	Formulation	kg ai/ha	kg ai/hL	Water L/ha	No.				
2005  <i>Florida</i> (Utah Tail)	250 SC	0.15	0.032	462	4		control	< 0.01	VA-FR-05-6042
						1	leaf stalks	5.00	
						7		<u>6.40</u> 1.40 1.40	
2005  <i>Michigan</i> (Greenbay)	250 SC	0.15	0.81	18.7	4		control	< 0.01	NL-FR-05-6043
						1	leaf stalks	<u>1.80</u>	
						7		1.30 0.98	
								0.54	
2005  <i>California</i> (Sonora)	250 SC	0.15	0.080	192	4		control	< 0.01	WC-FR-05-6044
						0	leaf stalks	3.20	
						1		7.40 <u>3.60</u> 3.40	
						3		1.70	
						5		2.90	
						7		1.30	
						9		2.90	
								1.50	
								1.60	
		0.62							
		0.83							
2005  <i>California</i> (T&A 29-1)	250 SC	0.16	0.089	175	4		control	< 0.01	WC-FR-05-6045
						1	leaf stalks	0.38	
						7		<u>0.74</u> 0.87 0.75	
2005  <i>California</i> (Conquistador)	250 SC	0.15	0.040	375	4		control	< 0.01	WC-FR-05-6046
						1	leaf stalks	<u>1.60</u>	
						7		1.10 0.93 0.91	
2005  <i>California</i> (Conquistador)	250 SC	0.15	0.036	417	4		control	< 0.01	WC-FR-05-6047
						1	leaf stalks	<u>7.80</u>	
						7		4.50 2.20 1.40	

## Mandipropamid

A total of six residue trials were carried out according to GAP ( $\pm 30\%$ ) in the United States in 2005 (Joseph, T, Hamilton, LS, 2007, NOA/446510/1075). In all trials, mandipropamid (NOA-446510 SC 250 g/L) was applied four times at 7 days intervals at a rate of 151.2 g ai/ha as a foliar application to spinach. The water rate was between 19–468 L/ha. The PHI was 1 days. A summary of the residue data from the trials is given in Table 49.

Table 49 Results of residue trials with mandipropamid conducted as a foliar application to spinach in US in 2005 (Joseph, T, Hamilton, LS, 2007, NOA/446510/1075)

SPINACH Year Location (variety)	Application					PHI days	Commodity	Residues, mg/kg mandipropamid	Ref. Reg.DocID. (Trial No.)
	Formulation	kg ai/ha	kg ai/hL	Water L/ha	No.				
2005  <i>New York</i> (Melody)	250 SC	0.16	0.81	19.3	4		control	< 0.01	5E-FR-05-6048
						1	leaves	10.3	
						7		<u>10.9</u> 2.80 1.40	
2005  <i>New Jersey</i> (Tyee)	250 SC	0.16	0.059	266	4		control	< 0.01	EB-FR-05-6049
						0	leaves	12.3	
						1		11.9	
								10.4	
						3		<u>11.0</u>	
								4.70	
						5		4.80	
								4.90	
						7		4.50	
9		3.10 3.00 2.60 1.40							
2005  <i>Texas</i> (Melody)	250 SC	0.15	0.086	179	4		control	< 0.01	SA-FR-05-6050
						1	leaves	7.40	
						7		<u>8.20</u> 2.00 1.60	
2005  <i>Colorado</i> (Melody)	250 SC	0.15	0.10	151	4		control	< 0.01	NM-FR-05-6051
						1	leaves	<u>10.2</u>	
						7		9.20 2.90 2.40	
2005  <i>California</i> (Hybrid 424)	250 SC	0.15	0.080	188	4		control	< 0.01	WC-FR-05-6052
						1	leaf stalks	9.10	
						7		<u>9.90</u> 4.10	

SPINACH Year Location (variety)	Application					PHI days	Commodity	Residues, mg/kg mandipropamid	Ref. Reg.DocID. (Trial No.)
	Formulation	kg ai/ha	kg ai/hL	Water L/ha	No.				
								4.20	
2005  California (Tigercat)	250 SC	0.16	0.078	199	4		control	< 0.01	WC-FR-05- 6053
						1	leaf stalks	<u>5.60</u>	
								5.10	
						7		1.30	
								1.50	

A total of 16 residue trials were carried out according to GAP ( $\pm 30\%$ ) in Europe (eight in the South and eight in the North) in 2003 and 2004 (Gill, JP, 2005, NOA/446510/0295; Gardinal, P, Ryan, J, 2004, NOA/446510/0176; Gardinal, P, Ryan, J, 2004, NOA/446510/0175; Gardinal, P, Ryan, J, 2004, NOA/446510/0177; Gill, JP, 2005, NOA/446510/0296; Kühne, RO, 2005, NOA/446510/0072; Gill, J P, 2005, NOA/446510/0328; Gill, JP, 2005, NOA/446510/0320; Gill, JP, 2005, NOA/446510/0329; Gill, JP, 2005, NOA/446510/0321; Gardinal, P, Ryan, J, 2004, NOA/446510/0186; Simon, P, 2005, NOA/446510/0222; Gardinal, P, Ryan, J, 2004, NOA/446510/0178; Gill, JP, 2005, NOA/446510/0322; Ryan, J, 2005, NOA/446510/0269; Ryan, J, 2005, NOA/446510/0270). In all trials, mandipropamid (A12975 EC 120 g/L) was applied six times at 6–9 day intervals at a rate of 142–165 g ai/ha as a foliar application to potatoes. The water rate was between 200–622 L/ha. The PHI was 2–3 days. A summary of the residue data from the trials is given in Table 50.

Table 50 Results of residue trials with mandipropamid conducted as a foliar application to potatoes in Europe between 2002 and 2005 (Gill, JP, 2005, NOA/446510/0295; Gardinal, P, Ryan, J, 2004, NOA/446510/0176; Gardinal, P, Ryan, J, 2004, NOA/446510/0175; Gardinal, P, Ryan, J, 2004, NOA/446510/0177; Gill, JP, 2005, NOA/446510/0296; Kühne, RO, 2005, NOA/446510/0072; Gill, J P, 2005, NOA/446510/0328; Gill, JP, 2005, NOA/446510/0320; Gill, JP, 2005, NOA/446510/0329; Gill, JP, 2005, NOA/446510/0321; Gardinal, P, Ryan, J, 2004, NOA/446510/0186; Simon, P, 2005, NOA/446510/0222; Gardinal, P, Ryan, J, 2004, NOA/446510/0178; Gill, JP, 2005, NOA/446510/0322; Ryan, J, 2005, NOA/446510/0269; Ryan, J, 2005, NOA/446510/0270)

POTATOES Country, Year Location (variety)	Application					PHI days	Commodity	Residues, mg/kg mandipropamid	Ref. Reg.DocID. (Trial No.)
	Formulation	kg ai/ha	kg ai/hL	Water L/ha	No.				
Spain, 2004  Seville (Carlita) Southern Europe	250 SC	0.153	0.030	509	6		control	< 0.01	ES-FR-04- 0013
						0	tuber	< 0.01	
						3		<u><math>\leq 0.01</math></u>	
						6		< 0.01	
						13		< 0.01	
						19		< 0.01	
France, 2003  Glisy (Bintje) Northern Europe	250 SC	0.157	0.052	300	6		control	< 0.01	03-6039
						0	tuber	< 0.01	
						3		<u><math>\leq 0.01</math></u>	
						7		< 0.01	
						14		< 0.01	
						22		< 0.01	

