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Chlorothalonil

NOTIFICATION OF AN ACTIVE SUBSTANCE UNDER COMMISSION REGULATION (EU) 844/2012

DOCUMENT M-CA, Section 6 Supplement

RESIDUES IN OR ON TREATED PRODUCTS, FOOD AND FEED

Version history[1]

Date	Data points containing amendments or additions and brief description	Document identifier and version number
21-08-2015	KCA 6.1/08. Final OECD summary of the storage stability of chlorothalonil metabolite R182281 in animal matrices under freezer storage conditions for up to two years included; all changes highlighted in yellow.	7 March 2015 updated 24/8/15
14-12-2015	KCA 6.1/04 revised report included for storage stability results up to 30 months; KCA 6.5.3/08 new wheat processing study included; all changes highlighted in green.	7 March 2015 updated 24/8/15 and 14/12/15
24-6-2016	CA 6.3.1 inclusion of field tomato residue trials, 8 northern and 8 southern conducted at 1x 1000 g a.s./ha as requested by the RMS. These new trials were ongoing during the course of the EU evaluation; all changes highlighted in turquoise.	7 March 2015 updated 24/8/15, 14/12/15, 24.6.16
3-8-2016	Removal of highlighted revision dates as provided in this table	7 March 2015 updated 24/8/15, 14/12/15, 24/6/16, 3/8/16

[1]It is suggested that applicants adopt a similar approach to showing revisions and version history as outlined in SANCO/10180/2013 Chapter 4 How to revise an Assessment Report

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CA 6 RESIDUES IN OR ON TREATED PRODUCTS, FOOD AND FEED

This document supports the application for renewal of the regulatory approval of chlorothalonil under Commission Implementing Regulation (EU) 844/2012 of 18 September 2012. This document reviews residues in or on treated products, food and feed, for chlorothalonil. The dossier preparation guidance (**SANCO/10181/2013**) states that all data and evaluations must be provided in the active substance(s) dossier. Therefore all relevant data for the representative use of A14111B (Syngenta Crop Protection); Chlorothalonil 500 g/L SC (Oxon Italia SpA) and ARY-0474-001 (Arysta LifeScience) is provided in this document. A combined representative GAP is provided in Appendix 1.

Chlorothalonil was included in Annex I of Council Directive 91/414/EEC (Commission Directive 2005/53/EC of 16 September 2005). This active substance is an approved active substance under Regulation (EC) 1107/2009 (repealing Commission Directive 91/414/EEC) as specified in Commission Implementing Regulation (EU) No. 540/2011 of 25 May 2011.

In accordance with Commission Implementing Regulation (EU) 844/2012, this document summarises new information which are relevant for the renewal of the approval of chlorothalonil under Regulation (EC) 1107/2009. Where appropriate this document refers to the Commission Implementing Regulation (EU) No. 540/2011 for chlorothalonil and to the Review Report for chlorothalonil(SANCO/4343/2000 final (revised), 28September 2006), and in particular the endpoints provided in Appendices I and II thereof.

This document covers data and risk assessments which were not part of the original dossier and which are necessary to reflect changes:

- In requirements under Commission Regulation (EU) No 283/2013, and the associated Annex, which repeals Commission Regulation (EU) No 544/2011 which, under Regulation (EC) 1107/2009, replaced the requirements of Annex II to Directive 91/414/EEC
- In scientific and technical knowledge since the approval or last renewal of the approval
- To representative uses

Where the conclusions of the EU review had specific areas of concern on chlorothalonil, new data and/or reviews and/or risk assessments have been provided. Where additional and/or new data on chlorothalonil are provided, a justification has been included.

Additional studies that are available and provide supplementary information that does not impact directly on the assessment and are therefore not relied upon are not included in the dossier however the studies have been summarised. These summaries are presented in Appendix 3 for information.

Details of the literature search undertaken can be found in M-CA Section 9. If a relevant scientifically peer-reviewed open literature reference has been identified for chlorothalonil or its major metabolites, it has been discussed within the relevant data point.

A major proposal in this document is the request for a change of definition of residue (DoR) of crops and animals for monitoring and risk assessment (see Point CA 6.7.1). To support this proposal a number of additional studies have been submitted. These include the metabolism studies on rotational crops and livestock, a new rotational crop study, new processing studies and new residue studies on tomato, barley and wheat. This has been made clear at the start of each section. Tomato, wheat, barley and potato are the representative crops in this submission and for this reason are the only crops to be included for dietary burden and risk assessment calculations. As the renewal of approval of chlorothalonil is supported by a

Task Force consisting of Syngenta CropProtection, Oxon Italia S.p.A. and Arysta LifeScience SAS, studies owned by different companies are presented in the following sections.

CA 6.1 Storage stability of Residues

Stability of residues during storage of samples

The stability of chlorothalonil was investigated in various crops and animal products. The studies were evaluated under Council Directive 91/414/EEC and are presented in the chlorothalonil monograph (**Vol.3, Annex B, Section B.7.6.2, January 2000**).

Commodity	Author/s	Issue Year	Report Number
Cherry	King C	1995	3064-88-0068-CR-003
Almond	King C, Wiedmann JL	1996	3064-88-0158-CR-003
Potato	Rose C	1995	3064-88-0095-CR-003
Carrot	Rose C	1995	3064-88-0096-CR-003
Celery	King C	1995	3064-88-0136-CR-003
Cucumber	King C, Wiedmann JL	1996	3064-88-0093-CR-003
Tomato	Hayes PC Jr, Kenyon RG	1996	3064-88-0083-CR-003
Wheat	Kenyon RG	1995	3064-88-0070-CR-003
Peanut	King C	1995	3064-88-0160-CR-003
Soya	Dvorak RS, Kenyon RG	1995	3064-88-0097-CR-003
Animal products	King C, Prince P	1995	5927-93-0329-CR-001

Resulting from the original evaluation of the results from these study reports, chlorothalonil levels appeared stable when stored as whole commodities under frozen storage conditions (at -7°C or below) for at least 2 years (almonds nutmeats and hulls) to 4 years (cherries, wheat, grain, tomatoes, cucumbers, carrots, soybeans and celery). In potatoes and peanuts, chlorothalonil levels tended to decrease upon long term storage, yet remained relatively stable during the first year and half year of storage, respectively. Relatively low and stable levels of R182281 (SDS-3701) and R611965 (SDS-46851) were detected in most commodities. Only in peanuts, R182281 and R611965 levels tended to increase upon prolonged storage, but the levels remained below 10%of the levels of chlorothalonil.

R182281 was stable for at least 12 months in animal products (milk, liver, muscle and fat) stored frozen (<-6°C).

Additional freezer storage stability studies not submitted for Annex I listing of chlorothalonil are now available and summaries are presented below.

Report:	K-CA 6.1/01. Anderson L and Chaggar S. (2007), Chlorothalonil (R44686) and R182281 (SDS3701): storage stability of field-incurred residues in homogenised crops stored deep frozen for up to two years. Syngenta, Jealott's Hill International Research Centre, Bracknell, United Kingdom. Syngenta Report Number T000559-06-REG. (Syngenta File No: R182281/0023).

Guidelines

Not stated but meets the requirements of Guideline: Commission of the European Communities: Storage Stability of Residue Samples (**SANCO 7032/V1/95 rev. 5 22/7/1997**).

GLP

The study was carried out according to the principles of Good Laboratory Practice.

EXECUTIVE SUMMARY

Samples of cucumber, tomato, whole melon, carrot root, carrot top (foliage), whole orange, barley grain, barley straw and soya beans containing incurred residues of chlorothalonil and R182281 from supervised residue trials were stored under frozen conditions (≤-18° C) and analysed at intervals up to 24 months (five sampling points). An additional analysis after 27 months storage was conducted for barley straw and soya bean samples only. The limit of quantification (LOQ) for both chlorothalonil and R182281 was 0.01 mg/kg.

Residues of chlorothalonil were stable for at least 24 months in tomato, cucumber, melon (high water crop group), barley grain (high starch group), for at least 27 months in soya bean (high oil group) and for 12 months in barley straw when stored in the freezer at ≤-18°C.

There was no apparent degradation of R182281 in tomatoes, oranges or soya bean. Measured residues of R182281 increased in cucumber, melon, carrots (root and foliage) and barely (grain and straw), probably via transformation of chlorothalonil to R182281. However, some of the incurred residues were below the LOQ of the method (0.01 mg/kg) and therefore difficult to quantify with accuracy and precision.

The study demonstrated that field incurred residues of chlorothalonil and R182281 remained stable on storage when prepared without the use of dry ice or acid.

I. MATERIALS AND METHODS

A. MATERIALS

A1. Test Materials

The purity of the analytical standards used in this study is listed in Table 6.1-1.

Table 6.1-1: Purity of analytical standards

Analyte	Standard reference no.	Purity (wt. %)
Chlorothalonil	AMS 237/2	99
R 182281 (SDS-3701)	ASJ10209-02	100

A2. Test Commodity

The test commodities were mature crops obtained from field trials.

A3. Test Facilities

The field phase of this study was performed at various locations in Europe and the USA. The analytical phase was performed at Syngenta, Jealott's Hill International Research Centre, Bracknell, Berkshire, RG42 6EY, UK.

B. STUDY DESIGN AND METHODS

B1. Fortification and Storage of Samples

Samples of tomato (variety "Petula"), cucumber (variety "Tiria"), whole melon, (variety "Ferreol"), whole orange (variety "Navelina"), carrot root and tops (variety "Solo"), barley straw and grain (variety "Landi") were obtained from a residue study conducted in Switzerland. Soya beans (variety "Pioneer 93M80") were obtained from a residue study conducted in the USA. In all trials application of chlorothalonil was made by foliar spray at a nominal rate of 4500 g a.s./ha (tomato, cucumber, melon, orange, carrot), 3000 g a.s./ha (barley) or 3430 g a.s./ha (soya bean). Mature harvest samples of tomato, cucumber, melon, orange, carrot and barley straw were homogenised by chopping (without dry ice). Samples of barley grain and soya bean were not prepared. Sub-samples of each commodity were stored under frozen conditions (≤18°C) and analysed in triplicate at intervals up to 24 months (five sampling points). An additional analysis after 27 months storage was conducted for barley straw and soya bean. The initial (0 month) samples were analysed in triplicate immediately after sample preparation.

B2. Analytical Method

Two methods of analysis were used. Analytical method SOP RAM 365/02 was used for samples taken at 0, 3, 6 and 12 months. The method validation is reported in report number R44686/3294. A full method description and validation data are presented in document M-CA Section 4, CA 4.1.2.

Commodity	Author/s	Issue Year	Report Number
Crops	Hargreaves, S.L.	2003	R44686/3321
Crops	Atkinson, S.	2003	R44686/3365

The method involved extraction of the samples with acetone/5M sulphuric acid followed by centrifugation. An aliquot of the extract was taken, partitioned into toluene and then subjected to C8 solid phase extraction (SPE) clean up. Chlorothalonil and R182281 were determined by gas liquid chromatography with mass selective detection (GC-MSD) using three fragment ions ($m/z > 100$) for quantification. R182281 was derivatised with trimethylsilyl diazomethane to produce methyl R182281 (R619464). The LOQ was 0.01 mg/kg for both analytes.

Analytical method SOP RAM 365/02 was replaced by method GRM005.01A for samples analysed after 24 and 27 months. The method validation is reported in report number R44686 /4046. A full method description and validation data are presented in document M-CA Section 4, CA 4.1.2.

Commodity	Author/s	Issue Year	Report Number
Crops	Chaggar, S.	2006	R44686 /4047
Crops	Chaggar, S.	2006	R44686/4046

The method involved extraction of the samples with acetone/5M sulphuric acid followed by centrifugation. For chlorothalonil aliquots of the extracts were diluted with water and subjected to SPE clean up, before analysis by GC-MSD. For R18221, aliquots of the sample extracts were diluted with acetonitrile: water and analysed by liquid chromatography tandem mass spectrometry (LC-MS/MS). The LOQ was 0.01 mg/kg for both analytes.

