European Commission

Renewal Assessment Report of the Inclusion of the Active Substance in Annex I of the Regulation (EC) 1107/2009

Oxamyl

Volume 3 (CA)
ANNEX B.7 Residue data

Rapporteur Member State: Italia
Co-Rapporteur Member State: France

January 2018

VERSION HISTORY

Date	Data points containing amendments or additions	Document identifier or version number
July 2017	First RAR of Italy	
January 2018	Revised RAR after comment CoRMS (France)	

TABLE OF CONTENTS

TABLE OF TABLES

TABLE OF FIGURES

B.7 RESIDUE DATA[1]

Unless specifically indicated, all reports in this section are submitt to address mandatory data requirements for the approval of active substance.

Unless specifically indicated, all tests submitted in this section, which involve vertebrate animals, address mandatory data requirements which could not be met with alternative methods. Studies were conducted according to prescribed guidelines.

Unless specifically indicated, this section does not contain reports of studies duplicating previous tests on vertebrate animals.

B.7.1 Storage stability of residues

Study already submitted to the EU.

B.7.1/01

Reference:**CA 6.1/03**	**Report**	Dubey, L., Steiner, C., Belgaid, R. (2002); Stability of oxamyl in different crops stored frozen **DuPont Report No.:** DuPont-4235 **Guidelines:** EU 7032/VI/1995 Rev 5 (1997) App. H **Deviations:** None **Testing Facility:** Battelle Europe-Centre de Recherche de Geneve, Geneva, Switzerland Testing Facility Report No.: A-11-00-04 **GLP:** Yes **Certifying Authority:** Not given

Executive summary:

This study showed that oxamyl is stable in crop matrices stored frozen at -18 ± 5°C for at least 24 months. This study supports residue data generated in crop matrices during the magnitude and decline of residue studies, processing studies, and field crop rotation studies. Crop samples from the storage stability study and the field studies were stored under similar conditions, extracted, and analysed following the procedures described in the analytical method reports DuPont-3702, DuPont-4722, and DuPont-11125, analytical methods for the quantitation of oxamyl in various crop matrices and their processed fractions. These methods are summarised in Volume 3 B.5

[1] Uses applied for to support the setting of MRLs for uses beyond the representative uses(s) should be clearly identified.

I. MATERIALS AND METHODS

A. MATERIALS

1.	Test material:	Oxamyl analytical standard
	Lot/Batch #:	D1410-376
	Purity:	100%
	Description:	White powder
	CAS#:	23135-22-0
2.	Test commodity:	
3.	Crop:	Potato, sugar beet, leaf lettuce, tomato, and orange
	Type:	Not available
	Variety:	Not available
	Botanical name:	Not available
	Crop part(s) or processed commodity:	Potato tuber, sugar beet root, leaf lettuce, tomato, and orange peel
	Sample size:	3 ± 0.1 g

B. STUDY DESIGN

The study was conducted during the period between 15-June-2000 and 02-July-2002 at the Battelle Europe-Centre de Recherche de Geneve in Geneva, Switzerland.

1. Test procedure

Control samples fortified with oxamyl at 0.5 mg/kg were stored over a period up to 24 months during which they were keept in a frozen condition (approximately -18°C) pending analysis. At intervals during the storage period, two stored fortified and three control samples were removed from storage for analysis. Two of the control samples were freshly fortified with oxamyl at 0.5 mg/kg and the five samples were analysed for oxamyl residues using the same analytical procedures that were employed for crop field residue studies.

2. Description of analytical procedures

Samples were analysed at 0 days, and after approximately 3, 6, 12, 18, and 24 months of frozen storage for oxamyl by an LC/column-switch/UV method (potato tuber, sugar beet root, leaf lettuce, and tomato samples; DuPont-3702) or an N-methyl carbamate pesticide multiresidue method (HPLC with post-column derivatisation followed by fluorescence detection) (orange peel samples; DuPont-4722). These methods are summarised in Volume 3 B5

II. RESULTS AND DISCUSSION

The average recoveries of Oxamyl from the representative fruit and vegetable matrices ranged from 70% to 91% following 24 months of storage. The normalized average recoveries of Oxamyl residues in potato tuber, sugar beet root, leaf lettuce, tomato and orange peel samples were 86% or greater than after 24 months storage.
There was no Oxamyl found in any of control samples.
The data indicate that when frozen samples of potato tuber, sugar beet root, leaf lettuce, tomato, and orange peel, intended for residue analyses, are stored for extended periods of at least 24 months, acceptable stability can be expected (see Table 1).

Table 1 Storage stability of oxamyl in potato tubers, sugar beet root, leaf lettuce, tomato, and orange peel

Crop commodity	Approximate Storage interval (months)	% Recovery				
		Freeze Stored Fortifications	Fresh Fortifications	Average Recovery		Normalised Recovery[a]
				Stored	Fresh	
Potato	0	---	83, 83	---	83	100
Tuber	3	73, 80	86, 78	77	82	94
	6	82, 73	80, 73	78	77	101
	12	88, 70	70, 79	79	75	105
	18	79, 81	85, 77	80	81	99
	24	61, 65, 79, 75[b]	86, 80, 85, 71[b]	70	81	86
Sugar Beet	0	---	77, 70	---	74	100
Root	3	81, 83	74, 85	82	80	103
	6	85, 83	75, 86	84	81	104
	12	73, 70	71, 74	72	73	99
	18	70, 68	76, 78	69	77	90
	24	66, 84	81, 78	75	80	94
Leaf Lettuce	0	---	96, 97	---	97	100
	3	77, 91	84, 78	84	81	104
	6	90, 86	86, 81	88	84	105
	12	86, 90	89, 93	88	91	97
	18	81,86	86, 83	84	85	99
	24	90, 91	100. 91	91	96	95
Tomato	0	---	84, 96	---	90	100
	3	87, 78	88, 78	83	83	100
	6	83, 91	75, 83	87	79	110
	12	85, 76	92, 77	81	85	95
	18	69, 73	73, 83	71	78	91
	24	82, 72	77, 88	77	83	93
Orange Peel	0	---	93, 96	---	95	100
	6	95, 87	86, 60	91	73	125
	12	94, 91	93, 93	93	93	100
	18	90, 86	96, 97	88	97	91

	24	84, 78	82, 89	81	86	94

[a] Normalised Recovery = (average freezer storage value/average fresh fortification value) × 100
[b] Initial analysis gave <70% recoveries for stored samples so the analysis was repeated. Results from both data sets are reported.

III. CONCLUSION

Oxamyl residues in representative watery, acidic, sugary, starchy, and oily fruit and vegetable matrices (potato tuber, sugar beet root, leaf lettuce, tomato, and orange peel) are stable for periods of storage at approx. -18°C for at least 24 months, a period which exceeds the longest time period for which samples were stored in the course of the residue trial studies.

(Dubey, L., Steiner, C., Belgaid, R., 2002)

Study submitted to the EU for the first time in this submission.

B.7.1/02

Reference: CA 6.1/01	**Report**	Cairns, S.D., Davidson, J. (2006); Storage stability of oxamyl in dried tobacco leaves **DuPont Report No.:** DuPont-17600 **Guidelines:** Directive 91/414/EEC, 7032/VI/95 Rev.5 (1997) **Deviations:** None **Testing Facility:** Charles River Laboratories (UK), Tranent, Scotland, UK Testing Facility Report No.: 26648 **GLP:** Yes **Certifying Authority:** Department of Health (U.K.)

Executive summary:

This study showed that oxamyl is stable in dried tobacco leaves stored frozen at approximately -20°C for at least 6 months. This study supports residue data generated in crop matrices during the magnitude and decline of residue studies, processing studies, and field crop rotation studies.

The stability of Oxamyl was studied by fortifying homogenized control dried tobacco samples with 0.1 mg/kg Oxamyl and storing the fortified samples in a freezer at ca. -20°C. The stored samples were analyzed at approximate time interval of 0, 1, 3 and 6 months of frozen storage. To verify method performance, unfortified homogenized control dried tobacco samples were stored frozen with the fortified samples to serve as analytical controls or freshly fortified samples at the time of analysis. Freshly fortified samples were fortified with 0.1 mg/kg of Oxamyl.

Freshly and/or stored fortified specimens were analysed for residues of Oxamyl following the procedures described in the analytical method report DuPont-17601 "Validation of an analytical method for the determination of Oxamyl in green, dried and fermented Tobacco leaves" This method is summarized in Volume 3 B.5.

The determined Limit of Quantification (LOQ) in tobacco was 0.010 mg/kg. The Limit of detection (LOD) was 0.007 mg/kg.

Oxamyl residues in fortified samples following freezer storage at ca -20°C are summarized in the table 2.

The average recoveries of Oxamyl from dried tobacco samples ranged from 69% to 87% following 6 months of frozen storage. The normalized average recoveries of Oxamyl residues in dried tobacco samples were 79% or greater after 6 months of storage. This indicates that Oxamyl is stable in dried tobacco when samples are storage in a freezer for up to 6 months at ca -20°C prior to analysis. There are no detectable Oxamyl residues found in any of the unfortified control samples.

I. MATERIALS AND METHODS

A. MATERIALS

1.	Test material:	Oxamyl analytical standard
	Lot/Batch #:	D1410-454
	Purity:	99.9%
	Description:	White powder
	CAS#:	23135-22-0
2.	Test commodity:	
3.	Crop:	Tobacco
	Type:	Not available
	Variety:	Not available
	Botanical name:	Not available
	Crop part(s) or processed commodity:	Dried tobacco leaves
	Sample size:	15 g

B. STUDY DESIGN

The study was conducted during the period between 05-September-2005 and 25-March-2006 at the Charles River Laboratories, Tranent, Edinburgh, UK.

1. Test procedure

Control samples fortified with oxamyl at 0.10 mg/kg were stored over a period up to 6 months during which they were kept in a frozen condition (approximately -20°C) pending analysis. At intervals during the storage period, 2 stored fortified and 3 control samples were removed from storage for analysis. Two of the control samples were freshly fortified with oxamyl at 0.10 mg/kg and the five samples were analysed.

2. Description of analytical procedures

Samples were analysed at 0, 1, 3, and 6 months of frozen storage for oxamyl by an LC-MS method (DuPont-17601). This method is summarized in Volume 3 B.5.

II. RESULTS AND DISCUSSION

The data indicate that when frozen samples of dried tobacco leaves are stored for extended periods of at least 6 months, acceptable stability can be expected (see Table 2).

Table 2 Storage stability of oxamyl in dried tobacco leaves

Crop commodity	Approximate Storage interval (months)	% Recovery				
		Freeze Stored Fortifications	Fresh Fortifications	Average Recovery		Normalised Recovery[a]
				Stored	Fresh	
Dried Tobacco	0	---	90, 90	---	90	100
	1	78, 72	95, 95	75	95	79
	3	78, 59[b]	82, 77	69	80	86
	6	90, 84	102, 116[b]	87	109	80

[a] Normalised Recovery = (average freezer storage value/average fresh fortification value) x 100
[b] Atypical result included in calculations

III. CONCLUSION

Oxamyl residues in dried tobacco leaves are stable for periods of storage at -20°C for at least 6 months, a period which exceeds the longest time period for which tobacco samples were stored in the course of the residue trial study.

(Cairns, S.D., Davidson, J., 2006)

Study submitted to the EU for the first time in this submission.

B.7.1/03

Reference: CA 6.1/02	Report:	Cairns, S.D., Woodmansey, L. (2013); Stability of oxamyl (DPX-D1410) in oranges stored frozen **DuPont Report No.:** DuPont-32189 **Guidelines:** Directive 91/414/EEC, 7032/VI/95 Rev.5 (1997) **Deviations:** None **Testing Facility:** Charles River Laboratories (UK), Tranent, Scotland, UK Testing Facility Report No.: 218451 **GLP:** Yes **Certifying Authority:** Department of Health (U.K.)

Executive summary:

This study showed that oxamyl is stable in ground oranges stored frozen at approximately -20°C for at least 12 months. This study supports residue data generated in crop matrices during the magnitude and decline of residue studies, processing studies, and field crop rotation studies. Crop samples from the storage stability study and the field studies were stored under similar conditions, extracted, and analysed following the procedures described in the analytical method report DuPont-33191, Method Validation for the Analysis of Oxamyl (DPX-D1410) in Representative Crop Commodities using LC-MS/MS. This method is summarized in Volume 3 B.5.

I. MATERIALS AND METHODS

A. MATERIALS

1.	Test material:	Oxamyl analytical standard
	Lot/Batch #:	D1410-222
	Purity:	99.3%
	Description:	Solid, powder
	CAS#:	23135-22-0
2.	Test commodity:	
3.	Crop:	Oranges
	Type:	Not available
	Variety:	Not available
	Botanical name:	Not available
	Crop part(s) or processed commodity:	Ground whole oranges
	Sample size:	15 g

B. STUDY DESIGN

The study was conducted during the period between 29 March 2011 and 06 December 2012 at Charles River Laboratories, Tranent, Edinburgh, UK.

1. Test procedure

Control samples fortified with oxamyl at 0.10 mg/kg were stored over a period up to 12 months during which time they were kept in a frozen condition (approximately -20°C) pending analysis. At intervals during the storage period, 2 stored fortified and 3 control samples were removed from storage for analysis. Two of the control samples were freshly fortified with oxamyl at 0.10 mg/kg and the five samples were analysed.

2. Description of analytical procedures

Samples were analysed at 0, 3, 6, 9 and 12 months of frozen storage for oxamyl by an LC-MS method (DuPont-33191). This method is summarised in Volume 3 B.5.II. RESULTS AND DISCUSSION

The data indicate that when frozen samples of oranges are stored for extended periods of at least 12 months, acceptable stability can be expected (see Table 3).

Table 3 Storage stability of oxamyl in whole oranges

Crop commodity	Fort level (ppm, mg/kg)	Storage interval (Months)	Stored (-20°C) recovered residues (ppm, mg/kg)		% Recovery						
					Stored (-20°C) Forts		Fresh forts		Average recovery		
									Stored	Fresh	Normalized[a]
Oxamyl											
Orange	0.10	0	--	--	--	--	93	87	--	90	--
	0.10	3	0.11	0.086	110	84	81	95	97	88	110
	0.10	6	0.11	0.10	109	101	109	98	105	104	101
	0.10	9	0.085	0.097	83	95	88	80	89	84	106
	0.10	12	0.104	0.102	102	100	115	90	101	102	99

[a] Normalized Recovery = average freezer storage recovery value/average fresh fortification recovery

III. CONCLUSION

Oxamyl residues in whole oranges are stable for periods of storage at -20°C for at least 12 months.

(Cairns, S.D., Woodmansey, L., 2013)

RMS comments and conclusion: The studies confirm that the residue of Oxamyl in whole orange are stable for at least 12 months when storage at -20°C, and that the residue of Oxamyl in Tobacco are stable for 6 months when storage at -20°C. The studies are perform on control samples that were fortified by Oxamyl Standard Solution.
The studies are acceptable.

Stability of residues in sample extracts

Stability of analyte residues in sample extracts were verified by the acceptable fortification recovery data summarised in each study. At least one or two fortifications were runn with each set of analytical samples. These fortifications were run with the specimens in each analysis set and were stored and treated in every way as the treated and control specimens in that set.

B.7.2 Metabolism, distribution and expression of residues

The comparative metabolism of ^{14}C-oxamyl in plants was studied in diverse crops *via* direct foliage, fruit, or soil applications under laboratory and/or field settings. Metabolism of oxamyl in plants included hydrolysis of the methylcarbamoyl group to yield the non-insecticidal oxamyl oxime (IN-A2213). IN-A2213 was demethylated before or after glucose conjugation to give IN-L2953 and/or its glucose conjugate. Conjugation of the glucosides of IN-A2213 and IN-L2953 with additional sugar residues was also observed. IN-A2213 (or oxamyl) may also be metabolised to IN-N0079, which is metabolised to IN-D2708 and ultimately incorporated into plant natural products. (For details on the metabolite structures please refer to Figure 3).

The major metabolic pathways in plants and animals were similar. Oxamyl was rapidly absorbed, extensively metabolised, and excreted in livestock. The major metabolites found in both lactating goats and laying hens were thiocyanate and radioactivity resulting from incorporation of the radioactivity into natural components (such as lactose). The metabolism of oxamyl proceeded rapidly in livestock animals with the formation of IN-A2213 by hydrolysis of the carbamate moiety. IN-A2213 (or oxamyl) was converted to IN-N0079, which was then degraded to cyanide. Cyanide was rapidly detoxified by the conversion to thiocyanate.

All metabolism studies were conducted using [1-^{14}C]oxamyl. The radiolabel in the 1-position is the most stable in the molecule and is appropriate for metabolism studies.

B.7.2.1 Plants

Plant metabolism studies in potatoes and studies on tobacco, tomatoes, peanuts, apples, and oranges were submitted as part of the EU Dossier in 2001 and included in the first EU approval review. A supplementary report to the 2001 potato metabolism study addressing further characterization efforts on the principal potato foliage metabolite, IN-QKT34, is summarized below. In addition, a new tomato metabolism study conducted to provide additional details on the nature of residues in fruits and fruiting vegetables following drip irrigation and foliar application is also summarized.

Study submitted in the EU Dossier in 2001 and included in the first EU approval review.

B.7.2.1/01

Reference: --	**Report:**	Harvey, J. (1973a); Metabolism and biodegradation of oxamyl **DuPont Report No.:** O/ME 4 **Guidelines:** Not given

1. Test material: [^{14}C]oxamyl
   Lot/Batch #: Not given
   Purity: Radiochemical purity - 99.5%

Materials and methods:

Samples of three soil types (fine sand soil, silt loam and sandy loam) were placed separately in 250 mL flasks. A stock solution of oxamyl in water was mixed into each soil to provide a concentration of 10 mg a.s./kg soil and the moisture was adjusted to 65% field capacity. All flasks were stoppered with foam bungs and incubated at 27°C. Soil microbial populations (fungi and bacteria) were determined at 1, 2, 4 and 8 weeks after treatment, using dilution plates.

A separate set of replicate 500 mL flasks containing soil (moisture content: 65% field capacity) treated with Oxamyl (10 mg a.s./kg soil) was set up to assess the effect of oxamyl on total microbial activity in the soil. The flasks were sealed and incubated at 27°C. Evolution of CO_2 was measured over an incubation period of nine weeks.

Findings:

Dilution plate study results presented in Table 4 show that oxamyl had no effect on populations of fungi or bacteria in any of the three soil types studied. There was an initial increase in fungal and bacterial populations compared to the control in the fine sand and silt loam soils treated with Oxamyl; this difference disappeared within two weeks after treatment. Soil microbial respiration was determined by soil CO2 evolution studies. These data are presented in Table 5 and show that soil microbial activity was unaffected by the presence of oxamyl.

Table 4 Effect of Oxamyl on soil microbial populations

	Micro-organisms per gram of soil [1]

Treatment	Fungi x 10^4				Bacteria x 10^6			
	Week 1	Week 2	Week 4	Week 8	Week 1	Week 2	Week 4	Week 8
Untreated control								
Fine sand soil	2.5	10.0	4.1	1.8	2.9	5.2	1.1	1.1
Silt loam soil	1.5	7.8	5.1	1.7	5.5	12.7	5.7	2.4
Sandy loam soil	0.9	4.4	3.0	1.5	3.3	3.0	0.9	0.8
Oxamyl treated[2]								
Fine sand soil	6.4	9.2	3.4	2.7	4.4	4.3	0.7	1.8
Silt loam soil	4.2	8.0	2.5	1.7	13.0	13.8	5.8	3.2
Sandy loam soil	0.9	4.5	2.4	1.7	1.9	3.3	1.1	0.8

[1] Fungi were isolated on peptone-dextrose rose bengal agar from 1/1000 dilutions; bacteria were isolated from 1/100 000 dilutions of Thornton's medium.
[2] Treatment rate 10 mg a.s./kg soil

Table 5 Effect of Oxamyl on production of CO_2 by soil micro-organisms

Treatment	CO_2 produced per 100 g soil (mg)				
	Week 1	Week 2	Week 4	Week 8[2]	Week 9
Untreated control					
Fine sand soil	24	44	79	134	385
Silt loam soil	29	47	74	121	347
Sandy loam soil	6	12	20	38	272
Oxamyl treated[1]					
Fine sand soil	23	41	73	124	367
Silt loam soil	29	46	72	118	343
Sandy loam soil	6	11	20	37	281

[1] Treated at a rate of 10 mg Oxamyl/kg soil
[2] Nutrients added after 8 weeks of incubation

The metabolism, distribution and expression of residues study O/ME 4, originally submitted under EU Rev8 Points IIA 6.1.2 and IIA 6.1.3 and conducted with test material [^{14}C]oxamyl. Guideline was not given. A review of this study indicates that it does not meet the current guideline (OECD Test Guideline 501: Metabolism in Crops). The study predates EU/EPA guidelines, and the required level of analytical details is not provided; however, the study provides supplemental information supporting the overall metabolism of oxamyl in plants.

RMS comments and conclusion: The study was evaluated during the first inclusion in Annex I of Directive 91/414/EEC. The conclusion was that "the study can be only used as supporting information and cannot be used as a primary source of metabolic data".

Study submitted in the EU Dossier in 2001 and included in the first EU approval review.

B.7.2.1/02

Reference: --	**Report:**	Han, J.C.-Y., Harvey, J. (1975); Additional studies of oxamyl in plants - characterization of ^{14}C-harvest residues in potato tubers

		DuPont Report No.: O/ME 8-75 **Guidelines:** Not given

1. Test material: [^{14}C]oxamyl
   Lot/Batch #: Not given
   Purity: Not given

The plants study O/ME 8-75, originally submitted under EU Rev8 Point IIA 6.1.1 and conducted with test material [^{14}C]oxamyl. Guideline was not given. A review of this study indicates that it does not meet the current guideline (OECD Test Guideline 501: Metabolism in Crops). The study predates EU/EPA guidelines, and the required level of analytical details is not provided; however, the study provides supplemental information supporting the overall metabolism of oxamyl in plants.

RMS comments and conclusion: The study was evaluated during the first inclusion in Annex I of Directive 91/414/EEC. The conclusion was that "the study can be only used as supporting information and cannot be used as a primary source of metabolic data".

Study submitted in the EU Dossier in 2001 and included in the first EU approval review.

B.7.2.1/03

Reference: --	**Report:**	Brown, A.M., Young, G.A., Swain, R.S. (2001); Metabolism of ^{14}C-oxamyl in potatoes **DuPont Report No.:** DuPont-4520 **Guidelines:** OPPTS 860.1300 (1996)

1. Test material: [^{14}C]oxamyl
   Lot/Batch #: 3410-085
   Purity: Radiochemical purity - >95%

Study submitted in the EU Dossier in 2003 and included in the first EU approval review.

B.7.2.1/04

Reference: --	**Report:**	Brown, A.M., Young, G.A., Swain, R.S. (2002); Metabolism of ^{14}C-oxamyl in potatoes **DuPont Report No.:** DuPont-4520, Supplement No. 1 **Guidelines:** OPPTS 860.1300 (1996)

1. Test material: [^{14}C]oxamyl
   Lot/Batch #: 3410-085
   Purity: Radiochemical purity - >95%

Study details:

The study was carried out by applying oxamyl at a rate equivalent to 8 kg as/ha to potatoes grown in plastic plots [49 mg of Oxamyl was added to each pot]. The application was made using an aqueous solution of oxamyl. The recommended GAP for the application of oxamyl to potatoes involves an application of between 4 and 5.5 kg as/ha so the current study is using an application rate of approximately 1.5N. The crop was harvested at 127 d post planting (4th of Jan 2001) and analysis was completed within 7 months of sampling. (31st of July 2001).

Distribution of ^{14}C:

The sampled crop was divided into foliage, potato peels and peeled potatoes and the total ^{14}C was determined in each fraction. The results are presented in Table 6 below.

Table 6 Total Radioactive Residues (TRR) present in potato tubers and foliage following the application of ^{14}C Oxamyl at a rate equivalent to 8.0 kg as/ha

Matrix.	**TRR present in mg/kg.**
Potato tubers (calculated)	0.81 mg/kg.
Potato peels.	1.11 mg/kg.
Potatoes, peeled.	0.86 mg/kg
Potato foliage.	1.51 mg/kg.
Note: The TRR in whole potatoes was calculated by combining the results from the potato peels and peeled potatoes.	

Characterisation and Identification of the residue components:

The EU guidelines require that all residue components which are present at a concentration greater than 0.05 mg/kg or 10% of the residue should be identified and all residues present in the range 0.01 to 0.05 mg/kg should be characterised.

Extractability of residues:

The potato samples were divided into potato peels, peeled potatoes and potato foliage. These three matrices were successively extracted by using
methanol
methanol:water(50:50) and in the case of the potato tubers and peels water.

The majority of the TRR was extracted into the methanol and methanol/water solutions (circa 90% for the potato tubers and at 78% for the potato foliage). The combined extracts were concentrated to the aqueous phase and the TRR residue was partitioned between ethyl acetate and water. This partitioning results in less than 0.5% of the ^{14}C partitioning into the organic (ethyl acetate) phase for potato tubers/ peels while 7.5% of the foliage ^{14}C transfers into the organic phase. In the course of this partitioning exercise between 10 and 20% of the TRR

is lost due to the formation of emulsions and precipitates. The emulsions and precipitates were not analysed to confirm this proposition.

The data confirms that residues resulting from the use of oxamyl are highly polar but are readily extractable, in the case of potato tubers, into methanol and methanol/water solutions. The 10% TRR residue in potato tubers which is not extractable is tightly bound in that only 3- 4% of the residue is released following acid/basic and enzymatic hydrolysis. The distribution of TRR residues following the different extraction and characterising procedures is presented in Table 7 below.

Table 7 Total radioactive residues in different potato matrices.

Potato Peels.			**Characterization and identification of residues.**		
Fraction	**%TRR**	**Residue (mg/kg).**	**Analyte**	**%TRR**	**Residue (mg/kg)**
Aqueous organic (MeOH/H2O) extract.	90.7	1.01	Polar(s) (at Rt = 2.8 min.) IN-D2708 (at Rt= 5.4 min.) Unknown (at Rt= 21.2 min.) Unknown (at	6.2 68.1 4.4 2.0 7.4	0.07 0.76 0.05 0.02 0.08
Organic	0.3	<0.01	Not quantitated due to the low levels present. No oxamyl or oxime detected.		
Aqueous	80.1	0.89	It was stated that the chromatographic profile was similar to that of the organic/aqueous extract.		
Total extractable	90.7	1.01			
Insoluble (non extractable	9.3	0.1			
Residues released by hydrolysis.	3.7	0.04	The bound residue was subjected to enzyme(cellusase), alkali (0.1N NaOH) and acid (1N HCl) hydrolysis.		
Residues bound following	5.6	0.06	The extracted sample was subjected to total ^{14}C analysis.		
Total residues.	100	1.11			
Peeled potato.			**Characterisation and identification of residues.**		
Fraction	**%TRR**	**Residue (mg/kg).**	**Analyte**	**%TRR**	**Residue (mg/kg)**
Aqueous organic (MeOH/H2O) extract.	91	0.79	Polar(s) (at Rt = 2.8 min.) Polar(s) (at Rt= 3.2 min.) IN-D2708 (at Rt= 5.8 min.)	4.0 2.1 70.8 8.2	0.03 0.02 0.61 0.07
Organic	0.5	<0.01	Not quantitated due to the low levels present. No oxamyl or oxime detected.		
Aqueous	75.6	0.65	It was stated that the chromatographic profile was similar to that of the organic/aqueous extract.		
Total extractable	91	0.79			
Insoluble (non extractable	9.0	0.08			
Residues released by hydrolysis.	3.0	0.03	The bound residue was subjected to enzyme(cellusase), alkali (0.1N NaOH) and acid (1N HCl) hydrolysis.		
Residues bound following	6.0	0.05	The extracted sample was subjected to total ^{14}C analysis.		
Total residues.	100	0.86			
Potato foliage.			**Characterisation and identification of residues.**		
Fraction	**%TRR**	**Residue (mg/kg).**	**Analyte**	**%TRR**	**Residue (mg/kg)**

Aqueous organic (MeOH/H2O) extract.	78.3	1.18	Polar(s) (at Rt = 3.25 min.) IN-D2708 (at Rt= 4.9 min.) Unknown (at Rt= 6.2 min.) Unknown (at Rt= 7.6 min) Unknown (at Rt= 20.2 min). Unknown (at Rt= 21.2 min) IN-A2213(Oxime) (at Rt=22.3min) Unknown (at	13.4 1.9 1.1 1.1 45.7 1.2 5.9 1.9 1.1 1.7	0.2 0.03 0.02 0.02 0.69 0.02 0.09 0.03 0.02 0.02
Organic	7.3	0.11			
Aqueous	49.6	0.75			
Total extractable	78.3	1.18			
Insoluble (non extractable	21.7	0.33			
Residues released by hydrolysis.	--	---	The bound residue was not subjected to hydrolysis.		
Total residues.	100	1.51			
Note: ^{14}C residue levels for unidentified fractions of the residue are presented as Oxamyl equivalents.					

Characterisation and identification of the ^{14}C residue in potatoes.

^{14}C residues were readily extracted from the potato tubers/peels using methanol and methanol/water extraction solutions.

The residue profile in both the peeled potatoes and in potato peels were very similar while the profile in the potato foliage was significantly different.

In potato tubers (peels and peeled)

- there was one major constituent residue present at circa 70% of the TRR. This residue was identified as the metabolite IN-D2708. IN-D2708 was identified by HPLC, TLC, co-chromatography with a reference standard and by methylation and re-analysis of the resultant derivative molecule.

- The remaining ^{14}C residues present in potato tubers were not identified. These residues were separated by HPLC and by TLC and were all present at a concentration less than 0.1 mg/kg Oxamyl equivalents.

- No residues of oxamyl or its oxime were detected in potato tubers.

- Of the ^{14}C residue which remained following methanol/water extraction, circa 10% of TRR, was very tightly bound as only 3-4% was released when it was subjected to hydrolysis both enzymatic and chemical.

In potato foliage the metabolic profile differs from that in potato tubers. The composition, number and range of metabolites is different to that in tubers and the main metabolite in potato tubers is at an insignificant level in the foliage.

- Residues of oxamyl (0.02 mg/kg) and its oxime (0.09 mg/kg) are present in potato foliage following treatment of soil with oxamyl at a rate of 8 kg as/ha. This is in contrast to the situation with tubers where these residues are not present.

- The main metabolite found in potato foliage, at 46% of the TRR, was characterised but no attempt was made to identify the molecule as part of the present study. In a subsequent supplementary study a significant effort was made to identify this molecule. The residue was analysed using HPLC, TLC, LC-MS and H-NMR with a view to determining its structure. It was predicted that the molecule was the glucoside derivative of oxamyl-oxime (IN-A2213) and much of the chromatographic and spectrophotometric data supported this view. In contrast to the conclusion of the supplementary study it is considered that this residue was not definitively shown to be the glucoside derivative of the oxime and that further data would need to be provided to demonstrate this fact. The fact that it was not possible to hydrolyse the molecule into its constituent parts and that the glucoside derivative was not synthesised did not assist the process for the identification of this metabolite. Apart from one further chromatographic fraction, close to the solvent front, and corresponding to 0.2 mg/kg of TRR the remaining unidentified foliage residue components, separated as part of the HPLC analysis, are present at a level less than 0.03 mg/kg of TRR.

- It is recognised that potato foliage is not used for either human food or as an animal feed so the composition of the residue present in the foliage is not critical from a residue definition point of view. The information obtained is useful for comparative purposes when assessing the metabolism of oxamyl in other crops following a different method of application.

Conclusion:

This study shows that following the use of oxamyl on potatoes as a granular application the only detectable residue present in potato tubers is the metabolite IN-D2708. Residues of oxamyl and oxamyl oxime are not present in potato tubers even when the application is made at 1.5N the recommended GAP.

The main identified component of the residue found in potato tubers and peels was the metabolite IN-D2708. This metabolite corresponded to circa 70% of the TRR and is the only metabolite present in potatoes following the application of oxamyl to soil.

The metabolite IN-D2708 should have none of the toxicological properties which one would associates with oxamyl as the carbamate fraction of the molecule is not present.

The plant metabolism study DuPont-4520, originally submitted under EU Rev8 Point IIA 6.1.1 and conducted with test material [^{14}C]oxamyl, was conducted under guideline OPPTS 860.1300 (1996). A review of this study indicates that it fully meets the current guideline (OECD Test Guideline 501: Metabolism in Crops).

The plants study DuPont-4520, Supplement No. 1, originally submitted under EU Rev8 Point IIA 6.1.1 and conducted with test material [^{14}C]oxamyl, was conducted under guideline OPPTS 860.1300 (1996). A review of this study indicates that it partially meets the current guideline (OECD Test Guideline 501: Metabolism in Crops). DuPont-4520, Supplement No. 1 addresses further characterization of potato foliage (non-RAC) residues. However, when submitted in conjunction with DuPont-4520 and DuPont 4520, Supplement No. 2, it adequately completes the understanding of oxamyl metabolism in potato plants.

RMS comments and conclusion: The study with its supplements No.1 and No.2 can be considered useful for the understanding of oxamyl metabolism in potato plants**.**

Study submitted in the EU Dossier in 2001 and included in the first EU approval review.

B.7.2.1/05

Reference:	**Report:**	Harvey, J. (1973b); Additional studies on the metabolism and biodegradation of oxamyl in plants - Period: May 1, 1973 to October 1, 1973
--		

		DuPont Report No.: O/ME 5 **Guidelines:** Not given

The plants study O/ME 5, originally submitted under EU Rev8 Points IIA 6.1.2 and IIA 6.1.3 and conducted with test material [^{14}C]oxamyl. Guideline was not given. A review of this study indicates that it does not meet the current guideline (OECD Test Guideline 501: Metabolism in Crops). The study predates EU/EPA guidelines, and the required level of analytical details is not provided; however, the study provides supplemental information supporting the overall metabolism of oxamyl in plants.

1. Test material: [^{14}C]oxamyl
   Lot/Batch #: Not given
   Purity: Not given

Conclusion (DAR 2003): This supplementary study was carried out to further identify the composition of the 14C residue present in treated peanut and tobacco plants.
The report presents facts and conclusions. It includes, however, the minimum of back-up supporting technical information and this absence of information from the study makes it difficult for the reviewer to assess the conclusions reached.
The study indicates that methanol is a very efficient solvent for the extraction of 14C containing residues from the treated plants.
The study indicates that, in peanut plants 4 weeks after treatment, the main 14C residue present is polar in nature. Two metabolites, metabolite A and metabolite A1, were isolated from this polar extract. Metabolite A was already identified as the glucose conjugate of Oxamyl-oxime. In this study metabolite A1 was a tentatively identified as being the glucose conjugate of the demethylated Oxamyl-oxime. Metabolite A1 is present at twice the level of Metabolite A in this extract fraction.
57% of the 14C present in peanut hay, which was treated twice, harvested from the mature crop was methanol extractable. Metabolites A and A' were not present in peanut hay in the harvested crop. Converting the methanol extract into its acetyl or methoxy derivatives enabled the extract to be solubilised in chloroform. Liquid chromatography and mass spectral analysis of the derivatised chloroform soluble extract indicated the presence of one compound which was designated as metabolite A11. The identity of this metabolite was not established in the present study but it was proposed that metabolite A11 was the glucose conjugate of the fully demethylated Oxamyl-oxime.

RMS comments and conclusion: The study was evaluated during the first inclusion in Annex I of Directive 91/414/EEC. The conclusion was that "the study can be only used as supporting information and cannot be used as a primary source of metabolic data".

Study submitted in the EU Dossier in 2001 and included in the first EU approval review.

B.7.2.1/06

Reference: --	**Report:**	Harvey, J. (1974); Additional studies on the metabolism of oxamyl in plants - I: Characterization of harvest residues in peanuts, apples and oranges (supplement 1) **DuPont Report No.:** O/ME 5, Supplement No. 1 **Guidelines:** Not given

1. Test material: [^{14}C]oxamyl

Lot/Batch #:	Not given
Purity:	Not given

The plants study O/ME 5, Supplement No. 1, originally submitted under EU Rev8 Points IIA 6.1.2, IIA 6.1.5, and IIA 6.1.6 and conducted with test material [^{14}C]oxamyl. Guideline was not given. A review of this study indicates it does not meet the current guideline (OECD Test Guideline 501: Metabolism in Crops). The study predates EU/EPA guidelines, and the required level of analytical details is not provided; however, the study provides supplemental information supporting the overall metabolism of oxamyl in plants.

Conclusion (DAR 2003): This report provides some new information with respect to the metabolism of oxamyl in apples and in oranges and details the work carried out to determine the composition of the 14C present in oxamyl treated peanut plants.
In mature peanut hay, following treatment with oxamyl, some of the 14C is present as Metabolite A11 (5% of TRR) and sugar conjugates. Enzyme hydrolysis using □-glucosidase released Metabolites A and A1.
Peanuts from Oxamyl treated plants contain low 14C residues at circa 1 mg/kg. 45% of this residue is non polar in nature while circa 35% of this residue is not solvent extractable. Cellulase hydrolysis releases 60% of this bound residue. None of the residues were identified.
Apples retained little surface residue 47 days following their treatment with oxamyl. The majority of the residue was present in the peeled apples of which 77% of TRR was soluble in ethyl acetate and consisted of oxamyl (16%) , Oxamyl-oxime (42%) and the DMCF (17%). 23% of the 14C present in apples was methanol extractable but was not soluble in ethyl acetate. 35% of this polar fraction was hydrolysed by □-glucosidase and corresponded to Metabolite A.
Oranges, when treated with 14C labelled oxamyl, retained 82% of the TRR in the rind. 96% of this 14C was methanol extractable and 34% was ethyl acetate soluble. The ethyl acetate fraction consisted of 9% parent oxamyl, 4% of its oxime and 29% of DMCF. Oxamyl (20%) is degraded to DMCF when it is exposed to freshly macerated orange rind for 15 minutes.
As in previous metabolism reports presented by the notifier, which were based on studies carried out in the early 1970's, conclusions are presented and a minimum of back-up supporting technical and analytical data is provided to substantiate the conclusions reached. This study is again considered to be supporting and is not considered to be a primary source of metabolism data

RMS comments and conclusion: The study was evaluated during the first inclusion in Annex I of Directive 91/414/EEC. The conclusion was that "the study can be only used as supporting information and cannot be used as a primary source of metabolic data".

Study submitted in the EU Dossier in 2001 and included in the first EU approval review.

B.7.2.1/07

Reference:	**Report:**	
--		Harvey, J. (1975); Additional studies on the metabolism of oxamyl in plants - II: Characterization of harvest residues - A: The polar fraction in oranges - period October 1, 1974 to June 1, 1975 **DuPont Report No.:** O/ME 5, Supplement No. 2 **Guidelines:** Not given

1. Test material: [^{14}C]oxamyl
   Lot/Batch #: Not given
   Purity: Not given

The plants study O/ME 5, Supplement No. 2, originally submitted under EU Rev8 Point IIA 6.1.5 and conducted with test material [^{14}C]oxamyl. Guideline was not given. A review of this study indicates that it does not meet the current guideline (OECD Test Guideline 501: Metabolism in Crops). The study predates EU/EPA guidelines, and the required level of analytical details is not provided; however, the study provides supplemental information supporting the overall metabolism of oxamyl in plants.

Conclusion (DAR 2003): This report is a follow on to an earlier study reported in section B.7.1.5.above. The additional information provided by this study shows that following the foliar application of Oxamyl to oranges the polar fraction of the 14C residue, part of the methanol extract, contains metabolites A and A1 in approximately equal amounts. The presentation of this report is similar to the other 1970's metabolism studies reported in that the results are presented but insufficient technical data and information is provided to allow the evaluator to fully assess the conclusions reached.

RMS comments and conclusion: The study was evaluated during the first inclusion in Annex I of Directive 91/414/EEC. The conclusion was that "the study can be only used as supporting information and cannot be used as a primary source of metabolic data".

Study submitted to the EU for the first time in this submission.

B.7.2.1/08

Reference: **CA 6.2.1/01**	**Report:**	Brown, A.M., McMillan, J.A., Young, G.A., Pierce, D., Schrass, K.H. (2008); Metabolism of ^{14}C-oxamyl in potatoes **DuPont Report No.:** DuPont-4520, Supplement No. 2 **Guidelines:** OPPTS 860.1300 (1996) **Deviations:** None **Testing Facility:** DuPont Stine-Haskell Research Center, Newark, Delaware, USA Testing Facility Report No.: DuPont-4520, Supplement No. 2 **GLP:** Yes **Certifying Authority:** Laboratories in the USA are not certified by any government agency, but are subject to regular inspections.

I. MATERIALS AND METHODS

The purpose of this supplementary study was to more fully define the nature of the major ^{14}C-oxamyl derived residues in foliage of potato plants grown in soil treated (at planting) with ^{14}C-oxamyl. Extracts used for this supplementary study were obtained from the main potato study (DuPont 4520, cited above).

In the main study, seed potatoes (cv. Red Pontiac) were treated with a single soil application (at planting) of a solution of ^{14}C-oxamyl (9.75 µCi/mg; 0.36 MBq/mg; >95% radiochemical purity) containing inert ingredients to simulate a Vydate 10L formulation at a rate of 8 kg as/ha (49 mg/pot). The pots were maintained in a greenhouse throughout the duration of the in-life portion of the study. Mature tubers and foliage were harvested 127 days after treatment. Foliage, which is not a food or feed item, was extracted to more fully elucidate the metabolic pathway in the potato plant. Total radioactive residues (TRR, combustion analysis) in treated foliage was 1.25 mg oxamyl equivalents/kg. The homogenized potato foliage was extracted with methanol and 50% aqueous methanol. The extracts were pooled and the radioactivity quantified by LSC. The major potato foliage metabolite (45.7% TRR, 0.69 mg/kg oxamyl equivalents) was tentatively characterized as IN-A2213 glucoside.

DuPont-4520, Supplement No. 1 described initial isolation, purification, and characterization efforts to support the proposed glucoside structure. DuPont-4520, Supplement No. 2 (this study) provides more definitive evidence to confirm the oxamyl oxime glucoside structure by comparison of the chromatographic, spectral and chemical behavior of the *in-plant* glucoside with that of an authentic reference standard (IN-QKT34).

Isolation of Major Foliage Metabolite: Additional quantities of IN-A2213 glucoside were extracted and isolated from potato foliage using procedures similar to those described in DuPont-4520, Supplement No. 1. Homogenized foliage was allowed to thaw, extracted, and the component of interest isolated. The aqueous (water containing 0.1% formic acid) methanol extracts (from 240 g of potato foliage) were concentrated to all aqueous and partitioned with ethyl acetate. The aqueous phase was taken to dryness, the residue dissolved in 0.1% formic acid:acetonitrile then subjected to C18 and Oasis HLB® (Waters Corp., Milford, MA) solid phase extraction (SPE; eluted with various concentrations of water containing 0.1% formic acid/ acetonitrile) followed by repetitive HPLC (Phenomenex Aqua C18 column held at 40°C using mobile phase gradients composed of water and acetonitrile containing 0.1% formic acid) with fraction collection. Fractions (R_T 15-32 min from twelve consecutive HPLC runs) containing the component of interest were combined and further purified by Oasis HLB® SPE (washed with varying concentrations of 0.1% formic acid/ acetonitrile then eluted with methanol). The concentrated methanol eluate was reconstituted in 0.1% formic acid and chromatographed repetitively. The component of interest was manually collected from successive HPLC runs using Hamilton PRP-1, Zorbax SB Phenyl and Shandon Hypercarb columns and mobile phase gradients composed of acetonitrile and water (or 0.1% formic acid) at 40°C and a flow rate of 1 mL/min.

Enzymatic Hydrolysis: Aliquots of the IN-A2213 glucoside isolate and the authentic IN-A2213 glucoside reference standard (IN-QKT34) were separately subjected to enzyme hydrolysis using β-glucosidase (Sigma Chemical Company, St. Louis, MO, G0395, Lot No. 119H4029) and α-glucosidase (Sigma Chemical Company, St. Louis, MO, G5003, Lot No. 081K7415) in buffer (buffered at pH 5 for β-glucosidase and at pH 6.8 for α-glucosidase) at 37°C for ca. 24 hours. After incubation, each sample was centrifuged, filtered, and analyzed by HPLC to qualitatively determine the nature of radioactivity after enzymatic digestion.

Acid Hydrolysis: Aliquots of the IN-A2213 glucoside isolate and IN-QKT34 were separately subjected to acid hydrolysis in 1N HCl at 60°C for *ca.* 18 hours. After incubation, each sample was neutralized with 1N NaOH, centrifuged, filtered, and analyzed by HPLC to qualitatively determine the nature of radioactivity after acid digestion.

LC-MS Analysis: Mass spectral data for IN-A2213, IN-QKT34, and the glucoside isolate were obtained in the positive ion mode with alternate full (90-800) and dependent LC-MS/MS scans of the protonated ion of interest [M+H]+. LC-MS was performed on a Hewlett-Packard 1100 HPLC (Agilent Technologies) coupled to a ThermoFinnigan LCQ Mass Spectrometer (Thermo Finnigan, San Jose, CA) equipped with an ElectroSpray Ionization (ESI) interface. Aliquots of IN-A2213, IN-QKT34, and the glucoside isolate were analysed with Zorbax SB Phenyl, Hamilton PRP-1, or Shandon Hypercarb HPLC columns using mobile phase gradients composed of acetonitrile and water (or 0.1% formic acid) at a flow rate of 1 mL/min. The column eluate was split using a mixing T prior to the mass spectrometer/radiochemical detector at an approximate 2:1 ratio. Radiochemical detection was performed using a Ramona 92 Radiochemical Flow Detector (Raytest USA, Inc., Wilmington, NC) equipped with a 200-µL solid cell or a Ramona Classic Radiochemical Flow equipped with a 300-µL liquid cell. UV and radiochromatograms were acquired with HPLC 3D ChemStation® software Version 10.02 (Agilent Technologies). Mass spectral data were acquired with LTQ software Xcalibur™ Version 1.4 (ThermoElectron).

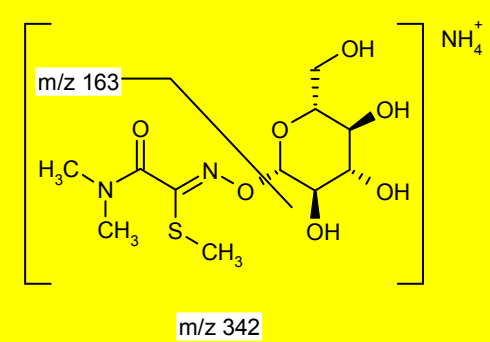
^{1}H-NMR: Proton NMR analysis of IN-QKT34 and the glucoside isolate were acquired on a Bruker Avance 600 MHz digital NMR spectrometer equipped with a 5 mm CP TCI 600S3 H-C/N-D-05 Z probe. Bruker TopSpin 1.3 Software was used for data acquisition and processing of proton 1D and 2D gradient COSY (COrrelation SpectroscopY) NMR spectra. TopSpin 2.1 software was used for 1D TOCSY (TOtal Correlation SpectroscopY) data acquisition and processing.

II. FINDINGS

Potato foliage from the original potato metabolism study was extracted and the *in-plant* glucoside isolated following a series of repetitive SPE and HPLC procedures. Aliquots of the glucoside isolate and the authentic IN-A2213 glucoside reference standard (IN-QKT34) were subjected to enzyme (α- and β-glucosidase) and acid (1N HCl) digestions. Comparisons of chromatographic and spectral (LC-MS and NMR) characteristics of the glucoside isolate and IN-QKT34 were conducted under identical experimental conditions. The HPLC chromatographic profile of each analyte remained essentially unchanged following enzyme and acid digestion with the exception of the ß-glucosidase/glucoside isolate digestion in which low levels of IN-A2213 were detected. These results indicate that neither IN-QKT34 nor the *in-plant* glucoside are cleaved to any significant extent under typical hydrolysis conditions.

ESI LC-MS (and LC-MS/MS) analyses of the glucoside isolate and IN-QKT34 reference standard were conducted under identical conditions. The full scan ESI spectrum of IN-QKT34 contained protonated ions at m/z 325 [M+H+], the ammonia adduct at m/z 342 ([M+NH_4]+), and a fragment at m/z 163 (consistent with a loss of glucose, Figure 1. The LC-MS and MS/MS of the potato foliage isolate were consistent with that of the authentic standard.

Figure 1 LC-MS fragmentation of IN-QKT34



One-dimensional 1H-NMR analysis of the glucose isolate and IN-QKT34 were conducted in D_2O. While sample impurities were present in the NMR of the isolate, overall the proton NMR spectrum of the isolate was consistent with that of IN-QKT34. IN-QKT34 proton assignments were confirmed by 2D gradient COSY and 1D TOCSY NMR experiments.

III. CONCLUSION

IN-QKT34, the glucose conjugate of IN-A2213, was synthesized and its structure confirmed by NMR and mass spectrometry. The chemical structure of the major metabolite isolated from ^{14}C-oxamyl treated potato foliage was confirmed by LC-MS/MS and NMR spectroscopy to be consistent with the standard IN-QKT34. The isolate and IN-QKT34 also demonstrated consistent chemical behavior under hydrolytic conditions. Neither IN-QKT34 nor the *in-plant* glucoside were cleaved to any significant extent after 18 hours digestion with enzymes (α- and β-glucosidase) and acid (1N HCl, 60°C).

(Brown, A.M., McMillan, J.A., Young, G.A., Pierce, D., Schrass, K.H., 2008)

RMS comments and conclusion: The study has been submitted for this renewal. It is appropriate for the purpose. The study gives the information on the major metaboliteIN-A2213 glucoside, as major metabolite in potato foliage, isolated and confirmed by LC/MS/MS and NMR spectroscopy.

Study submitted to the EU for the first time in this submission.

B.7.2.1/09

Reference: CA 6.2.1/02	**Report:**	Chapleo, S., Johnson, J. (2014); The metabolism of ^{14}C-oxamyl in tomato plants **DuPont Report No.:** DuPont-32188 **Guidelines:** OECD 501 (2007), OPPTS 860.1300 (1996), EC 1607/VI/97 Rev 2 (1999), 12 NohSan No. 8147 (2000), OECD 64 (2006), OECD 32 (2006) **Deviations:** None **Testing Facility:** Charles River Laboratories (UK), Tranent, Scotland, UK Testing Facility Report No.: 809961 **GLP:** Yes **Certifying Authority:** Department of Health (U.K.)

Executive summary:

The purpose of this study was to examine the metabolic fate of oxamyl in tomato plants.

Tomato plants (*cv.* Red Alert) were grown in a glasshouse at Charles River Laboratories and treated with [1-^{14}C]oxamyl, formulated with inert formulation ingredients to simulate Oxamyl 10SL, a 100 g/L aqueous formulation. Two application regimes were investigated: (a) multiple foliar applications and (b) multiple soil applications. The specific activities of the applied [^{14}C]oxamyl were 381.9 Bq/µg (10.3 µCi/mg) and 843.6 Bq/µg (22.8 µCi/mg) for the foliar and soil treatments, respectively. Total applications of 5 kg a.s./ha were made to separate groups of plants for each treatment regime. The first application was immediately after transplant at a target application of 2000 g a.s./ha for both treatment regimes. Three subsequent applications for both the foliar and soil experiments were carried out 14 days apart to achieve a 21 day pre harvest interval (PHI); the target rate for each application was 1000 g a.s./ha.

Immature fruit and foliage were sampled at 14DAT3 (14 days after treatment 3; immediately prior to the fourth application; BBCH 74). Ripe fruit and foliage were sampled at 7DAT4 (BBCH 81), 14DAT4 (soil application only; BBCH 81), and 21DAT4 (final harvest, BBCH 89). Samples which received the foliar treatment were surface rinsed in water and the rinsates retained for analysis.

Samples were milled and total radioactive residues (TRRs) determined by oxidative combustion prior to liquid scintillation counting (LSC). Portions of milled tissue were initially extracted with methanol, methanol: water (1:1, v/v), and water in succession. The remaining post extraction solids (PES) from 21DAT4 fruit and foliage were extracted sequentially with water, α-amylase, combined amyloglucosidase and cellulase, 0.1N NaOH (60°C), and 1N HCl (60°C). The surface washes and extracts containing significant radioactivity (≥0.01 mg/kg) were analysed by high performance liquid chromatography (HPLC) and characterisation of ^{14}C residues was accomplished by HPLC retention time comparison with that of the synthetic standards.

Foliar Application Regime: Fruit

TRRs in fruit at 7DAT4 and 21DAT4 were 0.72 and 0.99 mg/kg, respectively. The majority of the radioactivity (≥92.0% TRR) was extracted by surface washing and initial extraction with aqueous methanol under ambient

conditions. Oxamyl was the principal residue at 7DAT4 accounting for 31.2% TRR (0.223 mg/kg) and decreased to 2.9% TRR (0.027 mg/kg) at 21DAT4. Metabolites included IN-N0079 (9.0–12.5% TRR), IN-A2213 (5.3–9.7% TRR), IN-F3905 (3.5–4.6% TRR), IN-QKT34 (4.5–7.7% TRR) and unidentified components including a region of polar radioactivity (detected in the main HPLC system used for quantification; 31.7–52.4% TRR). The region of polar radioactivity isolated from the 21DAT4 sample was comprised of IN-D2708 (20.8% TRR), IN-KP532 (3.9% TRR), IN-KV998/IN-T2921 (unresolved; 0.7% TRR), and at least five other polar components (individually ≤8.8% TRR).

Exhaustive extraction of the post extraction solids (PES) from the 21DAT4 sample released an additional 5.2% TRR; the combined aqueous and enzyme extracts contained three unidentified polar metabolites (individually ≤3.0% TRR). Terminal unextracted residues in 21DAT4 fruit accounted for 2.8% TRR.

TLC analyses demonstrated possible low levels (<1.9% TRR) of glucose at 14DAT3, suggesting natural incorporation of the ^{14}C-label. Other components identified in the immature fruit included oxamyl (36.4% TRR, 0.523 mg/kg), IN-N0079, IN-QKT34, IN-A2213, and IN-F3905; each ≤7.9% TRR. The polar components in 14DAT3 fruit accounted for 35.2% TRR.

Foliar Application Regime: Foliage

TRRs in foliage at 7 and 21 DAT4 were 9.88 and 39.89 mg/kg, respectively. The majority of the radioactivity (≥96.8% TRR) was extracted by surface washing and initial extraction with aqueous methanol under ambient conditions. Oxamyl was the principal component (73.1–78.4% TRR, 7.219–31.297 mg/kg). Metabolites included IN-QKT34 (10.6–12.6% TRR), IN-N0079 (1.5–3.9% TRR), IN-A2213 (2.0–2.2% TRR), IN-L2953 (0.8% TRR), and unidentified metabolites including the polar metabolites (3.8–4.0% TRR) also detected in fruit.

Exhaustive extraction of the PES from the 21DAT4 sample released an additional 2.2% TRR; the combined aqueous and enzyme extracts contained oxamyl (<0.1% TRR, 0.010 mg/kg), IN-A2213, IN-QKT34, IN-N0079, and unidentified metabolites (≤0.3% TRR). Radioactivity in the base and acid extracts was characterised as polar and not extractable into dichloromethane. Terminal unextracted residues accounted for 0.5% TRR.

Soil Application: Fruit

TRRs in fruit at 7, 14, and 21DAT4 were 0.332–0.805 mg/kg. The majority of the radioactivity (≥90.4% TRR) was extracted in aqueous methanol under ambient conditions. Oxamyl was detected only in the 7DAT4 fruit (5.9% TRR, 0.047 mg/kg). Metabolites included IN-A2213 (8.4–11.0% TRR), IN-QKT34 (4.8–10.7% TRR), IN-F3905 (2.2–7.2% TRR), IN-L2953 (2.9% TRR), IN-N0079 (2.3–21.9% TRR), and unidentified metabolites including the polar components (35.4–60.2% TRR) detected in foliar-treated fruit and foliage. The region of polar radioactivity isolated from the 21DAT4 sample was comprised of IN-D2708 (21.3% TRR), IN-KP532 (5.2% TRR), IN-KV998/INT2921 (unresolved; 0.4% TRR), and at least three other polar components (individually ≤12.4% TRR).

Exhaustive extraction of the PES from the 21DAT4 sample released an additional 6.5% TRR; the combined aqueous and enzyme extracts contained 5 unidentified polar metabolites (0.1–3.7% TRR). Terminal unextracted residues in the 21DAT4 fruit accounted for 3.1% TRR.

Soil Application: Foliage

TRRs in foliage at 7, 14, and 21 DAT4 were 5.45–11.40 mg/kg. The majority of the radioactivity (≥91.5% TRR) was extracted in aqueous methanol under ambient conditions. Oxamyl accounted for 6.3–19.3% TRR (0.730–1.050 mg/kg). IN-QKT34 (35.2–62.6% TRR), IN-F3905 (1.3–3.2% TRR), IN-A2213 (3.8–7.6% TRR), IN-N0079 (2.8–4.4% TRR), IN-L2953 (1.6–3.5% TRR), and the polar unidentified metabolites (12.6–19.8% TRR) present in fruit were detected.

Exhaustive extraction of the PES from the 21DAT4 sample released an additional 6.7% TRR. The combined aqueous and enzyme extracts contained oxamyl (0.1% TRR, 0.018 mg/kg), IN-A2213, IN-QKT34, IN-N0079, and unidentified metabolites (0.9% TRR in total). Radioactivity in the base and acid extracts was characterised as polar and not extractable into dichloromethane. Terminal unextracted residues in 21DAT4 foliage accounted for 1.5% TRR.

Additional Characterisation of Polar Fruit Metabolites

The unidentified polar metabolites in 21DAT4 fruit (both treatment regimes) were characterised after solvent partitioning (aqueous fraction) and isolation to remove apolar components. The polar radioactivity was then subjected to enzyme digestion (β-glucosidase and cellulase), acid and base hydrolysis at elevated temperatures, derivatisation (methylation), and analyzed using various HPLC and TLC systems. The results from enzyme and hydrolytic treatments were inconclusive. HPLC profile changes were noted following enzyme treatment of the aqueous fraction; however, no apparent changes were observed following enzyme digestion, acid or base hydrolyses of a semi-purified polar isolate. Ten regions were evident after derivatisation with BF_3/methanol of which three accounted for 12.0–19.0% TRR and the others accounted for 1.8–7.1% TRR. Attempts to identify the metabolites by LC-MS after derivatization were unsuccessful. Low levels (<1.9% TRR) of ^{14}C glucose were tentatively identified in immature fruit suggesting incorporation of the ^{14}C-label into plant natural products. Comparative chromatography using varied stationary and mobile phases demonstrated that the unidentified fruit components, including the polars, did not co-elute with any available reference standards (IN-A2912, IN-M2583, IN-N2935, IN-SBY69, IN-U1966, IN-U1967, oxalic acid, IN-00699 [oxamide], IN-18474 [oxamic acid], or thiocyanate). Nor did radioactivity correspond to any of the reference standards following enzyme or hydrolytic incubations of polar fractions or isolates. No metabolites containing the intact carbamate moiety were observed.

