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Napropamide-M

Volume 3 – B.7 (AS)

Rapporteur Member State: United Kingdom

Version History

When	What
June 2017	Initial DAR

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B.7. RESIDUE DATA

Many of the studies presented below have been previously evaluated by Denmark for the Napropamide DAR (see B.7.8 for details of which studies have been previously evaluated). Much of the text presented below is therefore amended from the Danish evaluation for napropamide with additional detail included where necessary and the conclusions appropriately amended for napropamide-M. Note where the term napropamide has been used it refers to the napropamide racemate unless stated otherwise.

B.7.1. STORAGE STABILITY OF RESIDUES

Report:	CA 6.1/01. Norris, D. (2002a), Determination of the freezer storage stability of napropamide residues in samples of brassicas (to include cauliflower, cabbage and Brussels sprouts), over a maximum period of twelve months, in compliance with Good Laboratory Practice Company Report No. OA00567 B. Oxford Analytical Ltd., United Kingdom, GLP.

Untreated samples of cauliflower, cabbage and Brussels sprouts were fortified with napropamide at a concentration of 1 mg/kg and stored at – 20°C. Untreated samples were stored under the same condition. Method performance was assessed by the analysis of five untreated samples fortified at 1.0 mg/kg, to determine the procedural recovery. The storage period was 294 days for cauliflower, 341 days for cabbage and 222 days for brussel sprouts.

Analysis was conducted using analytical method OAN/A/125. The method has been considered acceptably validated in Volume 3- B.5.1.2 with an LOQ of 0.1 mg/kg. The method does not distinguish between R and S isomers and therefore determines only total napropamide in this study.

The results from the study are shown in Table B.7.1-1

Table B.7.1-1 Freezer storage stability of napropamide residues in different matrices

Crop	Storage interval (days)	Recovery of nominal fortified amount (%)	Mean recovery (%)
Cauliflower	294	95.8, 88.9, 92.9, 83.3, 85.6, 62.7	84.9
Cabbage	341	90.6, 89.6, 92.4, 88.9, 89.5, 89.3	90.1
Brussels sprouts	222	79.7, 76.4, 76.3, 73.9, 72.2	75.7

The mean recoveries in fortified samples was found to be 84.9 % in cauliflower after a storage period of 294 days, 90.1% in cabbage after a storage period of 341 days and 75.7% in Brussels sprouts after a storage period of 222 days.
There were no residues found in untreated samples.

The mean procedural recoveries for the fortifications were 94.2% for cauliflower, 99.1% for cabbage and 95.0% for Brussels sprouts.

Conclusion
Residues of napropamide are stable in samples of cauliflower, cabbage and Brussels sprouts for at least 341, 294 and 222 days, respectively under freezer storage at - 20°C.

Report:	CA 6.1/02. Brown, D. (2001), Study to determine the stability of napropamide residues in oilseed rape seed and specimens following frozen storage at ca. -18°C for 0 days, 1 month, 3, 6 and 12 months. Company Report No. AD/5287/US. Agrisearch UK Limited, United Kingdom, GLP.

Untreated samples of oilseed rape seeds were fortified at the fortification levels 0.2 and 1.0 mg/kg and stored at -18°C. Sampling intervals were 0, 3, 6 and 12 month after fortification. Untreated samples were stored under the

same condition. At each sampling interval 5 replicates from each fortification level were analysed.

Procedural recovery was performed concurrently with each fortification level by analysing one replicate of a new fortification at each sampling interval.

Analyses were performed using analytical method Napropamide/crops/DB/00/1. The method whilst not validated has been considered fit for purpose in Volume 3- B.5.1.2 with an LOQ of 0.05 mg/kg. The method does not distinguish between R and S isomers and therefore determines only total napropamide in this study.

The results from the study are shown in Table B.7.1-2

Table B.7.1-2 Freezer storage stability of napropamide residues in oilseed rape

Crop	Storage interval (months)	Fortification level (mg/kg)	Recovery of nominal fortified amount (%)	Mean recovery (%)	Procedural recovery
Oilseed rape seed	0	0.2	76.0, 80.5, 83.5, 80.5, 83.5	81	74
	1		74.0, 82.5, 79.0, 81.0, 88.5	81	86
	3		68.5, 63.0, 67.5, 73.0, 66.0	68	71
	6		85.5, 82.0, 91.5, 88.0, 96.5	89	89
	12		102, 104, 101, 99.5, 99.5	102	101
	0	1.0	84.7, 98.5, 81.3, 89.9, 89.7	89	80
	1		76.7, 88.9, 92.1, 86.2, 90.3	87	92
	3		79.4, 90.8, 65.0, 72.6, 64.7	75	84
	6		90.1, 86.2, 85.2, 85.9, 79.1	85	94
	12		103, 88.1, 107, 87.0, 82.9	94	95

Conclusion

The mean recoveries in the studies ranged from 68% to 102 %. The lowest recoveries were found at a 0.2 mg/kg fortification level after 3 months storage and ranged from 63% to 73%. This is not considered indicative of a decrease in residues on storage as procedural recovery at this time point was also low (71%) and all other mean recoveries for the other storage periods were 75% to 102%.

Residues of napropamide are stable in samples of oilseed rape seed for at least 1 year when stored at - 18°C or lower.

Storage stability summary and conclusion

Storage stability studies have been provided which demonstrate that residues of napropamide are stable when stored at -18ºC or below for up to 341 days in high water content commodities (cabbage) and 12 month in high oil content commodities (oil seed rape seed). Recovery after storage was > 75% in both studies, the data on napropamide can be considered acceptable to address the storage stability of napropamide-M.

B.7.2. METABOLISM, DISTRIBUTION AND EXPRESSION OF RESIDUES

B.7.2.1. Plants

Report:	CA 6.2.1/01. Ahmad, S. (2015), [naphthyl-1-^{14}C] napropamide-M: Metabolism in oilseed rape crop. Company Report No. AU-2012-49. Jai Research Foundation, USA. GLP.

Materials and methods

[^{14}C-1-naphthyl]-napropamide-M was used in the study. It was applied at 0.72 kg as/ha to bare soil in 4 containers, then incorporated into the top 2.5 cm soil layer. On the same day as application oilseed rape seeds were sown into each of the 4 pots. At application and sowing the pots were in a greenhouse, at BBCH 12 they were moved outside. Soil samples were collected at application. Whole plant samples were taken at BBCH 15-

22 and BBCH 51, soil and immature pods at BBCH 76, soil at BBCH 84, haulm and seed at BBCH 89. TRR were determined by combustion.

Soil samples, forage, pods and seeds were extracted and analysed as shown in Figure B.7.2.1-1 to B.7.2.1-4.

Figure B.7.2.1-1 Soil sample extraction and analysis.

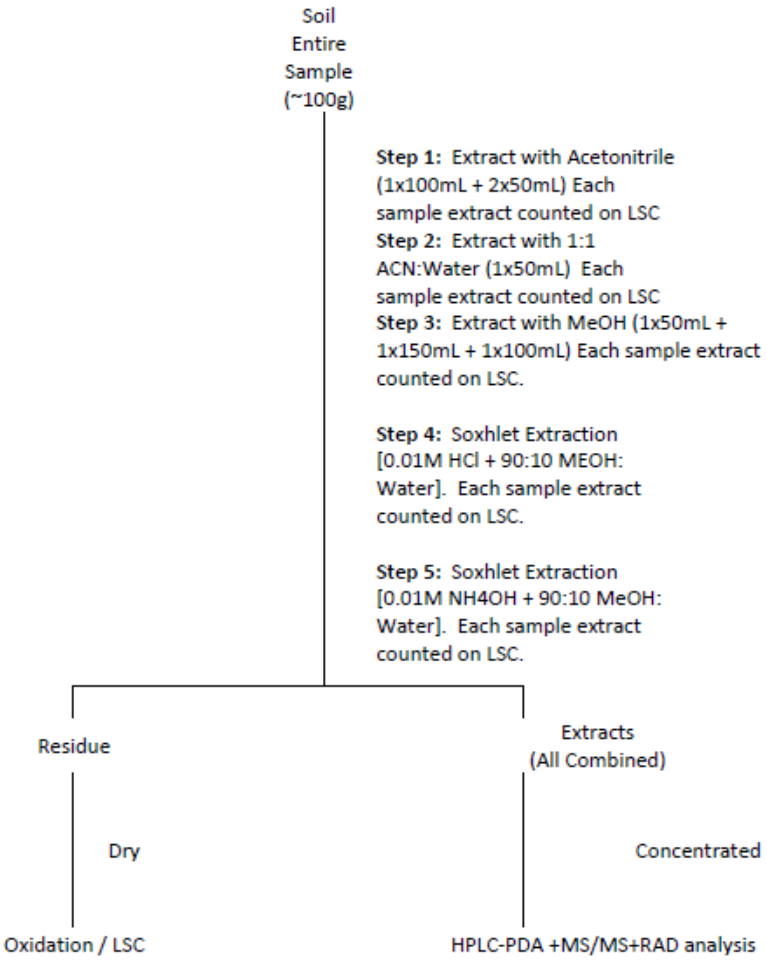


Figure B.7.2.1-2 Forage and immature pod extraction and analysis.

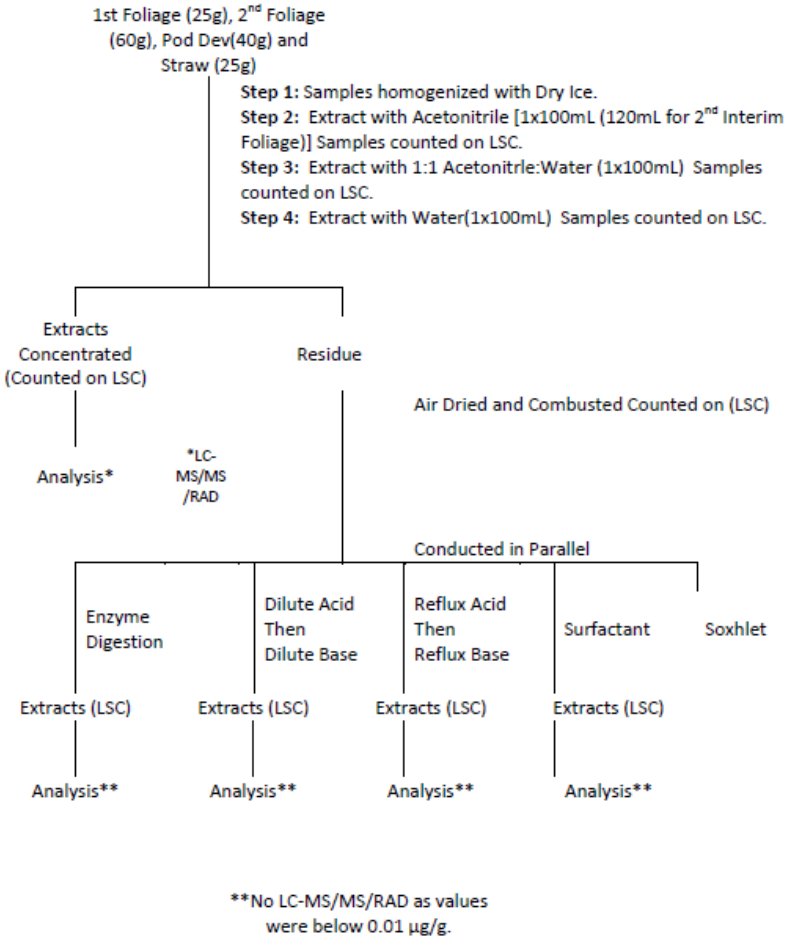


Figure B.7.2.1-3 Mature pods extraction and analysis.

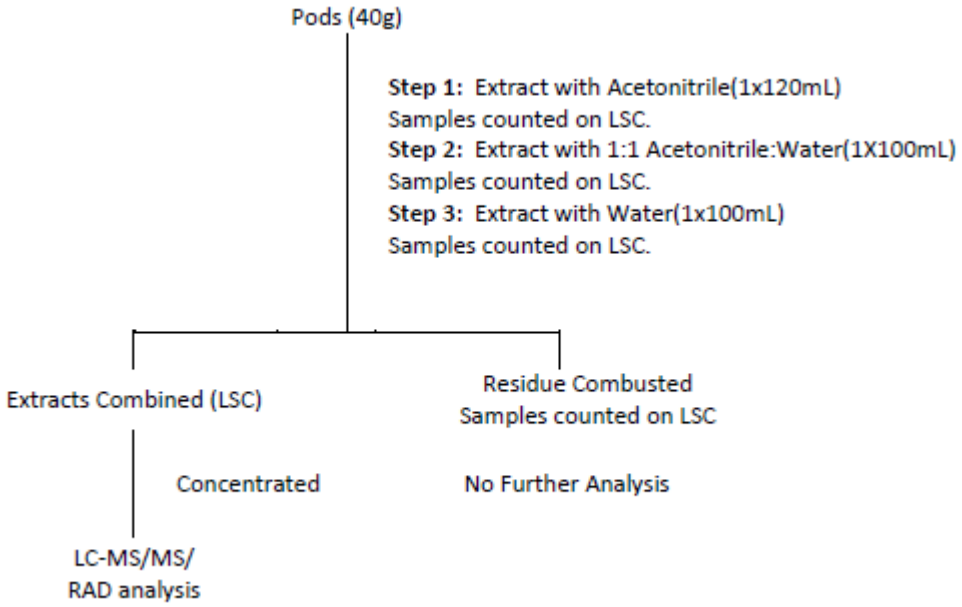
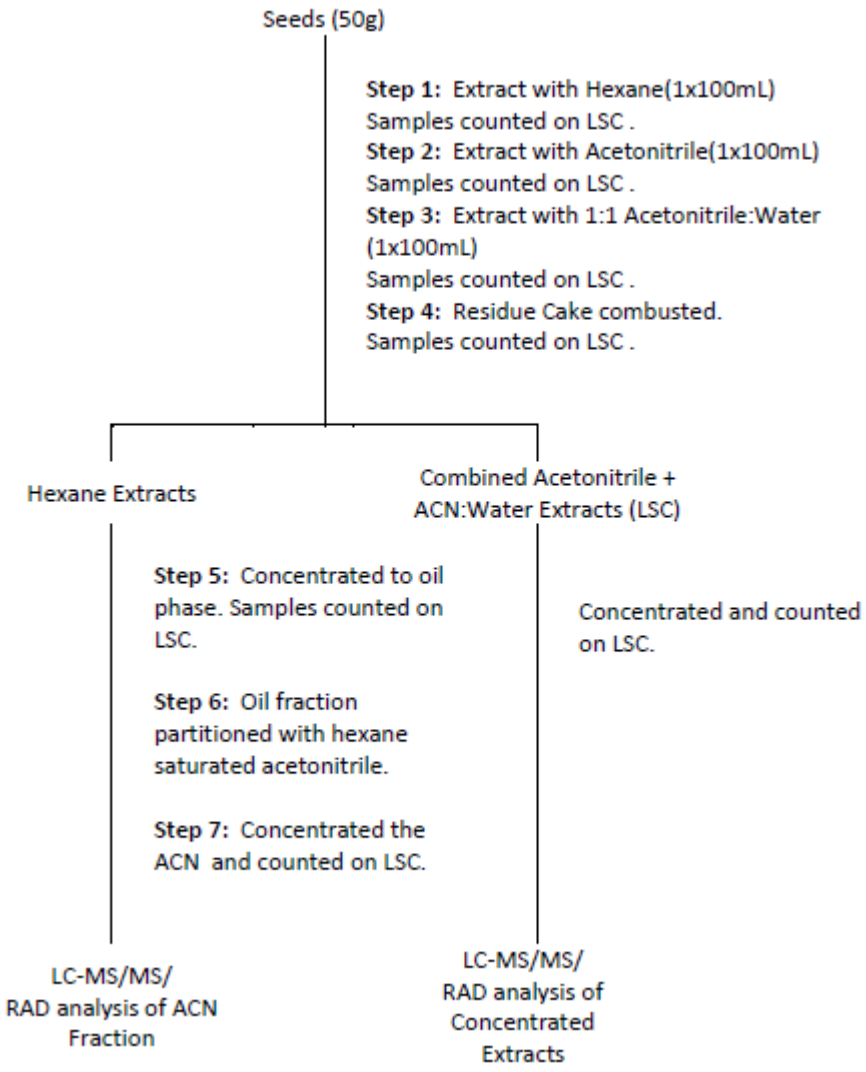


Figure B.7.2.1-4 Seed extraction and analysis



Results

The total radioactive residues (TRR) in foliage, pods, haulm, oilseeds and soil are shown in Table B.7.2.1.1.

Table B.7.2.1 -1 Total radioactive residue (mg napropamide equivalents/kg) in crop and soil

Sampling time	Crop part/Soil	TRR (mg/kg napropamide-M equivalents)[1]	Extractable residue mg/kg (%TRR)[1, 2]	Non extractable residue mg/kg (%TRR)1
Application / Sowing	Soil	0.088	0.0865 (98.3)	0.0015 (1.7)
Forage 1 (BBCH 15-22)	Foliage	0.0147	0.0090 (61.2)	0.0057 (38.8)
	Soil	0.125	0.1075 (86.0)	0.0175 (14.0)
Forage 2 (BBCH 51)	Foliage	0.0105	0.0059 (56.2)	0.0046 (43.8)
	Soil	0.086	0.0663 (77.1)	0.0197 (22.9)
Pod development (BBCH 76)	Pods	0.0077	0.0059 (76.6)	0.0018 (23.4)
	Foliage	0.1397	0.0723 (51.8)	0.0674 (48.2)
	Soil	0.068	0.0423 (62.2)	0.0257 (37.8)
BBCH 84	Soil	0.037	0.0135 (36.5)	0.0235 (63.5)
Harvest (BBCH 89)	Seeds	0.0170	0.0066 (38.8)	0.0104 (61.2)
	Haulm	0.2908	0.0805 (27.7)	0.2103 (72.3)

[1] - Values for soil average of four containers
[2] – Plant extraction in solvent /water prior to any exhaustive procedures (hexane or solvent for seeds)

Enzyme digestion liberated only small additional percentages of the TRR with dilute acid or reflux extraction liberating varying additional percentages of the TRR. The notifier hypothesises based on this that much of the residues are incorporated into endogenous plant material. The report suggests that due to the low levels of extractable radioactive residues found in seeds and pods, no further characterisation could be performed.

When N rates are considered the total extractable residues found are <0.01 mg/kg in seeds and pods. Early foliage samples (≤BBCH 51) have TER <0.01 mg/kg. Analysis of the foliage by HPLC indicated 8-10 components however these could not be correlated with any of the following reference standards:

Napropamide-M
L-Napropamide
DE-NPAM
NOPA
1-NAPHTHOL
NQ

It is noted that total extractable residues in foliage at BBCH 76 are 0.07 mg/kg and haulm at BBCH89 are 0.08 mg/kg. No significant peaks could be found in the TER from foliage at BBCH 76. The haulm TER comprised 6 unresolved peaks and 3 other minor components. These peaks could not be correlated with any of the reference standards listed above.

Report:	CA 6.2.1/02. Langford-Pollard, A.D. (2002), Napropamide oilseed rape metabolism Company Report No. UPH/028/14461. Huntingdon Life Sciences Ltd., United Kingdom. GLP.

Materials and methods

[^{14}C-1-naphthyl]-napropamide, radiochemical purity > 97% was used in the study. The study was conducted outdoors in England.

[^{14}C-1-naphthyl]-napropamide was isotopically diluted with non-radioactive labelled napropamide (purity 94 - 95%) and then diluted with Devrinol 2E blank formulation and incorporated into the upper 3-4 cm of soil in plastic containers corresponding to 2.0 kg as/ha. Rape seeds were sown in 4 containers with treated soil. In addition one untreated control container was set. Forage samples were taken 124 days after treatment (DAT) (forage 1) and 195 DAT (forage 2). Samples of pods were taken 256 DAT and harvest was 292 DAT. Soil samples were also taken at each sampling point. After harvesting the roots, foliage and the pods were separated. At harvest the seeds were removed from the pods and empty pods included with the foliage (haulm).

Plant material samples were extracted with acetonitrile and acetonitrile/water (1:1) and water. Oil seeds were extracted with hexane, acetonitrile and acetonitrile/water. The hexane extracts of oilseeds were characterised using solid phase extraction (silica) and by saponification. Exhaustive extraction of non-extractable residues was performed by incubation with enzymes, extraction with 0.1 M HCL, extraction with 0.1 M NAOH, reflux with 6 M HCL for 2 hours and reflux with 2 M NaOH, or 10 M NaOH for 2 hours. Samples were stored at < - 10°C until analysis which was performed within 5 weeks (15 weeks for forage 1). The total radioactive residues were determined by LSC or by combustion/LSC. TLC and HPLC were used for characterisation and identification of metabolites.

Fractionation of soil residues was performed by extraction with 0.5 M NaOH for 18 hours, followed by extraction with 0.5 M NaOH two times. Further extraction was performed twice with 1 M HCL and the extracts were pooled. The total radioactive residues were determined by LSC or by combustion/LSC. TLC and HPLC were used for characterisation and identification of metabolites.

HPLC analyses of solvent/water extract of forage 2, pods and remaining plant, and oil seeds and haulm at harvest was conducted within 5 weeks of sampling. Due to an error, definitive HPLC analysis of forage 1 solvent/water extracts was conducted within 15 weeks. A portion of the remaining plant from the pod development stage was re-extracted approximately 15 weeks after the initial extraction. The amount of radioactive components was similar to the original analysis indicating that napropamide and metabolites were stable for at least 15 weeks.

Results

The total radioactive residues (TRR) in foliage, pods, haulm, oilseeds and soil are shown in Table B.7.2.1-2.