II. RESULTS AND DISCUSSION

Method Validation

Procedural recoveries were determined using freshly fortified samples at each interval. Samples were fortified with chlorothalonil at 0.1 – 25 mg/kg or R182281 at 0.01 – 1.5 mg/kg. Individual recoveries, mean recoveries and %RSD are summarised in Table 6.1-2 (chlorothalonil) and Table 6.1-3 (R182281).

Table 6.1-2: Summary of procedural recoveries for chlorothalonil in crops

Crop	Fortification level (mg/kg)	Recovery (%)	Mean recovery (%)	RSD (%)
Tomato	1	81	89	12
	3	103, 101, 73, 75, 88, 91, 88, 87		
	5	98		
Cucumber	1	99	95	8.8
	2	98, 101, 92, 89, 94, 92, 85, 86		
	5	113		
Melon	0.1	90	98	7.8
	1	99, 97, 98, 113, 111, 93, 92, 96, 95		
Orange	0.1	79	95	6.6
	1	94		
	10	99, 101, 96, 93, 95, 99, 95, 100		
Carrot root	0.1	95	95	4.3
	1	99, 91, 91, 95, 103, 91, 97, 93, 91		
Carrot top	1	92	96	5.0
	5	94		
	25	103, 100, 89, 92, 92, 97, 97, 102		
Barley straw	5	100	96	5.1
	10	103		
	20	96, 104, 96, 99, 96, 94, 92, 99, 89, 89		
Barley grain	0.1	96, 77, 88	90	6.5
	1	86, 87, 94, 92, 95, 95, 89		
Soya bean	0.1	88	80	8.5
	1	81, 77, 93		
	1.5	79, 67, 76, 79		
	2.0	74, 76, 84, 82		

Recovery data were obtained by using method SOP RAM 365/02 and method GRM005.01A.

Table 6.1-3: Summary of procedural recoveries for R18221 in crops

Crop	Fortification level (mg/kg)	Recovery (%)	Mean recovery (%)	RSD (%)
Tomato	0.01	83, 101, 92, 87, 69, 72, 122, 94, 99, 101	92	16
	0.1	80		
	0.05	102		
Cucumber	0.01	107, 113, 105, 101, 97, 105, 101, 82, 100, 96	101	7.6
	0.1	97		
	0.05	105		
Melon	0.01	87, 107, 100, 106, 103, 109, 96, 110, 103	101	8.7
	0.1	85		
Orange	0.01	90	98	7.3
	0.02	97, 92, 114, 102, 102, 99, 97, 91		
	0.1	94		
Carrot root	0.01	83	96	10
	0.03	100, 108		
	0.04	99, 91, 101, 103, 101, 96		
	0.1	77		
Carrot top	0.01	108	107	9.4
	0.1	94		
	0.25	124, 128, 100, 104		
	0.3	100, 99, 108, 111, 108, 102		
Barley straw	0.1	108	105	6.8
	1	102, 99, 97, 106, 100, 109, 100, 98, 105		
	1.5	120, 115		
Barley grain	0.01	93, 86, 101, 96, 101	96	7.7
	0.05	99, 88, 106, 106		
	0.1	88		
Soya bean	0.01	76, 79	98	12
	0.02	112, 108, 83, 98, 94, 92, 101, 117		
	0.03	103, 106		
	0.1	99, 101		

Recovery data were obtained by using method SOP RAM 365/02 and method GRM005.01A

Storage Stability of Residues

The recoveries of chlorothalonil and R182281 in crops stored at ≤-18°C are summarised in Table 6.1-4 and Table 6.1-5, respectively. The results are not corrected for freshly fortified recoveries.

Table 6.1-4: Freezer storage stability for chlorothalonil in crops

Sampling interval (nominal months)	Sampling interval (actual days)	Uncorrected residue (mg/kg)	Mean uncorrected residue (mg/kg)	Mean procedural recovery (%)	Mean recovered uncorrected residue (%)
Tomato					
0	0	2.8, 2.7, 3.0	2.8	89	100
3	98	3.0, 2.7, 3.1	3.0	102	106
6	211	1.8, 1.9, 2.1	1.9	73	69
12	385	2.6, 2.7, 2.5	2.6	90	93
24	786	2.5, 2.5, 2.3	2.5	87	88
Cucumber					
0	7	1.8, 2.3, 1.5	1.9	106	100
3	104	1.6, 1.6, 1.6	1.6	99	86
6	209	1.4, 1.5, 1.5	1.5	90	78
12	383	1.4, 1.5, 1.4	1.4	93	76
24	784	1.6, 1.3, 1.3	1.4	85	76
Melon					
0	0	0.57, 0.65, 0.65, 0.79, 0.62	0.66	95	100
3	99	0.55, 0.52, 1.02	0.70	97	106
6	216	0.70, 0.66, 0.71	0.69	113	104
12	378	0.71, 0.41, 0.51	0.54	93	83
24	779	0.69, 0.53, 0.80	0.68	96	103
Orange					
0	0	11, 8.2, 8.9, 11, 11	10	87	100
3	102	8.0, 8.7, 8.6	8.4	100	84
6	223	7.6, 8.1, 8.3	8.0	95	80
12	404	8.5, 8.6, 8.2	8.4	97	84
24	788	8.0, 8.5, 7.8	8.1	97	81
Carrot root					
0	0	0.73, 0.69, 0.70, 0.71, 0.64	0.69	97	100
3	97	0.67, 0.62, 0.74	0.68	91	98
6	216	0.60, 0.62, 0.57	0.60	99	86
12	405	0.60, 0.61, 0.60	0.60	94	87
24	781	0.50, 0.52, 0.53	0.51	92	74
Carrot top					
0	0	101, 85, 94, 92, 87	92	93	100
3	92	92, 89, 87	89	101	97
6	211	79, 80, 73	77	91	84
12	400	90, 101, 94	95	95	103
24	784	77, 77, 73	75	100	82
Barley straw					
0	0	25, 25, 28, 24, 26	26	101	100
3	104	21, 21, 20	20	100	80

Sampling interval (nominal months)	Sampling interval (actual days)	Uncorrected residue (mg/kg)	Mean uncorrected residue (mg/kg)	Mean procedural recovery (%)	Mean recovered uncorrected residue (%)
6	209	18, 18, 20	18	97	72
12	406	19, 18, 17	18	95	70
24	790	15, 15, 16	15	95	59
27	840	13, 14, 15	14	89	53
Barley grain					
0	0	0.71, 0.80, 0.73, 0.74, 0.83	0.76	91	100
3	92	0.82, 0.82, 0.88	0.84	83	110
6	203	0.67, 0.80, 0.65	0.71	90	93
12	391	0.79, 0.76, 0.77	0.77	94	101
24	770	0.81, 0.58, 0.85	0.74	92	98
Soya bean					
0	0	1.4, 1.4, 1.3, 1.3, 1.4	1.4	84	100
3	91	1.4 ,1.3, 1.4	1.4	73	100
6	202	1.5, 1.6, 1.6	1.6	85	115
12	390	1.5, 1.4, 1.4	1.5	75	106
24	770	1.2, 0.69, 0.84	0.91	83	68
27	810	0.97, 1.2, 1.5	1.2	77	88

Percentage recovered residue = residue concentration / initial residue concentration using uncorrected residues x 100.
Calculations performed on unrounded values.
No residues were present above the LOQ in control samples.

Table 6.1-5: Freezer storage stability for R182281 in crops

Sampling interval (nominal months)	Sampling interval (actual days)	Uncorrected residue (mg/kg)	Mean uncorrected residue (mg/kg)	Mean procedural recovery (%)	Mean recovered uncorrected residue (%)
Tomato					
0	0	0.008, 0.008, 0.007, 0.009, 0.007	0.008	82	100
0	9	0.008, 0.009, 0.010		101	
3	98	0.008, 0.009	0.008	90	102
6	211	0.006, 0.007, 0.007	0.007	71	83
12	385	0.008, 0.01, 0.009	0.009	108	113
24	786	0.008, 0.009, 0.01	0.009	100	110
Cucumber					
0	0	0.004, 0.002, 0.002, 0.003, 0.004	0.004	102	100
0	7	0.003, 0.004, 0.005		109	
3	104	0.008, 0.010, 0.010	0.009	103	264
6	209	0.014, 0.017, 0.020	0.017	101	482
12	383	0.021, 0.016, 0.021	0.019	91	556
24	784	0.026, 0.024, 0.025	0.025	98	714
Melon					
0	0	0.003, 0.005, 0.005, 0.005, 0.003	0.004	86	100
3	99	0.004, 0.003, 0.005	0.004	103	97
6	216	0.005, 0.005, 0.006	0.006	105	140
12	378	0.005, 0.003, 0.006	0.004	103	111
24	779	0.009, 0.008, 0.008	0.009	106	220
Orange					
0	0	0.024, 0.014, 0.015, 0.028, 0.029	0.022	92	100
3	116	0.022, 0.021, 0.028	0.024	94	109
6	223	0.020, 0.019, 0.019	0.019	108	86
12	404	0.016, 0.020, 0.018	0.018	100	82

Sampling interval (nominal months)	Sampling interval (actual days)	Uncorrected residue (mg/kg)	Mean uncorrected residue (mg/kg)	Mean procedural recovery (%)	Mean recovered uncorrected residue (%)
24	788	0.016, 0.017, 0.018	0.017	94	77
Carrot root					
0	0	0.033, 0.030, 0.030, 0.033, 0.030	0.031	80	100
3	97	0.048, 0.042, 0.043	0.044	104	143
6	216	0.050, 0.047, 0.047	0.048	95	154
12	405	0.059, 0.063, 0.061	0.061	102	196
24	781	0.084, 0.076, 0.081	0.080	99	259
Carrot top					
0	0	0.28, 0.24, 0.25, 0.26, 0.26	0.26	101	100
3	92	0.45, 0.41, 0.42	0.40	126	157
3*	104	0.37, 0.42, 0.36		102	
6	211	0.42, 0.38, 0.38	0.39	99	153
12	400	0.50, 0.49, 0.51	0.50	108	194
24	784	0.60, 0.70, 0.58	0.62	105	243
Barley straw					
0	0	1.2, 1.2, 1.2, 1.1, 1.2	1.2	105	100
3	104	1.3, 1.4, 1.3	1.3	98	111
6	209	1.4, 1.5, 1.4	1.4	103	121
12	406	1.6, 1.6, 1.7	1.6	104	138
24	790	1.9, 2.0, 2.0	2.0	102	166
27	840	1.3, 1.0, 2.0	1.4	117	119
Barley grain					
0	0	0.052, 0.053, 0.053, 0.056, 0.057	0.054	90	100
3	92	0.066, 0.075, 0.072	0.071	94	131
6	203	0.114, 0.124, 0.112	0.117	106	215
12	391	0.067, 0.069, 0.068	0.068	94	125
24	770	0.089, 0.093, 0.097	0.093	98	172
Soya bean					
0	0	0.024, 0.021, 0.022	0.028	87	100

Sampling interval (nominal months)	Sampling interval (actual days)	Uncorrected residue (mg/kg)	Mean uncorrected residue (mg/kg)	Mean procedural recovery (%)	Mean recovered uncorrected residue (%)
0	0	0.036, 0.032, 0.035, 0.031, 0.032		90	
3	91	0.022, 0.020, 0.015	0.019	105	68
6	202	0.026, 0.029, 0.028	0.027	110	98
12	390	0.018, 0.024, 0.020	0.021	91	74
24	770	0.016, 0.014, 0.015	0.015	93	53
27	810	0.022, 0.022, 0.029	0.024	109	88

*reanalysis to confirm results as batch recovery was high
Percentage recovered residue = residue concentration / initial residue concentration using uncorrected residues x 100.
Calculations performed on unrounded values.
No residues were present above the LOQ in control samples.