Route of Metabolism

The route of metabolism in tomato plants was similar following both foliar and soil applications. Oxamyl was hydrolyzed to the-oxime, IN-A2213 (and its isomer IN-F3905), which was metabolized to IN-D2708 and other polar metabolites. IN-A2213 was conjugated with glucose to IN-QKT34 and de-methylated to form IN-L2953. IN-A2213 (or oxamyl) was also metabolized to the nitrile IN-N0079. Hydrolysis of the nitrile moiety of IN-N0079 to the amide yielded IN-T2921 and subsequent hydrolysis of the amide to the carboxylic acid yielded IN-D2708. *N*-Demethylation of IN-T2921 and IN-KV998 gave IN-D2708 and IN-KP532, respectively. The carbamate group was not present in any of the metabolites detected. Metabolism to components characterized as highly polar most likely results from more extensive metabolism of the 3 carbon (IN-KV998 and IN-KP532) or 4 carbon (IN-T2921 and IN-D2708) containing metabolites, or reincorporation into plant natural products of $14CO_2$ derived from soil-mediated mineralisation of oxamyl.

Radiovalidation of the Crop Residue Method for Oxamyl

Fruit and foliage (soil application regime) were extracted using the crop residue method for oxamyl. In 14DAT3 foliage, oxamyl was quantified as 2.2% TRR using the crop residue extraction method and 3.8% TRR using the more exhaustive metabolism method. For 21DAT4 foliage, oxamyl was quantified as 55.0% TRR using the crop residue extraction method and 72.6% TRR using the metabolism method. These values demonstrate that the crop residue extraction method is effective in extracting oxamyl.

I. MATERIALS AND METHODS

A. MATERIALS

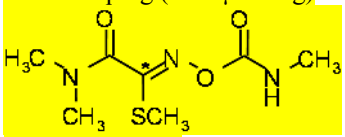
Test material (analytical standard):	Oxamyl analytical standard
Lot/Batch No:	D1410-222
Purity:	99.3%
Description:	Solid, powder
CAS No:	23135-22-0
Stability of test compound:	Stable under conditions of the study
Radiolabelled test material:	[1-^{14}C]Oxamyl
Lot/Batch #	Lot no. 3609149
Radiochemical purity:	99.2%
Specific activity:	0.84 MBq/mg (22.8 µCI/mg)
Chemical structure:	
Soil:	Sandy clay loam

Table 8 Soil physicochemical properties

Soil type	pH (in water)	Organic carbon (%)	CEC (meq/100g)
Sandy clay loam	7.2	2.3	18.6

B. EXPERIMENTAL

The study was conducted during the period 24 May 2011 to 21 October 2014 at Charles River Laboratories, Tranent, Scotland, EH33 2NE.

1. In-Life Phase

The in-life phase was conducted in temperature-controlled glasshouses at Charles River Laboratories, Tranent, EH33 2NE, Scotland. Plants were grown in pots containing John Innes No 1 compost prior to transplant into 10 L plastic containers filled with sandy clay loam soil.

Plants were subject to two separate application regimes: (a) multiple foliar applications and (b) multiple soil applications. Each regime comprised a first application immediately after transplant at 2000 g a.s./ha followed by three further applications 14 days apart at 1000 g a.s./ha to achieve a 21 day pre harvest interval (PHI).

2. Sampling

Fruit and foliage treated with [^{14}C]oxamyl were non-systematically sampled at 14DAT3, 7DAT4, 14DAT4 (soil treatment only), and 21DAT4.

3. Analytical Procedures

All plant samples from the foliar treatment regime were surface washed in water and the rinsates retained for analysis. All crop tissues (washed for the foliar regime) were pulverised in dry ice, which was allowed to sublime in a freezer set to maintain -20°C prior to determination of TRR by combustion analysis followed by liquid scintillation counting (LSC). Portions of samples (TRR >0.01 mg/kg) were

extracted with methanol followed by methanol:water (1:1, v/v) and water. Levels of radioactivity in each extract were determined by LSC. Selected samples (21DAT4) were extracted further with water (overnight), α-amylase (pH 7, 50°C, 2 × 72 h), a mixture of amyloglucosidase and cellulase (pH 5, 50°C, 2 × 48 h), NaOH (0.1N, 60°C, 2 × 6 h), and HCL (1N, 60°C, 2 × 6 h). The unextracted radioactivity in the post-extraction solids was determined by combustion analysis followed by LSC. Extractability was determined for each sample by summing radioactivity in the extracts and unextracted residue.

Extracts were analysed using reversed phase HPLC (Agilent 1100 HPLC); Aqua C18 column eluted with a gradient of water containing 0.1% formic acid, and acetonitrile. The effluent was passed through an on-line UV detector (254 nm) to detect reference standards. Quantification of radioactivity in the column effluent was confirmed by 20 second fraction collection (Gilson 204 fraction collector). HPLC using a Hamilton PRP (mobile phases: water and acetonitrile) and a Thermo Scientific Hypercarb (mobile phases: 0.1% trifluoroacetic acid in water and methanol) were used to confirm the presence of oxamyl, IN-A2213, IN-F3905, IN-QKT34, IN-N0079, and IN-L2953. Data were collected and evaluated using Atlas 2002 R1 or Laura v.4.0.4.101 data handling systems.

Polar radioactivity in 21DAT4 fruit (both regimes) was further characterised by solvent partitioning (aqueous fraction) and isolation (HPLC-fraction collection) to remove apolar components. Polar components were subjected to enzyme digestion (β-glucosidase and cellulase), acid and base hydrolysis at elevated temperatures, derivatisation (methylation), and analyzed using various HPLC and TLC systems to confirm the presence of IN-KP532, IN-D2708, and IN-T2921/IN-KV998 and ^{14}C-glucose.

II. RESULTS AND DISCUSSION

A. TOTAL RADIOACTIVE RESIDUES (TRRs)

Tomatoes were grown from seed in John Innes No 1 compost prior to transplant into a sandy clay loam soil. Tomatoes plants were subject to multiple applications of [^{14}C]oxamyl through foliar or soil application. Samples fruit and foliage were sampled at 14DAT3, 7DAT4, 14DAT4 (soil treatment only), and 21DAT4. Plant tissues were pulverised and extracted. The total radioactive residue (TRR) was determined as the sum of the radioactivity determined in each extract and in the post extraction solids (PES; Table 9).

1. Foliar Application Regime

TRRs in foliar treated fruit ranged from 0.716–1.434 mg/kg with the highest TRRs at 14DAT3. Foliar treated foliage residues were higher than for fruit and ranged from 4.775–39.894 mg/kg, with the highest levels at 21DAT4.

2. Soil Application Regime

TRRs in soil treated fruit ranged from 0.332–0.805 mg/kg with the highest TRRs at 7DAT4. Soil treated foliage residues were higher than the fruit and ranged from 5.451–11.398 mg/kg, with the highest levels at 21DAT4.

Table 9 Total radioactive residues in tomato fruit and foliage following application of [^{14}C]oxamyl

Foliar application: Total radioactive residues (mg/kg)[a]		
Days after treatment	**Fruit**	**Foliage**
14DAT3	1.434	4.775
7DAT4	0.716	9.883
21DAT4	0.990	39.894
Soil application: Total radioactive residues (mg/kg)[a]		
Days after treatment	**Fruit**	**Foliage**
14DAT3	0.721	11.321
7DAT4	0.805	5.451
14DAT4	0.332	7.143
21DAT4	0.655	11.398

[a] TRR values are the sum of extracted + unextracted radioactivity expressed as oxamyl equivalents on a fresh weight basis.

B. EXTRACTION AND CHARACTERISATION OF RESIDUES

The extractability of the ^{14}C residue in tomato plants was determined using methanol followed by methanol:water (1:1 v/v) and 100% water. Selected samples (21DAT4 fruit and foliage) were extracted further with water (overnight), α-amylase (pH 7, 50°C, 2 × 72 h), a mixture of amyloglucosidase and cellulase (pH 5, 50°C, 2 × 48 h), NaOH (0.1M, 60°C, 2 × 6 h), and HCL (1M, 60°C, 2 × 6 h). The unextracted radioactivity in the PES was determined by combustion analysis followed by LSC.

1. Extraction and characterisation of residues in fruit and foliage samples from the foliar application regime

Foliar Application: Fruit

The majority of the radioactivity was recovered in the surface wash and aqueous methanol extracts (≥ 92.0% TRR; Table 10). Oxamyl was the main component in fruit (0.027–0.523 mg/kg, 2.9–36.4% TRR). IN-N0079 (0.088–0.103 mg/kg, 7.2–12.5% TRR), IN-QKT34 (0.033–0.077 mg/kg, 4.5–7.7% TRR), IN-A2213 (0.038–0.096 mg/kg, 5.3–9.7% TRR), and IN-F3905 (0.033–0.114 mg/kg, 3.5-7.9% TRR) were detected in the fruit following a foliar treatment regime.

Table 10 Summary of radioactive residues in tomato fruit following multiple foliar application of [^{14}C]oxamyl

Fruit	14DAT3		7DAT4		21DAT4	
	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg
Identified components[a]						
Oxamyl[b]	36.4	0.523	31.2	0.223	2.9	0.027
IN-N0079	7.2	0.103	12.5	0.090	9.0	0.088
IN-QKT34	3.5	0.050	4.5	0.033	7.7	0.077
IN-A2213	5.7	0.081	5.3	0.038	9.7	0.096
IN-F3905	7.9	0.114	4.6	0.033	3.5	0.035
Analysis of polar isolate						
IN-D2708[c]	Not Conducted				20.8	0.206
IN-KP532[c]					3.9	0.038
IN-KV998/IN-T2921[c]					0.7	0.007
Uncharacterised fractions						
NaOH extract	Not Characterised Further				1.1	0.011
HCl extract					0.3	0.003
Unidentified components						
Number	1	-	3	-	12	-
Highest	35.2	0.504	31.7	0.227	8.8	0.087
Lowest	35.2	0.504	0.8	0.006	0.3	0.003
Unextracted	4.0	0.057	6.2	0.044	2.8	0.028

[a] Sum of components identified in fruit surface washes and tissue extracts
[b] The majority of parent (oxamyl) was found in the surface washes (1.2-35.6%TRR; 0.012-0.511 mg/kg); much lower concentrations were detected in the fruit extracts (0.8-1.7%TRR; 0.012-0.015 mg/kg).
[c] Quantified in 21DAT4 fruit by HPLC (IN-D2708, IN-KP532) and TLC (IN-KV998/ IN-T2921)

Polar metabolites accounted for 31.7–53.5% TRR. A polar isolate from the 21DAT4 sample contained IN-D2708 (0.206 mg/kg, 20.8% TRR), IN-KP532 (0.038 mg/kg, 3.9% TRR), unresolved IN-KV998/IN-T2921 (0.007 mg/kg, 0.7% TRR), and at least five other polar components (individually ≤8.8% TRR).

TLC (3 systems) indicated low levels (<1.9% TRR) of glucose at 14DAT3, suggesting incorporation of the ^{14}C-label into natural products. Other components in the 14DAT3 fruit included oxamyl (36.4% TRR, 0.523 mg/kg), IN-N0079, IN-QKT34, IN-A2213, and IN-F3905; each ≤7.9% TRR. The unidentified polar component(s) in 14DAT3 fruit accounted for 35.2% TRR.

The PES after aqueous methanol extraction accounted for 4.0–6.2% TRR in 14DAT3 and 21DAT4 fruit. The 21DAT4 sample was extracted further with water, α-amylase, combined amyloglucosidase and cellulase, 0.1M NaOH (*ca.* 60°C), and 1M HCl (*ca.* 60°C), overall releasing a further 5.2% TRR with individual fractions ≤2.4% TRR. Three unidentified polar metabolites at 0.3–3.0% TRR were detected in the combined water and enzyme fractions. The final unextracted residue was 2.8% TRR.

Foliar Application: Foliage

The majority of the radioactivity was recovered in the surface wash and aqueous methanol extracts (≥ 94.1% TRR; Table 11). Oxamyl was the main component in foliage accounting for 43.3-78.4%TRR (2.064–31.297 mg/kg). IN-N0079 (0.127–0.633 mg/kg, 1.5–3.9% TRR), IN-QKT34 (1.240–

4.241 mg/kg, 10.6–35.0% TRR), IN-A2213 (0.125–0.882 mg/kg, 2.0–2.6% TRR), and IN-L2953 (0.081 mg/kg, 0.8% TRR, 7DAT4 only) were identified in tomato foliage. Unidentified components accounted for 8.1%, 4.4%, and 3.8% TRR at 14DAT3, 7DAT4, and 21DAT4, respectively. Polar components were shown to be qualitatively similar to those in fruit by comparative 1D-TLC, therefore analysis of the polar radioactivity in fruit was regarded as adequate characterisation. Other metabolites that did not co-chromatograph with available reference (≤0.6% TRR) were also detected.

Table 11 Summary of radioactive residues in tomato foliage following multiple foliar application of [^{14}C]oxamyl

Foliage	14DAT3		7DAT4		21DAT4	
	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg
Identified components[a]						
Oxamyl[b]	43.3	2.064	73.1	7.219	78.4	31.297
IN-L2953	-	-	0.8	0.081	-	-
IN-N0079	2.6	0.127	3.9	0.393	1.5	0.633
IN-QKT34	35.0	1.673	12.6	1.240	10.6	4.241
IN-A2213	2.6	0.125	2.0	0.193	2.2	0.882
IN-F3905	1.7	0.082	-	-	-	-
Uncharacterised fractions						
NaOH extract	Not Characterised Further				0.7	0.279
HCl extract					0.7	0.279
Unidentified components						
Number	3	-	2	-	9	-
Highest	7.6	0.364	4.0	0.396	2.6	1.031
Lowest	0.5	0.025	0.4	0.042	<0.1	0.006
Unextracted	5.8	0.277	3.2	0.316	0.5	0.199

[a] Sum of components identified in foliage surface washes and tissue extracts
[b] Oxamyl was the principal component in foliage surface washes (21.9-36.7%TRR; 1.075-8.737 mg/kg) and extracts (20.8-56.5%TRR; 0.989-22.550 mg/kg).

The PES after aqueous methanol extraction accounted for 2.5–5.8% TRR. The 21DAT4 sample was extracted further with water, α-amylase, combined amyloglucosidase and cellulase, 0.1M NaOH (*ca.* 60°C), and 1M HCl (*ca.* 60°C), overall releasing a further 2.2% TRR with individual fractions ≤0.7% TRR. Oxamyl (<0.1 % TRR, 0.010 mg/kg), IN-A2213, IN-QKT34, IN-N0079, and unidentified metabolites at ≤0.3% TRR were detected in the combined aqueous and enzyme fractions. The radioactivity in the base and acid extracts was not partitioned into dichloromethane. The final unextracted residue was 0.5% TRR.

2. Extraction and characterisation of residues in fruit and foliage samples from the soil application regime

Soil Application: Fruit

The majority of the radioactivity was extracted using aqueous methanol (≥90.4% TRR). Oxamyl was detected at 14DAT3 and 7DAT4 only (0.028–0.047 mg/kg, 3.8–5.9% TRR; Table 12). IN-N0079 (0.013–0.073 mg/kg, 1.8–21.9% TRR), IN-QKT34 (0.016–0.071 mg/kg, 4.8–10.7% TRR), IN-A2213 (0.031–0.089 mg/kg, 8.4–11.5% TRR), IN-F3905 (0.029–0.058 mg/kg, 2.2–7.8% TRR), and IN-L2953 (0.023 mg/kg, 2.9% TRR, 7DAT4 only) were also detected in fruit. Extractable polar components

accounted for 35.4–60.2% TRR in the 7–21DAT4 fruit. A metabolite that did not co-chromatograph with the available reference standards accounted for ≤6.3% TRR.

Table 12 Summary of radioactive residues in tomato fruit following multiple soil application of [^{14}C]oxamyl

Fruit	14DAT3		7DAT4		14DAT4		21DAT4	
	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg
Identified components								
Oxamyl	3.8	0.028	5.9	0.047	-	-	-	-
IN-L2953	-	-	2.9	0.023	-	-	-	-
IN-N0079	1.8	0.013	-	-	21.9	0.073	2.3	0.015
IN-QKT34	9.6	0.070	8.4	0.068	4.8	0.016	10.7	0.071
IN-A2213	11.5	0.083	11.0	0.089	9.3	0.031	8.4	0.055
IN-F3905	7.8	0.056	7.2	0.058	2.2	0.007	4.4	0.029
Analysis of polar isolate								
IN-D2708[a]	Not Conducted						21.3	0.139
IN-KP532[a]							5.2	0.034
IN-KV998/IN-T2921[a]							0.4	0.003
Uncharacterised fractions								
NaOH extract	Not Characterised Further						1.2	0.008
HCl extract							0.4	0.003
Unidentified components								
Number	4	-	4		4	-	9	-
Highest	23.9	0.172	28.4	0.228	24.2	0.081	12.4	0.082
Lowest	3.1	0.022	6.3	0.051	0.8	0.003	0.1	0.001
Unextracted	8.3	0.060	9.5	0.076	5.6	0.019	3.1	0.020

[a] Quantified in 21DAT4 fruit by HPLC (IN-D2708, IN-KP532) and TLC (IN-KV998/ IN-T2921)

The main region of polar radioactivity isolated from the 21DAT4 sample was comprised of IN-D2708 (0.139 mg/kg, 21.3% TRR), IN-KP532 (0.034 mg/kg, 5.2% TRR), and three additional polar metabolites (≤12.4% TRR, 0.082 mg/kg). TLC analysis confirmed the presence of IN-KP532 and IN-D2708 together with IN-KV998 and/or IN-T2921 (unresolved; 0.003 mg/kg, 0.4% TRR) and five other unidentified metabolites (≤3.6% TRR).

The PES after aqueous methanol extraction accounted for 8.3–9.5% TRR. The 21DAT4 sample was extracted further with water, α-amylase, combined amyloglucosidase and cellulase, 0.1M NaOH (*ca.* 60°C), and 1M HCl (*ca.* 60°C), overall releasing a further 6.5% TRR with individual fractions accounting for ≤2.8% TRR. Five unidentified polar metabolites accounted for 0.1–3.7% TRR in the combined aqueous and enzyme fractions. The final unextracted residue was 3.1% TRR.

Soil Application: Foliage

The majority of the radioactivity was extracted using aqueous methanol (≥91.5% TRR). Oxamyl (0.730–1.527 mg/kg, 6.3–19.3% TRR), IN-N0079 (0.154–0.499 mg/kg, 2.8–4.4% TRR), IN-QKT34 (1.918–7.212 mg/kg, 35.2–63.7% TRR), IN-A2213 (0.189–0.447 mg/kg, 1.7–7.6% TRR), IN-F3905 (0.154–0.549 mg/kg, 1.3–4.9% TRR), and IN-L2953 (0.088–0.250 mg/kg, 1.6–3.5% TRR) were detected (Table 13). Polar radioactivity accounting for 6.7–19.8% TRR was shown to be qualitatively

similar to that in fruit by comparative 1D-TLC, and therefore, analysis of the polar radioactivity in fruit was regarded as adequate characterisation. Other metabolites that did not correspond to available reference standards accounted for ≤1.2% TRR and were not characterised further.

Table 13 Summary of radioactive residues in tomato foliage following multiple soil application of [^{14}C]oxamyl

Foliage	14DAT3		7DAT4		14DAT4		21DAT4	
	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg
Identified components								
Oxamyl	13.5	1.527	19.3	1.050	10.5	0.749	6.3	0.730
IN-L2953	-	-	1.6	0.088	3.5	0.250	-	-
IN-N0079	3.0	0.341	2.8	0.154	-	-	4.4	0.499
IN-QKT34	63.7	7.212	35.2	1.918	55.6	3.967	62.6	7.144
IN-A2213	1.7	0.189	7.6	0.416	4.9	0.348	3.8	0.447
IN-F3905	4.9	0.549	3.2	0.176	2.8	0.202	1.3	0.154
Uncharacterised fractions								
NaOH extract	Not Conducted						2.2	0.251
HCl extract							2.2	0.251
Unidentified components								
Number	3	-	6	-	3	-	12	-
Highest	6.0	0.674	18.1	0.986	12.6	0.894	11.1	1.268
Lowest	0.7	0.073	0.3	0.014	0.8	0.057	<0.1	0.005
Unextracted	6.0	0.679	8.0	0.436	8.6	0.614	1.5	0.171

The PES after aqueous methanol extraction accounted for 8.0–8.6% TRR. The 21DAT4 sample was further extracted with water, α-amylase, combined amyloglucosidase and cellulase, 0.1M NaOH (*ca*. 60°C), and 1M HCl (*ca*. 60°C), overall releasing a further 6.7% TRR (0.764 mg/kg) and with individual fractions ≤2.2% TRR. Oxamyl, IN A2213, IN-QKT34, IN-N0079, and several unidentified metabolites were detected at ≤ 0.6% TRR in the combined water and enzyme fractions. The radioactivity in the base and acid extracts was not partitioned into dichloromethane. The final unextracted residue was 1.5% TRR.

3. Further characterisation of the extractable polar residues in fruit

Aqueous methanol fruit extracts (21DAT4, soil application) were concentrated to remove organic solvent, partitioned against dichloromethane, acidified, and re partitioned with dichloromethane. The aqueous fraction contained the majority of the radioactivity (78.3% TRR). HPLC demonstrated the presence of IN-QKT34, IN-A2213, and two regions of polar radioactivity comprising 13.6% TRR and 49.4% TRR. Other HPLC methods showed these polar regions were comprised of multiple components including IN-D2708, IN-F3905, IN-KP532, and IN-T2921/IN-KV998 (unresolved) all individually ≤11.3% TRR, together with unidentified metabolites eluting near the void volume (12.9% TRR) and five metabolites (individually ≤3.2% TRR).

Whilst the HPLC profile showed changes following enzyme digestion of the aqueous fraction, no conclusive changes were apparent following enzyme digestion, acid or base hydrolyses of a semi-purified polar isolate. Aliquots of the polar isolate (21DAT4 soil regime) were separately subjected to enzyme digestion (β glucosidase, *ca*. 38°C, 6 hours) and acid (0.1M HCl, *ca*. 90°C, 6 hours) and base (0.1M NaOH, *ca*. 38°C, 6 hours) hydrolysis. Three distinct regions of polar radioactivity present in the

untreated sample remained unchanged after β-glucosidase and acid hydrolysis, while all radioactivity eluted as one peak in the void volume following alkaline hydrolysis. The results indicate that polar components were not readily cleaved under enzyme or hydrolytic conditions or that any components released were also polar.

Analysis under different chromatographic methods indicated that portions of the polar radioactivity were well retained under acidic conditions suggesting that one or more of the polar components had acidic properties. A concentrated aqueous extract from fruit (21DAT4, soil regime) was clarified by SPE and polar radioactivity isolated using sequential HPLC methods. The final isolate exhibited a prominent peak; however characterisation by LC-MS was unsuccessful.

Comparative chromatography using varied stationary and mobile phases demonstrated that the unidentified fruit components, including the polars, did not co-elute with available reference standards (oxamyl, IN-A2213, IN-A2912, IN-F3905, IN-KP532, IN-KV998, IN-L2953, IN-M2583, IN-N0079, IN-N2935, IN-QKT34, IN-SBY69, IN-T2921, IN-U1966, IN-U1967, oxalic acid, IN-18474 [oxamic acid], IN-00699 [oxamide], or thiocyanate). No components corresponding to the available standards were released upon enzyme digestion or acid/base hydrolysis of the concentrated aqueous fraction or polar isolate.

An aliquot of a polar concentrate (21 DAT4, soil regime) was derivatised using BF_3/methanol. Following derivatization, the radiochromatogram contained a new component. Attempts to characterize the component by LC-MS were unsuccessful. No diagnostic mass showing a sulphur ^{14}C isotope pattern was detected, and results were deemed inconclusive.

A representative fruit extract (14DAT3, foliar applications) was analysed by TLC in three systems together with ^{14}C-glucose. The analysis demonstrated the possible reincorporation of low levels of radioactivity (<1.9% TRR) into glucose.

4. Storage stability of residues

Samples were stored in a freezer set to maintain *ca.* -20°C, milled, and extracted within 23 days of harvest, and the initial extracts analysed within 37 days of extraction. Storage stability investigations were not conducted as initial extraction and chromatography was conducted within 6 months.

5. Identification of oxamyl and metabolites

The identities of the principal residue components were investigated by comparison of the extractable residues with authenticated analytical reference standards of oxamyl and metabolites. Oxamyl was present in the majority of samples as confirmed by co-chromatography using an authenticated reference standard. IN-A2213, IN-F3905, IN-QKT34, IN-N0079, IN-L2953, IN-KP532, IN-D2708, and IN-T2921/IN-KV998 were identified by co-chromatography in at least one contrasting chromatography system using authenticated reference standards. ^{14}C-Glucose was tentatively identified by 1D-TLC using an authenticated radiolabelled standard.

6. Proposed metabolic pathway

The route of metabolism was similar following both foliar and soil applications and was consistent with previous oxamyl plant metabolism studies. A proposed metabolic pathway is presented in Figure 2.

- Hydrolysis of the methylcarbamoyl group to yield the non-insecticidal oxamyl-oximes, IN-A2213, and IN-F3905
- IN-A2213 conjunction with glucose to form IN-QKT34
- IN-A2213 demethylation to give IN-L2953

- IN-A2213 (or oxamyl) metabolism to IN-N0079
- IN-N0079 metabolism (*via* IN-T2921) to IN-D2708
- IN-L2953 metabolism to IN-KP532 (*via* IN-KV998)

Metabolism to components characterized as highly polar are the likely result of more extensive metabolism of the 3 carbon (IN-KV998 and IN-KP532) or 4 carbon (IN-T2921 and IN-D2708) containing metabolites, and reincorporation into natural products of $^{14}CO_2$ possibly derived from soil microbial mineralisation of oxamyl. Direct soil application or soil interception during foliar application to immature plants at transplant would allow for ready oxamyl degradation to the soil degrade IN-D2708 and consequently available $^{14}CO_2$ for plant uptake.

III. CONCLUSION

Tomato plants were treated with [1-^{14}C]oxamyl, formulated to simulate Vydate 10L under both multiple foliar and multiple soil application regimes. The first application was immediately after transplant at 2000 g a.s./ha and three subsequent 1000 g a.s./ha applications were conducted 14 days apart to achieve a 21 day pre harvest interval (PHI).

TRRs in fruit ranged from 0.716–1.434 mg/kg for the foliar treatment and 0.332–0.805 mg/kg for the soil treatment. Values in foliage ranged from 4.775–39.894 mg/kg for the foliar treatment and 5.451–11.398 mg/kg for the soil treatment.

The majority of the radioactivity (≥90.4%) was extracted by surface washing (foliar regime only) and/or extraction with methanol, aqueous methanol, and water in succession. Further extraction of the 21DAT4 samples with water (ambient), α-amylase (50°C), combined amyloglucosidase and cellulase (50°C), 0.1M NaOH (60°C), and 0.1M HCl (60°C) released an additional 2.2–6.7% TRR, leaving final unextracted residues of 0.5–3.1% TRR.

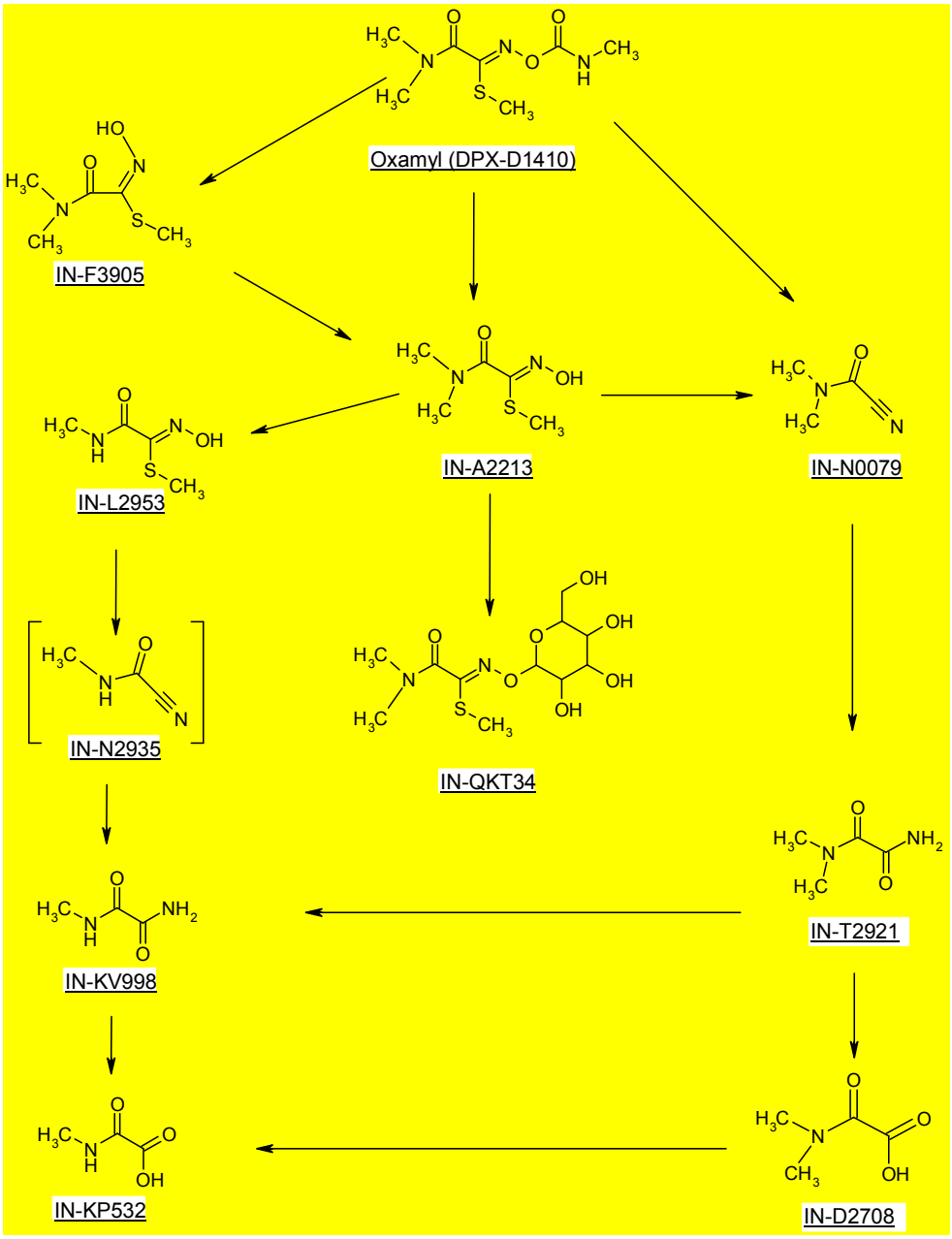
Highest oxamyl concentrations in fruit from the foliar treatment regime; oxamyl concentrations declined from 31.2% TRR (0.223mg/kg) at 7DAT4, to 2.9% TRR (0.027 mg/kg) at 21DAT4. Metabolites including IN-A2213, IN-L2953, IN-QKT34, IN-N0079, IN-F3905, IN-D2708, IN-KP532, and IN-KV998/IN-T2920 were detected in fruit and foliage from both treatment regimes.

Several (at least three) components more polar than IN-KP532 and IN-D2708 were detected in the fruit and foliage at each time point in each treatment regime. Efforts to further characterise these water-soluble polar metabolites included chromatographic, deconjugation, hydrolysis, derivatisation, and mass spectroscopic techniques were inconclusive. TLC indicated low levels of 14C-glucose in immature fruit (14DAT3 foliar regime) suggesting incorporation of radioactivity into plant natural products.

The metabolic pathway of oxamyl in tomato fruit and foliage included hydrolysis of the methylcarbamoyl group to yield the non-insecticidal oxamyl-oximes (IN-A2213 and IN-F3905). IN-A2213 was conjugated with glucose to yield IN-QKT74. IN-A2213 was demethylated to give IN-L2953. IN-A2213 (or oxamyl) was also metabolised to IN-N0079, which was further metabolised (*via* IN-T2921) to IN-D2708. A similar conversion of IN-L2953 to IN-KP532 (*via* IN-KV998) was observed. Highly polar components possibly resulting from re-incorporation of the radiolabel and/or polysaccharide conjugates were also detected.

(Chapleo, S., Johnson, J., 2014)

Figure 2 Proposed metabolic pathway of oxamyl in tomato



RMS comments and conclusion: The study has been submitted for this renewal. It is appropriate for the purpose.
The metabolism of oxamyl in tomatoes plants after foliar and soil treatments has been studied. The metabolic pathway of oxamyl in tomato fruit and foliage tissues included hydrolysis of the methylcarbamoyl group to yield the non-insecticidal oxamyloximes (IN-A2213 and IN-F3905). IN-A2213 was conjugated with glucose to yield IN-QKT74. IN-A2213 was demethylated to give IN-L2953. IN-A2213 (or oxamyl) was also metabolised to IN-N0079, which was further metabolised (via T2921) to IN-D2708. A similar conversion of IN-L2953 to IN-KP532 (via INKV998) was observed. The carbamate group was not present in any of the metabolites detected. Highly polar components possibly resulting from reincorporation (in part) of the radiolabel and/or polysaccharide conjugates were also observed.

B.7.2.2 Poultry

Study submitted in the EU Dossier in 2001 and included in the first EU approval review.

B.7.2.2/01

Reference: --	**Report:**	[redacted] (1994); Metabolism of [^{14}C]oxamyl in **DuPont Report No.:** AMR 2546-92 **Guidelines:** U.S. EPA 171-4 c,d

1. Test material: [1-^{14}C]oxamyl
   Lot/Batch #: 2868-235; 2868-229
   Purity: Radiochemical purity - 99.0% (2868-235); 98.5% (2868-229)

Study details:

[1-^{14}C]Oxamyl was fed to hens in capsule form at a nominal dose of 3.62 – 3.65 mg of oxamyl (equivalent to dietary intake of 36.3 to 42.5 mg/kg) for 3 days. This dosing regime is > 1000x times the expected dietary intake of oxamyl for hens arising from the consumption of treated potatoes. Samples of excreta were collected daily and stored frozen until analysed. Eggs were collected twice daily and were frozen until analysed. Volatiles were monitored daily from one group of hens. The hens were sacrificed 22 ± 2 hours post the final dose and samples of liver, muscle, skin, fat, kidney, blood, GI tract and GI contents were taken for analysis.

Distribution of ^{14}C:

^{14}C was measured in excreta, egg white, egg yolk, liver, kidney, fat, skin, blood, GI tract and contents and muscle. The results are presented in Table 14.

Table 14 Recovery of ^{14}C following the dosing of hens (group of 10) with Oxamyl at a target dose of circa 30 mg/kg in the diet.

Sample.	Mean ppm of Oxamyl equivalents.	Mean % of the total dose administered.
Excreta		71.4
Liver	2.01 ± 0.3	0.7
Kidneys	1.72 ± 0.29	0.2
Blood	2.02 ± 0.42	2.0
Br east muscle	0.442 ± 0.098	0.9
Thigh muscle.	0.675 ± 0.126	1.3
Skin.	0.714 ± 0.117	0.1
Fat	0.064 ± 0.03	0.1
G.I. tract.	0.933 ± 0.162	0.9
G.I. contents	0.784 ± 0.491	0.6
Egg yolk, 0-24h.	0.105 ± 0.099	0.13
Egg yolk, 24-48 h.	0.487 ± 0.13	
Egg yolk, 48-72h.	1.06 ± 0.17	
Egg white, 0-24h	0.321 ± 0.344	0.3
Egg white, 24-48h.	0.91 ± 0.239	
Egg white, 48-72h.	1.16 ± 0.07	
Total.		78.63

Extractability and characterisation of ^{14}C present in hen eggs, organs, tissues and excreta:

Excreta:
Excreta was extracted using methanol/water in the ratio sample:water:methanol (2:1:2). The resulting supernatant solution and the extracted solids were both analysed to determine the total ^{14}C oxamyl equivalents present in the different fractions.

Approximately 53.6% of the ^{14}C was extracted from the 0-24h fraction, 65.3% of the ^{14}C was extracted from the 24-48h fraction and 56.6% of the 14C ^{was} extracted from the 48-72h fraction.

Liver:
^{14}C-Liver residues were extracted using a sequence of solvents in increasing order of polarity, hexane, methylene chloride, Ethyl acetate and methanol/water.

< 1% of the ^{14}C-liver residues were extractable into hexane and dichloromethane. 24.3% of the 14C was extracted into ethyl acetate.

21.6% of the ^{14}C-liver residues were extracted into methanol/water.

The combined ethyl acetate and methanol/water extracts when treated with acetone resulted in 11.6% of the ^{14}C present precipitating from solution.

53.6% of the ^{14}C was not extractable using the solvents indicted. 61% of this non-solvent extractable 14C was solubilised when the extracted solids were treated with protease.

Details of the extractability of the ^{14}C-liver residues are presented in Table 15 below.

Egg yolk:
Egg yolk was extracted in a manner similar to that used for liver.

The majority of the ^{14}C-egg yolk residues were extracted into the methanol/water solvent solution indicating that the residue present was very polar in nature.

Details of the extractability of the ^{14}C-egg yolk residues are presented in Table 15 below.

Egg white:

Egg white was extracted in a manner identical to that for egg yolk.

Majority of the ^{14}C-egg white residues present were extracted into the methanol/water solvent solution confirming the polar nature of the residue.

Details of the extractability of the ^{14}C-egg white residues are presented in Table 15 below.

Breast muscle:

Breast muscle was extracted in a manner identical to that for eggs.

The majority of the ^{14}C-breast muscle residues were extracted into the methanol/water solvent solution confirming the polar nature of the residue.

Details of the extractability of the ^{14}C-residues in- breast muscleare presented in Table 15 below.

Thigh muscle:

Thigh muscle was extracted in a manner identical to that for breast muscle.

The majority of the ^{14}C-thigh muscle residues were extracted into the methanol/water solvent solution confirming the polar nature of the residue.

Details of the extractability of the ^{14}C residues in thigh muscle are presented in Table 15 below.

Table 15 Extractability of ^{14}C from organs and tissues % TRR (ppm)

Extracting solvent.	**Liver ^{14}C residues extracted.**	**Egg yolk ^{14}C residues extracted.**	**Egg white ^{14}C residues extracted.**	**Breast muscle ^{14}C residues extracted.**	**Thigh muscle ^{14}C residues extracted.**
Mean residue ^{14}C oxamyl equivalents.	2.01 mg/kg	0-24h 0.105 mg/kg 24-48h 0.487 mg/kg 48-72h 1.06 mg/kg	0-24h 0.321 mg/kg 24-48h 0.91 mg/kg 48-72h 1.16 mg/kg	0.442 mg/kg	0.675 mg/kg
Hexane.	0.23 (0.005)	0-24h 0.02 (<0.001)	0-24h 0.15(<0.001)	0.28 (0.001)	0.071 (<0.001)
		24-48h<0.001(<0.001)	24-48h 0.07 (<0.001)		
		48-72h 0.55 (0.006)	48-72h 0.08(<0.001)		
Methylene chloride	0.43 (0.009)	0-24h 8.86 (0.009)	0-24h 5.83 (0.019)	1.38 (0.006)	2.04 (0.014)
		24-48h 5.34 (0.026	24-48h 4.66(0.042)		
		48-72h 2.25 (0.024)	48-72h 2.81(0.033)		
Ethyl acetate.	24.3 (0.488)	0-24h 6.63 (0.007)	0-24h 1.52(0.005)	4.26 (0.018)	4.27 (0.029)
		24-48h 3.98 (0.019)	24-48h 2.99(0.027)		
		48-72h 7.85 (0.083)	48-72h 3.15 (0.037)		
Methanol/water	21.6 (0.434)	0-24h 130.7(0.137)	0-24h 114(0.462)	81.6 (0.36)	63.2 (0.425)
		24-48h 53.7 (0.261)	24-48h 95.6 (0.87)		
		48-72h 90.7 (0.961)	48-72h 84.2(0.976)		
Pronase supernatant following treatment of remaining solids	32.6 (0.655)				
Unextracted ^{14}C.	17.4 (0.35)	0-24h 11.3 (0.012)	0-24h 8.72(0.028	12.9 (0.057)	16.3 (0.11)
		24-48h 11.9 (0.058)	24-48h 7.8(0.069		
		48-72h 12.9 (0.137)	48-72h 10.8 (0.125)		
Total.	96.6 (1.941)	0-24h 157.5(0.165)	0-24h 130.22(0.514)	100.1 (0.442)	85.9 (0.578)
		24-48h 74.9 (0.364)	24-48h 111.1(1.008)		
		48-72h 114.3 (1.211)	48-72h 101(1.171)		
Note: Samples were sequentially extracted with the solvents as outlined above in the table. Following solvent extraction the remaining solids were subjected to pronase hydrolysis to release some of the bound residue. The Unextracted 14C residue was that which could not be solubilised by either solvent extraction or protase hydrolysis.					

Identification of residues present in hen tissues, organs, eggs and excreta:

Excreta:
HPLC analysis of excreta using a radiochemical detector indicates that the composition of the residue is similar for each of the 0-24, 24-48 and 48-72 hour samples. The 0-24h excreta was selected with a view to identifying it's constituent metabolites.

HPLC analysis of the 0-24h excreta extract indicates the presence of at least 9 different ^{14}C fractions.

Comparison of the retention times of the HPLC fractions with those of known standards shows the absence of Oxamyl, oxamyl sulphone, oxamyl sulphoxide, oxamyl oxime, *N*- methyl oxime and dimethyl cyanoformamide (DMCF) from excreta.

Thiocyanate was the main metabolite identified in excreta. It was identified using different HPLC systems and by precipitating the thiocyanate from the sample extract using silver nitrate. Thiocyanate was calculated to be present in the 0-24h fraction at 6.2% of the administered dose. The content of thiocyanate present in excreta and other tissues/organs is presented in

Table 16 below.

A second polar metabolite which co-eluted with thiocyanate in the initial HPLC (PRP- 1column) analytical run, was separated from the thiocyanate using a Hypercarb column but was not identified.

Oxamyl oxime sulphoxide was identified in excreta following the derivatisation of the sample extract with t-Butyldimethylchlorosilane. The identity was confirmed by comparison with a known standard and analysis by GC/MS. This metabolite was only found in excreta.

Oxalic acid, oxamic acid and urea were found in excreta in minor quantities and were tentatively identified as either their pentafluorobenzyl bromide or their t- Butyldimethylchlorosilane derivatives using GC/MS.

The anti-isomer of oxamyl oxime was also isolated and identified as a minor metabolite when reacted with t-Butyldimethylchlorosilane and analysed by GC/MS.

Liver:
45.9% of the ^{14}C-residues in liver was extractable into ethyl acetate and methanol/water. Remaining solids retained circa 50% of the liver radioactivity. These solids when treated with Pronase-E resulted in 32.6% of this non extractable ^{14}C residue being solubilised.

Oxamyl and its expected metabolites, as listed for excreta, were not identified in the liver extracts when analysed by HPLC.

HPLC analysis of the supernatant extract solution (ethyl acetate + methanol/water extract solution following the acetone precipitation of macromolecules) indicated the presence of one major ^{14}C fraction. Further analysis of this ^{14}C fraction showed that thiocyanate (HPLC, co- chromatography and thiocyanate precipitation with silver nitrate) was present (13.6% of TRR) along with another unidentified radioactivity (10.4% of the TRR). This was similar to the pattern found in excreta.

None of the ^{14}C containing metabolites solubilised following the enzymatic digestion of the extracted liver solids were identified.

Egg Yolk:
Table 15 above shows the extractability of the ^{14}C-residues egg yolk into the different solvents. The solubility data, where the majority of the ^{14}C is extractable into methanol/water, indicates that the vast majority of the radioactivity is polar in nature.

Oxamyl or its structurally related metabolites were not identified in egg yolk following HPLC analysis of the methanol/water extract.

Thiocyanate was the only metabolite identified in egg yolk. The levels present are indicated in

Table 16 below.

Egg white:
Table 15 above shows the extractability of the 14C residues from egg white. The majority of the radioactivity was extracted into methanol/water similar to egg yolks.

No oxamyl or its structurally related metabolites were identified in egg white. Thiocyanate was the only metabolite identified and the levels present are indicated in

Table 16 below.

Breast muscle:

The extractability of ^{14}C-residues from breast muscle was similar to that for other matrices with the majority of the radioactivity extractable into the methanol/water phase.

HPLC analysis of the methanol/water extract indicates that thiocyanate is present only as minor component of the ^{14}C.

No other metabolite was identified in breast muscle.

Thigh muscle:

The results for thigh muscle were similar to that for breast muscle with the exception that thiocyanate was present at circa 10% of the TRR as opposed to 4% for the breast muscle.

No other metabolite was identified.

Table 16 Concentration of Thiocyanate found in hen excreta, tissues and organs

Sample Analysed.	% TRR	Concentration in mg/kg (Oxamyl equivalents)	Concentration in mg/kg (Thiocyanate equivalents)
Excreta			
- 0-24 hour fraction	6.2		
- 24- 48 hour fraction.	2.9		
- 48- 72 hour fraction.	3.5		
Liver	13.6	0.273	0.072
Egg Yolk.			
- 0 – 24 hour eggs	33.5	0.035	0.009
- 24- 48 hour eggs.	17.7	0.086	0.023
- 48 – 72 hour eggs.	33.3	0.353	0.093
Egg White.			
- 0- 24 hour eggs	46.5	0.149	0.039
- 24- 48 hour eggs	36.3	0.33	0.087
- 48- 72 hour eggs.	26	0.301	0.08
Breast muscle.	4.1	0.018	0.005
Thigh muscle.	10.3	0.07	0.019

Stability data:

During the study a check was carried out on the storage stability of the samples by comparing HPLC chromatograms of sample extracts from day 0 with those taken from sample extracts following storage for circa 3 months. In the case of liver, egg yolk and muscle a comparison of the chromatographic data presented does not clearly demonstrate that the initial ^{14}C residue present is stable when samples of these matrices are stored for between 3 and 4 months.

Conclusion:

In this study hens were dosed a dietary intake of between 36 and 42mg/kg in the diet. This is considered to be vastly in excess (>1000x) of the expected intake of oxamyl for hens which is outlined in

Table 16. The resulting 14C containing residue levels found in hen tissues, organs and in eggs are similarly considered to be vastly in excess of what will be found following the application of Oxamyl to potatoes in granular form.

The study fully characterises the residue present in hens fed with ^{14}C labelled oxamyl. It can be concluded that the residue present is very polar in nature.

Oxamyl and its structurally related metabolites are not detected in any of the tissues, organs or eggs sampled from the test hens. Thiocyanate is the only metabolite identified in tissues, organs and eggs from this study, see

Table 16 above. This indicates that oxamyl is highly metabolised in hens to a level where the labelled imine carbon is incorporated into non oxamyl like metabolites.

Analysis of excreta shows that thiocyanate was again the major identified metabolite. Smaller quantities of oxamyl oxime sulphoxide, oxalic acid, urea, oxamic acid and the anti isomer of oxamyl oxime were identified in hen excreta and provides a partial picture of the degradation pathway for oxamyl in hens.

The present study indicates that oxamyl is highly metabolised.

21 % of the administered 14C was not recovered in the present study.

In the present study hens were dosed at a level which was vastly in excess (>1000x) of the expected residue levels likely to be present in poulty feed. The TRR residue present in hen tissues, organs and eggs (Table 14) following this feeding regime suggests that hens exposed to the oxamyl residues expected in a normal diet (

Table 16) will not contain any detectable oxamyl or oxamyl metabolite residues in edible poultry products.

On the basis of the predicted dietary intake of oxamyl in hens, see

Table 16 there is no requirement for poultry metabolism or feeding studies to be carried out for oxamyl.

The poultry study AMR 2546-92, originally submitted under EU Rev8 Point IIA 6.2.2 and conducted with test material [1-^{14}C]oxamyl, was conducted under guideline U.S. EPA 171-4 c,d. A review of this study indicates that it fully meets the current guideline (OECD Test Guideline 503: Metabolism in Livestock).

RMS comments and conclusion: The study was submitted during the first inclusion in annex I of Directive 91/414/EEC and fulfil the actual guidelines.

Study submitted in the EU Dossier in 2001 and included in the first EU approval review.

B.7.2.2/02

Reference: --	**Report:**	[redacted] (1990); Metabolism of (14C)-oxamyl in laying hens **t No.:** AMR 1005-87 **Guidelines:** U.S. EPA 171-4

1. Test material: [^{14}C]oxamyl
   Lot/Batch #: E52467-5
   Purity: Radiochemical purity - >97%

Study details:
The purpose of the study was to evaluate the
- route and rate of excretion of 14C from treated hens.
- Level of residue retained in hen tissues, organs and in eggs.
- Any significant residues found in eggs, tissues or in excreta.

The study itself involved the feeding of[1-^{14}C] Oxamyl, labelled at the imine carbon, to hens (in capsule form) at the nominal doses of 0.12mg (low dose, 1mg/kg in the diet.) and 2.4mg (high dose, 20mg/kg in the diet.) per treated group. This low dose feeding level corresponds to >100x times the predicted exposure as outlined in Table 17. Each dosing group consisted of 5 hens and the groups were dosed for 3 days. Hens were sacrificed 24 hours following the final dose.

Samples of excreta were collected on a daily basis and stored frozen until analysed. Samples were pooled by day and by treatment group. Eggs were collected on a daily basis, stored and were frozen until analysed. Samples were pooled by day and by treatment group. The hens were sacrificed 24 hours post the final dose and samples of liver, thigh muscle, breast muscle, fat, kidney and blood were taken for analysis.

Distribution of ^{14}C:

Radioactivity was measured in excreta, eggs, liver, kidney, fat, gut content and muscle. The results are presented in Table 17.

Table 17 % Recovery of ^{14}C following the dosing of hens (group of 5) with Oxamyl at a dose of 1 and 20 mg/kg in the diet

Sample./ Dose level.	Dose 1mg/kg in the diet (Mean conc in ppm of ^{14}C present).	Dose 20 mg/kg in the diet. (% of administered dose recovered.).
Excreta (total)	60.1	66.4
0 - 24h fraction	19.9 (0.46 ppm)	21.3 (8.4 ppm)
24 - 48 h fraction.	19.6 (0.38 ppm)	24.1 (10.83 ppm)
48 - 72 h fraction.	20.6 (0.45 ppm)	21.0 (9.05 ppm)
Eggs (total.)	0.1	0.2
0 - 24h fraction.	<0.1 (<0.01 ppm)	<0.1 (0.11 ppm)
24 - 48 h fraction.	Nd (<0.01 ppm)	0.1 (0.11 ppm)
48 - 72 h fraction.	0.1 (<0.01 ppm)	0.1 (0.12 ppm)
Cage washings.(total.)	6.4	7.1
0 - 24 h fraction.	2.0	2.2
24- 48 h fraction.	1.8	2.0
48 - 72 h fraction.	2.6	2.9
Liver.	0.3 (0.02 ppm)	0.4 (0.59 ppm)
Blood	(0.02 ppm)	(0.48 ppm)
Kidney	<0.1 (0.01 ppm)	0.1 (0.37 ppm)
Gut content.	0.1	0.1
Fat	(<0.01 ppm)	(0.03 ppm)
Muscle*.	0.2 (< 0.01 ppm)	0.2 (0.11 – 0.12 ppm)
Total.	67.2	74.5
* = An average of the thigh and breast muscle information and assuming that 40% of the total body weight is muscle.		

Extractability and characterisation of 14C present in hen eggs, organs, tissues and excreta:

Low dose:
Samples of excreta and liver, both no hydrolysed and hydrolysed (Methanolic HCl), from the low dose study were studied. The ^{14}C residue present in liver and excreta appears to be polar in nature as between 93.2 and 95.8% of the radioactivity present in the excreta was not extractable into ethyl acetate. 90.5% of the liver 14C was not extractable into ethyl acetate.

Between 54.5 and 63.2% of the radioactivity from HCl hydrolysed excreta was not extractable into the ethyl acetate.

69.9% of the 14C from HCl hydrolysed liver was not extractable into ethyl acetate. HPLC analysis of the excreta extract indicates that Oxamyl, oxime, DMCF and NDMO are not present. The no hydrolysed sample extract contained 2 main 14C fractions accounting for 55 and 25% respectively of the eluted radioactivity. The extract, following HCl hydrolysis, contained up to five radiolabelled fractions, 2 major and 3 minor, with the major peaks accounting for 70% of the eluted radioactivity.

HPLC analysis of the no hydrolysed liver extract shows the presence of two radioactive fractions similar to those found in excreta. These peaks accounted for 91 and 6% respectively of the 14C present. Hydrolysed liver extract contain two major and one minor 14C fractions. The major fractions account for 85% of the 14C present.

No ^{14}C containing metabolite present in the low dose excreta or liver extracts was identyfied.

High dose:
Excreta:
Excreta, freeze dried, was extracted with methanol (using a shaker and soxhlet extractor); methanolic sodium hydroxide; dichloromethane.

The solvent extracted solids were then hydrolysed overnight using 0.2N NaOH at 60°C. The resulting hydrolysis solution was filtered, neutralized, evaporated and then combined with the earlier solvent extracts.

Between 100.6 and 104.3% of the radioactivity present in excreta was extractable using the scheme described.

The sample extract was analysed using HPLC and TLC to determine its composition. Oxamyl, oxime, NDMO and DMCF were not detected in the sample extract. HPLC analysis of the 14C present in excreta showed the presence of one major 14C fraction accounting for between 75 and 100% of the excreta 14C in each of the 0-24h, 24- 48h and 48 –72h samples. TLC analysis of this HPLC fraction shows that it consists of up to six different 14C containing metabolic fractions. None of the 14C present was identyfied positively even though DMOA had similar chromatographic characteristics to one of the 14C fractions isolated.

Eggs:
Freeze dried eggs were exhaustively extracted with methanol. The extracted solids were then hydrolysed using methanolic sodium hydroxide (0.2 M, 60°C). This process extracts between 92 and 102% of the 14C present in eggs.

The extracts and hydrolysate were pooled and a portion was evaporated to dryness, re- constituted in acetonitrile/water and analysed using both HPLC and TLC systems as for excreta.

None of the 14C present in eggs was identified and it was demonstrated that residues of Oxamyl, oxime, NDMO and DMCF were not present. It was possible to fractionate the 14C present in the eggs into five component fractions.

Muscle:

Freeze dried muscle was exhaustively extracted with methanol. The extracts were combined, evaporated to dryness and re-constituted in water. This process extracts 82% of the 14C present in muscle.

The aqueous solution was then extracted using ethyl acetate (x3) and chloroform (x1). An aliquot of the extracted solution was cleaned up further by passing it through a C18 Sep-Pak cartridge prior to the sample being analysed using HPLC and TLC.

None of the ^{14}C present in muscle was identified in the study.

Liver:
Freeze dried liver was extracted with methanol (x4) and the solution centrifuged after each extraction. The combined extracts were combined and evaporated to near dryness before being re-constituted in water. This process extracts 66.9% of the 14C present in liver.

The re-constituted water solution was extracted with ethyl acetate(x1) and chloroform (x1) which removes 3.0% of the 14C from solution. An aliquot of this extracted water was evaporated to dryness, reconstituted in methanol and analysed by HPLC and TLC. This analysis showed the presence of up to 2 different 14C fractions, none of which were identified.

A portion of liver, following solvent extraction, was mixed with a solution of protease enzyme (Pronase-E) and incubated at 37°C for 24h. The resulting supernatant solution was filtered (0.45 micron filter), evaporated to dryness, reconstituted in HPLC mobile phase and analysed by HPLC. Analysis indicated the presence of one main 14C fraction. No residues of Oxamyl were detected in the sample.

A portion of solvent extracted liver was hydrolysed using HCl (110°C, 20 h). This solution was reacted with PITC (phenyl isothiocyanate) to derivatise any amino acids which may have been released by hydrolysis. The derivatised hydrolysate was evaporated to dryness and re- constituted in water. The pH of the solution was adjusted initially to pH 8-10 and then to pH 2-3. At each pH level the sample was extracted with di-ethyl ether. The ether extracts contained < 5% of the original 14C and the HPLC chromatograms were consistent with presence of PITC derivatives of amino acids. None of the PITC amino acid derivatives were identified in the study.

Conclusion:
Hens were fed at a dose level of circa 1 and 20 ppm in the diet for 3 days. The low dose is considered to be vastly in excess (>100x) of the predicted dietary intake of Oxamyl by hens as outlined in Table 17. Analysis of total 14C present indicates that at the lower dose total 14C residues will not exceed 0.02 ppm in hen tissues, organs and eggs.

Oxamyl appears to be rapidly metabolized as no residue of Oxamyl, oxime, NDMO and DMCF are not detected in any of the tissues, organ or eggs analysed.

Methanol is the most efficient solvent for extracting the incorporated 14C from the different sample matrices analysed. This is indicative of the very polar nature of the 14C present.

Less than 5% of the 14C present in liver was incorporated into amino acids. None of these amino acids were identified in the course of the study.

There was no explanation provided for the poor recovery of 14C relative to the dose administered. It was suggested that the 14C was eliminated as 14CO2 but this conclusion was not supported.

The study provides little information as to the metabolic pathway followed for the degradation of Oxamyl in hens due to the high level of degradation which occurs and the failure to identify any of the 14C containing metabolites formed.

The study demonstrates that if Oxamyl is applied to potatoes only in line with the indicated GAP there will be no detectable residues found in edible poultry products.

The poultry study AMR 1005-87, originally submitted under EU Rev8 Point IIA 6.2.2.1 and conducted with test material [14C]oxamyl, was conducted under guideline U.S. EPA 171-4. A review of this study indicates that it does not meet the current guideline (OECD Test Guideline 503: Metabolism in Livestock) and has been superseded with AMR 2546-92, cited above.

RMS comments and conclusion: The study was submitted during the first inclusion in annex I of Directive 91/414/EEC and fulfil the actual guidelines.

B.7.2.3 Lactating ruminants

Study submitted in the EU Dossier in 2001 and included in the first EU approval review.

B.7.2.3/01

Reference:	**Report:**	Belasco, I.J., Harvey, J. (1980); *In vitro* rumen metabolism of ^{14}C-labeled oxamyl and selected metabolites of oxamyl **DuPont Report No.:** AMR 09-80 **Guidelines:** Not given
--		

1. Test material: [1-^{14}C]oxamyl
   Lot/Batch #: Not given
   Purity: Radiochemical purity - >99%

Study details:

Rumen fluid was taken from a lactating cow and was placed in a series of 7 erlenmeyer flasks each containing a mixture of cellulose, starch, dextrose, urea and nutrient solutions. The contents of 3 flasks were supplemented with ^{14}C Oxamyl, a second group of 3 flasks were supplemented with N,N-dimethyl-1- cyanoformamide (DMCF) while the remaining flask was supplemented with the glucose conjugate of Oxamyl Oxime (metabolite A). The solutions were incubated at 38°C while purging with Nitrogen to maintain anaerobic conditions. Flasks were taken for analysis at 1, 6 and 24 hours in the case of Oxamyl and DMCF while the metabolite A flask was incubated for 24h. The flasks were then stored at -20°C until analysed.