Table B.7.2.1-2 Total radioactive residue (mg napropamide equivalents/kg) in crop and soil

Sampling time	Crop part/Soil	TRR	Extractable	Non extractable
Application	Soil	2.12	2.10 (99.5)	0.015 (0.7)
Forage 1 (124 DAT)	Foliage	0.334	0.334 (100)	-
	Soil	0.563	0.324 (57.6)	0.239 (42.4)
Forage 2 (195 DAT)	Foliage	0.119	0.119 (100)	-
	Soil	1.43	0.460 (37.5)	0.968 (62.5)
Pod development (256 DAT)	Pods	0.019	0.015 (81.1)	0.004 (18.9)
	Foliage	0.104	0.075 (72.3)	0.029 (27.7)
	Soil	0.593	0.113 (22.0)	0.481 (78.1)
Main Harvest (292 DAT)	Oilseeds	0.060	0.050 (83.4)	0.010 (16.6)
	Haulm	0.118	0.075 (63.9)	0.043 (36.1)
	Soil	0.508	0.061 (14.6)	0.447 (85.4)

As shown in Table B.7.2.1-2 TRR in forage declined from 0.334 mg/kg at 124 DAT to 0.119 mg/kg at 195 DAT. At the pod development stage, TRR values were 0.019 mg/kg in the pods and 0.104 mg/kg in the remaining plant. At 292 DAT (harvest) TRR values were 0.060 mg/kg and 0.118 mg/kg in oilseeds and haulm respectively. Furthermore it is shown that the extraction efficiency was 100% of TRR in forage 1 and 2, 81.1% in pods, 72.3% in foliage from pod development, 83.4% in oilseeds and 63.9% in haulm.

TRR in soil declined from 2.12 mg/kg at application to 0.508 mg/kg at harvest. Extraction efficiency declined from 99.5% of TRR at application to 14.6% at 292 DAT. The residue remaining after solvent extraction at harvest (85.4% of TRR, 0.447 mg/kg) was fractionated into a humin fraction (54.5% of TRR, 0.277 mg/kg), a humic acid fraction (4.0% of TRR, 0.020 mg/kg) and a fulvic acid fraction (26.9 of TRR, 0.137 mg/kg).

In Table B.7.2.1-3 and B.7.2.1-4 summarises of the results concerning TRR and identification and characterisation of this in forage samples, haulm and oilseeds are shown.

Table B.7.2.1-3 Summary of TRR and identification and characterisation of metabolites in forage 1 and 2 (in % of TRR and mg napropamide equivalents/kg).

	Forage 1		Forage 2	
	mg/kg	% of TRR	mg/kg	% of TRR
TRR	0.334	100	0.119	100
Extracted radioactivity	0.334	100	0.119	100
Napropamide	0.054	16.3	0.002	1.7
Polar fraction	0.083	25.9	0.051	43.0
Maximum amount of other individual component	0.024	7.3	0.006	5.1
Non extractable	nd	nd	nd	nd

nd not detected. Insufficient residue remained for analysis.

Table B.7.2.1-4 Summary of the TRR and identification and characterisation of metabolites in samples of haulm and oilseeds (in % of TRR and mg napropamide equivalents/kg).

	Oilseeds		Haulm	
	mg/kg	% of TRR	mg/kg	% of TRR
TRR	0.060	100	0.118	100
Extracted radioactivity	0.050	83.4	0.075	63.9
Napropamide	< 0.001	< 0.8	0.001	0.8
Polar fraction	0.013	21.0	0.014	12.2
Incorporation into oil fraction	0.011	19.1	na	na
Maximum amount of other individual component	0.002	3.8	0.007	6.1
Non extractable	0.010	16.6	0.043	36.1

nd not applicable

Forage sample 1 and forage sample 2
As shown in Table B.7.2.1-3 100 % of TRR could be extracted in forage 1 and 2, respectively. Napropamide accounted for 16.3% of TRR (0.054 mg/kg,) in forage 1 and 1.7 % of TRR (0.002 mg/kg) in forage 2, respectively. Furthermore at least eighteen and sixteen components could be characterised in forage 1 and 2, respectively. At least 4 of these components were found in the polar fraction, the largest of which amounted to 30% of TRR (0.036 mg/kg, forage 2). Component nine amounted to 7.3% of TRR (0.024 mg/kg) in forage 1 and 17.3% of TRR (0.021 mg/kg) in forage 2, respectively.
In summary 96.3% and 77.4% of TRR could be identified or characterised due to napropamide and at least eighteen components in forage 1 and sixteen components in forage 2, respectively.

Immature pod at the pod development stage
As shown in Table B.7.2.1-2 81.1% of TRR could be extracted from immature pod at the pod development stage and 18.9% was unextractable. Napropamide was not detected. The solvent/water extractable fraction accounted for 42.9% of TRR. At least thirteen components were seen in this fraction. One of these accounted for 27.9% (0.005 mg/kg) and 2 minor components accounted for 0.001 mg/kg (5.3%) and 0.002 mg/kg (8.2%), respectively. Enzyme treatment and acid and base hydrolysis released a further 38.2% of which each fraction accounted for < 0.003 mg/kg (17.2%). These fractions were not chromatographed. Thus only 42.9% of TRR could be characterised. No further investigations were conducted on the pod extracts as no single components or fractions exceeded 0.010 mg/kg.

Extracts of the foliage at the pod development
As shown in Table B.7.2.1-2 72.3% of TRR could be extracted and 27.7% was unextractable. Nine components were characterised and accounted for 45.7% of TRR. Component 9 accounted for 10.8% (0.011 mg/kg). All the other components accounted each for < 0.01 mg/kg. Enzyme treatment and acid and base hydrolysis released further radioactivity amounting to 26.6% of TRR of which most significant was obtained with 2 M NaOH (0.012 mg/kg, 11.9%). These fractions were not chromatographed. Thus a total of 45.7 % of TRR could be identified and characterised.
No further investigations were conducted as no single components or fractions exceeded 0.012 mg/kg.

Extracts of the haulm at harvest
As shown in Table B.7.2.1-4 63.9% of TRR could be extracted and 36.1% was unextractable. Napropamide accounted for 0.8% (0.001 mg/kg) and a polar fraction accounted for 12.2% (0.014 mg/kg). The polar fraction was further analysed by TLC and was resolved into 3 components, the largest accounting for 6.7% of TRR (0.008 mg/kg). Further 8 minor components were present in the solvent/water extraction, each amounting to < 0.01 mg/kg and in total accounting for 25% of TRR. Enzyme treatment and acid and base hydrolysis released further 26.3% of TRR of which the most significant amount was released by 2 M NaOH (0.016 mg/kg, 13.9% of TRR). These fractions were not chromatographed. Thus a total of 38% of TRR could be identified and characterised. No further investigations were conducted as no single component or fraction exceeded 0.016 mg/kg.

Oilseeds
It is seen from Table B.7.2.1-4 that 83.4% of TRR could be extracted from oilseeds and 16.6% was unextractable. The hexane extract of the oilseeds at harvest contained 26.1% of TRR (0.016 mg/kg) and contained mainly oil. SPE developed to separate napropamide from oil was used to characterise the radioactivity

and showed that 0.012 mg/kg (19.9% of TRR) was associated with the oil fraction. The hexane fraction was also saponified with base and showed that 0.011 mg/kg (19.1% of TRR) was associated with the free fatty acid fraction. Subsequent solvent/water extraction showed polar material accounting for 34.7% of TRR (0.021 mg/kg). One component in this fraction amounted to 0.013 mg/kg (21% of TRR) and 5 minor components each amounted to < 0.01 mg/kg. Further 10 component were seen in this fraction each amounting to < 0.001 mg/kg. The components in total accounted for 13.7% of TRR. Acid and base extractions released further radioactivity accounting for 22.6% of TRR, each fraction < 0.01mg/kg and they were not chromatographed. Thus a total of 60.8 % of TRR was identified and characterised. No further investigations were conducted as no single component or fraction exceeded 0.013 mg/kg.

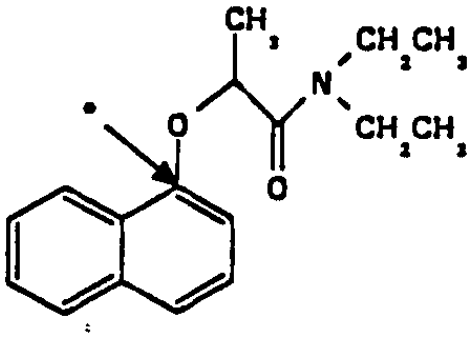
Conclusion

Extractability of the radioactivity from the forage samples was good, but a significant portion of radioactivity remained unextracted at the other sampling time points even after exhaustive extraction procedures. In forage 1, forage 2, immature pods at pod development stage, foliage at pod development stage, haulm at harvest and oilseeds a total of 96.3%, 77.4%, 42.9%, 45.5%, 37.6% and 60.8 %, respectively, was identified and characterised. The only component present at levels >0.05 mg/kg (0.054 mg/kg) was found in forage sample 1 and was identified as napropamide. The component detected in largest amount was detected in the polar fraction from forage 2 and accounted for 30% of TRR (0.036 mg/kg). Component nine also accounted for more than 10% of the TRR in the forage 2 sample (17.3% of TRR, 0.021 mg/kg) and the foliage from 256 DAT (10.8% of TRR, 0.011 mg/kg). Oil seed contained one which exceeded >0.01 mg/kg or >10% of the TRR. The component occurred in the polar fraction and accounted for 21% of TRR, 0.013 mg/kg. Saponification of the hexane extract from oilseeds showed that the radioactivity was associated with free fatty acid.

Report:	CA 6.2.1/03. Emburey, S., Joseph, R.S.I. (1992), Napropamide: Uptake and Metabolism in Cabbage. Company Report No. RJ1224B. ICI Agrochemicals, United Kingdom. GLP.

Materials and methods

[^{14}C-1-naphthyl]-napropamide, radiochemical purity 97.9 % was used in the study.



* Denotes position of ^{14}C-naphthyl-1 label.

The study was conducted in a glasshouse situated at Jealott`s Hill Research Station, Bracknell, Berkshire, England.

[^{14}C-1-naphthyl]-napropamide was isotopically diluted with non-radioactive labelled napropamide (purity 99.8 %) to give a specific activity of 4153.2 Bq μg^{-1} and then diluted with Devrinol 2E blank formulation. The test substance was incorporated into the upper 5 cm of sandy clay loam soil in pots corresponding to 2.5 kg as/ha. Cabbage plants at the 6-8 leaf stage were planted in 4 pots with treated soil. In addition one untreated control pot was set. The plants were harvested at maturity 55 – 60 days after soil treatment. Cabbages were separated into

samples of heart and outer leaf for analysis. Samples were stored at less than -10°C until analysis, which was performed within 3 month.

A sub sample from the four cabbage heart was combined, extracted and fractionated. Extractions were performed with ethanol and ethanol-water (70:30, v/v). Combined subsamples were partitioned with diethyl ether to give the fractions Ether 1 and Aqueous 1. Aqueous 1 was fractionated using a pre-conditioned C_{18} Bond-Elute column (SFE) to give Aqueous A and a 100% methanol fraction. The 100% methanol fraction was acid hydrolysed before being partioned with diethyl ether to give Aquoeus 2 and Ether 2. Further extraction of the unextracted fraction was performed with enzyme hydrolysis to give an unextracted fraction and a filtrate. The filtrate was partitioned with diethylether to give Ether 3 (not further analysed by TLC or HPLC) and Aqueous 3. Aqueous 3 was fractionated using SFE to give Aqueous B. TLC and/or HPLC analysis was used for characterisation and identification of metabolites. The extraction and fractionation procedure is shown in Figure B.7.2.1-5 and 7.2.1-6 below.

Figure B. 7.2.1-5: Fractionation of the cabbage heart

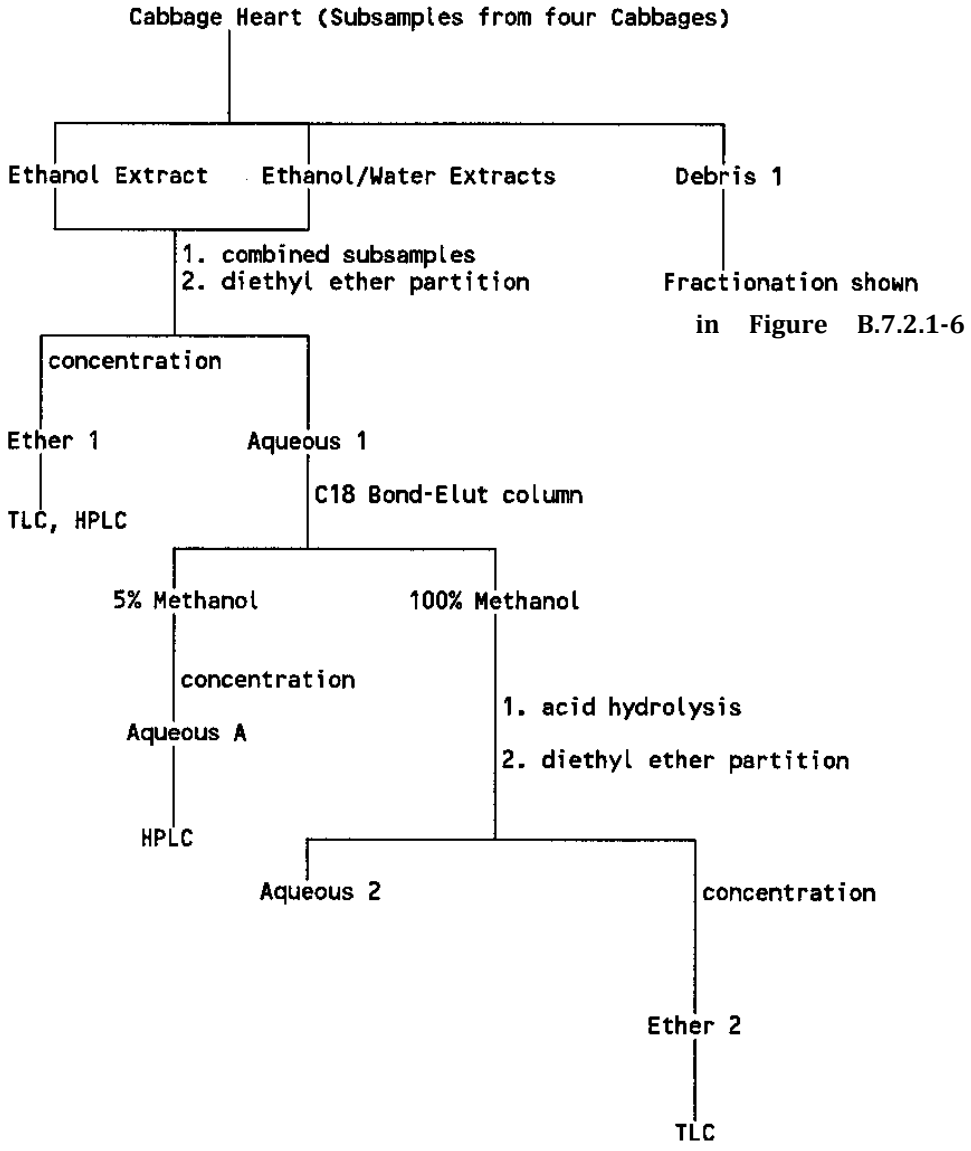
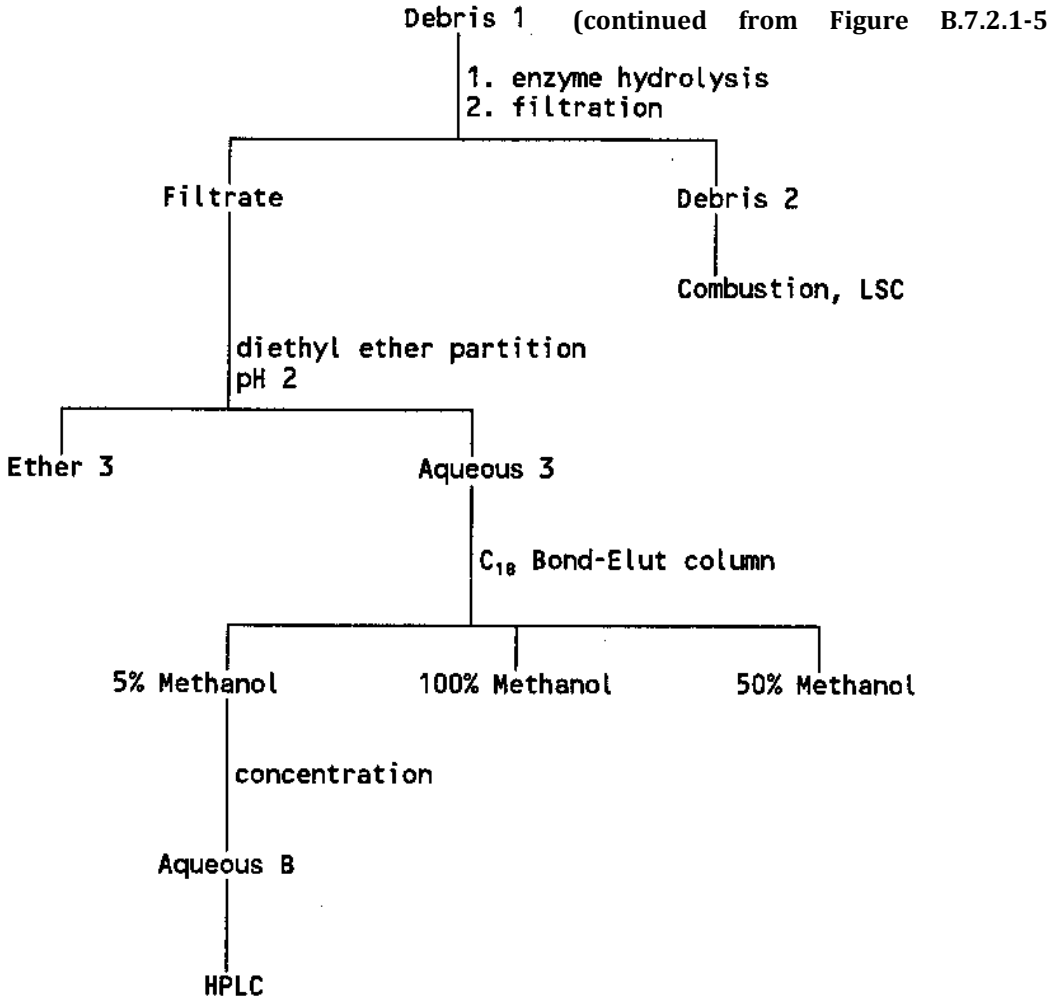


Figure B. 7.2.1-6: Fractionation of the cabbage heart debris



To determine the nature of the residue in the whole cabbage, a sub sample from each cabbage heart and outer leaves samples was combined, extracted, fractionated and analysed in the same way as the residue in the cabbage heart.
Also sub samples of cabbage heart and the whole cabbage from the control cabbage were fractionated and analysed which resulted in the following fractions: Ether 4, Ether 5, Aqueous 5, Aqueous C and D, 50% Methanol 1 and an unextracted fraction.

TRR was determined by combustion/LSC and by LSC on ethanol extract.

The metabolism study includes a study of storage stability of [^{14}C-1-naphthyl]-napropamide in cabbage heart and whole cabbage extracts. Residues were extracted from mature cabbage heart and the whole cabbage. Similar TLC profiles were observed after 17 month of storage at -10°C indicating that napropamide and its metabolites are stable in extracts of cabbage for up to 17 month at - 10°C.

Results

Analysis of control cabbage
In Table B.7.2.1-5 the results for the control cabbage are summarised.

Table B.7.2.1-5 Summary of ^{14}C-residues in control cabbage and outer leaves.

Sample (processed mass)	Mass (g)	Extracted residue mg/kg (% TRR)	Unextracted residue mg/kg (% TRR)	Total residue mg/kg
Cabbage heart	472.56	0.004 (55.2)	0.003 (44.8)	0.007
Outer leaves	218.36	0.003 (29.6)	0.006 (70.4%)	0.009

As shown in Table B.7.2.1-5 ^{14}C residues in control cabbage were 0.007 mg/kg and 0.009 mg/kg in cabbage heart and whole cabbage, respectively. The notifier has assumed that this activity was attributed to incorporation of $^{14}CO_2$ evolved from the treated soil in the test pots.

Analysis of cabbage heart and whole cabbage
Distributions of TRR in different fractions are shown in Table B.7.2.1-6 and B.7.2.1-7.

Table B.7.2.1-6 Distribution and nature of total radioactivity in various fractions from the extraction of the cabbage heart (2.5 kg as/ha treatment) in % of TRR and mg napropamide equivalents/kg.

Fraction	% of TRR	mg/kg	Nature of fraction
Ether 1 + Ether 2	18.3	0.023	Metabolites
Aqueous 2	5.0	0.006	Uncharacterised
Aqueous A	42.7	0.053	Sugars
Aqueous B	24.7	0.031	Sugars
Unextracted fraction	5.5	0.007	Uncharacterised
Other fractions	1.6	0.003	None > 1.2% (0.002 mg/kg)
Activity lost during fractionationation	2.2	0.003	
Sum	100	0.126	

Table B.7.2.1-7 Distribution and nature of radioactivity in various fractions from the extraction of the whole cabbage (2.5 kg as/ha treatment) in % of TRR and mg napropamide equivalents/kg

Fraction	% of TRR	mg/kg	Nature of fraction
Ether 4 + Ether 5	48.8	0.223	Metabolites
Aqueous 5	5.8	0.027	Unknowns
Aqueous C	9.0	0.041	Sugars
Aqueous D	7.2	0.033	Sugars
Unextracted fraction	9.9	0.045	Uncharacterised
50% Methanol 1	6.2	0.028	Unknowns
Other fractions	0.9	0.004	None > 0.7% (0.003 mg/kg)
Activity lost during fractionation	12.2	0.056	
Sum	100	0.457	

In Table B.7.2.1-8 and B.7.2.1-9 summaries of the distribution and characterisation of radioactivity in various fractions from extractions of the cabbage heart and the whole cabbage are shown. The metabolite levels, shown as % of TRR, are shown as sum of free and conjugated form of the metabolites. The total residues (%) for compounds characterised in more than one fraction are presented as sum of the residue found in each individual fraction.