III. CONCLUSIONS

Residues of chlorothalonil were stable for at least 24 months in tomato, cucumber, melon (high water crop group), barley grain (high starch group), for at least 27 months in soya bean (high oil group) and for 12 months in barley straw when stored in the freezer at ≤-18°C.

There was no apparent degradation of R182281 in tomatoes, oranges or soya bean. Measured residues of R182281 increased in cucumber, melon, carrots (root and foliage) and barely (grain and straw), probably via transformation of chlorothalonil to R182281. However, some of the incurred residues were below the LOQ of the method (0.01 mg/kg) and therefore difficult to quantify with accuracy and precision.

The study demonstrated that field incurred residues of chlorothalonil and R182281 remained stable during freezer storage when prepared without the use of dry ice or acid.

(Anderson L and Chaggar S, 2007)

Report:	K-CA 6.1/02. Anderson L. (2007), Chlorothalonil (R44686) and R182281 (SDS3701): storage stability in various crops prepared in acid and stored deep frozen for up to two years. Syngenta, Jealott's Hill International Research Centre, Bracknell, United Kingdom. Syngenta Report Number T005407-04-REG. (Syngenta File No: R44686/4298).

Guidelines

Not stated but meets the requirements of Guideline: Commission of the European Communities: Storage Stability of Residue Samples (**SANCO 7032/V1/95 rev. 5 22/7/1997**).

GLP

The study was carried out according to the principles of Good Laboratory Practice.

EXECUTIVE SUMMARY

Samples of strawberry, onion, broccoli, cauliflower, cucumber, tomato, melon, grape, Brussels sprout, cabbage, French bean, pea, apple, potato, carrot root, leek, plum, sugar beet root, olive and banana that had been homogenised in the presence of acid were fortified at 1 mg/kg with chlorothalonil and R182281. Triplicate samples were stored under frozen conditions (≤-18°C) and analysed at intervals up to 24 months (five sampling points). The LOQ for both chlorothalonil and R182281 was 0.01 mg/kg.

There was no significant decrease (>30% compared to the zero time value) in the levels of chlorothalonil in any crops over 24 months when stored at ≤-18°C.

Residues of chlorothalonil were found to be stable in crops representing the high water (onion, broccoli, cauliflower, cucumber, melon, tomato, Brussels sprout, cabbage, French bean, pea, apple, leek, plum, sugar beet root and banana), high oil (olives), high starch (potato, carrot root) and high acid (strawberry, grapes) crop groups for at least 24 months when stored in the freezer at ≤-18°C.

Residues of R182281 were stable for at least 24 months in broccoli, cauliflower, cucumber, melon, tomato, Brussels sprout, cabbage, French bean, pea, apple, leek, plum, sugar beet root and banana (high water crop group), olive (high oil crop group), potato, carrot root (high starch crop group) and strawberry (high acid crop group) when stored in the freezer at ≤-18°C. Residues of R182281 were found to be stable in grapes (high acid) for up to 3 months and were stable for less than 3 months in onions (high water) when stored frozen at ≤-18°C.

The study demonstrated that residues of chlorothalonil and R182281 remained stable during freezer storage when prepared in the presence of acid.

I. MATERIALS AND METHODS

A. MATERIALS

A1. Test Materials

The purity of the analytical standards used in this study is listed in Table 6.1-6.

Table 6.1-6: Purity of analytical standards

Analyte	Standard reference no.	Purity (wt. %)
Chlorothalonil	AMS 237/2	99
R 182281 (SDS-3701)	ASJ10209-02	100

A2. Test Commodity

The test commodities were strawberry, onion, broccoli, cauliflower, cucumber, tomato, melon (whole fruit), grape, Brussels sprout, cabbage, French bean, pea, apple, potato, carrot root, leek, plum (fruit minus stone), sugar beet root, olive (fruit minus stone) and banana (whole fruit). Samples were purchased from a local supermarket with the exception of the sugar beet root samples which were from the Syngenta control sample collection.

A3. Test Facilities

This study was performed at Syngenta, Jealott's Hill International Research Centre, Bracknell, Berkshire, RG42 6EY, UK.

B. STUDY DESIGN AND METHODS

B1. Fortification and Storage of Samples

Samples were partially homogenised, then 1M sulphuric acid was added at a ratio of 10% v/w before homogenisation was continued. The homogenised samples were fortified at 1.0 mg/kg with chlorothalonil and R182281 in acetone. Triplicate samples were stored under frozen conditions (≤-18°C) and analysed at intervals up to 24 months (five sampling points). Control samples were analysed at zero time and at each time point to ensure that no residues of chlorothalonil or R182281 were present at levels above 30% of the LOQ.

B2. Analytical Method

Analysis of the samples was performed according to analytical methods SOP RAM 365/01 and SOP 365/02 at intervals of 0, 3, 6, 12 and 24 months. RAM 365/02 was issued to correct a typographical error in method RAM 365/01 therefore the methods can be considered identical. The method validation is reported in report number R44686/3394. A full method description and validation data are presented in document M-CA Section 4, CA 4.1.2.

Commodity	Author/s	Issue Year	Report Number
Crops	Hargreaves, S.L.	2003	R44686/3321
Crops	Atkinson, S.	2003	R44686/3365

The method involved extraction of the samples with acetone/5M sulphuric acid followed by centrifugation. An aliquot of the extract was taken, partitioned into toluene and then subjected to SPE clean up. Chlorothalonil and R182281 were determined by GC-MSD using three fragment ions (m/z > 100) for quantification. R182281 was derivatised with trimethylsilyl diazomethane to produce methyl R182281 (R619464). The LOQ was 0.01 mg/kg for both analytes.

II. RESULTS AND DISCUSSION

Method Validation

Procedural recoveries were determined using freshly fortified samples at each interval. Samples were fortified with chlorothalonil and R182281 at 1.0 mg/kg. Individual recoveries, mean recoveries and %RSD are summarised in Table 6.1-7 (chlorothalonil) and Table 6.1-8 (R182281).

Table 6.1-7: Summary of procedural recoveries for chlorothalonil in crops

Crop	Fortification level (mg/kg)	Recovery (%)	Mean recovery (%)	RSD (%)
Strawberry	1.0	114, 100, 100, 101, 100, 102, 100, 103, 102, 100	102	4.1
Onion	1.0	92, 96, 100, 109, 95, 92, 96, 95, 103, 106, 89, 95	97	6.1
Broccoli	1.0	89, 90, 93, 92, 101, 99, 101, 103, 85, 88	94	6.8
Cauliflower	1.0	83, 91, 91, 97, 106, 100, 99, 101, 94, 92	95	6.9

Crop	Fortification level (mg/kg)	Recovery (%)	Mean recovery (%)	RSD (%)
Cucumber	1.0	105, 113, 96, 98, 106, 105, 102, 101, 91, 92	101	6.8
Melon	1.0	81, 88, 89, 91, 103, 104, 105, 105, 100, 93	96	9.0
Tomato	1.0	106, 110, 79, 91, 108, 108, 98, 101, 85, 92	98	11.0
Grape	1.0	90, 83, 87, 87, 107, 106, 104, 105, 89, 91	95	9.9
Brussels sprout	1.0	91, 92, 82, 96, 105, 112, 101, 106, 107, 106, 95, 91	99	9.0
Cabbage	1.0	105, 104, 93, 96, 103, 105, 101, 104, 98, 98	101	4.2
Green bean	1.0	99, 103, 94, 99, 109, 103, 101, 103, 96, 105	101	4.4
Pea	1.0	93, 91, 91, 95, 102, 99, 106, 113, 85, 99, 88, 93	96	8.3
Apple	1.0	98, 97, 92, 93, 100, 102, 104, 102, 93, 93	98	4.6
Potato	1.0	114, 110, 115, 109, 96, 94, 108, 107, 86, 81	102	11.7
Carrot root	1.0	94, 98, 91, 95, 102, 102, 97, 99, 92, 87	96	5.2
Leek	1.0	88, 87, 99, 100, 92, 89, 103, 107, 97, 102	96	7.4
Plum	1.0	92, 92, 92, 91, 112, 112, 106, 101, 78, 88	96	11.4
Banana (whole fruit)	1.0	98, 91, 98, 108, 102, 104, 109, 106, 75, 86	98	5.5
Sugar beet root	1.0	95, 97, 89, 94, 101, 98, 94, 109, 101, 99	98	11.2
Olive	1.0	101, 95, 83, 87, 108, 105, 93, 96, 91, 93	95	8.2

Table 6.1-8: Summary of procedural recoveries for R182281 in crops

Crop	Fortification level (mg/kg)	Recovery (%)	Mean recovery (%)	RSD (%)
Strawberry	1.0	123, 112, 98, 101, 99, 100, 91, 91, 98, 100	101	9.5
Onion	1.0	117, 116, 102, 105, 102, 95, 105, 109, 91, 94, 108, 112	105	8.0
Broccoli	1.0	114, 110, 113, 109, 103, 95, 96, 96, 97, 102	104	7.3
Cauliflower	1.0	100, 110, 93, 108, 105, 109, 100, 101, 107, 102	104	5.1
Cucumber	1.0	104, 108, 102, 83, 105, 102, 94, 99, 108, 101	101	7.5
Melon	1.0	87, 90, 90, 94, 104, 102, 99, 100, 103, 100	97	6.3

Crop	Fortification level (mg/kg)	Recovery (%)	Mean recovery (%)	RSD (%)
Tomato	1.0	101, 121, 90, 85, 99, 95, 102, 101, 109, 105, 91, 94, 94, 88	98	9.6
Grape	1.0	97, 89, 91, 89, 100, 95, 95, 98, 104, 105	96	5.9
Brussels sprout	1.0	101, 104, 86, 97, 102, 97, 96, 96, 105, 108	99	6.5
Cabbage	1.0	111, 108, 95, 96, 108, 110, 96, 96, 99, 99	102	6.6
Green bean	1.0	101, 89, 104, 109, 114, 104, 97, 94, 77, 81	97	12.2
Pea	1.0	95, 95, 98, 102, 113, 103, 103, 103, 104, 107	102	5.2
Apple	1.0	107, 109, 79, 78, 99, 97, 96, 96, 89, 87	94	11.3
Potato	1.0	108, 102, 106, 97, 110, 102, 97, 94, 95, 82	99	8.3
Carrot root	1.0	102, 102, 92, 93, 106, 103, 99, 94, 93, 91	98	5.6
Leek	1.0	93, 91, 103, 101, 100, 94, 97, 99, 92, 90	96	4.8
Plum	1.0	80, 82, 90, 87, 107, 106, 91, 95, 80, 81, 104, 107	92	11.7
Banana (whole fruit)	1.0	88, 79, 106, 106, 109, 105, 95, 94, 74, 72	98	3.5
Sugar beet root	1.0	94, 99, 97, 97, 105, 100, 93, 96, 98, 97	93	15.3
Olive	1.0	98, 93, 109, 111, 112, 102, 97, 95, 91, 82	99	9.7

Storage Stability of Residues

The recoveries of chlorothalonil and R182281 in various crops stored at ≤ -18°C are summarised in Table 6.1-9 and Table 6.1-10, respectively. The results are not corrected for freshly fortified recoveries.