Study results:

Analysis of the sample extracts gave the results as outlined in Table 18 and Table 19 below. Oxamyl is rapidly degraded with up to 40% having degraded, mainly to the Oxamyl oxime (14%) and DMCF (26.6%) within one

hour. At 6 hours Oxamyl is 99% degraded and both the Oxime and DMCF remain the main metabolites present in the rumen fluid solution. DMCF continues to degrade between 6 and 24 hours where it is transformed into the dimethyl oxamic acid (metabolite III) and dimethyloxamide (metabolite VII).

DMCF when placed in rumen fluid was rapidly metabolized over the 24 hours of the study. There is some evidence that metabolites III, IV and VII are formed but the levels present were very low.

Metabolite A (the glucose conjugate of Oxamyl Oxime) was incubated with rumen fluid for 24h. Less than 1% of the original metabolite A remained after 24 hours. The majority of the ^{14}C residue (70%) was present as DMCF while the remainder was unidentified and was polar in nature.

Table 18 Distribution of metabolites during <u>in-vitro</u> rumen incubation with ^{14}C-Oxamyl

Compound.	Distribution of ^{14}C %.		
	1 Hour	6 Hour	24 Hour.
Oxamyl	58.8	1.2	1.1
Oxamyl oxime (I)	14.0	42.5	66.9
Methyl N-hydroxy-N,N –dimethyl-1- thiooxamimidate (II).	n.d	1.9	1.4
N,N-dimethyloxamic acid (III).	0.4	0.9	4.6
N-methyloxamic acid (IV)	0.2	0.2	1.6
N,N-dimethyl –1-cyanoformamide (DMCF, V).	26.6	51.8	12.8
Methyl N[1]-methyl-N-[(methylcarbamoyl)oxy]-1- thiooxamimidate. (VI)	n.d	0.7	1.2
N,N-dimethyloxamide (VII)	n.d	0.8	10.4

Table 19 Distribution of metabolites during <u>in-vitro</u> rumen incubation with ^{14}C-Dimethyl cyanoformamide (DMCF)

Compound.	Distribution of ^{14}C , μCi.		
	1 Hour	6 Hour	24 Hour.
N,N-dimethyl –1-cyanoformamide (DMCF, V).	0.83	1.05	0.16
N,N-dimethyloxamic acid (III).	n.d.	n.d.	0.06
N-methyloxamic acid (IV)	n.d.	n.d.	0.07
N,N-dimethyloxamide (VII)	n.d.	n.d.	0.02

<u>Conclusion:</u>

The study was poorly presented in that the basis for these conclusions reached were not fully supported and no chromatographic data was provided.

The study is indicative of the speed at which Oxamyl and its metabolites degrade in rumen fluid. It is clear that Oxamyl is very labile in rumen fluid and when ingested by ruminant animals will be rapidly degraded.

The *in-vitro* rumen fluid study, a model study for ruminant metabolism, AMR 09-80, originally submitted under EU Rev8 Point IIA 6.2.1 and conducted with test material [1-^{14}C]oxamyl. Guideline was not given. A review of this study indicates that it does not meet the current guideline (OECD Test Guideline 503: Metabolism in Livestock); deviations include that it is a non-guideline *in-vitro* model study designed to address metabolism in rumen fluid collected from ruminants. This study should be regarded as supplemental information.

RMS comments and conclusion: The study was submitted during the first inclusion in annex I of Directive 91/414/EEC and can be considered useful to give information on ruminant metabolism.

Study submitted in the EU Dossier in 2001 and included in the first EU approval review.

B.7.2.3/02

Reference: --	**Report:**	[redacted] (1994); The metabolism of [^{14}C] oxamyl in lactating goats **nt Report No.:** AMR 2578-92 **Guidelines:** U.S. EPA 171-4

1. Test material: [1-^{14}C]oxamyl
   Lot/Batch #: 2868-235; 2868-229; D1410-222
   Purity: Radiochemical purity - 97.3%

Study details:
A lactating goat was dosed with 59.3mg of ^{14}C oxamyl for five consecutive days. This dose rate was equivalent to a dietary intake of 31 mg/kg food as consumed (34 mg/kg food on a dry weight basis.). Urine, faeces, cage wash and milk were collected on a daily basis while tissues and organs were collected 21 hours following the final dose. Volatile gases expired by the goat were monitored daily for ^{14}C activity. The objective of the study was to investigate the metabolism of oxamyl in ruminants and to identify and quantify the major metabolites present in goat milk and tissues.

Distribution of ^{14}C within the goat:
Analysis of urine, faeces and different goat tissues/matrices following its dosing with ^{14}C labeled oxamyl showed the manner in which the ^{14}C was distributed within and excreted from the animal over the 5 days of the study. The results are presented in Table 20 below. The results show that over the period of the study that 54.5% of the ^{14}C dose is excreted (faeces, urine or exhaled) with the vast majority being excreted in urine. Residues in milk increased over the course of the study so a steady state concentration of ^{14}C in milk was not achieved during the study.

Table 20 Distribution of the ^{14}C, as a % of total dose, in the goat following dosing with ^{14}C labelled Oxamyl . (Max residue mg/kg found in the sample)

Animal matrix.	^{14}C Oxamyl equivalents.

Urine	44.7% of the dose.
Cage rinse.	0.56% of the dose.
Faeces	7.2% of the dose
Milk	10.2% of the dose. (residue ranged from 1.66mg/kg on day 1 to 4.63 mg/kg on day 5).
Kidneys	0.2% of the dose (4.57 mg/kg)
Liver.	1.9% of the dose (8.39 mg/kg)
Muscle (not specified)	3.4% of the dose (1.29mg/kg)
Fat	1.2% of the dose (0.64 mg/kg)
Exhaled ^{14}C (NaOH trap.).	1.9% of the dose.
Moisture trapped ^{14}C.	0.15% of the dose.
Blood	5.2% of the dose.
Stomach contents	1.8% of the dose.
Intestinal contents.	1.8% of the dose.
Total ^{14} C accounted for.	80.25% of the dose.
Note: The study was carried out at a dosing level which is considered to be > 100x the potential dietary intake for ruminant animals arising from the consumption of potatoes treated with oxamyl, which is the only use being supported	

Characterisation of ^{14}C in tissues, organs and milk:
When ^{14}C labeled oxamyl is fed to a goat, at the rates indicated above, residues are distributed across all tissues, organs and in milk. Sequental extraction of the ^{14}C from these matrices was carried out and the results are presented in Table 21 below.

Table 21 Distribution of ^{14}C residues in different solvent extracts from goat matrices.

Solvent extract	Milk		Liver		Kidney		Muscle		Fat.	
	%	mg/kg	%	mg/kg	%	mg/kg	%	mg/kg	%	mg/kg
Hexane	1.12	0.05	0.02	0.002	0.04	0.002	0.08	0.001	0.2	0.001
Dichloromethane	2	0.09	0.21	0.02	0.87	0.04	0.23	0.003	0.86	0.005
Ethyl acetate			0.45	0.04	1.09	0.05	1.21	0.01	0.74	0.005
Methanol/water	72.5	2.99	29.7	2.34	36.1	1.7	55.6	0.63	66.9	0.41
Unextractable.	25.3	1.04	69.6	5.49	61.9	2.91	42.9	0.48	31.3	0.19
% of unextractable residue released by protease enzyme	> 90		75		93		92		98	
Total			100	7.89	100	4.7	100	1.13	100	0.61
^{14}C by LSC.			94	8.39	103	4.57	88	1.29	96	0.64

Note 1 : The ^{14}C was the content determined to be present using LSC as the analytical method.
Note 2: The milk sample data above were from 120 hours after study had commenced.

Milk:
The total ^{14}C residue in milk corresponded to 4.12 mg/kg oxamyl equivalents at 120h post commencement of the study.

75.8% of milk ^{14}C was extractable and 90% of the remaining 25.3% could be solubilised by enzyme hydrolysis using protease.

72.5% of the ^{14}C was extracted using methanol/water (2.99 mg/kg, 120 hour milk) while chloroform extracted (3.12% or 0.14 mg/kg) a much smaller quantity of the ^{14}C residue.

HPLC analysis of the chloroform fraction, after partitioning with hexane, indicated the presence of a number of different ^{14}C metabolite fractions. The main fraction, circa 0.025 mg/kg, was polar in nature. None of the constituents of these fractions were identified.

HPLC analysis of the methanol extract indicated that

>80% of this ^{14}C was polar in nature.
This polar fraction consisted of at least 7 different metabolites.
The main metabolite present was identified as thiocyanate. The concentration of this metabolite increased between the 24h and the 120h milk samples while the concentrations of the other metabolite fractions tended to decrease. Thiocyanate was present in 120h milk at a concentration of 0.52 mg/kg. Thiocyanate was identified by retention time comparison with a potassium thiocyanate standard and by derivatisation with pentafluorobenzyl bromide. The analysis of the pentafluorobenzyl derivative by GC/MS confirmed its identity.

25-30% of the milk (0.45- 1.04 mg/kg) ^{14}C was not solvent extractable. In excess of 90% of this ^{14}C was solubilised by enzyme hydrolysis using Pronase. HPLC analysis of the enzyme hydrolysate indicated the presence of one major polar fraction, subsequently determined to be thiocyanate, and up to 8 other metabolite fractions which were present at lower concentrations which varied between 0.01 and 0.1mg/kg oxamyl equivalents.

Residues of oxamyl, oxamyl-oxime, oxamyl sulphone, oxamyl sulphoxide, oxime sulphone, mono methyl oxime and dimethyl cyanoformamide were not detected in milk.

Liver:
Liver was sequentially extracted with the solvents hexane, dichloromethane, ethyl acetate and methanol/water. Little ^{14}C was extracted into the no polar solvents so the hexane, dichloromethane and ethyl acetate fractions were combined prior to analysis. This combined extract was brought to dryness, dissolved in acetonitrile and partitioned between acetonitrile (0.31% of ^{14}C at 0.026 mg/kg) and hexane (0.13% of ^{14}C at 0.01 mg/kg). The hexane fraction was not analysed further while the acetonitrile fraction (0.31% of the ^{14}C, 0.026 mg/kg) was analysed by HPLC. One major polar fraction was isolated.

No residues of oxamyl, oxime, oxamyl sulphone, oxamyl sulphoxide, oxime sulphone, mono methyl oxime and dimethyl cyanoformamide were detected in this fraction.

42.8% of ^{14}C present in liver was extracted into $MeOH/H_2O$. 24% of this ^{14}C was insoluble in acetone and precipitated from solution. The acetone soluble residue was fractionated using SPE (C18 BondElut) and 70.7% of the ^{14}C present (12.5% of TRR) was eluted with water and

16.7% (2.94% of TRR) was eluted with methanol. The methanol and water fractions were then analysed using HPLC.

- The water eluate had 2 major (La+Lb) and 3 minor metabolite fractions. Metabolite fractions La and Lb were analysed using alternative HPLC conditions. Fraction La contained 9 component sub-fractions [2 major components L1(0.18 mg/kg) and L5 (0.34 mg/kg) while the remainder were less than 0.05 mg/kg]. Fraction Lb contained 7 components all of which were present at a concentration less than 0.08 mg/kg.
- Fraction L1 was identified as the thiocyanate molecule (2.18% of ^{14}C, 0.18 mg/kg).
- Fraction L5 when analysed using a 3rd different HPLC method and was found to consist of 7 component sub-fractions. Two of these sub-fractions were present at concentrations of 0.06 and 0.07 mg/kg oxamyl equivalents. [60% of the ^{14}C was recovered in this analysis]. These two fractions had chromatographic retention times which corresponded to those of *N*-methyloxamic acid and *N*-methyloxamide.

The methanol eluate contained one major peak, which was identified as the thiocyanate metabolite (0.65% of ^{14}C or 0.05 mg/kg).

The no-extractable liver residues, pellet 1 (57% of liver ^{14}C), following methanol/water extraction and the methanol/water extractable residue which was not soluble in acetone, Pellet 2 (24% of liver ^{14}C) were both processed further and indicated the following

- Protease enzyme digestion released 75% of the ^{14}C present in pellet 1 and 100% of the ^{14}C present in pellet 2.
- HPLC analysis of both enzyme hydrolysate solutions indicated a similar chromatographic profile. Both contained 2 major peaks close to the solvent front indicating that the components were polar in nature. 90% of the associated ^{14}C was eluted in water following SPE clean-up of the protease hydrolysate. HPLC analysis of the aqueous fraction, using a Hypercarb column, gave similar chromatograms for both hydrolysate solutions. There were 3 main ^{14}C fractions present one of which corresponded to > 10% of the liver ^{14}C while the 2 remaining fractions contained less than 6% of the liver ^{14}C.

Acid/base hydrolysis of the enzyme hydrolysate solutions when compared with the results of acid/base hydrolysis of oxamyl confirmed that oxamyl was not present. It was unlikely that there were any oxamyl metabolites present in the no-extractable fraction which were structurally similar to parent oxamyl.

Kidney: Sequentially solvent extracted.
Little ^{14}C, <0.05 mg/kg, was found in the hexane, dichloromethane and ethyl acetate fractions. These fractions were combined, evaporated, taken up in acetonitrile and partitioned between acetonitrile (0.88%, 0.04 mg/kg) /hexane (0.01 mg/kg). HPLC analysis of the acetonitrile fraction indicated the presence of one main^{14}C fraction. No further analytical work was carried out on this organosoluble fraction.

MeOH/Water extracted 36.1% of ^{14}C of which 33.3% was acetone soluble. HPLC analysis of the acetone fraction contained one major, early eluting, polar ^{14}C fraction which in turn consisted of 2 components and 80% of ^{14}C. HPLC analysis, using alternative conditions, of this polar fraction showed the presence of 8 different ^{14}C fractions the largest of which, at 9.12%, corresponded to the thiocyanate metabolite.

The 2nd largest fraction, at 8.19% of the ^{14}C, had a similar retention time to the liver L5fraction. The study suggested that the composition of this fraction was similar to that of the liver fraction L5 but no further work was carried out to determine its composition.

Unextractable ^{14}C: This corresponded to 61.9% of the radioactivity present in liver. Protease hydrolysis released 93% of this ^{14}C. Analysis of this enzyme hydrolysate solution, using two different HPLC conditions, indicated the presence of three ^{14}C fractions which were considered to be similar to those found in the equivalent liver extract. No additional data was presented to confirm these conclusions.

Muscle: Muscle was sequentially extracted using the same solvent sequence as used for liver and kidney.
Little of the ^{14}C present in muscle was organosoluble at 2.52% or 0.014ppm. The methylene chloride and ethyl acetate extracts were combined, evaporated, dissolved in acetonitrile, partitioned between acetonitrile (0.79% of ^{14}C, 0.01 mg/kg) /hexane (0.04% of ^{14}C). HPLC analysis of the acetonitrile fraction indicated the presence of one polar fraction which did not correspond to any of the reference compounds (oxamyl, oxime, oxamyl sulphone, oxamyl sulphoxide, oxime sulphone, mono methyl oxime and dimethyl cyanoformamide) for which the sample was analysed.

MeOH/water extract contained 55.6% of the ^{14}C present in muscle (0.63 mg/kg). When analysed by HPLC eight different chromatographic fractions were isolated of which 2, thiocyanate (12.4% of the ^{14}C) and another fraction M4 (11.8% of ^{14}C, 0.13 mg/kg) were the only fractions with a ^{14}C content in excess of 0.05 mg/kg.(4% of the ^{14}C). The HPLC chromatogram fraction M4 had a similar retention time to the L5 liver fraction and was assumed to have a similar metabolite composition and profile. No additional information was provided to confirm this assumption.

The no-extractable muscle ^{14}C, (42.9% of ^{14}C, 0.49 mg/kg), was subjected to enzyme hydrolysis using protease and 92% of the ^{14}C was solubilised. HPLC analysis of the ^{14}C present in the hydrolysate indicated that it was

mainly polar in nature. The hydrolysis solution was purified using SPE and the polar aqueous eluate (24.8% of muscle ^{14}C) was was analysed by HPLC using a Hypercarb column. The resulting chromatograms were similar to those for the kidney and liver. No further data was presented. Acid and base hydrolysis of the enzyme hydrolysis solution indicate that the ^{14}C present in solvent extracted muscle residue was not present as Oxamyl or any closely related molecule.

Goat Fat: 1.2% of the administered ^{14}C (0.61mg/kg) was located in the Fat.
Less than 2% (0.01 mg/kg) of the fat ^{14}C was soluble in hexane, dichloromethane and ethyl acetate. No further studies were carried out to identify the constituents of this organo soluble fraction.

66.9% of the ^{14}C (0.41 mg/kg) was extractable into methanol/water. HPLC analysis indicated that the ^{14}C present was mainly polar in nature and did not correspond to any of the reference substances (oxamyl, oxime, oxamyl sulphone, oxamyl sulphoxide, oxime sulphone, mono methyl oxime and dimethyl cyanoformamide) for which the sample was analysed. Further HPLC analysis, using a Hypercarb column, of this polar fraction indicated the presence of 6 component fractions one of which, thiocyanate (31% of the ^{14}C, 0.19 mg/kg), was the major component present. The retention time of another component (7.43% of ^{14}C, 0.05 mg/kg) corresponded to that of *N*-methyloxamic acid and *N*-methyloxamide. No additional data was provided to identify these metabolites. The remaining fractions contained < 3% of the ^{14}C or <0.02 mg/kg.

Methanol/water unextractable residues contained 31.3% (0.19 mg/kg) of the ^{14}C. 98% of this ^{14}C was released following protease digestion. HPLC analysis, using two different sets of analytical conditions, of the digest produced chromatograms which were similar but not identical to those obtained from liver following the same enzyme digestion process.

Goat Urine: the 72 hour goat urine sample was analysed following centrifugation to remove any solids present.

92.3 % of the ^{14}C was soluble in the urine. 85.6% of this ^{14}C was present as a single major polar fraction (Hamilton PRP-1 column) with 4 other very minor fractions corresponding in total to < 2% of urine ^{14}C. Further HPLC analysis of the major polar fraction, using a Hypercarb column, separated the ^{14}C present in to a further eleven fractions. Five of these fractions each contained more than 5% of the urine ^{14}C. Analysis of three of these five fractions using a Bio-Rad Aminex HPX-87H column indicated that

- 2.54% of the radioactivity present in the urine was the thiocyanate.
- HPLC analysis + derivatisation with MTBSTFA and gc/ms analysis of the derivative confirmed the presence of the oxamide metabolite (10% of the ^{14}C.).
- HPLC analysis + derivatisation with MTBSTFA and analysis of the derivative using GC/MS confirmed the presence of *N*-methyloxamic acid (13% of ^{14}C in 72 h goat urine) and *N*-methyloxamide (5.44% of ^{14}C present in 72 h goat urine).

Analysis of the other two metabolite fractions containing > 5% of the urine ^{14}C did not provide any further information with respect to the composition of the metabolites present.

Identification of residues present in goat milk, urine, organs and tissues. :

Information is presented above with respect to the characterization and identification of residues present in goat tissues and in urine following its dosing with oxamyl.

The data presented indicates that oxamyl is highly metabolized when fed to a goat as residues of parent oxamyl, its oxime, sulphone and sulphoxide metaboltes, monomethyl oxime and dimethyl cyanoformamide are not detected in any tissue, organ or in urine. A detailed breakdown of the fractionation of the ^{14}C residue present in goat tissues and organs is presented in Table 22 below.

Only one metabolite, thiocyanate, was definitively identified and found in all tissues and organs analysed. Concentrations of thiocyanate vary from 2mg/kg in 120 hour milk to 0.14 mg/kg in muscle. Thiocyanate is formed following the complete degradation of oxamyl which results in the cyano group being released at which point it is metabolized to thiocyanate.

A tentative identification of the metabolites N-methyloxamide and N-methyloxamic acid was made in liver on the basis of comparative chromatographic retention times. No further information was provided, unlike the situation in urine, to confirm these metabolites in liver. The multiplicity of radioactivity in fractions present in the different tissues and organs is indicative of the degree to which oxamyl is metabolized.

The ^{14}C residue present in milk increased from 1.45 mg/kg at 24 hours to 4.12 mg/kg at 120 hours. Thiocyanate,which accounted for 48.5% of the ^{14}C in 120 hour milk, was the only metabolite identified. The remaining methanol/water extractable metabolites present in milk had a similar pattern, HPLC chromatogram, to those found in other tissues. Initially the majority of the ^{14}C present was characterized as being polar in nature (HPLC, Hamilton PRP-1 analytical column) and this polar fraction was found to consist of at least ten sub-fractions when analysed by HPLC using alternative analytical (Hypercarb column) conditions.

Information on the fractionation of the ^{14}C residue in milk is presented in Table 22 below.

Urine contained the greatest quantity of ^{14}C residues with 44.7% of the administered dose being recovered from this matrix. Analysis of urine, 72 hour sample, again indicated that oxamyl is highly metabolized with no oxamyl or structurally similar molecules being recovered in the urine. The greatest number of metabolites were isolated and identified in urine in comparison with the other tissues/organs analysed. Four metabolites being definitively identified in urine, see Table 22 below. The metabolites identified were thiocyanate, oxamide, *N*-methyloxamic acid and *N*-methyloxamide. The presence of these metabolites in urine confirms the rapid rate at which oxamyl is metabolized in the goat.

Storage stability of samples: ^{14}C analysis indicated that there was no significant loss of ^{14}C over the duration of the study. A limited number of chromatographic comparisons for urine, milk and liver indicated that the polar nature of the residue was consistent over the study period.

Conclusion:
In the present study oxamyl was fed to a goat at a level of 59.3 mg/day which is equivalent to 31mg/kg in the diet. This dosing level is vastly in excess (> 1000x times) of the dietary intake for goats arising from the consumption of potatoes treated with oxamyl in accordance with the recommended GAP. There are no detectable residues of Oxamyl present in potato tubers following granular treatment.

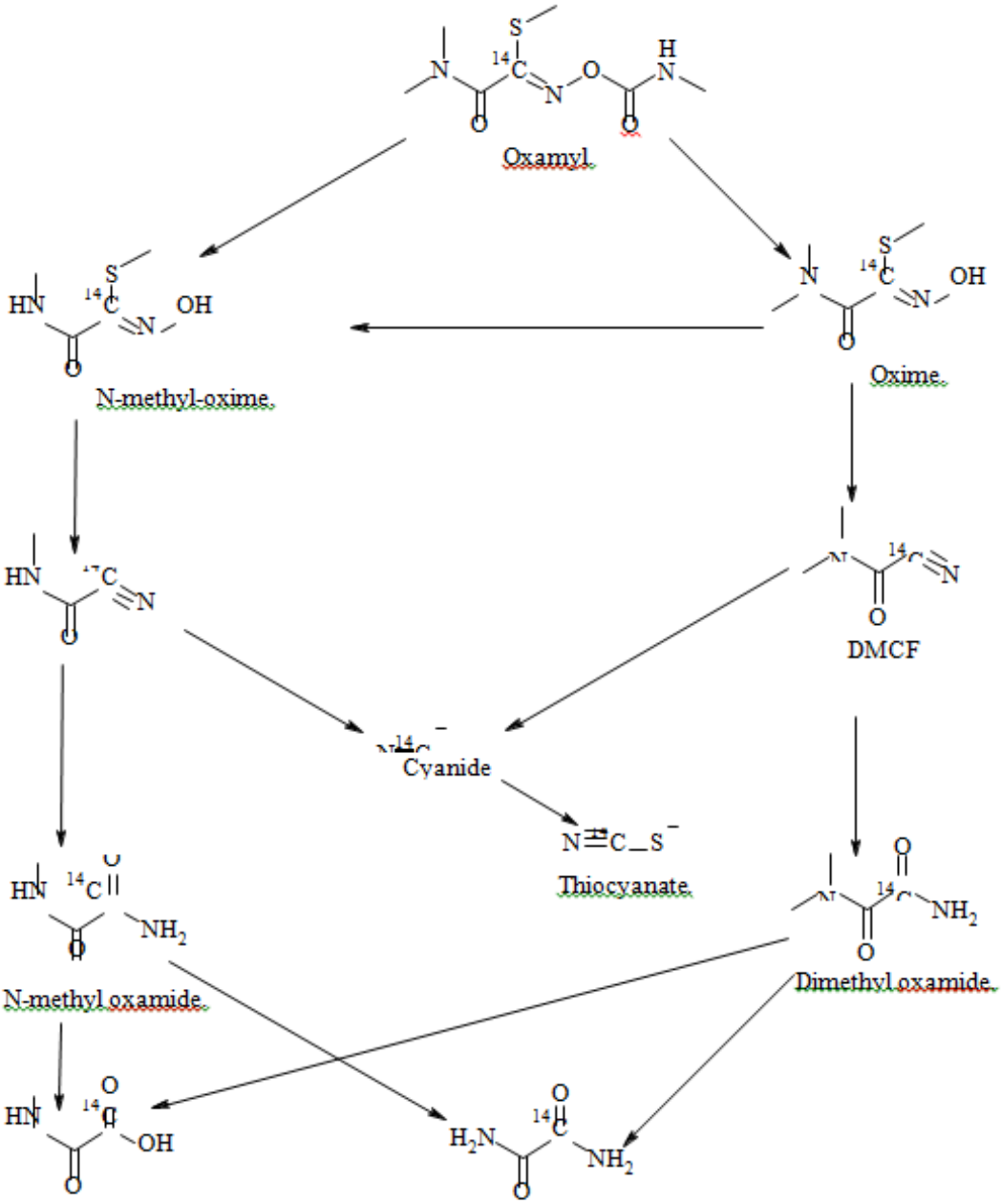
Oxamyl is highly metabolized in the goat where the main residue found in milk, tissues and organs is the thiocyanate metabolite. No residues of oxamyl , its oxime, DMCF or dimethyl oxamide were found in the goat.

Residues of the metabolites oxamide, *N*-methyloxamic acid and *N*-methyloxamide were found in urine and there was some evidence provided that the metabolites *N*-methyloxamic acid and *N*-methyloxamide may also be present in both liver and fat.

The remaining ^{14}C residue was not identifiable but could be separated chromatographically into a large number of discrete, mainly polar, fractions.

The metabolic process rapidly degrades oxamyl to its oxime or its mono-demethylated oxime. The mono demethylation process occurs rapidly and the presence of thiocyanate, *N*- methyloxamide, *N*-methyloxamic acid and oxamide as urine metabolites suggests that oxamyl degrades mainly through the mono methylcyanoformamide molecule to give the metabolites found in urine. A proposed metabolic pathway is presented in Figure B.7.2.1. below.

Figure B.7.2.1. Proposed Metabolic Pathway for Oxamyl degradation in a Lactating goat.



This study was carried out by dosing the goat at a level of circa 3 orders of magnitude greater than the expected goat dietary intake arising from the consumption of treated potatoes. If one extrapolates this data backward one can conclude, with reference to the information presented in Table 20 and in Table 22, that no detectable or identifiable residue will be present in goat milk, tissues or organs.

Table 22 Fractionation and identification of ^{14}C residues present in goat tissues.

Analytical details.		**Identity**	**% of Liver ^{14}C (conc mg/kg)**	**% of fat ^{14}C (conc mg/kg)**	**% of kidney ^{14}C (conc mg/kg)**	**% of muscle ^{14}C (conc mg/kg)**
Non extractable			57.2 (4.8)		63.9 (2.91)	
Organosoluble			<1			
MeOH/H_2O extractable residue.			42.8 (3.57)	66.9 (0.41)	36.1 (1.7)	55.6 (0.63)
Acetone soluble residue.			17.6 (1.47)	57 (0.35)	33.3	45.8 (0.52)
SPE aq. Eluate			12.5 (1.04)			
HPLC A (aq. Eluate)	Polar Frn A.		9.21	51 (0.31)	26.6	43.2 (0.49)
HPLC B.	Subfraction 1a	Thiocyanate	2.18 (0.18)	31 (0.19)	9.12	12.4 (0.14)
HPLC B.	Subfraction 2a		0.27 (0.02)	1.63 (0.01)	0.25	1.84 (0.02)
HPLC B.	Subfraction 3a		0.1 (0.01)	0.48 (0.003)	1.41	2.53 (0.03)
HPLC B.	Subfraction 4a		0.19 (0.02)	1.39 (0.01)	8.19	11.8 (0.13)
HPLC B.	Subfraction 5a		4.06 (0.34)	7.43 (0.05)	1.98	1.9 (0.02)
HPLC D.	Subfraction 5aa		0.08 (0.007)			
HPLC D.	Subfraction 5ab		0.35 (0.03)			
HPLC D.	Subfraction 5ac		0.14 (0.01)			
HPLC D.	Subfraction 5ad		0.05 (0.005)			
HPLC D.	Subfraction 5ae	N-methyl oxamic acid[1]	0.76 (0.06)			
HPLC D.	Subfraction 5af	N-methyl oxamide[1]	0.85 (0.07)	.		
HPLC D.	Subfraction 5ag		0.11 (0.01)			
HPLC B.	Subfraction 6a		0.26 (0.02)	2.79 (0.02)	1.84	3.58 (0.04)
HPLC B.	Subfraction 7a		0.44 (0.04)	0.65 (0.004)	0.25	1.26 (0.01)
HPLC B.	Subfraction 8a		0.18 (0.02)		0.92	2.88 (0.03)
HPLC B.	Subfraction 9a		0.26 (0.02)			
HPLC A.	Polar Frn B		2.02 (0.17)			
HPLC B	Subfraction 1b		0.07 (0.01)			
HPLC B.	Subfraction 2b		0.28 (0.03)			
HPLC B.	Subfraction 3b		0.89 (0.07)			
HPLC B.	Subfraction 4b		0.42 (0.03)			
HPLC B.	Subfraction 5b		0.06 (0.005)			
HPLC A.	Polar Frn. C		0.38 (0.03)			
HPLC A.	Polar Frn D.		0.46 (0.04)			
HPLC A.	Polar Frn. E.		0.08 (0.01)			
SPE MeOH eluate.			2.94 (0.25)			
HPLC A.	Fraction 1		2.05 (0.17)			
	Subfraction 1a	Thiocyanate	0.65 (0.05)			
	Subfraction 1b		0.09 (0.01)			
	Subfraction 1c		0.78 (0.06)			
	Subfraction 1d		0.08 (0.01)			
	Subfraction 1e		0.06 (0.005)			
	Subfraction 1f		0.07 (0.01)			
	Subfraction 1g		0.07 (0.01)			
	Subfraction 1h		0.08 (0.01)			
	Fraction 2		0.29 (0.02)			
	Fraction 3		0.24 (0.02)			
Non MeOH/H_2O extractable (Pellet 1)			57.2 (4.8)	31.3 (0.19)	61.9 (2.91)	42.9 (0.49)
Pellet 1 protease digest			43.3 (3.6)	30.6 (0.19)	57.6 (2.7)	39.4 (0.45)
HPLC A	Polar fraction.		37.9 (3.2)	26.5 (0.16)	47.5 (2.23)	24.8 (0.28)

HPLC B	Sub fraction 1		0.19 (0.02)	9.94 (0.06)	21.5 (1.01)	12.5 (0.14)
HPLC B	Sub fraction 2		0.6 (0.05)	1.71 (0.01)	3.28 (0.15)	1.88 (0.02)
HPLC B	Sub fraction 3		14.6 (1.22)	6.52 (0.04)	8.54 (0.4)	0.88 (0.01)
HPLC B	Sub fraction 4		4.26 (0.35)	0.96 (0.01)	2.27 (0.11)	4.52 (0.05)
HPLC B	Sub fraction 5		5.94 (0.5)	0.62 (<0.01)	1.24 (0.06)	0.96 (0.01)
HPLC B	Sub fraction 6		2.68 (0.22)	0.66 (<0.01)	2.24 (0.11)	1.8 (0.02)
HPLC B	Sub fraction 7		5.62 (0.47)	0.7 (<0.01)	2.04 (0.1)	
HPLC B	Sub fraction 8		1.23 (0.1)			
Extractable non acetone soluble, Pellet 2						
HPLC A.	Polar fraction		21.9 (1.83)			
	Subfraction 1		0.47 (0.04)			
	Subfraction 2		10.2 (0.85)			
	Subfraction 3		1.64 (0.14)			
	Subfraction 4		4.57 (0.38)			
	Subfraction 5		2.73 (0.23)			
	Subfraction 6		0.35 (0.03)			

Note 1: the identification of the N-methyl oxamide and N-methyloxamic acid in the liver extracts can only be considered as tentative as it was based only on comparative chromatographic retention times.
Note 2: HPLC A= analysis using a Hamilton PRP-1 analytical column. ; HPLC B = analysis using a Hypercarb analytical column. ; HPLC D = analysis using an Bio-Rad Aminex HPX-87H analytical column.
Note 3: The different fractions indicated in the above table correspond to the manner in which the ^{14}C is fractionated and when analysed using different HPLC conditions. Each fraction is assigned a number in the table but this does not mean that these fractions are identical when found in liver, muscle, kidney and fat.

Table 23 Fractionation and identification of ^{14}C residues present in goat milk and urine

Analytical details.		**Identity**	**% of Milk ^{14}C (conc mg/kg), [120 hour milk]**	**% of ^{14}C present in Urine**
Non extractable			25.3 (1.04)	
Organosoluble, chloroform extract.			2.13 (0.09)	
MeOH/H_2O extractable residue.			72.5 (2.99)	
HPLC A (aq. Eluate)	Polar Frn A.		58 (2.4)	85.6
HPLC B.	Subfraction 1a	Thiocyanate	36.1 (1.49)	5.42
HPLC D	Subfraction 1aa	Thiocyanate		2.54
HPLC B.	Subfraction 2a	Oxamide	3.63 (0.15) (this milk fraction does not correspond to oxamide)	10
HPLC B.	Subfraction 3a		1.13 (0.05)	23.6
HPLC D	Subfraction 3aa	N-methyl oxamic acid.		13
HPLC D	Subfraction 3ab	N-methyl oxamide		5.44
HPLC B.	Subfraction 4a		---	2.96
HPLC B.	Subfraction 5a		4.93 (0.2)	0.88
HPLC B.	Subfraction 6a		2.78 (0.11)	2.78
HPLC B.	Subfraction 7a		1.84 (0.08)	8.96
HPLC B.	Subfraction 8a		0.46 (0.02)	0.89
HPLC B.	Subfraction 9a		0.48 (0.02)	11.8
HPLC B	Subfraction 10a		0.36 (0.01)	1.1
HPLC B	Subfraction 11a.			0.72
HPLC A.	Polar Frn B		0.57 (0.02)	1.73
HPLC A.	Polar Frn. C		0.34 (0.01)	0.72
HPLC A.	Polar Frn D.		0.79 (0.03)	1.71

HPLC A.	Polar Frn. E.		1.32 (0.05)	1.77
HPLC A	Polar frn. F.			0.75
Non MeOH/H_2O extractable ^{14}C present in milk (Pellet 1)			25.3 (1.04)	
Pellet 1 protease digest, solubilised ^{14}C			23.3 (0.96)	
HPLC A	Polar fraction.		21.2 (0.87)	
HPLC B	Sub fraction 1	Thiocyanate	12.4 (0.51)	
HPLC B	Sub fraction 2		0.29 (0.01)	
HPLC B	Sub fraction 3		2.48 (0.1)	
HPLC B	Sub fraction 4		1.21 (0.05)	
HPLC B	Sub fraction 5		1.47 (0.06)	
HPLC B	Sub fraction 6		0.65 (0.03)	
HPLC B	Sub fraction 7		0.7 (0.03)	
HPLC B	Sub fraction 8		0.54 (0.02)	
HPLC B	Subfraction 9		0.64 (0.03)	
Lactose (tentative identification, comparison of rt in a single chromatographic system.			3.96 (0.16)	
Note 1: Oxamide, N-methyl oxamide and N-methyloxamic acid in urine were definitively identified using chromatography, derivatisation and gc/ms. **Note 2**: Urine was analysed following centrifugation to remove any solid materials present. **Note 3**: HPLC A= analysis using a Hamilton PRP-1 analytical column. ; HPLC B = analysis using a Hypercarb analytical column. HPLC D = analysis using an Bio-Rad Aminex HPX-87H analytical column. **Note 4**: The different fractions indicated in the above table relate to the manner in which the ^{14}C is fractionated when they are analysed using different HPLC conditions. Each fraction is assigned a number but this does not mean that these fractions are identical when found in both milk and urine.				

The lactating ruminants study AMR 2578-92, originally submitted under EU Rev8 Point IIA 6.2.1.1 and conducted with test material [1-^{14}C]oxamyl, was conducted under guideline U.S. EPA 171-4. A review of this study indicates that it fully meets the current guideline (OECD Test Guideline 503: Metabolism in Livestock).

RMS comments and conclusion: The study was submitted during the first inclusion in annex I of Directive 91/414/EEC and give information on goat metabolism and its metabolic pathway. The study fulfil the actual guideline on Metabolism in livestock (OECD 503).

B.7.2.4 Pigs

Metabolism studies to determine the nature of oxamyl derived residues in swine are not an EC requirement as consistent metabolism of oxamyl was observed in the laboratory rat, lactating goat, and laying hen studies.

B.7.2.5 Fish

DuPont recommends waiving the requirement for a fish metabolism study for oxamyl for the following reasons. Quantifiable residues (>0.01 mg/kg) of oxamyl are not expected in plant commodities (grains/seeds or potatoes) commonly used for the formulation of fish diets, thus the dietary burden of oxamyl for fish is negligible. Since oxamyl has a log P_{ow} <3 (-0.43 for a pH-value of 5), there is no potential for bioconcentration of the active substance in fish.

B.7.2.1 Comparison of plant and animal metabolic pathways

Oxamyl was extensively metabolised in livestock (goats and poultry), laboratory animals (rats), and in various crops. The major metabolic pathways in plants and animals were similar. The proposed overall pathway involves initial hydrolysis to IN-A2213. IN-A2213 or oxamyl is further metabolised to IN-N0079 with subsequent hydrolysis to IN-D2708. Details of metabolism following formation of these main metabolites differed between animals and plants.

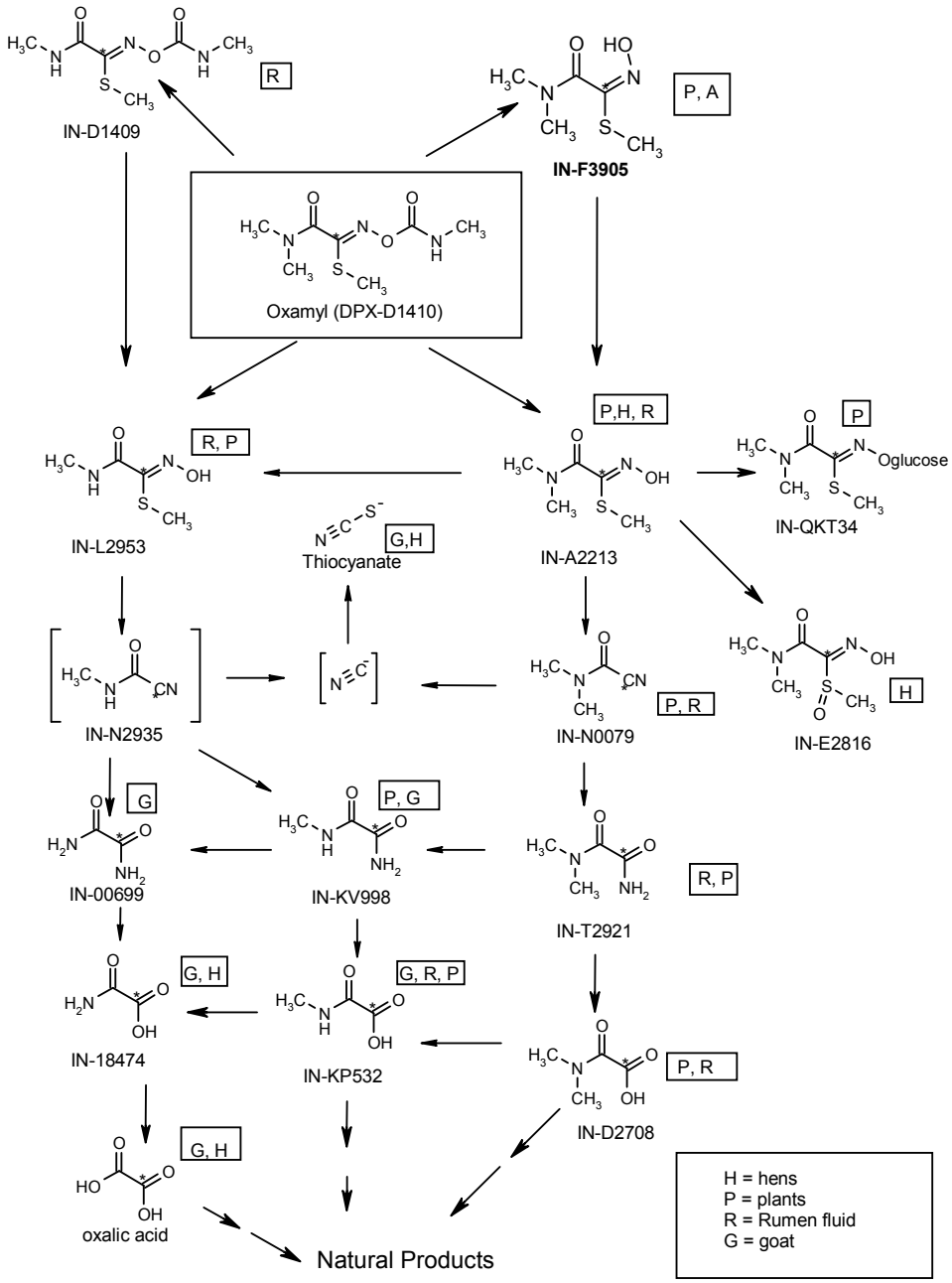
In plants, oxamyl hydrolysis to IN-A2213 may be followed by carbohydrate conjugation and/or *N*-demethylation (before or after IN-A2213 formation) resulting in IN-L2953 and its conjugates. IN-A2213 (or oxamyl) may also metabolise to IN-N0079 and its further breakdown products, including IN-D2708. Oxamyl residues may ultimately be reincorporated into plant natural products.

Oxamyl was rapidly absorbed, extensively metabolised, and excreted in livestock. The major metabolites found in both lactating goats and laying hens were thiocyanate and radioactivity resulting from incorporation of the radioactivity into natural components (such as lactose). No oxamyl was observed in the whole animal studies. Characterisation of tissue residues demonstrated fragmentation of oxamyl into numerous polar components, many released only through proteolytic digestion of tissues. *In vitro* rumen fluid metabolism studies demonstrated that oxamyl was extensively metabolised prior to absorption in goats. Rumen studies also provided the basis for establishing the metabolic conversion of oxamyl to thiocyanate. In rumen fluid, oxamyl was hydrolysed to IN-A2213, which metabolised to IN-N0079 (oxamyl could also form IN-N0079 directly through a Beckmann type rearrangement). Cyanide displacement from IN-N0079 would be detoxified as thiocyanate. Metabolites resulting from the N-demethylation of oxamyl and/or IN-A2213 (*e.g.*, IN-L2953 and IN-KP532) were also observed in rumen incubations. Demethylated metabolites (IN-KP532 and IN-KV998) were observed in goat livers and goat urine.

Rat metabolism study is presented in the mammalian toxicology section of the Oxamyl Volume 3 B6. The major route of elimination for oxamyl in rats was *via* urine. In rats, IN-N0079 conversion to thiocyanate was not observed; however, conjugates of the principal metabolites were found. Urinary metabolites included conjugates of IN-A2213 and IN-L2953. Conjugates of IN-D2708 and IN-KP532 were also observed.

The similarity in oxamyl metabolism between animals and plants indicates that the overall pathway (Figure 3) is consistent and is well defined.

Figure 3 Comparison of oxamyl plant and animal metabolic pathways



P = based on data from GLP potato and tomato metabolism studies; early non GLP studies show consistent pathways with additional carbohydrate conjugates of IN-A2213 and IN-L2953

B.7.3 Magnitude of residue trials in plants

Residue studies supportive of the renewal representative uses are summarized below. Residues relevant to MRL setting and dietary exposure assessment are underlined within the residue summary tables. The residues

identified are the highest residues per trial corresponding with an allowed use under the renewal representative GAP (ex., any sampling interval equal to or greater than the PHI and any number of applications up to the allowed maximum number of applications).

B.7.3.1 Potato

The renewal representative use for potatoes is in the CEU Regulatory zone. Oxamyl 10GR is applied in furrow, at the rate of 1.0 kg a.s./ha, at planting (BBCH 00) with an 90-d (12-week) PHI specified. Sixteen residue trials (8 NEU; 8 SEU) were conducted with higher use rates (3.0 kg a.s./ha in furrow or 4.0 to 5.5 kg a.s./ha broadcast at transplant) and/or later applications (6 applications from BBCH 0 to 69 for a total application rate of 4.2 kg a.s./ha).

In all trials, the residues were <0.01 mg/kg. With the lower application rate of 1.0 kg a.s./ha, residues will remain <0.01 mg/kg.

Study submitted in the EU Dossier in 2001 and included in the first EU approval review.

B.7.3.1/01

Reference: --	**Report:**	Françon, B., Belgaid, R., Jetzer, M., Steiner, C. (2000); Magnitude of residues of oxamyl in root and tuber vegetables (potatoes) following application of Oxamyl 10G Formulation - Europe, season 1999 **DuPont Report No.:** DuPont-2407 **Guidelines:** Directive 91/414/EEC (1991)

1. Test material: Oxamyl 10GR
   Lot/Batch #: D1410-394
   Purity: 100 g a.s./kg

Summary (DAR): The study was to determine the magnitude of residue of Oxamyl in root and tuber vegetables (potato) grown in EU following treatment with Oxamyl in order to support the re-registration and the JMPR evaluation of this compound, under maximum use pattern.
Oxamyl residues in field potatoes were studied at 8 test locations in 1999: Greece (2 locations), Spain (2 locations), The Netherlands (2 locations), and United Kingdom (2 location). One broadcast application of Oxamyl with incorporation was made art each test site, at planting, targeting approximately 5.5. kg oxamyl/ha. The plot were sampled for tubers at normal harvest (83-156 DALA) at the 8 sites. Oxamyl residue concentrations were determined in potato tubers by HPLC/CS/UV, with a limit of quantification (LOQ) of 0.002 mg/kg and a limit of detection of 0.01 mg/kg. There were no detectable oxamyl residues found in any treated or untreated control potato samples. Oxamyl residue following VIDATE® 10G treatment are summerized in the following table:

Test No.	Test Location	DALA	Average oxamyl residues (mg/kg) [a], [b] Tuber
1	Kilada, Greece	119	ND
2	Perithori, Greece	121	ND
3	La Algaida, Spain	86	ND
4	Los Palacios, Spain	83	ND
5	Angeren, The Netherlands	156	ND
6	Huissen, The Netherlands	135	ND
7	Whaley, United Kingdom	144	ND
8	Melbourne, United Kingdom	137	ND

(a) The designation "ND" is used for treated samples for which no oxamyl residue could be detected (below the limit of detection, < 0.01 mg/kg). These values are averages of duplicate sample determination.

(b) There were no peaks found for oxamyl in any of the control-sample chromatograms.

The magnitude of residues in potatoes study DuPont-2407, originally submitted under EU Rev8 Point IIA 6.3.1.1 and conducted with test material Oxamyl 10GR, was conducted under guideline Directive 91/414/EEC (1991). A review of this study indicates that it fully meets the current guideline (OECD Test Guideline 509: Crop field trials) but it was not conducted according to the proposed GAP.

RMS comments and conclusion: The study was performed according to the EU guideline for the crop field trials but it was not performed according to the critical GAP supported. The application dose is higher than the 25% of tolerance of the GAP, anyway the application can be considered a worst case. In addition the analytical method used to determine the residue is not in compliance with the actual EU guideline on analytical method for residue. The study is not acceptable.

Study submitted in the EU Dossier in 2001 and included in the first EU approval review.

B.7.3.1/02

Reference: --	**Report:**	Françon, B., Bass, R.V., Jernberg, K.M. (2001); Magnitude of residues of oxamyl in potatoes following application of Oxamyl 10G Formulation - Europe, season 2000 **DuPont Report No.:** DuPont-3939, Revision No. 1 **Guidelines:** Directive 91/414/EEC (1991)

1. Test material: Oxamyl 10GR
   Lot/Batch #: D1410-394
   Purity: 100 g a.s./kg

Summary DAR: This study was to determine the magnitude of residues of oxamyl in potato tuber specimens from plants grown in Europe, following treatment, immediately prior to planting, with Oxamyl 10G, in order to support the reregistration and the JMPR evaluation of this active substance as well as the registration of Oxamyl 10G formulated product, under maximum use pattern. Oxamyl is a DuPont nematicidally and insecticidally active substance used in Oxamyl 10G nematicide/insecticide formulated product. Oxamyl 10G contains 10% (w/w) oxamyl.

Oxamyl residues in potatoes were studied at 9 test locations in Europe during the 2000 field season. Magnitude of residues trials were carried out in Greece (2 locations), Spain (2 locations), The Netherlands (1 location) and United Kingdom (4 locations). One application of oxamyl (as Oxamyl 10G) was applied at planting, at target rates of approximately 4-kg oxamyl/ha for early varieties (Test Nos. 8 and 9) and 5.5-kg oxamyl/ha for common varieties (Test Nos. 1 to 7). The plots were sampled at harvest. Immediately after sampling, the tubers were brushed free of soil or rinsed gently to remove adhering soil and were deep frozen before subsequent analysis. Oxamyl residue concentrations were determined in potatoes by high performance liquid chromatography with post-column derivatization followed by fluorescence detection (HPLC/PCD/Fluor), with a 0.010-mg/kg Limit of Quantification (LOQ) and a 0.005-mg/kg Limit of Detection (LOD).

Oxamyl residues in potatoes from Oxamyl 10G treatment are summarized in the following table:

Crop, Country, Location, Year	Test Item	No of Applications	kg as/ha	Days After Last Application	Average Oxamyl Residues, (mg/kg) [(a), (b)]
Potato					
Greece, Kilada, 2000	DPX-D1410-394	1	5.665	140	ND
Greece Perithori, 2000	DPX-D1410-394	1	5.665	111	ND
Spain Guadalcacin, 2000	DPX-D1410-394	1	5.665	109	ND
Spain Algaida, 2000	DPX-D1410-394	1	5.665	102	ND
The Netherlands, Gelderland, 2000	DPX-D1410-394	1	5.666	135	ND
UK Spalding, 2000	DPX-D1410-394	1	5.682	137	ND
UK, Telford, 2000	DPX-D1410-394	1	5.734	138	ND
UK Melbourne, 2000	DPX-D1410-394	1	3.931	80	0.008
UK Elmton, 2000	DPX-D1410-394	1	4.120	83	ND
Average:					0.005

(a) The designation "ND" is used for treated specimens for which no oxamyl residue could be detected (below the Limit of Detection, < 0.005 mg/kg). These values are averages of duplicate specimen determination. For the purposes of calculating averages, 0.005 mg/kg was used for specimens with no detectable (ND) residues when averaging with a specimen containing detectable residues.

(b) There were no peaks found for oxamyl in any of the control-specimen chromatograms.

Detectable residues of oxamyl, 0.01 mg/kg, were found in one specimen from one location (Test No. 8, early variety potatoes, 80 DALA). All other specimens had non-detectable residues (<0.005 mg/kg).
The average recovery of oxamyl from potato at fortification levels of 0.010-0.10 mg/kg (ppm) was 80±10% (Rel.St.Dev. = 12%) for 7 fortification recoveries.

The magnitude of residues in potatoes study DuPont-3939, Revision No. 1, originally submitted under EU Rev8 Point IIA 6.3.1.1 and conducted with test material Oxamyl 10GR, was conducted under guideline Directive 91/414/EEC (1991). A review of this study indicates that it fully meets the current guideline (OECD Test Guideline 509: Crop field trials) but it was not conducted according to the proposed GAP.

RMS comments and conclusion: The study was performed according to the EU guideline for the crop field trials but it was not performed according to the critical GAP supported. The application dose is higher than the 25% of tolerance of the GAP, anyway the application can be considered a worst case. In addition the analytical method used to determine the residue is not in compliance with the actual EU guideline on analytical method for residue. The study is not acceptable.

Study submitted to the EU for the first time in this submission.

B.7.3.1/03

Reference: CA 6.3.1/01	**Report:**	Boissinot, J.-C., Cairns, S.D., Ward, L. (2007); Magnitude of oxamyl residues in potatoes following application of Vydate® 10G formulation–Europe 2006 **DuPont Report No.:** DuPont-19526 **Guidelines:** 91/414/EEC **Deviations:** None **Testing Facility:** Charles River Laboratories (UK), Tranent, Edinburgh, Scotland, UK Testing Facility Report No.: 689844 **GLP:** Yes **Certifying Authority:** Department of Health (U.K.)

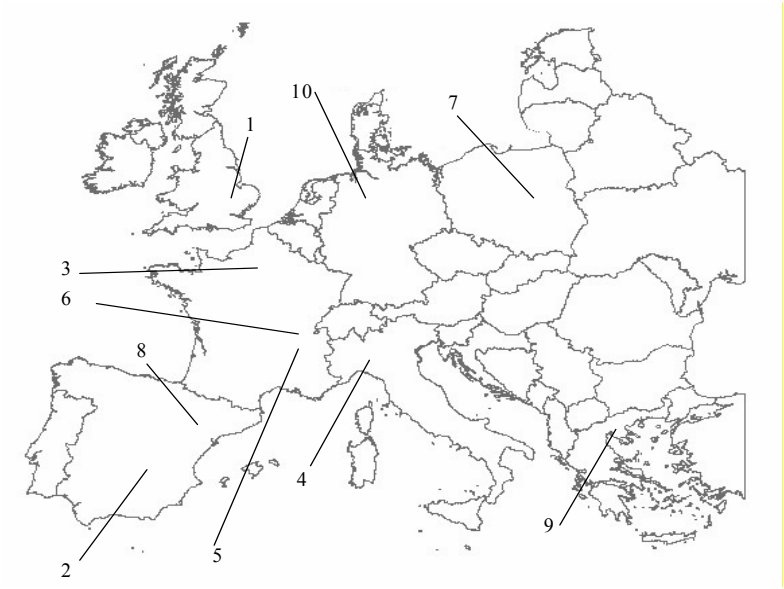
I. MATERIALS AND METHODS

The field program was conducted in 2006 at ten locations in the United Kingdom, Poland, Germany, France, Spain, Greece, and Italy. Ten test sites, all containing one control and one treated plot, were established in Europe. All trials were magnitude of residue tests. At each test site Oxamyl 10GR (DPX-D1410-477 or DPX-D1410-460) was applied once *via* granular soil application at the time of planting (Application A1). Application 1 (A1) was applied to main variety potatoes at a target application rate of 55.0 kg formulated product (fp)/ha (5.5 kg a.s./ha), at trials 1, 3-8, and 10. Oxamyl 10GR (DPX-D1410-477 or DPX-D1410-460) was applied to early variety potatoes at a target application rate of 40.0 kg formulated product (fp)/ha (4.0 kg a.s./ha) at trials 2 and 9.

For all trials, specimens of potatoes were collected at commercial harvest (92-153 days after application).

A total of ten magnitude of residue trials were conducted in United Kingdom, Poland, Germany, France, Spain, Greece, and Italy over one growing season (2006). A summary of these potato studies is given below. Locations of the trial sites are given in Figure 4.

Figure 4 Map: Oxamyl European potato test sites



No.	Location	No.	Location
1	St Osyth, Essex, England	6	Le Mas Rillier, Rhône-Alpes, France (south)
2	Olivares, Andalucia, Spain	7	Rozbity Kamień, Mazovian Region, Poland
3	Allouagne, Nord Pas-de-Calais, France (north)	8	Partida rec nou, Cami de l'Albi s/n, Alpicat, Lleida, Spain
4	Corana, Lombardia, Italy	9	Nea Magnesia, Thessaloniki, Central Macedonia, Greece
5	La Chapelle Villars, Rhône-Alpes, France (south)	10	Motterwitz, Saxony, Germany

A potato residue data summary (in mg/kg) is presented in Table 24.

To generate these data, the following analysis information pertains.

Analysis method: LC-MS method (DuPont-11125) developed as the oxamyl residue method for determining residues of oxamyl in/on crop matrices. This method is summarized in Oxamyl Volume 3 B5.

Analyte:	Oxamyl
Extraction:	Analyte extracted from crop matrix by homogenisation with an acetone, dichloromethane, petroleum ether mixture
Clean-up:	Aminopropyl SPE cartridge
Chromatography:	Reverse phase HPLC with C18 column
Detection:	Mass spectrometric detection (LC-MS) with 237.3 m/z ($M+NH_4$) used for quantification
Limit of Quantification:	0.005 mg/kg
Limit of Detection:	0.0033 mg/kg

Storage stability:

Treated specimens were stored at *ca* -18°C for no longer than 6 months between sampling and analysis.

Recovery data: Average recovery data for fortifications run concurrently with the treated samples are given in Table 24, to demonstrate the validity of the analytical method.