Table B.7.2.1-8 Summary of the distribution and characterisation of the radioactivity in various fraction from extraction in the cabbage heart in % of TRR and mg napropamide equivalents/kg

Component	% of TRR	mg/kg
Organosoluble radioactivity		
Napropamide	0.8	0.001
5-hydroxynapropamide(5-OH-NPAM)	1.2	0.002
Desethylnapropamide(DE-NPAM)	2.5	0.003
o-phthalic acid (PA)	0.5	0.001
1,4-Naphthoxyquinone(NQ)	0.8	0.001
Naphthoxy propionic acid (NOPA)	3.0	0.004
5-hydroxynaphthoxypropionic acid (5-OH –NOPA)	1.0	0.001
Unknowns	5.2	0.007
Remainder	3.4	0.004
• **Sum**	**18.4**	**0.024**
Aqueous soluble radioactivity		
Glucose	18.6	0.023
Fructose	13.0	0.016
Unknowns[a]	5.7	0.007
Losses on column	5.4	0.007
Aqueous (uncharacterised)	5.0	0.006
• **Sum**	**47.7**	**0.059**
Radioactivity resulting from enzyme hydrolysis of the unextracted fraction		
Sucrose	3.6	0.005
Glucose	12.4	0.016
Fructose	2.5	0.003
Unknowns[b]	3.0	0.004
Losses on column	3.2	0.004
Aqueous-soluble activity not analysed	1.6	0.002
Sum	**26.3**	**0.034**
Unextracted fraction	5.5	0.007
Radioactivity lost during fractionation	2.2	0.003

[a] Individual unknowns were not greater than 3.4% of the fraction (1.5% of TRR, 0.002 mg/kg)
[b] Individual unknowns were not greater than 8.2% of the fraction (2.0% of TRR, 0.003 mg/kg)

Table B.7.2.1-9 Summary of the distribution and characterisation of the radioactive residues in various fraction from extraction in the whole cabbage in % of TRR and mg napropamide equivalents/kg.

Component	% of TRR	mg/kg
Organosoluble radioactivity		
Napropamide	0.9	0.004
5-hydroxynapropamide(5-OH-NPMAM)	6.7	0.031
Naphthoxypropionamide (NOPAM)	0.2	0.001
Desethylnapropamide (DE-NPMAM)	2.3	0.011
5-hydroxydesethylnapropamide (5-OH-DE-NPAM)	2.0	0.009
O-phthalic acid (PA)	1.0	0.005
1.4. Naphthoxyquinone (NQ)	4.9	0.022
Naphthoxypropionic acid (NOPA)	2.9	0.013
5-hydroxynaphthoxypropionic acid (5-OH-NOPA)	1.7	0.008
Unknowns[a]	14.4	0.066
Remainder[b]	12.5	0.057
Sum	**49.5**	**0.227**
Aqueous soluble radioactivity		
Sucrose	0.2	0.001
Glucose	4.1	0.019
Fructose	3.1	0.014
Unknowns[b]	1.4	0.006
Losses on column	0.3	0.001
Radioactivity remaining in aqueous 5[c]	5.8	0.027
Aqueous radioactivity not analysed	0.2	0.001
• **Sum**	**15.1**	**0.066**
Radioactivity resulting from enzyme hydrolysis of the unextracted fraction		
Organosoluble activity not analysed	0.7	0.003
Sucrose	1.4	0.006
Glucose/fructose	3.8	0.017
Unknowns[d]	2.1	0.010
Activity in 50% methanol 1[e]	6.2	0.028
• **Sum**	**13.6**	**0.064**
Unextracted fraction	9.9	0.045
Radioactivity lost during fractionation	12.2	0.056

[a] The major unknown is = 3.0% of TRR, 0.014 mg/kg
[b] Individual unknowns were not greater than 3.4% of the fraction (0.3% of TRR, 0.001 mg/kg)
[c] Aqueous 5 contains at least two unknowns, the greatest of which accounts for 1.6% of TRR, 0.007 mg/kg
[d] Individual unknowns were not greater than 7.5% of the fraction (0.5% of TRR, 0.002 mg/kg)
[e] 50% methanol 1 contains at least one unknown, the greatest of which accounts for 3.8% of TRR, 0.017 mg/kg

Cabbage heart

TRR in cabbage heart was 0.126 mg/kg. As shown in Table B.7.2.1-8 a total of 66.1% of TRR (0.083 mg/kg) could be extracted. Enzyme hydrolysis released further 26.3% (0.034 mg/kg) leaving 5.5% (0.007 mg/kg) unextracted. Characterisation of the residues showed that napropamide accounted for 0.8% (0.001 mg/kg). Six other metabolites were identified of which the major metabolite was represented by naphthoxypropionic acid accounting for 3% (0.004 mg/kg).

Aqueous soluble radioactivity accounted for 47.7% of TRR and sucrose, glucose and fructose of which the major was glucose accounting for 18.6% (0.023 mg/kg) were identified in this fraction.

The radioactive contents in sugars are due to natural incorporation of $^{14}CO_2$ produced by the degradation of napropamide applied to the soil. The uptake of $^{14}CO_2$ is evident in control cabbage.

A total of 50.1% of TRR (0.063 mg/kg) was identified as sucrose, glucose and fructose, indicating the residue level due to napropamide and its metabolites were no greater than 0.063 mg/kg.

In conclusion 93.6% of TRR could be extracted and characterised from the cabbage heart. Of TRR 60.2% could be identified either as napropamide and its metabolites or as sugars resulting from natural incorporation. All unidentified components or fractions each accounted < 5% of TRR or (0.006 mg/kg) making no further identification practical or necessary.

Whole cabbage
TRR in the whole cabbage accounted for 0.457 mg/kg. As shown in Table B.7.2.1-9 a total of 64.6% of TRR (0.293 mg/kg) could be extracted and 9.9% (0.045 mg/kg) was unextractable. Enzyme hydrolysis released a further 13.6% (0.064 mg/kg).

Characterisation of residues showed that napropamide accounted for 0. 9% (0.004 mg/kg). Eight other metabolites were identified of which the major metabolite was 5-hydroxynapropamide accounting for 6.7% (0.031 mg/kg).

Aqueous soluble radioactivity accounted for 14.9% of TRR and was identified as sucrose, glucose and fructose. In the enzyme hydrolysed fraction sugars were also identified.
A total of 12.6% of TRR (0.058mg/kg) was identified as sucrose, glucose and fructose mg/kg, indicating the residue level due to napropamide and its metabolites were no greater than 0.399 mg/kg.

In conclusion 78% of TRR could be extracted and characterised from the cabbage heart. Of the TRR 65.2% could be identified either as napropamide and its metabolites or as sugars resulting from natural incorporation.

One unknown component characterised in the fraction enzyme hydrolysed accounted for 3.8% TRR (0.017 mg/kg). All other unidentified components or fractions each accounted for < 1.6% of TRR or (0.007 mg/kg) making no identification practical or necessary.

Conclusion
Cabbage, grown in soil incorporated with ^{14}C-napropamide, equivalent to 2.5 kg as/ha metabolise napropamide in the cabbage heart and the whole cabbage by a similar metabolic pathway. TRR in the cabbage heart and in the whole cabbage were 0.126 mg/kg and 0.457 mg/kg, respectively. These comprised of a trace of napropamide amounting to 0.8% of TRR (0.001 mg/kg) and 0.9% of TRR (0.004 mg/kg) in the cabbage heart and the whole cabbage, respectively. Six metabolites were identified in the cabbage heart and eight metabolites were identified in the whole cabbage. The metabolites identified were 5-hydroxynapropamide, naphthoxypropionamide, desethylnapropamide, 5-hydroxydesethylnapropamide, O-phthalic acid, 1.4-naphthoxyquinone, naphthoxypropionic acid and 5-hydroxynaphthoxypropionic acid which all were present in concentrations < 0.01 mg/kg. Natural sugars (from incorporation of 14CO2) accounted for 50.1% (0.063 mg/kg) and 12.6% (0.058 mg/kg) of TRR in the cabbage heart and whole cabbage respectively. All unidentified components of the residue were present in concentrations < 0.017 mg/kg and < 10% of TRR.

Report:	CA 6.2.1/04. Webb, J., Allin, R., Joseph, R.S.I. (1992), Napropamide: Uptake and Metabolism in Tomatoes Company Report No. RJ1153B. ICI Agrochemicals, United Kingdom. GLP.

Materials and methods
[^{14}C-1-naphthyl]-napropamide, radiochemical purity 97.9% was used in the study. The study was conducted in a glasshouse situated at Jealott`s Hill Research Station, Bracknell, Berkshire, England.

[^{14}C-1-naphthyl]-napropamide was isotopically diluted with non-radioactive labelled napropamide (purity 99.8%) to give a specific activity of 4153.2 Bq μg^{-1} and then diluted with Devrinol 2E blank formulation. The test substance was incorporated into the upper 5 cm of soil in pots corresponding to 2.5 kg as/ha. Tomato plants at the 4-6-leaf stage were used as test crops and planted in 3 pots with treated soil. In addition one untreated

control pot was set. The plants were grown to yield five trusses of tomato fruits on each of the three treated plants. Tomatoes were harvested as they ripened. Samples were stored at < -10°C until analysis within four month. The control tomatoes were harvested and stored in the same way.

Samples from truss two were extracted and fractionated prior to analysis by TLC. Extraction was performed with ethanol: water (70:30) before being partitioned with diethylether to give Ether 1 and Aqueous 1. Aqueous 1 was base hydrolysed and fractionated by SFE to give aqueous A and a 100% methanol fraction. The 100% methanol fraction was enzyme hydrolysed before being partitioned with diethyl ether to give Aqueous 2 and Ether 2. Aqueous 2 was fractionated by SFE to give an aqueous fraction, a 100% methanol fraction and a 50% methanol fraction. The 100% methanol fraction and the 50% methanol fraction were base hydrolysed and fractionated by SFE to give an aqueous fraction and a 100% methanol fraction. The 100% methanol fraction was enzyme hydrolysed before being partioned with diethylether to give Aqueous 3 and Ether 3. Aqueous 3 was partitioned with diethyl ether and acidified to pH 2 to give Aqueous 4 and Ether 4. Aqueous 4 was partitioned with ethyl acetate to give Aqueous 5 and Ethyl acetate 5. Further extraction of the unextracted fraction was performed with enzyme hydrolysis to give an unextracted fraction and a filtrate. The filtrate was partitioned with diethylether to give Ether 6 and Aqueous 6. Aqueous 6 was fractionated by SFE to give a 50% methanol fraction, a 100% methanol fraction and Aqueous B. Also control tomatoes were fractionated before analysis.

The total radioactive residues (TRR) in extracts were determined by LSC or by combustion/LSC. HPLC and/or TLC were used for characterisation and identification of metabolites.

The metabolism study included a study of the storage stability of [^{14}C-1-naphthyl]-napropamide in extractions of tomatoes. Extractions were performed on harvests from trusses one, two, three and five. Storage of up to 12 month at - 10°C all resulted in similar TLC profiles indicating that napropamide and its metabolites are stable in sample extracts from tomatoes for up to 12 months at - 10°C.

Results

In Table B.7.2.1-10 the distribution of TRR in the different fractions produced during fractionation is summarised.

Table B.7.2.1-10 Distribution of TRR in the different fractions produced during fractionation in % of TRR and mg napropamide equivalents/kg.

Fraction	% of TRR	mg/kg	Nature of the fraction
Ether 1 + Ether 2 + Ether 3 + Ether 4	31.2	0.016	Metabolites
Ethylacetate 5	5.4	0.0028	Unknowns
Aqueous 5	9.6	0.0049	Unknowns
Aqueous A + Aqueous B	31.2	0.016	Sugars
Unextracted	7.7	0.0039	No further work
Other fractions	6.3	0.0032	No > 2.3% (0.0012 mg/kg)
Activity lost during fractionation	8.6	0.0044	
Sum	100	0.0512	

From Table B.7.2.1-10 it is seen that TRR in truss two accounted for 0.051 mg/kg.

Summary of the characterisation of TRR in tomato fruit is presented in Table B.7.2.1-11. The metabolite levels, shown as % of TRR, are overall figures including of free and conjugated metabolites. The % of TRR shown for compounds identified in more than one fraction are calculated by adding the radioactivity found in each of the fractions.

Table B.7.2.1-11 Summary of the identification and characterisation of TRR in the tomato fruit in % of TRR and mg napropamide equivalents/kg.

Component	% of TRR	mg/kg
Organosoluble radioactivity		
Napropamide	0.4	0.0002
5-hydroxynapropamide(5-OH-NPAM)	2.4	0.0012
4-hydroxynapropamide (4-OH-NPAM)	0.2	0.0001
Desethylnapropamide (DE-NPAM)	1.6	0.0008
4-hydroxynapropamide (4-OH-DE-NPAM)	0.6	0.0003
5-hydroxydesethylnapropamide (5-OH-DE-NPAM)	4.5	0.0023
o-phthalic acid (PA)	6.1	0.0031
Naphthoxypropionic acid (NOPA)	1.5	0.0008
5-hydroxynaphthoxypropionic acid (5-OH-NOPA)	4.2	0.0021
4-hydroxynaphtoxypropionic acid (4-OH-NOPA)	1.2	0.0006
Unknowns	8.3[a]	0.0042
Remainder	5.1	0.0026
• **Sum**	**36.1**	**0.0201**
Aqueous soluble radioactivity		
Glucose	8.6	0.0044
Fructose	9.6	0.0049
Remainder	7.0	0.0036
Activity remaining in aqueous 5	9.6	0.0049
Aqueous radioactivity (not analysed)	4.0	0.0020
Sum	**38.8**	**0.0198**
Radioactivity resulting from enzyme hydrolysis of the unextracted fraction		
Organo soluble activity not analysed	0.4	0.0002
Glucose/sucrose	2.3	0.0012
Fructose	0.7	0.0004
Remainder	3.0	0.0015
Aqueous-soluble activity not analysed	1.3	0.0007
Sum	**7.7**	**0.004**
Activity remaining unextracted	8.3	0.0042
Activity lost during fractionation	8.6	0.0003

As shown in Table B.7.2.1-11 a total of 74.9% of TRR could be extracted. Enzyme hydrolysis released further 7.7% leaving 8.3% unextracted. During fractionation 8.6% was lost.

Characterisation and identification of residues showed that napropamide accounted for 0.4% (0.0002 mg/kg). Furthermore nine metabolites were identified, which individually accounted for between 0.2% and 6.1% of TRR (0.0001 – 0.0032 mg/kg).

Aqueous soluble radioactivity accounted for 38.8% of TRR. Of this 18% was identified as sugars due to natural incorporation of $^{14}CO_2$ formed from napropamide in soil. In the enzyme hydrolysed fraction sugars were also identified.
A total of 21.2% of TRR (0.011 mg/kg) was identified as sucrose, glucose and fructose, indicating the residue level due to napropamide and its metabolites were no greater than 0.04 mg/kg.

Conclusion
When tomatoes were grown in a glasshouse in soil treated with [^{14}C-1-naphthyl]-napropamide equivalent to 2.5 kg as/ha, total residue in the mature fruits was 0.051 mg/kg (of which 82.6% could be extracted and characterised). A total of 43.9% (0.022 mg/kg) could be identified either as napropamide and its metabolites or as sugars resulting from natural incorporation. Napropamide accounted for 0.4% (0.0002 mg/kg) and 9

metabolites were identified, e.g. 5-hydroxynapropamide, 4-hydroxynapropamide, desethylnapropamide, 4-hydroxydesethylnapropamide, 4-hydroxydesethylnapropamide, o-phthalic acid, naphthoxypropionic acid, 5-hydroxynaphthoxypropionic acid and 4-hydroxynaphthoxypropionic acid. All unidentified single components or fractions each accounted for 0.0049 mg/kg or < 9.6% of TRR making no further identification practical or necessary.

Report:	CA 6.2.1/05. Hurt, A.D., Joseph, R.S.I. (1992), Napropamide: Uptake and Metabolism in Apples Company Report No. RJ1128B. ICI Agrochemicals, United Kingdom. GLP.

Materials and methods

[^{14}C-1-naphthyl]-napropamide, radiochemical purity > 99%. [^{14}C-1-naphthyl]-napropamide was isotopically diluted with non-radioactive labelled napropamid (purity 99.8%) to give a specific activity of 207.2 Bq μg^{-1} and 201.3 Bq μg^{-1} for the first and second application solution, respectively. After this the substance was diluted with Devrinol 2E blank formulation. The study was conducted in England. The soil type was a medium clay loam. The two test plants (treated and control) were three-year-old Golden Delicious trees. [^{14}C-1-naphthyl]-napropamide solution was in the first application incorporated into the upper 5-8 cm of soil around the base of the apple tree, centred in an 4 m^2 plot at a rate corresponding to 4.61 kg as/ha. 151 days after the first treatment a second application was incorporated into the soil by watering at a rate corresponding to 4.53 kg as/ha. The overall application rate corresponded to 9.15 kg as/ha which is in accordance with the intended use. The first harvest of apples was at maturity 186 days after the first treatment and 35 days after the second treatment. The second harvest of apples was 550 DAT at maturity one year after the first harvest. All apple samples were stored frozen at < - 17°C until analysis which was performed within 13 days. TRR was determined using either combustion followed by LSC or by direct combustion analyses. Samples were extracted with ethanol: water (70:30 (v/v)).

Results

The TRR from samples determined by direct combustion was 0.0028 mg/kg, while it was 0.0032 mg/kg calculated by multiple extractions and combustion/LSC. In the second harvest 550 DAT TRR was 0.0090 mg/kg after direct combustion and 0.0105 mg/kg after multiple extraction and combustion/LSC.

In Table B.7.2.1-12 the fractionation of TRR into different extractions is summarised. The data obtained by multiple extractions and combustion/LSC are summarised.

Table B.7.2.1-12 Summary of the characterisation of the total radioactive residues in whole apple from first year`s harvest (186 DAT) and second year's harvest (550 DAT), (in % of TRR and mg napropamide equivalents/kg).

Fraction	First year harvest		Second year harvest	
	% of TRR	Residue level (mg/kg)	% of TRR	Residue level (mg/kg)
Whole apple	100	0.0032	100	0.0105
Aqueous soluble	61	0.0020	52.1	0.0055
Organosoluble	12	0.0004	<LOD	<LOD
Filter papers	2	0.00007	1	0.0001
Unextracted	25	0.0008	41.8	0.0044

As it is seen from Table B.7.2.1-12 none of the different fractions of extractions contained residues > 0.002 mg/kg napropamide equivalents so further characterisation was not performed.

Conclusion

When soil around an apple tree is treated at its base with [^{14}C-1-naphthyl]-napropamide, equivalent to 9.15 kg as/ha the mean TRR in mature apples was 0.0032 mg/kg. The mean residue in the second harvest one year later was 0.0105 mg/kg. No further characterisation was performed as no radioactive residues in the different fractions accounted for > 0.002 mg/kg.

Report:	CA 6.2.1/06. Spillner, C.J. (1983), Uptake and metabolism of [^{14}C] Devrinol in potatoes Company Report No. MRC-83-07. Stauffer Chemical Company, USA. Not to GLP.

Materials and methods
Test substance was [^{14}C]-napropamide, radiochemical purity 94.7%. Four sprouting seed potatoes were planted in each tub and grown in keeton loamy sand soil and treated with [^{14}C]- napropamide at a rate equivalent to 2.0 kg as/ha layered to a depth of 2.5 cm over the planted potatoes in a galvanised tubs. In addition control soil was prepared by incorporating non-radioactive napropamide at a rate of 2.2 kg as/ha. The study was conducted outdoor. Potato plants were harvested 61 DAT and were separated into potato foliage, peel and pulp for analysis. All samples were stored frozen (-18°C) until analyses. TRR were determined by combustion/LSC.

Plant samples were extracted with ethanol/water (7/3 v/v) followed by partition and fractionation. Partition was performed with chloroform/water. Deconjugation was performed with acid-hydrolysis and β-glycosidase. Soil samples were extracted with acetone for 16 hours. Characterisation and identification of metabolites was performed by TLC.

Results
Soil
TRR in soil declined from 4.91 mg/kg at 0 DAT sample to 0.92 mg/kg at the 61 DAT sample. 99.8 % of TRR (4.90 mg/kg) and 52.2% of TRR (0.48 mg/kg) could be extracted from the 0 DAT and the 61 DAT samples, respectively. At harvest napropamide was the major component accounting for 43% of TRR. Metabolites (desethyl napropamide, 1- napthoxypropionic acid, β- napropamide, hydroxy-1,4- naphthoquinone and hydroxylethyl napropamide) were found in very low concentrations (<0.036 mg/kg).

Potato Foliage
TRR was 1.13 mg/kg in foliage. 74.2% of this was organoextractable and 25.8% was unextractable. Napropamide accounted for 1.51% of TRR (0.02 mg/kg) and the metabolites 5-hydroxy-napropamide, 4-hydroxy-napropamide, desethyl-napropamide and 1,4-naphthoquinone were all found in concentrations < 0.013 mg/kg. The rest of the extracted material accounted for 69.4% of TRR and consisted of 16.2% unknown organosolubles, 13.9% unknown glucosides and other conjugates and 39.3% other unknown water solubles. All fractions accounted for < 0.01 mg/kg, so no further investigations were performed.