## Mandipropamid

POTATOES Country, Year <i>Location</i> (variety)	Application					PHI days	Commodity	Residues, mg/kg mandipropamid	Ref. Reg.DocID. (Trial No.)
	Formulation	kg ai/ha	kg ai/hL	Water L/ha	No.				
UK, 2004 <i>Duxford</i> (King Edward) Northern Europe	250 SC	0.15	0.075	200	6	0 3 7 14 21	control tuber	< 0.01 < 0.01 <u>≤ 0.01</u> < 0.01 < 0.01 < 0.01	03-6038
France, 2003 <i>Alpes de Hautes</i> (Agata) Southern Europe	250 SC	0.151	0.038	400	6	0 2 7 14 21	control tuber	< 0.01 < 0.01 <u>≤ 0.01</u> < 0.01 < 0.01 < 0.01	03-6040
Italy, 2004 <i>Pavia</i> (Lisetta) Southern Europe	250 SC	0.156	0.032	488	6	0 3 7 14 21	control tuber	< 0.01 < 0.01 <u>≤ 0.01</u> < 0.01 < 0.01 < 0.01	IT-FR-04-0170
Switzerland, 2002 <i>Vouvry</i> (Bintje) Northern Europe	250 SC	0.154	0.030	515	6	0 7 10 14 21	control tuber	< 0.01 <u>≤ 0.01</u> < 0.01 < 0.01 < 0.01 < 0.01	02-2011
France, 2004 <i>Somme</i> (Marabel) Northern Europe	250 SC	0.148	0.049	300	6	0 3 7 14 21	control tuber	< 0.01 < 0.01 <u>≤ 0.01</u> < 0.01 < 0.01 < 0.01	FR-FR-04-0166
UK, 2004 <i>Nottingham</i> (Cara) Northern Europe	250 SC	0.148	0.025	592	6	0 3 7 14 21	control tuber	< 0.01 < 0.01 <u>≤ 0.01</u> < 0.01 < 0.01 < 0.01	AF/8238/SY/1
France, 2004 <i>Alpes de Hautes</i>	250 SC	0.15	0.030	500	6	0	control tuber	< 0.01 < 0.01	FR-FR-04-0167

POTATOES Country, Year <i>Location</i> (variety)	Application					PHI days	Commodity	Residues, mg/kg mandipropamid	Ref. Reg.DocID. (Trial No.)
	Formulation	kg ai/ha	kg ai/hL	Water L/ha	No.				
(Berbere) Southern Europe						3 7		<u>≤ 0.01</u> < 0.01	
						14 21		< 0.01 < 0.01	
France, 2004 <i>Tar-et-Garonne</i> (Mona Lisa) Southern Europe	250 SC	0.153	0.051	300	6	0 3 7 14 21	control  tuber	< 0.01  < 0.01 <u>≤ 0.01</u> < 0.01 < 0.01 < 0.01	FR-FR-04- 0168
Netherlands, 2004 <i>Hank</i> (Bintje) Northern Europe	250 SC	0.155	0.060	259	6	0 3 7 14 21	control  tuber	< 0.01  0.02 <u>0.01</u> < 0.01 < 0.01 < 0.01	NL-FR-04- 0082
Switzerland, 2003 <i>Vouvry</i> (Bintje) Northern Europe	250 SC	0.155	0.030	518	6	0 3 7 14 21	control  tuber	< 0.01  < 0.01 <u>≤ 0.01</u> < 0.01 < 0.01 < 0.01	03-6042
Germany, 2003 <i>Großweitzschen- Niederranschütz</i> (Karlana) Northern Europe	250 SC	0.15	0.050	300	6	0 3 7 14 21	control  tuber	< 0.01  < 0.01 <u>≤ 0.01</u> < 0.01 < 0.01 < 0.01	gpo343103
France, 2003 <i>Grisolles</i> (Bintje) Southern Europe	250 SC	0.154	0.077	200	6	0 3 7 14 21	control  tuber	< 0.01  < 0.01 <u>≤ 0.01</u> < 0.01 < 0.01 < 0.01	03-6041
Switzerland, 2004 <i>Vouvry</i> (Bintje) Northern Europe	250 SC	0.151	0.025	603	6	0 3 7	control  tuber	< 0.01  < 0.01 <u>≤ 0.01</u> < 0.01	CH-FR-04- 0081

POTATOES Country, Year <i>Location</i> (variety)	Application					PHI days	Commodity	Residues, mg/kg mandipropamid	Ref. Reg.DocID. (Trial No.)
	Formulation	kg ai/ha	kg ai/hL	Water L/ha	No.				
						14 21		< 0.01 < 0.01	
Spain, 2003 <i>Madrid</i> (Red Pontiac) Southern Europe	250 SC	0.151	0.038	400	6	0 3 7 14 21	control tuber	< 0.01 < 0.01 <u>&lt; 0.01</u> < 0.01 < 0.01 < 0.01	03-6006
Spain, 2003 <i>Sevilla</i> (Monalisa) Southern Europe	250 SC	0.156	0.040	391	6	0 3 8 15 22	control tuber	< 0.01 0.01 <u>&lt; 0.01</u> < 0.01 < 0.01 < 0.01	03-6005

## FATE OF RESIDUES IN STORAGE AND PROCESSING

### *In processing*

The Meeting received information on the fate of mandipropamid residues during aqueous hydrolysis under conditions of pasteurisation and baking, brewing and boiling and sterilisation. Information was also provided on the fate of mandipropamid residues during the food processing of grapes and tomatoes.

An aqueous high temperature hydrolysis study was conducted during 2004 (McGill, C, 2004, NOA/446510/0208). [<sup>14</sup>C]-mandipropamid uniformly labelled in either the chlorophenyl ring or the methoxyphenyl ring was dissolved in aqueous sodium acetate buffers to produce solutions. The concentration of mandipropamid in all experiments ranged from 1.79 µg/mL to 2.30 µg/mL. For each radiolabel duplicate solutions were prepared at pH 4, 5 and 6 and were heated to temperatures of 90, 100 and 120°C for 20, 60 and 20 minutes respectively. These conditions are considered to be representative of pasteurisation, baking/brewing/boiling and sterilisation processes (Table 51). Solutions were allowed to cool prior to analysis. Solutions of the test materials at the same concentrations and pHs as the test substances were maintained at ambient temperature for 1 hour to act as controls. All solutions were shielded from light to minimise any photolytic effects. At time 0 and after 20 or 60 minutes incubation, the samples were taken and analysed by TLC and confirmed by HPLC.

Table 51 Hydrolysis products of mandipropamid at simulated processing (McGill, C, 2004, NOA/446510/0208)

Temperature (°C)	Time (min)	pH	Process Represented
90	20	4	Pasteurisation
100	60	5	Baking, Brewing, Boiling
120	20	6	Sterilisation

The recoveries of applied radioactivity were between 87.8% and 111.3% for the controls and between 98.9% and 115.9% for the heated samples. These results indicated that there were no losses

of radioactivity during the experimental procedures. Mandipropamid accounted for greater than 95% of the radioactivity present in each hydrolysate and control sample. No other discrete components were detected in any of the TLC systems and the identity of mandipropamid was further confirmed by HPLC. Mandipropamid is concluded to be hydrolytically stable under conditions representative of pasteurization, baking/brewing/boiling and sterilization. A summary of the radioactive recoveries is shown in Table 52.