Table 24 Residues of oxamyl in potato tubers from supervised trials

Renewal representative use: CEU Regulatory zone; Oxamyl 10GR, 1.0 kg a.s./ha in furrow; application at planting (BBCH 00); 90-d PHI								
GLP and trial details	**Crop/ Variety**	**Country**	**Application rate (kg a.s./ha)**	**Crop growth stage at last application and at final sampling**	**Spray concentration (kg a.s./hL)**	**DALA[a] (days)**	**Residues found (mg/kg)[b]**	**Recovery data**
DuPont-19526 Trial No. 1 GLP 2006	Potato/ Maris Piper	England, St. Osyth	5.2	BBCH 00, 49	NA	148	nd	Mean recovery =87% ± 4%, RSD = 5 (n = 4) at 0.005 mg/kg fortification Mean recovery = 92% ± 8%, RSD = 9 (n = 4) at 0.10 mg/kg fortification
DuPont-19526 Trial No. 2 GLP 2006	Potato/ Carlita (early variety)	Spain, Olivares	4.08	BBCH 00, 49	NA	97	nd	Mean recovery =87% ± 4%, RSD = 5 (n = 4) at 0.005 mg/kg fortification Mean recovery = 92% ± 8%, RSD = 9 (n = 4) at 0.10 mg/kg fortification
DuPont-19526 Trial No. 3 GLP 2006	Potato/ Amila	N. France, Allouagne	5.61	BBCH 00, 49	NA	153	nd	Mean recovery =87% ± 4%, RSD = 5 (n = 4) at 0.005 mg/kg fortification Mean recovery = 92% ± 8%, RSD = 9 (n = 4) at 0.10 mg/kg fortification
DuPont-19526 Trial No. 4 GLP 2006	Potato/ Annabella	Italy, Corona	5.61	BBCH 00, 49	NA	102	nd	Mean recovery =87% ± 4%, RSD = 5 (n = 4) at 0.005 mg/kg fortification Mean recovery = 92% ± 8%, RSD = 9 (n = 4) at 0.10 mg/kg fortification

Table 24 Residues of oxamyl in potato tubers from supervised trials (continued)

Renewal representative use: CEU Regulatory zone; Oxamyl 10GR, 1.0 kg a.s./ha in furrow; application at planting (BBCH 00); 90-d PHI								
GLP and trial details	**Crop/ Variety**	**Country**	**Application rate (kg a.s./ha)**	**Crop growth stage at last application and at final sampling**	**Spray concentration (kg a.s./hL)**	**DALA[a] (days)**	**Residues found (mg/kg)[b]**	**Recovery data**
DuPont-19526 Trial No. 5 GLP 2006	Potato/ Europa	S. France, La Chapelle Villars	5.61	BBCH 00, 49	NA	120	nd	Mean recovery =87% ± 4%, RSD = 5 (n = 4) at 0.005 mg/kg fortification Mean recovery = 92% ± 8%, RSD = 9 (n = 4) at 0.10 mg/kg fortification
DuPont-19526 Trial No. 6 GLP 2006	Potato/ Mona Lisa	S. France, La Mas Rillier	5.61	BBCH 00, 49	NA	132	nd	Mean recovery =87% ± 4%, RSD = 5 (n = 4) at 0.005 mg/kg fortification Mean recovery = 92% ± 8%, RSD = 9 (n = 4) at 0.10 mg/kg fortification
DuPont-19526 Trial No.7 GLP 2006	Potato/ Irga	Poland, Rozbity Kamien	5.61	BBCH 00-03, 49	NA	135	nd	Mean recovery =87% ± 4%, RSD = 5 (n = 4) at 0.005 mg/kg fortification Mean recovery = 92% ± 8%, RSD = 9 (n = 4) at 0.10 mg/kg fortification
DuPont-19526 Trial No. 8 GLP 2006	Potato/ Kenebec	Spain, Lleida	5.61	BBCH 00, 48	NA	92	nd	Mean recovery =87% ± 4%, RSD = 5 (n = 4) at 0.005 mg/kg fortification Mean recovery = 92% ± 8%, RSD = 9 (n = 4) at 0.10 mg/kg fortification

Table 24 Residues of oxamyl in potato tubers from supervised trials (continued)

Renewal representative use: CEU Regulatory zone; Oxamyl 10GR, 1.0 kg a.s./ha in furrow; application at planting (BBCH 00); 90-d PHI								
GLP and trial details	**Crop/ Variety**	**Country**	**Application rate (kg a.s./ha)**	**Crop growth stage at last application and at final sampling**	**Spray concentration (kg a.s./hL)**	**DALA[a] (days)**	**Residues found (mg/kg)[b]**	**Recovery data**
DuPont-19526 Trial No. 9 GLP 2006	Potato/ Agria (early variety)	Greece, Nea Magnesia	4.00	BBCH 00, 49	NA	100	nd	Mean recovery =87% ± 4%, RSD = 5 (n = 4) at 0.005 mg/kg fortification Mean recovery = 92% ± 8%, RSD = 9 (n = 4) at 0.10 mg/kg fortification
DuPont-19526 Trial No. 10 GLP 2006	Potato/ Prinzess	Germany, Motterwitz	5.61	BBCH 01, 49	NA	124	nd	Mean recovery =87% ± 4%, RSD = 5 (n = 4) at 0.005 mg/kg fortification Mean recovery = 92% ± 8%, RSD = 9 (n = 4) at 0.10 mg/kg fortification

[a] DALA = Days after last application
[b] nd = analyte peak not detected or peak <LOD (<0.0033 mg/kg)

II. RESULTS AND DISCUSSION

The residue studies presented were carried out in seven EU countries, Italy, Spain, France, Poland, the United Kingdom, Germany, and Greece, and provide data relevant to conditions in the northern and southern European regions.

All of the analytical work associated with the studies was performed at Charles River Laboratories, Tranent EH33 2NE, Scotland.

Northern and southern Europe

In the northern and southern European regions, no residues were detected (<0.0033 mg/kg) in potatoes in any of the ten magnitude of residue trials conducted in 2006, in which oxamyl was applied at 4.0 to 5.6 kg a.s./ha at planting (application growth stages BBCH 00-01) and mature tubers were harvested at 92-153 days after application.

Recovery values for fresh control fortifications run concurrently with treated samples in all the trials are summarised above. Mean recovery = 87% ± 4%, RSD = 5 (n = 4) at 0.005 mg/kg fortification. Mean recovery = 92% ± 8%, RSD = 9 (n = 4) at 0.10 mg/kg fortification and the relative standard deviations were approximately 20% or less for all trials. Therefore, the analytical methods used performed well for the determination of oxamyl in treated crops.

III. CONCLUSION

Overall consistent residue behaviour of oxamyl on potatoes was found in one season of study in the EU for application and sampling. The residue data show that residues in potato tubers collected at maturity were not detected (<0.0033 mg/kg) although the application rate was 4.0 to 5.6 kg a.s./ha at planting (application growth stages BBCH 00-01), an exaggerated rate versus the representative use rate supported here.

(Boissinot, J.-C., Cairns, S.D., Ward, L., 2007)

RMS comments and conclusion: The study was performed according to the EU guideline for the crop field trials but it was not performed according to the critical GAP supported. The application dose is higher than the 25% of tolerance of the GAP, anyway the application can be considered a worst case. 10 trials were performed in the NEU and SEU (4 trials NEU, 6 trials SEU), for all trials the determined residue were below the LOQ (<0.005 mg/kg). In addition the analytical method used to determine the residue is in compliance with the actual EU guideline on analytical method for residue.

The study can be considered appropriate for the evaluation and can be considered acceptable as worst case.

Study submitted to the EU for the first time in this submission.

B.7.3.1/04

Reference: **CA 6.3.1/03**	**Report:**	Zenide, D., Jetzer, M., Smyser, B.P. (2002); Magnitude of residues of oxamyl in potatoes following in-furrow application of Oxamyl 5G formulation - southern Europe, season 2001 **DuPont Report No.:** DuPont-5989 **Guidelines:** EU 7029/VI/1995 Rev 5 (1997) App. B **Deviations:** None **Testing Facility:** Battelle Europe-Centre de Recherche de Geneve, Geneva, Switzerland Testing Facility Report No.: A-11-01-17 **GLP:** Yes

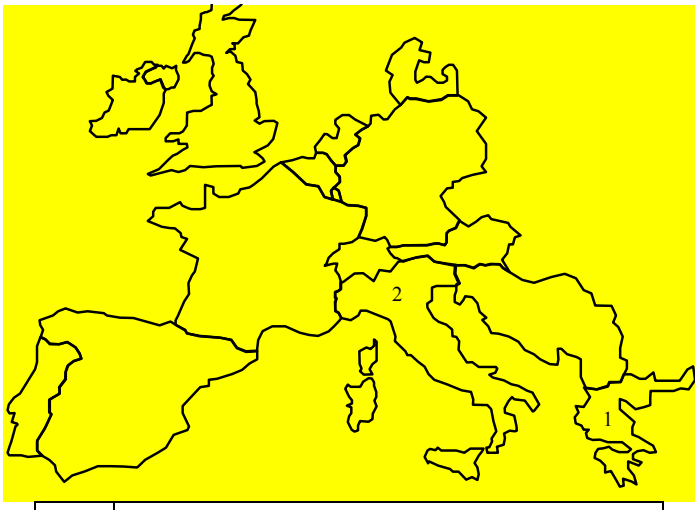
		Certifying Authority: Swiss Federal Department of the Interior (Switzerland)

I. MATERIALS AND METHODS

The field program was conducted in 2001 at 2 locations (one each in Italy and Greece). Oxamyl 5GR (DPX-D1410-419) was applied by in-furrow application with incorporation into the soil before planting at the rate of 3 kg a.s./ha. Specimens were collected at tuber maturity.

A total of 2 magnitudes of residue trials in southern Europe were conducted in one growing season (2001). A summary of these potato studies is given below. Locations of the potato trial sites are given in Figure 5.

Figure 5 Map: Oxamyl European potato test sites (DuPont-5989)



No.	Location
1	Polimilos, GR-50100, Kozani, Greece
2	Bagnarola di Budrio, 40050, Bologna, Italy

A potato residue data summary (in mg/kg) is presented in Table 25.

To generate these data, the following analysis and recovery information pertains.

Analysis method: N-methyl carbamate pesticide multiresidue method [DuPont-4722; HPLC with post-column derivatisation followed by fluorescence detection] for determining residues of oxamyl in/on a variety of crops. This method is summarized in Oxamyl Volume 3 B5.

Analyte:	Oxamyl
Internal Standard:	Trimethacarb (added prior to HPLC)
Extraction:	Analyte extracted from crop matrix with acetone
Clean-up:	Dichloromethane:petroleum ether partition followed by aminopropyl SPE
Chromatography:	HPLC
Post column hydrolysis:	0.2 M NaOH at 95°C
Derivatisation:	Fluorescent reagent at ambient temperature
Fluorescence Detection:	Excitation wavelength: 466 nm
	Emission wavelength: 330 nm
Limit of Quantification:	0.010 mg/kg
Limit of Detection:	0.005 mg/kg

Storage stability:

Treated specimens were stored at *ca* -18°C for less than 4 months between sampling and analysis.

Recovery data: Average recovery data for fortifications run concurrently with the treated samples are given in Table 25, to demonstrate the validity of the analytical method.

Table 25 Residues of oxamyl in potato tubers from supervised trials (DuPont-5989)

Renewal representative use: CEU Regulatory zone; Oxamyl 10GR, 1.0 kg a.s./ha in furrow; application at planting (BBCH 00); 90-d PHI								
GLP and trial details	**Crop**	**Country**	**Application rate (kg a.s./ha) Application method**	**Crop growth stage at application and at Sampling**	**Spray concentration (kg a.s./hL)**	**DALA[a]**	**Residues found (mg/kg)**	**Recovery data**
DuPont-5989 Trial No.1 GLP 2001	Potato/ Spunta	Greece, Polimilos, GR-50100, Kozani	3.0 In-furrow	BBCH 00, 49	not relevant for this test	112	ND[b]	Tubers: mean recovery = 75%, RSD = 2 (n = 2) in 0.010 mg/kg fortifications; mean recovery = 81%, RSD = 2 (n = 2) in 0.10 mg/kg fortifications
DuPont-5989 Trial No.2 GLP 2001	Potato/ Primura	Italy, Bagnarola di Budrio, 40050, Bologna	3.19 In-furrow	BBCH 00, 49	not relevant for this test	117	ND	Tubers: mean recovery = 75%, RSD = 2 (n = 2) in 0.010 mg/kg fortifications; mean recovery = 81%, RSD = 2 (n = 2) in 0.10 mg/kg fortifications

[a] DALA = Days after last application
[b] The designation "ND" is used for treated samples for which no oxamyl residue could be detected (below the limit of detection, <0.005 mg/kg).

II. RESULTS AND DISCUSSION

The residue studies presented were carried out in 2 different EU countries (Italy and Greece) and provide data relevant to conditions in the southern EU region.

All of the analytical work associated with the studies was performed at Battelle, Geneva Research Centres, CH-7, route de Drize, 1227 Carouge/Geneva, Switzerland. The analytical work was carried out during one time period for the 2001 residue trials.

Southern Europe

In the southern EU region, residues in potato tubers were not detected (<0.005 mg/kg) in samples collected at maturity (approximately 112-117 days after application) in the 2 magnitude of residue trials conducted in 2001 in which oxamyl was applied *via* in-furrow application at planting at approximately 3.0 kg oxamyl/ha.

Both sets of data show no detectable residues (<0.005 mg/kg) will be found when oxamyl is applied in accordance with GAP.

Mean recoveries (± RSD) for control potato samples fortified at 0.010 mg/kg and run concurrently with treated samples were 75% (±2%) and those fortified at 0.10 mg/kg were 81% (±2%). All the recoveries were within 70–110% and the relative standard deviations were less than 20% for all trials. Therefore, the analytical methods used performed well for the determination of oxamyl in treated crops.

III. CONCLUSION

Overall consistent residue behaviour of oxamyl on potatoes was found in one season of study in the southern EU for application and sampling. The residue data show that residues in potato tubers collected at maturity (approximately 112-117 days after application) were not detected (<0.005 mg/kg) although the application rate was 3 kg a.s./ha, an exaggerated rate versus the representative use rate supported here.

(Zenide, D., Jetzer, M., Smyser, B.P., 2002)

RMS comments and conclusion: The study was performed according to the EU guideline for the crop field trials but it was not performed according to the critical GAP supported. The application dose is higher than the 25% of tolerance of the GAP, anyway the application can be considered a worst case. 2 trials were performed in the SEU, for all trials the determined residue were below the LOQ (<0.01 mg/kg). In addition the analytical method used to determine the residue is in compliance with the actual EU guideline on analytical method for residue.

The study can be considered appropriate for the evaluation and can be considered acceptable as worst case.

Study submitted to the EU for the first time in this submission.

B.7.3.1/05

Reference: **CA 6.3.1/02**	**Report:**	Foster, A.C., Davidson, J., Cairns, S.D., Doran, A.M. (2003); Combined decline and magnitude of residues of oxamyl in main crop potatoes following applications of Oxamyl 10L formulation by drip irrigation - northern Europe, 2002 **DuPont Report No.:** DuPont-10297, Revision No. 1 **Guidelines:** EU 7029/VI/1995 Rev 5 (1997) App. B **Deviations:** None **Testing Facility:** Inveresk Research, Tranent, East Lothian, Scotland, UK Testing Facility Report No.: 682194, Amendment 2

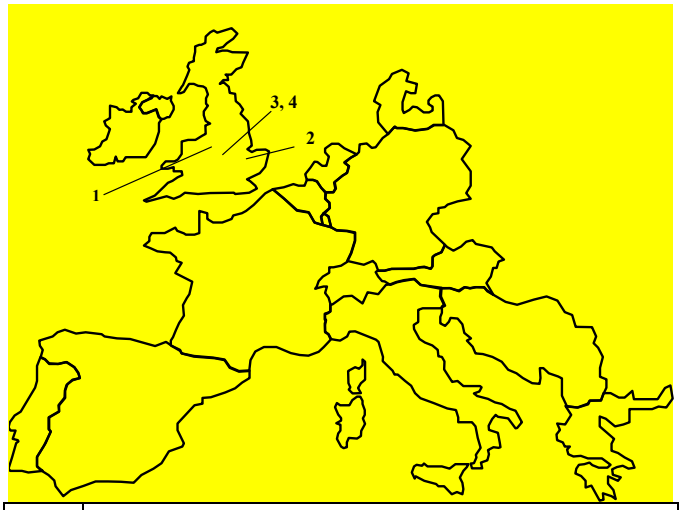
		GLP: Yes **Certifying Authority:** Department of Health (U.K.)

I. MATERIALS AND METHODS

The field program was conducted in 2002 at four locations in the United Kingdom. Oxamyl 10SL (DPX-D1410-424) was applied to potatoes six times at the rate of 0.7 kg a.s./ha/application for a seasonal application rate of 4.2 kg a.s./ha. The first application occurred on the day of planting. A 14-day spray interval was used between applications, with the last application occurring approximately 70 days after planting, when the crop was at growth stage BBCH 59–69.

A total of two magnitude of residue trials and two normal decline trials were conducted in the United Kingdom over one growing season (2002). A summary of these potato studies is given below. Locations of the trial sites are given in Figure 6.

Figure 6 Map: Oxamyl European potato test sites (DuPont-10297, Revision No. 1)



No.	Location
1	Newport, Shropshire, United Kingdom
2	Ely, Cambridgeshire, United Kingdom
3	Barrow-on-Trent, Derbyshire, United Kingdom
4	Melbourne, Derbyshire, United Kingdom

A potato residue data summary (in mg/kg) is presented in Table 26.

To generate these data, the following analysis and recovery information pertains.

Analysis method: LC-MS method (DuPont-11125) developed as the oxamyl residue method for determining residues of oxamyl in/on crop matrices. This method is summarized in Oxamyl Volume 3 B5.

Analyte:	Oxamyl
Extraction:	Analyte extracted from crop matrix by homogenisation with an acetone, dichloromethane, petroleum ether mixture
Clean-up:	Aminopropyl SPE cartridge
Chromatography:	Reverse phase HPLC with C18 column
Detection:	Mass spectrometric detection (LC-MS) with 237.3 m/z ($M+NH_4$) used for quantification
Limit of Quantification:	0.010 mg/kg
Limit of Detection:	0.007 mg/kg

Storage stability:

Treated specimens were stored at *ca* -18°C for no longer than 5 months between sampling and analysis.

Recovery data: Average recovery data for fortifications run concurrently with the treated samples are given in Table 26, to demonstrate the validity of the analytical method.

Table 26 Residues of oxamyl in potato tubers from supervised trials (DuPont-10297, Revision No. 1)

Renewal representative use: CEU Regulatory zone; Oxamyl 10GR, 1.0 kg a.s./ha in furrow; application at planting (BBCH 00); 90-d PHI								
GLP and trial details	**Crop/ Variety**	**Country**	**Application rate (kg a.s./ha)**	**Crop growth stage at last application and at sampling**	**Spray concentration (kg a.s./hL)**	**DALA[a] (days)**	**Residues found (mg/kg)**	**Recovery data**
DuPont-10297, Revision No. 1 Trial No. 1 GLP 2002	Potato/ Estima	United Kingdom, Newport, Shropshire	6 applications at 0.702	1) BBCH 59 2) BBCH 99	0.15- 0.19	73	nd[b]	Tuber: mean recovery = 70.4%, RSD = 2.4 (n = 4 in 0.010–0.10 mg/kg fortification range)
DuPont-10297, Revision No. 1 Trial No. 2 GLP 2002	Potato/ Maris Piper	United Kingdom, Ely, Cambridgeshire	6 applications at 0.702	1) BBCH 65 2) BBCH 97	0.15- 0.18	82	nd	Tuber: mean recovery = 70.4%, RSD = 2.4 (n = 4 in 0.010–0.10 mg/kg fortification range)
DuPont-10297, Revision No. 1 Trial No. 3 GLP 2002	Potato/ Russet Burbank	United Kingdom, Barrow-on-Trent, Derbyshire	6 applications at 0.702	1) BBCH 59 2) BBCH 59, 69, 69, 81, 99	0.15- 0.21	0 14 28 49 83	0.018 0.013 nd nd nd	Tuber: mean recovery = 70.4%, RSD = 2.4 (n = 4 in 0.010–0.10 mg/kg fortification range)
DuPont-10297, Revision No. 1 Trial No. 4 GLP 2002	Potato/ Wilja	United Kingdom, Melbourne, Derbyshire	6 applications at 0.702	1) BBCH 69 2) BBCH 69, 69, 70, 81, 99	0.17- 0.19	0 14 28 49 78	0.060 0.037 0.011 0.008 nd	Tuber: mean recovery = 70.4%, RSD = 2.4 (n = 4 in 0.010–0.10 mg/kg fortification range)

[a] DALA = Days after last application
[b] nd = analyte peak not detected (<0.007 mg/kg)

II. RESULTS AND DISCUSSION

The residue studies presented were carried out in one EU country, the United Kingdom, and provide data relevant to conditions in the northern European region.

All of the analytical work associated with the studies was performed at Charles River Laboratories, Tranent EH33 2NE, Scotland.

Northern Europe

In the northern European region, no residues were detected (<0.007 mg/kg) in mature potato tubers at 73-82 DALA in the four trials conducted in 2002 in which oxamyl was applied at 100% of GAP rate of application and at last application growth stages BBCH 59–69. In the two normal decline trials, residues declined from less than or equal to 0.060 mg/kg at 0 DALA until there were no residues detected (<0.007 mg/kg) at 78–83 DALA. The average half-life for oxamyl in potato tubers was 22.5 days.

All four sets of data show an overall consistent residue profile when oxamyl is applied under these conditions.

Recovery values for fresh control fortifications run concurrently with treated samples in all the trials were within 67.0–72.3% (n = 4) for potato tubers. Approximately 75% of the recoveries were within 70–110% and the relative standard deviations were less than 20% for all trials. Therefore, the analytical methods used performed well for the determination of oxamyl in treated crops.

III. CONCLUSION

Overall consistent residue behaviour of oxamyl on potatoes treated with Oxamyl 10SL was found in one season of study in the EU for application and sampling conducted to support the use of Oxamyl 10SL. The residue data show that residues decline in potato tubers with increasing DALA. Residues in potatoes from two decline trials decreased from less than or equal to 0.060 mg/kg immediately after the sixth and last application of oxamyl until no residues were detected (<0.007 mg/kg) at 78–83 DALA. The average half-life for oxamyl in potato tubers was 22.5 days. The residue data show that residues in potato tubers collected at maturity (approximately 73-83 DALA) were not detected (<0.007 mg/kg).

(Foster, A.C., Davidson, J., Cairns, S.D., Doran, A.M., 2003)

RMS comments and conclusion: The study was performed according to the EU guideline for the crop field trials. Four trials were conducted in the NEU at application rate according to the critical GAP supported with 6 application, instead one application as in the GAP supported. For all trials the determined residues were below the LOD (<0.007 mg/kg). In addition the analytical method used to determine the residue is in compliance with the actual EU guideline on analytical method for residue.

The study can be considered useful for the decline of residues.

B.7.3.2 Tomato

The renewal representative use for tomatoes is for use on tomatoes under protection. Oxamyl 10SL is applied at 5.5 kg a.s. 30 days before transplant (preplant solarisation), then at transplanting (2.0 kg a.s./ha) followed by three applications at 1.0 kg a.s./ha/application with a 10-day retreatment interval and a 28-day PHI.

Twenty-two residue trials were conducted on protected tomatoes including cherry tomatoes according to the in-season use pattern (the trials are divided in different plots where the different plots received an application of 2.0 kg a.s./ha followed by 1-3 applications with a rate of 1 kg a.s./ha).

In all trials, the residues were <0.01 mg/kg and are comparable to those including the addition of the pre-planting solarisation application according to the renewal representative use for tomatoes under protection (for details please refer to Point CA 6.3.4 in this document).

Study submitted to the EU for the first time in this submission.

B.7.3.2/01

Reference: **CA 6.3.2/02**	**Report:**	Boissinot, J.-C., Cairns, S.D., Ward, L. (2007b); Decline and magnitude of oxamyl residues in protected tomatoes (fruiting vegetables, solanacea) following application of Vydate® 10L formulation *via* drip irrigation - southern Europe 2006 **DuPont Report No.:** DuPont-19519, Revision No. 1 **Guidelines:** Directive 91/414/EEC **Deviations:** None **Testing Facility:** Charles River Laboratories (UK), Tranent, Scotland, UK **Testing Facility Report No.:** 689802 **GLP:** Yes **Certifying Authority:** Department of Health (U.K.), Entidad Nacional de Acreditacion (ENAC) (Spain), Groupe Interministeriel des Produits Chimiques (GIPC) (Paris, France), Ministero delle Politiche Agricole e Forestali (Italy), Ministry of Economy and Finance-Directorate General-General Chemical State Laboratory-Division of Environment (Greece)

Study submitted to the EU for the first time in this submission.

B.7.3.2/02

Reference: **CA 6.3.2/01**	**Report:**	Boissinot, J.-C., Cairns, S.D., Ward, L. (2007a); Decline and magnitude of oxamyl residues in protected cherry tomatoes (fruiting vegetables, solanacea) following application of Vydate® 10L formulation *via* drip irrigation - southern Europe 2006 **DuPont Report No.:** DuPont-19521 **Guidelines:** Directive 91/414/EEC **Deviations:** None **Testing Facility:** Charles River Laboratories (UK), Tranent, Scotland, UK Testing Facility Report No.: 689865 **GLP:** Yes **Certifying Authority:** Department of Health (U.K.), Entidad Nacional de Acreditacion (ENAC) (Spain), Groupe Interministeriel des Produits Chimiques (GIPC) (Paris, France), Ministero delle Politiche Agricole e Forestali (Italy), Ministry of Economy and Finance-Directorate General-General Chemical State Laboratory-Division of Environment (Greece)

I. MATERIALS AND METHODS

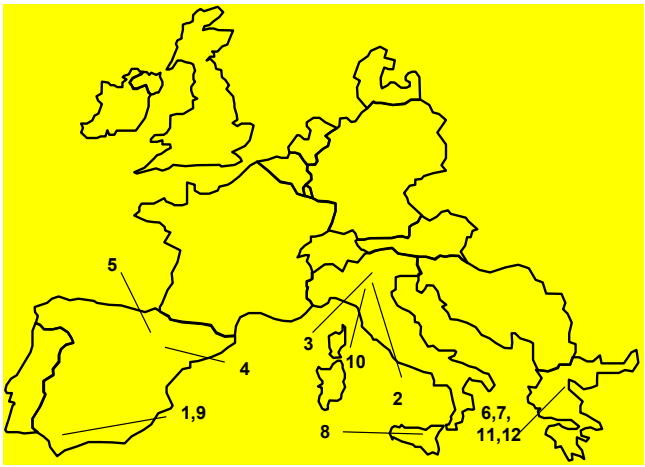
A field program was conducted in 2006 at twelve locations in Spain, Greece, and Italy. Eight trials were conducted on tomatoes and 4 trials were conducted on cherry tomatoes. Oxamyl 10SL (DPX-D1410-488) was applied three-four times *via* drip irrigation or representative technique. An application was made to each treated plot immediately after transplanting. Three treated plots at each trial site received two additional applications (Treatments 2, 3, 4). The other two treated plots at each trial site received three additional applications (Treatment 5, 6). These additional applications occurred at 10 day intervals triggered by the predicted first commercial harvest.

The first application was applied at a target application rate of 20.0 L formulated product (fp)/ha (2.0 kg a.s./ha). All other applications were applied at a target application rate of 10.0 L formulated product (fp)/ha (1.0 kg a.s./ha) for a seasonal application rate of 4.0 or 5.0 kg a.s./ha, respectively. Citric acid was used as an additive for all applications in all trials.

For all trials, specimens of protected tomatoes and cherry tomatoes were collected at -0 and 21 (Treatments 2 and 5), 28 (Treatments 3 and 6), and 35, 42, and 49 (Treatments 4 and 6) days after last application (DALA).

A total of twelve reverse decline residue trials were conducted in Spain, Italy, and Greece over one growing season (2006). A summary of these protected tomato and cherry tomato studies are given below. Locations of the trial sites are given in Figure 7.

Figure 7 Map: Oxamyl European protected tomato, including cherry tomato, test sites



No.	Location	No.	Location
1	Los Palacios, Andalucia, Spain	7	Nea Magnesia, Thessaloniki, Central Macedonia, Greece
2	Triginto di Mediglia, Lombardia, Italy	8	Contrada Pozzo Bollente, Vittoria, Italy
3	Roncoferraro, Lombardia, Italy	9	Los Palacios, Andalucia, Spain
4	Bellcaire d'Urgell, Lleida, Spain	10	Ascoli Piceno, Italy
5	Partida Foutanet, Lleida, Spain	11	Profitis, Thessaloniki, Central Macedonia, Greece
6	Profitis, Thessaloniki, Central Macedonia, Greece	12	Nea Magnesia, Thessaloniki, Central Macedonia, Greece

A protected tomato, including cherry tomato, residue data summary (in mg/kg) is presented in Table 27.

To generate these data, the following analysis information pertains.

Analysis method: LC-MS method (DuPont-11125) developed as the oxamyl residue method for determining residues of oxamyl in/on crop matrices. This method is summarized in Oxamyl Volume 3 B5.

Analyte:	Oxamyl
Extraction:	Analyte extracted from crop matrix by homogenisation with an acetone, dichloromethane, petroleum ether mixture
Clean-up:	Aminopropyl SPE cartridge
Chromatography:	Reverse phase HPLC with C18 column
Detection:	Mass spectrometric detection (LC-MS) with 237.3 m/z ($M+NH_4$) used for quantification
Limit of Quantification:	0.010 mg/kg
Limit of Detection:	0.007 mg/kg

Storage stability:

Treated specimens were stored at *ca* -18°C for no longer than 7 months between sampling and analysis.

Recovery data: Average recovery data for fortifications run concurrently with the treated samples are given in Table 27, to demonstrate the validity of the analytical method.

Table 27 Residues of oxamyl in protected tomatoes, including cherry tomatoes, from supervised trials

Renewal representative GAP: Oxamyl 10SL, 5.5 kg a.s. 30 days before transplant (preplant solarisation); 2.0 kg a.s. at transplanting followed by 3 applications at 1.0 kg a.s./ha/application, 10 days apart; 28-d PHI; all applications *via* drip irrigation								
GLP and trial details	**Crop/ Variety**	**Country**	**Application rate (kg a.s./ha)**	**Crop growth stage at last application and at final sampling**	**Spray concentration (kg a.s./hL)**	**DALA[a] (days)**	**Residues found (mg/kg)**	**Recovery data**
DuPont-19519, Revision No. 1 Trial No. 1 GLP 2006	Protected Tomato/ Eldiez	Spain, Los Palacios	2.07 + 1.04 + 1.04 2.07 + 1.04 + 1.04 2.07 + 1.04 + 1.04	BBCH 12+64+72, 81 BBCH 12+62+65, 81 BBCH 12+61+65, 81	NA NA NA	-0 (A3-1h) 21 28 35 42 49	nd[b] nd nd nd nd nd	Mean recovery = 76% ± 11%, RSD = 14 (n = 7) at 0.010 mg/kg fortification Mean recovery = 77% ± 10%, RSD = 13 (n = 8) at 0.10 mg/kg fortification
			2.07 + 1.04 + 1.04 + 1.04 2.07 + 1.04 + 1.04 + 1.04	BBCH 12+61+64+72, 81 BBCH 12+61+62+65, 81	NA NA	-0 (A4-1h) 21 28 35 42 49	nd nd nd nd nd nd	
DuPont-19519, Revision No. 1 Trial No. 2 GLP 2006	Protected Tomato/ Oskar	Italy, Triginto di Mediglia	2.07 + 1.04 + 1.04 2.07 + 1.04 + 1.04 2.07 + 1.04 + 1.04	BBCH 14+64+72, 83/87-89 BBCH 14+63+64, 83/87-89 BBCH 14+19-51+63-64, 87-89	NA NA NA	-0 (A3-1h) 21 28 35 42 49	0.008 nd nd nd nd nd	Mean recovery = 76% ± 11%, RSD = 14 (n = 7) at 0.010 mg/kg fortification Mean recovery = 77% ± 10%, RSD = 13 (n = 8) at 0.10 mg/kg fortification
			2.07 + 1.04 + 1.04 + 1.04 2.07 + 1.04 + 1.04 + 1.04	BBCH 14+62+64+72, 83/87-89 BBCH 14+19+63+64, 89	NA NA	-0 (A4-1h) 21 28 35 42 49	0.031 nd nd nd nd nd	

Table 27 Residues of oxamyl in protected tomatoes, including cherry tomatoes, from supervised trials (continued)

Renewal representative GAP: Oxamyl 10SL, 5.5 kg a.s. 30 days before transplant (preplant solarisation); 2.0 kg a.s. at transplanting followed by 3 applications at 1.0 kg a.s./ha/application, 10 days apart; 28-d PHI; all applications *via* drip irrigation								
GLP and trial details	**Crop/ Variety**	**Country**	**Application rate (kg a.s./ha)**	**Crop growth stage at last application and at final sampling**	**Spray concentration (kg a.s./hL)**	**DALA[a] (days)**	**Residues found (mg/kg)**	**Recovery data**
DuPont-19519, Revision No. 1 Trial No. 3 GLP 2006	Protected Tomato/ Carso	Italy, Ronco-ferraro	2.07 + 1.04 + 1.04	BBCH 14+61+63-71, 83	NA	-0 (A3-1h) 21	nd nd	Mean recovery = 76% ± 11%, RSD = 14 (n = 7) at 0.010 mg/kg fortification Mean recovery = 77% ± 10%, RSD = 13 (n = 8) at 0.10 mg/kg fortification
			2.07 + 1.04 + 1.04	BBCH 14+52+62, 83	NA	28	nd	
			2.07 + 1.04 + 1.04	BBCH 14+52+61, 86	NA	35 42 49	nd nd nd	
			2.07 + 1.04 + 1.04 + 1.04	BBCH 14+52+61+63-71, 83	NA	-0 (A4-1h) 21	nd nd	
			2.07 + 1.04 + 1.04 + 1.04	BBCH 14+21+52+62, 87-89	NA	28 35 42 49	nd nd nd nd	
DuPont-19519, Revision No. 1 Trial No. 4 GLP 2006	Protected Tomato/ Caramba	Spain, Lleida	2.07 + 1.04 + 1.04	BBCH 13-14+72+73, 78-82	NA	-0 (A3-1h) 21	nd nd	Mean recovery = 76% ± 11%, RSD = 14 (n = 7) at 0.010 mg/kg fortification Mean recovery = 77% ± 10%, RSD = 13 (n = 8) at 0.10 mg/kg fortification
			2.07 + 1.04 + 1.04	BBCH 13-14+51+72-73, 78-82	NA	28	nd	
			2.07 + 1.04 + 1.04	BBCH 13-14+26-27+22, 82-85	NA	35 42 49	nd nd nd	
			2.07 + 1.04 + 1.04 + 1.04	BBCH 13-14+29-51+72+73, 78-82	NA	-0 (A4-1h) 21 28	nd nd nd	
			2.07 + 1.04 + 1.04 + 1.04	BBCH 13-14+19+51+72-73, 83-85	NA	35 42 49	nd nd nd	

Table 27 Residues of oxamyl in protected tomatoes, including cherry tomatoes, from supervised trials (continued)

Renewal representative GAP: Oxamyl 10SL, 5.5 kg a.s. 30 days before transplant (preplant solarisation); 2.0 kg a.s. at transplanting followed by 3 applications at 1.0 kg a.s./ha/application, 10 days apart; 28-d PHI; all applications *via* drip irrigation								
GLP and trial details	**Crop/ Variety**	**Country**	**Application rate (kg a.s./ha)**	**Crop growth stage at last application and at final sampling**	**Spray concentration (kg a.s./hL)**	**DALA[a] (days)**	**Residues found (mg/kg)**	**Recovery data**
DuPont-19519, Revision No. 1 Trial No. 5 GLP 2006	Protected Tomato/ Caramba	Spain, Lleida	2.07 + 1.04 + 1.04	BBCH 13-14+ 71-72+75, 83	NA	-0 (A3-1h) 21	nd nd	Mean recovery = 76% ± 11%, RSD = 14 (n = 7) at 0.010 mg/kg fortification Mean recovery = 77% ± 10%, RSD = 13 (n = 8) at 0.10 mg/kg fortification
			2.07 + 1.04 + 1.04	BBCH 13-14+61+72, 78-83	NA	28	nd	
			2.07 + 1.04 + 1.04	BBCH 13-14+51+ 63-64, 78-85	NA	35 42 49	nd nd nd	
			2.07 + 1.04 + 1.04 + 1.04	BBCH 13-14+ 29-51+72+73, 83	NA	-0 (A4-1h) 21 28	nd nd nd	
			2.07 + 1.04 + 1.04 + 1.04	BBCH 13-14+19+51+ 72-73, 78-86	NA	35 42 49	nd nd nd	
DuPont-19519, Revision No. 1 Trial No. 6 GLP 2006	Protected Tomato/ Belladonna	Greece, Profitis	2.00 + 1.00 + 1.00	BBCH 12-13+ 53-61+66-72, 89	NA	-0 (A3-1h) 21	nd nd	Mean recovery = 76% ± 11%, RSD = 14 (n = 7) at 0.010 mg/kg fortification Mean recovery = 77% ± 10%, RSD = 13 (n = 8) at 0.10 mg/kg fortification
			2.00 + 1.00 + 1.00	BBCH 12-13+ 51-52+64-71, 89	NA	28	nd	
			2.00 + 1.00 + 1.00	BBCH 12-13+16+53, 89	NA	35 42 49	nd nd nd	
			2.00 + 1.00 + 1.00 + 1.00	BBCH 12-13+51+ 53-61+66-72, 89	NA	-0 (A4-1h) 21 28	nd nd nd	
			2.00 + 1.00 + 1.00 + 1.00	BBCH 12-13+16+ 51-52+64-71, 89	NA	35 42 49	nd nd nd	

Table 27 Residues of oxamyl in protected tomatoes, including cherry tomatoes, from supervised trials (continued)

Renewal representative GAP: Oxamyl 10SL, 5.5 kg a.s. 30 days before transplant (preplant solarisation); 2.0 kg a.s. at transplanting followed by 3 applications at 1.0 kg a.s./ha/application, 10 days apart; 28-d PHI; all applications *via* drip irrigation								
GLP and trial details	**Crop/ Variety**	**Country**	**Application rate (kg a.s./ha)**	**Crop growth stage at last application and at final sampling**	**Spray concentration (kg a.s./hL)**	**DALA[a] (days)**	**Residues found (mg/kg)**	**Recovery data**
DuPont-19519, Revision No. 1 Trial No. 7 GLP 2006	Protected Tomato/ Alma	Greece, Nea Magnesia	2.00 + 1.00 + 1.00	BBCH 12-13+ 62-63+66-72, 89	NA	-0 (A3-1h) 21	nd nd	Mean recovery = 76% ± 11%, RSD = 14 (n = 7) at 0.010 mg/kg fortification Mean recovery = 77% ± 10%, RSD = 13 (n = 8) at 0.10 mg/kg fortification
			2.00 + 1.00 + 1.00	BBCH 12-13+52+ 64-71, 89	NA	28	nd	
			2.00 + 1.00 + 1.00	BBCH 12-13+ 25-26+60-62, 89	NA	35 42 49	nd nd nd	
			2.00 + 1.00 + 1.00 + 1.00	BBCH 12-13+26-27+62-63+66-72, 89	NA	-0 (A4-1h) 21 28	nd nd nd	
			2.00 + 1.00 + 1.00 + 1.00	BBCH 12-13+25-26+52+64-71, 89	NA	35 42 49	nd nd nd	
DuPont-19519, Revision No. 1 Trial No. 8 GLP 2006	Protected Tomato/ Panarea	Italy, Vittoria	2.00 + 1.03 + 1.02	BBCH 102+64+67, 89	NA	-0 (A3-1h) 21	0.010 nd	Mean recovery = 76% ± 11%, RSD = 14 (n = 7) at 0.010 mg/kg fortification Mean recovery = 77% ± 10%, RSD = 13 (n = 8) at 0.10 mg/kg fortification
			2.02 + 1.02 + 1.02	BBCH 102+62+65, 89	NA	28	nd	
			2.04 + 1.02 + 1.02	BBCH 102+61+63, 89	NA	35 42 49	nd nd nd	
			2.04 + 1.02 + 1.02 + 1.02	BBCH 102+62+64+ 67, 89	NA	-0 (A4-1h) 21 28	0.012 nd nd	
			2.04 + 1.01 + 1.02 + 1.02	BBCH 102+61+62+ 65, 89	NA	35 42 49	nd nd nd	

Table 27 Residues of oxamyl in protected tomatoes, including cherry tomatoes, from supervised trials (continued)

Renewal representative GAP: Oxamyl 10SL, 5.5 kg a.s. 30 days before transplant (preplant solarisation); 2.0 kg a.s. at transplanting followed by 3 applications at 1.0 kg a.s./ha/application, 10 days apart; 28-d PHI; all applications *via* drip irrigation								
GLP and trial details	**Crop/ Variety**	**Country**	**Application rate (kg a.s./ha)**	**Crop growth stage at application and at sampling**	**Spray concentration (kg a.s./hL)**	**DALA[a] (days)**	**Residues found (mg/kg)**	**Recovery data**
DuPont-19521 Trial No. 1 GLP 2006	Protected cherry tomatoes/ Lupita	Spain, Los Palacios	2.07 + 1.04 + 1.04	BBCH 12+71+81, 81, 83	NA	-0 (A3-1h) 21	nd nd	Mean recovery = 76% ± 6%, RSD = 8 (n = 6) at 0.010 mg/kg fortification
			2.07 + 1.04 + 1.04	BBCH 12+66+71, 83	NA	28	nd	
			2.07 + 1.04 + 1.04	BBCH 12+63+66, 83, 83,83	NA	35 42 49	nd nd nd	Mean recovery = 76% ± 6%, RSD = 8 (n = 6) at 0.10 mg/kg fortification
			2.07 + 1.04 + 1.04 + 1.04	BBCH 12+65+71+81, 81, 83	NA	-0 (A4-1h) 21 28	0.019 nd nd	
			2.07 + 1.04 + 1.04 + 1.04	BBCH 12+63+66+71, 83,83, 83, 85	NA	35 42 49	nd nd nd	
DuPont-19521 Trial No. 2 GLP 2006	Protected cherry tomatoes/ Carminion de reuter	Italy, Ascoli Picelo	2.02 + 1.00 + 1.01	BBCH 18+64+ 81, 80-81 85	NA	-0 (A3-1h) 21	nd nd	Mean recovery = 76% ± 6%, RSD = 8 (n = 6) at 0.010 mg/kg fortification
			2.00 + 1.00 + 1.01	BBCH 18+51+77, 85	NA	28	nd	
			2.03 + 1.01 + 1.00	BBCH 18+25+54, 85, 86-87, 87-88	NA	35 42 48	nd nd nd	Mean recovery = 76% ± 6%, RSD = 8 (n = 6) at 0.10 mg/kg fortification
			2.01 + 1.01 + 1.01 + 1.00	BBCH 18+29+64+82, 80-81, 85	NA	-0 (A4-1h) 21 28	nd nd nd	
			2.01 + 1.02 + 1.01 + 1.01	BBCH 18+24+51+77, 85, 86-87, 87-88, 88-89	NA	35 41 49	nd nd nd	

Table 27 Residues of oxamyl in protected tomatoes, including cherry tomatoes, from supervised trials (continued)

Renewal representative GAP: Oxamyl 10SL, 5.5 kg a.s. 30 days before transplant (preplant solarisation); 2.0 kg a.s. at transplanting followed by 3 applications at 1.0 kg a.s./ha/application, 10 days apart; 28-d PHI; all applications *via* drip irrigation								
GLP and trial details	**Crop/ Variety**	**Country**	**Application rate (kg a.s./ha)**	**Crop growth stage at application and at sampling**	**Spray concentration (kg a.s./hL)**	**DALA[a] (days)**	**Residues found (mg/kg)**	**Recovery data**
DuPont-19521 Trial No. 3 GLP 2006	Protected cherry tomatoes/ Winner	Greece, Profitis	2.00 + 1.00 + 1.00	BBCH 12-13+66-72+ 72-74, 72-74, 89	NA	-0 (A3-1h) 21	nd nd	Mean recovery = 76% ± 6%, RSD = 8 (n = 6) at 0.010 mg/kg fortification Mean recovery = 76% ± 6%, RSD = 8 (n = 6) at 0.10 mg/kg fortification
			2.00 + 1.00 + 1.00	BBCH 12-13+63-65+ 67-73, 89	NA	29	nd	
			2.00 + 1.00 + 1.00	BBCH 12-13+52-54+ 65-71, 89, 89,89	NA	35 42 49	nd nd nd	
			2.00 + 1.00 + 1.00 + 1.00	BBCH 12-13+60-63+66-72+72-74, 72-74, 89	NA	-0 (A4-1h) 21 29	nd nd nd	
			2.00 + 1.00 + 1.00 + 1.00	BBCH 12-13+25-27+63-65+67-73, 89, 89,89,89	NA	36 43 50	nd nd nd	

Table 27 Residues of oxamyl in protected tomatoes, including cherry tomatoes, from supervised trials (continued)

Renewal representative GAP: Oxamyl 10SL, 5.5 kg a.s. 30 days before transplant (preplant solarisation); 2.0 kg a.s. at transplanting followed by 3 applications at 1.0 kg a.s./ha/application, 10 days apart; 28-d PHI; all applications *via* drip irrigation								
GLP and trial details	**Crop/ Variety**	**Country**	**Application rate (kg a.s./ha)**	**Crop growth stage at application and at sampling**	**Spray concentration (kg a.s./hL)**	**DALA[a] (days)**	**Residues found (mg/kg)**	**Recovery data**
DuPont-19521 Trial No. 4 GLP 2006	Protected cherry tomatoes/ Winner	Greece, Nea Magnesia	2.00 + 1.00 + 1.00	BBCH 12-13+62-64+66-73, 72, 89	NA	-0 (A3-1h)	nd	Mean recovery = 76% ± 6%, RSD = 8 (n = 6) at 0.010 mg/kg fortification Mean recovery = 76% ± 6%, RSD = 8 (n = 6) at 0.10 mg/kg fortification
			2.00 + 1.00 + 1.00			20	nd	
			2.00 + 1.00 + 1.00	BBCH 12-13+55-57+ 64-72, 89	NA	28	nd	
				BBCH 12-13+26-27+ 61-64, 89, 89,89	NA	34	nd	
						41	nd	
						49	nd	
			2.00 + 1.00 + 1.00 + 1.00	BBCH 12-13+52-55+62-64+66-73, 72, 89	NA	-0 (A4-1h)	nd	
			2.00 + 1.00 + 1.00 + 1.00			20	nd	
						28	nd	
				BBCH 12-13+26-27+ 55-57+64-72, 89, 89 89,89	NA	35	nd	
						42	nd	
						49	nd	

[a] DALA = Days after last application
[b] nd = analyte peak not detected or peak <LOD (<0.007 mg/kg)

II. RESULTS AND DISCUSSION

The residue studies presented were carried out in three EU countries, Italy, Spain, and Greece, and provide data relevant to conditions in the southern European region for protected tomatoes.

All of the analytical work associated with the studies was performed at Charles River Laboratories, Tranent EH33 2NE, Scotland.

Southern Europe

In the southern European region, no residues were detected (<0.007 mg/kg) in protected tomatoes or cherry tomatoes in the twelve reverse decline residue trials conducted in 2006 in which oxamyl was applied in accordance with the defined good agricultural practice.

The average half-life for oxamyl in protected tomatoes, including cherry tomatoes, following the method of application studied, could not be determined since, for the majority of the samples analysed, no residues were detected.

Recovery values for fresh control fortifications run concurrently with treated samples in all the trials are summarised above. Mean recovery from tomatoes fortified at 0.010 mg/kg was 76% ± 11%, RSD = 14 (n = 7) while mean recovery from tomatoes fortified at 0.10 mg/kg was 77% ± 10%, RSD = 13 (n = 8). Mean recovery from cherry tomatoes fortified at 0.010 mg/kg was 76% ± 6%, RSD = 8 (n = 6) while the mean recovery from cherry tomatoes fortified at 0.10 mg/kg was 76% ± 6%, RSD = 8 (n = 6). Therefore, the analytical methods used performed well for the determination of oxamyl in treated crops.

III. CONCLUSION

Overall consistent residue behaviour of oxamyl on protected tomatoes, including cherry tomatoes, was found in one season of study in the EU for application and sampling conducted according to the in-season use pattern. The residue data show that residues were not detected (<0.007 mg/kg) in protected tomatoes, including cherry tomatoes, collected 28 days or more after the last application.

(Boissinot, J.-C., Cairns, S.D., Ward., L., 2007b;
Boissinot, J.-C., Cairns, S.D., Ward., L., 2007a)

RMS comments and conclusion: The studies conducted in compliance with the EU guideline for the crop field trials. ~~Twenteen~~ Twelve trials were conducted in the SEU at application rate according to the critical GAP supported for all trials the determined residues were below the LOD (<0.007 mg/kg). In addition, the analytical method is compliance with the actual EU guideline on analytical method for residue.

The study can considered useful for the residues evalution and can be considered acceptable.

Study submitted to the EU for the first time in this submission.

B.7.3.2/03

Reference: **CA 6.3.2/03**	**Report:**	Haigh, I., Hoskins, M. (2011); Decline and magnitude of oxamyl residues in protected tomatoes, including cherry tomatoes (fruiting vegetables, solanacea) following application of Oxamyl 10L formulation *via* drip irrigation - southern Europe, 2009-10 **DuPont Report No.:** DuPont-29313 **Guidelines:** Directive 91/414/EEC **Deviations:** None **Testing Facility:** Charles River Laboratories (UK), Tranent, Scotland, UK

		Testing Facility Report No.: 695156 **GLP:** Yes **Certifying Authority:** Department of Health (U.K.), Entidad Nacional de Acreditacion (ENAC) (Spain)

I. MATERIALS AND METHODS

The field program was conducted in 2009-10 at fourteen locations in Spain, Greece, and Italy. Each test contained one control plot and five treated plots. Oxamyl (DPX-D1410-518, Oxamyl 10SL) was applied *via* drip irrigation or representative technique. An application was made to each treated plot immediately after transplanting followed by one, two or three applications with a targeted 10±1 day re-treatment interval between applications 2-4 and a minimum 10 ± 1 day re-treatment interval between applications 1 and 2.

The first application was applied at a target application rate of 20.0 L formulated product (fp)/ha (2.0 kg a.s./ha). All other applications were applied at a target application rate of 10.0 L fp/ha (1.0 kg a.s./ha) for a seasonal application rate of 3.0 to 5.0 kg a.s./ha, respectively. All applications were made in acidified water (pH 5–6) but no surfactant was added to the tank mix.

The following table summarizes the targeted design for each test conducted.

Table 28 Targeted test design (DuPont-29313)

Test no.	Test type[a]	Formulation	Number of applications	Rate per application (kg a.s./ha)	Retreatment interval (days)	Application volume[b] (L/ha)	DALA[c] (days)
1, 2, 3	revDEC	Oxamyl 10SL	4	A1: 2.0 A2-A4: 1.0	A1: immediately after transplant A2-A4: 10 ± 1	2000	30
			4	A1: 2.0 A2-A4: 1.0	A1: immediately after transplant A2-A4: 10 ± 1	2000	45
			3	A1: 2.0 A2-A3: 1.0	A1: immediately after transplant A2-A3: 10 ± 1	2000	70
			2	A1: 2.0 A2: 1.0	A1: immediately after transplant A2: 10 ± 1	2000	80
			4	A1: 2.0 A2-A4: 1.0	A1: immediately after transplant A1-A4: 10 ± 1	2000	Not specified
4, 5, 6, 7	revDEC	Oxamyl 10SL	2	A1: 2.0 A2: 1.0	A1: immediately after transplant A2: 10 ± 1	2000	<25
			3	A1: 2.0 A2-A3: 1.0	A1: immediately after transplant A2-A3: 10 ± 1	2000	30
			4	A1: 2.0 A2-A4: 1.0	A1: immediately after transplant A2-A4: 10 ± 1	2000	35
			4	A1: 2.0 A2-A4: 1.0	A1: immediately after transplant A2-A4: 10 ± 1	2000	50
			4	A1: 2.0 A2-A4: 1.0	A1: immediately after transplant A1-A4: 10 ± 1	2000	Not specified
8, 9, 10	revDEC	Oxamyl 10SL	1	A1: 2.0	A1: immediately after transplant	2000	Not specified
			3	A1: 2.0 A2-A3: 1.0	A1: immediately after transplant A2-A3: 10 ± 1	2000	30
			4	A1: 2.0 A2-A4: 1.0	A1: immediately after transplant A2-A4: 10 ± 1	2000	35
			4	A1: 2.0 A2-A4: 1.0	A1: immediately after transplant A2-A4: 10 ± 1	2000	50
			4	A1: 2.0 A2-A4: 1.0	A1: immediately after transplant A1-A4: 10 ± 1	2000	Not specified

Table 28 Targeted test design (DuPont-29313) (continued)

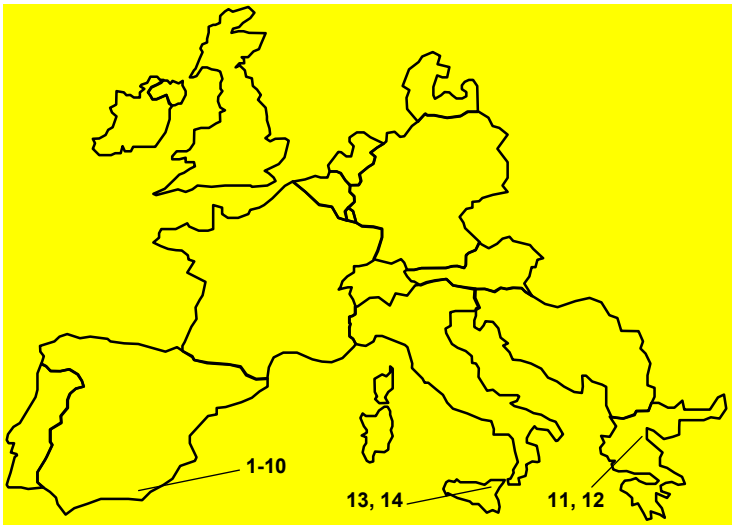
Test no.	Test type	formulation	Number of applications	Rate per application (kg a.s./ha)	Retreatment interval (days)	Application volume[b] (L/ha)	DALA[c] (days)
11, 12	revDEC	Oxamyl 10SL	4	A1: 2.0 A2-A4: 1.0	A1: immediately after transplant A2-A4: 10 ± 1	2000	30
			3	A1: 2.0 A2-A3: 1.0	A1: immediately after transplant A2-A3: 10 ± 1	2000	50
			2	A1: 2.0 A2: 1.0	A1: immediately after transplant A2: 10 ± 1	2000	60
			1	A1: 2.0	A1: immediately after transplant	2000	Not specified
			4	A1: 2.0 A2-A4: 1.0	A1: immediately after transplant A1-A4: 10 ± 1	2000	Not specified
13, 14	revDEC	Oxamyl 10SL	4	A1: 2.0 A2-A4: 1.0	A1: immediately after transplant A2-A4: 10 ± 1	2000	30
			4	A1: 2.0 A2-A4: 1.0	A1: immediately after transplant A2-A4: 10 ± 1	2000	45
			4	A1: 2.0 A2-A4: 1.0	A1: immediately after transplant A2-A4: 10 ± 1	2000	60
			4	A1: 2.0 A2-A4: 1.0	A1: immediately after transplant A2-A4: 10 ± 1	2000	75
			4	A1: 2.0 A2-A4: 1.0	A1: immediately after transplant A1-A4: 10 ± 1	2000	Not specified

[a] revDEC = reverse decline of residue (individual treatment plots for each sampling interval)
[b] G = Irrigation applied before, during and after application of test substance.
[c] DALA = Days after last application (days between last application and sampling)

For all test sites, specimens were collected at specified days after last application (DALA) or, if not specified, specimens were collected at first commercial harvest.

A total of fourteen reverse decline residue trials were conducted in Spain, Italy, and Greece over one growing season (2009-10). A summary, of these protected tomatoes, including cherry tomato fruit, studies is given below. Locations of the trial sites are given in Figure 8.

Figure 8 Map: Oxamyl European protected tomato/cherry tomato fruit test sites



No.	Location	No.	Location
1	Castell de Ferro, Andalucia, Spain	8	Ruescas, Andalucia, Spain
2	Castell de Ferro, Andalucia, Spain	9	Ruescas, Andalucia, Spain
3	Albuñol, Andalucia, Spain	10	Ruescas, Andalucia, Spain
4	Las Norias de Daza, Andalucia, Spain	11	Nea Magnisia, Thessaloniki, Greece
5	Las Norias de Daza, Andalucia, Spain	12	Nea Magnisia, Thessaloniki, Greece
6	La Mojonera, Andalucia, Spain	13	Contrada Dirillo, Sicily, Italy
7	Puebla de Vicar, Andalucia, Spain	14	Contrada Bosco Rotondo, Sicily, Italy

A protected tomato, including cherry tomato, fruit residue data summary (in mg/kg) is presented in Table 29.

To generate these data, the following analysis information pertains.

Analysis method: LC-MS method (DuPont-11125) developed as the oxamyl residue method for determining residues of oxamyl in/on crop matrices. This method is summarized in Oxamyl Volume 3 B5.

Analyte:	Oxamyl
Extraction:	Analyte extracted from crop matrix by homogenisation with an acetone, dichloromethane, petroleum ether mixture
Clean-up:	Aminopropyl SPE cartridge
Chromatography:	Reverse phase HPLC with C18 column
Detection:	Mass spectrometric detection (LC-MS) with 237.3 m/z ($M+NH_4$) used for quantification
Limit of Quantification:	0.010 mg/kg
Limit of Detection:	0.007 mg/kg

Storage stability:

Treated specimens were stored at *ca* -18°C for no longer than 6 months between sampling and analysis.

Recovery data: Average recovery data for fortifications run concurrently with the treated samples are given in Table 29 to demonstrate the validity of the analytical method.