Potato peel
TRR in peel amounted to 0.54 mg/kg of which 63.2% (0.34 mg/kg) could be extracted. Trace of napropamide, 1.11% (< 0.01 mg/kg), was found and metabolites similar to those found in foliage were present in concentrations < 0.01 mg/kg.

Potato pulp
TRR in pulp amounted to 0.11 mg/kg of which 44.8% (0.05 mg/kg) was extracted and 55.2% unextracted (0.059 mg/kg). No napropamide was detected in pulp and only 1.1% of the TRR was identified as traces of metabolites o-naphthalic acid, 1.4-naphthoxyquinone, and 1-naphthol (< 0.01 mg/kg).

Conclusion
In potatoes, grown in soil treated with [^{14}C]-napropamide equivalent to 2.0 kg as/ha, total residues in foliage was 1.13 mg/kg. In the potato peel and pulp TRR at harvest were 0.54 mg/kg and 0.11 mg/kg, respectively. The residues in foliage comprised a trace of napropamide (1.11% of TRR, < 0.01 mg/kg) and at least 4 extracted metabolites identified as 5-hydroxy-napropamide, 4-hydroxy-napropamide, desethyl-napropamide and 1,4-naphthoquinone which all were present in concentrations of <0.01 mg/kg. Similar pattern was seen in potato peel. No napropamide were found in potato pulp and only traces of the metabolites o-naphthalic acid, 1,4-naphthoxyquinone, and 1-naphthol were identified, all present in concentrations < 0.01 mg/kg. In peel and pulp the unextractable fractions accounted for 36.8% and 55.2% of TRR, respectively.

Metabolism, distribution and expression of residues in plants summary and conclusion

Six metabolism studies conducted on plants have been provided. The details of the studies have been summarised in Table B.7.2.1-13 below.

Table B.7.2.1-13: Summary of the primary plant metabolism studies

Crop groups	**Crop**	**Label position**	**Application and sampling details**				**Study**
			Method	**Rate**	**No**	**Sampling (DAT)**	
Fruit crops	Tomato	^{14}C-1-naphthyl]-napropamide	Soil incorporated to top 5cm. Glasshouse study. Tomato seedlings transplanted into treated soil at 4-6 leaf stage.	Corresponding to 2.5 kg as/ha	1	Tomatoes harvested as they ripen.	Webb, J., Allin, R., Joseph, R.S.I. (1992)
	Apple	^{14}C-1-naphthyl]-napropamide	Soil incorporated to top 5-8 cm around 3 year old trees. Then second application 155 days later watered on.	1) Corresponding to 4.61 kg as/ha. 2) Corresponding to 4.53 kg as/ha. Total= 9.15 kga s/ha	2	At harvest 35 days after last treatment and 550 DAT.	Hurt, AD, Joseph, R.S.I, 1992
Root crops	Potato	[^{14}C-1-naphthyl]-napropamide	Soil incorporated to top 2.5cm. Outdoor pot study.	Corresponding to 2 kg as/ha.	1	At harvest 61 days after last treatment.	Spillner,C.J. , 1983
Leafy crops	Cabbage	[^{14}C-1-naphthyl]-napropamide	Soil incorporated to top 5cm. Glasshouse study. Cabbage seedlings transplanted into treated soil at 6-8 leaf stage.	Corresponding to 2.5 kg as/ha	1	55-60 DAT. Cabbage heart and whole cabbage.	Emburey & Joseph (1992)
Pulses/Oilseeds	Oilseed rape	[^{14}C-1-naphthyl]-napropamide	Soil incorporated to top 3-4 cm. Outdoor Rape seeds sown into treated soil	Corresponding to 2.0 kg as/ha	1	Forage 124 and 195 DAT and immature pods 256 DAT and harvestable pods 292 DAT	Langford-Pollard A.D., 2002
	Oilseed rape	[^{14}C-1-naphthyl]-napropamide-M	Soil incorporated to top 2.5 cm. Rape seeds sown into treated soil. Kept in glasshouse until BBCH 12, then outdoors.	Corresponding to 0.72 kg as/ha	1	Forage at BBCH 15, 22 and 51, pods and foliage at GS 76 and pods, straw and seed at BBCH 84.	Ahmad, S. (2015)

All of the studies except for the Ahmad, 2015 study have been previously evaluated in the Napropamide DAR which concluded as follows:

The metabolism of napropamide has been investigated in cabbage (leafy crops), tomatoes (fruiting vegetables), oilseed rape (oilseed), potatoes (root and tuber) and apples (fruit). In all cases except the apple study, plants were sown in soil treated with [^{14}C]-napropamide. The metabolism of napropamide in the four crop categories is similar.
In cabbage, tomatoes, oilseed rape and potato peel napropamide was detected in trace amounts (<0.01 mg/kg). No napropamide was detected in potato pulp.

In cabbage and tomatoes seven and nine metabolites were detected, respectively. In potato pulp and peel traces of several metabolites, all < 0.01 mg/kg were detected. In oilseed rape up to eighteen components were detected. In forage from oilseed a significant amount of unmetabolised napropamide was detected (0.054 mg/kg). Here all other components were present at < 0.05 mg/kg, although some accounted for > 10% of TRR in forage samples and foliage from immature plants. In all other cases metabolites were found in amounts < 0.01 mg/kg and < 10% of TRR.

In the metabolism study in apples in which soil around apple trees was treated with [^{14}C]-napropamide, TRR in the mature fruit was negligible (< 0.01 mg/kg).

The metabolism of napropamide involved the following routes:

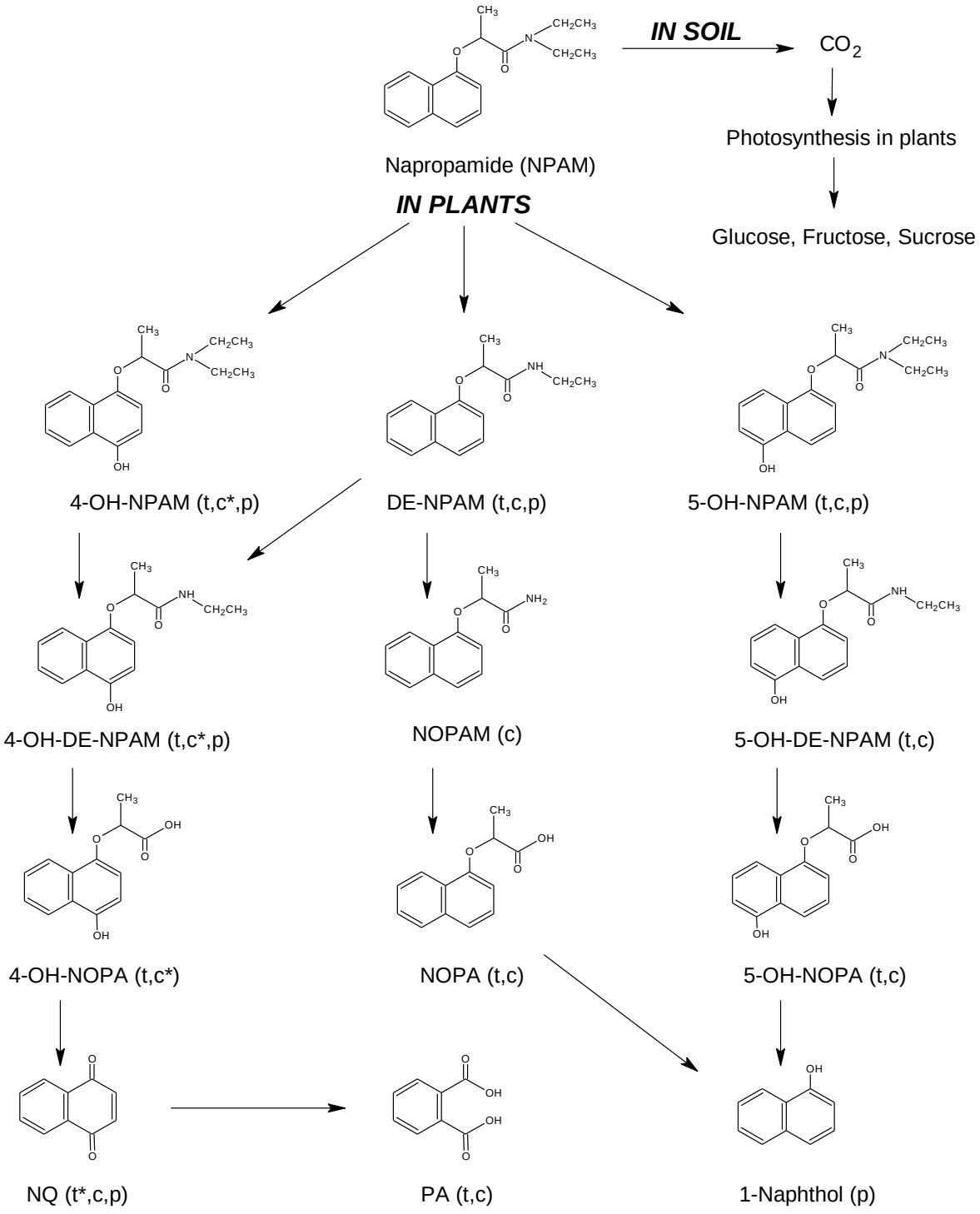
1) *Desethylation to desethylnapropamide (DE-NPAM) followed by further desethylation to naphthoxypropionamide (NOPAM) and then hydrolyses to naphthoxypropionic acid (NOPA).*
2) *Hydroxylation of position 5 in the ring to give 5-hydroxynapropamide (5-OH-NPAM), which is the major metabolite in whole cabbage, followed by desethylation of this compound to give 5-hydroxydesethylnapropamide (5-OH-DE-NPAM). This was hydrolysed to give 5-hydroxynaphthoxypropionic acid (5-OH-NOPA).*
3) *Hydroxylation of position 4 in the ring to give 4-hydroxy-napropamide (4-OH-NPAM), desethylation of this compound to give 4-hydroxynaphthoxypropionic acid (4-OH-NOPA). Oxidation of this compound resultet in 1.4-naphthoxyquinone (NQ) and further oxidation of (NQ) gives compound o-phthalic acid (PA). NQ and PA were only found in conjugated forms.*

Rapporteur has evaluated that the metabolic pattern found in leafy crops, fruiting vegetables, root and tuber vegetables are similar. In oilseed rape napropamide is metabolised extensively since up to eighteen compounds are seen. RMS supposes that the metabolic pattern of napropamide in oilseed is similar to the metabolism found in the three crop categories. No further studies are required for elucidating the metabolic pathway of napropamide in plants.

The metabolic pathway for napropamide in plants is the same as in the rat.

In Figure B.7.2.1-7 the proposed metabolic pathway of napropamide as presented in the Napropamide DAR is reproduced.

Figure B.7.2.1-7 Proposed metabolic pathway for napropamide in plants



t = Tomato, c = cabbage, p = potato

* = not identified but assumed to be intermediate

A residue definition of napropamide in plants for both monitoring and risk assessment was therefore proposed. During peer review concerns were raised that the use of napropamide as a residue definition could substantially

underestimate the total toxicological burden. This was summarised in the EFSA conclusion (EFSA Journal 2010; 8(4):1565) :

The RMS proposed to restrict the residue definition to napropamide for monitoring and risk assessment. This was agreed by the PRAPeR 35 meeting of experts. It was however noted that the definition for risk assessment may underestimate by 1 to 2 orders of magnitude the global toxicological burden, considering the ratio between the parent compound and all metabolites produced by plant metabolism. This was however considered of no consequence in the final outcome of the risk assessment, given the very low portion of the ADI used. The possible change in the ratio of constituting isomers by plant metabolism or due to environmental conditions was also considered by the meeting of experts. It was considered that the impact on consumer safety would not be an issue in this case, as the exposure is minimal.

For this consideration of napropamide-M one additional metabolism study has been provided (Ahmad, 2015) where dosing with napropamide-M was performed on soil in which oilseed rape was then cultivated. Although significant attempts to extract residues were performed in the study very little characterisation was possible. The study was performed at approximately 1N and significant extractable residues (above 0.01 mg/kg in food and >0.05 mg/kg in feed) were only found in foliage at pod development and haulm at maturity. Considering the low levels of residues found in rapeseed and the margin of safety shown in the consumer risk assessment additional studies to elucidate further potential differences in napropamide and napropamide –M metabolism are not considered warranted.

B.7.2.2. Poultry

Report:	CA 6.2.2/01. [redacted] (1993). Metabolism of orally administered multiple doses in the laying hen. Company Report No. RJ1408B. [redacted] GLP.

Materials and methods: As test substance a mixture of [^{14}C-1-naphthyl]-napropamide, radiochemical purity > 99% and unlabelled napropamide (purity 99.8 %) was used. The radiochemical purity of the mixture was 98.3 % and the specific activity was 2190 Bq μg^{-1}.

Animals: Ten laying hens (denoted hen 110 to 120) 30 weeks old and with a body weight on the arrival of 1.9-2.2 kg. The animals were acclimatised for a period prior dosing.

Dose administration: Each hen received once daily an oral dose of 1.145 mg [^{14}C-1-naphthyl]-napropamide in gelatine capsules over a period of ten consecutive days (equivalent to approximately 0.57 mg/kg bw/day). The diet contained a mean of 8.3 mg/kg [^{14}C-1-naphthyl]-napropamide which corresponds to an exaggerated dose due to the fact that detectable residues (≥ 0.01 mg/kg) are not expected in feed items based on the intended uses.

Sample collection: Excreta were collected from the hens during the 24 hours prior to the first radioactive dose and then twice a day, in the morning and in the afternoon before dosing. The samples were stored at - 15°C until analysis. Eggs were collected twice daily, in the morning and in the afternoon prior to dosing from 2 days before the first dose and until termination of the hens. The eggs were kept refrigerated at 0-4°C prior to analysis. The hens were sacrificed between 23 and 24 hours after the final dose. Tissue samples of skin plus subcutaneous fat, peritoneal fat, leg muscle, breast muscle, liver, kidney and gastrointestinal tract and contents were taken for analysis.

Radioactivity analysis: The levels of TRR were measured by combustion/LSC (HRC method) or by extraction, combustion and LSC (ICI method).

Liver from hen 112 was initially extracted with acetonitrile yielding an extractable part and an unextractable part. Further hydrolysis was performed with acid. The use of acid hydrolysis did not release significant amounts of unextractable TRR therefore enzyme hydrolysis was used to further characterise the residues in liver. Only sub samples of the livers from hen 111 and hen 113 are used in the study.

Extraction procedure: Egg yolk samples were sequentially homogenised with acetonitrile, acetonitrile/water (1:1, v/v) and water. Liquid-liquid partitions were carried out with hexane. Liver samples were sequentially extracted with acetonitrile, acetonitrile/water (1:1, v/v). Liquid-liquid partitions were carried out with ethyl

acetate and diethyl ether. Enzyme hydrolysis was performed with β-glucuronidase, pancreatin, peptidase and sulfatase to characterize conjugated metabolites. Base hydrolysis and acid hydrolysis was performed with (0.1 M, 1 M or 4 M) sodium hydroxide solution, respectively. The final aqueous fraction resulting from extraction and fractionation of the liver required clean up and was fractionated using SFE. Further extractions of the unextractable fractions from liver and egg yolk was performed with acetonitrile and base hydrolysed before being partitioned with ethyl acetate. A subsample from the liver was also treated with enzyme (pancreatin).

Chromatographic analysis: TLC was used to characterise radioactive compounds in sample extracts.

Results:
Following the administration of ^{14}C-napropamide to hen 111 and 113 a total of 92.1% of the administered dose was excreted during the dosing period and 2.5% was detected in cage washings.

In Table B.7.2.2-1 the mean concentrations of radioactivity in tissues from hen 110 to 120 are shown.

Table B.7.2.2-1 Mean concentrations of radioactivity in edible tissues of ten hens after 10 daily oral doses of [^{14}C]-napropamide in gelatine capsules (1.2 mg/day)

mg ^{14}C-napropamide equivalent/kg	
Tissue	Mean (mg/kg)
Liver	0.105
Kidney	0.046
Leg Muscle	0.00330
Breast muscle	0.00274
Skin and subcutaneous fat	0.00779
Peritoneal fat	0.00345

As shown in Table B.7.2.2-1 the highest concentrations of radioactivity were detected in liver (0.105 mg/kg) and kidney (0.046 mg/kg). No further characterisation was performed on TRR from the hen kidney. Characterisation was only performed on TRR in liver.

Liver from hen 111 and 113 were extracted and metabolites were identified. Mean total radioactive residue in these two livers amounted to 0.0982 mg/kg. Of this only 29.5% (0.0289 mg/kg) could be extracted with acetonitrile and acetonitrile/water while 70% (0.0687 mg/kg) remained unextractable. Enzymes and base hydrolysis of the unextracted fraction released the majority of the TRR 59.1% (0.058 mg/kg) leaving 10.9% unextractable. 13.7% of TRR (0.0135 mg/kg) was identified as napthoxypropionic acid and 2,5% of TRR (0.0025 mg/kg) was identified as desethylnapropamide. Other components and fractions each amounted to < 0.01 mg/kg, so further identification was not performed.

The mean concentrations of radioactivity in egg whites were in the range of 0.00518 mg/kg to 0.00713 mg/kg. The levels were constant throughout the study and according to the low levels no further characterisation was performed.

Residue levels in the egg yolks rose from 0.0061 mg/kg on day 2 to 0.0373 mg/kg and 0.0419 mg/kg on days 6 and 10, respectively. The mean total radioactive residue (TRR) found in the egg yolks (sub samples from day 3 to day 10) from hen 115 was 0.035 mg/kg. 75.7% of TRR (0.0265) mg/kg was organosoluble, 21.2% of TRR (0.0074 mg/kg) was aqueous soluble, and 6.5% was unextracted. A further 1.5% of TRR (0.0005 mg/kg) remained in the first acetonitrile wash. napropamide was identified and accounted for 5.2% of TRR (0.0018 mg/kg). The metabolites desethylnapropamide, 4-hydroxydesethylnapropamide and naphthoxypropionic acid accounted for 4.1% (0.0014 mg/kg), 3.9% (0.0018 mg/kg) and 6.4% of TRR (0.0022 mg/kg), respectively. No other single components or fractions were at levels > 0.01 mg/kg, so further identification was not performed.

Conclusion
When [^{14}C-1-naphthyl]-napropamide was administered orally to ten laying hen for ten consecutive days at an exaggerated dose rate, napropamide was rapidly metabolised and excreted by hens with 92.1% of the dose (mean value of two hens) being excreted during the dosing period.
The radioactive residue level in the egg whites was constant throughout the study and very low (< 0.01 mg/kg) and was therefore not further characterised.

In the egg yolk a residue level of 0.035 mg/kg was found. Of this 5.2% (0.0018 mg/kg) was identified as napropamide, 4.1% (0.0014 mg/kg) as desethylnapropamide, 3.9% (0.0018 mg/kg) as 4-hydroxydesethyl napropamide and 6.4% (0.0022 mg/kg) as naphthoxypropionic acid. No other single components or fractions occurred at levels > 0.01 mg/kg, so further identification was not performed.

B.7.2.3. Lactating ruminants

Report:	CA 6.2.3/01. [redacted] [redacted] (1993). Metabolism of orally administered multiple doses in the lactating goat. Company Report No. RJ1388B. [redacted] GLP.

Materials and methods

Test substance: A mixture of [^{14}C-1-naphthyl]-napropamide, radiochemical purity > 99% and unlabelled napropamide (purity 99.8 %) was used as a test substance. The radiochemical purity of the mixture was 98.8 % and the specific activity was 2190 Bq μg^{-1}.

Animals: Two lactating goats aged 2 years with a body weight of 65 kg. The two goats were acclimatised for a period of three days prior to administration of the first dose.

Dose administration: Each goat received twice a day an oral administration of [^{14}C-1-naphthyl]-napropamide in gelatine capsules over a period of four consecutive days. The dose rate was 9.9 mg/kg feed of [^{14}C-1-naphthyl]-napropamide (0.38-0.51 mg/kg bw/day).

Sample collection: Urine and faeces were collected 24 hours prior to the first dose and hereafter with 24-hour intervals up to and including 23 hours after the last dose. The goats were milked twice daily, in the morning and in the afternoon prior to dosing. The goats were sacrificed 23 and 24 hours after the final dose and liver, kidney, omental fat, subcutaneous fat, perirenal fat, muscle from foreleg and rump, gastrointestinal tract, urine from bladder and bile were immediately collected.

Radioactivity analysis: The levels of radioactivity were measured in all samples of excreta, cage washings, milk and tissues by LSC or by LSC following combustion.

Extraction procedure: Tissue samples were repeatedly homogenised with acetonitrile/water (1:1; v/v). Further homogenisation was performed on goat 2 samples only, using dichloromethane and chloroform/methanol (2:1; v/v) on the kidney and chloroform/methanol (2:1, v/v) on the liver. Liquid-liquid partitions were carried out with ethyl acetate and diethyl ether. Some of the extracts were treated with enzymes (sulfatase, lipase, pancreatin and papain) to characterise conjugated metabolites. Acid hydrolysis was performed with hydrochloric acid. Using SFE some of the aqueous fractions were fractionated.

Chromatographic analysis: TLC was used to characterise radioactive compounds in sample extracts.

Results
In Table B.7.2.2-2 the recovered radioactivity found in milk, urine, faeces and tissues is shown.

Table 7.2.2-2 Percent total radioactivity as cumulative dose recovered in milk, excreta and tissues

	% of total doses		
Tissue	Animal 1	Animal 2	Mean
Liver	0.178	0.162	0.170
Kidneys	0.008	0.006	0.007
Milk	0.071	0.096	0.084
Urine	47.8	48.2	48.0
Bladder contents	0.085	NS	0.043
Cage washings	2.17	1.16	1.67
Faeces	38.6	41.8	40.2
Total recovery	88.9	91.4	90.2

The metabolism study showed that the majority of the radiolabelled dose administered to the two goats was excreted in urine (47.8 – 48.2%) and faeces (38.6 – 41.8%) after four days. TRR in milk accounted for (0.071-0.096%) of the administered dose. Total recovery of radioactivity accounted for 88.9 – 91.4%.