Table 52 Radioactive recovery for hydrolysates of mandipropamid at simulated processing (McGill, C, 2004, NOA/446510/0208)

Hydrolysis conditions	Label	%Reactive Recovery <sup>a</sup>	<sup>14</sup> C-mandipropamid <sup>b</sup>	Remainder <sup>b</sup>
pH6, 120 °C	Chlorophenyl	109.3	104.2	5.1
		115.9	111.1	4.9
pH5, 100 °C	Chlorophenyl	98.9	95.7	3.3
		107.8	103.9	4.0
pH4, 90 °C	Chlorophenyl	108.8	105.9	3.0
		101.2	99.8	1.5
pH6, 120 °C	Methoxyphenyl	109.8	107.1	2.9
		108.4	106.4	2.1
pH5, 100 °C	Methoxyphenyl	103.7	101.1	2.6
		104.1	102.1	2.1
pH4, 90 °C	Methoxyphenyl	104.2	102.4	1.8
		103.5	102.9	0.7

<sup>a</sup> % figures from LSC assay of reaction solutions.

<sup>b</sup> % figures for identified components based on mean average from TLC data, may vary slightly from LSC due to rounding errors, does not include any discrete components.

A residue field trial was conducted in Northern France during 2003, in which mandipropamid formulated as A-12946 C, a suspension concentrate (SC) containing 250 g mandipropamid per litre, was applied to grapes (Ryan, J, 2005, NOA446510/0355). Four applications, separated by intervals of 10–11 days, were made at a concentration of 15 g ai/hL using a water volume of 1000 L/ha. Twenty-two days after the final application samples (approximately 100 kg) of treated and untreated grape bunches were harvested and transported at ambient temperature to the processing facility.

Two mass balance processing studies were conducted where the grape bunches were processed into red wine using either a ‘maceration’ process or a ‘heating of the must’ process. One mass balance and one follow-up processing studies were conducted and the grape bunches were processed into red grape juice. Samples of grape bunches prior to processing, and wine, juice and many of the intermediates and processing by-products were analysed for residues of mandipropamid using method RAM 415/01. The mandipropamid residues in grapes prior to processing and in wine, grape juice and wet and dry pomace are presented in Table 53.

Table 53 Mandipropamid residues in grape and processed fractions resulting from supervised trials in France (Ryan, J, 2005, NOA446510/0355)

GRAPES Country, Year, location (variety)	Application					PHI days	Commodity	Residues, mg/kg mandipropamid	Ref
	Form	kg ai/ha	kg ai/hL	water (L/ha)	no.				
France, 2003 <i>Maisdon</i> (Muscadet)	250 SC	0.15	0.015	1000	4	22	whole fruit	0.08 <sup>a</sup>	03-6062 By maceration
							young wine	0.01	
							6 month wine	0.01	

GRAPES Country, Year, location (variety)	Application					PHI days	Commodity	Residues, mg/kg mandipropamid	Ref
	Form	kg ai/ha	kg ai/hL	water (L/ha)	no.				
							wet pomace dry pomace	0.23 0.62	
							young wine 6 month wine wet pomace dry pomace	< 0.01 < 0.01 0.19 0.55	By heating of the must
							pasteurised juice wet pomace dry pomace	0.02 0.15 0.39	From grape juice
							pasteurised juice wet pomace dry pomace	0.02 0.21 0.54	From grape juice

<sup>a</sup> Mean mandipropamid residue on grape bunches prior to processing

Two residue field trials were conducted in California, USA during 2003, in which mandipropamid formulated as A-12946 C, a suspension concentrate (SC) containing 250 g mandipropamid per litre, was applied to grapes (Joseph, T, 2005, NOA446510/0424). In each trial two treated plots were present; each received four applications, separated by intervals of 6–7 days, at rates of 149–157 g ai/ha to the first (1×) treated plot and at 752–783 g ai/ha to the second (5×) treated plot. Samples of treated and untreated grapes were harvested 14 days after the final application from one trial and 28 days after the final application from the second trial. The samples were then transported at ambient temperature to the processing facility.

Two follow-up processing studies were conducted where grapes were processed into white wine, grape juice and raisins. Samples of grapes, prior to processing, wine, juice and raisins were analysed for residues of mandipropamid by method RAM 415/01 with some minor modifications. The mandipropamid residues in grape bunches, prior to processing, and in wine, grape juice and wet and dry pomace are presented in Table 54.

Table 54 Mandipropamid residues in grapes and processed fractions resulting from supervised trials in USA (Joseph, T, 2005, NOA446510/0424)

GRAPES Year Location (variety)	Application					PHI days	Commodity	Residues, mg/kg mandipropamid	Ref
	Form	kg ai/ha	kg ai/hL	water (L/ha)	no.				
2003 California (Red Flames (Seedless))	250 SC	0.15	0.012	1227	4	14	control	< 0.01	WC-FR-006-03
							whole fruit	0.21 <sup>a</sup>	
							juice	0.05	
							raisin	0.44	
							young wine	0.23	
	aged wine	0.39							
	0.76	0.062	1226	4	14	whole fruit	0.46 <sup>a</sup>		
						juice	0.34		
						raisin	3.50		



GRAPES Year Location (variety)	Application					PHI days	Commodity	Residues, mg/kg mandipropamid	Ref
	Form	kg ai/ha	kg ai/hL	water (L/ha)	no.				
							young wine aged wine	1.30 1.40	
2003 <i>California</i> (Thompson seedless)	250 SC	0.15	0.014	1073	4	28	control	< 0.01	WC-FR-007-03
whole fruit juice raisin young wine aged wine							0.36 0.07 1.60 0.35 0.23		
	0.77	0.072	1070	4	28	whole fruit juice raisin young wine aged wine	1.10 0.45 4.30 1.10 0.94		

<sup>a</sup> Mean mandipropamid residue on grape prior to processing.

A residue field trial was conducted in Greece during 2004 in which mandipropamid formulated as A-12946 C, a suspension concentrate (SC) containing 250 g mandipropamid per litre, was applied to grapes (Ryan J, 2005, NOA446510/0430). Two applications, separated by an interval of 10 days, were made at 299 g ai/ha. Ten days after the final application samples of treated and untreated grape bunches were harvested.

One mass balance and three follow-up processing studies were conducted where the grape bunches were processed into raisins. Grapes bunches were dried in the sun for 15 days after which raisins and stems were collected. Samples of grapes, prior to processing, and raisins with stems were analysed for residues of mandipropamid using method RAM 415/01. The mandipropamid residues in grape bunches prior to processing, and in wine, grape juice and wet and dry pomace are presented in Table 55.

Table 55 Mandipropamid residues in grapes and processed fractions resulting from supervised trials in Greece (Ryan, J, 2005, NOA446510/0430)

GRAPES Year Location (variety)	Application					PHI days	Commodity	Residues, mg/kg mandipropamid	Ref
	Form	kg ai/ha	kg ai/hL	water (L/ha)	no.				
2004 <i>Dendro Korinthias</i> (cv Black Corinth)	250 SC	0.30	0.030	996	2	10	control	< 0.01	
						fruit	0.54		
25						raisin	1.80 <sup>a</sup>		

<sup>a</sup> Mean mandipropamid residue on raisin.