Table 29 Residues of oxamyl in protected tomatoes and cherry tomatoes fruit from supervised trials

Renewal representative GAP: Oxamyl 10SL, 5.5 kg a.s. 30 days before transplant (preplant solarisation); 2.0 kg a.s. at transplanting followed by 3 applications at 1.0 kg a.s./ha/application, 10 days apart; 28-d PHI; all applications *via* drip irrigation								
GLP and trial details	**Crop/ Variety**	**Country**	**Application rate (kg a.s./ha)**	**Crop growth stage at application and at sampling**	**Spray concentration (kg a.s./hL)**	**DALA[a] (days)**	**Residues found[b] (mg/kg)**	**Recovery data**
DuPont-29313 Trial No. 1 GLP 2009-10	Protected Cherry Tomato/ Cupido	Spain, Castell de Ferro	2.074, 1.037, 1.037, 1.037	BBCH 14 + 65 + 67 + 69 + 84	NA	37	nd	Mean recovery = 85% ± 5%, RSD = 6 (n = 10) at 0.010 mg/kg fortification Mean recovery = 83% ± 4%, RSD = 4 (n = 10) at 0.10 mg/kg fortification Overall Mean recovery= 84% ± 4%, RSD = 5
			2.074, 1.037, 1.037, 1.037	BBCH 14 + 61 + 64 + 65 + 84	NA	52	nd	
			2.074, 1.037, 1.037, 1.037	BBCH 14 + 15-51 + 52 + 62 + 84	NA	67	nd	
			2.074, 1.037, 1.037	BBCH 14 + 15-51 + 52 + 84	NA	77	nd	
			2.074, 1.037	BBCH 14 + 15-51 + 84	NA	87	nd	
DuPont-29313 Trial No. 2 GLP 2009-10	Protected Cherry Tomato/ DRC 524	Spain, Castell de Ferro	2.074, 1.037, 1.037, 1.037	BBCH 13 + 62 + 63 + 64 + 89	NA	48	nd	Mean recovery = 85% ± 5%, RSD = 6 (n = 10) at 0.010 mg/kg fortification Mean recovery = 83% ± 4%, RSD = 4 (n = 10) at 0.10 mg/kg fortification Overall Mean recovery= 84% ± 4%, RSD = 5
			2.074, 1.037, 1.037, 1.037	BBCH 13 + 61 + 62 + 62 + 89	NA	63	nd	
			2.074, 1.037, 1.037, 1.037	BBCH 13 + 17-51 + 54 + 62 + 89	NA	78	nd	
			2.074, 1.037, 1.037	BBCH 13 + 17-51 + 54 + 89	NA	88	nd	
			2.074, 1.037	BBCH 13 + 17-51 + 89	NA	98	nd	

Table 29 Residues of oxamyl in protected tomatoes and cherry tomatoes fruit from supervised trials (continued)

EU critical GAP: Oxamyl 10SL, 5.5 kg a.s. 30 days before transplant (preplant solarisation); 2.0 kg a.s./ha at transplanting followed by 3 applications at 1.0 kg a.s./ha/application, 10 days apart; all applications *via* drip irrigation; 28-d PHI								
GLP and trial details	**Crop/ Variety**	**Country**	**Application rate (kg a.s./ha)**	**Crop growth stage at application and at sampling**	**Spray concentration (kg a.s./hL)**	**DALA[a] (days)**	**Residues found[b] (mg/kg)**	**Recovery data**
DuPont-29313 Trial No. 3 GLP 2009-10	Protected Cherry Tomato/ Catalina	Spain, Albuňol	2.074, 1.037, 1.037, 1.037	BBCH 12 + 52 + 61 + 65 + 85	NA	58	nd	Mean recovery = 85% ± 5%, RSD = 6 (n = 10) at 0.010 mg/kg fortification Mean recovery = 83% ± 4%, RSD = 4 (n = 10) at 0.10 mg/kg fortification Overall Mean recovery= 84% ± 4%, RSD = 5
			2.074, 1.037, 1.037, 1.037	BBCH 12 + 17 + 51 + 53 + 85	NA	73	nd	
			2.074, 1.037, 1.037, 1.037	BBCH 12 + 13 + 16 + 19 + 85	NA	88	nd	
			2.074, 1.037, 1.037	BBCH 12 + 13 + 16 + 85	NA	98	nd	
			2.074, 1.037	BBCH 12 + 13 + 85	NA	108	nd	
DuPont-29313 Trial No. 4 GLP 2009-10	Protected Tomato/ Zinac	Spain, Las Norias de Daza	2.074, 1.037	BBCH 12 + 72 + 84	NA	57	nd	Mean recovery = 85% ± 5%, RSD = 6 (n = 10) at 0.010 mg/kg fortification Mean recovery = 83% ± 4%, RSD = 4 (n = 10) at 0.10 mg/kg fortification Overall Mean recovery= 84% ± 4%, RSD = 5
			2.074, 1.037, 1.037	BBCH 12 + 53 + 53-71 + 84	NA	62	nd	
			2.074, 1.037, 1.037, 1.037	BBCH 12 + 19 + 52 + 53/71 + 84	NA	67	nd	
			2.074, 1.037, 1.037, 1.037	BBCH 12 + 16 + 19 + 51 + 84	NA	82	nd	
			2.074, 1.037, 1.037, 1.037	BBCH 12 + 14 + 16 + 19 + 84	NA	92	nd	

Table 29 Residues of oxamyl in protected tomatoes and cherry tomatoes fruit from supervised trials (continued)

EU critical GAP: Oxamyl 10SL, 5.5 kg a.s. 30 days before transplant (preplant solarisation); 2.0 kg a.s./ha at transplanting followed by 3 applications at 1.0 kg a.s./ha/application, 10 days apart; all applications *via* drip irrigation; 28-d PHI								
GLP and trial details	**Crop/ Variety**	**Country**	**Application rate (kg a.s./ha)**	**Crop growth stage at application and at sampling**	**Spray concentration (kg a.s./hL)**	**DALA[a] (days)**	**Residues found[b] (mg/kg)**	**Recovery data**
DuPont-29313 Trial No. 5 GLP 2009-10	Protected Tomato/ Bernal	Spain, Las Norias de Daza	2.074, 1.037	BBCH 12 + 72 + 82	NA	68	nd	Mean recovery = 85% ± 5%, RSD = 6 (n = 10) at 0.010 mg/kg fortification Mean recovery = 83% ± 4%, RSD = 4 (n = 10) at 0.10 mg/kg fortification Overall Mean recovery= 84% ± 4%, RSD = 5
			2.074, 1.037, 1.037	BBCH 12 + 53 + 53/71 + 82	NA	73	nd	
			2.074, 1.037, 1.037, 1.037	BBCH 12 + 19 + 51 + 53/71 + 82	NA	78	nd	
			2.074, 1.037, 1.037, 1.037	BBCH 12 + 18 + 19 + 51 + 82	NA	93	nd	
			2.074, 1.037, 1.037, 1.037	BBCH 12 + 14 + 18 + 19 + 82	NA	103	nd	
DuPont-29313 Trial No. 6 GLP 2009-10	Protected Tomato/ Denis	Spain, La Mojonera	2.074, 1.037	BBCH 15 + 52 + 83	NA	55	nd	Mean recovery = 85% ± 5%, RSD = 6 (n = 10) at 0.010 mg/kg fortification Mean recovery = 83% ± 4%, RSD = 4 (n = 10) at 0.10 mg/kg fortification Overall Mean recovery= 84% ± 4%, RSD = 5
			2.074, 1.037, 1.037	BBCH 15 + 51 + 52 + 83	NA	60	nd	
			2.074, 1.037, 1.037, 1.037	BBCH 15 + 19 + 19 + 51 + 83	NA	65	nd	
			2.074, 1.037, 1.037, 1.037	BBCH 15 + 19 + 19 + 19 + 83	NA	80	nd	
			2.074, 1.037, 1.037, 1.037	BBCH 15 + 17 + 19 + 19 + 83	NA	90	nd	

Table 29 Residues of oxamyl in protected tomatoes and cherry tomatoes fruit from supervised trials (continued)

EU critical GAP: Oxamyl 10SL, 5.5 kg a.s. 30 days before transplant (preplant solarisation); 2.0 kg a.s./ha at transplanting followed by 3 applications at 1.0 kg a.s./ha/application, 10 days apart; all applications *via* drip irrigation; 28-d PHI								
GLP and trial details	**Crop/ Variety**	**Country**	**Application rate (kg a.s./ha)**	**Crop growth stage at application and at sampling**	**Spray concentration (kg a.s./hL)**	**DALA[a] (days)**	**Residues found[b] (mg/kg)**	**Recovery data**
DuPont-29313 Trial No. 7 GLP 2009-10	Protected Tomato/ Enate	Spain, Puebla de Vicar	2.074, 1.037	BBCH 13 + 72 + 85	NA	54	nd	Mean recovery = 85% ± 5%, RSD = 6 (n = 10) at 0.010 mg/kg fortification Mean recovery = 83% ± 4%, RSD = 4 (n = 10) at 0.10 mg/kg fortification Overall Mean recovery= 84% ± 4%, RSD = 5
			2.074, 1.037, 1.037	BBCH 13 + 52/71 + 72 + 85	NA	59	nd	
			2.074, 1.037, 1.037, 1.037	BBCH 13 + 19 + 32 + 71 + 85	NA	64	nd	
			2.074, 1.037, 1.037, 1.037	BBCH 13 + 17 + 18 + 31 + 85	NA	79	nd	
			2.074, 1.037, 1.037, 1.037	BBCH 13 + 15 + 17 + 18 + 85	NA	89	nd	
DuPont-29313 Trial No. 8 GLP 2009-10	Protected Tomato/ Octydia	Spain, Ruescas	2.074, 1.037, 1.037	BBCH 13 + 64 + 68 + 83	NA	45	nd	Mean recovery = 85% ± 5%, RSD = 6 (n = 10) at 0.010 mg/kg fortification Mean recovery = 83% ± 4%, RSD = 4 (n = 10) at 0.10 mg/kg fortification Overall Mean recovery= 84% ± 4%, RSD = 5
			2.074, 1.037, 1.037, 1.037	BBCH 13 + 51 + 59 + 65 + 83	NA	50	nd	
			2.074, 1.037, 1.037, 1.037	BBCH 13 + 16 + 19 + 53 + 83	NA	65	nd	
			2.074, 1.037, 1.037, 1.037	BBCH 13 + 14 + 16 + 19 + 83	NA	75	nd	
			2.074	BBCH 13 + 83	NA	105	nd	

Table 29 Residues of oxamyl in protected tomatoes and cherry tomatoes fruit from supervised trials (continued)

EU critical GAP: Oxamyl 10SL, 5.5 kg a.s. 30 days before transplant (preplant solarisation); 2.0 kg a.s./ha at transplanting followed by 3 applications at 1.0 kg a.s./ha/application, 10 days apart; all applications *via* drip irrigation; 28-d PHI								
GLP and trial details	**Crop/ Variety**	**Country**	**Application rate (kg a.s./ha)**	**Crop growth stage at application and at sampling**	**Spray concentration (kg a.s./hL)**	**DALA[a] (days)**	**Residues found[b] (mg/kg)**	**Recovery data**
DuPont-29313 Trial No. 9 GLP 2009-10	Protected Tomato/ Pristila	Spain, Ruescas	2.074, 1.037, 1.037	BBCH 13 + 65 + 68 + 83	NA	45	nd	Mean recovery = 85% ± 5%, RSD = 6 (n = 10) at 0.010 mg/kg fortification Mean recovery = 83% ± 4%, RSD = 4 (n = 10) at 0.10 mg/kg fortification Overall Mean recovery= 84% ± 4%, RSD = 5
			2.074, 1.037, 1.037, 1.037	BBCH 13 + 51 + 59 + 66 + 83	NA	50	nd	
			2.074, 1.037, 1.037, 1.037	BBCH 13 + 16 + 19 + 53 + 83	NA	65	nd	
			2.074, 1.037, 1.037, 1.037	BBCH 13 + 14 + 16 + 19 + 83	NA	75	nd	
			2.074	BBCH 13 + 83	NA	105	nd	
DuPont-29313 Trial No. 10 GLP 2009-10	Protected Tomato/ Tya	Spain, Ruescas	2.074, 1.037, 1.037	BBCH 14 + 65 + 68 + 84	NA	47	nd	Mean recovery = 85% ± 5%, RSD = 6 (n = 10) at 0.010 mg/kg fortification Mean recovery = 83% ± 4%, RSD = 4 (n = 10) at 0.10 mg/kg fortification Overall Mean recovery= 84% ± 4%, RSD = 5
			2.074, 1.037, 1.037, 1.037	BBCH 14 + 51 + 59 + 65 + 84	NA	52	nd	
			2.074, 1.037, 1.037, 1.037	BBCH 14 + 17 + 19 + 53 + 84	NA	67	nd	
			2.074, 1.037, 1.037, 1.037	BBCH 14 + 15 + 17 + 19 + 84	NA	77	nd	
			2.074	BBCH 14 + 84	NA	107	nd	

Table 29 Residues of oxamyl in protected tomatoes and cherry tomatoes fruit from supervised trials (continued)

EU critical GAP: Oxamyl 10SL, 5.5 kg a.s. 30 days before transplant (preplant solarisation); 2.0 kg a.s./ha at transplanting followed by 3 applications at 1.0 kg a.s./ha/application, 10 days apart; all applications *via* drip irrigation; 28-d PHI								
GLP and trial details	**Crop/ Variety**	**Country**	**Application rate (kg a.s./ha)**	**Crop growth stage at application and at sampling**	**Spray concentration (kg a.s./hL)**	**DALA[a] (days)**	**Residues found[b] (mg/kg)**	**Recovery data**
DuPont-29313 Trial No. 11 GLP 2009-10	Protected Cherry Tomato/ Corbus	Greece, Nea Magnisia	2.000, 1.000, 1.000, 1.000	BBCH 16 + 53/61 + 62 + 63 + 81	NA	28	nd	Mean recovery = 85% ± 5%, RSD = 6 (n = 10) at 0.010 mg/kg fortification Mean recovery = 83% ± 4%, RSD = 4 (n = 10) at 0.10 mg/kg fortification Overall Mean recovery= 84% ± 4%, RSD = 5
			2.000, 1.000, 1.000, 1.000	BBCH 16 + 18/51 + 53/61 + 62 + 81	NA	37	nd	
			2.000, 1.000, 1.000	BBCH 16 + 52/61 + 53/61 + 81	NA	47	nd	
			2.000, 1.000	BBCH 16 + 52/61 + 81	NA	55	nd	
			2.000	BBCH 16 + 81	NA	70	nd	
DuPont-29313 Trial No. 12 GLP 2009-10	Protected Tomato/ Victor	Greece, Nea Magnisia	2.000, 1.000, 1.000, 1.000	BBCH 18 + 53/61 + 62 + 63 + 81	NA	28	nd	Mean recovery = 85% ± 5%, RSD = 6 (n = 10) at 0.010 mg/kg fortification Mean recovery = 83% ± 4%, RSD = 4 (n = 10) at 0.10 mg/kg fortification Overall Mean recovery= 84% ± 4%, RSD = 5
			2.000, 1.000, 1.000, 1.000	BBCH 18 + 19/51 + 53/61 + 62 + 81	NA	37	nd	
			2.000, 1.000, 1.000	BBCH 18 + 52/61 + 53/61 + 81	NA	47	nd	
			2.000, 1.000	BBCH 18 + 52/61 + 81	NA	55	nd	
			2.000	BBCH 18 + 81	NA	70	nd	

Table 29 Residues of oxamyl in protected tomatoes and cherry tomatoes fruit from supervised trials (continued)

EU critical GAP: Oxamyl 10SL, 5.5 kg a.s. 30 days before transplant (preplant solarisation); 2.0 kg a.s./ha at transplanting followed by 3 applications at 1.0 kg a.s./ha/application, 10 days apart; all applications *via* drip irrigation; 28-d PHI								
GLP and trial details	**Crop/ Variety**	**Country**	**Application rate (kg a.s./ha)**	**Crop growth stage at application and at sampling**	**Spray concentration (kg a.s./hL)**	**DALA[a] (days)**	**Residues found[b] (mg/kg)**	**Recovery data**
DuPont-29313 Trial No. 13 GLP 2009-10	Protected Cherry Tomato/ Genio	Italy, Contrada Dirillo	2.042, 1.028, 1.029, 1.026	BBCH 13 + 63 + 65 + 66 + 81	NA	31	nd	Mean recovery = 85% ± 5%, RSD = 6 (n = 10) at 0.010 mg/kg fortification Mean recovery = 83% ± 4%, RSD = 4 (n = 10) at 0.10 mg/kg fortification Overall Mean recovery= 84% ± 4%, RSD = 5
			2.042, 1.031, 1.025, 1.024	BBCH 13 + 62 + 63 + 64 + 81	NA	48	nd	
			2.052, 1.026, 1.025, 1.031	BBCH 13 + 61 + 61 + 62 + 81	NA	62	nd	
			2.052, 1.026, 1.022, 1.031	BBCH 13 + 14 + 18 + 61 + 81	NA	76	nd	
			2.061, 1.027, 1.030, 1.029	BBCH 13 + 14 + 18 + 61 + 81	NA	76	nd	
DuPont-29313 Trial No. 14 GLP 2009-10	Protected Tomato/ Rovente	Italy, Contrada Bosco Rotondo	2.054, 1.031, 1.028, 1.028	BBCH 12 + 61 + 63 + 64 + 81	NA	31	nd	Mean recovery = 85% ± 5%, RSD = 6 (n = 10) at 0.010 mg/kg fortification Mean recovery = 83% ± 4%, RSD = 4 (n = 10) at 0.10 mg/kg fortification Overall Mean recovery= 84% ± 4%, RSD = 5
			2.058, 1.030, 1.029, 1.029	BBCH 12 + 61 + 61 + 62 + 81	NA	46	nd	
			2.052, 1.028, 1.031, 1.028	BBCH 12 + 16 + 19 + 61 + 81	NA	60	nd	
			2.054, 1.026, 1.030, 1.027	BBCH 12 + 14 + 15 + 18 + 81	NA	74	nd	
			2.054, 1.025, 1.030, 1.027	BBCH 12 + 14 + 15 + 18 + 81	NA	74	nd	

NA = Not applicable
[a] DALA = Days after last application
[b] The designation "nd" is used for treated samples for which no peak was observed or residue was <LOD (below the limit of detection; <0.007 mg/kg).

II. RESULTS AND DISCUSSION

The residue studies presented were carried out in three EU countries, Italy, Spain, and Greece, and provide data relevant to conditions in the southern European region.

All of the analytical work associated with the studies was performed at Charles River Laboratories, Tranent EH33 2NE, Scotland.

Southern Europe

In the southern European region, no residues were detected (<0.007 mg/kg) in protected tomatoes or cherry tomatoes in the four reverse decline residue trials conducted in 2009-10 in which oxamyl was applied in accordance with the in-season use pattern.

Recovery values for fresh control fortifications run concurrently with treated samples in all the trials are summarised above. Mean recovery from tomatoes and cherry tomatoes fortified at 0.010 mg/kg was 85% ± 5%, RSD = 6 (n = 10) while the mean recovery from tomatoes and cherry tomatoes fortified at 0.10 mg/kg was 83% ± 4%, RSD = 4 (n = 10). Therefore, the analytical methods used performed well for the determination of oxamyl in treated crops.

III. CONCLUSION

Overall consistent residue behaviour of oxamyl on protected tomatoes and cherry tomatoes was found in one season of study in the EU for application and sampling conducted according to the in-season use pattern. The residue data show that residues were <0.007 mg/kg in protected tomatoes and cherry tomatoes from four trials treated with a single application at transplanting followed by 3 applications throughout development and collected 28 days or more after the last application.

(Haigh, I., Hoskins, M., 2011)

RMS comments and conclusion: The study conducted according to the EU guideline for the crop field trials. Fourteen trials were conducted in the SEU at application rate according to the critical GAP supported.For all trials the determined residues were below the LOD (<0.007 mg/kg). In addition, the analytical method is compliance with the actual EU guideline on analytical method for residue.

The study can considered useful for residues evaluation and can be considered acceptable.

Study submitted to the EU for the first time in this submission.

B.7.3.2/04

Reference: CA 6.3.2/04	**Report:**	Haigh, I., Cairns, S. (2012); Decline and magnitude of oxamyl residues in protected tomatoes, including cherry tomatoes (fruiting vegetables, solanacea) following application of Oxamyl 10L formulation *via* drip irrigation - southern Europe 2010-2011 **DuPont Report No.:** DuPont-31506 **Guidelines:** Directive 91/414/EEC **Deviations:** None **Testing Facility:** Charles River Laboratories (UK), Tranent, Scotland, UK Testing Facility Report No.: 696228 **GLP:** Yes **Certifying Authority:** Department of Health (U.K.), Entidad Nacional de Acreditacion (ENAC) (Spain)

I. MATERIALS AND METHODS

The field program was conducted in 2010-2011 at seven locations in Spain, Greece, and Italy. Each test contained one control and four treated plots. Oxamyl 10SL (DPX-D1410-527) was applied *via* drip irrigation.

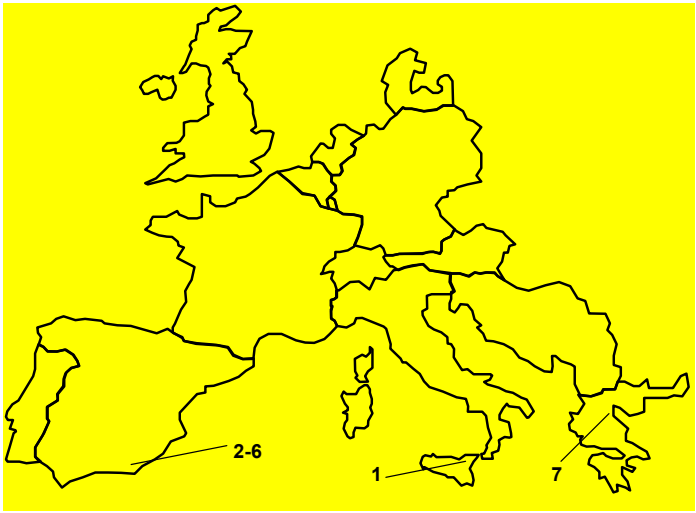
An application was made to each treated plot immediately after transplanting followed by three additional applications. These additional applications occurred at 10-day intervals triggered by the predicted first commercial harvest.

The first application was applied at a target application rate of 20.0 L formulated product (fp)/ha (2.0 kg a.s./ha). All other applications were applied at a target application rate of 10.0 L formulated product (fp)/ha (1.0 kg a.s./ha) for a seasonal application rate of 5.0 kg a.s./ha.

For Tests 1-6, specimens of protected tomatoes and cherry tomatoes were collected at *ca.* 20, 30, 45, and 60 days after last application (DALA). For Test 7 specimens of protected tomatoes were collected at *ca.* 45, 55, 70, and 85 DALA.

A total of seven reverse decline residue trials were conducted in Spain, Italy, and Greece over one growing season (2010-2011). A summary of these protected tomatoes and cherry tomatoes studies is given below. Locations of the trial sites are given in Figure 9.

Figure 9 Map: Oxamyl European protected tomato and cherry tomato test sites



No.	Location	No.	Location
1	Contrada Rinazze di Strada, Sicily, Italy	5	Venta del Viso, Andalucia, Spain
2	Campohermoso, Andalucia, Spain	6	La Mojonera, Andalucia, Spain
3	Campohermoso, Andalucia, Spain	7	Almyros, Greece
4	El Ejido, Andalucia, Spain		

A protected tomato and cherry tomato residue data summary (in mg/kg) is presented in Table 30.

To generate these data, the following analysis information pertains.

Analysis method: LC-MS/MS method (DuPont-33191) developed as the oxamyl residue method for determining residues of oxamyl in/on crop matrices. This method is summarized in Oxamyl Volume 3 B5.

Analyte:	Oxamyl
Extraction:	Analyte extracted from crop matrix by homogenization followed by shaking with a mixture of organic solvents (acetone, dichloromethane and petroleum ether)
Clean-up:	Samples are passed through an aminopropyl SPE cartridge and eluted with 1% decanol in dichloromethane.
Chromatography:	Analytical Column: Phenomenex Luna C18, 2.0 mm × 100 mm, 3 µm, 100Å
Detection:	LC-MS/MS using positive turbo ion spray. Target ion transition of 237.1/72.0, confirmatory ion transition of 237.1/90.1.
Limit of Quantification:	0.010 mg/kg
Limit of Detection:	0.003 mg/kg

Storage stability:

Treated specimens were stored at *ca* -18°C for no longer than 8 months between sampling and analysis.

Recovery data: Average recovery data for fortifications run concurrently with the treated samples are given in Table 30 to demonstrate the validity of the analytical method.

Table 30 Residues of oxamyl in protected tomato and cherry tomato from supervised trials

EU critical GAP: Oxamyl 10SL, 5.5 kg a.s. 30 days before transplant (preplant solarisation); 2.0 kg a.s./ha at transplanting followed by 3 applications at 1.0 kg a.s./ha/application, 10 days apart; all applications *via* drip irrigation; 28-d PHI								
GLP and trial details	**Crop/ Variety**	**Country**	**Application rate (kg a.s./ha)**	**Crop growth stage at Last Application**	**Spray concentration (g a.s./hL)**	**DALA[a] (days)**	**Residues found[b] (mg/kg)**	**Recovery data**
DuPont-31506 Trial No. 1 GLP 2010-2011	Protected Cherry Tomato/ Genio	Italy, Contrada Rinazze di Strada, Sicily	2.12 + 1.06 + 1.06 + 1.06	BBCH 65	NA	20	0.005	Mean recovery = 91% ± 19%, RSD = 21 (n = 4) at 0.010 mg/kg fortification Mean recovery = 80% ± 7%, RSD = 8 (n = 4) at 0.10 mg/kg fortification
			2.12 + 1.06 + 1.06 + 1.06	BBCH 64	NA	30	nd	
			2.11 + 1.06 + 1.06 + 1.06	BBCH 63	NA	43	nd	
			2.12 + 1.06 + 1.06 + 1.06	BBCH 62	NA	58	nd	
DuPont-31506 Trial No. 2 GLP 2010-2011	Protected Cherry Tomato/ Genio	South Spain, Campohermoso, Andalucia	2.13 + 1.01 + 1.01 + 1.01	BBCH 72	NA	21	nd	
			2.13 + 1.07 + 1.01 + 1.01	BBCH 69	NA	30	nd	
			2.13 + 1.07 + 1.07 + 1.01	BBCH 63	NA	45	nd	
			2.13 + 1.07 + 1.07 + 1.07	BBCH 53	NA	60	nd	
DuPont-31506 Trial No. 3 GLP 2010-2011	Protected Cherry Tomato/ Santawest	South Spain, Campohermoso, Andalucia	2.13 + 1.01 + 1.01 + 1.01	BBCH 72	NA	21	0.003	Mean recovery = 91% ± 19%, RSD = 21 (n = 4) at 0.010 mg/kg fortification Mean recovery = 80% ± 7%, RSD = 8 (n = 4) at 0.10 mg/kg fortification
			2.13 + 1.07 + 1.01 + 1.01	BBCH 69	NA	30	nd	
			2.13 + 1.07 + 1.07 + 1.01	BBCH 63	NA	45	nd	
			2.13 + 1.07 + 1.07 + 1.07	BBCH 53	NA	60	nd	
DuPont-31506 Trial No. 4 GLP 2010-2011	Protected Tomato/ Zinac	South Spain, El Ejido, Andalucia	2.13 + 1.07 + 1.01 + 1.01	BBCH 72	NA	21	0.003	
			2.13 + 1.07 + 1.07 + 1.01	BBCH 69	NA	31	nd	
			2.13 + 1.07 + 1.07 + 1.07	BBCH 65	NA	45	nd	
			2.13 + 1.07 + 1.07 + 1.07	BBCH 53	NA	60	nd	
DuPont-31506 Trial No. 5 GLP 2010-2011	Protected Tomato/ Mayoral	South Spain, Venta del Viso, Andalucia	2.13 + 1.07 + 1.01 + 1.01	BBCH 72	NA	21	nd	Mean recovery = 91% ± 19%, RSD = 21 (n = 4) at 0.010 mg/kg fortification Mean recovery = 80% ± 7%, RSD = 8 (n = 4) at 0.10 mg/kg fortification
			2.13 + 1.07 + 1.07 + 1.01	BBCH 69	NA	30	nd	
			2.13 + 1.07 + 1.07 + 1.07	BBCH 65	NA	45	nd	
			2.13 + 1.07 + 1.07 + 1.07	BBCH 55	NA	60	nd	

Table 30 Residues of oxamyl in protected tomato and cherry tomato from supervised trials (continued)

EU critical GAP: Oxamyl 10SL, 5.5 kg a.s. 30 days before transplant (preplant solarisation); 2.0 kg a.s./ha at transplanting followed by 3 applications at 1.0 kg a.s./ha/application, 10 days apart; all applications *via* drip irrigation; 28-d PHI								
GLP and trial details	**Crop/ Variety**	**Country**	**Application rate (kg a.s./ha)**	**Crop growth stage at Last Application**	**Spray concentration (g a.s./hL)**	**DALA[a] (days)**	**Residues found[b] (mg/kg)**	**Recovery data**
DuPont-31506 Trial No. 6 GLP 2010-2011	Protected Tomato/ Realeza	South Spain, La Mojonera, Andalucia	2.13 + 1.01 + 1.01 + 1.01	BBCH 72	NA	21	0.006	Mean recovery = 91% ± 19%, RSD = 21 (n = 4) at 0.010 mg/kg fortification Mean recovery = 80% ± 7%, RSD = 8 (n = 4) at 0.10 mg/kg fortification
			2.13 + 1.01 + 1.01 + 1.01	BBCH 69	NA	31	0.004	
			2.13 + 1.07 + 1.07 + 1.01	BBCH 64	NA	44	nd	
			2.13 + 1.07 + 1.07 + 1.07	BBCH 54	NA	60	nd	
DuPont-31506 Trial No. 7 GLP 2010-2011	Protected Tomato/ Belladonna	Greece, Almyros, Central Greece	2.12 + 1.00 + 1.00 + 1.00	BBCH 54-55/64	NA	45	nd	Mean recovery = 91% ± 19%, RSD = 21 (n = 4) at 0.010 mg/kg fortification Mean recovery = 80% ± 7%, RSD = 8 (n = 4) at 0.10 mg/kg fortification
			2.12 + 1.00 + 1.00 + 1.00	BBCH 53-54/63	NA	54	nd	
			2.12 + 1.06 + 1.00 + 1.00	BBCH 52-53/61	NA	69	nd	
			2.12 + 1.06 + 1.06	BBCH 52/61	NA	84	nd	

[a] DALA = Day after last application
[b] nd = analyte peak not detected or peak <LOD (<0.003 mg/kg)

II. RESULTS AND DISCUSSION

The residue studies presented were carried out in three EU countries, Italy, Spain, and Greece, and provide data relevant to conditions in the southern European region.

All of the analytical work associated with the studies was performed at Charles River Laboratories, Tranent EH33 2NE, Scotland.

Southern Europe

In the southern European region, residues ranged from <0.003 to 0.004 mg/kg in protected tomatoes and cherry tomatoes, treated with a single application at transplanting followed by 3 applications throughout development and collected 21 days or more after the last application.

Concurrent recoveries from untreated tomato samples fortified at the LOQ (0.010 mg/kg) to 10× LOQ (0.10 mg/kg) ranged from 64-105%. Mean recoveries (± standard deviation) for control protected tomato samples fortified at 0.010 mg/kg were 91% (±19) and for control protected tomato samples fortified at 0.10 mg/kg were 80% (±7). Therefore, the analytical methods used performed well for the determination of oxamyl in treated crops.

III. CONCLUSION

Overall consistent residue behaviour of oxamyl on protected tomatoes and cherry tomatoes was found in one season of study in the EU for application and sampling conducted according to the in-season use pattern. . The residue data show that residues ranged from <0.003 to 0.004 mg/kg in protected tomatoes and cherry tomatoes, treated with a single application at transplanting followed by 3 applications throughout development and collected 28 days or more after the last application.

(Haigh, I., Cairns, S., 2012)

RMS comments and conclusion: The study performed according to the EU guideline for the crop field trials. ~~Fourteen~~Seven trials were conducted in the SEU at application rate according to the critical GAP supported.For all trials the determined residues were below the LOD (<0.007 mg/kg). In addition, the analytical method is compliance with the actual EU guideline on analytical method for residue.

The study can considered useful for residues evaluation and can be considered acceptable.

B.7.3.3 Tobacco

The renewal representative use for tobacco is in the SEU Regulatory zone. Oxamyl 10GR is applied at planting (BBCH 00) in furrow, at the rate of 3.0 kg a.s./ha, or broadcast at the rate of 5.5 kg a.s./ha.

Five residue trials were conducted with Oxamyl 10GR or Oxamyl 5GR applied at the GAP rates or higher (in furrow application at 3.5 kg a.s./ha or as broadcast application with 5.5-5.9 kg a.s./ha).

In all trials, the residues in green tobacco leaves were <0.01 mg/kg.

Study submitted to the EU for the first time in this submission.

B.7.3.3/01

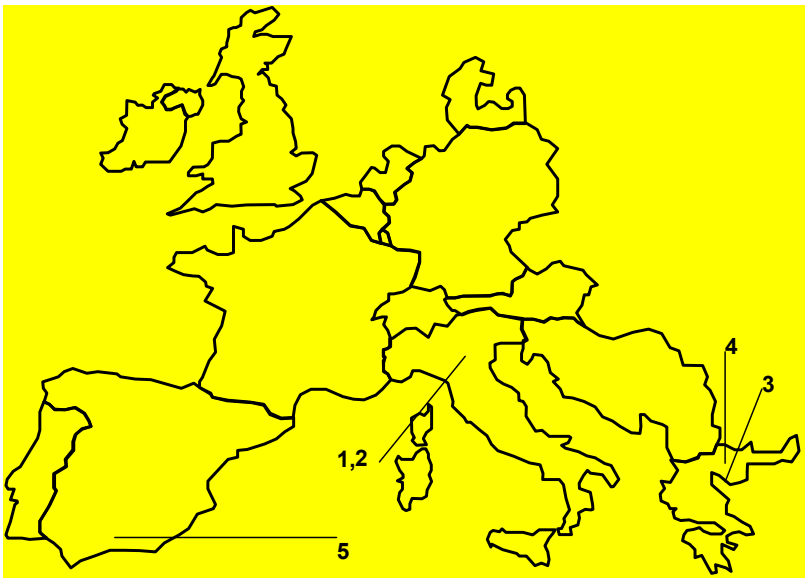
Reference: **CA 6.3.3/01**	**Report:**	Anderson, I., Cairns, S.D. (2006); Decline and magnitude of oxamyl residues in fermented tobacco leaves following granular application of Vydate® 5G or 10G and low pressure soil application of Vydate 10L® - southern Europe, 2005 **DuPont Report No.:** DuPont-14667 **Guidelines:** Directive 91/414/EEC **Deviations:** None **Testing Facility:** Charles River Laboratories (UK), Tranent, Scotland, UK Testing Facility Report No.: 26498 **GLP:** Yes **Certifying Authority:** Department of Health (U.K.), Entidad Nacional de Acreditacion (ENAC) (Spain), Ministero delle Politiche Agricole e Forestali (Italy)

I. MATERIALS AND METHODS

The field program was conducted in 2005 at five locations in Spain, Greece, and Italy. Oxamyl residues were determined in/on tobacco leaves (green, dried, and dried, fermented) in Europe following treatment with Oxamyl 10GR, Oxamyl 5GR, or Oxamyl 10SL insecticide. Oxamyl 10GR (DPX-D1410-460) or Oxamyl 5GR (DPX-D1410-481) was applied by granular applicator at the rate of 5.5 kg a.s./ha (3.5 kg a.s./ha in-furrow). The application was made at transplant when the crop was at growth stage BBCH 12–15. Oxamyl 10SL (DPX-D1410-461) was applied four times by foliar application to separate plots. Oxamyl 10SL was applied at the rate of 1.5 kg a.s./ha/application for a season application rate of 6.0 kg a.s./ha. The applications were made every 14 days starting at transplant when the crop was at growth stages BBCH 12–19.

A total of 5 magnitude of residue trials in southern Europe were conducted over one growing season (season 2005). A summary of residue data on tobacco is given below. Locations of the tobacco trial sites are given in Figure 10.

Figure 10 Map: Oxamyl tobacco test sites



No.	Country
1	Bovolone (Verona), Veneto, Italy
2	Bovolone (Verona), Veneto, Italy
3	Thessaloniki, Central Macedonia, Greece
4	Pieria, Central Macedonia, Greece
5	Santa Fe – Granada, Spain

Tobacco 'green leaves,' 'dried leaves,' and 'dried fermented leaves' residue data summaries (in mg/kg) are presented in Table 31and Table 32.

To generate these data, the following analysis information pertains.

Analysis method: Specimens were analysed for oxamyl by LC-MS based on method DuPont-17601. This method is summarized in Oxamyl Volume 3 B5.

Analyte:	Oxamyl
Extraction:	Analyte extracted from crop matrix by homogenisation with acetonitrile
Clean-up:	Removal of lipids using hexane followed by an aminopropyl SPE cartridge
Chromatography:	Reverse phase HPLC with C18 column
Detection:	Mass spectrometric detection (LC-MS) with 237.3 m/z ($M+NH_4$) used for quantification
Limit of Quantification:	0.010 mg/kg
Limit of Detection:	0.007 mg/kg

Storage stability:

Treated specimens were stored at *ca* -18°C for no longer than 6 months between sampling and analysis.

Recovery data: Average recovery data for fortifications run concurrently with the treated samples are given in Table 31 and Table 32 to demonstrate the validity of the analytical method.

Table 31 Residues of oxamyl in tobacco leaves from supervised trials following applications of Oxamyl 10GR or Oxamyl 5GR

Renewal representative GAP: SEU; One 5.5 kg a.s./ha application (broadcast) or one 3.0 kg a.s./ha application (in-furrow) of Oxamyl 10GR at transplant										
							Residues found[b] (mg/kg)			
GLP and trial details	Crop/ Variety	Country	Application rate (kg a.s./ha)	Crop growth stage at Applications and at Sampling	Spray conc (kg a.s./hL)	DALA[a]	Green leaves	Dried leaves	Dried, Fermented leaves	Recovery data
DuPont-14667 Trial No. 1 GLP 2005	Tobacco/ Burley	Bovolone (Verona), Veneto, Italy	5.900 - broadcast	BBCH 14–15 BBCH 49	NA	94	nd	nd	nd	Green Leaves: mean recovery = 93%, RSD = 14 (n = 8) in 0.010–0.10 mg/kg fortification range; Dried Leaves: mean recovery = 92%, RSD = 8 (n = 10) in 0.010–0.40 mg/kg fortification range; Dried Fermented Leaves: mean recovery = 92%, RSD = 1 (n = 4) in 0.010–0.10 mg/kg fortification range)
DuPont-14667 Trial No. 2 GLP 2005	Tobacco/ Bright	Bovolone (Verona), Veneto, Italy	5.900 - broadcast	BBCH 14–15 BBCH 49	NA	105	nd	nd	nd	Green Leaves: mean recovery = 93%, RSD = 14 (n = 8) in 0.010–0.10 mg/kg fortification range; Dried Leaves: mean recovery = 92%, RSD = 8 (n = 10) in 0.010–0.40 mg/kg fortification range; Dried Fermented Leaves: mean recovery = 92%, RSD = 1 (n = 4) in 0.010–0.10 mg/kg fortification range)

Table 31 Residues of oxamyl in tobacco leaves from supervised trials following applications of Oxamyl 10GR or Oxamyl 5GR (continued)

Renewal representative GAP: SEU; One 5.5 kg a.s./ha application (broadcast) or one 3.0 kg a.s./ha application (in-furrow) of Oxamyl 10GR at transplant										
GLP and trial details	Crop/ Variety	Country	Application rate (kg a.s./ha)	Crop growth stage at Applications and at Sampling	Spray conc (kg a.s./hL)	DALA[a]	Residues found[b] (mg/kg)			Recovery data
							Green leaves	Dried leaves	Dried, Fermented leaves	
DuPont-14667 Trial No. 3 GLP 2005	Tobacco/ Basmas	Thessaloniki, Central Macedonia, GR-57020, Greece	3.495 – in-furrow	BBCH 12–13 BBCH 49	NA	78	nd	0.020	nd	Green Leaves: mean recovery = 93%, RSD = 14 (n = 8) in 0.010–0.10 mg/kg fortification range; Dried Leaves: mean recovery = 92%, RSD = 8 (n = 10) in 0.010–0.40 mg/kg fortification range; Dried Fermented Leaves: mean recovery = 92%, RSD = 1 (n = 4) in 0.010–0.10 mg/kg fortification range)
DuPont-14667 Trial No. 4 GLP 2005	Tobacco/ Katerinis	Pieria, Central Macedonia, GR-60100, Greece	3.495 – in-furrow	BBCH 12–13 BBCH 49	NA	78	nd	nd	nd	Green Leaves: mean recovery = 93%, RSD = 14 (n = 8) in 0.010–0.10 mg/kg fortification range; Dried Leaves: mean recovery = 92%, RSD = 8 (n = 10) in 0.010–0.40 mg/kg fortification range; Dried Fermented Leaves: mean recovery = 92%, RSD = 1 (n = 4) in 0.010–0.10 mg/kg fortification range)

Table 31 Residues of oxamyl in tobacco leaves from supervised trials following applications of Oxamyl 10GR or Oxamyl 5GR (continued)

Renewal representative GAP: SEU; One 5.5 kg a.s./ha application (broadcast) or one 3.0 kg a.s./ha application (in-furrow) of Oxamyl 10GR at transplant										
GLP and trial details	**Crop/ Variety**	**Country**	**Application rate (kg a.s./ha)**	**Crop growth stage at Applications and at Sampling**	**Spray conc (kg a.s./hL)**	**DALA[a]**	**Residues found[b] (mg/kg)**			**Recovery data**
							Green leaves	**Dried leaves**	**Dried, Fermented leaves**	
DuPont-14667 Trial No. 5 GLP 2005	Tobacco/ Burley	Santa Fe, Granada, Andalucia, Spain	5.500 – broadcast	BBCH 13–14 BBCH 92	NA	105	nd	nd	nd	Green Leaves: mean recovery = 93%, RSD = 14 (n = 8) in 0.010–0.10 mg/kg fortification range; Dried Leaves: mean recovery = 92%, RSD = 8 (n = 10) in 0.010–0.40 mg/kg fortification range; Dried Fermented Leaves: mean recovery = 92%, RSD = 1 (n = 4) in 0.010–0.10 mg/kg fortification range)

[a] DALA = Days after last application b
[b] nd = analyte peak not detected or peak <LOD (<0.007 mg/kg)

Table 32 Residues of oxamyl in tobacco leaves (solanaceae) from supervised trials following applications of Oxamyl 10SL

Renewal representative GAP: SEU, One 5.5 kg a.s./ha application (broadcast) or one 3.0 kg a.s./ha application (in-furrow) of Oxamyl 10GR at transplant										
GLP and trial details	Crop/ Variety	Country	Application rate (kg a.s./ha)	Crop growth stage at Applications and at Sampling	Spray conc (kg a.s./hL)	DALA[a]	Residues found[b] (mg/kg)			Recovery data
							Green leaves	Dried leaves	Dried, Fermented leaves	
DuPont-14667 Trial No. 1 GLP 2005	Tobacco/ Burley	Bovolone (Verona), Veneto, Italy	1.497 1.434 1.475 1.484	BBCH 14–15 BBCH 15–16 BBCH 17 BBCH 19 BBCH 49	0.15 0.15 0.15 0.15	50	nd	nd	nd	Green Leaves: mean recovery = 93%, RSD = 14 (n = 8) in 0.010–0.10 mg/kg fortification range; Dried Leaves: mean recovery = 92%, RSD = 8 (n = 10 in 0.010–0.40 mg/kg fortification range; Dried Fermented Leaves: mean recovery = 92%, RSD = 1 (n = 4) in 0.010–0.10 mg/kg fortification range
DuPont-14667 Trial No. 2 GLP 2005	Tobacco/ Bright	Bovolone (Verona), Veneto, Italy	1.506 1.425 1.484 1.490	BBCH 14–15 BBCH 15–16 BBCH 17 BBCH 19 BBCH 49	0.15 0.15 0.15 0.15	61	nd	nd	nd	Green Leaves: mean recovery = 93%, RSD = 14 (n = 8) in 0.010–0.10 mg/kg fortification range; Dried Leaves: mean recovery = 92%, RSD = 8 (n = 10 in 0.010–0.40 mg/kg fortification range; Dried Fermented Leaves: mean recovery = 92%, RSD = 1 (n = 4) in 0.010–0.10 mg/kg fortification range

Table 32 Residues of oxamyl in tobacco leaves (solanaceae) from supervised trials following applications of Oxamyl 10SL (continued)

Renewal representative GAP: SEU, One 5.5 kg a.s./ha application (broadcast) or one 3.0 kg a.s./ha application (in-furrow) of Oxamyl 10GR at transplant										
GLP and trial details	Crop/ Variety	Country	Application rate (kg a.s./ha)	Crop growth stage at Applications and at Sampling	Spray conc (kg a.s./hL)	DALA[a]	Residues found[b] (mg/kg)			Recovery data
							Green leaves	Dried leaves	Dried, Fermented leaves	
DuPont-14667 Trial No. 3 GLP 2005	Tobacco/ Basmas	Thessaloniki, Central Macedonia, GR-57020, Greece	1.498 1.500 1.464 1.524	BBCH 12–13 BBCH 14–15 BBCH 16/59 BBCH 19/60 BBCH 49	0.15 0.15 0.15 0.15	36	0.041	0.32	0.012	Green Leaves: mean recovery = 93%, RSD = 14 (n = 8) in 0.010–0.10 mg/kg fortification range; Dried Leaves: mean recovery = 92%, RSD = 8 (n = 10 in 0.010–0.40 mg/kg fortification range; Dried Fermented Leaves: mean recovery = 92%, RSD = 1 (n = 4) in 0.010–0.10 mg/kg fortification range
DuPont-14667 Trial No. 4 GLP 2005	Tobacco/ Katerinis	Pieria, Central Macedonia, GR-60100, Greece	1.484 1.443 1.444 1.479	BBCH 12–13 BBCH 14 BBCH 16 BBCH 19 BBCH 49	0.15 0.15 0.15 0.15	36	0.010	0.021	nd	Green Leaves: mean recovery = 93%, RSD = 14 (n = 8) in 0.010–0.10 mg/kg fortification range; Dried Leaves: mean recovery = 92%, RSD = 8 (n = 10 in 0.010–0.40 mg/kg fortification range; Dried Fermented Leaves: mean recovery = 92%, RSD = 1 (n = 4) in 0.010–0.10 mg/kg fortification range

Table 32 Residues of oxamyl in tobacco leaves (solanaceae) from supervised trials following applications of Oxamyl 10SL (continued)

Renewal representative GAP: SEU, One 5.5 kg a.s./ha application (broadcast) or one 3.0 kg a.s./ha application (in-furrow) of Oxamyl 10GR at transplant										
							Residues found[b] (mg/kg)			
GLP and trial details	Crop/ Variety	Country	Application rate (kg a.s./ha)	Crop growth stage at Applications and at Sampling	Spray conc (kg a.s./hL)	DALA[a]	Green leaves	Dried leaves	Dried, Fermented leaves	Recovery data
DuPont-14667 Trial No. 5 GLP 2005	Tobacco/ Burley	Santa Fe-Granada, Andalucia, 18195, Spain	1.491 1.500 1.500 1.511	BBCH 13–14 BBCH 15 BBCH 15 BBCH 18 BBCH 92	0.15 0.15 0.15 0.15	64	nd	nd	nd	Green Leaves: mean recovery = 93%, RSD = 14 (n = 8) in 0.010–0.10 mg/kg fortification range; Dried Leaves: mean recovery = 92%, RSD = 8 (n = 10 in 0.010–0.40 mg/kg fortification range; Dried Fermented Leaves: mean recovery = 92%, RSD = 1 (n = 4) in 0.010–0.10 mg/kg fortification range

[a] DALA = Days after last application
[b] nd = analyte peak not detected or peak <LOD (<0.007 mg/kg)

II. RESULTS AND DISCUSSION

The residue studies presented were carried out in three European countries and provide data relevant to conditions in southern Europe to support granular application of oxamyl at transplant of tobacco and foliar application of oxamyl on tobacco.

All of the analytical work associated with the studies was performed at Charles River Laboratories, Tranent EH33 2NE, Scotland. The analytical work was carried out during one time period for the 2005 residue trials.

Southern Europe

In the five trials conducted in 2005, following application of Oxamyl 5GR or Oxamyl 10GR at 100-117% of GAP rate of application at transplanting, oxamyl residues were not detected (<0.007 mg/kg) in green, dried, or dried fermented tobacco leaves at 78-105 DALA with the exception of 0.020 mg/kg residues in dried leaves from one trial. In the five trials conducted in 2005, following 4 applications of Oxamyl 10SL at 1.5 kg a.s./ha/application and at last application growth stages BBCH 18–19, oxamyl residues in green, dried, and dried fermented tobacco leaves, ranged from not detected to 0.041 mg/kg, from not detected to 0.32 mg/kg, and from not detected to 0.012 mg/kg, respectively, at 36-54 DALA.

All sets of data show an overall consistent residue profile.

Recovery values for fresh control fortifications run concurrently with treated samples in all the trials are summarised in Table 31 and Table 32. Approximately 80% or more of the recoveries were within 70–110% and the relative standard deviation was approximately 20% or less across all trials. Therefore, the analytical methods used performed well for the analytical determinations in the treated/untreated crop.

III. CONCLUSION

Overall consistent residue behaviour of oxamyl on tobacco leaves was found for one season of study in southern Europe, for application and sampling conducted according to the renewal representative GAP. Residues in green tobacco leaves, dried tobacco leaves and dried, fermented tobacco leaves were not detected (<0.007 mg/kg) in green, dried, or dried fermented tobacco leaves at 78-105 DALA with the exception of 0.020 mg/kg residues in dried leaves from one trial.

(Anderson, I., Cairns, S.D., 2006)

RMS comments and conclusion : The study was performed according to the EU guideline for the crop field trials. Ten trials were conducted in the SEU at application rate according to the critical GAP supported.For all trials the determined residues were below the LOD (<0.007 mg/kg). In addition, the analytical method is compliance with the actual EU guideline on analytical method for residue.

The study can considered useful for residues evaluation.

B.7.3.4 Solarisation

The renewal representative use of solarisation is for vegetables grown under protection. Oxamyl 10SL is applied a minimum of 30 days prior to transplanting (preplant solarisation), at the rate of 5.5 kg a.s./ha. For tomatoes, this preplant solarisation application is followed at transplanting with a rate of 2.0 kg a.s./ha followed by three applications at 1.0 kg a.s./ha/application with a 10-day retreatment interval and a 28-day PHI.

Four residue bridging trials were conducted to support Oxamyl 10SL for use in solarisation applications. In all trials, the residues in fruiting vegetables (cherry tomatoes or courgettes) harvested following in-season applications at the critical GAP were comparable regardless of the addition of the preplanting solarisation applications.

Study submitted to the EU for the first time in this submission.

B.7.3.4/01

Reference: CA 6.3.4/01	**Report:**	Aitken, A., Cairns, S. (2013); Decline and magnitude of oxamyl residues in protected courgettes (fruiting vegetables, cucurbits) and cherry tomatoes (fruiting vegetables, solanacea) following application of Oxamyl 10L formulation via drip irrigation - Europe - 2012 **DuPont Report No.:** DuPont-35356 **Guidelines:** EC Commission Directive 91/414/EEC, OECD 509, SANCO/825/00 rev.8.1 (16/11/2010) **Deviations:** None **Testing Facility:** Charles River Laboratories (UK), Charles River, Tranent, Scotland, UK, Offenbach, Bieber, Germany Testing Facility Report No.: 697787 **GLP:** Yes **Certifying Authority:** Department of Health (U.K.), Entidad Nacional de Acreditacion (ENAC) (Spain)

I. MATERIALS AND METHODS

This study determined the magnitude of residues of oxamyl in/on protected courgettes and protected cherry tomatoes in Europe following treatment with Oxamyl 10L during the 2012 growing season. The test item solution was applied *via* drip irrigation. This study supports the registration of Oxamyl 10L for use in solarisation applications (applications made under plastic 30 days prior to transplant for control of nematodes) on protected fruiting vegetables.

The number, location, test type, and test system (protected courgettes and protected cherry tomatoes, with the variety being common of the representative growing areas) per growing season used in this study are given as follows.

Table 33 Number, location, test type, and test system per growing season for DuPont-35356

Growing season	Test no.	Regulatory region	Country	Location, region	Test type[a]	Crop/Variety[b]
2012	1	southern EU	Spain	Los Palacios, Andalucia	MOR	Protected Cherry Tomato/ Daterino
2012	2	southern EU	Spain	Los Palacios, Andalucia	MOR	Protected Courgette/ Jedida
2012	3	southern EU	Sicily, Italy	Contrada Moglie, Acate (Ragusa)	MOR	Protected Cherry Tomato/ Panarea
2012	4	southern EU	Greece	Nea Magnisia, Thessaloniki, Central Macedonia	MOR	Protected Courgette/ Ezra F1

[a] MOR = magnitude of residue
[b] varieties used were common of the representative growing areas

This was the targeted design of each type of test conducted.

Table 34 Targeted design of each type of test conducted for DuPont-35356

Test no.	Test type[a]	Formulation	No. of appl.	Rate per appl. (kg a.s./ha)	Retreatment interval (days)[b]	Spray volume (L/ha)	DALA[c]
1 and 3	MOR	Oxamyl 10L	4	A1: 2.0 A2-A4: 1.0	A1: 0 DAT A2:10±1 DBA3 A3: 10±1 DBA4 A4: 28±3 DBH	2000	28
			5	A1: 5.5 A2: 2.0 A3-A5: 1.0	A1: 30 DPT A2: 0 DAT A3: 10±1 DBA4 A4: 10±1 DBA5 A5: 28±3 DBH	2000	
2 and 4	MOR		2	A1: 2.0 A2: 1.0	A1: 0 DAT A2: 45±5 DBH	2000	45
			3	A1: 5.5 A2: 2.0 A3: 1.0	A1: 30 DPT A2: 0 DAT A3: 45±5 DBH	2000	

[a] MOR = magnitude of residue
[b] DAT = Days after transplanting; DBA = Days before application; DBH = Days before harvest; DPT: Days prior to transplanting
[c] DALA = Days after last application (days between last application and sampling)

Specimens at each indicated sampling interval were collected at the first commercial harvest date or, in the case of Test 1 where fruits were slow to mature, at 30 DALA and at commercial harvest. There were no surfactants/additives included in the spray mixture.

A summary of the residue tests conducted is given below. Locations of the test sites are given as follows.

Figure 11 Map: Oxamyl solarisation test sites

Test no.	Country	Location, region
1	Spain	Los Palacios, Andalucia
2	Spain	Los Palacios, Andalucia
3	Sicily, Italy	Contrada Moglie, Acate (Ragusa)
4	Greece	Nea Magnisia, Thessaloniki, Central Macedonia

A residue data summary (in mg/kg) is provided below.

To generate these data, the following analysis, recovery and stability information pertains.

Analysis method:

Method ID:	DuPont-33191, Charles River Laboratories Analytical Method No. 1901, "The Determination of Oxamyl (DPX-D1410) in Representative Crop Commodities Using LC-MS/MS''. This method is summarized in Oxamyl Volume 3 B5.
Analyte(s):	Oxamyl
Extraction Solvent/Technique:	Analyte extracted from crop matrix by homogenization followed by shaking with a mixture of organic solvents (acetone, dichloromethane and petroleum ether)
Cleanup Strategies:	Samples are passed through an aminopropyl SPE cartridge and eluted with 1% decanol in dichloromethane.
Chromatography:	Analytical Column: Phenomenex Luna C18, 2.0 mm x 100 mm, 3 µm, 100Å
Detection	LC-MS/MS using positive turbo ion spray. Target ion transition of 237.1/72.0, confirmatory ion transition of 237.1/90.1.
Limit of Quantification:	0.010 mg/kg
Limit of Detection:	0.003 mg/kg

Storage stability:

Treated specimens were stored at *ca* -18°C for no longer than 8 months between sampling and analysis.

Recovery data: Average recovery data for fortifications run concurrently with the treated samples are given in Table 35 to demonstrate the validity of the analytical method.

Table 35 Residues of oxamyl in protected cherry tomatoes and courgettes

Renewal representative GAP: Oxamyl 10SL, 5.5 kg a.s. 30 days before transplant (preplant solarisation); 2.0 kg a.s. at transplanting followed by 3 applications at 1.0 kg a.s./ha/application, 10 days apart; 28-d PHI; all applications *via* drip irrigation								
GLP and trial details	**Crop/ Variety**	**Country**	**Application rate (kg a.s./ha)**	**Crop growth stage at last application and at final sampling**	**Spray conc. (kg a.s./hL)**	**DALA[a] (days)**	**Residues found[b] (mg/kg)**	**Recovery data**
DuPont-35356 Trial No. 1 GLP 2012	Protected Cherry Tomato/ Daterino	Spain, Los Palacios	2.134 + 1.067 + 1.067 + 1.067	BBCH 12+63+63+71, 74+81	NA	30 42	nd nd	Mean recovery = 73% (n = 2) at 0.010 mg/kg fortification Mean recovery = 73% (n = 2) at 0.10 mg/kg fortification
			5.869 + 2.134 + 1.067 + 1.067 + 1.067	Preplant+BBCH 12+63+63+71, 74+81	NA	30 42	nd nd	
DuPont-35356 Trial No. 2 GLP 2012	Protected Courgette/ Jedida	Spain, Los Palacios	2.134 + 1.067	BBCH 12+16, 89	NA	41	0.003	Mean recovery = 72% (n = 2) at 0.010 mg/kg fortification Mean recovery = 74% (n = 2) at 0.10 mg/kg fortification
			5.869 + 2.134 + 1.067	Preplant+ BBCH 12+16, 89	NA	41	nd	
DuPont-35356 Trial No. 3 GLP 2012	Protected Cherry Tomato/ Panarea	Italy, Contrada Moglie, Acate (Ragusa), Sicily,	2.122 + 1.065 + 1.063 + 1.066	BBCH 13+62+64+71, 81	NA	28	0.008	Mean recovery = 73% (n = 2) at 0.010 mg/kg fortification Mean recovery = 73% (n = 2) at 0.10 mg/kg fortification
			5.856 + 2.128 + 1.065 + 1.064 + 1.065	Preplant+ BBCH 13+62+64+71, 81	NA	28	0.006	
DuPont-35356 Trial No. 4 GLP 2012	Protected Courgette/ Ezra F1	Greece, Nea Magnisia, Thessaloniki, Central Macedonia,	2.134 + 1.067	BBCH 11+15, 79	NA	45	nd	Mean recovery = 72% (n = 2) at 0.010 mg/kg fortification Mean recovery = 74% (n = 2) at 0.10 mg/kg fortification
			5.869 + 2.134 + 1.067	Preplant+ BBCH 11+15, 79	NA	45	nd	

[a] DALA = Days after last application
[b] nd = analyte peak not detected or peak <LOD (<0.003 mg/kg)

II. RESULTS AND DISCUSSION

The residue studies presented in the dossier were carried out in the indicated regulatory region(s) and provide data relevant to conditions in those regions.

All of the analytical work associated with the studies was performed at Charles River Laboratories. All of the analyses were carried out between the following dates, the date that the first field specimen was extracted and the date that the last field specimen was analyzed: 20 May 2013 to 07 June 2013.

EU

Residues detected in treated samples following applications made starting at transplant ranged from <0.003 mg/kg (nd) to 0.008 mg/kg. Residues detected in treated samples with an additional solarisation application made 29 days (Test 1) or 30 days (Tests 2, 3 and 4) prior to transplant ranged from <0.003 mg/kg (nd) to 0.006 mg/kg. These residue data indicate the added solarisation application does not cause higher residues in the fruit at harvest.

All tests show an overall consistent residue profile when oxamyl is applied in accordance with the defined good agricultural practice. No oxamyl residues were detected in untreated courgettes or cherry tomatoes.

Concurrent recoveries from untreated tomato samples fortified at the LOQ (0.010 mg/kg) to 10× LOQ (0.10 mg/kg) ranged from 71–75%. Mean recoveries (± standard deviation) for control tomato samples fortified at both levels (0.010 mg/kg and 0.10 mg/kg) were 73% (±3).

Concurrent recoveries from untreated courgette samples fortified at the LOQ (0.010 mg/kg) to 10× LOQ (0.10 mg/kg) ranged from 68–76%. Mean recoveries (± standard deviation) for control courgette samples fortified at both levels (0.010 mg/kg and 0.10 mg/kg) were 73% (±5). Therefore, the analytical methods used perform well for the determination of oxamyl in treated crops.

III. CONCLUSION

Overall consistent residue behaviour was found in EU for application and sampling conducted to support the use of Oxamyl 10SL for solarisation applications.

(Aitken, A., Cairns, S., 2013)

RMS comments and conclusion: The study performed according to the EU guideline for the crop field trials. Four trials performed in the SEU at application rate according to the critical GAP supported. For all trials the determined residues were below the LOD (<0.007 mg/kg). These residue data indicate the added solarisation application does not cause higher residue in the fruit at harvest. In addition, the analytical method used to determine the residue is according to the actual EU guideline on analytical method for residue.

The study can considered useful for residues evaluation.

B.7.4 Feeding studies

The proposed GAP for oxamyl involves application to only one potential animal feed crop - potatoes. Residues in potato tubers when treated in accordance with the proposed GAP are <0.01 mg/kg. These low feed residues result in livestock dietary burdens <0.004 mg/kg bw/day. The Commission Regulation (EU) No 283/2013 states livestock feeding studies shall not be required where intake is below except in cases where the residue, that is to say the active substance, its metabolites or breakdown products, as defined in the residue definition for risk assessment, tends to accumulate. In the case of oxamyl, livestock feeding studies are not required since anticipated residues in the entire diet received are less than 0.004 mg/kg bw/day.