In Table B.7.2.2-3 the concentrations of radioactivity in milk are shown. After the last dosing the radioactivity quickly decreased.

Table B.7.2.2-3 Combined 24-hourly average concentrations of radioactivity in milk from goats during and after twice-daily oral doses of [^{14}C-1-naphthyl]-napropamide.

	TRR (mg napropamide equivalents /kg)		
Time (hours)	Animal 1	Animal 2	Mean
0 – 24	0.0066	0.0070	0.0068
24 – 48	0.0084	0.0088	0.0086
48 – 72	0.0092	0.0086	0.0089
72 – 96	0.0094	0.0080	0.0087
96 – 102	0.0050	0.0027	0.0039

In Table B.7.2.2-4 TRR in tissues is shown.

Table B.7.2.2-4 Concentration of radioactivity in tissues expressed as mg equivalents napropamide/kg.

	TRR (mg napropamide equivalents /kg)		
Tissue	Animal 1	Animal 2	Mean
Liver	0.140	0.165	0.153
Kidneys	0.0394	0.0335	0.0365
Subcutaneous fat	0.0069	0.0097	0.0083
Omental fat	0.0050	0.0048	0.0049
Perirenal fat	0.0044	0.0043	0.0044
Foreleg muscle	0.0027	0.0027	0.0027
Rump muscle	0.0022	0.0020	0.0021

At sacrifice the highest mean concentration of total radioactivity was detected in the liver (0.153 mg/kg). In kidneys a mean of 0.0365 mg/kg was present while mean concentrations in fat (subcutaneous fat, omental fat and perirenal fat) ranged from 0.0044 to 0.0083 mg/kg. In rump muscle and foreleg muscle, respectively, 0.0021 mg/kg and 0.0027 mg/kg were detected.

Characterisation of the TRR in the liver showed that 18.9% (0.032 mg/kg) of TRR could be extracted. Of this 0.3% of TRR (< 0.001 mg/kg) was identified as napropamide and desethyl-napropamide. Further extraction of the unextracted fraction resulted in bound residue accounting for 40.0% of TRR (0.065 mg/kg which was found to be associated with precipitated proteins. After fractionation all single fractions and components amounted to less than 0.01 mg/kg so further investigation was not performed. Altogether 58.9% was characterised and identified.
Characterisation of the TRR in kidney showed that 63.5% of TRR (0.022 mg/kg) could be extracted. Of this 1.8% (0.001 mg/kg) was identified as napropamide. All other single fractions and components amounted to less than 0.01 mg/kg so further investigation was not performed.

Conclusion
When [^{14}C-1-naphthyl]-napropamide was administered orally to two lactating goats at a dose rate corresponding to 9.9 mg/kg feed the radioactivity in liver and kidney was 0.153 mg/kg and 0.0365 mg/kg, respectively. In other tissues and milk TRR were very low (< 0.01 mg/kg). Traces of napropamide and desethyl-napropamide were identified in the liver (<0.001 mg/kg). In the kidney napropamide amounted to 0.001 mg/kg. All other single fractions and components amounted to < 0.01 mg/kg so no further characterisation was required.

B.7.2.4. Pigs

A metabolism study in pigs has not been provided and is not required.

B.7.2.5. Fish

A metabolism study in fish is not required.

B.7.2.6 Metabolism, distribution and expression of residues in animals summary and conclusion

No detectable residues of napropamide-M are present in plant commodities therefore expected residues intakes by livestock are <0,004 mg/kg bw/day and metabolism studies in animals (and a residue definition for animal commodities) are not necessary. Napropamide metabolism studies have however been conducted in lactating goats and laying hens. In both goats and hens napropamide is rapidly excreted and extensively metabolised. No feeding studies were conducted given that the animal exposure is minimal.

B.7.3. MAGNITUDE OF RESIDUE TRIALS IN PLANTS

The following intended uses have been provided as shown in Table B.7.3-1.

Note brassica vegetable crops refers to

Broccoli (calabrese, Broccoli raab, Chinese broccoli), cauliflower, brussels sprout, Head cabbage (pointed head cabbage, red cabbage, savoy cabbage, white cabbage) Chinese cabbage (Indian or Chinese) mustard, pak choi, Chinese flat cabbage/ai goo choi), choi sum, Peking cabbage/pe-tsa) kale (Borecole/curly kale, collards, Portuguese Kale, Portuguese cabbage, cow cabbage) and kohl rabi.

Table B.7.3-1.: Intended uses

Crop and/or situation (a)	Member State or Country	Product name	F G or I (b)	Pests or Group of pests controlled (c)	Preparation		Application				Application rate per treatment			PHI (days) (m)	Remarks
					Type (d-f)	Conc. a.s. (i)	method kind (f-h)	range of growth stages & season (j)	number min-max (k)	Interval between application (min)	kg a.s /hL min-max (l)	Water L/ha min-max	kg a.s./ha min-max (l)		
Winter oilseed rape	All zones	HBW03	F	Annual grasses and broad-leaved weeds	SC	450 g/L	Broadcast soil spray and incorporation	Pre-sowing, summer-autumn	1	na	0.255-0.3825	200-300	0.765	na	
Winter oilseed rape	All zones	HBW03	F	Annual grasses and broad-leaved weeds	SC	450 g/L	Broadcast soil spray only, no incorporation	Pre-sowing, summer-autumn	1	na	0.255-0.3825	200-300	0.765	na	
Brassica vegetable crops[1]	All zones	HBW03	F	Annual grasses and broad-leaved weeds	SC	450 g/L	Broadcast soil spray and incorporation	Pre-planting / pre-sowing, spring-summer	1	na	0.1275-0.3825	200-600	0.765	na	Treatment is made to soil prior to sowing or transplanting of crops
Brassica vegetable crops[1]	All zones	HBW03	F	Annual grasses and broad-leaved weeds	SC	450 g/L	Broadcast soil spray only, no incorporation	Pre-planting / pre-sowing, spring-summer	1	na	0.1275-0.3825	200-600	0.765	na	Treatment is made to soil prior to sowing or transplanting of crops
Brassica vegetable crops[1]	All zones	HBW03	F	Annual grasses and broad-leaved weeds	SC	450 g/L	Broadcast soil spray only, no incorporation	Post-sowing, pre-emergence / BBCH 00-08, spring-summer	1	na	0.1275-0.3825	200-600	0.765	na	Treatment is made to soil post-sowing but not post-transplanting of crops
Winter oilseed rape	All zones	HBW03	F	Annual grasses and broad-leaved weeds	SC	450 g/L	Broadcast soil spray only, no incorporation	Post-sowing, pre-emergence / BBCH 00-08, summer-autumn	1	na	0.255-0.3825	200-300	0.765	na	

[1] Broccoli (calabrese, Broccoli raab, Chinese broccoli), cauliflower, brussels sprout, Head cabbage (pointed head cabbage, red cabbage, savoy cabbage, white cabbage) Chinese cabbage (Indian or Chinese) mustard, pak choi, Chinese flat cabbage/ai goo choi), choi sum, Peking cabbage/pe-tsa) kale (Borecole/curly kale, collards, Portuguese Kale, Portuguese cabbage, cow cabbage) and kohl rabi.

(a) For crops, the EU and Codex classifications (both) should be taken into account; where relevant, the use situation should be described (e.g. fumigation of a structure)
(b) Outdoor or field use (F), greenhouse application (G) or indoor application (I)
(c) *e.g.* biting and sucking insects, soil born insects, foliar fungi, weeds
(d) *e.g.* wettable powder (WP), emulsifiable concentrate (EC), granule (GR)
(e) CropLife International Technical Monograph no 2, 6th Edition. Revised May 2008. Catalogue of
(i) g/kg or g/L. Normally the rate should be given for the active substance (according to ISO) and not for the variant in order to compare the rate for same active substances used in different variants (e.g. fluoroxypyr). **In certain cases, where only one variant is synthesised, it is more appropriate to give the rate for the variant (e.g. benthiavalicarb-isopropyl).**
(j) Growth stage range from first to last treatment (BBCH Monograph, Growth Stages of Plants, 1997, Blackwell, ISBN 3-8263-3152-4), including where relevant, information on season at time of

pesticide formulation types and international coding system (f) All abbreviations used must be explained (g) Method, e.g. high volume spraying, low volume spraying, spreading, dusting, drench (h) Kind, *e.g.* overall, broadcast, aerial spraying, row, individual plant, between the plant- type of equipment used must be indicated	application (k) Indicate the minimum and maximum number of applications possible under practical conditions of use (l) The values should be given in g or kg whatever gives the more manageable number (e.g. 200 kg/ha instead of 200 000 g/ha or 12.5 g/ha instead of 0.0125 kg/ha (m) PHI - minimum pre-harvest interval

B.7.3.1 Brassica vegetables

The following seven study reports were submitted detailing residue trials conducted on brassicas in Northern and Southern Europe:

CA 6.3.1/01A. Field phase. A. Bamber (2001) The production of brassica samples after one pre-plant application of Devrinol. UPL Europe Ltd, Unpublished report No.: 688-00-UPL-BRA. GLP

CA 6.3.1/01B. Analytical report. D. Norris (2002b) Determination of napropamide residues in samples of brassicas treated with Devrinol in compliance with Good Laboratory Practice. UPL Europe Ltd, Unpublished report No.: OA00567. GLP

CA 6.3.1/02. D. Clark (2002a) To determine the magnitude of napropamide residues at harvest in the raw agricultural commodity head cabbage resulting from a single overall application of Devrinol 45FL in the UK during 2001. UPL Europe Ltd, Unpublished report No.: AS/5631/US. GLP

CA 6.3.1/03. D. Clark (2002b) To determine the magnitude of napropamide residues at harvest in the raw agricultural commodity cauliflower resulting from a single overall application of Devrinol 45FL in the UK during 2001. UPL Europe Ltd, Unpublished report No.: AS/5633/US. GLP

CA 6.3.1/04. D. Clark (2002c) To determine the magnitude of napropamide residues at harvest in the raw agricultural commodity Brussels sprouts resulting from a single overall application of Devrinol 45FL in the UK during 2001. UPL Europe Ltd, Unpublished report No.: AS/5634/US. GLP

CA 6.3.1/05. M Balluff (2005a) Determination of residues of napropamide after a single application with soil incorporation of Devrinol 45FL in head cabbage outdoor, Southern Europe, 2004/2005. UPL Europe Ltd, Unpublished report No.: 20044048/I1-FPCA. GLP

CA 6.3.1/06. M Balluff (2005b) Determination of residues of napropamide after a single application with soil incorporation of Devrinol 45FL in head cauliflower outdoor, Southern Europe, 2004/2005. UPL Europe Ltd, Unpublished report No.: 20044048/I1-FPCF. GLP

Twentyseven residue trials on brassica vegetables have been submitted. All trials were performed using a single application of napropamide formulated as 450 g/l suspension concentrate. The formulation was applied to the soil using a commercial sprayer at about 1.0 kg as/ha napropamide prior to transplanting of the seedlings. In Table B.7.3.1-1 to Table B.7.3.1-3 details of the trials are given which show that at harvest in all cases residues of napropamide were below the LOQ. The LOQ was 0.1 mg/kg in the trials from 2000 and 0.01 mg/kg in all other trials. Procedural recoveries for all trials were within 77- 106%, one unacceptable procedural recovery occurred in Clark, 2002c, AS/5634/US but samples from this batch were reextracted.

It should be noted that all the brassica trials have been provided with an application rate listed as napropamide which is a racemate of the R and S isomer. Therefore all the application rates have been halved to be appropriate to napropamide-M. On this basis the application rate for the trials is between 0.48 to 0.53 kg as/ha which is not within ±25% of the GAP (0.765 kg as/ha). However the residues in all trials have been shown to be <LOQ. In addition the residues have been determined as napropamide the racemate form. Therefore the residues of napropamide-M could also be half of that shown in the trials. Even if residues at twice the current LOQ were to be found in trials at the proposed GAP there is a considerable margin of safety for the risk assessment based on the proposed ADI (0.3 mg/kg bw/day).

With respect to MRLs for the proposed use the data available indicates that the proposed uses would be unlikely to exceed the current MRLs listed in Regulation 396/2005 for napropamide for brassica vegetables (0.05* mg/kg).

Trials relevant to the representative uses

Crop		Napropamide (mg/kg)	MRL[+]	HR[+]	STMR[+]
Cauliflower	NEU	4 x <0.1, <0.01, 3 x <0.01	0.02*	0.02	0.02
	SEU	2 x <0.01			
Cabbage	NEU	3 x <0.1, 4 x <0.01			
	SEU	2 x <0.01			
Brussels sprout	NEU	4 x <0.1 4 x <0.01			
	SEU	-			

[+]Note as the residues are determined as napropamide in the available residue trials, residues have been doubled to enable a conservative risk assessment to be conducted.

The residues in all trials were demonstrated to be below the LOQ (0.01 and 0.1 mg napropamide/kg). The following extrapolation is possible for applications before the edible part of the crop is formed (i.e. BBCH 16). Based on the residues being <LOQ in all the trials 8 trials on cabbage and 8 trials on cauliflower are not considered to be required and a reduced data set is acceptable.

8 trials on head cabbages (0242020) + 8 trials on cauliflower (0241020) → **Whole subgroups (a) flowering brassica (0241000) and (b) head brassica (0242000)**

Note extrapolation cannot be made to leafy brassicas (0243000) or kohl rabi see SANCO 7525/VI/95 Rev. 10.2

Full details of the residue trials are shown in Table 7.3.1-1, Table 7.3.1-2 and Table 7.3.1-3 below. Note where storage periods are greyed out this indicates that the storage period exceeds the storage period supported by the available storage stability data. Where the method used has been greyed out this indicates that the method used has not been sufficiently validated (see Vol 3 B.5.1.2).

Table B.7.3.1-1 Residue trial summary for cauliflower

Northern Europe											
Trial No./ Location/ Year	*Commodity/ Variety*	*Formulation*	*Application rate per treatment*			*Dates of treatment or no. of treatments and last date*	*Growth stage at last treatment or date*	*Portion analyzed*	*Residues (mg/kg)*	*PHI (days)*	*Remarks*
			kg a.s./ ha	*Water (l/ha)*	*kg a.s./hl*				***Napropamide***		
UK, 2000 688/CAUL/1	Cauliflower	SC 450 g/l	1.045 napropamide equivalent to 0.52 napropamide-M	209.7	0.5	1	Pre-planting	Head	<0.1	78	Norris 2002 b, OA 00567 Analytical Method OAN/A/125 Procedural recovery= 88-103% Maximum storage period 310 days.
UK, 2000 688/CAUL/2	Cauliflower	SC 450 g/l	0.989 napropamide equivalent to 0.49 napropamide-M	198.6	0.5	1	Pre-planting	Head	<0.1	163	Norris 2002 b, OA 00567 Analytical Method OAN/A/125 Procedural recovery= 88-103% Maximum storage period 310 days.
UK, 2000 688/CAUL/3	Cauliflower	SC 450 g/l	1.013 napropamide equivalent to 0.51 napropamide-M	203.3	0.5	1	Pre-planting	Head	<0.1	104	Norris 2002 b, OA 00567 Analytical Method OAN/A/125 Procedural recovery= 88-103% Maximum storage period 310 days.

Northern Europe											
Trial No./ Location/ Year	*Commodity/ Variety*	*Formulation*	*Application rate per treatment*			*Dates of treatment or no. of treatments and last date*	*Growth stage at last treatment or date*	*Portion analyzed*	*Residues (mg/kg)*	*PHI (days)*	*Remarks*
			kg a.s./ ha	*Water (l/ha)*	*kg a.s./hl*				***Napropamide***		
UK, 2000 688/CAUL/4	Cauliflower	SC 450 g/l	1.038 napropamide equivalent to 0.52 napropamide-M	208.3	0.5	1	Pre-planting	Head	<0.1	136	Norris 2002 b, OA 00567 Analytical Method OAN/A/125 Procedural recovery= 88-103% Maximum storage period 310days.
UK, 2001 AS/5633/US/2	Cauliflower	SC 450 g/l	1.003 napropamide equivalent to 0.50 napropamide-M	198	0.5	1	Pre-planting	Head	<0.01	91	Clark, 2002b, AS/5633/US Analytical Method EMK/00/1 Procedural recovery= 90-98% Maximum storage period 100 days.
UK, 2001 AS/5633/US/3	Cauliflower	SC 450 g/l	1.013 napropamide equivalent to 0.51 napropamide-M	200	0.5	1	Pre-planting	Head	<0.01	70	Clark, 2002b, AS/5633/US Analytical Method EMK/00/1 Procedural recovery= 90-98% Maximum storage period 237 days.

Northern Europe											
Trial No./ Location/ Year	*Commodity/ Variety*	*Formulation*	*Application rate per treatment*			*Dates of treatment or no. of treatments and last date*	*Growth stage at last treatment or date*	*Portion analyzed*	*Residues (mg/kg)*	*PHI (days)*	*Remarks*
			kg a.s./ ha	*Water (l/ha)*	*kg a.s./hl*				***Napropamide***		
UK, 2001 AS/5633/US/4	Cauliflower	SC 450 g/l	1.018 napropamide equivalent to 0.51 napropamide-M	201	0.5	1	Pre-planting	Head	<0.01	70	Clark, 2002b, AS/5633/US Analytical Method EMK/00/1 Procedural recovery= 90-98% Maximum storage period 173 days.
Southern Europe											
I04W061R Italy	Cauliflower-Frimon	SC 450 g/l	1.022 napropamide equivalent to 0.51 napropamide-M	307	0.33	1	Pre-planting	Mature inflorescence	<0.01	98	M Balluff (2005b), 20044048/I1-FPCF Analytical method HPLC- MS/MS as described in above study report. Procedural recovery= 98-102% Maximum storage period 172 days.

Northern Europe											
Trial No./ Location/ Year	*Commodity/ Variety*	*Formulation*	*Application rate per treatment*			*Dates of treatment or no. of treatments and last date*	*Growth stage at last treatment or date*	*Portion analyzed*	*Residues (mg/kg)*	*PHI (days)*	*Remarks*
			kg a.s./ ha	*Water (l/ha)*	*kg a.s./hl*				***Napropamide***		
I04W062R Italy	Cauliflower-Freedom	SC 450 g/l	0.972 napropamide equivalent to 0.49 napropamide-M	292	0.33	1	Pre-planting	Mature inflorescence	<0.01	85	M Balluff (2005b), 20044048/I1-FPCF Analytical method HPLC- MS/MS as described in above study report. Procedural recovery= 98-102% Maximum storage period 176 days.

Table B.7.3.1- 2 Residue trial summary for head cabbage

Northern Europe											
Trial No./ Location/ Year	*Commodity/ Variety*	*Formulation*	*Application rate per treatment*			*Dates of treatment or no. of treatments and last date*	*Growth stage at last treatment or date*	*Portion analyzed*	*Residues (mg/kg)*	*PHI (days)*	*Remarks*
			kg a.s./ ha	*Water (l/ha)*	*kg a.s./hl*				***Napropamide***		
UK, 2000 688/CAB/5	Head cabbage	SC 450 g/l	0.995 napropamide equivalent to 0.50 napropamide-M	200	0.5	1	Pre-planting	Head	<0.1	58	Norris, 2002b, OA00567 Analytical Method OAN/A/125 Procedural recovery= 84-106% Maximum storage period 356 days.
UK, 2000 688/CAB/6	Head cabbage	SC 450 g/l	0.962 napropamide equivalent to 0.48 napropamide-M	193	0.5	1	Pre-planting	Head	<u>≤0.1</u>	188	Norris, 2002b, OA00567 Analytical Method OAN/A/125 Procedural recovery= 84-106% Maximum storage period 101 days.
UK, 2000 688/CAB/7	Head cabbage	SC 450 g/l	1.037 napropamide equivalent to 0.52 napropamide-M	208	0.5	1	Pre-planting	Head	<u>≤0.1</u>	72	Norris, 2002b, OA00567 Analytical Method OAN/A/125 Procedural recovery= 84-106% Maximum storage period 287 days.

Northern Europe											
Trial No./ Location/ Year	*Commodity/ Variety*	*Formulation*	*Application rate per treatment*			*Dates of treatment or no. of treatments and last date*	*Growth stage at last treatment or date*	*Portion analyzed*	*Residues (mg/kg)*	*PHI (days)*	*Remarks*
			kg a.s./ ha	*Water (l/ha)*	*kg a.s./hl*				***Napropamide***		
UK, 2000 688/CAB/8	Head cabbage	SC 450 g/l	0.957 napropamide equivalent to 0.48 napropamide-M	192	0.5	1	Pre-planting	Head	<0.1	55	Norris, 2002b, OA00567 Analytical Method OAN/A/125 Procedural recovery= 84-106% Maximum storage period 282 days.
UK, 2001 AS/5631/US/1	Head cabbage	SC 450 g/l	1.013 napropamide equivalent to 0.51 napropamide-M	200	0.5	1	Pre-planting	Head	<0.01	125	Clark,2002a, AS/5631/US Analytical Method EMK/00/1 Procedural recovery= 77-80% Maximum storage period 123 days.
UK, 2001 AS/5631/US/2	Head cabbage	SC 450 g/l	1.028 napropamide equivalent to 0.51 napropamide-M	203	0.5	1	Pre-planting	Head	<0.01	124	Clark, 2002a, AS/5631/US Analytical Method EMK/00/1 Procedural recovery= 77-80% Maximum storage period 51 days.