A residue field trial was conducted in Southern France during 2004, in which mandipropamid formulated as A-12946 C, a suspension concentrate (SC) containing 250 g mandipropamid per litre, was applied to tomatoes (Gill, JP, 2005, NOA446510/0436). Four applications, separated by an interval of 7 days, were made at rates of 490–515 g ai/ha. Three days after the final application samples (approximately 100 kg) of treated and untreated tomatoes were harvested and transported at ambient temperature to the processing facility.

One mass balance and three follow-up processing studies were conducted where the tomatoes were processed into tomato juice, tomato puree, canned tomatoes and washed tomatoes. Samples of tomatoes prior to processing and tomato juice, tomato puree, canned tomatoes and washed tomatoes and many of the intermediates and processing by-products were analysed for residues of mandipropamid using method RAM 415/01. The mandipropamid residues in tomatoes prior to processing and in washed tomatoes, canned tomatoes, tomato puree and tomato juice are presented in Table 56.

Table 56 Mandipropamid residues in tomatoes and processed fractions resulting from supervised trials in France (Gill, JP, 2005, NOA446510/0436)

TOMATOES  Year Location (variety)	Application					PHI days	Commodity	Residues, mg/kg mandipropamid	Ref	
	Form	kg ai/ha	kg ai/hL	water (L/ha)	no.					
2004 <i>Hérault</i> (Isola)	250 SC	0.50	0.13	400	4	3	control	< 0.01	FR-FR-04-0129B	
							unwashed fruit	0.36 <sup>a</sup>		
							washed fruit	0.07		
							wet pomace	0.33		
							dry pomace	2.0		
							juice	0.33		
							puree	0.41		
							canned fruit	0.12		
							unwashed fruit	0.36 <sup>a</sup>		FR-FR-04-0129F1
							washed fruit	0.10		
							wet pomace	0.46		
							dry pomace	1.90		
							juice	0.45		
							puree	0.34		
							canned fruit	0.18		
							unwashed fruit	0.36 <sup>a</sup>	FR-FR-04-0129F2	
							washed fruit	0.09		
							wet pomace	0.35		
							dry pomace	1.30		
							juice	0.31		
							puree	0.49		
							canned fruit	0.11		
							unwashed fruit	0.36 <sup>a</sup>	FR-FR-04-0129F3	
							washed fruit	0.18		
wet pomace	0.30									
dry pomace	1.20									
juice	0.37									
puree	0.41									
canned fruit	0.14									

Table 57 Summary of processing factors for mandipropamid residues. The factors are calculated from the data recorded in tables in this section

Raw agricultural commodity (RAC)	Processed commodity	Calculated processing factors	Median or best estimate
Grapes	Pasteurised juice	0.25, 0.25	0.25
	Juice	0.19, 0.24, 0.41, 0.74	0.33
	Yong wine	< 0.13, 0.13, 0.97, 1.00, 1.10, 2.83	1.00
	Aged wine	< 0.13, 0.13, 0.64, 0.85, 1.86, 3.04	0.85
	raisin	2.10, 3.33, 3.91, 4.44, 7.61	3.91
	Wet pomace	1.88, 2.38, 2.63, 2.88	2.51
	Dry pomace	4.88, 6.75, 6.88, 7.75	6.82
Tomatoes	Juice	0.86, 0.92, 1.03, 1.25	0.98
	Canned tomatoes	0.31, 0.33, 0.39, 0.50	0.36
	Washed tomatoes	0.19, 0.25, 0.28, 0.50	0.27
	Puree	0.94, 1.14, 1.14, 1.36	1.14
	Wet pomace	0.83, 0.92, 0.97, 1.28	0.95
	Dry pomace	3.33, 3.61, 5.28, 5.56	4.45

## RESIDUES IN ANIMAL COMMODITIES

### *Direct animal treatments*

Mandipropamid is not used for direct animal treatments.

### *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.

## RESIDUES IN FOOD IN COMMERCE OR AT CONSUMPTION

There are no data on market-basket monitoring studies available for mandipropamid.

## NATIONAL RESIDUE DEFINITIONS

Information was provided on national residue definitions for mandipropamid.

### *USA*

Commodities of plant origin except root and tuber vegetables: mandipropamid.

Commodities of root and tuber vegetables: mandipropamid + SYN500003.

### *Brazil*

Commodities of plant origin: mandipropamid.

**APPRAISAL**

Mandipropamid or 2-(4-chlorophenyl)-*N*-[3-methoxy-4-(prop-2-ynyloxy)phenethyl]-2-(prop-2-ynyloxy)acetamide belongs to the mandelamide chemical class of fungicides and is a synthetic fungicide intended for the control of Oomycete fungal pathogens in a range of crops.

The following abbreviations are used for the metabolites discussed below:

NOA458422	2-(4-Chlorophenyl)- <i>N</i> -[2-(4-hydroxy-3-methoxyphenyl)-ethyl]-2-prop-2-ynyl- oxy-acetamide
CGA380778	2-(4-Chlorophenyl)-2-hydroxy- <i>N</i> -[2-(3-methoxy-4-prop-2-ynyloxyphenyl)-ethyl] -acetamide
SYN521195	2-(4-Chlorophenyl)- <i>N</i> -[2-(3-hydroxy-4-prop-2-ynyloxyphenyl)-ethyl]-2-prop- 2-ynyl-oxy-acetamide
CGA380775	2-(4-Chlorophenyl)-2-hydroxy- <i>N</i> -[2-(4-hydroxy-3-methoxyphenyl)-ethyl]-acetamide
SYN500003	(4-Chlorophenyl)-prop-2-ynyloxy-acetic acid
SYN524199	(4-chloro-phenyl)-(3,4,5-trihydroxy-6-hydroxymethyl-tetrahydro-pyran-2- yloxy)-acetic acid
CGA155705	4-chloro-benzoic acid
SYN 508792	2-(4-chloro-phenyl)- <i>N</i> -{2-[3-methoxy-4-(3,4,5-trihydroxy-6-hydroxymethyl-tetrahydro-pyran-2-yloxy)-phenyl]-ethyl}-2-prop-2-ynyloxy-acetamide
SYN 508793	malonyl-O-glycoside of NOA 458422
SYN536638	<i>N</i> -[2-(4-Allyloxy-3-methoxyphenyl)-ethyl]-2-(4-chlorophenyl)-2-prop-2- ynyloxy-acetamide

***Animal metabolism***

The Meeting received information on the fate of orally-dosed mandipropamid in lactating goats.

The principal route of metabolism in goats includes demethylation of the methoxy phenyl functionality to generate the phenol moiety and the removal of either or both of the propargyl side chains to generate the corresponding alcohol or phenol functionalities. The metabolite patterns in the lactating goat and in rats presented qualitatively similar (See the toxicology review in this Report for more details on laboratory animal metabolism).

[<sup>14</sup>C]mandipropamid, radiolabelled uniformly in either the chlorophenyl or methoxyphenyl ring, was administered orally at doses equivalent to 27–49 mg/kg in the total diet to lactating goats once daily for seven consecutive days. The majority of the radioactivity was excreted in the faeces and urine. For the [<sup>14</sup>C]chlorophenyl treated goats, 46% of the administered dose was excreted in the faeces and 30% and 33% in the urine. For the remaining goat treated with [<sup>14</sup>C]methoxyphenyl mandipropamid, 49% of the administered radioactivity was excreted in the faeces and 33% in the urine.