Table 6.1-9: Freezer storage stability for chlorothalonil at 1.0 mg/kg in crops

Sampling interval (nominal months)	Sampling interval (actual days)	Uncorrected residue (mg/kg)	Mean uncorrected residue (mg/kg)	Mean procedural recovery (%)	Mean recovered uncorrected residue (%)
Strawberry					
0	0	1.06, 0.97, 1.03	1.02	107	100
3	93	1.02, 1.00, 1.00	1.00	101	99
6	184	1.00, 0.96, 0.87	0.94	101	93
12	408	0.88, 0.99, 0.95	0.94	102	92
24	749	1.00, 0.96, 0.95	0.97	101	95
Onion					
0	0	0.92, 1.05, 0.94	0.97	94	100
3	92, 96	0.77, 0.78, 0.72, 0.78, 0.82, 0.70	0.76	99	78
6	187	0.86, 0.83, 0.82	0.84	95	86
12	408	0.94, 0.92, 0.91	0.92	104	95
24	749	0.87, 0.91, 0.90	0.89	92	92
Broccoli					
0	0	0.86, 0.86, 1.02	0.92	90	100
3	95	1.09, 1.01, 0.92	1.01	92	110
6	187	0.91, 0.89, 0.84	0.88	100	96
12	410	0.96, 0.96, 0.92	0.95	102	103
24	748	0.83, 0.80, 0.83	0.82	87	89
Cauliflower					
0	0	0.96, 0.79, 0.93	0.89	87	100
3	105	0.96, 0.90, 1.00	0.96	94	107
6	189	0.99, 1.17, 0.95	1.04	103	116
12	408	0.96, 0.94, 0.88	0.92	100	104
24	750	1.06, 1.02, 1.04	1.04	93	117
Cucumber					
0	0	0.99, 1.04, 1.03	1.02	109	100
3	104	0.86, 0.87, 0.94	0.89	97	87
6	188	1.03, 0.93, 0.98	0.98	105	96
12	406	0.93, 0.93, 0.89	0.92	102	90
24	750	0.94, 0.83, 0.78	0.85	91	84
Tomato					
0	0	0.92, 0.82, 1.02	0.92	108	100
3	98	0.84, 0.85, 0.82	0.84	85	91
6	118	0.94, 0.95, 1.01	0.97	108	105
12	410	0.94, 0.93, 0.83	0.90	100	98
24	747	0.90, 0.84, 0.86	0.87	88	94

Sampling interval (nominal months)	Sampling interval (actual days)	Uncorrected residue (mg/kg)	Mean uncorrected residue (mg/kg)	Mean procedural recovery (%)	Mean recovered uncorrected residue (%)
Melon					
0	0	0.91, 0.84, 092	0.89	84	100
3	102	0.88, 0.91, 0.82	0.87	90	98
6	187	0.97, 1.03, 0.97	0.99	104	111
12	405	0.94, 0.98, 0.96	0.96	105	108
24	748	0.94, 0.89, 1.02	0.95	97	107
Grape					
0	0	0.84, 0.89, 0.87	0.87	87	100
3	101	0.87, 0.88, 0.85	0.87	87	100
6	185	1.08, 1.01, 1.04	1.04	107	121
12	402	1.05, 1.03, 1.01	1.03	104	119
24	745	0.87, 0.89, 0.82	0.86	90	99
Brussels sprout					
0	0	0.85, 0.83, 0.89	0.86	91	100
3	103	0.88, 0.81, 0.82, 0.92, 1.04, 1.02	0.92	99	106
6	187	0.97, 1.01, 0.93	0.97	104	114
12	405	0.94, 0.83, 0.83	0.87	107	101
24	744	0.84, 0.80, 0.85	0.83	93	97
Head cabbage					
0	0	1.00, 0.92, 1.00	0.97	105	100
3	101	0.91, 0.85, 0.87	0.88	94	90
6	185	0.89, 0.91, 0.87	0.89	104	92
12	405	0.91, 0.95, 0.91	0.92	102	95
24	745	0.94, 0.92, 0.91	0.92	98	95
French bean					
0	0	1.01, 1.08, 0.97	1.02	101	100
3	103	0.99, 0.95, 0.96	0.97	96	95
6	187	0.93, 1.10, 1.07	1.04	106	102
12	405	1.05, 1.04, 1.10	1.06	102	104
24	746	1.01, 1.03, 0.97	1.00	101	99
Pea					
0	0	0.91, 0.90, 0.83	0.88	92	100
3	102	0.89, 0.91, 0.86	0.89	93	101
6	187	0.96, 0.85, 1.00	0.93	101	106
12	405	0.95, 0.98, 0.94	0.95	110	109
24	746, 759	0.85, 0.86, 0.89, 0.88, 0.82	0.86	92	98

Sampling interval (nominal months)	Sampling interval (actual days)	Uncorrected residue (mg/kg)	Mean uncorrected residue (mg/kg)	Mean procedural recovery (%)	Mean recovered uncorrected residue (%)
Apple					
0	0	0.89, 0.90, 0.86	0.88	101	100
3	100	0.91, 0.93, 0.96	0.93	93	106
6	185	1.06, 0.97, 1.10	1.05	101	119
12	403	0.89, 0.91, 1.00	0.93	103	106
24	735	1.02, 0.93, 0.92	0.96	93	109
Potato					
0	0	1.07, 1.04, 1.10	1.07	112	100
3	86	1.08, 1.14, 1.16	1.13	112	105
6	169	0.93, 0.93, 0.93	0.93	95	87
12	387	1.05, 1.08, 1.04	1.06	107	99
24	730	0.96, 0.94, 0.89	0.93	83	87
Carrot root					
0	0	0.94, 0.91, 0.90	0.92	96	100
3	99	0.96, 0.94, 0.96	0.95	93	104
6	183	1.05, 1.03, 1.04	1.04	102	114
12	401	1.01, 1.02, 0.96	1.00	98	109
24	740	0.92, 0.96, 1.00	0.96	89	105
Leek					
0	0	0.84, 0.83, 0.82	0.83	87	100
3	99	0.96, 0.89, 0.91	0.92	99	111
6	186	0.96, 0.88, 0.87	0.90	90	109
12	404	0.96, 0.97, 0.96	0.96	105	116
24	741	1.17, 1.08, 1.00	1.08	100	130
Plum					
0	0	0.92, 0.97, 0.91	0.93	92	100
3	98	0.90, 0.97, 0.95	0.94	91	101
6	181	1.13, 1.09, 1.05	1.09	112	117
12	400	0.99, 0.97, 0.97	0.98	103	105
24	737	0.94, 0.90, 0.90	0.91	83	98
Sugar beet root					
0	0	0.95, 0.97, 0.87	0.93	96	100
3	91	0.99, 0.91, 0.91	0.94	92	101
6	174	0.99, 0.97, 1.09	1.02	99	109
12	393	1.04, 1.01, 1.04	1.03	102	111
24	730	0.86, 1.08, 1.12	1.02	100	110

Sampling interval (nominal months)	Sampling interval (actual days)	Uncorrected residue (mg/kg)	Mean uncorrected residue (mg/kg)	Mean procedural recovery (%)	Mean recovered uncorrected residue (%)
Olive					
0	0	0.98, 0.96, 0.96	0.97	98	100
3	91	0.88, 0.89, 0.88	0.88	85	91
6	175	1.08, 1.19, 1.18	1.15	107	119
12	393	0.95, 0.97, 0.95	0.96	95	99
24	733	0.82, 0.86, 0.92	0.87	92	90
Banana (whole fruit)					
0	0	0.94, 0.93, 0.86	0.91	95	100
3	91	1.03, 1.07, 1.03	1.04	103	114
6	175	1.08, 1.07, 1.06	1.07	103	117
12	393	0.99, 1.03, 1.04	1.02	108	112
24	730	0.93, 0.84, 0.86	0.88	80	96

Percentage recovered residue = residue concentration / initial residue concentration using uncorrected residues x 100.
Calculations performed on unrounded values.
No residues were present above the LOQ in control samples.

Table 6.1-10: Freezer storage stability for R182281 at 1.0 mg/kg in crops

Sampling interval (nominal months)	Sampling interval (actual days)	Uncorrected residue (mg/kg)	Mean uncorrected residue (mg/kg)	Mean procedural recovery (%)	Mean recovered uncorrected residue (%)
Strawberry					
0	0	1.15, 1.08, 1.08	1.10	117	100
3	93	0.85, 0.85, 0.84	0.85	100	77
6	184	0.80, 0.75, 0.72	0.76	99	69
12	408	0.70, 0.78, 0.76	0.75	91	68
24	479	0.80, 0.78, 0.76	0.78	99	71
Onion					
0	0	1.11, 1.14, 1.18	1.14	117	100
3	92, 96	0.66, 0.61, 0.60, 0.60, 0.59, 0.60	0.61	102	54
6	187	0.58, 0.53, 0.61	0.58	107	50
12	408	0.42, 0.47, 0.44	0.44	92	39
24	749	0.76, 0.60, 0.68	0.68	110	59
Broccoli					
0	0	1.16, 1.08, 1.17	1.14	112	100
3	95	0.98, 1.03, 1.02	1.01	111	89
6	187	0.89, 0.96, 0.96	0.94	99	82
12	410	0.86, 0.87, 0.90	0.88	96	77
24	748	0.97, 1.00, 0.86	0.94	100	83
Cauliflower					
0	0	1.02, 0.96, 0.92	0.97	105	100
3	105	0.88, 0.86, 0.91	0.88	101	91
6	189	0.80, 0.85, 0.81	0.82	107	85
12	408	0.85, 0.87, 0.98	0.90	101	93
24	750	0.98, 1.14, 1.12	1.08	105	112
Cucumber					
0	0	1.01, 1.02, 0.94	0.99	106	100
3	104	0.83, 0.87, 0.91	0.87	92	88
6	188	0.91, 0.81, 0.88	0.87	103	88
12	406	0.79, 0.77, 0.75	0.77	96	78
24	750	0.93, 0.93, 0.88	0.92	105	92
Tomato					
0	0	1.00, 0.90, 1.12	1.00	111	100
3	98	0.74, 0.76, 0.72, 0.83, 0.81, 0.77	0.77	93	77
3	108	0.96, 0.93, 0.93	0.94	102	94
6	188	0.84, 0.83, 0.87	0.84	107	84
12	410	0.79, 0.73, 0.68	0.73	92	73
24	747	0.78, 0.77, 0.82	0.79	91	78

Sampling interval (nominal months)	Sampling interval (actual days)	Uncorrected residue (mg/kg)	Mean uncorrected residue (mg/kg)	Mean procedural recovery (%)	Mean recovered uncorrected residue (%)
Melon					
0	0	0.92, 0.85, 0.94	0.90	89	100
3	102	0.84, 0.89, 0.79	0.84	92	93
6	187	0.85, 0.88, 0.86	0.86	103	96
12	405	0.78, 0.81, 0.79	0.79	100	88
24	748	0.88, 0.82 ,0.87	0.85	101	95
Grape					
0	0	0.92, 0.94, 0.92	0.93	93	100
3	101	0.71, 0.72, 0.67	0.70	90	75
6	185	0.64, 0.59, 0.63	0.62	98	67
12	402	0.55, 0.43, 0.43	0.47	96	51
24	745	0.48, 0.67, 0.59	0.58	104	62
Brussels sprout					
0	0	0.96, 1.01, 0.97	0.98	103	100
3	103	0.94, 0.87, 0.96	0.92	91	94
6	187	0.99, 1.00, 0.95	0.98	99	100
12	405	0.94, 0.90, 0.94	0.93	96	95
24	744	1.16, 1.10, 1.08	1.11	103	113
Head cabbage					
0	0	1.01, 1.08, 1.04	1.04	110	100
3	101	0.90, 0.93, 0.94	0.92	95	88
6	185	0.95, 0.97, 0.96	0.96	109	92
12	405	0.85, 0.86, 0.86	0.86	96	83
24	745	0.93, 0.94, 0.94	0.94	99	90
French bean					
0	0	0.95, 1.00, 0.97	0.98	95	100
3	103	1.00, 1.02, 0.95	0.99	107	102
6	187	0.91, 1.02, 1.00	0.98	109	100
12	405	0.90, 0.97, 0.92	0.93	96	95
24	746	0.86, 0.74, 0.88	0.83	79	85
Pea					
0	0	0.95, 0.91, 0.83	0.90	95	100
3	102	0.99, 1.07, 1.03	1.03	100	115
6	187	0.99, 0.82, 0.99	0.93	108	104
12	405	0.94, 0.95, 0.95	0.94	103	105
24	746	1.14, 1.18, 1.10	1.14	105	127