Northern Europe											
Trial No./ Location/ Year	*Commodity/ Variety*	*Formulation*	*Application rate per treatment*			*Dates of treatment or no. of treatments and last date*	*Growth stage at last treatment or date*	*Portion analyzed*	*Residues (mg/kg)*	*PHI (days)*	*Remarks*
			kg a.s./ ha	*Water (l/ha)*	*kg a.s./hl*				***Napropamide***		
UK, 2001 AS/5631/US/3	Head cabbage	SC 450 g/l	1.038 napropamide equivalent to 0.52 napropamide-M	205	0.5	1	Pre-planting	Head	<0.01	91	Clark, 2002a, AS/5631/US Analytical Method EMK/00/1 Procedural recovery= 77-80% Maximum storage period 157 days.
UK, 2001 AS/5631/US/4	Head cabbage	SC 450 g/l	1.048 napropamide equivalent to 0.52 napropamide-M	207	0.5	1	Pre-planting	Head	<0.01	124	Clark, 2002a, AS/5631/US Analytical Method EMK/00/1 Procedural recovery= 77-80% Maximum storage period 100 days.

Trial No./ Location/ Year	*Commodity/ Variety*	*Formulation*	*Application rate per treatment*			*Dates of treatment or no. of treatments and last date*	*Growth stage at last treatment or date*	*Portion analyzed*	*Residues (mg/kg)*	*PHI (days)*	*Remarks*
			kg a.s./ ha	*Water (l/ha)*	*kg a.s./hl*				***Napropamide***		
Southern Europe											
I04W045R Italy 2004	Head cabbage, Castello	SC 450 g/l	0.989 napropamide equivalent to 0.49 napropamide-M	297	0.33	1	Pre-planting	Mature head	<u><0.01</u>	84	Balluff, 2005a, 20044048/I1- FPCA Analytical method HPLC- MS/MS as described in above study report. Procedural recovery= 95-102% Maximum storage period 193 days.
I04W060R Italy 2004	Head cabbage, Cape Horn	SC 450 g/l	0.972 napropamide equivalent to 0.49 napropamide-M	292	0.33	1	Pre-planting	Mature head	<u><0.01</u>	100	Balluff, 2005a, 20044048/I1- FPCA Analytical method HPLC- MS/MS as described in above study report. Procedural recovery= 95-102% Maximum storage period 161 days.

Table B.7.3.1-3 Residue trial summary for brussels sprout

Northern Europe											
Trial No./ Location/ Year	*Commodity/ Variety*	*Formulation*	*Application rate per treatment*			*Dates of treatment or no. of treatments and last date*	*Growth stage at last treatment or date*	*Portion analyzed*	*Residues (mg/kg)*	*PHI (days)*	*Remarks*
			kg a.s./ ha	*Water (l/ha)*	*kg a.s./hl*				*Analyte 1 Analyte 2*		
UK, 2000 688/SPR/9	Brussels sprouts	SC 450 g/l	1.030 napropamide equivalent to 0.52 napropamide-M	207	0.5	1	Pre-planting	Brussels sprouts	<0.1	201	Norris, 2002b, OA00567 Analytical method OAN/A/125 Procedural recovery= 92-106% Maximum storage period 197 days.
UK, 2000 688/SPR/10	Brussels sprouts	SC 450 g/l	0.980 napropamide equivalent to 0.49 napropamide-M	197	0.5	1	Pre-planting	Brussels sprouts	<0.1	190	Norris, 2002b, OA00567 Analytical method OAN/A/125 Procedural recovery= 92-106% Maximum storage period 218 days.
UK, 2000 688/SPR/11	Brussels sprouts	SC 450 g/l	1.057 napropamide equivalent to 0.53 napropamide-M	212	0.5	1	Pre-planting	Brussels sprouts	<0.1	161	Norris, 2002b, OA00567 Analytical method OAN/A/125 Procedural recovery= 92-106% Maximum storage period 252days.

Northern Europe											
Trial No./ Location/ Year	*Commodity/ Variety*	*Formulation*	*Application rate per treatment*			*Dates of treatment or no. of treatments and last date*	*Growth stage at last treatment or date*	*Portion analyzed*	*Residues (mg/kg)*	*PHI (days)*	*Remarks*
			kg a.s./ ha	*Water (l/ha)*	*kg a.s./hl*				*Analyte 1 Analyte 2*		
UK, 2000 688/SPR/12	Brussels sprouts	SC 450 g/l	0.991 napropamide equivalent to 0.50 napropamide-M	199	0.5	1	Pre-planting	Brussels sprouts	<0.1	155	Norris, 2002b, OA00567 Analytical method OAN/A/125 Procedural recovery= 92-106% Maximum storage period 259 days.
UK, 2001 AS/5634/US/1	Brussels sprouts	SC 450 g/l	1.033 napropamide equivalent to 0.52 napropamide-M	204	0.5	1	Pre-planting	Brussels sprouts	<0.01	174	Clark, 2002c, AS/5634/US Analytical Method EMK/00/1 Procedural recovery= 81-95% Maximum storage period 258 days.
UK, 2001 AS/5634/US/2	Brussels sprouts	SC 450 g/l	1.028 napropamide equivalent to 0.51 napropamide-M	203	0.5	1	Pre-planting	Brussels sprouts	<0.01	176	Clark, 2002c, AS/5634/US Analytical Method EMK/00/1 Procedural recovery= 81-95% Maximum storage period 105 days.

Northern Europe											
Trial No./ Location/ Year	*Commodity/ Variety*	*Formulation*	*Application rate per treatment*			*Dates of treatment or no. of treatments and last date*	*Growth stage at last treatment or date*	*Portion analyzed*	*Residues (mg/kg)*	*PHI (days)*	*Remarks*
			kg a.s./ ha	*Water (l/ha)*	*kg a.s./hl*				*Analyte 1 Analyte 2*		
UK, 2001 AS/5634/US/3	Brussels sprouts	SC 450 g/l	0.891 napropamide equivalent to 0.45 napropamide-M	176	0.5	1	Pre-planting	Brussels sprouts	<0.01	186	Clark, 2002c, AS/5634/US Analytical Method EMK/00/1 Procedural recovery= 81-95% Maximum storage period 108 days.
UK, 2001 AS/5634/US/4	Brussels sprouts	SC 450 g/l	1.028 napropamide equivalent to 0.51 napropamide-M	203	0.5	1	Pre-planting	Brussels sprouts	<0.01	198	Clark, 2002c, AS/5634/US Analytical Method EMK/00/1 Procedural recovery= 81-95% Maximum storage period 73 days.

B.7.3.2 Oilseed rape

The following four study reports were submitted detailing residue trials conducted on oilseed rape in Northern and Southern Europe:

CA 6.3.2/01. G. Chadwick (2015) d-napropamide 450 g/L Determination of residues of d-napropamide after one application of d-napropamide 450 g/L SC to winter oilseed rape at 3 sites in Northern Europe and 4 sites in Southern Europe 2012. UPL Europe Ltd, Unpublished report No.: S12-03756. GLP

CA 6.3.2/02. T. Goodband (2002) To determine the magnitude of napropamide residues at harvest in the raw agricultural commodity oilseed rape resulting from a single overall application of Devrinol 45FL to the ground in Northern France (2000-2002). UPL Europe Ltd, Unpublished report No.: AF/5056/US. GLP

CA 6.3.2/03. J. Pay, N.D. Simmons (1990) Napropamide: Residues in oil seed rape from trials carried out in West Germany during 1988. UPL Europe Ltd, Unpublished report No.: RJ0829B. GLP

CA 6.3.2/04. N.D. Simmons (1992a) Napropamide: Residues in oil seed rape from trials carried out in Denmark during 1990. UPL Europe Ltd, Unpublished report No.: RJ1006B. GLP

Eighteeen trials on oilseed rape have been submitted. Four residue trials were carried out in northern France on oilseed rape in 2001 using a single application of napropamide (450 g/l SC). The formulation was applied to bare soil at 1.26 or 1.28 kg Napropamide /ha and incorporated to a depth of 5 cm prior to sowing. This equates to 0.63 to 0.64 kg Napropamide-M/ha which is within ±25% of the GAP (0.765 kg as/ha).

Five residue trials were carried out in West Germany on oilseed rape in 1988 using a single application of napropamide (190 g/l) combined with trifluranil (240 g/l), as an SC/CS formulation (note the trifluranil was encapsulated). At the same sites replicate trials were carried out using a single application of napropamide, formulated as an EC formulation with trifluralin. In both cases the formulations were applied to the bare soil at a rate of 0.95 kg as/ha for napropamide and within 2 days after application incorporated to a depth of 5 cm, before drilling oilseed rape. This equates to 0.48 kg Napropamide-M/ha which is not within ±25% of the GAP (0.765 kg as/ha).

Two residue trials were carried out in Denmark on oilseed rape in 1990 using a single application of napropamide, formulated as Treflan Plus, a mixture containing 190 g/l napropamide and 240 g/l trifluralin in an SC formulation. The formulation was applied to bare soil at either 0.475 kg as/ha or 0.95 kg as/ha and incorporated to a depth of 5 cm within one hour after application. This equates to 0.24 and 0.48 kg napropamide-M/ha respectively which is not within ±25% of the GAP (0.765 kg as/ha).

Seven residue trials were carried out (3 in NEU, 4 in SEU) on oilseed rape in 2012/13 using a single application of napropamide- M, formulated as D-Devrinol 45 SC. The formulation was applied to bare soil with no incorporation 1-2 days post sowing of oilseed rape at 0.74-0.77 kg as/ha, which corresponds to the intended use.

As shown in Table B.7.3.2-1 residues at harvest in all cases were below or equal to the LOQ. Procedural recoveries for rape seed in all trials were within 71- 106%, for whole plants recoveries were within 66-101% and for immature pods 61-91 %.

There are sufficient residue trial data to support the proposed use based on the Napropamide-M residue trials; the napropamide trials pertinent to the GAP are also shown in the below table as supporting information.

Trials relevant to the proposed use

Crop		Napropamide-M	Napropamide	MRL required	HR	STMR
Oilseed rape	NEU	3 x <0.01	4 x <0.05	0.01	0.01	0.01
	SEU	4 x <0.01				

With respect to MRLs for the proposed use the data available indicates that the proposed uses would be unlikely to exceed the current MRLs listed in Regulation 396/2005 for napropamide for oilseed rape (0.1 mg/kg).

Table B.7.3.2-1 Residue trial summary for oilseed rape-

Northern Europe											
Trial No./ Location/ Year	*Commodity/ Variety*	*Formulation*	*Application rate per treatment*			*Dates of treatment or no. of treatments and last date*	*Growth stage at last treatment or date*	*Portion analyzed*	*Residues (mg/kg)*	*PHI (days)*	*Remarks*
			kg a.s./ ha	*Water (l/ha)*	*kg a.s./hl*				*Napropamide*		
France, 2001 AS/5056/US/1	Oilseed rape	SC, 450 g/l	1.26 napropamide equivalent to 0.63 kg napropamide -M	200	0.63	1	Pre-sowing	Seed	<0.05	319	Goodband, 2002, AF/5056/US Analytical method Napropamide/Crops /DB/00/1. Procedural recovery= 71-84% Maximum storage period 186 days.
France, 2001 AS/5056/US/2	Oilseed rape	SC, 450 g/l	1.279 napropamide equivalent to 0.64 kg napropamide -M	203	0.63	1	Pre-sowing	Seed	<0.05	315	Goodband, 2002, AF/5056/US Analytical method Napropamide/Crops /DB/00/1. Procedural recovery= 71-84% Maximum storage period 185 days.

Northern Europe											
Trial No./ Location/ Year	*Commodity/ Variety*	*Formulation*	*Application rate per treatment*			*Dates of treatment or no. of treatments and last date*	*Growth stage at last treatment or date*	*Portion analyzed*	*Residues (mg/kg)*	*PHI (days)*	*Remarks*
			kg a.s./ ha	*Water (l/ha)*	*kg a.s./hl*				*Napropamide*		
France, 2001 AS/5056/US/3	Oilseed rape	SC, 450 g/l	1.279 napropamide equivalent to 0.64 kg napropamide -M	203	0.63	1	Pre-sowing	Seed	<0.05	311	Goodband, 2002, AF/5056/US Analytical method Napropamide/Crops /DB/00/1. Procedural recovery= 71-84% Maximum storage period 193 days.
France, 2001 AS/5056/US/4	Oilseed rape	SC, 450 g/l	1.26 napropamide equivalent to 0.63 kg napropamide -M	200	0.63	1	Pre-sowing	Seed	<0.05	303	Goodband, 2002, AF/5056/US Analytical method Napropamide/Crops /DB/00/1. Procedural recovery= 71-84% Maximum storage period 192 days.

Northern Europe											
Trial No./ Location/ Year	*Commodity/ Variety*	*Formulation*	*Application rate per treatment*			*Dates of treatment or no. of treatments and last date*	*Growth stage at last treatment or date*	*Portion analyzed*	*Residues (mg/kg)*	*PHI (days)*	*Remarks*
			kg a.s./ ha	*Water (l/ha)*	*kg a.s./hl*				*Napropamide*		
Germany, 1988 RS-8837-B1	Oilseed rape	SC, 190 g/l napropamide	0.95 equivalent to 0.48 kg napropamide -M	400	0.2375	1	Pre-sowing	Whole plant	<0.02 <0.02 <0.02	57 215 256	Pay *et al* 1990, RJ0829B Analytical method ARAM 177 Procedural recovery Whole plant= 66-101% Pods=61-91% Seed=79-106% Maximum storage period Whole plant S1 458 d, S2 & S3 300d Pods 231 days Seed 181 days
								Pods	<0.05	284	
								Seed	<0.05	343	
		EC, 95g/l napropamide	0.95 equivalent to 0.48 kg napropamide -M	400	0.2375	1	Pre-sowing	Whole plant	<0.02 <0.02 <0.02	57 215 256	
								Pods	<0.05	284	
								Seed	<0.05	343	
		EC, 190 g/l napropamide	0.95 equivalent to 0.48 kg napropamide -M	400	0.2375	1	Pre-sowing	Whole plant	<0.02 <0.02	57 215 256	
								Pods	<0.05	284	
								Seed	<0.05	343	

Northern Europe											
Trial No./ Location/ Year	*Commodity/ Variety*	*Formulation*	*Application rate per treatment*			*Dates of treatment or no. of treatments and last date*	*Growth stage at last treatment or date*	*Portion analyzed*	*Residues (mg/kg)*	*PHI (days)*	*Remarks*
			kg a.s./ ha	*Water (l/ha)*	*kg a.s./hl*				*Napropamide*		
Germany, 1988 RS-8837-B2	Oilseed rape	SC 190 g/l napropamide	0.95 equivalent to 0.48 kg napropamide -M	400	0.2375	1	Pre-sowing	Whole plant	<0.02 <0.02 <0.02	61 215 255	Pay *et al* 1990, RJ0829B Analytical method ARAM 177 Procedural recovery Whole plant= 66-101% Pods=61-91% Seed=79-106% Maximum storage period Whole plant S1 458 d, S2 & S3 300d Pods 231 days Seed 181 days
								Pods	<0.05	285	
								Seed	<0.05	336	
		EC, 95g/l napropamide	0.95 equivalent to 0.48 kg napropamide -M	400	0.2375	1	Pre-sowing	Whole plant	<0.02 <0.02 <0.02	61 215 255	
								Pods	<0.05	285	
								Seed	<0.05	336	
		EC, 190 g/l napropamide	0.95 equivalent to 0.48 kg napropamide -M	400	0.2375	1	Pre-sowing	Whole plant	<0.02 <0.02 <0.02	61 215 285	
								Pods	<0.05	285	
								Seed	<0.05	336	

Northern Europe											
Trial No./ Location/ Year	*Commodity/ Variety*	*Formulation*	*Application rate per treatment*			*Dates of treatment or no. of treatments and last date*	*Growth stage at last treatment or date*	*Portion analyzed*	*Residues (mg/kg)*	*PHI (days)*	*Remarks*
			kg a.s./ ha	*Water (l/ha)*	*kg a.s./hl*				*Napropamide*		
Germany, 1988 RS-8837-E2	Oilseed rape	SC, 190 g/l napropamide	0.95 equivalent to 0.48 kg napropamide -M	400	0.2375	1	Pre-sowing	Whole plant	0.01 <0.02 <0.02	83 225 247	Pay *et al* 1990, RJ0829B Analytical method ARAM 177 Procedural recovery Whole plant= 66-101% Pods=61-91% Seed=79-106% Maximum storage period Whole plant S1 458 d, S2 & S3 300d Pods 231 days Seed 181 days
								Pods	<0.05	278	
								Seed	<0.05	328	
		EC, 95g/l napropamide	0.95 equivalent to 0.48 kg napropamide -M	400	0.2375	1	Pre-sowing	Whole plant	<0.02 <0.02 <0.02	83 225 247	
								Pods	<0.05	278	
								Seed	<0.05	328	

Northern Europe											
Trial No./ Location/ Year	*Commodity/ Variety*	*Formulation*	*Application rate per treatment*			*Dates of treatment or no. of treatments and last date*	*Growth stage at last treatment or date*	*Portion analyzed*	*Residues (mg/kg)*	*PHI (days)*	*Remarks*
			kg a.s./ ha	*Water (l/ha)*	*kg a.s./hl*				*Napropamide*		
Germany, 1988 RS-8837-E2	Oilseed rape	EC, 190 g/l napropamide	0.95 equivalent to 0.48 kg napropamide -M	400	0.2375	1	Pre-sowing	Whole plant	<0.02 <0.02 <0.02	83 225 278	Pay *et al* 1990, RJ0829B Analytical method ARAM 177 Procedural recovery Whole plant= 66-101% Pods=61-91% Seed=79-106% Maximum storage period Whole plant S1 458 d, S2 & S3 300d Pods 231 days Seed 181 days
								Pods	<0.05	278	
								Seed	<0.05	328	

Northern Europe											
Trial No./ Location/ Year	*Commodity/ Variety*	*Formulation*	*Application rate per treatment*			*Dates of treatment or no. of treatments and last date*	*Growth stage at last treatment or date*	*Portion analyzed*	*Residues (mg/kg)*	*PHI (days)*	*Remarks*
			kg a.s./ ha	*Water (l/ha)*	*kg a.s./hl*				*Napropamide*		
Germany, 1988 RS-8837-G1	Oilseed rape	SC, 190 g/l napropamide	0.95 equivalent to 0.48 kg napropamide -M	400	0.2375	1	Pre-sowing	Whole plant	<0.02 <0.02 <0.02	68 230 254	Pay *et al* 1990, RJ0829B Analytical method ARAM 177 Procedural recovery Whole plant= 66-101% Pods=61-91% Seed=79-106% Maximum storage period Whole plant S1 458 d, S2 & S3 300d Pods 231 days Seed 181 days
								Pods	<0.05	289	
								Seed	<0.05	328	
		EC, 95g/l napropamide	0.95 equivalent to 0.48 kg napropamide -M	400	0.2375	1	Pre-sowing	Whole plant	<0.02 <0.02 <0.02	68 230 254	
								Pods	<0.05	289	
								Seed	<0.05	328	
		EC, 190 g/l napropamide	0.95 equivalent to 0.48 kg napropamide -M	400	0.2375	1	Pre-sowing	Whole plant	<0.02 <0.02 <0.02	68 230 254	
								Pods	<0.05	289	
								Seed	<0.05	328	

Northern Europe											
Trial No./ Location/ Year	*Commodity/ Variety*	*Formulation*	*Application rate per treatment*			*Dates of treatment or no. of treatments and last date*	*Growth stage at last treatment or date*	*Portion analyzed*	*Residues (mg/kg)*	*PHI (days)*	*Remarks*
			kg a.s./ ha	*Water (l/ha)*	*kg a.s./hl*				*Napropamide*		
Denmark, 1990 DK10-90-S121	Oilseed rape	Treflan Plus SC, 190g/l, napropamide	0.95 equivalent to 0.48 kg napropamide -M	200	0.475	1	Pre-sowing	Siliques/pod	<0.05 <0.05	126 133	Simmons, 1992a, RJ1006B Analytical method ARAM 177 Procedural recovery= 92-102% Maximum storage period 175 days
								Seed	<0.05	145	
		Treflan Plus SC, 190 g/l, napropamide	0.475 equivalent to 0.24 kg napropamide -M	200	0.2375	1	Pre-sowing	Siliques/pod	<0.05 <0.05	126 133	
								Seed	<0.05	145	
Denmark, 1990 DK10-90-S122	Oilseed rape	Treflan Plus SC, 190g/l, napropamide	0.95 equivalent to 0.48 kg napropamide -M	200	0.475	1	Pre-sowing	Siliques/pod	<0.05 <0.05	120 131	Simmons, 1992a, RJ1006B Analytical method ARAM 177 Procedural recovery= 92-102% Maximum storage period 162 days
								Seed	<0.05	147	
		Treflan Plus SC, 190 g/l, napropamide	0.475 equivalent to 0.24 kg napropamide -M	200	0.2375	1	Pre-sowing	Siliques/pod	<0.05 <0.01	120 131	
								Seed	<0.05	147	

Northern Europe											
Trial No./ Location/ Year	*Commodity/ Variety*	*Formulation*	*Application rate per treatment*			*Dates of treatment or no. of treatments and last date*	*Growth stage at last treatment or date*	*Portion analyzed*	*Residues (mg/kg)*	*PHI (days)*	*Remarks*
			kg a.s./ ha	*Water (l/ha)*	*kg a.s./hl*				***Napropamide-M***		
S12-03756-01 United Kingdom 2012/13	Oilseed rape	D-devrinol 45 SC	0.740 napropamide-M	204	0.36	1	Pre-emergence (BBCH 00)	Mature seed	<0.01	343	Chadwick, 2015, S12-03756 Analytical method M792 (based on JRFA AU-265R0) Procedural recovery= 89-103% Maximum storage period 150 days.
S12-03756-02 Germany 2012/13	Oilseed rape	D-devrinol 45 SC	0.760 napropamide -M	212	0.36	1	Pre-emergence	Mature seed	<0.01	320	Chadwick, 2015, S12-03756 Analytical method M792 (based on JRFA AU-265R0) Procedural recovery= 89-103% Maximum storage period 181 days.
S12-03756-04 North France 2012/13	Oilseed rape	D-devrinol 45 SC	0.750 napropamide -M	209	0.36	1	Pre-emergence	Mature seed	<0.01	318	Chadwick, 2015, S12-03756 Analytical method M792 (based on JRFA AU-265R0) Procedural recovery= 89-103% Maximum storage period 182 days.