The study results show no significant differences between the metabolic profiles of the two radiolabelled treatments. All metabolites identified contained both the chlorophenyl and methoxyphenyl moieties, indicating no cleavage of the amide bond between the two aromatic rings. TRRs were low in milk ( $\leq 0.01$  mg/kg), muscle (0.03% TRR, 0.005 mg/kg), and fat (0.01% TRR,  $\leq 0.021$  mg/kg), and highest in liver (0.11% TRR, 0.48 mg/kg) and kidney (0.01% TRR, 0.13 mg/kg). Unchanged parent mandipropamid comprised the majority of the residue in goat fat (75–77% TRR),

and only a small proportion of the residue in goat milk (7.9% TRR) and liver (0.8–1.4% TRR), and was not detected in kidney.

The metabolite NOA 458422 was a significant residue in kidney at 15–18% TRR (0.018–0.024 mg/kg) but was a minor residue in liver at 5.3–5.8% TRR (0.025–0.028 mg/kg). Metabolites CGA 380775, CGA 380778, SYN 505503, SYN 521195, and SYN 518495 were identified as minor residues in kidney (each  $\leq$  9.3% TRR,  $<$  0.02 mg/kg) and liver (each  $\leq$  7.3% TRR,  $\leq$  0.04 mg/kg).

### *Plant metabolism*

The Meeting received plant metabolism studies with mandipropamid on grapes, lettuce, potatoes and tomatoes.

Metabolism studies of mandipropamid in four different crop types (fruit–grapes, leafy vegetables–lettuce, root and tuber vegetables–potato and fruiting vegetables–tomato) demonstrated that metabolism of mandipropamid was similar in the foliar parts, and that the compound undergoes extensive metabolism to form a range of metabolites which are more polar than the parent. Unchanged mandipropamid remained as the major component in all aerial crop parts (ranging from approximately 40% to 94% TRR). A consistent degradation pathway was demonstrated by the four different crop studies though fewer metabolites were identified in lettuce due to a shorter period of exposure to the chemical prior to harvest. In lettuce, grapes, tomatoes and potato leaves, no individual metabolite released by room temperature extraction accounted for  $>$  4.5% TRR mandipropamid equivalents. In peel and flesh of potato tubers, the major metabolite (SYN 500003) accounted for 13% and 11% TRR respectively, but was at very low concentrations ( $\leq$  0.006 mg/kg mandipropamid equivalents).

When grape vines were treated six times with [ $^{14}$ C]mandipropamid (chlorophenyl- and methoxyphenyl-label) at a nominal application rate of 150 g ai/ha (1 $\times$  rate) and 450 g ai/ha (3 $\times$  rate), parent compound was found as the major component at all time points accounting for 54–80% of TRR. Several additional components (such as NOA 458422, CGA380778) were detected in the room temperature extracts of the fruit samples of which the largest fraction accounted for a maximum of only 3.8% TRR or 0.040 mg/kg. The metabolite patterns in the overdose studies were very comparable to those found in the 1 $\times$  rate experiments. The majority of the radioactivity in the fruit was present on the surface, accounting for 79–89% TRR. Of the remaining radioactivity 8–13% TRR was extractable using acetonitrile:water (80:20 v/v) leaving a maximum of 9% TRR unextracted. The majority of the radioactivity (83–91% TRR) in the leaves was extractable using acetonitrile:water (80:20 v/v) leaving a maximum of 17% unextracted. Parent mandipropamid was identified as the major component of the residue in all fruit samples from both labels, ranging from 79 to 80% TRR in the 0 day PHI samples and reducing to 54–59% TRR in the 28 day PHI samples.

When lettuce plants were treated twice with [ $^{14}$ C]mandipropamid (chlorophenyl- and methoxyphenyl-label) at a nominal recommended application rate of 150 g ai/ha, parent mandipropamid was the largest component of the residue accounting for 82–94% TRR. Four metabolites were identified, all of which contained both the chlorophenyl and methoxyphenyl rings. NOA458422 and CGA380778 were present both as free metabolites at maximum levels of 1.1% TRR (0.018 mg/kg) and also as conjugated metabolites at maximum levels of 0.4% TRR (0.005 mg/kg). SYN521195 and CGA380775 were only present as conjugated metabolites at maximum levels of 0.2% TRR (0.003 mg/kg). No significant difference was found between the profiles of lettuce samples derived from the two radiolabelled experiments.

Six foliar applications of [chlorophenyl-(U)- $^{14}$ C]mandipropamid or [methoxyphenyl- (U)- $^{14}$ C]mandipropamid were made to potato plants at a rate of 150 g ai/ha. TRRs in peel and flesh samples were 0.040–0.59 mg/kg and were comparable with both labels and at both PHIs (7 and 21 days). TRRs in potato leaves were much higher, ranging from 2.7–6.3 mg/kg. No significant difference was found between the profiles of the leaf samples derived from the two radiolabelled experiments. Parent mandipropamid was identified as the largest component of the residue in the leaves accounting for 40–61% TRR. Three other metabolites all containing both the chlorophenyl and methoxyphenyl rings (NOA458422, CGA380775 and CGA380778) were identified at much lower

levels than parent ranging from 0.4–1.8% TRR. A significant difference was found between the profiles of the peel and flesh samples derived from the two radiolabel experiments; however within each experiment the peel and flesh profiles were similar. Parent mandipropamid was identified in the peel samples at a maximum level of 4.2% TRR (0.002 mg/kg) but was not detected in the flesh. Three small acidic molecules, containing only the chlorophenyl ring, were identified in both the peel and flesh samples. These were SYN500003, SYN524199 and CGA155705 and were detected at maximum levels of 13% TRR, 7.2% TRR and 2.1% TRR respectively (maximum individual residue level of only 0.006 mg/kg). No metabolites containing only the methoxyphenyl ring were identified. Radioactivity remaining in the debris after initial extraction was further investigated using an acidic microwave extraction. A significant proportion of the radioactivity was solubilised and was shown to be mainly comprised of glucose (10–30% TRR) and a second component (7–16% TRR) proposed to be an intermediate breakdown product formed during the acid hydrolysis of starch.

Tomato plants were treated with four foliar applications of [<sup>14</sup>C]mandipropamid (chlorophenyl- and methoxyphenyl-label) at a rate of 276 g ai/ha and 295 g ai/ha at 2 week intervals, followed by two further treatments at a rate of 147 g ai/ha and 149 g ai/ha in weekly intervals, resulting in a total use rate of 867 g ai/ha. Tomato fruits and leaves/foilage were harvested at 5 intervals: 0, 3, 7, 14 and 28 days after the last application (DALA). Parent compound was the major residue in fruits (61–80% TRR) and leaves (66–76% TRR). Most of the applied radioactivity remained on the surface of the fruits (69–87% TRR). Five metabolites were identified by co-chromatography with reference standards or by LC-NMR and LC-MS as CGA 380775, CGA 380778, NOA 458422, SYN 508792 and SYN 508793 and were present in a range of 0.003 mg/kg and 0.013 mg/kg.