Sampling interval (nominal months)	Sampling interval (actual days)	Uncorrected residue (mg/kg)	Mean uncorrected residue (mg/kg)	Mean procedural recovery (%)	Mean recovered uncorrected residue (%)
Apple					
0	0	0.98, 0.90, 0.92	0.93	98	100
3	100	0.73, 0.70, 0.73	0.72	78	77
6	185	0.83, 0.79, 0.81	0.81	98	87
12	403	0.69, 0.71, 0.76	0.72	96	77
24	735	0.77, 0.73, 0.76	0.75	88	81
Potato					
0	0	1.02, 0.97, 1.05	1.01	105	100
3	86	0.97, 0.90, 1.00	0.96	101	94
6	169	0.96, 0.95, 1.00	0.97	106	96
12	387	0.84, 0.89, 0.86	0.87	95	85
24	730	0.94, 0.91, 0.91	0.92	88	91
Carrot root					
0	0	1.01, 0.98, 0.97	1.02	102	100
3	99	0.94, 0.93, 0.88	0.92	93	90
6	183	0.98, 0.91, 0.99	0.96	104	94
12	401	0.91, 0.94, 0.90	0.91	97	90
24	740	0.91, 0.94, 0.98	0.94	92	93
Leek					
0	0	0.89, 0.94, 0.90	0.91	92	100
3	99	0.80, 0.69, 0.74	0.74	102	82
6	186	0.70, 0.68, 0.66	0.68	97	75
12	404	0.68, 0.68, 0.68	0.68	98	75
24	741	0.64, 0.68, 0.65	0.66	91	73
Plum					
0	0	0.83, 0.82, 0.82	0.82	81	100
3	98	0.81, 0.83, 0.77	0.80	89	97
6	181	0.84, 0.85, 0.84	0.84	106	102
12	400	0.71, 0.68, 0.70	0.70	93	85
24	737, 745	0.67, 0.63, 0.43, 0.77, 0.74, 0.79	0.67	93	79
Sugar beet root					
0	0	0.99, 1.04, 0.93	0.99	96	100
3	91	0.95, 0.85, 0.91	0.92	97	93
6	174	0.89, 0.90, 0.97	0.92	103	93
12	393	0.89, 0.87, 0.88	0.88	94	89
24	730	0.85, 0.92, 0.93	0.90	97	91

Sampling interval (nominal months)	Sampling interval (actual days)	Uncorrected residue (mg/kg)	Mean uncorrected residue (mg/kg)	Mean procedural recovery (%)	Mean recovered uncorrected residue (%)
Olive					
0	0	0.97, 0.93, 0.99	0.96	95	100
3	91	1.10, 1.14, 1.14	1.13	110	117
6	175	0.92, 0.96, 0.95	0.94	107	98
12	393	0.93, 0.94, 0.93	0.93	96	97
24	733	0.96, 0.94, 0.97	0.96	87	100
Banana (whole fruit)					
0	0	0.76, 0.77, 0.72	0.75	83	100
3	91	0.95, 1.00, 0.95	0.97	106	129
6	175	0.95, 0.95, 0.92	0.94	107	125
12	393	0.77, 0.82, 0.81	0.80	95	107
24	730	0.70, 0.64, 0.64	0.66	73	88

Percentage recovered residue = residue concentration / initial residue concentration using uncorrected residues x 100.
Calculations performed on unrounded values.
No residues were present above the LOQ in control samples.

III. CONCLUSIONS

Residues of chlorothalonil were stable for at least 24 months in onion, broccoli, cauliflower, cucumber, melon, tomato, Brussels sprout, cabbage, French bean, pea, apple, leek, plum, sugar beet root and banana (high water crop group), olive (high oil crop group), potato, carrot root (high starch crop group) strawberry and grape (high acid crop group) when stored in the freezer at ≤-18°C.

Residues of R182281 were stable for at least 24 months in broccoli, cauliflower, cucumber, melon, tomato, Brussels sprout, cabbage, French bean, pea, apple, leek, plum, sugar beet root and banana (high water crop group), olive (high oil crop group), potato, carrot root (high starch crop group) and strawberry (high acid crop group) when stored in the freezer at ≤-18°C. Residues of R182281 were found to stable in grapes (high acid) for up to 3 months and were stable for less than 3 months in onions (high water) when stored frozen at ≤-18°C.

The study demonstrated that residues of chlorothalonil and R182281 remained stable during freezer storage when prepared in the presence of acid.

(Anderson L, 2007)

Report:	K-CA 6.1/03. Brown D., (2014), Chlorothalonil - Storage stability of residues of chlorothalonil and R182281 in cereal straw for up to 12 months. Eurofins Agroscience Service Chem Ltd, Derbyshire, United Kingdom. Report Number S12-01844. Syngenta File No: R044686_11076.

Guidelines

OECD Guideline for Testing of Chemicals No. 506, Stability of Pesticide Residues in Stored Commodities, adopted 16 October 2007

EPA Residue Chemistry Test Guidelines, OPPTS 860.1380, Storage Stability Data, August 1996

Commission of the European Communities: Storage Stability of Residue Samples (**SANCO 7032/V1/95 rev. 5 22/7/1997**).

GLP

The study was carried out according to the principles of Good Laboratory Practice.

EXECUTIVE SUMMARY

Samples of cereal straw were fortified at 0.5 mg/kg with chlorothalonil or R182281. Triplicate samples were stored under frozen conditions (≤-18°C) and analysed at intervals up to 12 months (five sampling points). The LOQ for both chlorothalonil and R182281 was 0.01 mg/kg.

There was no significant decrease (>30% compared to the zero time value) in the levels of chlorothalonil in cereal straw over 9 months and no significant decrease in the observed residue levels of R182281 in cereal straw over 12 months when stored at ≤-18°C.

Residues of chlorothalonil in cereal straw were stable for 9 months and residues of R182281 in cereal straw were stable for at least 12 months when stored deep frozen at -18°C.

I. MATERIALS AND METHODS

A. MATERIALS

A1. Test Materials

The purity of the analytical standards used in this study is listed in Table 6.1-11.

Table 6.1-11: Purity of analytical standards

Analyte	Standard reference no.	Purity (wt. %)
Chlorothalonil	638406	99.6
R 182281	P2	98.7

A2. Test Commodity

The test commodity was untreated homogenised cereal straw taken from other studies conducted by the test facility.

A3. Test Facilities

This study was performed at Eurofins Agroscience Services Chem Ltd, Slade Lane, Wilson, Melbourne, Derbyshire, DE73 8AG, UK

B. STUDY DESIGN AND METHODS

B1. Fortification and Storage of Samples

Homogenised samples were fortified at 0.5 mg/kg with either chlorothalonil in acidified toluene or R182281 in acidified acetone. Triplicate samples were stored under frozen conditions (≤-18°C) and analysed at intervals up to 12 months (five sampling points). Control samples were analysed at zero time

and at each time point to ensure that no residues of chlorothalonil or R182281 were present at levels above 30% of the LOQ.

B2. Analytical Method

Analysis of the samples was performed according to analytical method GRM005.01.A at intervals of 0, 1, 3, 6, 9 and 12 months. The method validation is reported in report number R44686 /4046. A full method description and validation data are presented in document M-CA Section 4, CA 4.1.2.

Commodity	Author/s	Issue Year	Report Number
Crops	Chaggar, S.	2006	R44686 /4047
Crops	Chaggar, S.	2006	R44686/4046

The method involved extraction of the samples with acetone/5M sulphuric acid followed by centrifugation. For chlorothalonil determination, aliquots are taken and diluted with water followed by SPE clean up using a C8 cartridge. Chlorothalonil residues were eluted from the SPE cartridges using toluene. The final volume of the extracts was adjusted to 4 mL using acidified toluene. Chlorothalonil is analysed by GC-MSD.

For the determination of R182281, aliquots of the extracts are taken and diluted with acetonitrile: water (50/50, v/v) to a volume of 10 ml. Final determination of R182281 is by LC-MS/MS. The LOQ was 0.01 mg/kg for both analytes.

II. RESULTS AND DISCUSSION

Method Validation

Procedural recoveries were determined using freshly fortified samples at each interval. Samples were fortified with chlorothalonil or R182281 at 0.5 mg/kg. Individual recoveries, mean recoveries and %RSD are summarised in Table 6.1-12 (chlorothalonil) and Table 6.1-13 (R182281).

Table 6.1-12: Summary of procedural recoveries for chlorothalonil in cereal straw

Recovery at zero time (%)	Recovery at 1 month (%)	Recovery at 3 months (%)	Recovery at 6 months (%)	Recovery at 9 months (%)	Recovery at 12 months (%)	Mean recovery (%)	RSD (%)
94, 95	100, 104	94, 99	97, 94	90, 94	91, 87	95	5

Table 6.1-13: Summary of procedural recoveries for R182281 in cereal straw

Recovery at zero time (%)	Recovery at 1 month (%)	Recovery at 3 months (%)	Recovery at 6 months (%)	Recovery at 9 months (%)	Recovery at 12 months (%)	Mean recovery (%)	RSD (%)
100, 101	103, 103	102, 101	95, 101	99, 102	95, 91	99	4

Storage Stability of Residues

The recoveries of chlorothalonil and R182281 in cereal straw stored at ≤ -18°C are summarised in Table 6.1-14 and Table 6.1-15, respectively. The results are not corrected for freshly fortified recoveries.

Table 6.1-14: Freezer storage stability for chlorothalonil at 0.5 mg/kg in cereal straw

Sampling interval (nominal months)	Sampling interval (actual days)	Uncorrected residue (mg/kg)	Mean uncorrected residue (mg/kg)	Mean procedural recovery (%)	Mean recovered uncorrected residue (%)
0	0	0.49, 0.49, 0.49	0.49	95	100
1	29	0.48, 0.48, 0.48	0.48	102	98
3	91	0.42, 0.43, 0.43	0.43	97	87
6	182	0.38, 0.38, 0.37	0.38	96	77
9	274	0.35, 0.34, 0.35	0.35	92	74
12	367	0.31, 0.30, 0.31	0.31	89	63

Percentage recovered residue = residue concentration / initial residue concentration using uncorrected residues x 100.
Calculations performed on unrounded values.
No residues were present above the LOQ in control samples.

Table 6.1-15: Freezer storage stability for R182281 at 0.5 mg/kg in cereal straw

Sampling interval (nominal months)	Sampling interval (actual days)	Uncorrected residue (mg/kg)	Mean uncorrected residue (mg/kg)	Mean procedural recovery (%)	Mean recovered uncorrected residue (%)
0	0	0.51, 0.50, 0.52	0.51	100	100
1	29	0.50, 0.51, 0.51	0.51	103	100
3	91	0.50, 0.50, 0.50	0.50	102	98
6	182	0.49, 0.49, 0.47	0.48	98	95
9	274	0.49, 0.50, 0.52	0.51	100	99
12	367	0.50, 0.47, 0.41	0.46	93	91

Percentage recovered residue = residue concentration / initial residue concentration using uncorrected residues x 100.
Calculations performed on unrounded values.
Residue in control sample for 9 month time point was 31% of the LOQ.