In addition, Commission Regulation (EU) No 283/2013 states livestock feeding studies shall be provided where metabolism studies indicate that residues at levels of above 0.01 mg/kg may occur in edible animal tissue, milk, eggs or fish, taking into account the residue levels in potential feeding stuffs, obtained at the 1 × dose rate, calculated on the dry weight basis. In metabolism studies submitted and evaluated in the Oxamyl Draft Assessment Report 2004 with oxamyl in livestock, no residues of oxamyl were found (<0.01 mg/kg) in human

foodstuffs - milk, eggs, or edible tissues. Consequently, feeding studies are not necessary to assess human exposure to oxamyl from animal food sources.

B.7.4.1 Poultry

As discussed in Point CA 6.4 above, poultry feeding studies are not necessary to assess human exposure to oxamyl from animal food sources.

B.7.4.2 Ruminants

As discussed in Point CA 6.4 above, ruminant feeding studies are not necessary to assess human exposure to oxamyl from animal food sources.

B.7.4.3 Pigs

As discussed in Point CA 6.4 above, pig (swine) feeding studies are not necessary to assess human exposure to oxamyl from animal food sources.

B.7.4.4 Fish

As discussed in Point CA 6.4 above, fish feeding studies are not necessary to assess human exposure to oxamyl from animal food sources.

B.7.5 Effects of processing

Commission Regulation (EU) No 283/2013 states that processing studies are not necessary "if no significant (>0.1 mg/kg) or no analytically quantifiable residues occur in the plant product being processed". No oxamyl residues (≤0.01 mg/kg) were found in commonly processed commodities (potatoes, tomato, tobacco) at the time of harvest or during residue decline studies. Consequently, processing studies are not required.

However, a study investigating the nature of the residue following high-temperature hydrolysis simulating industrial processing and/or household preparation was conducted, submitted and evaluated as part of the Annex I inclusion of oxamyl in 2004.

In addition, in Point CA 6.5.3 below, data from a follow-up study discussed. In one study, the transfer of residues from raw potato tubers to potato tubers following baking, boiling and microwave preparation investigated and is summarised as supplementary data.

B.7.5.1 Nature of the residue

A study investigating the nature of the oxamyl residue following high-temperature hydrolysis simulating industrial processing and/or household preparation was conducted, submitted and evaluated in the Oxamyl Draft Assessment Report, Volume 3, Annex B.7, 2004. Oxamyl was stable under pasteurisation conditions, degraded (57.8% remaining) under baking/boiling conditions, and completely degraded under sterilisation conditions. The only degradation product was the oxime metabolite.

Study submitted in the EU Dossier in 2001 and included in the first EU approval review.

B.7.5.1/01

Reference: --	**Report:**	Lee, D.Y. (2001); Hydrolysis to investigate the nature of potential residues of oxamyl in products resulting from industrial processing or household preparation **DuPont Report No.:** DuPont-4025

		Guidelines: 7035/VI/95, rev 5 (1997)

1. Test material: [1-^{14}C]oxamyl
   Lot/Batch #: HOTC 417
   Purity: Radiochemical purity - >96%

Study Objectives:
Effects of pasteurization involved the preparation of sterile solutions at pH=4 which are heated to 90°C for 20 minutes.

Effects of baking, brewing or boiling were studied by preparing sterile solutions at pH5 and heating them to 100°C for 60 minutes.

Effects of sterilization were studied by preparing sterile solutions at pH6 and heating them at 120°C for 20 minutes.

The Oxamyl was present in each of the test solutions at a concentration of circa 19.0 µg/litre.

Samples were analysed for total ^{14}C present and also to determine the presence of parent and metabolites.

Results:
Oxamyl does not degrade when subject to pasteurization.

When Oxamyl was treated using the "brewing/baking/boiling" conditions it degraded to 57.8% of the original amount present. The only metabolite formed was oxamyl-oxime which accounted for 41.42% of total ^{14}C.

Oxamyl degrades completely when treated using the sterilizing conditions indicated above. Under these conditions Oxamyl degrades completely to its oxime.

Conclusion:
This study indicates that Oxamyl is stable at pH 4 and 90°C for 20 minutes. When the temperature is increased to 100°C, at pH 5, Oxamyl becomes increasing labile and is degraded rapidly to its Oxime at 120°C at pH 6.

The nature of the residue study DuPont-4025, originally submitted under EU Rev8 Point IIA 6.5.1 and conducted with test material [1-14C]oxamyl, was conducted under guideline 7035/VI/95, rev 5 (1997). A review of this study indicates that it fully meets the current guideline (OECD Test Guideline 507: Nature of the Pesticide Residues in Processed Commodities - High Temperature Hydrolysis).

RMS comments and conclusion: The study is acceptable.

B.7.5.2 Distribution of the residue in peel and pulp

Pulp and peel are not relevant to the representative crops proposed for oxamyl use.

B.7.5.3 Magnitude of residues in processed commodities

Study submitted to the EU for the first time in this submission.

B.7.5.3/01

Reference: CA 6.5.3/01	**Report:**	Foster, A. (2009); Magnitude of oxamyl residues in potatoes and potato processed fractions following exaggerated rate applications of Oxamyl 10G formulation - Europe 2009 **DuPont Report No.:** DuPont-27667 **Guidelines:** Directive 91/414/EEC **Deviations:** None **Testing Facility:** Charles River Laboratories (UK), Tranent, Scotland, UK Testing Facility Report No.: 694126 **GLP:** Yes **Certifying Authority:** Department of Health (U.K.)

I. MATERIALS AND METHODS

A potato processing study was to determine the magnitude of residues of oxamyl in/on raw potato tubers and processed fractions of potato tubers in Europe following exaggerated treatment with Oxamyl 10GR during the 2009 growing season to allow estimates of transfer factors to processed commodities. The granular test item formulation was applied manually. Three tests consisting of three different early potato varieties planted in control and treated boxes containing acidic compost (pH 4.0-.5) were established in northern Europe. All three tests were processing tests, from which samples for uncooked and cooked (processed) specimens were generated. In all tests, Oxamyl 10GR (DPX-D1410-516) was applied six times commencing with Application A1 on the day of tuber planting. Application A2 was repeated after 28 days followed at 7-day intervals with applications A3-A6 inclusive. Application A1 was applied at a target application rate of 16.5 g fp/m2 (16.5 kg a.s./ha). Application A2–A6 inclusive were applied at a target application rate of 5.5 g fp/m2 (5.5 kg a.s./ha) for a seasonal target application of 44 kg a.s./ha, 8× the critical EU GAP. Early variety potatoes, planter boxes containing low pH compost, an exaggerated at-plant application rate and an exaggerated number of applications were employed, after review by the UK Chemicals Regulation Directorate (CRD), to produce quantifiable oxamyl residues in the raw potato tubers to allow adequate estimates of transfer factors. The study use patterns are summarized in Table 36.

The magnitudes of residues in the raw potato tubers are not representative of residues following on-label use of oxamyl.

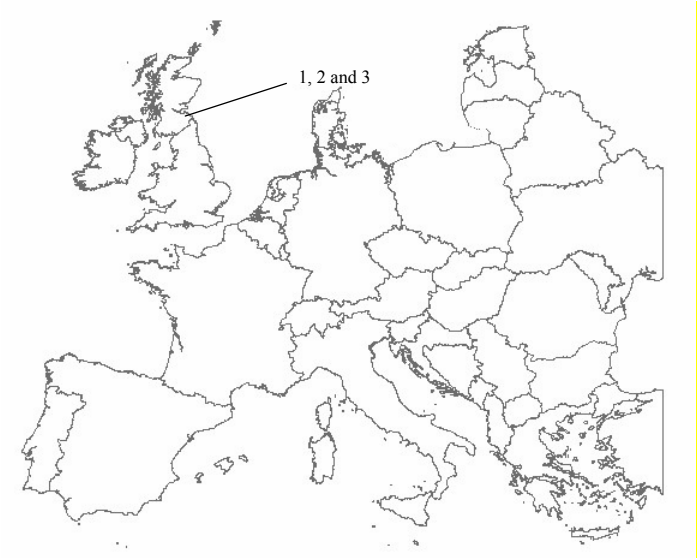
Table 36 Study use pattern – potato tubers

Test Identification (City, State/Region, Country, Year, Variety)	EP[a]	Application						Tank Mix Adjuvants	Ref
		Method/ Timing[b]	Vol (L/ha)	kg a.s./ha	g a.s./hL	RTI[c] Days	Total Rate kg a.s./ha		
Test 01 (Tranent, East Lothian, UK, 2009, Rocket)	10 GR	Manual – A1 at planting; A2-A6 every 7 days starting 28 days after A1	NA[d]	16.33 5.45 5.45 5.45 5.45 5.45	NA	- 28 7 7 7 7	43.58	NA	DuPont-27667
Test 02 (Tranent, East Lothian, UK, 2009, Arran Pilot)	10 GR	Manual – A1 at planting; A2-A6 every 7 days starting 28 days after A1	NA	16.33 5.45 5.45 5.45 5.45 5.45	NA	- 28 7 7 7 7	43.58	NA	DuPont-27667
Test 03 (Tranent, East Lothian, UK, 2009, Wilja)	10 GR	Manual – A1 at planting; A2-A6 every 7 days starting 28 days after A1	NA	16.33 5.45 5.45 5.45 5.45 5.45	NA	- 28 7 7 7 7	43.58	NA	DuPont-27667

[a] EP = End-use Product, Oxamyl 10GR
[b] DBH = Days before harvest
[c] Retreatment Interval
[d] Not applicable for granular application

A total of three residue processing field tests in northern Europe were conducted. Locations of the test sites are given in the following figure.

Figure 12 Map: Oxamyl potato processing field test sites



Reference, Test No	Location
DuPont-27667, 1	Tranent, Edinburgh, UK
DuPont-27667, 2	Tranent, Edinburgh, UK
DuPont-27667, 3	Tranent, Edinburgh, UK

For all tests, bulk specimens of potato tubers were collected at maturity, 46 days after the last application. Initially, per test, one raw potato tuber control specimen together with three raw potato tuber treated specimens were submitted for analysis. Following the determination of detectable oxamyl residues in the raw agricultural commodity (uncooked potato tubers), a cooking phase was conducted to generate cooked potato tuber specimens (separate baked, boiled and microwaved specimens). The cooking phase occurred three days after harvesting the bulk potato tuber samples. During these three days the bulk uncooked samples were stored in a cool, dark location which simulated commercial practice. All the analysed specimens (raw and cooked) were unpeeled and had been lightly washed to remove adhering compost at the time of harvest.

A data summary (in mg/kg) is presented in Table 37.

To generate these data, the following analysis, stability and recovery information pertains.

Analysis method:	LC-MS method (DuPont-11125) developed as the oxamyl residue method for determining residues of oxamyl in/on crop matrices. This method is summarized in Oxamyl Volume 3 B5.
Analyte:	Oxamyl
Extraction:	Analyte extracted from crop matrix by homogenization followed by shaking with a mixture of organic solvents (acetone, dichloromethane and petroleum ether)
Clean-up:	Samples are passed through an aminopropyl SPE cartridge and eluted with 1% decanol in dichloromethane.
Chromatography:	Analytical Column: Agilent Hypersil ODS, 2.1 mm × 100 mm, 3 µm
Detection:	Mass spectrometer detection (MS) in positive electrospray mode. Selective ion monitoring for 237.3 m/z.
LOQ:	0.005 mg/kg

Storage stability: Raw and processed potato tuber samples were stored at *ca* -18°C (±5°C) for less than 1 month between sampling and analysis.

Table 37 Residues of oxamyl in potato commodities from supervised tests

Country, location, year, test no., variety	Application				DALA[a]	Residues (mg/kg)[b, c]			
						Potatoes			
	Formulation test item	BBCH: last appln.	Appln No.	kg a.s./ha		Whole uncooked tubers	Baked tubers	Boiled tubers	Micro-waved tubers
UK, Tranent East Lothian, 2009, 1, Rocket	Untreated	-	-	-	Control	nd	nd	nd	nd
	Oxamyl 10GR	501-505	A1 A2 A3 A4 A5 A6	16.33 5.45 5.45 5.45 5.45 5.45	46	0.077 0.11 0.10	0.017 0.011	nd nd	nd nd
UK, Tranent East Lothian, 2009, 2, Arran Pilot	Untreated	-	-	-	Control	nd	nd	nd	nd
	Oxamyl 10GR	501	A1 A2 A3 A4 A5 A6	16.33 5.45 5.45 5.45 5.45 5.45	46	0.11 0.10 0.057	0.0094 0.0056	nd nd	nd nd
UK, Tranent East Lothian, 2009, 3, Wilja	Untreated	-	-	-	Control	nd	nd	nd	nd
	Oxamyl 10GR	309	A1 A2 A3 A4 A5 A6	16.33 5.45 5.45 5.45 5.45 5.45	46	0.086 0.070 0.053	nd nd	nd nd	nd nd

[a] Days after last application
[b] The designation "nd" is used for samples for which no peak was observed or residue was <LOD (below the limit of detection; <0.0033 mg/kg). For calculations, 0.0033 mg/kg was used for specimens with no detectable (nd) residues.
[c] Three replicate samples of whole uncooked tubers were taken for analysis. Two replicate samples of tubers were taken to be processed by baking, boiling or microwaving.

Recovery data: Average recovery data for fortifications run concurrently with the treated specimens are given below to demonstrate the validity of the analytical method.

Table 38 Summary of concurrent recoveries of oxamyl from potato commodities

Matrix	Fortification level in ppm (mg/kg)	Sample size (n)	Recoveries (%)	Mean ± std. dev. (RSD) (% ± %(%))
Raw tubers	0.005 0.10	2 2	81, 85 90, 96	83 ± 3 (3) 93 ± 4 (4)
Microwaved baked tubers	0.005 0.10	2 2	114, 92 95, 95	103 ± 15 (15) 94 ± 2 (2)
Boiled tubers	0.005 0.10	2 2	156[a], 97 99, 114	NA 107 ± 11 (10)
Baked tubers	0.005 0.10	2 2	85, 91 92, 91	88 ± 4 (5) 91 ± 1 (1)

[a] Value excluded from calculations.

II. RESULTS AND DISCUSSION

The residue processing studies presented herein were carried out in the UK and provide data relevant to the home preparation of potatoes.

All of the analytical work associated with the tests presented herein was performed at Charles River Laboratories, Tranent, EH33 2NE, Scotland. The analytical work was carried out during July 2009.

Average oxamyl residues in triplicate specimens of raw potato tubers ranged from 0.070 to 0.096 mg/kg. Following light washing plus baking, boiling, or microwaving of potatoes average oxamyl residues in duplicate specimens were reduced.

Median transfer factors of oxamyl residues in prepared commodities compared to residues in the unprocessed tubers were 0.08 (range: <0.1-0.15), <0.1 (all: <0.1), and <0.1 (all: <0.1) for baked tubers, boiled tubers, or microwaved tubers, respectively. Transfer factors are summarized in Table 39.

All 4 sets of data show an overall consistent residue profile when active is applied in accordance with GAP.

The mean overall percent recovery for oxamyl from 15 control unpeeled potato tubers freshly fortified at 0.005 and 0.10 mg/kg (uncooked, microwaved, boiled, and baked) was 94 ± 9% (RSD = 10). Most of the recoveries were within 70–120% and the relative standard deviations were less than 20% for all tests. Therefore, the analytical methods used performed well for the determination of oxamyl in raw and processed potatoes.

Table 39 Transfer factors from potato processing study with oxamyl

Country, location, year, test no., variety	RAC	Processed commodity	Total rate (kg a.s./ha)	DALA/ PHI (days)	Average residues (mg/kg) [a]	Transfer factor [b]
UK, Tranent, East Lothian, 2009, 1, Rocket	Potato tubers	---	43.58	46	0.096	--
		Baked tubers			0.014	0.15
		Boiled tubers			nd	<0.1
		Microwaved tubers			nd	<0.1
UK, Tranent, East Lothian, 2009, 2, Arran Pilot	Potato tubers	---	43.58	46	0.089	--
		Baked tubers			0.0075	0.08
		Boiled tubers			nd	<0.1
		Microwaved tubers			nd	<0.1
UK, Tranent, East Lothian, 2009, 3, Wilja	Potato tubers	---	43.58	46	0.070	--
		Baked tubers			nd	<0.1
		Boiled tubers			nd	<0.1
		Microwaved tubers			nd	<0.1

[a] The designation "nd" is used for treated specimens for which no peak was observed or residue was <LOD (below the limit of detection; <0.0033 mg/kg). For calculations, the LOQ (0.01 mg/kg) was used for fractions with no detectable (nd) residues.
[b] Transfer Factor = Oxamyl residues in processed commodity/ Oxamyl residues in unprocessed potato tubers.

III. CONCLUSION

Overall consistent residue behaviour of oxamyl in/on potato tubers during processing was found in one season of study in the EU. Early variety potatoes, planter boxes containing low pH compost, an exaggerated at-plant application rate, and an exaggerated number of applications were employed to produce quantifiable oxamyl residues in the raw potato tubers to allow adequate estimates of transfer factors. The magnitudes of residues in the raw potato tubers are not representative of residues following on-label use of oxamyl.

Average oxamyl residues in triplicate specimens of raw potato tubers ranged from 0.070 to 0.096 mg/kg. Following light washing plus baking, boiling, or microwaving of potatoes average oxamyl residues in duplicate specimens were reduced.

Median transfer factors of oxamyl residues in prepared commodities compared to residues in the unprocessed tubers were 0.08 (range: <0.1-0.15), <0.1 (all: <0.1), and <0.1 (all: <0.1) for baked tubers, boiled tubers, or microwaved tubers, respectively.

(Foster, A., 2009)

RMS comments and conclusion: The study is acceptable. These residue data indicate the added solarisation application does not cause high residues in the processed commodities. ~~fruit at harvest~~.

B.7.5.4 Overview of processing studies

Processed commodity	Number of tests	High PF	Median PF	Reference
Potato tubers, baked	3	0.15	0.08	DuPont-27667
Potato tubers, boiled	3	<0.1	<0.1	DuPont-27667
Potato tubers, microwaved	4	<0.1	<0.1	DuPont-27667

B.7.6 Residues in rotational crops

Three confined rotational crop studies were conducted, submitted, and evaluated in the Oxamyl Draft Assessment Report, Volume 3, Annex B.7, 2004. The studies were conducted with ^{14}C-oxamyl applied to the soil and the soil aged for 30, 120, and/or 363 days. Significant ^{14}C-oxamyl residues remained in the soil at planting in all three studies, allowing for assessment of the potential for accumulation of oxamyl derived residues in rotational crops (beets, cabbage, sorghum, barley, and lettuce). In the confined rotational crop studies, oxamyl, IN-A2213, and IN-D2708 were identified at concentrations >0.01 mg/kg (oxamyl equivalents) in barley, beet, cabbage, and lettuce commodities planted 30 and 120 days after soil treatments of 9 and 20 kg oxamyl/ha. These components have been previously identified in plant metabolism studies and all were present in the soil at planting. The identification of these components and the characterisation of several tentatively identified metabolites (IN-KP532, IN-T2921, IN-L2953, and IN-N0079) in barley planted 30 days after soil treatment at 8 kg oxamyl/ha further support the metabolic profile in the rotated crop. The proposed metabolic pathway of oxamyl in rotated crops is consistent with the pathway seen in plants following oxamyl application at planting or postemergence (see Point CA 6.2 in this document) and verifies the residue definition for food of plant origin as parent oxamyl only.

At four residue trial locations in the northern EU, oxamyl residues were determined in rotational crops planted in a field that had previously contained potatoes treated with Oxamyl 10GR applied at planting at 5.0–5.5 kg a.s./ha. Oxamyl residues in succeeding crops (lettuce, carrot roots and tops, and cereal grain, hay, and straw) planted 80 and 120 days after Oxamyl 10GR application and harvested at maturity were <0.007 mg/kg.

At two residue trial locations in the southern EU, oxamyl residues were determined in rotational crops planted in protected plots that had previously contained melons treated with Oxamyl 10SL applied at 6.0 kg a.s./ha/season. Oxamyl residues in succeeding crops (lettuce and radish roots and radish tops) planted *ca.* 30, 60, 90, and 120 days after Oxamyl 10SL application and harvested at maturity were <0.007 mg/kg.

B.7.6.1 Metabolism in rotational crops

Study submitted in the EU Dossier in 2001 and included in the first EU approval review.

B.7.6.1/01

Reference:	**Report:**	Harvey, J. (1978); Crop rotation study with ^{14}C-oxamyl in the greenhouse **DuPont Report No.:** O/ME 34 **Guidelines:** Not given
--		

1. Test material: [^{14}C]oxamyl
   Lot/Batch #: Not given
   Purity: Not given

Study Details:

Soil was treated at a rate equivalent to 8.9 kg as/ha using a foliar application. The soil was aged for both 30 and 120 days. Samples were taken for analysis at both 30 and 120 days to determine the quantity and composition of the ^{14}C remaining in the soil.

Beet, cabbage and sorghum seeds were cultivated in both 30 and 120d aged pots and grown to maturity. At maturity the crops were harvested and analysed for total ^{14}C and characterized in terms of the quantity of ^{14}C extracted into methanol and partitioning into ethyl acetate.

Results:

^{14}C Oxamyl degrades rapidly in sandy loam soil. After 30 days 52% of the ^{14}C had been lost completely while at 120d 88% of the ^{14}C was lost. It was suggested that this loss occurred as $^{14}CO2$ but no confirmatory information was provided. At 30 days post application 19% of the applied dose Oxamyl is still present in soil but at 120d post application it has practically disappeared as only 0.3% of the applied dose remains.

At 30d and 120d residues of ^{14}C present in the cultivated crops were determined and are as listed in Table 40 below.

Table 40 ^{14}C residues present in crops grown on soil treated with ^{14}C Oxamyl and aged for 30 and 120 days.

	ppm ^{14}C-residues (calculated as ^{14}C-Oxamyl equivalents)		
Sample type.	**Total ^{14}C present**	**Ethyl acetate soluble ^{14}C residues.**	**Oxamyl + Oxime equivalents.**
30 day aged soil crops			
Beet leaves.	4.2	0.47	0.12
Beet Roots.	0.6	0.02	----
Cabbage head	0.6	0.04	0.01
Sorghum fodder	2.2	0.18	0.06
Sorghum seed.	1.1	0.02	-----
120 day aged soil crops.			
Beet leaves	0.15	0.02	----
Beet Roots.	0.07	<0.01	-----
Cabbage head.	0.15	0.01	-----
Sorghum fodder.	0.18	0.02	-----
Sorghum seed.	0.15	0.01	------

Conclusion:

The study is quite basic in the manner in which it is presented. Results and conclusions are presented but the supporting chromatographic and analytical information is not included in the study.

The study indicates that Oxamyl is rapidly degraded in soil and that total 14C residues are rapidly dissipated.

The study indicates that residues of Oxamyl and its oxime are present at low levels in the leafy portions of the crops cultivated in Oxamyl treated soil 30 days after application. No residues of Oxamyl and its oxime are found in plants grown on the soil 120 day after application. The study does not provide data as to the ratios of Oxamyl to Oxime present in these plant parts.

The metabolism in rotational crops study O/ME 34, originally submitted under EU Rev8 Point IIA 6.6 and conducted with test material [^{14}C]oxamyl. Guideline was not given. A review of this study indicates that it partially meets the current guideline (OECD 502: Metabolism in Rotational Crops). The study predates EU/EPA guidelines and the required level of analytical details is not provided. However, when submitted in conjunction with AMR 1190-88 and DuPont 4518, it adequately completes the understanding of metabolism in rotational crops.

RMS comments and conclusion: The study can considered useful to understand the metabolism in rotational crops. The study is acceptable.

Study submitted in the EU Dossier in 2001 and included in the first EU approval review.

B.7.6.1/02

Reference: --	**Report:**	Hawkins, D.R., Mayo, B.C., Pollard, A.D., Donschak, A.W. (1990); The confined accumulation of [^{14}C] oxamyl in rotational crops **DuPont Report No.:** AMR 1190-88 **Guidelines:** U.S. EPA 165-1 (1982)

1. Test material: [1-^{14}C]oxamyl
   Lot/Batch #: HOTC 311
   Purity: Radiochemical purity - >97%

Study Details:

Soil was treated at a rate equivalent to 17.8 kg as/ha using a foliar application. The soil was aged for 30, 120 and 363 days. When the aging interval was reached the rotational crops barley, beetroot and lettuce were planted and grown to maturity. Soil samples were taken on the day of application, time of planting and at maturity to determine the concentration and nature of the remaining ^{14}C. Representative crop samples were analysed to determine the total ^{14}C present and where significant residues were present the sample extracts were analysed further to determine the nature of the residue.

Results:

Sandy loam soil, from the UK, was collected and used in the present study. Details of the ^{14}C present in soil at the different study intervals are presented in Table 40. The information provided indicates that the total ^{14}C present in soil following the application of Oxamyl has a t1/2 of circa 76 days in this soil. This is approximately 2x that estimated in the study presented above.

The extractability of ^{14}C from soil, using methanol and methanol/water, decreases from day 0 when 97% of the residue can be extracted to 3.9% of the residue being extractable from the 363 day aged soil.

The ^{14}C residue present in soil aged for 30 and 120 days is of the same order of magnitude but it is clear from the data presented in Table B.7.9.1.2.2. below that there is much greater uptake of ^{14}C residue into plants for those grown in the 30d aged soil as opposed to those grown on the120 day aged soil. This is probably linked to the increased polarity of the residue and the associated difficulty in it being extracted from soil over time.

Control samples of barley, beetroot and lettuce all contain ^{14}C residues ranging from 0.5 to 3.7 µg/g of Oxamyl equivalent residues for 30day aged soil cultivations. Lower levels were found for the 120 and 363 day aged soil cultivations. It was indicated that this residue was most likely to be due to degradation of Oxamyl and re-incorporation of the ^{14}CO2 formed back into the control plants. The control plants were cultivated within the same growth room so this explanation is reasonable.

Samples were extracted using Methanol and methanol/water. These extracts were analysed by TLC. The results of these analyses detailing the concentrations of oxamyl and oxamyl oxime present in the cultivated crops are presented in

Table 41 below. The extracts were also found to contain up to 4 different polar fractions which were not identified during the study apart from the ^{14}C remaining at the origin of the TLC plate and that which was not extracted by the solvents used.

Table 41 ^{14}C-Oxamyl equivalent (μg equivalent/g dry weight soil) residues present in soil samples both pre and post aging and at harvest.

	30- day aged soil		120 day aged soil.		363 day aged soil.	
Soil Samples.	Treated soil	Control soil	Treated soil	Control soil.	Treated soil	Control soil.
0 day soil after						
Barley soil	18	<0.09	21	<0.09	17	<0.09
Beetroot soil	14	<0.09	16	<0.09	20	<0.09
Lettuce soil	20	<0.09	16	<0.09	18	<0.09
Mean soil residue.	17 ±3		18 ± 3		18 ±2	
Aged (at sowing)						
Barley soil	5.1	<0.18	4.6	<0.14	0.31	<0.02
Beetroot soil.	22	<0.18	10	<0.14	0.96	<0.02
Lettuce soil.	12	<0.18	7.1	<0.14	0.65	<0.02
Mean soil residue.	13 ± 8		7.2 ± 2.7		0.64±0.33	
At Harvest						
Barley forage soil.	2.2 (+41 day)	0.03	3.4 (+130 day)	<0.15	0.42 (+374 day)	<0.02
Barley soil	13 (+170d)	<0.05	4.5 (+274 day)	<0.06	1.1 (+527 day)	<0.02
Beetroot soil	1.4 (+ 126 d)	<0.11	1.2 (+238 day)	<0.03	1.1 (+466 day)	<0.04
Lettuce soil	1.0 (+ 126 d)	<0.11	3.1 (+207 day)	<0.14	0.87 (+427day)	<0.04

Table 42 Total ^{14}C-Oxamyl equivalent (μg equivalent/g of crop) residues present in crops grown on soil aged for 30, 120 and 363 days.

	30- day aged soil		120 day aged soil.		363 day aged soil.	
Crops (days following planting).	Treated soil	Control soil	Treated soil	Control soil.	Treated soil	Control soil.
Barley.						
- Forage. (10-11d)	21	1.3	1.7	<0.09	0.05	<0.02
- Straw. (140- 170d)	38	2.9	5.2	0.73	0.29	0.1
- Chaff (140-170d)	24	3.7	3.6	0.62	0.19	0.1
- Grain. (140- 170d)	7.2	3.0	1.3	0.37	0.11	0.06
Beetroot.						
- Foliage (90-120d)	24	0.5	6.8	0.08	0.08	<0.04
- Peel. (90- 120d)	14	2	2.3	0.16	0.24	<0.07
- Root. (90- 120d)	7.1	2	0.86	0.13	0.04	<0.04
Lettuce.						
- Total lettuce (60- 100d)	3.1	0.5	0.27	0.11	0.03	<0.03

Table 43 The concentration of Oxamyl and Oxamyl oxime (μg of Oxamyl equivalents/g sample) present in crops grown on soils aged for 30 and 120 days

	Soil aged for 30 days.		Soil aged for 120 days.	
Crop/sample.	**Oxamyl**	**Oxime**	**Oxamyl**	**Oxime.**
Soil (at time of planting)	8.3	0.9	1.7	1.3
Barley				
- Forage	12	2.2	0.53	0.3
- Straw.	5.9	0.99	0.16	0.08
- Chaff	1.5	0.89	0.08	0.08
- Seed	<0.03	<0.03	<0.01	<0.01
Beetroot.				
- Foliage	2.5	1.4	<0.06	<0.06
- Root peel	<0.11	0.29	<0.01	<0.01

- Root.	0.13	0.33	<0.01	0.04
Lettuce	0.18	0.12	<0.01	<0.01

Note: Samples were analysed using TLC. Confirmation of the residues was by TLC using different analytical conditions. The degree to which TLC can be used to accurately identify and quantify residues of Oxamyl and it's oxime when present is complex sample matrices is considered to be limited. It is felt that the values presented above should be considered as being indicative of the residue levels

Conclusions:

Oxamyl was applied to soil at a rate of circa 3x the recommended potato GAP. Any residues found would be expected therefore to be far greater than the levels found following normal usage of Oxamyl. This report studies the uptake and distribution of Oxamyl from soil aged for 30, 120 and 363 days into the crops Barley, Beetroot and Lettuce.

The study shows that Oxamyl and its oxime are present in both beetroot and lettuce when cultivated on soil aged the 30 days. Residues are not detectable in these crops when grown on soil aged for 120 days. In the case of barley higher residues of Oxamyl and its oxime are found in the forage and straw in the crop grown on soil aged for 30 days with significantly reduced levels present in the same crop fractions when grown on soil aged for 120 days. No residues of Oxamyl or its oxime were found in barley grain in the soils aged for both 30 and 120 days. This data is presented in Table 43 above.

Apart from Oxamyl and its oxime no other compound was identified in these rotational crops.

The potential of TLC to accurately identify and quantify the components of complex sample extracts is considered to be limited. It is felt that, due to these limitations, the residue levels of Oxamyl and its oxime found in the crops analysed are indicative only.

At least 4 other ^{14}C fractions are isolated using TLC when the sample extracts are analysed. None of the components of these fractions were identified but they were considered to be polar in nature on the basis of their TLC behaviour.

If crops are cultivated in soil treated with Oxamyl within 30 days of treatment residues of Oxamyl and its oxime are detected in these crops. It is necessary, to ensure that MRL's will not be exceeded, to place a label restriction which indicates that following crops should not be planted within 120 days following application. Moreover, EFSA Journal 2010;8(10):1830 also concludes that the studies on nature of residues in succeeding crops "*also indicated that if crops are planted within 120 days of oxamyl application then residues of oxamyl and oxamyl oxime may occur in the roots and aerial parts of these crops. In order to minimize the possibility of residues being detected in the rotational crops EFSA recommends the setting of a restriction to crop rotation"*.

The metabolism in rotational crops study AMR 1190-88, originally submitted under EU Rev8 Point IIA 6.6 and conducted with test material [1-^{14}C]oxamyl, was conducted under guideline U.S. EPA 165-1 (1982). A review of this study indicates that it partially meets the current guideline (OECD 502: Metabolism in Rotational Crops). The required level of analytical details and characterization are not provided. However, when submitted in conjunction with O/ME 34 and DuPont 4518, it adequately completes the understanding of metabolism in rotational crops.

RMS comments and conclusion: The study is not complete due to the lack on analytical data and characterisathion. Anyway, if we conseder also the study DuPont 4518 it possible to have a full set of information.

Study submitted in the EU Dossier in 2001 and included in the first EU approval review.

B.7.6.1/03

Reference:	**Report:**	Brown, A. M., Young, G. A., Swain, R. S. (2001); Accumulation of residues in

--		confined rotational crops (barley) after soil treatment with ^{14}C-oxamyl **DuPont Report No.:** DuPont-4518 **Guidelines:** OPPTS 860.1850 (1996)

1. Test material: [1-^{14}C]oxamyl
   Lot/Batch #: D1410-367
   Purity: Radiochemical purity - >95%

Study submitted in the EU Dossier in 2003 and included in the first EU approval review.

B.7.6.1/04

Reference: --	**Report:**	Brown, A. M., Young, G. A., Swain, R. S. (2002); Accumulation of residues in confined rotational crops (barley) after soil treatment with ^{14}C-oxamyl **DuPont Report No.:** DuPont-4518, Supplement No. 1 **Guidelines:** OPPTS 860.1850 (1996)

1. Test material: [1-^{14}C]oxamyl
   Lot/Batch #: D1410-367
   Purity: Radiochemical purity - >95%

Study Details:
Soil was treated at a rate equivalent to 8 kg as/ha. The soil was aged outdoors for 30 days prior to planting the rotational crop of barley was then grown to maturity in a glasshouse. The objectives of the current study were to:

Determine the level of uptake into the rotational crop, barley.

To compare the metabolites found in barley with the results of previous studies.

To determine the nature of the terminal residue present in the raw commodity when the levels were in the range 0.01 to 0.05mg/kg or greater.

Samples taken were stored frozen until they were analysed.

Soil samples were taken at treatment, at planting, at hay sampling and at final harvest and were stored frozen until analysis.

Samples were analysed by extraction of the residue using methanol, methanol/water and finally water. Samples were analysed by LSC, HPLC and TLC.

Distribution of ^{14}C in soil and barley:
Analysis of soil residues at day 0, 30, 93 and 166 showed that the extractability of the residue decreased rapidly from 94.8% of TRR at day 0 to 7% of TRR at day 166. There was a corresponding decrease in the concentration of Oxamyl present over the same time period.

The results of this analysis are presented in Table 44 below, and indicate that the t1/2 for Oxamyl in soil is very short with only 14.8% of the soil ^{14}C remaining as Oxamyl after 30 days.

Table 44 Total Radioactive Residues in Aqueous Organic soil Extracts.

	Total ^{14}C residues, Oxamyl equivalents; % TRR (mg/kg)			
	Day 0	**Day 30**	**Day 93**	**Day 166**
Total Residues	5.51	0.65	0.35	0.54
Aqueous Organic extractable	94.8 (5.22)	32.9 (0.21)	16.2 (0.06)	7.0 (0.04)
Oxamyl	78.8 (4.34)	14.8 (0.1)	8.8 (0.03)	1.0 (0.01)
IN-A2213	1.5 (0.08)	2.3 (0.02)	0.8 (<0.01)	0.5 (<0.01)
IN-D2708	11.2 (0.62)	3.2 (0.02)	1.7 (0.01)	0.8 (0.01)
Others.	2.7 (0.15)	8.4 (0.06)	3.8 (0.01)	4.1 (0.02)

Analysis of TRR in soil and crop samples shows that ^{14}C residues reduce, as expected, from the levels found in forage to those found in grain and straw. Details of these levels are presented in Table 45 below.

Table 45 TRR residues (TRR's) in soil and barley samples following application of ^{14}C-Oxamyl

Timing and method of application.	**Matrix.**	**Days after planting**	**Total ^{14}C Residues as mg oxamy equivalents/ kg. (TRR based on combustion**
A single application to the soil surface 30 days before planting.	Day 0 soil (treatment)		5.51
	Day 30 soil (planting)		0.65
	Forage	20	6.71 (7.17)
	Day 93 soil (Hay collection)		0.35
	Hay.	63	1.19 (1.42)
	Day 166 soil (final harvest)		0.54
	Straw.	136	1.58 (1.79)
	Grain.	136	0.32 (0.26)

Characterisation and identification of radioactive residues:

Soil samples were taken for analysis at day 0, 30, 93 and 166 and the ^{14}C present showed a rapid decline between day 0 and day 30. After day 30 the ^{14}C residues present did not change substantially. The extractability of the ^{14}C residue changes substantially with time however with 94.8% being extractable at day 0 dropping to 32.9% at day 30, 16.2% at day 93 and finally dropping to 7% at day 166. Over this time period there is also a substantial reduction in the levels of Oxamyl present in soil while the residues of the metabolites IN-D2708 and IN- A2213 remain relatively stable. This information is presented in Table 44 above.

Barlely grain: The major extractable component of grain was identified as metabolite IN-D2708. This was identified by both HPLC and TLC using co-chromatography and by derivatisation of the metabolite with trimethylsilyl diazomethane and comparison with a comparative standard reference molecule. Oxamyl and its oxime were not detected in grain. Hydrolysis of the extracted insoluble fraction with cellulase, alkali and acid released a further 7.9%, 3.2% and 2.0% of the TRR respectively (= a total of 13% of the TRR released by hydrolysis). 27% of the TRR remained unextractable. The presence of IN-D2708 as the major metabolite in barley grain corresponds to the situation in potato tubers where the same metabolite corresponded to 70% of the residue present.

Barley Forage: 88.8% of the ^{14}C residue present in forage was solvent extractable. Analysis of this extract showed the presence of thirteen different ^{14}C fractions, see Table 45 below. Oxamyl and its metabolites IN-D2708 and IN-A2213 are the main identified constituents of the ^{14}C residue present in forage. Other smaller quantities of the ^{14}C present in the forage behave chromatographically similar to the metabolites IN-KP532, IN-L2953 and IN-N0079. Six other unknown ^{14}C fractions were isolated but not identified chromatographically and did not correspond to any of the other Oxamyl metabolites studied.

Barley Hay: TRR in barley hay is present at circa 20% of that in forage. The ^{14}C residue is metabolized to a far greater extent in comparison to that in forage with resulting lower levels of Oxamyl (0.07 mg/kg), Oxamyl oxime (0.06 mg/kg) and metabolite IN-D2708 (0.1mg/kg) present in the hay. A total of sixteen different ^{14}C

containing metabolite fractions were found in the hay of which the main fraction, corresponding to 0.48 mg/kg(40% of TRR), was stated to be the glucoside of the oxime (metabolite IN-A2213). No analytical data was presented to support this conclusion. As in the case of barley forage the metabolites IN-KP532, IN-T2921, IN-L2953 and IN-N0079 were tentatively identified on the basis of their chromatographic behaviour. Information is presented in Table 45 below detailing the composition of the ^{14}C present in barley hay. Hydrolysis of the insoluble ^{14}C fraction with cellulase, alkali and acid resulted in 3.4%, 5.4% and 1.4% of the ^{14}C being solubilised respectively.

Barley Straw: Barley straw contained approximately 30% higher level of ^{14}C than that present in hay. The extractability of the ^{14}C present in straw, at 71.7%, is less than that in hay and fewer ^{14}C fractions, nine in total, were isolated when the sample extracts were analysed. The main straw metabolite appears to be the same as the main component of the ^{14}C residue in hay. This metabolite was tentatively identified as being the glucoside of the oxime (metabolite IN- A2213) but no further supporting analytical data was provided in the study. Hydrolysis of the insoluble straw residue using cellulase, alkali and acid released 4.5, 5.3 and 5.9% of the ^{14}C respectively. None of the hydrolysis products were identified.

Stability data: No stability data was generated as part of the current study.

Table 46 Total ^{14}C residues present in Barley grain, straw, forage and hay.

	Residues in Barley grain.			Residues in Barley forage			Residues in Barley Hay			Residues in Barley Straw.		
	Analyte	%TRR	mg/kg	Analyte	%TRR	mg/kg	Analyte	%TRR	mg/kg	Analyte	%TRR	mg/kg
Aqueous/ organic (MeOH/ H_2O) extract.	Polar (Rt 2.6 min) IN-D2708 (Rt = 1.8m)	4.0 51.3	0.01 0.16	Polar (Rt= 3.9 min) IN-KP532* (Rt =4.4 min) IN-D2708 (Rt= 5.2 min) IN-L2953* (Rt= 17.9min) IN-N0079* (Rt= 18.4 min) Unknown (Rt= 20.3 min) Unknown (Rt=21.8 min.) IN-A2213 (Rt=22.3 min) Unknown (Rt= 22.8 min) Unknown (Rt=23.7 min.) Unknown (Rt= 24 min) Unknown (Rt=24.5 min.)	1.4 0.8 3.4 1.4 0.6 24.4 1.1 13.4 1.4 1.5 1.8 2.2 24.0	0.09 0.06 0.23 0.09 0.04 1.64 0.08 0.9 0.1 0.1 0.12 0.14 1.61	Polar (Rt= 3.4 min) IN-KP532* (Rt =4.4 min) IN-D2708 (Rt= 5.4 min) IN-T2921* (Rt=6.4 min) Unknown (Rt=12.6 min) IN-L2953* (Rt= 18.7min) IN-N0079* (Rt= 19.2 min) Unknown (Rt=21.2 min.) IN-A2213 (Rt=23.3 min) Unknown (Rt= 24.6 min) Oxamyl (Rt= 26.4 min) Others (5 components, <0.01)	3.1 2.2 8.2 1.7 1.3 6.2 2.0 40.4 4.6 1.5 5.9 3.5	0.04 0.03 0.1 0.02 0.02 0.07 0.02 0.48 0.06 0.02 0.07 0.04	Polar (Rt= 3.4 min) IN-KP532* (Rt =4.2 min) IN-D2708 (Rt= 5.6 min) IN-T2921* (Rt= 6.9 min) IN-N0079* (Rt= 19.3 min) Unknown (Rt= 21.1 min) IN-A2213 (Rt=23.3 min) Oxamyl (Rt= 26.4 min) Others (1 component <0.01)	1.2 1.0 2.9 1.0 13.1 28.3 6.3 6.0 0.6	0.02 0.02 0.05 0.02 0.21 0.45 0.1 0.09 0.01
Total characterized/ identified		55.3	0.17		77.4	5.2		80.6	0.97		60.4	0.97
Total Extractable.		60.3	0.19		88.8	5.96		84.3	1.0		71.7	1.13
Insoluble.		39.7	0.13		11.2	0.75		15.7	0.19		28.3	0.44
Total Hydrolysis (Enzyme, alkali and acid digestion of insoluble fraction.).		13.0	0.04		Not carried out.			10.2	0.12		15.7	0.24
Remaining bound residues		26.7	0.09		11.2	0.75		5.5	0.07		12.5	0.2
Total.		100	0.32		100	6.71		100	1.19		100	1.57

Note 1: Insoluble plant residues are those which are not extractable with the aqueous organic solvent and reflects the ^{14}C retained in the extracted pellet.
Note 2: Insoluble residues were treated successively with enzyme (cellulase), alkali (0.1N NaOH) and acid (1N HCl) to determine what portion of the ^{14}C could be solubilised in this way. The ^{14}C released is called the "Total Hydrolysis" residue.
Note 3: * = these metabolites were not fully identified. Their chromatographic behaviour was consistent with that of their corresponding standards but full confirmatory data was not provided.

Conclusion:
The information presented shows that Oxamyl is very labile in soil and degrades with a t1/2 of less than 30 days.

^{14}C residues in barley forage, hay, straw and grain becomes less extractable as one goes from forage/hay to grain and straw.

TRR exceed 0.3 mg/kg in all barley fractions analysed.

Residues of Oxamyl will not be detectable in barley grain when barley is grown on Oxamyl treated soil.

Oxamyl and its oxime are both detected in the barley forage, hay and straw samples analysed. In grain metabolite IN-D2708, at 50% of TRR, is the main component of the residue present.

The same major ^{14}C metabolite fraction found in hay is also the main component present in straw. This metabolite elutes earlier than Oxamyl-oxime, was resistant to enzyme and acid hydrolysis, and is believed to be the glucose conjugate of the oxime (metabolite IN-A2213). No further data was provided to support this conclusion.

On the basis of the proposed residue definition for oxamyl in residues of Oxamyl will not detectable in barley grain when grown as a rotational crop. It is however possible that detectable residues of Oxamyl and its oxime will be detected in barley straw grown on soil within 30 days of Oxamyl being applied to the soil. This data is consistent with the conclusions of the study reported in section B.7.6.1. above. It is considered prudent in this situation that product labels carry a warning to this effect to ensure that there are no MRL exceedances when rotational crops are planted within 30 days of Oxamyl applications.

The metabolism in rotational crops study DuPont-4518, originally submitted under EU Rev8 Point IIA 6.6 and conducted with test material [1-^{14}C]oxamyl, was conducted under guideline OPPTS 860.1850 (1996). A review of this study indicates that it partially meets the current guideline (OECD 502: Metabolism in Rotational Crops); deviations include only a 30-day rotational interval in a cereal crop (barley) was studied. However, when submitted in conjunction with O/ME 34 and AMR 1190-88, it adequately completes the understanding of metabolism in rotational crops.

The metabolism in rotational crops study DuPont-4518, Supplement No. 1, originally submitted under EU Rev8 Point IIA 6.6.2 and conducted with test material [1-^{14}C]oxamyl, was conducted under guideline OPPTS 860.1850 (1996). A review of this study indicates that it partially meets the current guideline (OECD 502: Metabolism in Rotational Crops); deviations include it addresses further characterization of oxamyl residues in one crop (barley) following a 30-day rotational interval. However, when submitted in conjunction with DuPont-4518, O/ME 34, and AMR 1190-88, it adequately completes the understanding of metabolism in rotational crops.

RMS comments and conclusion: The information submitte in this study with the information in the studies O/ME 34 and AMR 1190-88 adequately completes the understanding of metabolism in rotational crops.

B.7.6.2 Magnitude of residues in rotational crops

Study submitted to the EU for the first time in this submission.

B.6.6.2/01

Reference: CA 6.6.2/01	**Report:**	Anderson, I., Cairns, S., Hansford, R.J. (2007); Field crop rotation study with Vydate® 10G (DPX-D1410) - Europe 2005/6 **DuPont Report No.:** DuPont-16669 **Guidelines:** Directive 91/414/EEC **Deviations:** None **Testing Facility:** Charles River Laboratories (UK), Tranent, Scotland, UK

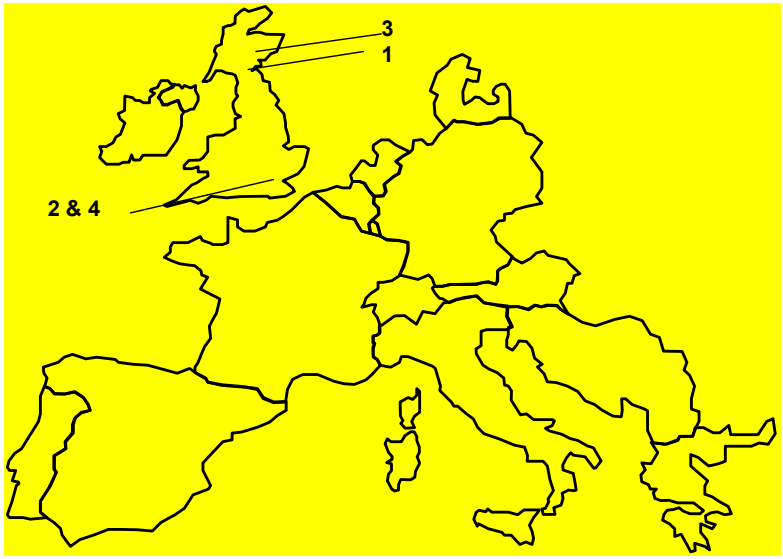
		Testing Facility Report No.: 687171 **GLP:** Yes **Certifying Authority:** Department of Health (U.K.)

I. MATERIALS AND METHODS

The field program was conducted in 2005-2006 at 4 locations in the UK. Oxamyl 10GR (DPX-D1410-460) was applied at 4.9 - 5.5 kg a.s./ha to potatoes at planting (growth stage BBCH 03). Potatoes were removed at 80 or 120 days after the application to allow planting of succeeding crops at the targeted Plantback Intervals, PBIs.

A total of 4 rotational crop trials (in northern Europe) for each of the succeeding crop types, representative leafy vegetables, root vegetables, and small-grain cereals (field lettuce, field carrot, winter barley, and winter wheat) were conducted in one growing season (2005-6). A summary of these rotational crop studies is given below. Locations of the trial sites are given in Figure 13.

Figure 13 Map: Oxamyl 10GR rotational crop test sites



Test No.	Country	Location, Region
1	UK (North)	Aberlady, East Lothian. UK
2	UK (South)	Ramsey, Harwich, Essex. UK
3	UK (North)	Monikie, Dundee, Angus. UK
4	UK (South)	Ramsey, Harwich, Essex, UK

A rotational crop residue data summary (in mg/kg) is presented in Table 47.

To generate these data, the following analysis and recovery information pertains.

Analysis method: Specimens were analysed for oxamyl by LC-MS based on method DuPont-17601. This method is summarized in Oxamyl Volume 3 B5..

Analyte:	Oxamyl
Extraction:	Analyte extracted from crop matrix by homogenisation with acetonitrile
Clean-up:	Removal of lipids using hexane followed by an aminopropyl SPE cartridge
Chromatography:	Reverse phase HPLC with C18 column
Detection:	Mass spectrometric detection (LC-MS) with 237.3 m/z ($M+NH_4$) used for quantification
Limit of Quantification:	0.010 mg/kg
Limit of Detection:	0.007 mg/kg

Recovery data: Average recovery data for fortifications run concurrently with the treated samples are given in Table 47 to demonstrate the validity of the analytical method.

Storage stability: All samples were analysed within 18 months of sampling. Oxamyl residues in representative crop matrices (lettuce, tomato, sugar beet root, potato tuber, and orange peel) were found to be stable for at least 18 months following freezer storage at -18°C (see Point CA 6.1.1 in this document). Therefore, no degradation is expected to have occurred between harvest and analysis.

Table 47 Residues of oxamyl in rotational crop commodities from supervised trials (DuPont-16669)

Renewal representative use: CEU; Potato; Oxamyl 10GR, 1.0 kg a.s./ha in furrow; application at planting (BBCH 00); 90-d PHI Renewal representative use: SEU; Tobacco; Oxamyl 10GR, 5.5 kg a.s./ha application (broadcast) or one 3.0 kg a.s./ha application (in-furrow) at transplant								
Test Identification (City, State/Region, Country, Year)	**EP[a]**	**Season 2 Crop/ Variety**	**Commodity or Matrix**	**Total Rate kg a.s./ha**	**Harvest DAP[b]**	**PBI[c] (days)**	**Residue ppm (mg/kg) [d]**	**Recovery data**
Test 01 (Aberlady, East Lothian, UK 2005/2006)	Oxamyl 10GR	Lettuce/ Diamond (closed head variety)	Heads	5.295	39	81	nd	Lettuce mean recovery = 73%, RSD = 4 (n = 2) at 0.010 mg/kg fortification Lettuce mean recovery = 70%, RSD = 2 (n = 2) at 0.10 mg/kg fortification
			Heads		47	120	nd	
		Carrot/ Nairobi F1	Root		86	81	nd	Carrot root mean recovery = 72%, RSD = 13 (n = 6) at 0.010 mg/kg fortification Carrot root mean recovery = 79%, RSD = 3 (n = 6) at 0.10 mg/kg fortification
			Tops		86		nd	Carrot tops mean recovery = 83%, RSD = 12 (n = 4) at 0.010 mg/kg fortification Carrot tops mean recovery = 79%, RSD = 6 (n = 4) at 0.10 mg/kg fortification
			Root		138	120	nd	Carrot root mean recovery = 72%, RSD = 13 (n = 6) at 0.010 mg/kg fortification Carrot root mean recovery = 79%, RSD = 3 (n = 6) at 0.10 mg/kg fortification
			Tops		138		nd	Carrot tops mean recovery = 83%, RSD = 12 (n = 4) at 0.010 mg/kg fortification Carrot tops mean recovery = 79%, RSD = 6 (n = 4) at 0.10 mg/kg fortification

Table 47 Residues of oxamyl in rotational crop commodities from supervised trials (continued)

Critical GAP for Oxamyl 10GR-treated crops: 5.5 kg a.s./ha with application at Planting/Transplanting

Test Identification (City, State/Region, Country, Year)	EP[a]	Season 2 Crop/ Variety	Commodity or Matrix	Total Rate kg a.s./ha	Harvest DAP[b]	PBI[c] (days)	Residue ppm (mg/kg) [d]	Recovery data
Test 02 (Ramsey, Harwich, Essex, UK.2005/2006)	Oxamyl 10GR	Lettuce/ Majesty (open head variety)	Heads	5.276	90	80	nd	Lettuce mean recovery = 73%, RSD = 4 (n = 2) at 0.010 mg/kg fortification Lettuce mean recovery = 70%, RSD = 2 (n = 2) at 0.10 mg/kg fortification
			Heads		50	120	nd	
		Carrot/ Bangor F1	Root		90	80	nd	Carrot root mean recovery = 72%, RSD = 13 (n = 6) at 0.010 mg/kg fortification Carrot root mean recovery = 79%, RSD = 3 (n = 6) at 0.10 mg/kg fortification
			Tops		90		nd	Carrot tops mean recovery = 83%, RSD = 12 (n = 4) at 0.010 mg/kg fortification Carrot tops mean recovery = 79%, RSD = 6 (n = 4) at 0.10 mg/kg fortification
			Root		114	120	nd	Carrot root mean recovery = 72%, RSD = 13 (n = 6) at 0.010 mg/kg fortification Carrot root mean recovery = 79%, RSD = 3 (n = 6) at 0.10 mg/kg fortification
			Tops		114		nd	Carrot tops mean recovery = 83%, RSD = 12 (n = 4) at 0.010 mg/kg fortification Carrot tops mean recovery = 79%, RSD = 6 (n = 4) at 0.10 mg/kg fortification

Table 47 Residues of oxamyl in rotational crop commodities from supervised trials (continued)

Critical GAP for Oxamyl 10GR-treated crops: 5.5 kg a.s./ha with application at Planting/Transplanting

Test Identification (City, State/Region, Country, Year)	EP[a]	Season 2 Crop/ Variety	Commodity or Matrix	Total Rate kg a.s./ha	Harvest DAP[b]	PBI[c] (days)	Residue ppm (mg/kg) [d]	Recovery data
Test 03 (Monikie, Dundee, Angus. UK 2005/2006)	Oxamyl 10GR	Winter Barley/ Siberia	Hay	4.926	305	80	nd	Cereal hay mean recovery =102%, RSD = 3 (n = 2) at 0.010 mg/kg fortification Cereal hay mean recovery = 94%, RSD = 2 (n = 2) at 0.10 mg/kg fortification
			Grain		349		nd	Cereal grain mean recovery =109%, RSD = 6 (n = 2) at 0.010 mg/kg fortification Cereal grain mean recovery = 97%, RSD = 1 (n = 2) at 0.10 mg/kg fortification
			Straw		349		nd	Cereal straw mean recovery =91%, RSD = 16 (n = 2) at 0.010 mg/kg fortification Cereal straw mean recovery = 81%, RSD = 13 (n = 2) at 0.10 mg/kg fortification
			Hay		266	119	nd	Cereal hay mean recovery =102%, RSD = 3 (n = 2) at 0.010 mg/kg fortification Cereal hay mean recovery = 94%, RSD = 2 (n = 2) at 0.10 mg/kg fortification
			Grain		310		nd	Cereal grain mean recovery =109%, RSD = 6 (n = 2) at 0.010 mg/kg fortification Cereal grain mean recovery = 97%, RSD = 1 (n = 2) at 0.10 mg/kg fortification
			Straw		310		nd	Cereal straw mean recovery =91%, RSD = 16 (n = 2) at 0.010 mg/kg fortification Cereal straw mean recovery = 81%, RSD = 13 (n = 2) at 0.10 mg/kg fortification

Table 47 Residues of oxamyl in rotational crop commodities from supervised trials (continued)

Critical GAP for Oxamyl 10GR-treated crops: 5.5 kg a.s./ha with application at Planting/Transplanting

Test Identification (City, State/Region, Country, Year)	EP[a]	Season 2 Crop/ Variety	Commodity or Matrix	Total Rate kg a.s./ha	Harvest DAP[b]	PBI[c] (days)	Residue ppm (mg/kg) [d]	Recovery data
Test 04 (Ramsey, Harwich, Essex, UK. 2005/ 2006)	Oxamyl 10GR	Winter Wheat/ Einstein	Hay	5.462	299	80	nd	Cereal hay mean recovery =102%, RSD = 3 (n = 2) at 0.010 mg/kg fortification Cereal hay mean recovery = 94%, RSD = 2 (n = 2) at 0.10 mg/kg fortification
			Grain		324		nd	Cereal grain mean recovery =109%, RSD = 6 (n = 2) at 0.010 mg/kg fortification Cereal grain mean recovery = 97%, RSD = 1 (n = 2) at 0.10 mg/kg fortification
			Straw		324		nd	Cereal straw mean recovery =91%, RSD = 16 (n = 2) at 0.010 mg/kg fortification Cereal straw mean recovery = 81%, RSD = 13 (n = 2) at 0.10 mg/kg fortification
			Hay		259	120	nd	Cereal hay mean recovery =102%, RSD = 3 (n = 2) at 0.010 mg/kg fortification Cereal hay mean recovery = 94%, RSD = 2 (n = 2) at 0.10 mg/kg fortification
			Grain		284		nd	Cereal grain mean recovery =109%, RSD = 6 (n = 2) at 0.010 mg/kg fortification Cereal grain mean recovery = 97%, RSD = 1 (n = 2) at 0.10 mg/kg fortification
			Straw		284		nd	Cereal straw mean recovery =91%, RSD = 16 (n = 2) at 0.010 mg/kg fortification Cereal straw mean recovery = 81%, RSD = 13 (n = 2) at 0.10 mg/kg fortification

[a] EP = End-use Product
[b] DAP = Days after planting = number of days between sowing and sampling of succeeding crop commodities
[c] PBI = Plantback interval = number of days between last application to treated crop and sowing of succeeding crops
[d] The designation "nd" is used for treated specimens for which no peak was observed or residue was <LOD (below the limit of detection; <0.007 mg/kg)

II. RESULTS AND DISCUSSION

The crop rotation residue studies presented were carried out in one EU country and provide data relevant to conditions in the European region to support granular application of oxamyl to crops.

All of the analytical work associated with the studies was performed at Charles River Laboratories, Tranent EH33 2NE, Scotland. The analytical work was carried out during one time period for the 2005/6 residue trials.