Southern Europe											
Trial No./ Location/ Year	*Commodity/ Variety*	*Formulation*	*Application rate per treatment*			*Dates of treatment or no. of treatments and last date*	*Growth stage at last treatment or date*	*Portion analyzed*	*Residues (mg/kg)*	*PHI (days)*	*Remarks*
			kg a.s./ ha	*Water (l/ha)*	*kg a.s./hl*				*Napropamide-M*		
S12-03756-05 South France 2012/13	Oilseed rape	D-Devrinol 45 SC	0.770 napropamide -M	213	0.36	1	Pre-emergence	Mature seed	<0.01	283	Chadwick, 2015, S12-03756 Analytical method M792 (based on JRFA AU-265R0) Procedural recovery= 89-103% Maximum storage period 200 days.
S12-03756-06 South France 2012/13	Oilseed rape	D-Devrinol 45 SC	0.750 napropamide -M	208	0.36	1	Pre-emergence	Mature seed	<0.01	300	Chadwick, 2015, S12-03756 Analytical method M792 (based on JRFA AU-265R0) Procedural recovery= 89-103% Maximum storage period 186 days.
S12-03756-07 Italy 2012/13	Oilseed rape	D-Devrinol 45 SC	0.770 napropamide -M	213	0.36	1	Pre-emergence	Mature seed	<0.01	273	Chadwick, 2015, S12-03756 Analytical method M792 (based on JRFA AU-265R0) Procedural recovery= 89-103% Maximum storage period 216 days.

Southern Europe											
Trial No./ Location/ Year	*Commodity/ Variety*	*Formulation*	*Application rate per treatment*			*Dates of treatment or no. of treatments and last date*	*Growth stage at last treatment or date*	*Portion analyzed*	*Residues (mg/kg)*	*PHI (days)*	*Remarks*
			kg a.s./ ha	*Water (l/ha)*	*kg a.s./hl*				*Napropamide-M*		
S12-03756-08 Spain 2012/13	Oilseed rape	D-Devrinol 45 SC	0.750 napropamide -M	209	0.36	1	Pre-emergence	Mature seed	<0.01	216	Chadwick, 2015, S12-03756 Analytical method M792 (based on JRFA AU-265R0) Procedural recovery= 89-103% Maximum storage period 200 days.

B.7.4. FEEDING STUDIES

The following input values have been used to calculate the dietary burden:

Table B. 7.4-1: Input values for the dietary burden calculation

Feed commodity	Median dietary burden		Maximum dietary burden	
	(mg/kg)	Comment	(mg/kg)	Comment
Cabbage heads, leaves	0.02	STMR	0.02	HR
Kale, leaves	0.02	STMR	0.02	HR
Canola (rapeseed meal)	0.02	STMR*PF [α]	0.02	STMR*PF [α]
Rape, meal	0.02	STMR*PF [α]	0.02	STMR*PF [α]

[α]Default processing factor from the OECD animal model has been used. Note both canola and rape meal appear in the OECD animal model, however for MRL purposes canola and oilseed rape are considered to have the same commodity code.

Table B.7.4-2: Estimated maximum animal intakes (mg/kg bw/day)

Animals	**Median burden** (mg/kg bw)	**Maximum burden** (mg/kg bw)	**Above 0.004 mg /kg bw**	**Maximum burden** (mg/kg DM)	**Highest contributing commodities**	
Beef cattle	0.001	0.001	No	0.03	Cabbage, heads	leaves
Dairy cattle	0.001	0.001	No	0.03	Cabbage, heads	leaves
Ram/Ewe	0.001	0.001	No	0.02	Cabbage, heads	leaves
Lamb	0.001	0.001	No	0.02	Cabbage, heads	leaves
Pig (breeding)	0.0004	0.0004	No	0.02	Cabbage, heads	leaves
Pig (finishing)	0.0001	0.0001	No	0.00	Canola	meal
Poultry broiler	0.0003	0.0003	No	0.00	Canola	meal
Poultry layer	0.001	0.001	No	0.01	Cabbage, heads	leaves
Turkey	0.0003	0.0003	No	0.00	Canola	meal

Expected residues intakes by livestock are <0.004 mg/kg bw/day and therefore feeding studies are not required.

B.7.5. EFFECTS OF PROCESSING

Residues in brassica vegetables and oilseed rape seed are expected to be <0.01 mg/kg therefore processing studies are not required.

B.7.6. RESIDUES IN SUCCEEDING OR ROTATIONAL CROPS

B.7.6.1. Metabolism in rotational crops

Report:	CA 6.6.1/01. Parker, S., Steel, T.R., Harris, M., Hurt, A.D., Allin, R. (1993), Napropamide: uptake and metabolism in confined rotational crops. Company Report No. RJ1348B. ICI Agrochemicals, United Kingdom. GLP.

Materials and methods
Testsubstance: [^{14}C-1-naphthyl]-napropamide, radiochemical purity 98.3% prepared as a Devrinol 2E formulation. The formulation was isotopically diluted with [^{13}C-1-naphthyl]-napropamide, radiochemical purity 98.5% and [^{12}C-1-naphthyl]-napropamide, radiochemical purity 99.8% in the ratio 1:2:2. The activity of the test substance was 1628 Bq/ug.

The study was conducted in a glasshouse in England. The devrinol 2E-formulation was incorporated into the upper 5 cm of the sandy loam soil in pots corresponding to 4.8 kg as/ha.

The rotational crops spring wheat, carrot and lettuce were planted 60, 180 and 364 days after soil treatment (DAT). At each interval two pots of wheat were planted, the first for mature crop and the second for forage. Only one pot of carrots and lettuce were planted. At each interval one pot of each wheat, carrots and lettuce were also planted in untreated pots. Wheat was harvested at maturity and wheat forage was harvested at growth stage 45-55. Carrot tops and roots and lettuce were sampled at maturity. Soil cores were taken at treatment, planting and harvest. Samples were stored in freezer at - 6°C to - 26°C until analysis within 6 month.

Cabbage seedlings were planted in the 60 DAT pots. The report states that the purpose of planting cabbage prior to the 60 day interval was an attempt to reduce the level of napropamide in the soil and hence reduce the possibility of phytotoxic effects at an interval which does not reflect normal use. Cabbage seedlings were harvested after 4 weeks (28 DAT). Cabbage seedlings were not analysed in the study.

The total radioactive residues (TRR) in solutions were determined by LSC or by combustion/LSC. Crop samples were cut into small sections, combined, extracted and fractionated. Extractions were performed with ethanol, ethanol:water (70:30 v/v) and then water. Extracts were combined and partitioned with diethyl ether. Partition fractions were then concentrated for TLC analyses.

Since the fractionation of the residue and the TLC profiles of the organic and aqueous fraction were broadly similar, further analyses of the aqueous fraction and the unextracted fraction were only conducted on all crop parts 60 DAT. Notifier considered these fractions to be representative of the same fraction at the 180 DAT and 364 DAT. To support this, further analyses on the aqueous fraction and the unextracted fraction was also conducted on the 180 DAT and 364 DAT wheat straw fractions.

Further analysis of aqueous fraction: a sub-sample of the aqueous phase was concentrated and acidified to pH 2 with HCl. Methanol was added and the solution was applied to a C_{18} Mega Bond Elut column eluted with methanol:water (5:95 v/v), methanol, methanol:water (50:50 v/v) and methanol:water (50:50 v/v pH 2). The methanol:water (5:95 v/v) eluate fraction was concentrated to near dryness, redissolved in 0.01M calcium sulphate and analysed for free sugars by HPLC. The other fractions were combined and rotary evaporated to dryness, refluxed with 1M HCl for 2 hours, filtered, partitioned with diethyl acetate. A C_{18} solid phase separation was used to isolate conjugated sugars.

The unextracted fraction obtained from the initial extractions was subsequently extracted by refluxing with strong acid (1 M HCL, 2 hours), strong base (5 M NaOH, 24 hours) and with enzymes in an attempt to characterise the residue. These additional extracts were quantified by LSC. TLC and HPLC were used to identify

residues.

Soil
Soil cores were extracted with methanol:water (60:40), centrifuged, filtered and analysed by LSC and TLC. The unextracted fraction was combusted prior to LSC.

Storage stability
The analyses of lettuce planted 60 DAT were performed within the first 6 month of storage and again within 21 months of storage. Comparison of the results showed that there were no significant differences between TRR in the different fractionations as well as the TLC profiles. All remained unchanged. This indicated that napropamide and its metabolites were stable over the period of time the samples were stored.

Results
Radioactive residues in control crops indicated that natural incorporation of $^{14}CO_2$ after degradation of radiolabelled napropamide in soil to $^{14}CO_2$ might occur. In wheat grain the control residue, as a percentage of the treated residue, increased from 48.8% 60 DAT to 56.7% 180 DAT and 97.7% 364 DAT.

Notifier refers to two references in which it is shown that microbial degradation producing carbon dioxide is the major degradation pathway for napropamide in soil. Uptake of $^{14}CO_2$, followed by incorporation into natural plant constituents. Natural incorporation was confirmed by the identification of ^{4}C-labelled free and deconjugated sugars in all crop samples.

A summary of TRR detected in each commodity sampled at 60, 180 and 360 DAT is shown in Table B.7.6.1-1.

Table B.7.6.1-1 Summary of TRR (mg ^{14}C-napropamide equivalents/kg) detected in crops at 60, 180 and 364 DAT

	TRR (mg ^{14}C-napropamide equivalents/kg)		
Crop sample	60 DAT (mg/kg)	180 DAT (mg/kg)	364 DAT(mg/kg)
Wheat grain	0.10	0.04	0.11
Wheat forage	0.41	0.08	0.10
Wheat straw	1.85	0.50	0.78
Carrot root	0.14	0.06	0.04
Carrot top	0.16	0.10	0.08
Lettuce	0.08	0.06	0.04

As shown in Table B.7.6.1-1 the total radioactive residue determined ranged from 1.85 mg/kg in wheat straw 60 DAT to 0.04 mg/kg in lettuce and carrot 364 DAT.

It is seen from Table B.7.6.1-1 that there was a slight overall increase of TRR in wheat grain from 60 DAT to 364 DAT. In wheat forage and straw an overall decrease from 60 DAT to 364 DAT representing 24% and 42 % were seen. In both cases a slight increase in TRR from 180 DAT to 364 DAT were seen. Since residues in control crops only can arise from natural incorporation, the notifier considers that these increases in the rotational crop also may arise from incorporation into natural constituents.

In carrot root, carrot top and lettuce a decrease was seen from 60 DAT to 364 DAT. However the rate of decrease was smaller between 180 DAT to 364 DAT, probably attributed to the increased levels of $^{14}CO_2$ in glasshouse at the 364 day interval increasing the significance of natural incorporation.

The residues identified fell into two main categories, an organic soluble fraction and an aqueous soluble fraction. Napropamide and its metabolites were found in the organic soluble fraction and sugars were found in the aqueous soluble fraction. Napropamide, its metabolites and the sugars were all found in both free and conjugated forms.

The distribution of TRR between the organic, aqueous and unextracted fractions for the different crops at 60, 180 and 364 DAT are presented in Table B.7.6.1-2.

Table B.7.6.1-2 Distribution of TRR in the organic, aqueous and the unextracted fractions for the crops at 60, 180 and 364 DAT.

	(mg ^{14}C-napropamide equivalents/kg)/ %TRR								
Fraction	Organic fraction			Aqueous fraction			Unextracted		
DAT	60 DAT	180 DAT	364 DAT	60 DAT	180 DAT	364 DAT	60 DAT	180 DAT	364 DAT
Wheat grain	< 0.003 3.0	0.002 5.0	0.005 4.5	0.02 20.0	0.007 17.5	0.01 9.1	0.07 70.0	0.03 75.0	0.09 81.8
Wheat forage	0.02 4.9	0.006 7.5	0.008 8.0	0.2 48.8	0.03 37.5	0.04 40.0	0.19 46.3	0.04 50.0	0.05 50.0
Wheat straw	0.06 3.2	0.02 4.0	0.03 3.8	0.87 47.0	0.22 44.0	0.32 41.0	0.85 45.9	0.25 50.0	0.42 53.8
Carrot root	0.08 57.1	0.03 50.0	0.02 50.0	0.03 21.4	0.01 16.7	0.01 25.0	0.04 28.6	0.01 16.7	0.01 25.0
Carrot top	0.04 25.0	0.04 40.0	0.02 25.0	0.05 31.3	0.03 30.0	0.03 37.5	0.07 43.8	0.03 30.0	0.03 37.5
Lettuce	0.008 10.0	0.01 16.7	0.004 10.0	0.03 37.5	0.03 50.0	0.02 50.0	0.04 50.0	0.03 50.0	0.01 25.0

In Table B.7.6.1-3 summaries of identified residues in wheat grain, wheat forage, lettuce, carrot root and top 60 DAT, 180 DAT and 364 DAT are presented. Results for wheat straw are shown in Table B.7.6.1-4.

Table B.7.6.1-3 Summaries of identified residues (mg ^{14}C-napropamide equivalents/kg) in wheat grain, wheat forage, lettuce, carrot root and top 60, 180 and 364 DAT.

	Wheat grain			Wheat Forage			Carrot root			Carrot top			Lettuce		
TRR (mg/kg)	0.10	0.04	0.11	0.41	0.08	0.10	0.14	0.06	0.04	0.16	0.10	0.08	0.08	0.06	0.04
Residue	60 DAT mg/kg % of TRR	180 DAT mg/kg % of TRR	364 DAT mg/kg % of TRR	60 DAT mg/kg % of TRR	180 DAT mg/kg % of TRR	364 DAT mg/kg % of TRR	60 DAT mg/kg % of TRR	180 DAT mg/kg % of TRR	364 DAT mg/kg % of TRR	60 DAT mg/kg % of TRR	180 DAT mg/kg % of TRR	364 DAT mg/kg % of TRR	60 DAT mg/kg % of TRR	180 DAT mg/kg % of TRR	364 DAT mg/kg % of TRR
Napropamide				0.006 1.5	0.0007 0.9	0.003	0.05 35.7	0.02 33.3	0.0092 2.9	0.01 6.3	0.01 10	0.007 7.0	0.001 1.3	0.001 1.7	0.0009 2.3
Desethylnapropamide (DE-NPAM)				0.005 1.2	0.0003 0.4	0.0004	0.02 4.3	0.009 15.0	0.004 10	0.02 12.5	0.02 20	0.01 12.5	0.002 2.5	0.002 3.3	0.0009 2.3
1.4-naphthoquinone (NQ)										0.001 0.6					
Sucroce	0.009 9			0.008 2.0			0.008 5.7			0.004 2.5			0.001 1.3		
Glucose	0.02 20			0.02 4.8			0.005 3.6			0.008 5.0			0.005 6.3		
Fructose	0.008 8			0.02 4.8			0.006 4.3			0.009 5.6			0.006 7.5		
Unknowns Minimum Maximum				18 0.0001 0.02	3 0.0003 0.003	6 0.0001 0.0004	1 0.001	3 0.0002 0.0004	1 0.0001	7 0.0005 0.008	3 0.0003 0.0013	5 0.0002 0.001	8 0.0001 0.001	5 0.0002 0.005	5 0.0001 0.0006

Wheat grain 60 DAT

As shown in Table B.7.6.1-3 no napropamide or metabolites were found in wheat grain but only sucrose, glucose and fructose. Sugars were released from the unextracted fraction by acid hydrolysis and accounted for 37% of TRR.

Wheat grain 180 DAT and 364 DAT

As shown in Table B.7.6.1-2 the organic and the aqueous fractions in all cases accounted for ≤ 0.01 mg/kg. The unextracted fraction accounted for 0.03 mg/kg (75%) and 0.09 mg/kg (81.8%) 180 DAT and 364 DAT, respectively. The large amount 0.09 mg/kg 364 DAT in the unextracted fraction is probably due to uptake of $^{14}CO_2$, followed by incorporation into natural plant constituents.

Wheat forage 60 DAT

It is shown in Table B.7.6.1-3 that napropamide and desethylnapropamide were found in trace amounts ≤ 0.005 mg/kg. Sucrose, glucose and fructose were found and amounted to ≤ 0.02 mg/kg. One unknown exceeded 0.01

mg/kg, i.e. 0.02 mg/kg (4.9%). It was released from the aqueous fraction by acid hydrolysis. It was co-chromatographed with so-called coloured green co-extractives, indicating that it was associated with natural constituents.

Carrot root 60 DAT
It is shown from Table B.7.6.1-3 that napropamide accounted for 0.05 mg/kg (35.7%) and desethylnapropamide 0.02 mg/kg (14.3%). Sucrose, glucose and fructose were all found in trace amount ≤ 0.0008 mg/kg. Thus a total of 63.6% of TRR was identified in carrot root 60 DAT.

Carrot root 180 and 364 DAT
It is shown that napropamide and desethylnapropamide were found 180 and 364 DAT each amounting to ≤ 0.02 mg/kg. The aqueous fraction and the unextracted fraction both accounted for ≤ 0.01 mg/kg.

Carrot top 60 DAT
Napropamide and desethylnapropamide amounted to 0.01 and 0.02 mg/kg, respectively. 1,4-naphthoquinone amounted to 0.001 mg/kg. Sucrose, glucose and fructose each amounted to ≤ 0.004 mg/kg.

Lettuce 60 DAT
Napropamide and desethylnapropamide were each found in trace amounts ≤ 0.002 mg/kg. Sucrose, glucose and fructose were found in trace amount, each ≤ 0.006 mg/kg.

Wheat straw 60 DAT, 180 DAT and 363 DAT
In Table B.7.6.1-4 summaries of identified residues in wheat straw 60 DAT, 180 DAT and 364 DAT are shown.

Table B.7.6.1-4 Summary of identified residues (mg ^{14}C-napropamide equivalents/kg) in wheat straw 60, 180 and 364 DAT.

Residue	TRR (mg/kg) 60 DAT % of TRR	TRR (mg/kg) 180 DAT % of TRR	TRR (mg/kg) 364 DAT % of TRR
Napropamide	0.02 1.1	0.009 1.8	0.01 1.3
Desethylnapropamide (DE-NPAM)	0.01 0.5	0.004 0.8	0.009 1.2
5-hydroxy-napropamide (5-OH-NPAM)	0.05 2.7	0.01 2.0	0.009 1.2
5-hydroxy-desethylnapropamide (5-OH-DE-NPAM)	0.03 1.6	0.005 1.0	0.005 0.6
4-hydroxy-desethylnapropamide (4-OH-DE-NPAM)	nd	0.01 2.0	0.004 0.5
Naphthoxypropionic acid (NOPA)	0.03 1.6	0.008 1.6	0.02 2.6
5-hydroxynaphthoxy-propionic acid (5-OH-NOPA)	0.03 1.6	0.006 1.2	0.005 0.6
4-hydroxynaphthoxy-propionic acid (4-OH-NOPA)	nd	0.005 1.0	0.003 0.4
O-phthalic acid (PA)	0.004 0.2	nd	nd
Sucrose	0.04 2.2	< 0.007 < 1.4	0.006 0.8
Glucose	0.03 1.6	< 0.005 < 1.0	0.009 1.2
Fructose	0.08 4.3	< 0.009 < 1.8	0.002 0.3
Unknowns Minimum Maximum	10 0.004 0.009	7 0.002 0.007	8 0.002 0.01

nd not detected

Napropamide is found in largest amount 60 DAT amounting to 0.02 mg/kg. All metabolites amounted to ≤ 0.05

mg/kg 60 DAT, ≤ 0.01 mg/kg 180 DAT and ≤ 0.02 mg/kg 364 DAT, respectively.

Soil
Analysis of soil cores showed that napropamide degraded rapidly in pots amounting to 4.29 mg/kg (95.3% of TRR) at day 0 and 0.05 mg/kg (4.3% of TRR) at day 477. Besides napropamide, naphthoxypropionic acid was the only significant metabolite detected, at levels up to 0.20 mg/kg (12.4% of TRR). Desethylnapropamide and naphthoxypropionamide were detected at trace levels ≤ 0.01 mg/kg.

B.7.6.2. Magnitude of residues in rotational crops

Report:	CA 6.6.2. Simmons, N.D. (1992), Napropamide: Residue levels in soil and rotated winter wheat, following application to oil seed rape, from trials carried out in Germany during 1988-90. UPL Europe Ltd, Report No. RJ1035B. United Kingdom. GLP. **(Field report)** Purser, D. (1991), Napropamide : Determination of residues in crop and soil. UPL Europe Ltd, Unpublished report No. : 38/155D + Amendment No. 1. **(Analytical report)**

Materials and methods
Unlabelled napropamide was incorporated to a depth of 5 cm before drilling winter oil seed rape. The trial site was located in Germany. Each trial consisted of four plots, one control and three treated plots. Each treated plot received a different formulation of napropamide, either 190 g as/l (SC/CS formulation), 190 g as/l (EC formulation) or 95 g as/l (EC formulation), all corresponding to about 0.95 kg as/ha. The oil seed rape was harvested in autumn 1989 and the soil cultivated to a depth of 30 cm and a succeeding crop of winter wheat was sown in each plot. Samples of immature wheat and mature grain and straw were taken during the following season. At each sampling time soil samples were also taken. Residue analysis was performed using method ARAM 177 for wheat crop samples and ARAM 178 for soil samples see Vol 3 B.5.1.2.