### *Environmental fate in soil*

The Meeting received information on the environmental fate of mandipropamid in soil, including studies on aerobic soil metabolism and crop rotational studies.

#### *Aerobic soil metabolism*

Numerous soil studies were performed, under laboratory conditions, to evaluate the route and rate of [<sup>14</sup>C]mandipropamid labelled in the chlorophenyl ring or the methoxyphenyl ring. Degradation in a wide range of soil types (pH, organic matter, texture, origin) under varying test (temperature, concentration of active ingredient, soil humidity) and incubation conditions (aerobic, anaerobic, microbially active, sterile) were evaluated. The formation and degradation of non-extractable (bound) residues and mineralisation to carbon dioxide represent the main overall pathway for the metabolism of parent compound in soil. In active soils, mandipropamid residues were readily mineralized to [<sup>14</sup>C]carbon dioxide and accounted for up to 9–45% of applied radioactivity after 120 days (average from 21 studies = 23%), and resulted in non-extractable soil residue levels that reached maximum levels at up to 19–44% of applied radioactivity after 120 days (average from 21 studies = 33%). In less active soils, the mineralization rate to carbon dioxide was lower. A number of metabolites were observed in aerobic degradation studies following the degradation of mandipropamid, namely CGA380778 (≤ 6.0%), NOA458422 (≤ 1.7%) and CGA380775 (< 1%), SYN536638 (≤ 3.2%) and SYN500003 (< 1%).

#### *Aqueous photolysis*

The photolysis study conducted with [methoxyphenyl-(U)-<sup>14</sup>C]mandipropamid at a concentration of 1 mg/L in sterile buffer solution at pH 7 and 25 °C. The samples were irradiated for periods up to the equivalent of 17 days summer sunlight. The estimated half-life DT<sub>50</sub> was 34 h of continuous irradiation. At least 16 degradates were formed, none of which represented > 5% of the applied radioactivity.

### *Aqueous hydrolysis*

The hydrolysis study conducted with [ethyl-1-<sup>14</sup>C]mandipropamid at a concentration of 1 mg/L in sterile buffer solution at pH 4, 5, 7 and 9 at 50 °C for seven days and at pH 5, 7 and 9 at 25 °C for 32 days. The recovery for all samples was between 92.7 and 105.7% of the applied radioactivity. No degradation of the test substance was observed under all conditions.

### *Confined rotational crop*

In two outdoor confined rotational crop studies in Switzerland, soil was treated directly with [<sup>14</sup>C]mandipropamid labelled in the chlorophenyl ring or methoxyphenyl ring. Crops of lettuce, radish and wheat were sown into the treated soil at intervals of 29, 58, 120 and 365 days after treatment and were grown to maturity and harvested. Wheat forage was harvested at 50% maturity. Uptake of residues was quite limited with the only identified components being mandipropamid ( $\leq 0.023$  mg/kg), CGA380778 ( $\leq 0.009$  mg/kg) and NOA458422 ( $\leq 0.016$  mg/kg) all of which were identified in the primary crop metabolism studies. Levels of mandipropamid or any other metabolite in succeeding crops would not be expected to exceed 0.03 mg/kg. Since such low radioactive residues were found in analysed fractions of these rotational crop samples, mandipropamid is not readily taken up by succeeding crops.

### *Methods of analysis*

The Meeting received descriptions and validation data for analytical methods for residues of mandipropamid in raw agricultural commodities.

Crop samples were extracted with acetonitrile:water (80:20 v/v), extracts were centrifuged and aliquots diluted with water prior to being cleaned-up using polymeric solid-phase extraction cartridges. Residues of mandipropamid were quantified with HPLC-MS-MS. Method DFG S19 with HPLC-MS/MS was suitable for enforcement for agricultural commodities. LOQ values are at 0.01 mg/kg for various plant matrices.

Numerous recovery data on a wide range of substrates were provided from validation testing of the methods, which showed that the methods were valid over the relevant concentration ranges.

### *Stability of pesticide residues in stored analytical samples*

The Meeting received information on the freezer storage stability of residues of mandipropamid in plant commodities.

Residues were stable (less than 30% disappearance) in various plant matrices (tomatoes, grapes, potatoes, lettuce, cucumbers, wheat and soya bean and processed commodities) for at least up to 1 year when stored frozen at -20 °C.

### *Residue definition*

The composition of the residue in the metabolism studies, the available residue data in the supervised trials, the toxicological significance of metabolites, the capabilities of enforcement analytical methods and the national residue definitions already operating all influence the decision on residue definition.

As indicated the metabolism of mandipropamid was investigated in grapes, lettuce, potatoes and tomatoes. Except for potato tubers unchanged parent compound formed the major part of the residue in these studies. The cleavage products NOA458422, CGA380778 and CGA380775 were identified or observed in all four crops. All metabolites were of minor importance. The major metabolite (SYN 500003) in potato tubers accounted for up to 13% TRR and was present at very low levels ( $\leq 0.006$  mg/kg). Parent mandipropamid was identified in the peel samples at a maximum level of 4.2% TRR (0.002 mg/kg) but was not detected in the flesh.

A metabolism study on lactating goats showed unchanged parent 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.

The octanol-water partition coefficient of mandipropamid ( $\log K_{ow} = 3.2$ ) implied that mandipropamid may be fat-soluble. However, in the goat metabolism study, TRR in fat was about four times as high as that in liver and in the rat metabolism study, TRRs in fat and muscle were at similar levels. Based on the above information, the Meeting agreed that mandipropamid is not fat-soluble.

Based on the available comparative plant metabolism studies and lactating goat metabolism studies, the Meeting recommended the following residue definition for mandipropamid:

Definition of the residue for compliance with the MRL or for estimation of the dietary intake for plant and animal commodities: *mandipropamid*.

### ***Results of supervised residue trials on crops***

The Meeting received supervised trials data for mandipropamid on grapes, onion, broccoli, cabbages, cucumbers, cantaloupe, summer squash, tomatoes, peppers, mustard greens, lettuce and potatoes.

#### *Grapes*

Twelve trials were conducted on grape vines in the USA (maximum GAP: 0.15 kg ai/ha, four applications, 14-day PHI) in 2003. In all trials conducted at the maximum USA GAP, the ranked order of residues, median underlined, were: 0.20, 0.21, 0.22, 0.28, 0.38, 0.43, 0.59, 0.62, 0.63, 0.69, 0.76 and 0.85 mg/kg.

The Meeting estimated a maximum residue level and an STMR value for mandipropamid in grapes of 2 and 0.43 mg/kg, respectively.

#### *Spring onions*

Three trials were conducted on green onions in the USA (maximum GAP: 0.15 kg ai/ha, three applications, 7-day PHI) in 2004. The ranked order of residues, median underlined, was: 0.25, 0.48 and 1.74 mg/kg.

As there were only three trials in accordance with GAP, it was decided that a maximum residue level should be proposed that was higher than highest residue to allow for possible large uncertainty. The Meeting estimated a maximum residue level and an STMR value for mandipropamid in spring onions of 7 and 0.48 mg/kg, respectively.

#### *Bulb onions, dry*

In 2004 eight trials were conducted on bulb onions in the USA at the maximum US GAP (0.15 kg ai/ha, four applications, 7-day PHI). The ranked order of residues, median underlined, were: < 0.01, < 0.01, < 0.01, < 0.01, < 0.01, 0.01, 0.02 and 0.04 mg/kg.