Europe

In 2005-6, at four trial locations in the UK, magnitude of oxamyl residues were determined in rotational crops planted in a field that had previously contained potatoes treated with Oxamyl 10GR applied at 4.9–5.5 kg a.s./ha at planting. Oxamyl residues in succeeding crops (lettuce, carrot roots and tops, and cereal grain, hay, and straw) planted 80 and 120 days after Oxamyl 10GR application and harvested at maturity were <0.007 mg/kg.

III. CONCLUSION

Overall consistent residue behaviour of oxamyl on rotational crops planted in fields that had previously contained potatoes treated at planting with Oxamyl 10GR at 4.9 - 5.5 kg a.s./ha was found in a season of study in the EU. Oxamyl residues in succeeding crops (lettuce, carrot roots and tops, and cereal grain, hay, and straw) planted 80 and 120 days after Oxamyl 10GR application to potatoes, and harvested at maturity were <0.007 mg/kg.

(Anderson, I., Cairns, S., Hansford, R.J., 2007)

RMS comments and conclusion: The study presented is compliance with the EU guidelines for crop rotational and gives analytical information on the residue behavior of Oxamyl on rotational crops (lettuce, carrot root and tops, ceral grain, hay and straw) treated with the 10GR product. The study is acceptable.

Study submitted to the EU for the first time in this submission.

B.7.6.2/02

Reference: **CA 6.6.2/02**	**Report:**	Old, J., Boissinot, J.-C., Cairns, S., McConnell, K. (2009); Protected crop rotation study with Oxamyl 10L (DPX-D1410) - Europe 2007/8 **DuPont Report No.:** DuPont-16693 **Guidelines:** Directive 91/414/EEC **Deviations:** None **Testing Facility:** Charles River Laboratories (UK), Tranent, Scotland, UK Testing Facility Report No.: 686361 **GLP:** Yes **Certifying Authority:** Department of Health (U.K.)

I. MATERIALS AND METHODS

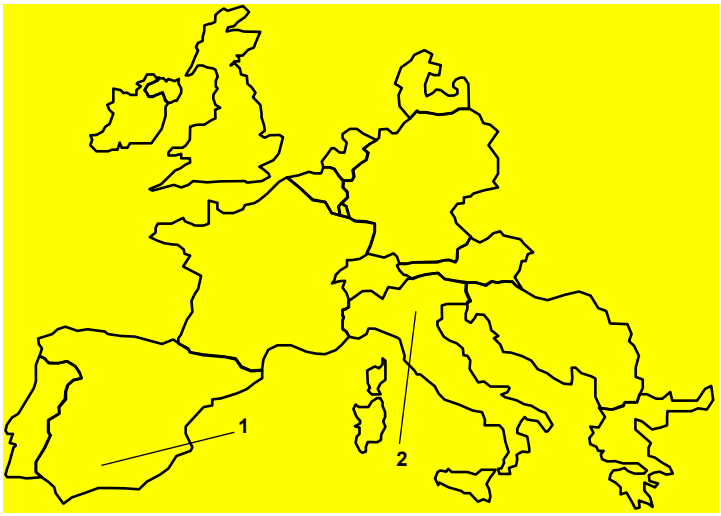
The field program was conducted in 2007-8 at two locations in southern EU. Oxamyl 10SL (DPX-D1410-488) was applied by simulated drip irrigation immediately after transplanting melons (application A1) and four additional times (A2-A5) with the last application being 21 days before melon harvest. Applications A2-A5 were made on a 10-day retreatment interval. Oxamyl 10SL application A1 was made at a target application rate of 2 kg a.s./ha and applications A2-A5 were made at a target application rate of 1 kg a.s./ha.

For all tests, Season 1 crops (melons) were removed after the final application to allow the following crops (Season 2 crops) to be planted at the targeted plant-back intervals, PBIs of *ca.* 30, 60, 90 or 120 days. In both tests the Season 2 crops were protected lettuce and protected radish (*i.e.* 8 treated subplots; 2 crops × 4 PBIs and 4 untreated subplots; 2 crops × 2 PBIs).

Two rotational crop trials in southern Europe under protection for representative leafy vegetables and root vegetables were conducted in one growing season (2007-2008). Cereals grown in rotation under protection are not possible and were not investigated.

A summary of these rotational crop studies is given below. Locations of the trial sites are given in Figure 14.

Figure 14 Map: Oxamyl 10SL rotational crop test sites



Test No.	Country	Location, Region
1	Spain	Los Palacios, Andalucía
2	Italy	Roncoferraro, Lombardia

A rotational crop residue data summary (in mg/kg) is presented in Table 48.

To generate these data, the following analysis and recovery information pertains.

Analysis method: Specimens were analysed for oxamyl by LC-MS based on method DuPont-17601. This method is summarized in Oxamyl Volume 3 B5.

Analyte:	Oxamyl
Extraction:	Analyte extracted from crop matrix by homogenisation with acetonitrile
Clean-up:	Removal of lipids using hexane followed by an aminopropyl SPE cartridge
Chromatography:	Reverse phase HPLC with C18 column
Detection:	Mass spectrometric detection (LC-MS) with 237.3 m/z ($M+NH_4$) used for quantification
Limit of Quantification:	0.010 mg/kg
Limit of Detection:	0.007 mg/kg

Recovery data: Average recovery data for fortifications run concurrently with the treated samples are given in Table 48 to demonstrate the validity of the analytical method.

Storage stability: All samples were analysed within 12 months of sampling. Oxamyl residues in representative crop matrices (lettuce, tomato, sugar beet root, potato tuber, and orange peel) were found to be stable for at least 18 months following freezer storage at -18°C (see Point CA 6.1.1 in this document). Therefore, no degradation is expected to have occurred between harvest and analysis.

Table 48 Residues of oxamyl in rotational crop commodities from supervised trials (DuPont-16693)
EU critical GAP for Oxamyl 10SL-treated crops: 2.0 kg a.s./ha at transplanting followed by 3 applications at 1.0 kg a.s./ha/application, 10 days apart; all applications *via* drip irrigation

Test Identification (City, State/Region, Country, Year)	EP[a]	Season 2 Crop/ Variety	Total Rate kg a.s./ha	Commodity or Matrix	Harvest DAP[b]	PBI[c] (days)	Residue ppm (mg/kg) [d]	Recovery data
Test 01 (Los Palacios, Andalucía, Spain, 2007/ 2008)	Oxamyl 10SL	Lettuce/ Filipu	6 (120% cGAP)	Heads	63	30	nd	Lettuce mean recovery = 93% (n = 2) at 0.010 mg/kg fortification Lettuce mean recovery = 66% (n = 2) at 0.10 mg/kg fortification
				Heads	52	60	nd	
				Heads	43	93	nd	
				Heads	45	120	nd	
		Radish/ Largo Comun		Roots	63	30	nd	Radish root mean recovery=65% (n = 2) at 0.010 mg/kg fortification Radish root mean recovery=82% (n = 2) at 0.10 mg/kg fortification Radish tops mean recovery=86% (n = 2) at 0.010 mg/kg fortification Radish tops mean recovery=88% (n = 2) at 0.10 mg/kg fortification
				Tops			nd	
				Roots	52	60	nd	
				Tops			nd	
				Roots	43	93	nd	
				Tops			nd	
				Roots	45	120	nd	
				Tops			nd	
Test 02 (Roncoferraro, Lombardia, Italy, 2007)	Oxamyl 10SL	Lettuce/ Justine	6 (120% cGAP)	Heads	38	30	nd	Lettuce mean recovery = 93% (n = 2) at 0.010 mg/kg fortification Lettuce mean recovery = 66% (n = 2) at 0.10 mg/kg fortification
				Heads	39	60	nd	
				Heads	45	92	nd	
				Heads	49	124	nd	
		Radish/ National		Roots	58	30	nd	Radish root mean recovery=65% (n = 2) at 0.010 mg/kg fortification Radish root mean recovery=82% (n = 2) at 0.10 mg/kg fortification Radish tops mean recovery=86% (n = 2) at 0.010 mg/kg fortification Radish tops mean recovery=88% (n = 2) at 0.10 mg/kg fortification
				Tops			nd	
				Roots	53	60	nd	
				Tops			Not Sampled	
				Roots	45	92	nd	
				Tops			nd	
				Roots	49	124	nd	
				Tops			nd	

[a] EP = End-use Product
[b] DAP = Days after planting = number of days between sowing and sampling of succeeding crop commodities
[c] PBI = Plantback interval = number of days between last application to treated crop and sowing of succeeding crops
[d] The designation "nd" is used for treated specimens for which no peak was observed or residue was <LOD (below the limit of detection; <0.007 mg/kg)

II. RESULTS AND DISCUSSION

The crop rotation residue studies presented were carried out in two EU countries and provide data relevant to protected conditions in the European region to support application of oxamyl to crops.

All of the analytical work associated with the studies was performed at Charles River Laboratories, Tranent EH33 2NE, Scotland. The analytical work was carried out between February and June 2008.

Europe

In 2007-2008, at two trial locations in Italy and Spain, magnitude of oxamyl residues were determined in rotational crops planted in a field that had previously contained melons treated with Oxamyl 10SL applied at 2.0 kg a.s./ha at planting followed by 4 applications at 1.0 kg a.s./ha. Oxamyl residues in succeeding crops (lettuce and radish roots and radish tops) planted *ca.* 30, 60, 90, and 120 days after Oxamyl 10SL application and harvested at maturity were <0.007 mg/kg.

III. CONCLUSION

Overall consistent residue behaviour of oxamyl on rotational crops planted in fields that had previously contained melons treated with Oxamyl 10SL applied at 2.0 kg a.s./ha at planting followed by 3 applications at 1.0 kg a.s./ha was found in a season of study under protection in the EU. Oxamyl residues in succeeding crops (lettuce and radish roots and radish tops) planted *ca.* 30, 60, 90, and 120 days after Oxamyl 10SL application and harvested at maturity were <0.007 mg/kg.

(Old, J., Boissinot, J-C., Cairns, S., McConnell, K., 2009)

RMS comments and conclusion: The study presented is compliance with the EU guidelines for crop rotational and gives analytical information on the residue behavior of Oxamyl on rotational crops (lettuce, radish root and tops) treated with the 10SL product. The study is acceptable.

B.7.7 Proposed residue definitions and maximum residue levels

B.7.8 Proposed residue definitions

Proposed residue definition (crop)

Metabolism of [^{14}C]oxamyl was investigated in two GLP studies in potatoes and tomatoes following soil and/ or foliar treatment regimes. These metabolism studies with representative root/tuber vegetables (potatoes) and fruit/fruiting vegetables (tomatoes) along with supplementary information from earlier studies in tobacco, peanuts, apples, and oranges (summarized in the Oxamyl Draft Assessment Report, Volume 3, Annex B.7, 2004) demonstrate an overall consistent route of metabolism across all studied crops/crop groups regardless of the treatment regime. The treatment and sampling regimes for potato and tomato along with conditions for earlier studies are summarised in Table 49.

Table 49 Summary of the treatment and sampling regimes for potato and tomato along with conditions for earlier studies

	Potato		Peanut		Tobacco	Tomato			Orange/Apple
	In-furrow + foliar application	**Soil application[a]**	**Foliar application**	**In-furrow + foliar application**	**Foliar or soil application**	**Fruit application**	**Foliar application[b]**	**Soil application[b]**	**Fruit application**
Variety:	Kennebec (in pots in greenhouse)	Red Pontiac (in pots in greenhouse)	Field grown	Field grown	Xanthi (in pots in greenhouse)	Bonny Best (in pots in greenhouse)	Red Alert (in pots in greenhouse)	Red Alert (in pots in greenhouse)	Hamlin/ Jonathan
Application rates (kg ai/ha):	3.36 (pre-plant, in-furrow) 0.56 + 4 @ 1.12 (foliar)	8	2.24	1.68 (pre-plant, in-furrow) 2 @ 1.12 (foliar)	1. 10 mg/plant (foliar) 2. 6 mg/kg (soil) 3. 0.48 or 2.4 g/L (foliar) 4. 6.72 kg/ha (soil)	0.37 mg/fruit (spot application to fruit)	One at 2 and 3 at 1	One at 2 and 3 at 1	1.4 g/L/1.2 g/L (brushed on fruit)
Number of applications:	1 pre-plant; 5 foliar	1	2	1 pre-plant; 2 foliar	1	1	4	4	1
Total applied dose (kg ai/ha):	8.4	8	4.48	3.92	See application rate	0.37 mg/fruit	5	5	1.4 g/L/1.2 g/L
First application (growth stage):	Pre-plant	At plant	three weeks after plant emergence	Pre-plant	Seedlings or at-plant	Applied to green fruit	At transplant	At transplant	Unspecified, brushed onto fruit on a tree
Interval between applications:	10 days (foliar)	Not applicable	4 weeks	24 and 76 days after planting	Not applicable	Not applicable	14 days (for applications 2-4)	14 days (for applications 2-4)	Not applicable
Growth conditions:	Greenhouse	Greenhouse	Open field	Open field	1. Growth chamber 2, 3. Greenhouse 4. Open field	Greenhouse	Greenhouse	Greenhouse	Open orchard
Sampling Intervals:	Maturity	Maturity	Prior to second appl; Maturity	40 and 70 days after last application	1,2,3,4. 0-4 weeks after application 4. maturity	7, 11, 14 and 21 days after treatment	Prior to last treatment; 7, 14, 21 days after last treatment	Prior to last treatment; 7, 14, 21 days after last treatment	6 weeks/ 47 days after treatment
Harvested Samples:	Tubers	Foliage, Tubers	Immature plants, green hay, mature peanuts	Whole plant, mature nutmeats	Whole plants, roots	Fruit	Immature fruit, mature fruit, foliage		Juice and rind from mature fruit; Peel and pulp from mature fruit

[a] DuPont 4520
[b] DuPont 32188

Oxamyl was readily metabolised in plants *via* IN-A2213 and IN-N7009 to IN-D2708. IN-A2213 was conjugated with glucose to IN-QKT34 and demethylated to IN-L2953. IN-L2953 was further metabolised to IN-KP532. Oxamyl was ultimately incorporation into plant natural products (*e.g.*, glucose) and components characterized as highly polar likely resulting from more extensive metabolism of the 3 carbon (IN-KV998 and IN-KP532) or 4 carbon (IN-T2921 and IN-D2708) containing metabolites, and reincorporation of 14C carbon dioxide into plant natural products.

It is generally recognised that carbamate insecticides lose their biological activity upon cleavage of the carbamate moiety. Oxamyl, like other methyl carbamate insecticides inhibits acetylcholinesterase (AChE) in the nervous system. AChE hydrolyses oxamyl's carbamate ester resulting in carbamylation and inhibition of the AChE enzyme. Therefore, oxamyl metabolites in which the carbamate ester moiety has been either hydrolysed or metabolically degraded are not expected to be toxicologically active by this mechanism. According to metabolism studies conducted with [^{14}C]oxamyl in plants and toxicology studies on oxamyl and five principal metabolites (IN-A2213, IN-N0079, IN-D2708, IN-T2921, and IN-L2953; none containing the carbamate moiety) summarised in the Draft Assessment Report (Oxamyl DAR, Volume 3, Annex B.6 and Annex B.7, 2004) and as stated in the Reasoned Opinion from EFSA following the Article 12 Review, the parent oxamyl is the only relevant substance included in the definition of the residue for enforcement and risk assessment in commodities of plant origin. This definition was pending one additional metabolism study investigating the nature of residues in fruits and fruiting vegetables following drip irrigation. The study, summarised in Point 7.2.1 in this document, confirms the residue definition for enforcement and risk assessment in commodities of plant origin as the parent oxamyl only.

Proposed residue definition (food of animal origin)

There are no significant terminal residues in milk, eggs or meat anticipated; therefore, no residue definition is required. For purposes of monitoring and risk assessment, the EU residue definition in plant and livestock (food) matrices is as oxamyl (Oxamyl DAR, Volume 3, Annex B.6 and Annex B.7, 2004).

B.7.8.1 Proposed maximum residue levels (MRLs) and justification of the acceptability of the levels proposed

Proposed maximum residue levels (MRLs)

EU MRLs for oxamyl are listed in SANCO/12783/2011, Annex II-1, Revision No. 7, voted on 16/September/2013 and issued on 18/September/2013. MRLs are not set on tobacco; however, a guideline residue level is proposed. The established/proposed MRLs are well supported by the residues data presented in Point CA 6.3 for the representative uses. Justifications that the established MRLs are supported by the summarized data are provided in the following points. The established/proposed MRLs are summarised in the following table.

Table 50 Summary of approved oxamyl MRLs - Commodities of plant origin for representative uses

Commodities	CXLs (mg/kg)	EU current MRL (mg/kg)	Proposed EU MRL/GRL (mg/kg)
Potato	None established	0.01[a]	0.01[a]
Tomato	2	0.01[a]	0.01[a]
Tobacco	None established	None established	0.01[a,b]

[a] Indicates lower limit of analytical determination

[b] This GRL falls within the one approved/pending use in place in Italy with a different GAP and formulation that will be supported after Annex I Renewal of oxamyl.

B.7.8.1.1 Justification for proposed MRL

Justification for proposed MRL—potato tubers

The renewal representative use for oxamyl on potatoes specifies 1 application of Oxamyl 10GR at 1.0 kg a.s./ha in-furrow at planting/transplanting with harvest at maturity (minimum 12 weeks). The residue data that support the establishment of the oxamyl potato MRL are derived from trials conducted in the 2001 and 2006 growing seasons. A total of 16 trials (8 trials in the northern region and 8 trials in the southern region) all resulted in non-detectable residues: 10 × <0.0033 mg/kg, 2 × <0.005 mg/kg. Trials were conducted with higher use rates (3.0 kg a.s./ha in furrow or 4.0 to 5.5 kg a.s./ha broadcast at transplant) and/or later applications (6 applications from BBCH 0 to 69 for a total application rate of 4.2 kg a.s./ha). With the lower application rate and/or earlier

application timing for the representative use, residues will remain <0.01 mg/kg. These residue data support an MRL for oxamyl in potato tubers of 0.01 mg/kg.

Justification for proposed MRL—tomato

The renewal representative uses for tomatoes grown under protection include a pre-plant solarisation use followed by an in-season use. Oxamyl 10SL is applied a minimum of 30 days prior to transplanting at the rate of 5.5 kg a.s./ha. At transplant, there is 1 drip irrigation application of Oxamyl 10SL at 2.0 kg a.s./ha at transplanting followed by 3 drip irrigation applications of 1.0 kg a.s./ha starting from BBCH 11, 10 days apart, with a 28-day PHI. Twenty-two residue trials were conducted on protected tomatoes including cherry tomatoes according to the in-season use pattern. Two bridging trials on cherry tomatoes and two bridging trials on courgettes were conducted to demonstrate residues are not impacted by the pre-plant solarisation applications. The residue data that support the establishment of the oxamyl tomato MRL are derived from trials conducted in the 2006, 2009-2010, and 2010-2011 growing seasons. A total of 24 trials resulted in <0.01 mg/kg residues. These residue data support an MRL for oxamyl in tomato of 0.01 mg/kg.

Justification for proposed GRL—tobacco

The renewal representative use for oxamyl on tobacco specifies 1 application of Oxamyl 10GR in furrow at the rate of 3.0 kg a.s./ha, or broadcast at the rate of 5.5 kg a.s./ha at planting/transplanting with harvest a minimum of 35 days later. The residue data that support the establishment of the oxamyl tobacco GRL are derived from trials conducted in the 2005 growing seasons. In five trials conducted in the SEU, the residues in green tobacco leaves were <0.01 mg/kg. These residue data support a GRL for oxamyl in green tobacco leaves of 0.01 mg/kg and falls within the one approved/pending use in place in Italy with a different GAP and formulation that will be supported after Annex I Renewal of oxamyl.

RMS comments and conclusion: The proposed MRLs are in compliance to the actual MRL for Oxamyl (EU Regulation No. 61/2014). No modification are required.

B.7.8.2 Proposed maximum residue levels (MRLs) and justification of the acceptability of the levels proposed for imported products (import tolerance)

No import tolerance MRLs for oxamyl are included with this submission.

B.7.9 Proposed safety intervals

Pre-harvest intervals (in days) for each relevant crop

Potato:

The renewal representative use specifies one application at transplant with a minimum 84-day (12-week) PHI. The residue data submitted support that time of application.

Tomato:

The PHI for tomatoes is 28 days. The residue data submitted reflect that time of application.

Tobacco:

The renewal representative use specifies one application at transplant with harvest of green leaves at maturity. The residue data submitted support that time of application.

Re-entry period (in days) for livestock, to area to be grased

Exposure of animals to oxamyl through the diet has studied in livestock metabolism studies. The exposure of livestock to oxamyl as result of potato culls in feed is less than that dosed in the livestock metabolism studies. No oxamyl residues above the limit of quantification (0.010 mg/kg) was found in milk, eggs, and edible tissues in livestock metabolism studies submitted and evaluated in the Oxamyl Draft Assessment Report Volume 3, Annex B.7, 2004. Due to no expectation of residues in milk, eggs, and edible tissues, establishing a re-entry period prior to livestock grazing is not necessary.

Re-entry period (in hours or days) for man to crops, buildings or spaces treated

Oxamyl-containing products applied directly to the soil, predominantly by incorporation or in-furrow application of granules at planting time or by drip irrigation; therefore, contamination of crop foliage is negligible. Worker exposure to crop protection chemicals is primarily by contact with treated foliage of crop plants, so risk of exposure to oxamyl is negligible. Degradation in soil, generally long pre-harvest application intervals, and low dermal penetration of the active substance further reduce the likelihood of significant worker exposure to oxamyl. Therefore, establishment of a re-entry period is not justified.

Withholding period (in days) for animal feedingstuffs

Exposure of animals to oxamyl through the diet studied in livestock metabolism studies. The exposure of livestock to oxamyl as result of potato culls in feed is less than that dosed in the livestock metabolism studies. No oxamyl residues above the limit of quantification (0.010 mg/kg) found in milk, eggs, and edible tissues. Due to no expectation of residues in milk, eggs, and edible tissues, establishing a withholding period for animal feedingstuffs is not necessary.

Waiting period (in days) between last application and sowing or planting the crops protected

Establishment of a waiting period between the last application and sowing or planting crops is not applicable since application made at planting/transplanting and after sowing.

Waiting period (in days) between application and handling treated product

Post-harvest treatment is not relevant for oxamyl.

Waiting period (in days) between last application and sowing or planting succeeding crops

When they treated according to the proposed GAP and grown under realistic field conditions, the concentration of oxamyl residues found in rotational crops planted 30-120 days after the application of oxamyl anticipated to be low. Therefore, no plantback waiting period proposed beyond the time necessary to prepare the field for the succeeding crop.

B.7.10 Estimation of the potential and actual exposure through diet and other sources

The ADI, ARfD and NOAEL for inhalation for oxamyl are summarised in the table below.

Endpoint	Value (mg/kg bw/d)	Study	Safety factor	Reference
Acceptable Daily Intake (ADI)	0.001	Acute neurotoxicity study in rat	100	EFSA Scientific Report 2005
Acute Reference Dose (ARfD)	0.001		100	
NOAEL, inhalation	0.1		Not applicable for the NOAEL	

[a] The only available inhalation study is an acute inhalation toxicity study. Therefore, the short- and intermediate-term inhalation endpoints are based on the acute neurotoxicity study in the rat. Since the chronic dietary endpoint is also based on the acute neurotoxicity study in the rat, this study better predicts effects for inhalation exposure that is greater than one day.

TMDI calculations

The calculation of the TMDI was performed using the maximum residue limit (MRL) for all crops to estimate the TMDI.

The summary of the calculation using the EFSA model rev 2.0 is presented in Appendix I. With the current EFSA model, the highest TMDI value in %ADI of oxamyl is 6.8% of the ADI. The highest calculated TMDI was for the UK infant.

NEDI calculations

The TMDI were 6.8% of the ADIs for oxamyl. Therefore, no further refinements to the long-term dietary exposure assessment were conducted.

RMS comments and conclusion: The results of the TMDI calculation indicates that a long-term intake of residue of Oxamyl is unlikely to present a public health concern.

IESTI calculations

The calculation of the IESTI was performed taking into account potatoes and tomatoes, the representative use crops. Since residues in the supervised residue trials were less than the limit of quantification in the edible portions, the LOQ's are used to estimate the IESTI. For potato tubers, the highest transfer factor observed for commodities prepared for consumption (0.15 for baked potatoes) was applied to the LOQ. Residue inputs used were:

- tomatoes: 0.01 mg/kg
- potato tubers: 0.01 mg/kg × 0.15 = 0.0015 mg/kg

The summary table found in Appendix I to this document.

RMS comments and conclusion: The results of the IESTI calcultation shows that a short term intake is unlikely to present a public health concern for tomato and potato.

Exposure *via* water

PEC_{gw} values for oxamyl metabolites IN-A2213 and IN-D2708 exceeded 0.1 µg/L but were less than 0.75 µg/L. From a risk management point of view, the exposure of consumers to metabolites 'non-relevant' in the hazard assessment at levels less than 0.75 µg/L is considered acceptable (threshold of concern approach) and therefore, for metabolites IN-A2213 and IN-D2708, no further assessment was conducted.

Inhalation Risk Assessment

It assumed that the greatest exposure to oxamyl will come from cigarettes. A conservative exposure estimate assuming oxamyl residues remain intact and are 100% inhaled during smoking indicates the Margin of Exposure (MOE) is 17500, much higher than the target MOE of 100.

$$\text{MOE} = \frac{\text{NOAEL, inhalation}}{\text{Exposure, tobacco}}$$

$$\text{Exposure} = \frac{\text{\# of cigarettes per day} \times \text{g tobacco/cigarette} \times \text{conversion factor} \times \text{mg oxamyl/kg tobacco}}{\text{average adult bodyweight}}$$

$$\text{MOE} = \frac{0.1}{20 \times 1 \times 0.001 \times 0.02 \div 70} = \frac{0.1}{0.000006} = 17500$$

Where,

- NOAEL, inhalation = 0.1 mg/kg bw/day

- # cigarettes per day = 20[2]
- g tobacco/cigarette = 1
- conversion factor = 0.001 kg/1 g
- Highest residues in dried tobacco leaves = 0.02 mg oxamyl/kg.
- average adult bodyweight = 70 kg

B.7.11 Other studies

Variability of residues in individual raw commodities

Study submitted to the EU for the first time in this submission.

B.7.10/01

Reference: CA 6.10/05	**Report:**	Zenide, D., Jetzer, M., Smyser, B.P. (2003); Unit-to-unit variability of residues of oxamyl in cucumbers (edible-peel cucurbits) grown in green/plastic houses following applications of Oxamyl 10L formulation by drip irrigation - southern Europe, season 2002 **DuPont Report No.:** DuPont-9459 **Guidelines:** 7029/VI/95, Rev 5 (1997) **Deviations:** None **Testing Facility:** Battelle Europe-Centre de Recherche de Geneve, Geneva, Switzerland Testing Facility Report No.: A-11-02-03 **GLP:** Yes **Certifying Authority:** Not given

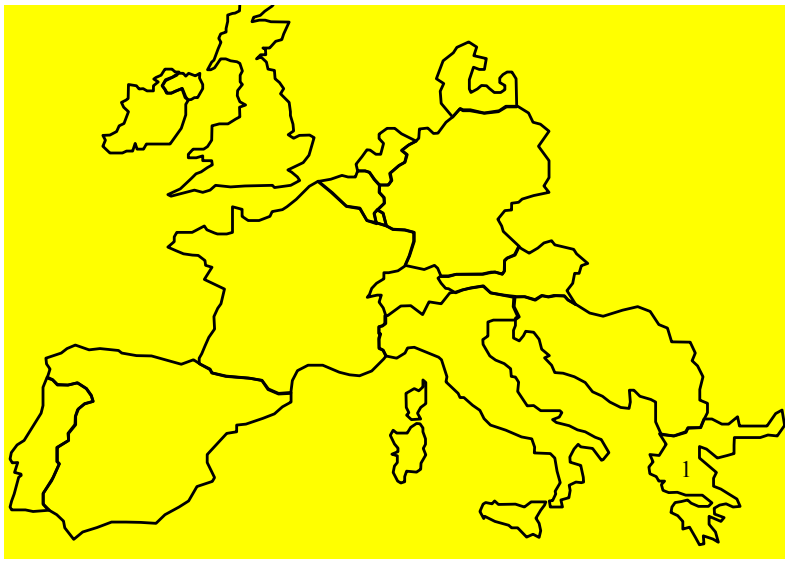
I. MATERIALS AND METHODS

The field program was conducted in 2002 at 1 location in southern Europe (Greece) on cucumbers. Oxamyl 10SL (DPX-D1410-424) was applied five times at 1.2 kg a.s./ha *via* drip irrigation on a 14-day application interval with a 3-day PHI. Phosphoric acid was used as an additive for all applications.

A total of 1 unit-to-unit variability trial in southern Europe was conducted in one growing season (2002). A summary of this trial is given below. The location of the trial site is given in Figure 15.

[2] Reference: Average U.S. smoker smokes 15 cigarettes per day. (Pierce, J.P., *et al*. 1989. Tobacco Use in 1986 – Methods and Basic Tabulations from Adult Use of Tobacco Survey. U.S. Dept. of Health and Human Services Publication Number OM90-2004. Office on Smoking and Health, Rockville, Maryland.)

Figure 15 Map: Oxamyl European cucumber unit-to-unit variability test site



No.	Location
1	Profitis, GR-57200, Thessaloniki, Greece

A cucumber individual unit residue data summary (in mg/kg) is presented in Table 51.

To generate these data, the following analysis information pertains.

Analysis method: N-methyl carbamate pesticide multiresidue method [DuPont-4722; HPLC with post-column derivatisation followed by fluorescence detection] for determining residues of oxamyl in/on a variety of crops. This method summarized in Volume 3 B5

Analyte:	Oxamyl
Internal Standard:	Trimethacarb (added prior to HPLC)
Extraction:	Analyte extracted from crop matrix with acetone
Clean-up:	Dichloromethane:petroleum ether partition followed by aminopropyl SPE
Chromatography:	HPLC using Zorbax® C8 LC column
Post column hydrolysis:	0.2 M NaOH at 95°C
Derivatisation:	Fluorescent reagent at ambient temperature
Fluorescence Detection:	Excitation wavelength: 466 nm Emission wavelength: 330 nm
Limit of Quantification:	0.010 mg/kg
Limit of Detection:	0.005 mg/kg

Recovery data: Average recovery data for fortifications run concurrently with the treated samples are given in Table 51, to demonstrate the validity of the analytical method.

Table 51 Residues of oxamyl in individual cucumber fruits from supervised trials

GLP and trial details	Crop	Country	Application rate (kg a.s./ha)	Crop growth stage at application and at sampling	Spray concentration (kg a.s./hL)	DALA[a]	Individual fruit residues found (mg/kg)[b] [in ascending order]	Recovery data
DuPont-9459, Trial No. 1 GLP 2002	Cucumber/ Z-14	Greece, Profitis, GR-57200, Thessaloniki	1) 1.2 2) 1.2 3) 1.2 4) 1.2 5) 1.2	BBCH 13, 15, 71, 81, 89, 89	not relevant for this test	3	nd, nd, nd, nd, 0.006, 0.007, 0.011, 0.018, 0.020, 0.020, 0.020, 0.026, 0.032, 0.032, 0.046, 0.049, 0.050, 0.054, 0.058, 0.067, 0.083, 0.087, 0.10, 0.11, 0.11, 0.12, 0.12, 0.14, 0.17, 0.22, 0.060, 0.22	Mean recovery = 78%, RSD = 4% (n = 5) in 0.010 mg/kg fortifications; Mean recovery = 72%, RSD = 6 (n = 5) in 0.10 mg/kg fortifications; Recovery = 70% (n = 1) in 0.20 mg/kg fortification
						Average =	**0.060**	
						Maximum =	**0.22**	
						Rel.ST.Dev =	**93%**	
						Median =	**0.048**	
						Variability factor[c] =	**3.7**	

[a] DALA = Days after last application
[b] For calculation purposes, 0.005 mg/kg (LOD) was used for specimens with no detectable (nd) residues.
[c] Variability factor = Maximum Residue/Average Residue = 0.22 (mg/kg)/0.060 (mg/kg)

II. RESULTS AND DISCUSSION

The unit-to-unit variability study was carried out in one EU country and provides data relevant to protected conditions in the southern European region.

All of the analytical work associated with the studies was performed at Battelle, Geneva Research Centres, CH-7, route de Drize, 1227 Carouge/Geneva, Switzerland. The analytical work was carried out during one time for the 2002 residue trials.

Oxamyl residues in 30 individual cucumber fruit treated 5 times at 1.2 kg a.s./ha *via* drip irrigation and collected 3 days after the last application, ranged from not detectable (<0.005 mg/kg) to 0.22 mg/kg. The overall average was 0.060 mg/kg (RSD = 93%) and the median was 0.048 mg/kg. The unit-to-unit variability factor was 3.7, calculated by dividing the maximum individual residue by the overall average residue.

Recovery values for fresh control fortifications run concurrently with treated samples in all the trials are summarised above. Approximately 80% or more of the recoveries were within 70–110% and the relative standard deviation was approximately 20% or less. Therefore, the analytical methods used performed well for the determination of oxamyl in treated crops.

III. CONCLUSION

Oxamyl residues in 30 individual cucumber fruit treated 5 times at 1.2 kg a.s./ha *via* drip irrigation and collected 3 days after the last application, ranged from not detectable (<0.005 mg/kg) to 0.22 mg/kg. The overall average was 0.060 mg/kg (RSD = 93%) and the median was 0.048 mg/kg. The unit-to-unit variability factor was 3.7, calculated by dividing the maximum individual residue by the overall average residue.

(Zenide, D., Jetzer, M., Smyser, B.P., 2003)

RMS Comments and Conclusions: The study conducted according tot he EU guidelines give information on the variability factor on cucumber fruit. The study is acceptable.

Effect on the residue level in wildlife feed items

DuPont has conducted several studies to assess the magnitude of oxamyl residues in wildlife feed items (ground dwelling arthropods, earthworms, weed seedlings, pollen, guttation drops, nectar) and dust from applications to which wildlife is exposed, providing input information for wildlife exposure assessments. These residue studies are summarised below.

Study submitted to the EU for the first time in this submission.

B.7.10/02

Reference: CA 6.10/04	**Report:**	Schwarz, A., Eichler, M. (2014); Oxamyl (DPX-D1410) 10SL: Field study on residues in arthropods, earthworms and seedlings (wildlife food items) **DuPont Report No.:** DuPont-40221 **Guidelines:** EFSA guidance document on risk assessment for birds and mammals (2009) **Deviations:** None **Testing Facility:** IBACON, Rossdorf, Germany Testing Facility Report No.: 87371126 **GLP:** Yes **Certifying Authority:** Hess. Ministerium fur Umwelt, Energie, Landwirtschaft and Verbraucherschutz

Executive summary

The purpose of the study was to determine the residues of oxamyl in ground dwelling arthropods, earthworms and weed seedlings after Oxamyl 10SL application in furrow during potato planting.

The study was conducted on agricultural fields in the vicinity of Groß-Zimmern, Landkreis Darmstadt-Dieburg, Germany. Within three separate test sites of at least 1 ha size each, plots (1 per test site) were established. The plots were treated separately with a spray solution prepared for each plot. Due to the independence of the plots (different fields, different spray solutions) it is possible to see the plots as separate tests.

The application simulated a commercial application during planting of potatoes. Each plot was treated separately. Application was performed according to Good Agricultural Practice with a commercial potato planting machine (Heiss All-in-One Profi). Application was done in the furrow with 2 nozzles (Hardi weiss) per furrow. The distance between the nozzle pairs was 75 cm resulting in a working width of 3 m for the 4 nozzle pairs.

A constant pressure (6 bar) and driving speed (4 kilometer per hour) ensured sufficient and constant output of the test item solution.

The application rate was 2.0 kg a.s./ha corresponding to 20 L product/ha (based on the nominal content of a.s.).

On the day of application and at intervals following the application samples of arthropods, earthworms and weed seedlings were taken. These samples were transported to the lab and deep frozen. After the samples were analyzed for the oxamyl content.

The study provides field data on the distribution and decline of oxamyl residues in three different matrices (arthropods, earthworms and weed seedlings) which can be used as food items by birds and mammals.

In general all three matrices showed oxamyl residues which rose and declined over time.

I. MATERIALS AND METHODS

A. MATERIALS

1.	Test material:	Oxamyl 10SL
	Lot/Batch #:	D1410-569
	Purity:	100 g a.s./L (nominal)
	Description:	Liquid
	CAS #:	None for the formulation; 23135-22-0 for oxamyl active substance
	Stability of test compound:	96.6% of the oxamyl remains in the delivery vehicle after one hour under agitation
2.	Control:	No control was needed for this kind of test. Untreated arthropods and weeds collected prior to application and untreated earthworms from IBACON´s established breeding programs were used as control matrices for the analytical phase.
	Test vehicle:	Tap water
3.	Test System	
	Species:	Arthropods, Earthworms and Weeds
	Source:	Natural occurring populations
4.	Environmental conditions	
	Temperature:	Natural conditions

B. STUDY DESIGN AND METHODS

1. Experimental start/completion

27-May-2014 to 28-June-2014

2. Experimental treatments

The purpose of the study was to determine the residues of oxamyl in ground dwelling arthropods, earthworms and weed seedlings after Oxamyl 10SL application in furrow during potato planting.

According to Regulation (EC) No 1107/2009 the possible adverse effects of crop protection products on birds and mammals have to be assessed.

The product is a nematicide used during the planting of potatoes. After the spray application into the furrow, the active substance may transfer to ground-dwelling arthropods and earthworms as well as weed seedlings.

The study was conducted on agricultural fields in the vicinity of Groß-Zimmern, Landkreis Darmstadt-Dieburg, Germany. Within three separate test sites of at least 1 ha size each, plots (1 per test site) were established. The plots were treated separately with a spray solution prepared for each plot. Due to the independence of the plots (different fields, different spray solutions) it is possible to see the plots as separate tests.

The application simulated a commercial application during planting of potatoes. Each plot was treated separately. Application was performed according to Good Agricultural Practice with a commercial potato planting machine (Heiss All-in-One Profi). Application was done in the furrow with 2 nozzles (Hardi weiss) per furrow. The distance between the nozzle pairs was 75 cm resulting in a working width of 3 m for the 4 nozzle pairs.

A constant pressure (6 bar) and driving speed (4 kilometer per hour) ensured sufficient and constant output of the test item solution.

The target application rate was 2.0 kg a.s./ha corresponding to 20 L product/ha (based on the nominal content of a.s.).

3. Observations

During the sampling dates (5 days prior to application; 1, 2, 4, 7, 10, 14, 17, and 21 days after application), samples of ground dwelling arthropods were taken from each test. Pitfall traps were used for the sampling of ground dwelling arthropods. The traps were installed prior to the application (20 pitfall traps per plot), then removed and installed again directly after the application with 80 pitfall traps per plot, which were placed between the rows. The traps were opened approximately 24 hours for each sampling date. The traps were sheltered by a transparent lid in order to protect the traps from rainfall. During the non-sampling periods, the pitfall traps were closed with a lid.

After sampling the collected arthropods were transferred to the lab. The arthropods were killed by freezing in a deep freezer and the content of all pitfall traps per plot was combined in one sampling bottle later in the lab. The composition of the pooled arthropod sample (per day and plot) was determined to taxonomic groups (*e.g.*, Coleoptera, Arachnida, Isopoda, Dermaptera, Diptera, Hymenoptera). The number of individuals per taxonomic group was determined and the fresh weight of a taxonomic group was determined.

During the sampling dates 0, 1, 3, 6, 9, 13, 16 and 20 days after application, 10 earthworm samples were taken from each plot by randomly selecting an area for each sample inside the plot with a metal frame of 50 cm * 50 cm. The sample targeted every aspect of a potato field, the space between furrows and the furrow itself. The area within this frame was dug out to a depth of 25 - 30 cm and the soil was searched for earthworms. The whole earthworms were transferred in polyethylene bottles (1 bottle per plot per sampling period), counted and weighed in the lab before being deep frozen in a deep freezer.

During the sampling dates 6, 7, 9, 13, 16, 20, 26 and 46 days after application, 10 weed seedling samples or samples from re-grown weeds were taken from each plot by randomly selecting an area for each sample inside the plot with a frame of 100 cm * 100 cm. The sample area contained the furrow as well as areas between the furrows. The main focus for sampling was laid on weed seedlings growing from the furrow as it was assumed that the highest exposure would occur in this location. The foliage of the plants within the area was sampled and transferred into a plastic bag (1 per plot) and weighed in the lab before being deep frozen in a deep freezer.

As all samples were transported to the lab after the sampling of the last plot, the maximum time between sampling and freezing was 6 hours at maximum.

II. RESULTS AND DISCUSSION

A. FINDINGS

Residue values ranging from <LOD to 0.042 mg a.s./kg were found in the matrix "Arthropods". The highest values were found at 14 to 21 days after application.

Table 52 Residues of oxamyl in arthropods

	Plot 1			Plot 2			Plot 3		
Days after appl.	Number of individuals	Total weight [g]	Conc. analysed [mg a.s./kg]	Number of individuals	Total weight [g]	Conc. analysed [mg a.s./kg]	Number of individuals	Total weight [g]	Conc. analysed [mg a.s./kg]
-5	526	4.13	<LOD	712	41.185	<LOD	1369	24.545	<LOD
1	1243	32.087	<LOD	1161	55.692	<LOD	1231	42.732	<LOQ
2	714	9.42	<LOD	750	14.349	<LOD	514	6.437	<LOQ
4	1074	9.053	<LOQ	1113	32.704	<LOD	1306	12.236	0.017
7	660	21.369	<LOQ	1097	88.594	<LOQ	1759	41.11	<LOQ
10	841	14.905	<LOD	1107	32.980	<LOD	1532	18.892	<LOQ
14	399	5.843	0.040	527	6.022	<LOD	748	4.998	<LOQ
17	524	4.840	0.015	585	9.470	0.014	698	5.010	0.013
21	533	4.568	0.015	679	7.005	0.042	710	6.025	0.032

LOQ = Limit of Quantification = 0.01 mg oxamyl/kg
LOD = Limit of Detection = 0.0026 mg oxamyl/kg

Oxamyl residues found in earthworms ranged from <LOD to 0.047 mg a.s./kg with the highest values occurring 0 to 6 days after application. An exception to these low residue values occurred in the day 0 sample from Test 3 with a residue of 1.5 mg a.s./kg, possibly due to soil contamination in the earthworm sample. All residues declined to <LOQ by the end of the experimental phase.

These findings indicate that the earthworms were exposed to the soil containing oxamyl with the residues rising and quickly declining.

Table 53 Residues of oxamyl in earthworms

	Plot 1			Plot 2			Plot 3		
Days after appl.	Number of individuals	Total weight [g]	Conc. analysed [mg a.s./kg]	Number of individuals	Total weight [g]	i	Number of Individuals	Total weight [g]	Conc. analysed [mg a.s./kg]
0	39	14.192	<LOQ	>100	87.296	0.011	58	20.879	1.544[a]
1	69	16.199	<LOD	147	50.005	<LOQ	71	19.581	0.013
3	40	8.649	<LOQ	196	60.171	0.047	84	14.140	0.019
6	34	10.562	0.021	87	33.162	<LOQ	77	16.735	0.021
9	30	10.570	<LOD	88	34.424	<LOQ	58	13.052	<LOQ
13	25	6.833	0.014	105	52.560	<LOD	83	20.675	<LOD
16	35	6.752	<LOD	128	37.804	<LOD	114	18.368	<LOD
20	27	3.900	<LOD	106	28.580	<LOD	147	31.491	<LOD

[a] residue was confirmed with triplicate analysis
LOQ = Limit of Quantification = 0.01 mg oxamyl/kg
LOD = Limit of Detection = 0.0026 mg oxamyl/kg

For weed seedlings the sampling started 6 days after application. The delayed sampling occurred for two reasons. First, weeds were not present following preparation of the field for planting and application. Second, residue studies in crop commodities following application to soil show residues in crop commodities are low on the day of application, rise in the 1-2 weeks following application and then decline. Consistent with this

expectation, residue values in weed seedling samples rose from 6 days after application with the highest residue values observed on days 13 and 16 after application. The residue values in the weed samples declined through 46 days after application to low concentrations.

These data indicate oxamyl was taken up by the weed seedlings and metabolised.

Table 54 Residues of oxamyl in weeds

	Plot 1		Plot 2		Plot 3	
Days after appl.	Total weight [g]	Conc. analysed [mg a.s./kg]	Total weight [g]	Conc. analysed [mg a.s./kg]	Total weight [g]	Conc. analysed [mg a.s./kg]
6	50.475	0.012	94.277	<LOQ	104.354	<LOQ
7	38.606	<LOQ	37.322	0.017	85.233	<LOD
9	45.572	<LOD	108.929	<LOD	109.914	0.036
13	24.160	0.069	21.248	1.728	21.584	3.657
16	26.351	2.646	18.811	2.324	32.022	0.010
20	19.383	0.742	18.005	0.534	28.778	2.135
26	122.868	0.169	114.758	0.560	110.772	0.208
46	148.562	<LOD	92.957	0.015	168.47	0.036

LOQ = Limit of Quantification = 0.01 mg oxamyl/kg
LOD = Limit of Detection = 0.0026 mg oxamyl/kg

III. CONCLUSIONS

The study provides field data on the distribution and decline of oxamyl residues in three different matrices (arthropods, earthworms and weed seedlings) which can be used as food items by birds and mammals.

In general all three matrices showed oxamyl residues which rose and declined over time.

(Schwarz, A., Eichler, M., 2014)

RMS Comments and Conclusions: The study conducted gives information on the distribution and decline of Oxamyl residue in arthropods, earthworms and weed seedlings as food for birds. The study is acceptable.

Study submitted to the EU for the first time in this submission.

B.7.10/03

Reference: CA 6.10/03	**Report:**	Scherer, F. (2015); Oxamyl (DPX-D1410) 10GR: Investigating the deposition of dust from in-furrow application of granules containing oxamyl and determination of residues of oxamyl in guttation fluid of potato in United Kingdom during 2014 **DuPont Report No.:** DuPont-38691 **Guidelines:** SANCO/3029/99 rev. 4, 7029/VI/95 (rev. 5) to Directive 91/414/EEC, BBA Drift Guideline VII, 2-1.1 (1992) **Deviations:** None **Testing Facility:** Eurofins Agroscience Services EcoChem GmbH, Niefern-Öschelbronn, Germany Testing Facility Report No.: S14-02913 **GLP:** Yes **Certifying Authority:** Landesanstalt Fur Umwelt, Messungen Und Naturschutz Baden-Wurttemberg

Executive summary

Potential residues of Oxamyl 10GR in the deposition of dust during in furrow application of granules containing oxamyl and the determination of residues of oxamyl in guttation fluid of potato plants was evaluated following the guideline BBA Drift Guideline VII, 2-1.1 (1992), 7029/VI/95 (rev. 5) to Directive 91/414/EEC and Regulations (EU) 283/2013 and 284/2013 implementing Regulation (EC) 1107/2009.

The field part of this study was conducted at one location (three trials) in the United Kingdom 2014. The trials were located in Northern UK (Yorkshire).

The study included one test item Treatment group (T): Oxamyl 10GR as granule application during planting of potatoes. Granules were drilled at a target rate of 30 kg Oxamyl 10GR/ha (equivalent to 3.0 kg a.s./ha based on nominal loading of a.s.).

The applications were done on 10 September 2014 for trial S14-02913-01, 11 September 2014 for trial S14-02913-02 and 15 September 2014 S14-02913-03 (United Kingdom).

The dust generated during application of granules was collected using Petri-dishes filled with glycerol/water, horizontally arranged on the soil surface at distances from 1 m, 3 m, 5 m, 10 m and 20 m from the sowing area (zero line). Residues of oxamyl were determined in the dust catching solution as a measure of the oxamyl available in the dust. Residue of oxamyl were also determined in guttation fluid from potato plants. Samples of guttation fluid were taken in all trials. The first samplings for each trial were done as soon as a minimum of 50% of the plants had emerged on the plot until 28/29 DAE (days after emergence).

The samples were analysed at Eurofins Agroscience Services Chem Ltd. (Wilson), United Kingdom, for residues of oxamyl with a level of quantification (LOQ) of 0.001 mg/L. Recovery values from dust catching solution fortified both in the field and the laboratory at levels down to 0.000008 mg/L ranged from 98 to 107%, indicating the method was suitable for the determination of oxamyl in dust catching solution at levels below the typical LOQ.

I. MATERIALS AND METHODS

A. MATERIALS

1.	Test material:	Oxamyl 10GR
	Lot/Batch #:	D1410-570
	Purity:	Nominal: 100 g/L oxamyl active substance
	Description:	solid
	CAS#:	None for the formulation; 23135-22-0 for oxamyl active substance
	Stability of test compound:	98.5% of the oxamyl remains in the delivery vehicle after one hour under agitation
2.	Control:	None
	Test vehicle:	Not applicable
3.	Environmental conditions (in-life period)	
	Temperature:	(From date of planting to last sampling on test item treatment plot): Mean: 12.3°C; Min: -1.5°C; Max: 22.0°C (Trial S14-02913-01, UK) Mean: 12.2°C; Min: -1.5°C; Max: 22.0°C (Trial S14-02913-02, UK) Mean: 11.9°C; -1.5°C; Max: 22.0°C (Trial S14-0213-03, UK)
	Precipitation:	Sum of rainfall (from date of planting to last sampling on test item treatment plot): 102.0 mm (trial S14-02913-01, UK) 108.2 mm (trial S14-02913-02, UK) 113.3 mm (trial S14-02977-03, UK)
	Photoperiod:	Natural light conditions

B. STUDY DESIGN AND METHODS

1. Experimental start/completion

10-September-2014 to 19-February-2015

2. Experimental treatments

In the test item treatment (T) potatoes were planted and the test item Oxamyl 10GR was applied at the same time in all three trials at a nominal rate of 30 kg/ha (equivalent to 3.0 kg a.s./ha). During the application wind had to be perpendicular towards the drilling direction (90°±30°) with a speed between 1 m/s and 5 m/s

No control plots were used.

3. Observations

Dust generated during the drilling of the granules was collected in petri dishes filled with a glycerol/water liquid. Residues of oxamyl were measured in the dust catching solution.

Residues of oxamyl were measured by analysis of guttation fluid samples from potato plants. Guttation fluid was collected with micro-pipettes (25 µL) *via* capillary forces.

II. RESULTS AND DISCUSSION

A. FINDINGS

The validity criteria for the environmental test conditions were fulfilled for mean values of all the three trials. The average wind speed during seeding of trial S14-02913-01 was 3.7 m/s ± 0.43 m/s. The wind deviated in average 6.8° ± 6.83° from the desired perpendicular direction to sowing during drilling. For S14-02913-02 the average wind speed during drilling was 2.7 m/s ± 1.33 m/s and the average deviation to the intended wind direction was 7.5° ± 25.24°. For S14-02913-03 the average wind speed during drilling was 3.0 m/s ± 0.40 m/s and the average deviation to the intended wind direction was 0.6° ± 7.68°.

The soil moisture content of the upper 5 cm of soil was 9.80% (S14-02913-01), 8.25 % (S14-02913-02) and 7.43% (S14-02913-03) of the fresh weight of soil.

For all three trials residues of oxamyl in Petri dishes were below the limit of quantification (LOQ = 0.001 mg/L). However, the method was suitable for the determination of oxamyl in dust catching solution at levels below the typical LOQ and the measured residue values were used to calculate the residue decline.

Residues decline constantly from the 1 m distance from the zero line to the 20 m distance. The residue values at 20 m were less than 40% the concentration found in the 1 m distance. Below is a table with the 90th percentile as % of the field rate calculated over the individual petri dishes of all three trials.

Table 55 Oxamyl residues in dust catching solution following application to potatoes at planting

Distance to zero line [m]	S14-02913-01 to S14-02913-03 90th percentile of oxamyl residues mg/ha	S14-02913-01 to S14-02913-03 90th percentile % of field rate mg/ha
1	19.97	0.00067
3	16.72	0.00056
5	16.38	0.00055
10	11.70	0.00039
20	7.56	0.00026

Guttation

All guttation fluid samples could be taken and those were analysed for residues of oxamyl.

Residues of oxamyl in guttation fluid of potato plant specimens from trial S14-02913-01 were in the range of 7.363 mg/kg to 46.789 mg/kg with the highest value at 3DAE. There were residues found in all samples taken with the lowest value measured in the last sampling collects at 28 DAE.

Residues of oxamyl in guttation fluid of potato plant specimens from trial S14-02913-02 were in the range of 6.107 mg/kg to 38.828 mg/kg with the highest value at 14DAE. There were residues found in all samples taken with the lowest value measured from the sampling collects at 18DAE. Residues in later samplings were higher with 22.549 mg/L at 22DAE and 20.835 mg/L at 29DAE.

Residues of oxamyl in guttation fluid of potato plant specimens from trial S14-02913-03 were in the range of 11.844 mg/kg to 58.390 mg/kg with the highest value at 6DAE. There were residues found in all samples taken with the lowest value measured in the last sampling collects at 28 DAE.

The summarized results of the guttation fluid analysis from test item treatment plots are given in the following table.

Table 56 Residues of oxamyl in guttation fluid samples from potato plants of the test item treatment plots

	S14-02913-01	S14-02913-02	S14-02913-03
Sampling DAE[a]	Residue [mg/L]		
0	25.121[b]	16.500[b]	16.952[b]
1	23.187	15.495[b]	17.051[b]
2	14.483	N/A[c]	N/A
3	**46.789**[d]	18.566[b]	31.090[b]
4	16.577	16.046[b]	31.338[b]
5	N/A	12.385	13.905
6	17.700	16.584	**58.390**
8	13.477	23.494	27.633
10	29.680	20.450	55.934
12	25.061	9.665	26.274
14	32.691	**38.828**	27.673
18	30.321[b]	6.107	23.500
22	13.371	22.549[b]	25.692[b]
28	7.363	N/A	11.844[b]
29	N/A	20.835[b]	N/A

[a] DAE: Days after emergence of 50% of plants
[b] Sampled under plastic tunnel
[c] N/A: Not available, sample was taken the following days
[d] Bold values mark maximum residue values
LOQ = Limit of quantification (0.001 mg/L)

III. CONCLUSIONS

From the results, it can be concluded that only very low amounts of dust from granules of the test item Oxamyl 10GR is produced and distributed during an in-furrow application during potato planting. Wind conditions during the dust exposure part of this study were within the range given in the study plan. All residue values recorded at distances from 1 m to 20 m to the zero line were below the LOQ (0.001 mg/L), but were measurable. However, because the method was suitable for the determination of oxamyl in dust catching solution at levels below the typical LOQ, analysis of the measured residue values shows a clear decline of the residues from 1 m to 20 m. Particle size of the granules was homogenous with only very low amounts of material below the 125 µm mesh size.

In the guttation fluid samples, residues of oxamyl between 6.107 mg/L and 58.390 mg/kg were found. Residues declined in two of the three trials towards the end of the sampling period.

(Scherer, F., 2015)

RMS comments and conclusion: The study is according tot the EU guideline and it conclude that residue in guttation fluid are in the range 6.107mg/L – 58.390 mg/L. The study is acceptable.

Study submitted to the EU for the first time in this submission.

B.7.10/04

Reference: CA 6.10/01	**Report:**	Knäbe, S. (2015); Oxamyl (DPX-D1410) 10GR: Determination of residues of oxamyl in guttation fluid of sugar beet plants in Germany 2014 **DuPont Report No.:** DuPont-41321 **Guidelines:** 7029/VI/95 (rev. 5) to Directive 91/414/EEC, EU 283/2013, EU 284/2013, EC 1107/2009, SANCO/3029/99 rev. 4 **Deviations:** None **Testing Facility:** Eurofins Agroscience Services EcoChem GmbH, Niefern-Öschelbronn, Germany Testing Facility Report No.: S14-02977 **GLP:** Yes **Certifying Authority:** Landesanstalt Fur Umwelt, Messungen Und Naturschutz Baden-Wurttemberg

Executive summary

The exposure of pollinating insects (*e.g.*, honeybees) to potential residues of Oxamyl 10GR in guttation fluid of sugar beet plants was tested following the guideline 7029/VI/95 (rev. 5) to Directive 91/414/EEC and Regulations (EU) 283/2013 and 284/2013 implementing Regulation (EC) 1107/2009.

The field part of this study was conducted at five locations (five trials) in Northern and Southern Germany 2014. Three trials were located in Northern Germany (Niedersachsen) and two trials in Southern Germany (Baden-Württemberg).

The study included one test item treatment group T and one control group C at each location:

- Treatment group (T): Oxamyl 10GR for sugar beet, as granule application during drilling of sugar beet; drilling of granule at a target rate of 25 kg Oxamyl 10GR/ha (equivalent to 2.5 kg a.s./ha based on nominal loading of a.s.)
- Control group C: untreated

The applications were done on 30-May-2014 for trial S14-02977-01, S14-02977-02, and S14-02977-03 (Northern Germany) and on 03-July-2014 for trial S14-02977-04 and S14-02977-05 (Southern Germany). The granule application was done on the days of seeding at a nominal rate of 2.5 kg a.s./ha.

Oxamyl residues were determined in guttation fluid from sugar beet plants. Samples of guttation fluid were not taken in all trials as no guttation fluid was available. The first samplings (C and T) were done as a minimum of 50% of the plants were emerged on the plot until 38 DAE (days after emergence).

The samples were analysed at Eurofins Agroscience Services EcoChem GmbH (Niefern), Germany, for residues of oxamyl with a level of quantification (LOQ) of 0.001 mg/kg.

I. MATERIALS AND METHODS

A. MATERIALS

1. Test material: Oxamyl 10GR
   Lot/Batch #: D1410-570
   Purity: Nominal: 100 g/L oxamyl active substance
   Description: solid
   CAS#: None for the formulation; 23135-22-0 for oxamyl active substance
   Stability of test compound: 98.5% of the oxamyl remains in the delivery vehicle after 1 hour under agitation
2. Control: Untreated
   Test vehicle: Not applicable
3. Environmental conditions (in-life period)
   Temperature: (From date of planting to last sampling on test item treatment plot):
   Mean: 18.9°C; Min: 5.5°C; Max: 34.2°C
   (Trial S14-02977-01, Northern Germany)
   Mean: 17.1°C; Min: 4.4°C; Max: 32.7°C
   (Trial S14-02977-02, Northern Germany)
   Mean: 18.0°C; Min: 3.3°C; Max: 30.8°C
   (Trial S14-02977-03, Northern Germany)
   Mean: 19.5°C; Min: 5.9°C; Max: 36.1°C
   (Trial S14-02977-04, Southern Germany)
   Mean: 19.7°C; Min: 7.3°C; Max: 36.1°C
   (Trial S14-02977-05, Southern Germany)
   Precipitation: Sum of rainfall (from date of planting to last sampling on test item treatment plot):
   106.3 mm (trial S14-02977-01, Northern Germany)
   122.4 mm (trial S14-02977-02, Northern Germany)
   106.3 mm (trial S14-02977-03, Northern Germany)
   109.6 mm (trial S14-02977-04, Southern Germany)
   176.7 mm (trial S14-02977-05, Southern Germany)
   Photoperiod: Natural light conditions

B. STUDY DESIGN AND METHODS

1. Experimental start/completion

   30-May-2014 to 08-December-2014

2. Experimental treatments

   In the test item treatment (T), sugar beet seeds were drilled, and the test item Oxamyl 10GR was applied on the same day in all five trials at a nominal rate of 25 kg/ha (equivalent to 2.5 kg a.s./ha).