Due to the steady decline of chlorothalonil residues overtime, additional analysis was undertaken at 9 months and 12 months. The sample sets fortified with chlorothalonil were also analysed for R182281 to assess whether the decline of chlorothalonil was due to conversion to R182281.

A total chlorothalonil residue was calculated as the sum of chlorothalonil (from Table 6.1-14) and R182281. The residue equivalent to chlorothalonil was calculated using a conversion factor based on the molecular weight of chlorothalonil and metabolite R182281 (265.9/247.5=1.0743). The results are presented in Table 6.1-16.

Table 6.1-16: Reanalysis of samples fortified with chlorothalonil at 0.5 mg/kg in cereal straw for R182281

Sampling interval (nominal months)	Sampling interval (actual days)	Uncorrected residue as R182281 (mg/kg)	Uncorrected residue as chlorothalonil equivalents (mg/kg)	Chlorothalonil residue from Table 6.1-14 (mg/kg)	Total chlorothalonil residues (mg/kg)	Mean recovered uncorrected residue (%)
9	274	0.013, 0.015, 0.013	0.014, 0.016, 0.014	0.35, 0.34, 0.35	0.36, 0.36, 0.36	73
12	367	0.017, 0.013, 0.016	0.018, 0.014, 0.017	0.31, 0.30, 0.31	0.33, 0.31, 0.33	67

III. CONCLUSIONS

There was no significant decrease (>30% as compared to the zero-time value) in the residue levels of chlorothalonil after deep frozen storage for 9 months however a significant decrease (>30%) was observed at the 12 month time point. Some of the reduction in levels of chlorothalonil may have been due to degradation to R182281.

No significant decrease (>30% as compared to the zero-time value) was observed in the residue values of R182281 in cereal straw after deep frozen storage for 12 months.

(Brown D, 2014)

~~**Report:**~~	~~K-CA 6.1/04. Watson G. (2014), Chlorothalonil - Storage stability of residues of R611965 in crop matrices stored frozen for up to two years, interim report for 12 months storage. Eurofins Agroscience Service Chem Ltd, Derbyshire, United Kingdom. Report Number S12-04611. Syngenta File No: R611965_10004.~~

Report:	K-CA 6.1/04. Gasso-Brown D (2015), Chlorothalonil - Storage stability of residues of R611965 in crop matrices stored frozen for up 30 months. Eurofins Agroscience Service Chem Ltd, Derbyshire, United Kingdom. Report Number S12-04611. Syngenta File No: R611965_10041

Guidelines

OECD Guideline for Testing of Chemicals No. 506, Stability of Pesticide Residues in Stored Commodities, adopted 16 October 2007

EPA Residue Chemistry Test Guidelines, OPPTS 860.1380, Storage Stability Data, August 1996

Commission of the European Communities: Storage Stability of Residue Samples (**SANCO 7032/V1/95 rev. 5 22/7/1997**).

GLP

The study was carried out according to the principles of Good Laboratory Practice.

EXECUTIVE SUMMARY

Samples of wheat grain, tomato, lentil, orange and soy bean were fortified at 0.5 mg/kg with R611965. Duplicate samples were stored under frozen conditions (≤-18°C) and analysed at intervals up to 12 months (five sampling points). The LOQ for R611965 was 0.01 mg/kg.

There was no significant decrease (>30% compared to the zero time value) in the levels of R611965 in the crops tested over 12 months when stored at ≤-18°C. Degradation of more than 30% of R611965 from the zero time point was observed in the 3, 9 and 12 month time-points for soya bean and the 24 month time point for oranges, although the recoveries for later time points are within the accepted range demonstrating that residues are stable over the 30 month period.

Residues of R611965 were found to be stable in crops representing the high water (tomato), high acid (orange), high starch (wheat grain), high protein (lentil) and high oil (soya bean seed) crop groups for at least ~~12~~ 30 months when stored in the freezer at ≤-18°C.

Stock standards of R611965 in methanol and calibration standards of R611965 in methanol / ultra-pure water (50/50, v/v) were stable for a period of approximately 6.5 months storage when stored in the dark in a refrigerator.

I. MATERIALS AND METHODS

A. MATERIALS

A1. Test Materials

The purity of the analytical standard used in this study is listed in Table 6.1-17.

Table 6.1-17: Purity of analytical standards

Analyte	Standard reference no.	Purity (wt. %)
R 611965	MES 134/1	96

A2. Test Commodity

The test commodities were untreated homogenised wheat grain and soya beans taken from other studies conducted by the test facility, and organic oranges, tomatoes and lentils purchased from a local supermarket.

A3. Test Facilities

This study was performed at Eurofins Agroscience Services Chem Ltd, Slade Lane, Wilson, Melbourne, Derbyshire, DE73 8AG, UK

B. STUDY DESIGN AND METHODS

B1. Fortification and Storage of Samples

Homogenised samples were fortified at 0.5 mg/kg with R611965 in methanol. Duplicate samples were stored under frozen conditions (≤-18°C) and analysed at intervals up to 12 months (five sampling points). Control samples were analysed at zero time and at all other time points to ensure that no residues of R611965 were present at levels above 30% of the LOQ.

B2. Analytical Method

Analysis of the samples was performed according to analytical method GRM005.06.A at intervals of 0, 1, 3, 6, 9, 12, 18 and 30 months. The method validation is reported in report number R611965_50001. A full method description and validation data are presented in document M-CA Section 4, CA 4.1.2.

Commodity	Author/s	Issue Year	Report Number
Crops	McDonald, T.J.	2012	R611965/50000
Crops	McDonald, T.J.	2012	R611965/50001

The method involved extraction of the samples with acetone/5M sulphuric acid followed by centrifugation. An aliquot of the extract was taken, evaporated and reconstituted in methyl tert-butyl ether (MTBE). A liquid-liquid partition was performed three times and the organic layer transferred to a concentration tube. Extracts were concentrated and reconstituted in water: methanol 50:50 (v/v). Final determination was by LC-MS/MS, monitoring for the primary transition (m/z 268→224) and the confirmatory transition (m/z 266→222). The LOQ was 0.01 mg/kg.

II. RESULTS AND DISCUSSION

Method Validation

Procedural recoveries were determined using freshly fortified samples at each interval. Samples were fortified with R611965 at 0.5 mg/kg. Individual recoveries, mean recoveries and %RSD are summarised in Table 6.1-18.

In order to assess the stability of standard solutions of R611965, the instrument response of stored stock and calibration solutions were compared to those of freshly prepared standards. After 6.5 months refrigerated storage the difference in response was < 10% therefore the standard solutions were shown to be stable for approximately 6.5 months.

Table 6.1-18: Summary of procedural recoveries for R611965 in crops

~~Recovery at zero time (%)~~	~~Recovery at 1 month (%)~~	~~Recovery at 3 months (%)~~	~~Recovery at 6 months (%)~~	~~Recovery at 9 months (%)~~	~~Recovery at 12 months (%)~~	~~Mean recovery (%)~~	~~RSD (%)~~
~~**Wheat grain**~~							
~~99, 108~~	~~93, 92~~	~~117, 103~~	~~105, 104~~	~~-~~	~~92, 98~~	~~101~~	~~8~~
~~**Tomato**~~							
~~99, 107~~	~~97, 94~~	~~99, 96~~	~~107, 95~~	~~-~~	~~104, 107~~	~~101~~	~~5~~
~~**Lentil**~~							
~~102, 103~~	~~94, 91~~	~~108, 110~~	~~111, 105~~	~~-~~	~~99, 105~~	~~103~~	~~6~~
~~**Orange**~~							
~~107, 107~~	~~89, 95~~	~~100, 100~~	~~109, 111~~	~~-~~	~~107, 104~~	~~103~~	~~6~~
~~**Soya bean**~~							
~~104, 104~~	~~88, 90~~	~~108, 99~~	~~98, 96~~	~~102, 102~~	~~99, 96~~	~~99~~	~~6~~

Recovery at zero time (%)	Recovery at 1 month (%)	Recovery at 3 months (%)	Recovery at 6 months (%)	Recovery at 9 months (%)	Recovery at 12 months (%)	Recovery at 18 months (%)	Recovery at 24 months (%)	Recovery at 30 months (%)	Mean recovery (%)	RSD (%)
Wheat grain										
99, 108	93, 92	117, 103	105, 104	-	92, 98	105, 104	106, 108	88, 90	101	8.0
Tomato										
99, 107	97, 94	99, 96	107, 95	-	104, 107	90, 92	103, 101	88, 94	98	6.1
Lentil										
102, 103	94, 91	108, 110	111, 105	-	99, 105	101, 102	108, 109	86, 89	101	7.7
Orange										
107, 107	89, 95	100, 100	109, 111	-	107, 104	101, 99	100, 96	85, 90	100	7.5
Soya bean										
104, 104	88, 90	108, 99	98, 96	102, 102	99, 96	104, 103	60, 59	93, 93	94	15

Storage Stability of Residues

The recoveries of R611965 in various crops stored at ≤ -18°C are summarised in Table 6.1-19 below. The results are not corrected for freshly fortified recoveries.

Table 6.1-19: Freezer storage stability for R611965 at 0.5 mg/kg in crops

Sampling interval (nominal months)	Sampling interval (actual days)	Uncorrected residue (mg/kg)	Mean uncorrected residue (mg/kg)	Mean procedural recovery (%)	Mean recovered uncorrected residue (%)
Wheat grain					
0	0	0.52, 0.50, 0.52	0.51	103	100
1	31	0.40, 0.41	0.40	92	79
3	91	0.46, 0.50	0.48	110	93
6	182	0.40, 0.42	0.41	104	80
12	365	0.42, 0.45	0.43	95	84
18	547	0.41,0.41	0.41	104	79
24	734	0.48,0.47	0.48	107	93
30	915	0.47,0.44	0.45	89	88
Tomato					
0	0	0.52, 0.50, 0.54	0.52	103	100
1	31	0.47, 0.46	0.47	96	89
3	91	0.50, 0.48	0.49	98	94
6	181	0.56, 0.54	0.55	101	106
12	367	0.52, 0.55	0.53	105	102
18	546	0.49,0.49	0.47	91	91
24	733	0.49, 0.50	0.50	102	95
30	916	0.49, 0.48	0.48	91	93
Lentil					
0	0	0.52. 0.53. 0.54	0.53	103	100
1	31	0.47. 0.42	0.44	93	84
3	91	0.47. 0.45	0.46	109	86
6	182	0.45. 0.49	0.47	105	88
12	365	0.50. 0.50	0.50	102	94
18	547	0.42, 0.43	0.43	102	80
24	734	0.48, 0.51	0.49	109	93
30	917	0.49, 0.47	0.48	87	91
Orange					
0	0	0.50, 0.54, 0.52	0.52	107	100
1	31	0.45, 0.46	0.45	92	87
3	94	0.49, 0.46	0.47	100	91
6	181	0.51, 0.55	0.53	110	102
12	367	0.52, 0.50	0.51	106	98
18	546	0.50, 0.49	0.50	100	95
24	733	0.33, 0.30	0.31	98	60†
30	916	0.47, 0.45	0.46	87	89
Soya bean					
0	0	0.53, 0.54, 0.52	0.53	104	100
1	31	0.39, 0.41	0.40	89	75
3	94	0.32, 0.34	0.33	104	62

Sampling interval (nominal months)	Sampling interval (actual days)	Uncorrected residue (mg/kg)	Mean uncorrected residue (mg/kg)	Mean procedural recovery (%)	Mean recovered uncorrected residue (%)
6	186	0.37, 0.38	0.38	97	71
9	276	0.34, 0.39	0.36	102	68
12	367	0.45, 0.42	0.44	97	82
18	546	0.34, 0.35	0.34	103	65†
30	916	0.41, 0.39	0.40	93	75

Percentage recovered residue = residue concentration / initial residue concentration using uncorrected residues x 100.
Calculations performed on unrounded values.
No residues were present above the LOQ in control samples.
†Degradation of more than 30% of R611965 from the zero time point, however results for later time points are within the accepted range implying residues are stable over the 30 month period.