The Meeting estimated a maximum residue level and an STMR value for mandipropamid in bulb onions (dry) of 0.1 and 0.01 mg/kg, respectively.

#### *Broccoli*

In 2004 six supervised trials were conducted on broccoli in the USA at the maximum GAP (0.15 kg ai/ha, four applications, 1-day PHI). The ranked order of residues on broccoli, median underlined, were: 0.29, 0.35, 0.43, 0.44, 0.57 and 0.70 mg/kg.

The Meeting estimated a maximum residue level and an STMR value for mandipropamid in broccoli of 2 and 0.435 mg/kg, respectively.



*Cabbage, head*

In 2004 six supervised trials were conducted on cabbages in the USA (maximum GAP: 0.15 kg ai/ha, four applications, 1-day PHI). The ranked order of residues on cabbage with wrapper leaves, median underlined, was: 0.90, 1.10, 1.11, 1.30, 1.60 and 1.80 mg/kg. The ranked order of residues on wrapper leaves of cabbages and cabbages without wrapper leaves, median underlined, was: 1.90, 2.30, 2.90, 4.20, 5.50 and 5.80 mg/kg and < 0.01, < 0.01, < 0.01, < 0.01, 0.05, 0.31 mg/kg, respectively.

The Meeting estimated a maximum residue level and an STMR value for mandipropamid in cabbages of 3 and 0.01 mg/kg respectively.

*Cucumbers*

In 2004 seven trials were conducted on cucumbers in the USA (maximum GAP: 0.15 kg ai/ha, four applications, 0-day PHI). The ranked order of residues on cucumbers, median underlined, was: 0.01, 0.02, 0.02, 0.02, 0.05, 0.05 and 0.07 mg/kg.

The Meeting estimated a maximum residue level and an STMR value for mandipropamid in cucumbers of 0.2 and 0.02 mg/kg, respectively.

*Melons*

Six trials were conducted on cantaloupe in the USA in 2004 (maximum GAP: 0.15 kg ai/ha, four applications, 0-day PHI). The ranked order of residues, median underlined, was: 0.06, 0.07, 0.11, 0.12, 0.19 and 0.26 mg/kg.

The Meeting estimated a maximum residue level and an STMR value for mandipropamid in melons, except watermelon, of 0.5 and 0.115 mg/kg, respectively.

*Summer squash*

Five trials were conducted on summer squash in the USA 2004 (maximum GAP: 0.15 kg ai/ha, four applications, 0-day PHI). The ranked order of residues, median underlined, was: 0.02, 0.03, 0.04, 0.07 and 0.08 mg/kg.

The Meeting estimated a maximum residue level and an STMR value for mandipropamid in squash of 0.2 and 0.04 mg/kg, respectively.

*Tomatoes*

Eleven trials were conducted on tomatoes in the USA in 2003 and 2004 (maximum GAP: 0.15 kg ai/ha, four applications, 1-day PHI). The ranked order of residues on tomato, median underlined, was: 0.02, 0.03, 0.03, 0.06, 0.06, 0.06, 0.06, 0.08, 0.09, 0.12 and 0.20 mg/kg.

The Meeting estimated a maximum residue level and an STMR value for mandipropamid in tomato of 0.3 and 0.06 mg/kg, respectively.

*Peppers*

Nine trials were conducted on sweet and chilli peppers in the USA in 2003 and 2004 (maximum GAP: 0.15 kg ai/ha, four applications, 1-day PHI). The residues on sweet peppers were 0.04, 0.07, 0.09, 0.12, 0.17 and 0.34 mg/kg, while the residues on chilli peppers were 0.11, 0.22 and 0.38 mg/kg.

As the residues were in the same range, the Meeting agreed to combine all data sets to support a MRL for peppers. The combined residues, in ranked order, median underlined, were: 0.04, 0.07, 0.09, 0.11, 0.12, 0.17, 0.22, 0.34 and 0.38 mg/kg.

The Meeting estimated a maximum residue level and an STMR value for mandipropamid in peppers of 1 and 0.12 mg/kg, respectively.

Under consideration of the default concentration factor of 7 for dried chilli pepper, the Meeting estimated a maximum residue level and an STMR value for mandipropamid in dried chilli peppers of 10 mg/kg and 0.84 mg/kg.

#### *Leafy vegetables*

Eleven trials were conducted on head and leaf lettuce in the USA in 2005 (maximum GAP on leafy vegetables: 0.15 kg ai/ha, four applications, 1-day PHI). The residues on leaf lettuce, median underlined, were 1.90, 4.50, 5.30, 5.70, 7.80 and 7.90 mg/kg, while the residues on head lettuce without wrapper leaves, median underlined, were: 1.60, 2.70, 3.50, 6.10 and 9.60 mg/kg.

Five trials were conducted on mustard greens in the USA in 2004 (maximum GAP on leafy vegetables: 0.15 kg ai/ha, four applications, 1-day PHI). The ranked order of residues on mustard greens, median underlined, were: 1.20, 4.00, 4.50, 4.50 and 11.5 mg/kg.

Six trials were conducted on spinach in the USA in 2005 (maximum GAP on leafy vegetables: 0.15 kg ai/ha, four applications, 1-day PHI). The residues on spinach, median underlined, were: 5.60, 8.20, 9.90, 10.2, 10.9 and 11.0 mg/kg.

The Meeting noted that the residue data populations, following treatment according to US GAP for leafy vegetables were similar, on head and leaf lettuce, mustard greens and spinach, and could be combined. The combined residues, in ranked order, median underlined, were: 1.20, 1.60, 1.90, 2.70, 3.50, 4.00, 4.50 (3), 5.30, 5.60, 5.70, 6.10, 7.80, 7.90, 8.20, 9.60, 9.90, 10.2, 10.9, 11.0 and 11.5 mg/kg.

The Meeting estimated a maximum residue level and an STMR value for mandipropamid in leafy vegetables of 25 and 5.65 mg/kg respectively.

#### *Celery*

Six trials were conducted on celery in the USA in 2005 (maximum GAP: 0.15 kg ai/ha, four applications, 1-day PHI). The residues on celery, median underlined, were: 0.74, 1.60, 1.80, 3.60, 6.40 and 7.80 mg/kg.

The Meeting estimated a maximum residue level and an STMR value for mandipropamid in celery of 20 and 2.70 mg/kg, respectively.

#### *Potato*

The Meeting received information on supervised residue trials on potatoes in France, Germany, Italy, the Netherlands, Spain, Switzerland and the UK.

Supervised trials were conducted on potato, in Germany (maximum GAP, 0.15 kg ai/ha, four applications, 7-day PHI), in France (no GAP provided), in Italy (no GAP provided), in the Netherlands (maximum GAP: 0.15 kg ai/ha, six applications, no PHI) and in Spain (no GAP provided), in Switzerland (no GAP provided), in the UK (maximum GAP: 0.15 kg ai/ha, four applications, 3-day PHI) in 2002, 2003 and 2004.

The Meeting noted that residues in the tuber were below the LOQ (< 0.01 mg/kg) in all trials conducted in France (six trials), Germany (one trial), Italy (one trial), the Netherlands (one trial), Spain (three trials), Switzerland (three trials), the UK (two trials), and agreed to combine all data from the 17 trials utilizing the British GAP. The Meeting estimated a maximum residue level and an STMR value for mandipropamid in potato of 0.01\* and 0.01 mg/kg, respectively.