   In the control plots of all trials, untreated sugar beet seeds were sown on the same day as in the test item treatment plots.

3. Observations

   Oxamyl residues were determined in guttation fluid samples from sugar beet plants. Guttation fluid was collected with micro-pipettes (20–40 µL) *via* capillary forces.

II. RESULTS AND DISCUSSION

A. FINDINGS

All guttation fluid samples available were analysed for residues of oxamyl.

For all trials analysed, no residues of oxamyl were detected at or above the limit of detection (LOD = 0.0003 mg/kg) in any of the untreated guttation fluid samples of sugar beet plants specimens.

No specimens were collected from trial S14-02977-01 because no guttation occurred during each of the sampling dates.

The single residue value of oxamyl in guttation fluid of treated sugar beet plant specimens from trial S14-02977-02 was at 0.0484 mg/kg (only one specimen collected at 31 days after emergence of 50% of plants, DAE).

Residues of oxamyl in guttation fluid of treated sugar beet plant specimens from trial S14-02977-03 were in the range of 0.208 to 1.43 mg/kg with the highest value at 22 DAE. For this trial, no guttation occurred from 1 to 14 DAE; only three specimens were available (18, 22, and 31 DAE).

Residues of oxamyl in guttation fluid of treated sugar beet plant specimens from trial S14-02977-04 were in the range of 0.0025 to 4.02 mg/kg and from trial S14-02977-05 in the range of 0.0082 to 129 mg/kg (specimens collected from 1 to 38 and 36 DAE, respectively). For both trials, highest residues were found at 5 DAE (4.02 and 129 mg/kg, respectively).

The summarised results of the guttation fluid analysis from test item treatment plots are given in the following table.

Table 57 Residues of oxamyl in guttation fluid samples from sugar beet plants of the test item treatment plots

Trial no.	Plot/Treatment	DAE[a]	Residue (mg/kg)
S14-02977-01	T	1	No guttation
		2	
		3	
		4	
		5	
		6	
		8	
		10	
		12	
		14	
		18	
		22	
		28	
		35	
S14-02977-02	T	1	No guttation
		2	
		3	
		4	
		5	
		6	
		8	
		10	
		12	
		14	
		18	
		22	
		31	**0.0484[b]**
		35	No guttation
S14-02977-03	T	1	No guttation
		2	
		3	
		4	
		5	
		6	
		8	
		10	
		12	
		14	
		18	1.23
		22	**1.43**
		31	0.208
		35	No guttation

Table 57 Residues of oxamyl in guttation fluid samples from sugar beet plants of the test item treatment plots (continued)

Trial no.	Plot/Treatment	DAE[a]	Residue (mg/kg)
S14-02977-04	T	1	0.0463
		2	0.0432
		3	2.27
		4	No guttation
		5	**4.02**
		6	No guttation
		8	0.021
		11	0.0096
		12	1.21
		14	0.373
		19	0.52
		24	0.439
		28	0.358
		38	0.0025
S14-02977-05	T	1	11.8
		2	31.6
		3	17.8
		4	73.9
		5	**129**
		6	46.9
		8	26.7
		11	6.24
		12	5.77
		14	3.7
		19	24.9
		22	4.41
		29	0.201
		36	0.0082

[a] DAE: Days after emergence of 50% of plants
[b] Bold and underlined values mark maximum residue values

III. CONCLUSIONS

It can be concluded that granule application of the test item Oxamyl 10GR during sugar beet drilling resulted in residues of oxamyl active substance above the limit of quantification (LOQ) of 0.001 mg/kg in guttation fluid from sugar beet plants. In the guttation fluid samples, residues of oxamyl were between 0.0025 and 129 mg/kg. Residues declined towards the end of the sampling period.

(Knäbe, S., 2015)

RMS comments and conclusion: The study is according tot the EU guideline and it conclude that residue in guttation fluid are present in the renge from 0.0025 mg/kg – 129 mg/kg. The study is acceptable.

Study submitted to the EU for the first time in this submission.

B.7.10/05

Reference: CA 6.10/02	**Report:**	Mack, P. (2015); Oxamyl (DPX-D1410) 10GR: Determination of residues of oxamyl in pollen, nectar, flowers, and guttation fluid of tobacco in southern Europe 2014

		DuPont Report No.: DuPont-41322, Revision No. 1 **Guidelines:** 7029/VI/95 (rev. 5) to Directive 91/414/EEC, EU 283/2013, EU 284/2013, EC 1107/2009, SANCO/3029/99 rev. 4 **Deviations:** None **Testing Facility:** Eurofins Agroscience Services EcoChem GmbH, Niefern-Öschelbronn, Germany Testing Facility Report No.: S14-02978 **GLP:** Yes **Certifying Authority:** Landesanstalt Fur Umwelt, Messungen Und Naturschutz Baden-Wurttemberg, Groupe Interministeriel des Produits Chimiques (GIPC) (Paris, France), Ministry of Economy and Finance-Directorate General-General Chemical State Laboratory-Division of Environment (Greece)

Executive summary

The exposure of pollinating insects (*e.g.*, honeybees) to potential residues of Oxamyl 10GR in nectar, pollen, flowers, and guttation fluid of tobacco plants was evaluated following the guideline 7029/VI/95 (rev. 5) to Directive 91/414/EEC and Regulations (EU) 283/2013 and 284/2013 implementing Regulation (EC) 1107/2009 and SANCO/3029/99 rev. 4.

The field part of this study was conducted at five locations (five trials) in Southern Europe in 2014. Three trials were located in Southern France (Pyrénées Orientales), and two trials were located in Greece.

The study included one test item treatment group T and one control group C at each location:

- Treatment group (T): Oxamyl 10GR for tobacco; planting of tobacco plants and treatment with granules in furrow at a rate of 30 kg/ha (equivalent to 3 kg a.s./ha based on nominal content of a.s.)
- Control group C: untreated

Planting of tobacco plants was done on 27-May-2014 for trials S14-02978-01 to S14-02978-03, on 02-June-2014 for trial S14-02978-04, and on 06-June-2014 for S14-02978-05, according to good agricultural practice. The test item granules were applied in furrow on the day of planting at a nominal rate of 3 kg a.s./ha.

Oxamyl residues were determined in pollen, nectar, and flower samples from tobacco plants. No samples of guttation fluid were taken for any trials as no guttation fluid was available on the tobacco plants. Samples of pollen could not be taken in trials S14-02978-01, S14-02978-02, and S14-02978-03. In trials S14-02978-04 and S14-02978-05 pollen samples were taken on 1 sampling day in the control plots and on 3 sampling days in the test item treatment plots. Nectar samples in all trials were taken on 1 sampling day in the control plots and on 3 sampling days in the test item treatment plots. Flower samples in all trials were taken on 1 sampling day in the control plots and on 3 sampling days in the test item treatment plots.

For all five trials, the nectar was collected from the flowers with the capillary method using micro-pipettes (10-50 µL). On each sampling day, at least 12 different locations across the plot were sampled. The pollen was sampled by beating the flowers into a tray and cleaning the samples afterwards from impurity with tweezers. On each sampling day, at least 12 different locations across the plot were sampled. Flower samples were taken by cutting the flower heads from at least 12 different locations across the plot.

The samples were analysed at Eurofins Agroscience Services EcoChem GmbH (Niefern), Germany, for residues of oxamyl with a level of quantification (LOQ) of 0.001 mg/kg.

I. MATERIALS AND METHODS

A. MATERIALS

1.	Test material:	Oxamyl 10GR
	Lot/Batch #:	D1410-570
	Purity:	Nominal: 100 g/L oxamyl active substance
	Description:	solid
	CAS#:	None for the formulation; 23135-22-0 for oxamyl active substance
	Stability of test compound:	98.5% of the oxamyl remains in the delivery vehicle after one hour under agitation
2.	Control:	Untreated
	Test vehicle:	Not applicable
3.	Environmental conditions (in-life period)	
	Temperature:	(From date of planting to last sampling on test item treatment plot): Mean: 23.8°C; Min: 10.9°C; Max: 43.5°C (Trial S14-02978-01, France) Mean: 24.6°C; Min: 10.4°C; Max: 48.7°C (Trial S14-02978-02, France) Mean: 25.0°C; Min: 9.6°C; Max: 43.1°C (Trial S14-02978-03, France) Mean: 24.0°C; Min: 9.9°C; Max: 35.2°C (Trial S14-02978-04, Greece) Mean: 23.7°C; Min: 14.8°C; Max: 35.2°C (Trial S14-02978-05, Greece)
	Precipitation:	Sum of rainfall (from date of planting to last sampling on test item treatment plot): 114.5 mm (trial S14-02978-01, France) 95.0 mm (trial S14-02978-02, France) 65.0 mm (trial S14-02978-03, France) 62.2 mm (trial S14-02978-04, Greece) 104.4 mm (trial S14-02978-05, Greece)
	Photoperiod:	Natural light conditions

B. STUDY DESIGN AND METHODS

1. Experimental start/completion

27-May-2014 to 14-February-2015

2. Experimental treatments

Treatment group (T): Oxamyl 10GR for tobacco; planting of tobacco plants and treatment with granules in furrow at a rate of 30 kg/ha (equivalent to 3 kg a.s./ha based on nominal content of a.s.).

In the control plots of all trials, tobacco plants were planted on the same day as in the test item treatment plots.

3. Observations

Oxamyl residues were determined in pollen, nectar, and flower samples from tobacco plants. Nectar from flowers was collected with micro-pipettes (10–50 µL) *via* capillary forces. The pollen was sampled either by beating the flowers into a tray and cleaning the samples afterwards from impurity with tweezers. Flower samples were taken by cutting the flower heads by hand.

II. RESULTS AND DISCUSSION

A. FINDINGS

All nectar, pollen, and flower samples available were analysed for residues of oxamyl.

1. Nectar

No residues of oxamyl were detected at or above the limit of quantification (0.001 mg/kg) in untreated nectar samples from trial -01, -02, -03, and -05 at the beginning of flowering (BBCH 61-65). For trial -04, a residue of oxamyl was found at 0.0018 mg/kg.

No residues of oxamyl were detected at or above the limit of detection (0.0003 mg/kg) in treated nectar samples from trial -01, -02, and -03 at three sampling dates (BBCH 61–69). From trial -04, residues of oxamyl were in the range of 0.0021 to 0.0170 mg/kg and from trial -05 in the range of 0.0021 to 0.0080 mg/kg.

2. Pollen

No specimens were available from trial -01, -02, and -03. For trials -04 and -05, no residues of oxamyl were detected at or above the limit of quantification (0.001 mg/kg) in any of the untreated pollen samples of tobacco plant specimens taken at the beginning of flowering (BBCH 61).

Residues of oxamyl in treated pollen samples from trial -04 were detected in the range of 0.0211 to 0.5352 mg/kg. Residues from trial -05 were below the limit of quantification (0.001 mg/kg). Pollen samples were taken at three sampling dates (BBCH 62–65).

3. Flowers

For all trials, no residues of oxamyl were detected at or above the limit of quantification (0.001 mg/kg) in any of the untreated flower samples of tobacco plant specimens taken at the beginning of flowering (BBCH 61–65).

Residues of oxamyl were detected in flower samples from trial -01 in the range of below the limit of detection (0.0003 mg/kg) to 0.0010 mg/kg. No residues of oxamyl were detected at or above the limit of detection (0.0003 mg/kg) in flower specimens from trial -02 and -03. Residues of oxamyl in flower samples from trial -04 were in the range of below the limit of quantification (0.001 mg/kg) to 0.0177 mg/kg and from trial -05 in the range of 0.0015 to 0.0187 mg/kg. Flower samples were taken at three sampling dates (BBCH 61–69).

4. Guttation fluid

No guttation fluid samples could be taken as no guttation occurred in tobacco plants.

The summarised results of the nectar, pollen, and flower sample analysis are given in the following tables.

Table 58 Residues of oxamyl in nectar samples from tobacco plants of the test item treatment plots

Trial no.	Plot/Treatment	Timing[a]	Residue[b] (mg/kg)
S14-02978-01	T[c]	BBCH 61	n.d.[d]
		BBCH 65	n.d.
		BBCH 65–69	n.d.
S14-02978-02		BBCH 61	n.d.
		BBCH 65	n.d.
		BBCH 65	n.d.
S14-02978-03		BBCH 61	n.d.
		BBCH 64–65	n.d.
		BBCH 67–69	n.d.
S14-02978-04		BBCH 62	0.0033[e]
		BBCH 63–64	**0.0170**[f]
		BBCH 65	0.0021
S14-02978-05		BBCH 62	0.0021[g]
		BBCH 63–64	**0.0080**
		BBCH 65	0.0022

[a] BBCH: according to Meier 2001
[b] LOQ: 0.001 mg/kg
[c] T: Treated specimen
[d] n.d.: Not detectable (<LOD = 0.0003 mg/kg)
[e] Mean result from determination of replicate samples (0.0023 mg/kg, 0.0042 mg/kg)
[f] Bold and underlined values mark maximum residue values
[g] Mean result from determination from replicate samples (0.0022 mg/kg, 0.0020 mg/kg)

Table 59 Residues of oxamyl in pollen samples from tobacco plants of the test item treatment plots

Trial no.	Plot/Treatment	Timing[a]	Residue[b] (mg/kg)
S14-02978-01	T[c]	BBCH 61	No specimen available
		BBCH 65	No specimen available
		BBCH 65–69	No specimen available
S14-02978-02		BBCH 61	No specimen available
		BBCH 65	No specimen available
		BBCH 65	No specimen available
S14-02978-03		BBCH 61	No specimen available
		BBCH 64–65	No specimen available
		BBCH 67–69	No specimen available
S14-02978-04		BBCH 62	0.0211[d]
		BBCH 63–64	**0.5352**[e,f]
		BBCH 65	0.0403[g]
S14-02978-05		BBCH 62	**<LOQ (0.0008)**
		BBCH 63–64	<LOQ (0.0006)
		BBCH 65	<LOQ (0.0003)

[a] BBCH: according to Meier 2001
[b] LOQ: 0.001 mg/kg
[c] T: Treated specimen
[d] Mean result from determination from replicate samples (n.d., 0.0421 mg/kg)
[e] Bold and underlined values mark maximum residue value
[f] Mean result from determination from replicate samples (<LOQ (0.0004 mg/kg), 1.070 mg/kg)
[g] Mean result from determination from replicate samples (<LOQ (0.0003 mg/kg), 0.0802 mg/kg)

Table 60 Residues of oxamyl in flower samples from tobacco plants of the test item treatment plots

Trial no.	Plot/Treatment	Timing[a]	Residue[b] (mg/kg)
S14-02978-01	T[c]	BBCH 61	0.0010
		BBCH 65	n.d.[d]
		BBCH 65–69	n.d.
S14-02978-02		BBCH 61	n.d.
		BBCH 65	n.d.
		BBCH 65	n.d.
S14-02978-03		BBCH 61	n.d.
		BBCH 64–65	n.d.
		BBCH 67–69	n.d.
S14-02978-04		BBCH 62	<LOQ (0.0006)
		BBCH 63–64	0.0177
		BBCH 65	0.0026
S14-02978-05		BBCH 62	0.0028[e]
		BBCH 63–64	**0.0187**[f]
		BBCH 65	0.0015

[a] BBCH: according to Meier 2001
[b] LOQ: 0.001 mg/kg
[c] T: Treated specimen
[d] n.d.: Not detectable (<LOD = 0.0003 mg/kg)
[e] Mean result from determination from replicate samples (0.0031 mg/kg, 0.0025 mg/kg)
[f] Bold and underlined values mark maximum residue value

III. CONCLUSIONS

It can be concluded that granule application of the test item Oxamyl 10GR during tobacco planting resulted in residues of oxamyl active substance above the limit of quantification (LOQ) of 0.001 mg/kg in nectar, pollen, and flowers from tobacco plants.

Residues of oxamyl in the test item treatment of trials S14-02978-04 and -05 were highest for all matrices at the second sampling date at BBCH 63–64, with one exception. For flowers of trial S14-02978-01, the highest value was found at the first sampling (BBCH 61). Afterwards residues declined for all matrices taken in all trials.

Residues were found in pollen samples of trial S14-02978-04 with values between 0.0003 mg/kg (<LOQ) and 0.5352 mg/kg. Residues of nectar were found between 0.0021 and 0.017 mg/kg, and residues of flowers between 0.0006 mg/kg (<LOQ) and 0.0187 mg/kg.

(Mack, P, 2015)

RMS comments and conclusion: The study is according tot the EU guideline and it conclude that residue in nectar, pollen, and flowers from tobacco plants are present. The study is acceptable.

B.7.11.1 Effect on the residue level in pollen and bee products

DuPont recommends waiving the requirement for residue levels in pollen and bee products for the following reasons: This is a new requirement introduced by Regulation No 283/2013. It did not exist in Regulation No 544/2011, and no guidelines/guidance exists at this stage on how to address the requirement (Commission communication No 2013/C 95/01). In addition, DuPont is not aware of guidelines harmonised at the EU or international level that could valuably be followed to generate such data and permit a meaningful interpretation.

B.7.12 References relied on

List of information, tests and studies which are considered as relied upon by the RMS for the evaluation with a view to the approval of the active substance.

Studies marked in yellow are submitted for the first time.

Sorted by Annex Point

Data requirement no., reference no.	Author(s)	Year	Title Source Company Report No. GLP or GEP Status (where relevant) Published or not	Vertebrate study Y/N	Data protection Y/N	Justification if data protection is claimed	Owner
B.7.1/01	Dubey, L., Steiner, C., Belgaid, R.	2002	Stability of oxamyl in different crops stored frozen Battelle Europe-Centre de Recherche de Geneve DuPont-4235 GLP: Yes Published: No	N	Yes at MS level	The study is necessary for the regulatory decision, conducted according to GLP and has not previously been protected or submitted in some MS.	DuPont
B.7.1/02	Cairns, S.D., Davidson, J.	2006	Storage stability of oxamyl in dried tobacco leaves Charles River Laboratories (UK) DuPont-17600 GLP: Yes Published: No	N	Yes at MS level	The study is necessary for the regulatory decision, conducted according to GLP and has not previously been protected or submitted in some MS.	DuPont
B.7.1/03	Cairns, S.D., Woodmansey, L.	2013	Stability of oxamyl (DPX-D1410) in oranges stored frozen Charles River Laboratories (UK) DuPont-32189 GLP: Yes Published: No	N	Y	The study is necessary for the regulatory decision, conducted according to GLP and has not previously been protected or submitted.	DuPont
B.7.2.1/01	Harvey, J.	1973a	Metabolism and biodegradation of oxamyl DuPont Experimental Station, DuPont Haskell Laboratory O/ME 4 Previously submitted at the EU level for Annex I inclusion Published: No	N	N	DuPont	

Data requirement no., reference no.	Author(s)	Year	Title Source Company Report No. GLP or GEP Status (where relevant) Published or not	Vertebrate study Y/N	Data protection Y/N	Justification if data protection is claimed	Owner
B.7.2.1/02	Han, J.C.-Y., Harvey, J.	1975	Additional studies of oxamyl in plants - characterization of ^{14}C-harvest residues in potato tubers DuPont Experimental Station O/ME 8-75 Previously submitted at the EU level for Annex I inclusion Published: No	N	N	DuPont	
B.7.2.1/03	Brown, A.M., Young, G.A., Swain, R.S.	2001	Metabolism of ^{14}C-oxamyl in potatoes DuPont Stine-Haskell Research Center DuPont-4520 Previously submitted at the EU level for Annex I inclusion Published: No	N	N	DuPont	
B.7.2.1/04	Brown, A.M., Young, G.A., Swain, R.S.	2002	Metabolism of ^{14}C-oxamyl in potatoes DuPont Stine-Haskell Research Center DuPont-4520, Supplement No. 1 Previously submitted at the EU level for Annex I inclusion Published: No	N	N	DuPont	
B.7.2.1/05	Harvey, J.	1973b	Additional studies on the metabolism and biodegradation of oxamyl in plants - Period: May 1, 1973 to October 1, 1973 DuPont Experimental Station O/ME 5 Previously submitted at the EU level for Annex I inclusion Published: No	N	N	DuPont	

Data requirement no., reference no.	Author(s)	Year	Title Source Company Report No. GLP or GEP Status (where relevant) Published or not	Vertebrate study Y/N	Data protection Y/N	Justification if data protection is claimed	Owner
B.7.2.1/06	Harvey, J.	1974	Additional studies on the metabolism of oxamyl in plants - I: Characterization of harvest residues in peanuts, apples and oranges (supplement 1) DuPont Experimental Station O/ME 5, Supplement No. 1 Previously submitted at the EU level for Annex I inclusion Published: No	N	N	DuPont	
B.7.2.1/07	Harvey, J.	1975	Additional studies on the metabolism of oxamyl in plants - II: Characterization of harvest residues - A: The polar fraction in oranges - period October 1, 1974 to June 1, 1975 DuPont Experimental Station O/ME 5, Supplement No. 2 Previously submitted at the EU level for Annex I inclusion Published: No	N	N	DuPont	
B.7.2.1/08	Brown, A.M., McMillan, J.A., Young, G.A., Pierce, D., Schrass, K.H.	2008	Metabolism of ^{14}C-oxamyl in potatoes DuPont Stine-Haskell Research Center DuPont-4520, Supplement No. 2 GLP: Yes Published: No	N	Y	The study is necessary for the regulatory decision, conducted according to GLP and has not previously been protected or submitted.	DuPont
C B.7.2.1/09	Chapleo, S., Johnson, J.	2014	The metabolism of ^{14}C-oxamyl in tomato plants Charles River Laboratories (UK) DuPont-32188 GLP: Yes Published: No	N	Y	The study is necessary for the regulatory decision, conducted according to GLP and has not previously been protected or submitted.	DuPont

Data requirement no., reference no.	Author(s)	Year	Title Source Company Report No. GLP or GEP Status (where relevant) Published or not	Vertebrate study Y/N	Data protection Y/N	Justification if data protection is claimed	Owner
B.7.2.2/01	[redacted]	1994	Metabolism of [^{14}C]oxamyl in laying hens [redacted] ex I inclusion Published: No	Y	N	DuPont	
B.7.2.2/02	[redacted]	1990	Metabolism of (^{14}C)-oxamyl in laying hens [redacted] n superceded with AMR 2546-92 Published: No		N		DuPont
B.7.2.3/01	Belasco, I.J., Harvey, J.	1980	In vitro rumen metabolism of ^{14}C-labeled oxamyl and selected metabolites of oxamyl DuPont Experimental Station AMR 09-80 Previously submitted at the EU level for Annex I inclusion Published: No	N	N	DuPont	
B.7.2.3/02	[redacted]	1994	The metabolism of [^{14}C] oxamyl in lactating goats [redacted] ex I inclusion Published: No	Y	N	DuPont	

Data requirement no., reference no.	Author(s)	Year	Title Source Company Report No. GLP or GEP Status (where relevant) Published or not	Vertebrate study Y/N	Data protection Y/N	Justification if data protection is claimed	Owner
B.7.3.1/01	Françon, B., Belgaid, R., Jetzer, M., Steiner, C.	2000	Magnitude of residues of oxamyl in root and tuber vegetables (potatoes) following application of Oxamyl 10G Formulation - Europe, season 1999 Battelle Europe-Centre de Recherche de Geneve DuPont-2407 Previously submitted at the EU level for Annex I inclusion Published: No	N	N	DuPont	
B.7.3.1/02	Françon, B., Bass, R.V., Jernberg, K.M.	2001	Magnitude of residues of oxamyl in potatoes following application of Oxamyl 10G Formulation - Europe, season 2000 Battelle Europe-Centre de Recherche de Geneve DuPont-3939, Revision No. 1 Previously submitted at the EU level for Annex I inclusion Published: No	N	N	DuPont	
B.7.3.1/03	Boissinot, J.-C., Cairns, S.D., Ward, L.	2007	Magnitude of oxamyl residues in potatoes following application of Vydate® 10G formulation–Europe 2006 Charles River Laboratories (UK) DuPont-19526 GLP: Yes Published: No	N	Y	The study is necessary for the regulatory decision, conducted according to GLP.	DuPont

Data requirement no., reference no.	Author(s)	Year	Title Source Company Report No. GLP or GEP Status (where relevant) Published or not	Vertebrate study Y/N	Data protection Y/N	Justification if data protection is claimed	Owner
B.7.3.1/04	Zenide, D., Jetzer, M., Smyser, B.P.	2002	Magnitude of residues of oxamyl in potatoes following in-furrow application of Oxamyl 5G formulation - southern Europe, season 2001 Battelle Europe-Centre de Recherche de Geneve DuPont-5989 GLP: Yes Published: No	N	Yes at MS level	The study is necessary for the regulatory decision, conducted according to GLP and has not previously been protected or submitted in some MS.	DuPont
B.7.3.1/05	Foster, A.C., Davidson, J., Cairns, S.D., Doran, A.M.	2003	Combined decline and magnitude of residues of oxamyl in main crop potatoes following applications of Oxamyl 10L formulation by drip irrigation - northern Europe, 2002 Inveresk Research DuPont-10297, Revision No. 1 GLP: Yes Published: No	N	Yes at MS level	The study is necessary for the regulatory decision, conducted according to GLP and has not previously been protected or submitted in some MS.	DuPont
B.7.3.2/01	Boissinot, J.-C., Cairns, S.D., Ward, L.	2007b	Decline and magnitude of oxamyl residues in protected tomatoes (fruiting vegetables, solanacea) following application of Vydate® 10L formulation *via* drip irrigation - southern Europe 2006 Charles River Laboratories (UK) DuPont-19519, Revision No. 1 GLP: Yes Published: No	N	Y	The study is necessary for the regulatory decision, conducted according to GLP.	DuPont

Data requirement no., reference no.	Author(s)	Year	Title Source Company Report No. GLP or GEP Status (where relevant) Published or not	Vertebrate study Y/N	Data protection Y/N	Justification if data protection is claimed	Owner
B.7.3.2/02	Boissinot, J.-C., Cairns, S.D., Ward, L.	2007a	Decline and magnitude of oxamyl residues in protected cherry tomatoes (fruiting vegetables, solanacea) following application of Vydate® 10L formulation *via* drip irrigation - southern Europe 2006 Charles River Laboratories (UK) DuPont-19521 GLP: Yes Published: No	N	Y	The study is necessary for the regulatory decision, conducted according to GLP.	DuPont
B.7.3.2/03	Haigh, I., Hoskins, M.	2011	Decline and magnitude of oxamyl residues in protected tomatoes, including cherry tomatoes (fruiting vegetables, solanacea) following application of Oxamyl 10L formulation *via* drip irrigation - southern Europe, 2009-10 Charles River Laboratories (UK) DuPont-29313 GLP: Yes Published: No	N	Y	The study is necessary for the regulatory decision, conducted according to GLP and has not previously been protected or submitted.	DuPont
B.7.3.2/04	Haigh, I., Cairns, S.	2012	Decline and magnitude of oxamyl residues in protected tomatoes, including cherry tomatoes (fruiting vegetables, solanacea) following application of Oxamyl 10L formulation *via* drip irrigation - southern Europe 2010-2011 Charles River Laboratories (UK) DuPont-31506 GLP: Yes Published: No	N	Y	The study is necessary for the regulatory decision, conducted according to GLP and has not previously been protected or submitted.	DuPont

Data requirement no., reference no.	Author(s)	Year	Title Source Company Report No. GLP or GEP Status (where relevant) Published or not	Vertebrate study Y/N	Data protection Y/N	Justification if data protection is claimed	Owner
B.7.3.3/01	Anderson, I., Cairns, S.D.	2006	Decline and magnitude of oxamyl residues in fermented tobacco leaves following granular application of Vydate® 5G or 10G and low pressure soil application of Vydate 10L® - southern Europe, 2005 Charles River Laboratories (UK) DuPont-14667 GLP: Yes Published: No	N	Y	The study is necessary for the regulatory decision, conducted according to GLP.	DuPont
B.7.3.4/01	Aitken, A., Cairns, S.	2013	Decline and magnitude of oxamyl residues in protected courgettes (fruiting vegetables, cucurbits) and cherry tomatoes (fruiting vegetables, solanacea) following application of Oxamyl 10L formulation *via* drip irrigation - Europe - 2012 Charles River Laboratories (UK), Charles River DuPont-35356 GLP: Yes Published: No	N	Y	The study is necessary for the regulatory decision, conducted according to GLP.	DuPont
B.7.5.1/01	Lee, D.Y.	2001	Hydrolysis to investigate the nature of potential residues of oxamyl in products resulting from industrial processing or household preparation DuPont Stine-Haskell Research Center DuPont-4025 Previously submitted at the EU level for Annex I inclusion Published: No	N	N	DuPont	

Data requirement no., reference no.	Author(s)	Year	Title Source Company Report No. GLP or GEP Status (where relevant) Published or not	Vertebrate study Y/N	Data protection Y/N	Justification if data protection is claimed	Owner
B.7.5.3/01	Foster, A.	2009	Magnitude of oxamyl residues in potatoes and potato processed fractions following exaggerated rate applications of Oxamyl 10G formulation - Europe 2009 Charles River Laboratories (UK) DuPont-27667 GLP: Yes Published: No	N	Y	The study is necessary for the regulatory decision, conducted according to GLP.	DuPont
B.7.6.1/01	Harvey, J.	1978	Crop rotation study with ^{14}C-oxamyl in the greenhouse DuPont Experimental Station O/ME 34 Previously submitted at the EU level for Annex I inclusion Published: No	N	N	DuPont	
B.7.6.1/02	Hawkins, D.R., Mayo, B.C., Pollard, A.D., Donschak, A.W.	1990	The confined accumulation of [^{14}C] oxamyl in rotational crops Huntingdon Research Centre AMR 1190-88 Previously submitted at the EU level for Annex I inclusion Published: No	N	N	DuPont	
B.7.6.1/03	Brown, A. M., Young, G. A., Swain, R. S.	2001	Accumulation of residues in confined rotational crops (barley) after soil treatment with ^{14}C-oxamyl DuPont Stine-Haskell Research Center DuPont-4518 Previously submitted at the EU level for Annex I inclusion Published: No	N	N	DuPont	

Data requirement no., reference no.	Author(s)	Year	Title Source Company Report No. GLP or GEP Status (where relevant) Published or not	Vertebrate study Y/N	Data protection Y/N	Justification if data protection is claimed	Owner
B.7.6.1/04	Brown, A. M., Young, G. A., Swain, R. S.	2002	Accumulation of residues in confined rotational crops (barley) after soil treatment with ^{14}C-oxamyl DuPont Stine-Haskell Research Center DuPont-4518, Supplement No. 1 Previously submitted at the EU level for Annex I inclusion Published: No	N	N	DuPont	
B.7.6.2/01	Anderson, I., Cairns, S., Hansford, R.J.	2007	Field crop rotation study with Vydate® 10G (DPX-D1410) - Europe 2005/6 Charles River Laboratories (UK) DuPont-16669 GLP: Yes Published: No	N	Y	The study is necessary for the regulatory decision, conducted according to GLP.	DuPont
B.7.6.2/02	Old, J., Boissinot, J.-C., Cairns, S., McConnell, K.	2009	Protected crop rotation study with Oxamyl 10L (DPX-D1410) - Europe 2007/8 Charles River Laboratories (UK) DuPont-16693 GLP: Yes Published: No	N	Y	The study is necessary for the regulatory decision, conducted according to GLP.	DuPont
B.7.10/01	Zenide, D., Jetzer, M., Smyser, B.P.	2003	Unit-to-unit variability of residues of oxamyl in cucumbers (edible-peel cucurbits) grown in green/plastic houses following applications of Oxamyl 10L formulation by drip irrigation - southern Europe, season 2002 Battelle Europe-Centre de Recherche de Geneve DuPont-9459 GLP: Yes Published: No	N	Yes at MS level	The study is necessary for the regulatory decision, conducted according to GLP and has not previously been protected or submitted in some MS.	DuPont

Data requirement no., reference no.	Author(s)	Year	Title Source Company Report No. GLP or GEP Status (where relevant) Published or not	Vertebrate study Y/N	Data protection Y/N	Justification if data protection is claimed	Owner
B.7.10/02	Schwarz, A., Eichler, M.	2014	Oxamyl (DPX-D1410) 10SL: Field study on residues in arthropods, earthworms and seedlings (wildlife food items) IBACON DuPont-40221 GLP: Yes Published: No	N	Y	The study is necessary for the regulatory decision, conducted according to GLP and has not previously been protected or submitted	DuPont
B.7.10/03	Scherer, F.	2015	Oxamyl (DPX-D1410) 10GR: Investigating the deposition of dust from in-furrow application of granules containing oxamyl and determination of residues of oxamyl in guttation fluid of potato in United Kingdom during 2014 Eurofins Agroscience Services EcoChem GmbH DuPont-38691 GLP: Yes Published: No	N	Y	The study is necessary for the regulatory decision, conducted according to GLP and has not previously been protected or submitted.	DuPont
B.7.10/04	Knäbe, S.	2015	Oxamyl (DPX-D1410) 10GR: Determination of residues of oxamyl in guttation fluid of sugar beet plants in Germany 2014 Eurofins Agroscience Services EcoChem GmbH DuPont-41321 GLP: Yes Published: No	N	Y	The study is necessary for the regulatory decision, conducted according to GLP and has not previously been protected or submitted.	DuPont

Data requirement no., reference no.	Author(s)	Year	Title Source Company Report No. GLP or GEP Status (where relevant) Published or not	Vertebrate study Y/N	Data protection Y/N	Justification if data protection is claimed	Owner
B.7.10/05	Mack, P.	2015	Oxamyl (DPX-D1410) 10GR: Determination of residues of oxamyl in pollen, nectar, flowers, and guttation fluid of tobacco in southern Europe 2014 Eurofins Agroscience Services EcoChem GmbH DuPont-41322, Revision No. 1 GLP: Yes Published: No	N	Y	The study is necessary for the regulatory decision, conducted according to GLP and has not previously been protected or submitted.	DuPont

Sorted by Author

Data requirement no., reference no.	Author(s)	Year	Title Source Company Report No. GLP or GEP Status (where relevant) Published or not	Vertebrate study Y/N	Data protection Y/N	Justification if data protection is claimed	Owner
B.7.3.4/01	Aitken, A., Cairns, S.	2013	Decline and magnitude of oxamyl residues in protected courgettes (fruiting vegetables, cucurbits) and cherry tomatoes (fruiting vegetables, solanacea) following application of Oxamyl 10L formulation *via* drip irrigation - Europe - 2012 Charles River Laboratories (UK), Charles River DuPont-35356 GLP: Yes Published: No	N	Y	The study is necessary for the regulatory decision, conducted according to GLP.	DuPont
B.7.6.2/01	Anderson, I., Cairns, S., Hansford, R.J.	2007	Field crop rotation study with Vydate® 10G (DPX-D1410) - Europe 2005/6 Charles River Laboratories (UK) DuPont-16669 GLP: Yes Published: No	N	Y	The study is necessary for the regulatory decision, conducted according to GLP.	DuPont
B.7.3.3/01	Anderson, I., Cairns, S.D.	2006	Decline and magnitude of oxamyl residues in fermented tobacco leaves following granular application of Vydate® 5G or 10G and low pressure soil application of Vydate 10L® - southern Europe, 2005 Charles River Laboratories (UK) DuPont-14667 GLP: Yes Published: No	N	Y	The study is necessary for the regulatory decision, conducted according to GLP.	DuPont

Data requirement no., reference no.	Author(s)	Year	Title Source Company Report No. GLP or GEP Status (where relevant) Published or not	Vertebrate study Y/N	Data protection Y/N	Justification if data protection is claimed	Owner
B.7.2.2/01	[redacted]	1994	Metabolism of [^{14}C]oxamyl in laying hens [redacted] ex I inclusion Published: No	Y	N	DuPont	
B.7.2.3/01	Belasco, I.J., Harvey, J.	1980	In vitro rumen metabolism of ^{14}C-labeled oxamyl and selected metabolites of oxamyl DuPont Experimental Station AMR 09-80 Previously submitted at the EU level for Annex I inclusion Published: No	N	N	DuPont	
B.7.3.1/03	Boissinot, J.-C., Cairns, S.D., Ward, L.	2007	Magnitude of oxamyl residues in potatoes following application of Vydate® 10G formulation–Europe 2006 Charles River Laboratories (UK) DuPont-19526 GLP: Yes Published: No	N	Y	The study is necessary for the regulatory decision, conducted according to GLP.	DuPont
B.7.3.2/01	Boissinot, J.-C., Cairns, S.D., Ward, L.	2007b	Decline and magnitude of oxamyl residues in protected tomatoes (fruiting vegetables, solanacea) following application of Vydate® 10L formulation *via* drip irrigation - southern Europe 2006 Charles River Laboratories (UK) DuPont-19519, Revision No. 1 GLP: Yes Published: No	N	Y	The study is necessary for the regulatory decision, conducted according to GLP.	DuPont

Data requirement no., reference no.	Author(s)	Year	Title Source Company Report No. GLP or GEP Status (where relevant) Published or not	Vertebrate study Y/N	Data protection Y/N	Justification if data protection is claimed	Owner
B.7.3.2/02	Boissinot, J.-C., Cairns, S.D., Ward, L.	2007a	Decline and magnitude of oxamyl residues in protected cherry tomatoes (fruiting vegetables, solanacea) following application of Vydate® 10L formulation *via* drip irrigation - southern Europe 2006 Charles River Laboratories (UK) DuPont-19521 GLP: Yes Published: No	N	Y	The study is necessary for the regulatory decision, conducted according to GLP.	DuPont
B.7.6.1/03	Brown, A. M., Young, G. A., Swain, R. S.	2001	Accumulation of residues in confined rotational crops (barley) after soil treatment with ^{14}C-oxamyl DuPont Stine-Haskell Research Center DuPont-4518 Previously submitted at the EU level for Annex I inclusion Published: No	N	N	DuPont	
B.7.6.1/04	Brown, A. M., Young, G. A., Swain, R. S.	2002	Accumulation of residues in confined rotational crops (barley) after soil treatment with ^{14}C-oxamyl DuPont Stine-Haskell Research Center DuPont-4518, Supplement No. 1 Previously submitted at the EU level for Annex I inclusion Published: No	N	N	DuPont	

Data requirement no., reference no.	Author(s)	Year	Title Source Company Report No. GLP or GEP Status (where relevant) Published or not	Vertebrate study Y/N	Data protection Y/N	Justification if data protection is claimed	Owner
B.7.2.1/08	Brown, A.M., McMillan, J.A., Young, G.A., Pierce, D., Schrass, K.H.	2008	Metabolism of ^{14}C-oxamyl in potatoes DuPont Stine-Haskell Research Center DuPont-4520, Supplement No. 2 GLP: Yes Published: No	N	Y	The study is necessary for the regulatory decision, conducted according to GLP and has not previously been protected or submitted.	DuPont
B.7.2.1/03	Brown, A.M., Young, G.A., Swain, R.S.	2001	Metabolism of ^{14}C-oxamyl in potatoes DuPont Stine-Haskell Research Center DuPont-4520 Previously submitted at the EU level for Annex I inclusion Published: No	N	N	DuPont	
B.7.2.1/04	Brown, A.M., Young, G.A., Swain, R.S.	2002	Metabolism of ^{14}C-oxamyl in potatoes DuPont Stine-Haskell Research Center DuPont-4520, Supplement No. 1 Previously submitted at the EU level for Annex I inclusion Published: No	N	N	DuPont	
B.7.1/02	Cairns, S.D., Davidson, J.	2006	Storage stability of oxamyl in dried tobacco leaves Charles River Laboratories (UK) DuPont-17600 GLP: Yes Published: No	N	Yes at MS level	The study is necessary for the regulatory decision, conducted according to GLP and has not previously been protected or submitted in some MS.	DuPont

Data requirement no., reference no.	Author(s)	Year	Title Source Company Report No. GLP or GEP Status (where relevant) Published or not	Vertebrate study Y/N	Data protection Y/N	Justification if data protection is claimed	Owner
B.7.1/03	Cairns, S.D., Woodmansey, L.	2013	Stability of oxamyl (DPX-D1410) in oranges stored frozen Charles River Laboratories (UK) DuPont-32189 GLP: Yes Published: No	N	Y	The study is necessary for the regulatory decision, conducted according to GLP and has not previously been protected or submitted.	DuPont
C B.7.2.1/09	Chapleo, S., Johnson, J.	2014	The metabolism of ^{14}C-oxamyl in tomato plants Charles River Laboratories (UK) DuPont-32188 GLP: Yes Published: No	N	Y	The study is necessary for the regulatory decision, conducted according to GLP and has not previously been protected or submitted.	DuPont
B.7.2.2/02	[redacted]	1990	Metabolism of (^{14}C)-oxamyl in laying hens [redacted] n superceded with AMR 2546-92 Published: No		N		DuPont
B.7.1/01	Dubey, L., Steiner, C., Belgaid, R.	2002	Stability of oxamyl in different crops stored frozen Battelle Europe-Centre de Recherche de Geneve DuPont-4235 GLP: Yes Published: No	N	Yes at MS level	The study is necessary for the regulatory decision, conducted according to GLP and has not previously been protected or submitted in some MS.	DuPont

Data requirement no., reference no.	Author(s)	Year	Title Source Company Report No. GLP or GEP Status (where relevant) Published or not	Vertebrate study Y/N	Data protection Y/N	Justification if data protection is claimed	Owner
B.7.5.3/01	Foster, A.	2009	Magnitude of oxamyl residues in potatoes and potato processed fractions following exaggerated rate applications of Oxamyl 10G formulation - Europe 2009 Charles River Laboratories (UK) DuPont-27667 GLP: Yes Published: No	N	Y	The study is necessary for the regulatory decision, conducted according to GLP.	DuPont
B.7.3.1/05	Foster, A.C., Davidson, J., Cairns, S.D., Doran, A.M.	2003	Combined decline and magnitude of residues of oxamyl in main crop potatoes following applications of Oxamyl 10L formulation by drip irrigation - northern Europe, 2002 Inveresk Research DuPont-10297, Revision No. 1 GLP: Yes Published: No	N	Yes at MS level	The study is necessary for the regulatory decision, conducted according to GLP and has not previously been protected or submitted in some MS.	DuPont
B.7.3.1/02	Françon, B., Bass, R.V., Jernberg, K.M.	2001	Magnitude of residues of oxamyl in potatoes following application of Oxamyl 10G Formulation - Europe, season 2000 Battelle Europe-Centre de Recherche de Geneve DuPont-3939, Revision No. 1 Previously submitted at the EU level for Annex I inclusion Published: No	N	N	DuPont	

Data requirement no., reference no.	Author(s)	Year	Title Source Company Report No. GLP or GEP Status (where relevant) Published or not	Vertebrate study Y/N	Data protection Y/N	Justification if data protection is claimed	Owner
B.7.3.1/01	Françon, B., Belgaid, R., Jetzer, M., Steiner, C.	2000	Magnitude of residues of oxamyl in root and tuber vegetables (potatoes) following application of Oxamyl 10G Formulation - Europe, season 1999 Battelle Europe-Centre de Recherche de Geneve DuPont-2407 Previously submitted at the EU level for Annex I inclusion Published: No	N	N	DuPont	
B.7.3.2/04	Haigh, I., Cairns, S.	2012	Decline and magnitude of oxamyl residues in protected tomatoes, including cherry tomatoes (fruiting vegetables, solanacea) following application of Oxamyl 10L formulation *via* drip irrigation - southern Europe 2010-2011 Charles River Laboratories (UK) DuPont-31506 GLP: Yes Published: No	N	Y	The study is necessary for the regulatory decision, conducted according to GLP and has not previously been protected or submitted.	DuPont
B.7.3.2/03	Haigh, I., Hoskins, M.	2011	Decline and magnitude of oxamyl residues in protected tomatoes, including cherry tomatoes (fruiting vegetables, solanacea) following application of Oxamyl 10L formulation *via* drip irrigation - southern Europe, 2009-10 Charles River Laboratories (UK) DuPont-29313 GLP: Yes Published: No	N	Y	The study is necessary for the regulatory decision, conducted according to GLP and has not previously been protected or submitted.	DuPont

Data requirement no., reference no.	Author(s)	Year	Title Source Company Report No. GLP or GEP Status (where relevant) Published or not	Vertebrate study Y/N	Data protection Y/N	Justification if data protection is claimed	Owner
B.7.2.1/02	Han, J.C.-Y., Harvey, J.	1975	Additional studies of oxamyl in plants - characterization of ^{14}C-harvest residues in potato tubers DuPont Experimental Station O/ME 8-75 Previously submitted at the EU level for Annex I inclusion Published: No	N	N	DuPont	
B.7.2.1/01	Harvey, J.	1973a	Metabolism and biodegradation of oxamyl DuPont Experimental Station, DuPont Haskell Laboratory O/ME 4 Previously submitted at the EU level for Annex I inclusion Published: No	N	N	DuPont	
B.7.2.1/05	Harvey, J.	1973b	Additional studies on the metabolism and biodegradation of oxamyl in plants - Period: May 1, 1973 to October 1, 1973 DuPont Experimental Station O/ME 5 Previously submitted at the EU level for Annex I inclusion Published: No	N	N	DuPont	

Data requirement no., reference no.	Author(s)	Year	Title Source Company Report No. GLP or GEP Status (where relevant) Published or not	Vertebrate study Y/N	Data protection Y/N	Justification if data protection is claimed	Owner
B.7.2.1/06	Harvey, J.	1974	Additional studies on the metabolism of oxamyl in plants - I: Characterization of harvest residues in peanuts, apples and oranges (supplement 1) DuPont Experimental Station O/ME 5, Supplement No. 1 Previously submitted at the EU level for Annex I inclusion Published: No	N	N	DuPont	
B.7.2.1/07	Harvey, J.	1975	Additional studies on the metabolism of oxamyl in plants - II: Characterization of harvest residues - A: The polar fraction in oranges - period October 1, 1974 to June 1, 1975 DuPont Experimental Station O/ME 5, Supplement No. 2 Previously submitted at the EU level for Annex I inclusion Published: No	N	N	DuPont	
B.7.6.1/01	Harvey, J.	1978	Crop rotation study with ^{14}C-oxamyl in the greenhouse DuPont Experimental Station O/ME 34 Previously submitted at the EU level for Annex I inclusion Published: No	N	N	DuPont	

Data requirement no., reference no.	Author(s)	Year	Title Source Company Report No. GLP or GEP Status (where relevant) Published or not	Vertebrate study Y/N	Data protection Y/N	Justification if data protection is claimed	Owner
B.7.6.1/02	Hawkins, D.R., Mayo, B.C., Pollard, A.D., Donschak, A.W.	1990	The confined accumulation of [^{14}C] oxamyl in rotational crops Huntingdon Research Centre AMR 1190-88 Previously submitted at the EU level for Annex I inclusion Published: No	N	N	DuPont	
B.7.10/04	Knäbe, S.	2015	Oxamyl (DPX-D1410) 10GR: Determination of residues of oxamyl in guttation fluid of sugar beet plants in Germany 2014 Eurofins Agroscience Services EcoChem GmbH DuPont-41321 GLP: Yes Published: No	N	Y	The study is necessary for the regulatory decision, conducted according to GLP and has not previously been protected or submitted.	DuPont
B.7.5.1/01	Lee, D.Y.	2001	Hydrolysis to investigate the nature of potential residues of oxamyl in products resulting from industrial processing or household preparation DuPont Stine-Haskell Research Center DuPont-4025 Previously submitted at the EU level for Annex I inclusion Published: No	N	N	DuPont	
B.7.2.3/02	[redacted]	1994	The metabolism of [^{14}C] oxamyl in lactating goats [redacted] ex I inclusion Published: No	Y	N	DuPont	

Data requirement no., reference no.	Author(s)	Year	Title Source Company Report No. GLP or GEP Status (where relevant) Published or not	Vertebrate study Y/N	Data protection Y/N	Justification if data protection is claimed	Owner
B.7.10/05	Mack, P.	2015	Oxamyl (DPX-D1410) 10GR: Determination of residues of oxamyl in pollen, nectar, flowers, and guttation fluid of tobacco in southern Europe 2014 Eurofins Agroscience Services EcoChem GmbH DuPont-41322, Revision No. 1 GLP: Yes Published: No	N	Y	The study is necessary for the regulatory decision, conducted according to GLP and has not previously been protected or submitted.	DuPont
B.7.6.2/02	Old, J., Boissinot, J.-C., Cairns, S., McConnell, K.	2009	Protected crop rotation study with Oxamyl 10L (DPX-D1410) - Europe 2007/8 Charles River Laboratories (UK) DuPont-16693 GLP: Yes Published: No	N	Y	The study is necessary for the regulatory decision, conducted according to GLP.	DuPont
B.7.10/03	Scherer, F.	2015	Oxamyl (DPX-D1410) 10GR: Investigating the deposition of dust from in-furrow application of granules containing oxamyl and determination of residues of oxamyl in guttation fluid of potato in United Kingdom during 2014 Eurofins Agroscience Services EcoChem GmbH DuPont-38691 GLP: Yes Published: No	N	Y	The study is necessary for the regulatory decision, conducted according to GLP and has not previously been protected or submitted.	DuPont
B.7.10/02	Schwarz, A., Eichler, M.	2014	Oxamyl (DPX-D1410) 10SL: Field study on residues in arthropods, earthworms and seedlings (wildlife food items) IBACON DuPont-40221 GLP: Yes Published: No	N	Y	The study is necessary for the regulatory decision, conducted according to GLP and has not previously been protected or submitted	DuPont

Data requirement no., reference no.	Author(s)	Year	Title Source Company Report No. GLP or GEP Status (where relevant) Published or not	Vertebrate study Y/N	Data protection Y/N	Justification if data protection is claimed	Owner
B.7.3.1/04	Zenide, D., Jetzer, M., Smyser, B.P.	2002	Magnitude of residues of oxamyl in potatoes following in-furrow application of Oxamyl 5G formulation - southern Europe, season 2001 Battelle Europe-Centre de Recherche de Geneve DuPont-5989 GLP: Yes Published: No	N	Yes at MS level	The study is necessary for the regulatory decision, conducted according to GLP and has not previously been protected or submitted in some MS.	DuPont
B.7.10/01	Zenide, D., Jetzer, M., Smyser, B.P.	2003	Unit-to-unit variability of residues of oxamyl in cucumbers (edible-peel cucurbits) grown in green/plastic houses following applications of Oxamyl 10L formulation by drip irrigation - southern Europe, season 2002 Battelle Europe-Centre de Recherche de Geneve DuPont-9459 GLP: Yes Published: No	N	Yes at MS level	The study is necessary for the regulatory decision, conducted according to GLP and has not previously been protected or submitted in some MS.	DuPont

APPENDIX I – EFSA Primo Model - Oxamyl

OXAMYL

Prepare workbook for refined calculations

Undo refined calculations

Status of the active substance:		Code no.	
LOQ (mg/kg bw):		proposed LOQ:	
Toxicological end points			
ADI (mg/kg bw/day):	0,01	ARfD (mg/kg bw):	0,01
Source of ADI:		Source of ARfD:	
Year of evaluation:		Year of evaluation:	

Explain choice of toxicological reference values.

The risk assessment has been performed on the basis of the MRLs collected from Member States in April 2006. For each pesticide/commodity the highest national MRL was identified (proposed temporary MRL = pTMRL).

The pTMRLs have been submitted to EFSA in September 2006.

Chronic risk assessment - refined calculations

	TMDI (range) in % of ADI minimum - maximum
	1 7
No of diets exceeding ADI:	—

Highest calculated TMDI values in % of ADI	MS Diet	Highest contributor to MS diet (in % of ADI)	Commodity / group of commodities	2nd contributor to MS diet (in % of ADI)	Commodity / group of commodities	3rd contributor to MS diet (in % of ADI)	Commodity / group of commodities	pTMRLs at LOQ (in % of ADI)
6,8	UK Infant	3,9	Milk and cream,	1,0	Sugar beet (root)	0,3	Potatoes	
6,8	NL child	2,9	Milk and cream,	0,6	Apples	0,6	Potatoes	
6,7	FR toddler	4,0	Milk and cream,	0,5	Potatoes	0,3	Apples	
6,3	UK Toddler	2,3	Sugar beet (root)	2,1	Milk and cream,	0,4	Wheat	
5,4	DE child	1,4	Milk and cream,	1,2	Apples	0,4	Wheat	
4,9	WHO Cluster diet B	0,9	Wheat	0,3	Milk and cream,	0,3	Tomatoes	
4,5	FR infant	2,6	Milk and cream,	0,4	Potatoes	0,3	Carrots	
4,1	DK child	1,3	Milk and cream,	0,6	Wheat	0,4	Rye	
3,9	IE adult	0,4	Sweet potatoes	0,3	Milk and cream,	0,2	Maize	
3,7	ES child	1,3	Milk and cream,	0,4	Wheat	0,3	Cocoa (fermented beans)	
3,3	SE general population 90th percentile	1,2	Milk and cream,	0,4	Potatoes	0,3	Wheat	
3,1	WHO cluster diet E	0,4	Wheat	0,4	Potatoes	0,3	Milk and cream,	
2,9	WHO cluster diet D	0,7	Wheat	0,5	Milk and cream,	0,4	Potatoes	
2,9	WHO regional European diet	0,5	Milk and cream,	0,4	Potatoes	0,3	Wheat	
2,8	WHO Cluster diet F	0,4	Milk and cream,	0,4	Wheat	0,3	Potatoes	
2,4	NL general	0,7	Milk and cream,	0,3	Potatoes	0,2	Wheat	
2,1	PT General population	0,5	Potatoes	0,4	Wheat	0,2	Wine grapes	
2,1	ES adult	0,5	Milk and cream,	0,2	Wheat	0,1	Oranges	
1,8	FR all population	0,4	Wine grapes	0,3	Wheat	0,3	Milk and cream,	
1,8	UK vegetarian	0,4	Sugar beet (root)	0,3	Milk and cream,	0,2	Wheat	
1,7	DK adult	0,5	Milk and cream,	0,2	Wheat	0,1	Potatoes	
1,7	IT kids/toddler	0,7	Wheat	0,2	Other cereal	0,1	Tomatoes	
1,6	UK Adult	0,4	Sugar beet (root)	0,3	Milk and cream,	0,2	Wheat	
1,6	LT adult	0,4	Milk and cream,	0,3	Potatoes	0,2	Apples	
1,5	FI adult	0,6	Milk and cream,	0,1	Potatoes	0,1	Coffee beans	
1,2	IT adult	0,4	Wheat	0,1	Tomatoes	0,1	Apples	
1,0	PL general population	0,3	Potatoes	0,2	Apples	0,1	Tomatoes	

Conclusion:

The estimated Theoretical Maximum Daily Intakes (TMDI), based on pTMRLs were below the ADI.

A long-term intake of residues of OXAMYL is unlikely to present a public health concern.

Acute risk assessment /children - refined calculations						Acute risk assessment / adults / general population - refined calculations					
The acute risk assessment is based on the ARfD.											
For each commodity the calculation is based on the highest reported MS consumption per kg bw and the corresponding unit weight from the MS with the critical consumption. If no data on the unit weight was available from that MS an average European unit weight was used for the IESTI calculation.											
In the **IESTI 1** calculation, the variability factors were 10, 7 or 5 (according to JMPR manual 2002), for lettuce a variability factor of 5 was used. In the **IESTI 2** calculations, the variability factors of 10 and 7 were replaced by 5. For lettuce the calculation was performed with a variabilty factor of 3.											
Threshold MRL is the calculated residue level which would leads to an exposure equivalent to 100 % of the ARfD.											
Unprocessed commodities											
No of commodities for which ARfD/ADI is exceeded (IESTI 1):		---	**No of commodities for which ARfD/ADI is exceeded (IESTI 2):**		---	**No of commodities for which ARfD/ADI is exceeded (IESTI 1):**		---	**No of commodities for which ARfD/ADI is exceeded (IESTI 2):**		---
IESTI 1	*)	**)	**IESTI 2**	*)	**)	**IESTI 1**	*)	**)	**IESTI 2**	*)	**)
Highest % of ARfD/ADI	Commodities	pTMRL/ threshold MRL (mg/kg)	Highest % of ARfD/ADI	Commodities	pTMRL/ threshold MRL (mg/kg)	Highest % of ARfD/ADI	Commodities	pTMRL/ threshold MRL (mg/kg)	Highest % of ARfD/ADI	Commodities	pTMRL/ threshold MRL (mg/kg)
15,4	Potatoes	0,01 / -	15,2	Melons	0,01 / -	5,3	Pumpkins	0,01 / -	5,3	Pumpkins	0,01 / -
15,2	Melons	0,01 / -	12,4	Milk and milk	0,01 / -	5,0	Aubergines (egg	0,02 / -	5,0	Aubergines (egg plants)	0,02 / -
13,3	Oranges	0,01 / -	12,2	Watermelons	0,01 / -	4,1	Watermelons	0,01 / -	4,1	Watermelons	0,01 / -
12,4	Milk and milk	0,01 / -	11,0	Potatoes	0,01 / -	3,9	Melons	0,01 / -	3,9	Melons	0,01 / -
12,2	Watermelons	0,01 / -	10,1	Pineapples	0,01 / -	3,6	Chinese cabbage	0,01 / -	3,6	Chinese cabbage	0,01 / -
No of critical MRLs (IESTI 1)			---			**No of critical MRLs (IESTI 2)**			---		
Processed commodities											
No of commodities for which ARfD/ADI is exceeded:		---				**No of commodities for which ARfD/ADI is exceeded:**		---			
		***)						***)			
Highest % of ARfD/ADI	Processed commodities	pTMRL/ threshold MRL (mg/kg)				Highest % of ARfD/ADI	Processed commodities	pTMRL/ threshold MRL (mg/kg)			
5,1	Apple juice	0,01 / -				1,0	Orange juice	0,01 / -			
5,0	Orange juice	0,01 / -				0,7	Apple juice	0,01 / -			
4,3	Carrot, juice	0,01 / -				0,4	Bread/pizza	0,01 / -			
3,3	Grape juice	0,01 / -				0,4	Wine	0,01 / -			
1,8	Peach juice	0,01 / -				0,3	Pineapples preserved	0,01 / -			
*) The results of the IESTI calculations are reported for at least 5 commodities. If the ARfD is exceeded for more than 5 commodities, all IESTI values > 90% of ARfD are reported.											
**) pTMRL: provisional temporary MRL											
***) pTMRL: provisional temporary MRL for unprocessed commodity											
Conclusion:											
For OXAMYL IESTI 1 and IESTI 2 were calculated for food commodities for which pTMRLs were submitted and for which consumption data are available.											
No exceedance of the ARfD/ADI was identified for any unprocessed commodity.											
For processed commodities, no exceedance of the ARfD/ADI was identified.											