III. CONCLUSIONS

There was no significant decrease (>30% as compared to the zero-time value) in the observed residue levels of R611965 after deep frozen storage for 12 months. Degradation of more than 30% of R611965 from the zero time point was observed in the 3 and 9 month time-points for soya bean, although the recoveries for later time points are within the accepted range demonstrating that residues are stable over the ~~12~~ 30 month period.

(Watson G, 2014)

Report:	K-CA 6.1/05. Krainz A. (2007), Chlorothalonil: Frozen storage stability in wheat (grain and straw). RCC Ltd, Switzerland. Report Number A71256. Syngenta File No: R044686_11197.

Guidelines

Commission of the European Communities: Storage Stability of Residue Samples (**SANCO 7032/V1/95 rev. 5 22/7/1997**).

GLP

The study was carried out according to the principles of Good Laboratory Practice.

EXECUTIVE SUMMARY

Samples of wheat grain and straw were fortified at 0.2 mg/kg with chlorothalonil. Triplicate samples were stored under frozen conditions (-20°C) and analysed at intervals up to 3 months (three sampling points). The LOQ for chlorothalonil was 0.01 mg/kg.

Residues of chlorothalonil were stable in wheat grain and straw for at least 3 months when stored in the freezer at -20°C.

I. MATERIALS AND METHODS

A. MATERIALS

A1. Test Materials

The purity of the analytical standard used in this study is listed in Table 6.1-20.

Table 6.1-20: Purity of analytical standards

Analyte	Standard reference no.	Purity (wt. %)
Chlorothalonil	337-98B	98

A2. Test Commodity

The test commodities were untreated homogenised wheat grain and straw taken from other studies conducted by the test facility.

A3. Test Facilities

This study was performed at RCC Ltd, Analytics, Zelgliweg 1, CH-4452 Itingen, Switzerland.

B. STUDY DESIGN AND METHODS

B1. Fortification and Storage of Samples

Homogenised samples were fortified at 0.2 mg/kg with chlorothalonil in toluene. Triplicate samples were stored under frozen conditions (-20°C) and analysed at intervals up to 3 months (three sampling points). Control samples were analysed at zero time and at all other time points to ensure that no residues of chlorothalonil were present at levels above 30% of the LOQ.

B2. Analytical Method

Analysis of the samples was performed according to analytical method A75813 at intervals of 0, 1, and 3 months. The method validation is reported in report number A75813 and A71188. A full method description and validation data are presented in document M-CA Section 4, CA 4.1.2.

Commodity	Author/s	Issue Year	Report Number
Tomato	Krainz, A.	2006	A75813
Wheat	Krainz, A.	2006	A71188

The method involved extraction of the samples with acetone/5M sulphuric acid followed by centrifugation. An aliquot of the extract was taken, diluted and subjected to SPE (C18) clean up, before analysis by gas chromatography with electron capture detection (GC-ECD) using two columns of different polarity for quantification and confirmation. The LOQ was 0.01 mg/kg.

II. RESULTS AND DISCUSSION

Method Validation

Procedural recoveries were determined using freshly fortified samples at each interval. Samples were fortified with chlorothalonil at 0.2 mg/kg. Individual recoveries, mean recoveries and %RSD are summarised in Table 6.1-21.

Table 6.1-21: Summary of procedural recoveries for chlorothalonil in wheat grain and straw

Recovery at zero time (%)	Recovery at 1 month (%)	Recovery at 2 months (%)	Recovery at 3 months (%)	Mean recovery (%)	RSD (%)
Wheat grain					
101, 95, 92, 94	90	81	72	89	11
Wheat straw					
88, 95, 103, 111	88	83	71	91	14

Storage Stability of Residues

The recoveries of chlorothalonil in cereal crops stored at -20°C are summarised in Table 6.1-22 below. The results are presented both corrected and uncorrected for freshly fortified recoveries.

Table 6.1-22: Freezer storage stability for chlorothalonil at 0.2 mg/kg in cereal crops

Sampling interval (nominal months)	Sampling interval (actual days)	Uncorrected residue (mg/kg)	Mean uncorrected residue (mg/kg)	Mean recovered uncorrected residue (%)	Procedural recovery (%)	Mean corrected residue (mg/kg)	Mean recovered corrected residue (%)
Wheat grain							
0	0	0.20, 0.19, 0.19, 0.19	0.19	100	-	0.19	-
1	32	0.15, 0.17, 0.15	0.16	83	90	0.19	100
2	62	0.19, 0.19, 0.19	0.19	99	81	0.19	100
3	99	0.13, 0.13, 0.13	0.13	67	72	0.19	100
Wheat Straw							
0	0	0.18, 0.19, 0.21, 0.22	0.20	100	-	0.20	-
1	32	0.20, 0.19, 0.21	0.20	100	88	0.20	100
2	62	0.21, 0.21, 0.22	0.21	107	83	0.20	100
3	92	0.18, 0.20, 0.22	0.20	99	71	0.20	100

Percentage recovered residue = residue concentration / initial residue concentration x 100.
Calculations performed on unrounded values.
No residues were present above the LOQ in control samples.

III. CONCLUSIONS

There was no significant decrease in the observed residue levels of chlorothalonil in cereal grain and straw after deep frozen storage for 3 months when results were corrected for procedural recoveries.

(Krainz A, 2007)

Report:	K-CA 6.1/06. Heillaut C and Anderson L. (2007), R613636: storage stability of residues in processed crop commodities stored deep frozen for up to two years. ADME Bioanalyses, Vergèze, France. Syngenta Report Number T007198-04-REG. (Syngenta File No: R613636/0003).

Guidelines

Not stated but meets the requirements of Guideline: Commission of the European Communities: Storage Stability of Residue Samples (**SANCO 7032/V1/95 rev. 5 22/7/1997**).

GLP

The study was carried out according to the principles of Good Laboratory Practice.

EXECUTIVE SUMMARY

Samples of processed barley (pearl barley and beer), processed wheat (bran and flour), processed peanut (meal and oil), processed tomato (juice, paste and puree) and processed legumes (cooked beans with pods) were fortified with the chlorothalonil metabolite R613636 at 0.10 mg/kg, stored under frozen conditions (≤-18° C) and analysed at intervals up to 24 months (four time points). The LOQ was 0.01 mg/kg.

There was no significant decrease in the levels of R613636 in any processed commodity tested over 24 months. Residues of R613636 were therefore stable for at least 24 months in all processed commodities when stored in the freezer at ≤-18°C.

I. MATERIALS AND METHODS

A. MATERIALS

A1. Test Materials

The purity of the analytical standard used in this study is listed in Table 6.1-23.

Table 6.1-23: Purity of analytical standards

Analyte	Standard reference no.	Purity (wt. %)
R613636	ASJ10214-01	99

A2. Test Commodity

The peanut meal, tomato paste and tomato puree were prepared by Syngenta to US guidelines. The pearl barley, beer, wheat bran, wheat flour, peanut oil, tomato juice and beans with pods were purchased from UK supermarkets.

A3. Test Facilities

Sample preparation and analysis up to and including the 12 month storage interval was performed at Syngenta, Jealott's Hill International Research Centre, Bracknell, Berkshire, RG42 6EY, UK. Samples for the 24 month analysis were analysed at ADME Bioanalyses, 75, Chemin de Sommières, F-30310 Vergèze, France.

B. STUDY DESIGN AND METHODS

B1. Fortification and Storage of Samples

The peanut meal was homogenised to remove lumps. The beans with pods were boiled in water for 15-20 minutes, drained, cooled, frozen and then chopped with dry ice. The pearl barley was ground in an ultracentrifugal mill.

Samples (10 g) of pearl barley, beer, wheat bran, wheat flour, peanut meal, peanut oil, cooked beans with pods, tomato juice, tomato paste and tomato puree were fortified with R613636 in acetone at 0.10 mg/kg. Triplicate samples were stored under frozen conditions (≤-18°C) and analysed at intervals up to 24 months (four time points). Control samples were analysed at the zero time and at each time point.

B2. Analytical Method

Analysis of the samples was performed according to analytical method RAM 464/01 at intervals of 0, 3, 6, 12 and 24 months.

The method involved extraction of the samples by homogenisation with acetone: 5M sulphuric acid (95:5, v: v). After centrifugation, aliquots were diluted with water and cleaned by solid phase extraction. Final determination was by HPLC coupled to a triple quadrupole mass spectrometer in selected reaction monitoring mode (LC-MS/MS). The LOQ was 0.01 mg/kg.

The method validation is reported in report number RJ3626B. A full method description and validation data are presented in document M-CA Section 4, CA 4.1.2.

Commodity	Author/s	Issue Year	Report Number
Cereal processed products	Chagger, S.	2005	RJ3626B
Peanut oil	Chagger, S.	2005	RJ3626B
Tomato puree	Chagger, S.	2005	RJ3626B

II. RESULTS AND DISCUSSION

Method Validation

Procedural recoveries were determined using freshly fortified samples at each interval. Samples were fortified with R613636 at 0.1 mg/kg. Individual recoveries, mean recoveries and %RSD are summarised in Table 6.1-24.

Table 6.1-24: Summary of procedural recoveries for R613636 in processed commodities

Recovery at zero time (%)	Recovery at 3 months (%)	Recovery at 6 months (%)	Recovery at 12 months (%)	Recovery at 24 months (%)	Mean recovery (%)	RSD (%)
Pearl barley						
112, 105	94, 96	95, 90	89, 91	92, 85	95	8
Beer						
101, 99	104, 107	98, 106	95, 100	91, 87	89	3
Wheat bran						
114, 110	77, 80	96, 97	66, 65	92, 93	89	19
Wheat flour						
106, 100	102, 103	88, 95	88, 95	96, 107	98	7
Peanut meal						
99, 102	86, 88	80, 72	88, 80	103, 100	90	12
Peanut oil						
98, 97	86, 98	102, 99	76, 78	94, 90	92	10
Cooked beans with pods						
101, 96	111, 112	99, 105	91, 90	94, 92	99	8
Tomato juice						
95, 113	93, 102	108, 102	99, 95	94, 91	99	7
Tomato paste						
96, 96	101, 108	99, 91	93, 86	86, 90	95	7
Tomato puree						
104, 99	108, 105	102, 100	95, 91	92, 89	99	7

Storage Stability of Residues

The recoveries of R613636 in processed commodities stored at ≤-18°C are summarised in Table 6.1-25. The results are not corrected for freshly fortified recoveries.