#### *Animal feedstuffs*

##### *Wrapper leaves of head cabbage*

Six supervised trials were conducted on cabbage in the USA in 2004 (described above). The ranked order of residues on cabbage wrapper leaves, median underlined, were: 1.90, 2.30, 2.90, 4.20, 5.50 and 5.80 mg/kg.

The Meeting estimated an STMR and a high residue values for mandipropamid in wrapper leaves of cabbage of 3.55 and 5.80 mg/kg, respectively.

### *Fate of residues during processing*

The Meeting received information on the fate of mandipropamid residues during aqueous hydrolysis under conditions of pasteurization and baking, brewing, boiling and sterilisation. Information was also provided on the fate of mandipropamid residues during the processing of grapes and tomatoes.

Mandipropamid was stable during the simulation of pasteurization (pH 4, 90 °C), baking, boiling, brewing (pH 5, 100 °C) or sterilisation (pH 6, 120 °C).

The processing factors for raisins (3.91), wet pomace (2.51), dry pomace (6.82), wine (0.85) and juice (0.33) were applied to the estimated STMR for grapes (0.43 mg/kg) to produce STMR-P values for raisins (1.68 mg/kg), wet pomace (1.16 mg/kg), dry pomace (2.93 mg/kg), wine (0.366 mg/kg) and grape juice (0.14 mg/kg). The processing factor for raisins (3.91) was applied to the grape residue data (highest value 0.85 mg/kg) to produce an estimated highest value for dried grapes (3.32 mg/kg).

The Meeting estimated a maximum residue level for mandipropamid in dried grapes (currants, raisins, sultanas) of 5 mg/kg.

The processing factors for wet pomace (0.95), dry pomace (4.45), juice (0.98), puree (1.14) and canned tomatoes (0.36) were applied to the estimated STMR for tomatoes (0.06 mg/kg) to produce STMR-P values for wet pomace (0.057 mg/kg), dry pomace (0.27 mg/kg), juice (0.059 mg/kg), puree (0.068) and canned tomatoes (0.022).

### *Farm animal dietary burden*

The Meeting estimated the dietary burden of mandipropamid in farm animals on the basis of the diets listed in the Annex 6 of the 2006 JMPR Report. Calculation from highest residue and STMR-P values provides the levels in feed suitable for estimating MRLs, while calculation from STMR and STMR-P values for feed is suitable for estimating STMR values for animal commodities. The percentage dry matter is taken as 100% when the highest residue levels and STMRs are already expressed as dry weight.

#### *Estimated maximum and mean dietary burdens of farm animals*

Dietary burden calculations for beef cattle, dairy cattle, poultry (layer and broiler) are provided in Annex 6 of the 2008 Report of the JMPR. The calculations were made according to the animal diets from the US–Canada, EU and Australia in the OECD Table (Annex 6 of the 2006 JMPR Report).

The calculations are then summarized and the highest dietary burdens (underlined) are selected for MRL and STMR estimates on animal commodities.

		Animal dietary burden, mandipropamid, ppm of dry matter diet		
		US–Canada	EU	Australia
Beef cattle	Max	0.02	<u>7.75</u>	1.56
	Mean	0.02	4.75	0.73
Dairy cattle	Max	0.01	<u>7.75<sup>a</sup></u>	1.56
	Mean	0.13	4.75 <sup>b</sup>	0.73
Poultry - broiler	Max	0	1.94 <sup>c</sup>	0
	Mean	0	0.01	0
Poultry - layer	Max	0	1.94	0
	Mean	0	1.19 <sup>d</sup>	0

<sup>a</sup> Highest maximum beef or dairy cattle dietary burden suitable for MRL estimates for mammalian meat and milk.

<sup>b</sup> Highest mean beef or dairy cattle dietary burden suitable for STMR estimates for mammalian meat and milk.

<sup>c</sup> Highest maximum poultry broiler and layer dietary burden suitable for MRL estimates for poultry meat and eggs.

<sup>d</sup>Highest mean poultry broiler and layer dietary burden suitable for STMR estimates for milk.

### ***Farm animal feeding studies***

No animal feeding studies on ruminants are available. The lactating goat metabolism study was used to evaluate the dietary burden for ruminants. In the metabolism study, in which [<sup>14</sup>C]mandipropamid equivalent to 27 – 49 ppm in the diet was orally administered to lactating goats for 7 consecutive days, highest residue parent compound (0.019 mg/kg) was found in fat. Given the low estimated animal burden (about one fourth of the administered level), no parent compound is expected to be present more than 0.005 mg/kg in tissues or milk.

For poultry, no feeding and metabolism studies are available. In addition, no analytical method for animal commodities was submitted for mandipropamid in animal commodities. The Meeting agreed that no maximum residue level could be estimated for animal commodities.

### **RECOMMENDATIONS**

On the basis of the data from supervised trials, the Meeting concluded that the residue concentrations listed below are suitable for establishing MRLs and for assessing IEDIs.

Definition of the residue (for compliance with the MRL and for estimation of dietary intake for plant and animal commodities): *mandipropamid*.

CCN	Commodity	MRL, mg/kg	STMR or STMR-P, mg/kg
VB 0400	Broccoli	2	0.435
VB 0041	Cabbage, head	3	0.01
VS 0624	Celery	20	2.70
HS 0444	Chilli peppers (dry)	10	0.84
VC 0424	Cucumber	0.2	0.02
FB 0269	Grapes	2	0.43
DF 0269	Dried grapes (= Currants, Raisins and Sultanas)	5	1.68
	Wet pomace		1.16
	Dry pomace		2.93
	Wine		0.366
	Juice		0.14
VL 0053	Leafy Vegetables	25	5.65
VC 0046	Melons, except Watermelon	0.5	0.115
VL 0485	Mustard greens	See Leafy veg	
VA 0385	Onion, bulb	0.1	0.01
VO 0051	Peppers	1	0.12
VR 0589	Potatoes	0.01*	0.01
VA 0389	Spring onion	7	0.48
VC 0431	Squash, summer	0.2	0.04
VO 0448	Tomato	0.3	0.06
-	Juice		0.059
-	Puree		0.068
-	Canned tomatoes		0.022
-	Wet pomace		0.057
-	Dry pomace		0.27

\* At or about the limit of quantification.

## DIETARY RISK ASSESSMENT

*Long-term intake*

The evaluation of mandipropamid resulted in recommendations for MRLs and STMR values for raw and processed commodities. Data on consumption were available for 17 food commodities and were used to calculate dietary intake. The results are shown in Annex 3 of the 2008 Report of the JMPR.

The International Estimated Daily Intakes (IEDIs) of mandipropamid, based on the STMRs estimated for 17 commodities, were 0–3% of the maximum ADI of 0.2 mg/kg bw for the thirteen GEMS/Food regional diets. The Meeting concluded that the long-term intake of residues of mandipropamid resulting from its uses that have been considered by JMPR is unlikely to present a public health concern.

*Short-term intake*

The 2008 JMPR decided that an ARfD was unnecessary. The Meeting therefore concluded that the short-term intake of mandipropamid residues is unlikely to present a public health concern.

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