Results
Residues of napropamide in immature wheat and mature grain and straw were reported to be below the LOQ (0.01 mg/kg) in all samples with the exception of one immature wheat sample that contained 0.04 mg/kg napropamide.

Analysis of soil samples showed that soils contained only low residue levels of napropamide (0.01mg/kg - 0.04 mg/kg).

It is noted that in Vol 3 B.5.1.2 method ARAM 178 and ARAM 177 have not been considered fully validated but have been considered fit for purpose with an LOQ of 0.1 mg/kg in soil, 0.05mg/kg in oilseed rape seed and 0.02 mg/kg in whole oilseed rape plant (see Vol 3 B.5.1.2). Following the submission of additional data (see Vol 3 B.5.1.2) an LOQ of 0.01mg/kg in wheat (whole plant straw and grain) using method ARAM 177 and 0.01 mg/kg in soil using method ARAM 178 has been confirmed.

Table B.7.6.2-1 Summary of residues trials in winter wheat rotated after oilseed rape- crop residue results

Doc. No. Trial Ref Location Crop Year	Application				Napropamide residues (mg/kg)	Crop part	DAA (days)
	No.	kg a.s./ha (product)	Spray Vol. L/ha	Timing			
CA 6.6.2/01 RS-8837-B1 Germany Rotated winter wheat 1988-1990	1	0.950 (190 SC)	400	Pre-sowing primary crop (OSR)	<0.01 <0.01 <0.01	Immature plant Mature grain Mature straw	595 717 717
	1	0.950 (190 EC)	400	Pre-sowing primary crop (OSR)	0.04 <0.01 <0.01	Immature plant Mature grain Mature straw	595 717 717
CA 6.6.2/01 RS-8837-B2 Germany Rotated winter wheat 1988-1990	1	0.950 (190 SC)	400	Pre-sowing primary crop (OSR)	<0.01 <0.01 <0.01	Immature plant Mature grain Mature straw	600 714 714
	1	0.950 (190 EC)	400	Pre-sowing primary crop (OSR)	<0.01 <0.01 <0.01	Immature plant Mature grain Mature straw	600 714 714
CA 6.6.2/01 RS-8837-E1 Germany Rotated winter wheat 1988-1990	1	0.950 (190 SC)	400	Pre-sowing primary crop (OSR)	<0.01 <0.01 <0.01	Immature plant Mature grain Mature straw	589 700 700
	1	0.950 (190 EC)	400	Pre-sowing primary crop (OSR)	<0.01 <0.01 <0.01	Immature plant Mature grain Mature straw	589 700 700
CA 6.6.2/01 RS-8837-E2 Germany Rotated winter wheat 1988-1990	1	0.950 (190 SC)	400	Pre-sowing primary crop (OSR)	<0.01 <0.01 <0.01	Immature plant Mature grain Mature straw	588 702 702
	1	0.950 (190 EC)	400	Pre-sowing primary crop (OSR)	<0.01 <0.01 <0.01	Immature plant Mature grain Mature straw	588 702 702
CA 6.6.2/01 RS-8837-G1 Germany Rotated winter wheat 1988-1990	1	0.950 (190 SC)	400	Pre-sowing primary crop (OSR)	<0.01 <0.01 <0.01	Immature plant Mature grain Mature straw	623 710 710
	1	0.950 (190 EC)	400	Pre-sowing primary crop (OSR)	<0.01 <0.01 <0.01	Immature plant Mature grain Mature straw	623 710 710

Table B.7.6.2-2 Summary of residues trials in winter wheat rotated after oilseed rape- soil residue results

Doc. No. Trial Ref Location Crop Year	Application				Napropamide residues (mg/kg)	Crop part	DAA (days)
	No.	kg a.s./ha (product)	Spray Vol. L/ha	Timing			
CA 6.6.2/01 RS-8837-B1 Germany Rotated winter wheat 1988-1990	1	0.950 (190 SC)	400	Pre-sowing primary crop (OSR)	0.01 <0.01	Soil Soil	595 717
	1	0.950 (190 EC)	400	Pre-sowing primary crop (OSR)	0.01 0.01	Soil Soil	595 717
CA 6.6.2/01 RS-8837-B2 Germany Rotated winter wheat 1988-1990	1	0.950 (190 SC)	400	Pre-sowing primary crop (OSR)	0.01 0.01	Soil Soil	600 714
	1	0.950 (190 EC)	400	Pre-sowing primary crop (OSR)	<0.01 0.04	Soil Soil	600 714
CA 6.6.2/01 RS-8837-E1 Germany Rotated winter wheat 1988-1990	1	0.950 (190 SC)	400	Pre-sowing primary crop (OSR)	<0.01 <0.01	Soil Soil	589 698
	1	0.950 (190 EC)	400	Pre-sowing primary crop (OSR)	<0.01 <0.01	Soil Soil	589 698
CA 6.6.2/01 RS-8837-E2 Germany Rotated winter wheat 1988-1990	1	0.950 (190 SC)	400	Pre-sowing primary crop (OSR)	<0.01 <0.01	Soil Soil	588 702
	1	0.950 (190 EC)	400	Pre-sowing primary crop (OSR)	<0.01 <0.01	Soil Soil	588 702
CA 6.6.2/01 RS-8837-G1 Germany Rotated winter wheat 1988-1990	1	0.950 (190 SC)	400	Pre-sowing primary crop (OSR)	<0.01 <0.01	Soil Soil	611 710
	1	0.950 (190 EC)	400	Pre-sowing primary crop (OSR)	0.01 <0.01	Soil Soil	611 710

Conclusion

When wheat is grown as a rotational crop to oil seed rape, which had originally received napropamide using different types of formulation at a rate corresponding to 0.95 kg as/ha, residues of napropamide in mature wheat grain and straw was < 0.01 mg/kg. In one immature wheat sample napropamide amounted to 0.04 mg/kg. Soil samples taken at crop harvest indicated residues in soil ≤0.04 mg/kg.

Summary

A napropamide rotational crop metabolism study and rotational crop trials for wheat (grown after oilseed rape) have been provided. Both of the studies have been previously evaluated in the napropamide DAR which concluded as follows:

The cultivation of certain crops within one year after the use of napropamide may cause problems due to phytotoxic effects. A confined rotational crop study was carried out using carrots, lettuce, and wheat as succeeding crops, planted 60, 180 and 360 days after soil treatment at 4800 g a.s./ha. This application rate is 5N in case of brassicas, 4N in case of oilseed rape, and 2N in case of tomatoes. Under these circumstances the TRR were ranging from 0.08 (lettuce) to 0.41 mg/kg (wheat forage) for the 60 days interval, and decreased to 0.04 (lettuce and carrot roots) to 0.11 mg/kg (wheat grain) for the 360 days interval. Unchanged napropamide was found in mature commodities at levels generally below 0.01 mg/kg, except in carrot roots, where the levels were 0.05 and 0.02 mg/kg for the 60 days and 180 days intervals, respectively. Two metabolites were identified,

suggesting that the metabolism in rotational crops is similar to that in primary crops. In a field study, where wheat was cultivated as a rotational crop to oilseed rape, residues in straw and grains were below the LOQ of 0.01 mg/kg.
The information available suggests a potential for low but measurable napropamide residues in rotational crops, particularly in root crops. The RMS proposed a waiting period of 180 days from the use of napropamide before planting or sowing rotational crops. This should be considered at Member State level.

The conclusions from the napropamide EU peer review can be considered appropriate for napropamide-M. Residues are low in succeeding crops and the data suggests residues will be <0.01 mg/kg after 180 days.

The PEC_{soil} accumulation for Napropamide-M is suggested to be 1.5979 mg/kg (see Vol 1, 2.8.6); this equates to an application rate of approximately 1198 g as/ha, at this rate significant residues in following crops are not expected as long as the interval between last application and planting of succeeding crops is in excess of180 days.

It is noted that the rotational crop metabolism study indicates that residues of napropamide will be ≤0.01 mg/kg in food after a 60 day plant back interval. However the 60 day plantback interval pots also included cabbage seedlings which were not tested. Therefore it is possible residues in food could be higher if this co-planting had not occurred.

It is noted that due to crop safety concerns and fate considerations the following replant restrictions (see Vol 1, 3.3.1) have been recommended:

Only supported uses, including brassica vegetable crops and winter oilseed rape, may be drilled/transplanted as following crops. Crops may be drilled only in the following planting season of the next calendar year.

Based purely on rotational crop concerns a plantback interval of 180 days would be recommended; however the efficacy and fate recommendation restricts use to the primary crops (brassica vegetables and winter oilseed rape), residues in following crops (even with accumulation) are not expected to significantly exceed the residues found in the primary crops in Section B.7.3.

B.7.7. OTHER STUDIES

B.7.7.1. Effect on the residue level in pollen and bee products

Bee and pollen studies have not been submitted and are not required until harmonised guidance has been agreed.

B.7.8. REFERENCES RELIED ON

7.8.1 Literature search

The following databases were searched :

Anabstr - Analytical abstracts
Biosis
Caplus - chemical abstracts plus
Chemlist
Embase - The Excerpta Medica database
Scisearch
Toxcenter
Medline
Rtecs- Registry of Toxic Effects of Chemical Substances
Science Direct
PubMed

Wiley Online Library

The search was restricted to publications within the last ten years.

Search criteria :

- Napropamide, synonyms and CAS numbers were used
- Relevant metabolite, synonyms and CAS numbers were used
- Suitable terms relating to the assessment of residues were used.
- Metabolites were not searched in combination with residue terms due to their non-significant levels in the residues assessment.

Consideration of relevance. The criteria for residues were:

1. Clearly defined test material
2. Well characterised and relevant test system
3. Acceptable mass balance for radiolabelled testing
4. Use of validated and acceptable analytical methods
5. Clear relevance to regulatory process or actual use of the active substance

In total 600 records were retrieved and screened by reviewers. The RMS (UK) considers the search criteria adequate. After a rapid assessment for relevance of the 600 records retrieved only two were regarded as possibly relevant. It is noted that the relevance criteria 4 could severely limit the number of studies considered relevant. However the rapid assessment of relevance is based only on the abstract and title of the paper; therefore it is unlikely in practice that criteria 4 can be applied at this stage.

Two full text documents were assessed in detail and excluded after detailed assessment of their relevance. If included they would not be expected to affect the outcome of the residues assessment:

Author(s)	Year	Title	Source	Reason(s) for not including this study in the dossier
Cui, Li-E.; Yang, Hong¶CS Jiangsu Key Laboratory of Pesticide Science, College of Science, Nanjing¶ Agricultural University, Nanjing, Peop. Rep. China	2011	Accumulation and residue of napropamide in alfalfa (Medicago sativa)¶ and soil involved in toxic response	Journal of Hazardous Materials (2011), 190(1-3), 81-86	The study is not a regulatory guideline study and has no adverse impact. Does not meet relevance criteria, therefore does not fulfil residue studies / dietary risk relevance criteria
Nougadere, Alexandre; Reninger, Jean-Cedric; Volatier, Jean-Luc; Leblanc, Jean-Charles CS, Chemicals Exposure and Quantitative Risk Assessment Unit, Office of Scientific Support for Risk Assessment, Risk Assessment Department French Agency for Food, Environmental and Occupational Health Safety	2011	Chronic dietary risk characterization for pesticide residues: A ranking and scoring method integrating agricultural uses and food¶ contamination data	Food and Chemical Toxicology (2011), 49(7), 1484-1510	The study is not relevant for supported uses or consumer risk, therefore does not fulfil residue studies / dietary risk relevance criteria

7.8.2 References

Data Point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Vertebrate study Y/N	Data protection claimed Y/N	Justification if data protection is claimed	Owner	Previous evaluation
Ahmad, S.	CA 6.2.1/01	2015	[naphthyl-1-14C] napropamide-M: Metabolism in oilseed rape crop Company Report No. AU-2012-49 Jai Research Foundation, USA GLP, Unpublished **Study submitted to meet data requirements**	N	N	NA	UPL	None
Balluf, M.	CA 6.3.1/05	2005a	Determination of residues of napropamide after a single application with soil incorporation of Devrinol 45FL in head cabbage outdoor, Southern Europe, 2004/2005 Company Report No. 20044048/I1-FPCA GAB Biotechnologie GmbH, Germany GLP, Unpublished **Study submitted to meet data requirements**	N	N	NA	UPL	None
Balluf, M.	CA 6.3.1/06	2005b	Determination of residues of napropamide after a single application with soil incorporation of Devrinol 45FL in head cauliflower outdoor, Southern Europe, 2004/2005 Company Report No. 20044048/I1-FPCF GAB Biotechnologie GmbH, Germany GLP, Unpublished **Study submitted to meet data requirements**	N	N	NA	UPL	None
Bamber, A.	CA 6.3.1/01A	2001	The production of brassica samples after one pre-plant application of Devrinol Company Report No. 688-00-UPL-BRA Oxford Agricultural Trials Ltd., United Kingdom GLP, Unpublished **Study submitted to meet data requirements**	N	N	NA	UPL	None
Brown, D.	CA 6.1/02	2001	Study to determine the stability of napropamide residues in oilseed rape seed and specimens following frozen storage at ca. -18°C for 0 days, 1 month, 3, 6 and 12 months Company Report No. AD/5287/US Agrisearch UK Limited, United Kingdom GLP, Unpublished **Study submitted to meet data requirements**	N	N	NA	UPL	Evaluated in the DAR for napropamide (racemate). RMS = Demark, September 2005)

Data Point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Vertebrate study Y/N	Data protection claimed Y/N	Justification if data protection is claimed	Owner	Previous evaluation
Chadwick, G.	CA 6.3.2/01	2015	d-napropamide 450 g/L Determination of residues of d-napropamide after one application of d-napropamide 450 g/L SC to winter oilseed rape at 3 sites in Northern Europe and 4 sites in Southern Europe 2012 Company Report No. S12-03756 Eurofins Agroscience Services Ltd., United Kingdom GLP, Unpublished **Study submitted to meet data requirements**	N	N	NA	UPL	None
Clark, D.	CA 6.3.1/02	2002a	To determine the magnitude of napropamide residues at harvest in the raw agricultural commodity head cabbage resulting from a single overall application of Devrinol 45FL in the UK during 2001 Company Report No. AS/5631/US Agrisearch UK Limited, United Kingdom GLP, Unpublished **Study submitted to meet data requirements**	N	N	NA	UPL	Evaluated in the DAR for napropamide (racemate). RMS = Demark, September 2005)
Clark, D.	CA 6.3.1/03	2002b	To determine the magnitude of napropamide residues at harvest in the raw agricultural commodity cauliflower resulting from a single overall application of Devrinol 45FL in the UK during 2001 Company Report No. AS/5633/US Agrisearch UK Limited, United Kingdom GLP, Unpublished **Study submitted to meet data requirements**	N	N	NA	UPL	Evaluated in the DAR for napropamide (racemate). RMS = Demark, September 2005)
Clark, D.	CA 6.3.1/04	2002c	To determine the magnitude of napropamide residues at harvest in the raw agricultural commodity Brussels sprouts resulting from a single overall application of Devrinol 45FL in the UK during 2001 Company Report No. AS/5634/US Agrisearch UK Limited, United Kingdom GLP, Unpublished **Study submitted to meet data requirements**	N	N	NA	UPL	Evaluated in the DAR for napropamide (racemate). RMS = Demark, September 2005)
Emburey, S., Joseph, R.S.I.	CA 6.2.1/03	1992	Napropamide: Uptake and Metabolism in Cabbage Company Report No. RJ1224B ICI Agrochemicals, United Kingdom GLP, Unpublished **Study submitted to meet data requirements**	N	N	NA	UPL	Evaluated in the DAR for napropamide (racemate). RMS = Demark, September 2005)

Data Point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Vertebrate study Y/N	Data protection claimed Y/N	Justification if data protection is claimed	Owner	Previous evaluation
Goodband, T.	CA 6.3.2/02	2002	To determine the magnitude of napropamide residues at harvest in the raw agricultural commodity oilseed rape resulting from a single overall application of Devrinol 45FL to the ground in Northern France (2000-2002) Company Report No. AF/5056/US Agrisearch UK Limited, United Kingdom GLP, Unpublished **Study submitted to meet data requirements**	N	N	NA	UPL	Evaluated in the DAR for napropamide (racemate). RMS = Demark, September 2005)
[redacted]	CA 6.2.2/01	1993	Napropamide: Metabolism of orally administered multiple doses in the laying hen Company Report No. RJ1408B [redacted] GLP, Unpublished **Study submitted to meet data requirements**	Y	N	NA	UPL	Evaluated in the DAR for napropamide (racemate). RMS = Demark, September 2005)
Hurt, A.D., Joseph, R.S.I.	CA 6.2.1/05	1992	Napropamide: Uptake and Metabolism in Apples Company Report No. RJ1128B ICI Agrochemicals, United Kingdom GLP, Unpublished **Study submitted to meet data requirements**	N	N	NA	UPL	Evaluated in the DAR for napropamide (racemate). RMS = Demark, September 2005)
Langford-Pollard, A.D.	CA 6.2.1/02	2002	Napropamide oilseed rape metabolism Company Report No. UPH/028/14461 Huntingdon Life Sciences Ltd., United Kingdom GLP, Unpublished **Study submitted to meet data requirements**	N	N	NA	UPL	Evaluated in the DAR for napropamide (racemate). RMS = Demark, September 2005)
Norris, D.	CA 6.1/01	2002a	Determination of the freezer storage stability of napropamide residues in samples of brassicas (to include cauliflower, cabbage and Brussels sprouts), over a maximum period of twelve months, in compliance with Good Laboratory Practice Company Report No. OA00567 B Oxford Analytical Ltd., United Kingdom GLP, Unpublished **Study submitted to meet data requirements**	N	N	NA	UPL	Evaluated in the DAR for napropamide (racemate). RMS = Demark, September 2005)
Norris, D.	CA 6.3.1/01B	2002b	Determination of napropamide residues in samples of brassicas treated with Devrinol in compliance with Good Laboratory Practice Company Report No. OA00567 Oxford Analytical Ltd., United Kingdom GLP, Unpublished **Study submitted to meet data requirements**	N	N	NA	UPL	Evaluated in the DAR for napropamide (racemate). RMS = Demark, September 2005)

Data Point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Vertebrate study Y/N	Data protection claimed Y/N	Justification if data protection is claimed	Owner	Previous evaluation
Parker, S., Steel, T.R., Harris, M., Hurt, A.D., Allin, R.	CA 6.6.1/01	1993	Napropamide: Uptake and metabolism in confined rotational crops Company Report No. RJ1348B ICI Agrochemicals, United Kingdom GLP, Unpublished **Study submitted to meet data requirements**	N	N	NA	UPL	Evaluated in the DAR for napropamide (racemate). RMS = Demark, September 2005)
Pay, J., Simmons, N.D.	CA 6.3.2/03	1990	Napropamide: Residues in oil seed rape from trials carried out in West Germany during 1988 Company Report No. RJ0829B ICI Agrochemicals, United Kingdom GLP, Unpublished **Study submitted to meet data requirements**	N	N	NA	UPL	Evaluated in the DAR for napropamide (racemate). RMS = Demark, September 2005)
Purser, D.	CA 6.6.2/01B	1991	Napropamide: Determination of residues in crop and soil + Amendment No. 1 Company Report No. 38/155D Hazleton UK, United Kingdom GLP, Unpublished **Study submitted to meet data requirements**	N	N	NA	UPL	Evaluated in the DAR for napropamide (racemate). RMS = Demark, September 2005)
Simmons, N.D.	CA 6.3.2/04	1992a	Napropamide: Residues in oil seed rape from trials carried out in Denmark during 1990 Company Report No. RJ1006B ICI Agrochemicals, United Kingdom GLP, Unpublished **Study submitted to meet data requirements**	N	N	NA	UPL	Evaluated in the DAR for napropamide (racemate). RMS = Demark, September 2005)
Simmons, N.D.	CA 6.6.2/01A	1992b	Napropamide: Residue levels in soil and rotated winter wheat, following application to oil seed rape, from trials carried out in Germany during 1988-90 Company Report No. RJ1035B ICI Agrochemicals, United Kingdom GLP, Unpublished **Study submitted to meet data requirements**	N	N	NA	UPL	Evaluated in the DAR for napropamide (racemate). RMS = Demark, September 2005)
Spillner, C.J.	CA 6.2.1/06	1983	Uptake and metabolism of [14C] Devrinol in potatoes Company Report No. MRC-83-07 Stauffer Chemical Company, USA Not GLP, Unpublished **Study submitted to meet data requirements**	N	N	NA	UPL	Evaluated in the DAR for napropamide (racemate). RMS = Demark, September 2005)
Webb, J., Allin, R., Joseph, R.S.I.	CA 6.2.1/04	1992	Napropamide: Uptake and Metabolism in Tomatoes Company Report No. RJ1153B ICI Agrochemicals, United Kingdom GLP, Unpublished **Study submitted to meet data requirements**	N	N	NA	UPL	Evaluated in the DAR for napropamide (racemate). RMS = Demark, September 2005)

Data Point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Vertebrate study Y/N	Data protection claimed Y/N	Justification if data protection is claimed	Owner	Previous evaluation
[redacted]	CA 6.2.3/01	1993	Napropamide: Metabolism of orally administered multiple doses in the lactating goat Company Report No. RJ1388B [redacted] GLP, Unpublished **Study submitted to meet data requirements**	Y	N	NA	UPL	Evaluated in the DAR for napropamide (racemate). RMS = Demark, September 2005)