Table 6.1-25: Freezer storage stability for R613636 in processed commodities

Sampling interval (nominal months)	Sampling interval (actual days)	Uncorrected residue (mg/kg)	Mean uncorrected residue (mg/kg)	Mean procedural recovery (%)	Mean recovered uncorrected residue (%)
Pearl barley					
0	0	0.09, 0.10, 0.10	0.10	108	100
3	106	0.09, 0.09, 0.09	0.09	95	102
6	218	0.10, 0.09, 0.09	0.09	92	95
12	359	0.09, 0.09, 0.09	0.09	90	89
24	787	0.10, 0.09, 0.09	0.09	88	93
Beer					
0	0	0.10, 0.09, 0.10	0.10	100	100
3	92	0.11, 0.11, 0.10	0.11	105	111
6	215	0.11, 0.10, 0.10	0.10	107	103
12	348	0.10, 0.10, 0.10	0.10	97	102
24	770	0.08, 0.09, 0.09	0.09	89	92
Wheat bran					
0*	0	0.12, 0.11, 0.12	0.11	112	100
3*	73	0.08, 0.09, 0.09	0.09	78	76
6*	196	0.10, 0.09, 0.09	0.09	96	81
12*	330	0.07, 0.07, 0.08	0.07	65	61
24*	750	0.08, 0.09, 0.10	0.09	93	79
Wheat flour					
0	0	0.10, 0.10, 0.10	0.10	103	100
3	109	0.09, 0.10, 0.10	0.10	103	99
6	221	0.09, 0.10, 0.10	0.10	92	99
12	362	0.09, 0.09, 0.09	0.09	91	92
24	789	0.10, 0.11, 0.11	0.11	101	113
Peanut meal					
0	0	0.08, 0.09, 0.09	0.09	101	100
3	85	0.09, 0.08, 0.08	0.08	87	97
6	208	0.07, 0.07, 0.08	0.07	76	86
12	342	0.08, 0.08, 0.08	0.08	84	93
24	762	0.10, 0.10, 0.10	0.10	101	119
Peanut oil					
0	0	0.10, 0.09, 0.09	0.09	97	100
3	106	0.10, 0.09, 0.08	0.09	92	85
6	217	0.08, 0.08, 0.08	0.08	101	82
12	363	0.09, 0.08, 0.08	0.08	77	90
24	792	0.09, 0.09, 0.09	0.09	92	96
Cooked beans with pods					
0	0	0.09, 0.10, 0.09	0.10	98	100
3	104	0.11, 0.11, 0.11	0.11	111	113
6	224	0.09, 0.10, 0.09	0.10	102	100

Sampling interval (nominal months)	Sampling interval (actual days)	Uncorrected residue (mg/kg)	Mean uncorrected residue (mg/kg)	Mean procedural recovery (%)	Mean recovered uncorrected residue (%)
12	357	0.09, 0.09, 0.09	0.09	90	93
24	782	0.10, 0.10, 0.08	0.09	93	96
Tomato juice					
0	0	0.12, 0.11, 0.11	0.11	104	100
3	105	0.09, 0.10, 0.09	0.09	98	82
6	216	0.11, 0.10, 0.10	0.10	105	94
12	362	0.10, 0.09, 0.09	0.09	97	83
24	790	0.09, 0.10, 0.09	0.09	93	84
Tomato paste					
0	0	0.10, 0.09, 0.10	0.10	96	100
3	92	0.10, 0.10, 0.10	0.10	104	107
6	212	0.09, 0.09, 0.09	0.09	95	94
12	345	0.09, 0.09, 0.09	0.09	90	95
24	772	0.09, 0.09, 0.09	0.09	88	96
Tomato puree					
0	0	0.10, 0.10, 0.09	0.10	102	100
3	92	0.11, 0.11, 0.11	0.11	106	111
6	212	0.10, 0.10, 0.10	0.10	101	99
12	349	0.10, 0.10, 0.11	0.10	93	103
24	770	0.09, 0.09, 0.09	0.09	90	93

Percentage recovered residue = residue concentration / initial residue concentration using uncorrected residues x 100.
Calculations performed on unrounded values.
* Wheat bran residues and recoveries were corrected for any apparent residue in the untreated control samples. No residues were present above the LOQ in other control samples.

III. CONCLUSIONS

Residues of R613636 were stable in pearl barley, beer, wheat bran, wheat flour, peanut meal, peanut oil, cooked beans with pods, tomato juice, tomato paste and tomato puree for at least 24 months when stored in the freezer at ≤-18°C.

(Heillaut C and Anderson L, 2007)

Report:	K-CA 6.1/07. Krainz A. (2007a), SDS-3701: Frozen storage stability in bovine muscle, fat, liver, kidney and cow's milk. RCC Ltd, Switzerland. Report Number A71278. Syngenta File No: R182281_10018.

Guidelines

Commission of the European Communities: Storage Stability of Residue Samples (**SANCO 7032/V1/95 rev. 5 22/7/1997**).

GLP

The study was carried out according to the principles of Good Laboratory Practice.

EXECUTIVE SUMMARY

Samples of bovine muscle, fat, liver, kidney and cow's milk were fortified at 0.2 mg/kg with R182281. Triplicate samples were stored under frozen conditions (-20°C) and analysed at intervals up to 3 months (three sampling points). The LOQ for R182281 was 0.01 mg/kg.

Residues of R182281 were stable in bovine muscle, fat, liver, kidney and cow's milk for at least 3 months when stored in the freezer at -20°C.

I. MATERIALS AND METHODS

A. MATERIALS

A1. Test Materials

The purity of the analytical standard used in this study is listed in Table 6.1-26.

Table 6.1-26: Purity of analytical standards

Analyte	Standard reference no.	Purity (wt. %)
R182281 (SDS-3701)	BJQ-impurity 246-001	95

A2. Test Commodity

The test commodities were untreated homogenised bovine muscle, fat, liver, kidney taken from a local butcher. Cow's milk was obtained from a regional distributor.

A3. Test Facilities

This study was performed at RCC Ltd, Analytics, Zelgliweg 1, CH-4452 Itingen, Switzerland.

B. STUDY DESIGN AND METHODS

B1. Fortification and Storage of Samples

Homogenised samples were fortified at 0.2 mg/kg with R182281 in acetonitrile. Triplicate samples were stored under frozen conditions (-20°C) and analysed at intervals up to 3 months (three sampling points). Control samples were analysed at zero time and at all other time points to ensure that no residues of chlorothalonil were present at levels above 30% of the LOQ.

B2. Analytical Method

Analysis of the samples was performed according to analytical method A71201 at intervals of 0, 1, and 3 months. The method validation is reported in study report number A71201. A full method description and validation data are presented in document M-CA Section 4, CA 4.2.

Commodity	Author/s	Issue Year	Report Number
Products of animal origin	Krainz, A.	2007	A71201
Products of animal origin	Abellán, M.	2008	S10168

The method involved extraction of the samples of muscle, kidney and liver with acetone/sulphuric acid (95/5, v/v) followed by centrifugation. Samples of milk were extracted with acetonitrile and centrifuged. Samples of fat were extracted with acetonitrile and partitioned with acetonitrile saturated hexane.

Aliquots of all extracts were diluted with methanol/water (1/1, v/v) before analysis by LC-MS/MS monitoring the ion transitions *m/z* 245→175 (quantitation) and *m/z* 245→182 (confirmation). The LOQ was 0.01 mg/kg.

II. RESULTS AND DISCUSSION

Method Validation

Procedural recoveries were determined using freshly fortified samples at each interval. Samples were fortified with R182281 at 0.02 mg/kg. Individual recoveries, mean recoveries and %RSD are summarised in Table 6.1-27.

Table 6.1-27: Summary of procedural recoveries for R182281 in products of animal origin

Recovery at zero time (%)	Recovery at 1 month (%)	Recovery at 2 months (%)	Recovery at 3 months (%)	Mean recovery (%)	RSD (%)
Bovine muscle					
72, 80, 79, 78	77	74	68	75	6
Bovine fat					
93, 95, 95, 95	91	98	98	95	3
Bovine liver					
83, 79, 72, 80	73	94	87	81	10
Bovine kidney					
93, 95, 96, 100	93	91	85	93	5
Cow's milk					
103, 102, 106, 104	101	101	102	103	2

Storage Stability of Residues

The recoveries of R182281 in animal matrices stored at -20°C are summarised in Table 6.1-28 below. The results are not corrected for freshly fortified recoveries.

Table 6.1-28: Freezer storage stability for R182281 at 0.2 mg/kg in animal products

Sampling interval (nominal months)	Sampling interval (actual days)	Uncorrected residue (mg/kg)	Mean uncorrected residue (mg/kg)	Procedural recovery (%)	Mean recovered uncorrected residue (%)
Bovine muscle					
0	0	0.14, 0.16, 0.16, 0.16	0.16	-	100
1	34	0.17, 0.16, 0.16	0.16	77	100
2	62	0.16, 0.15, 0.15	0.15	74	94
3	92	0.14, 0.14, 0.14	0.14	68	88
Bovine fat					
0	0	0.19, 0.19, 0.19, 0.19	0.19	-	100
1	32	0.18, 0.18, 0.18	0.18	91	95
2	60	0.19, 0.18, 0.20	0.19	98	100
3	90	0.17, 0.18, 0.17	0.17	98	89
Bovine liver					
0	0	0.17, 0.16, 0.15, 0.16	0.16	-	100
1	34	0.17, 0.16, 0.15	0.16	73	102
2	62	0.20, 0.20, 0.20	0.20	94	127
3	92	0.19, 0.18, 0.19	0.18	87	116
Bovine kidney					
0	0	0.19, 0.19, 0.19, 0.20	0.19	-	100
1	29	0.18, 0.18, 0.18	0.18	93	95
2	56	0.19, 0.19, 0.19	0.19	91	98
3	92	0.17, 0.18, 0.19	0.18	85	94
Cow's milk					
0	0	0.21, 0.20, 0.21, 0.21	0.21	-	100
1	36	0.21, 0.20, 0.21	0.21	101	100
2	63	0.19, 0.19, 0.19	0.19	101	90
3	93	0.20, 0.19, 0.20	0.20	102	95

Percentage recovered residue = residue concentration / initial residue concentration using uncorrected residues x 100.
Calculations performed on unrounded values.
No residues were present above the LOQ in control samples.

III. CONCLUSIONS

Residues of R182281 were stable in bovine muscle, fat, liver, kidney and cow's milk for at least 3 months when stored in the freezer at -20°C.

(Krainz A, 2007a)

~~**Report:**~~	~~K-CA 6.1/08. Amic S. (2014), Chlorothalonil - Storage stability of chlorothalonil metabolite R182281 in animal matrices under freezer storage conditions for up to two years, interim report for 18 months storage. Eurofins Agroscience Service Chem SAS, Vergèze, France. Report Number S12-04421. Syngenta File No: R182281_10008.~~

Guidelines

OECD Guideline for Testing of Chemicals No. 506, Stability of Pesticide Residues in Stored Commodities, adopted 16 October 2007

EPA Residue Chemistry Test Guidelines, OPPTS 860.1380, Storage Stability Data, August 1996

Commission of the European Communities: Storage Stability of Residue Samples (**SANCO 7032/V1/95 rev. 5 22/7/1997**).

GLP

The study was carried out according to the principles of Good Laboratory Practice.

EXECUTIVE SUMMARY

Samples of bovine tissues (liver and muscle), bovine milk and poultry eggs were fortified at 0.5 mg/kg with R182281. Duplicate samples were stored under frozen conditions (-20°C) and analysed at intervals up to 18 months (five sampling points). The LOQ for R182281was 0.01 mg/kg.

There was no significant decrease (>30% compared to the zero time value) in the levels of R182281 in animal matrices tested over 18 months when stored at -20°C.

Residues of R182281 were found to be stable in bovine liver and muscle, bovine milk and hens eggs groups for at least 18 months when stored in the freezer at -20°C.

I. MATERIALS AND METHODS

A. MATERIALS

A1. Test Materials

The purity of the analytical standard used in this study is listed in Table 6.1-29.

Table 6.1-29: Purity of analytical standards

Analyte	Standard reference no.	Purity (wt. %)
R 182281	P2	98.7

A2. Test Commodity

The test commodities were untreated homogenised bovine tissues (liver and muscle), bovine milk and poultry eggs purchased from a local supermarket.

A3. Test Facilities

This study was performed at Eurofins Agroscience Services Chem SAS, 75 Chemin de Sommières, 30310 Vergèze, France.

B. STUDY DESIGN AND METHODS

B1. Fortification and Storage of Samples

Homogenised samples were fortified at 0.5 mg/kg with R182281 in acetone/ hydrochloric acid (100:5 v/v). Duplicate samples were stored under frozen conditions (-20°C) and analysed at intervals up to 18 months (five sampling points). Control samples were analysed at zero time and at all other time points to ensure that no residues of R182281 were present at levels above 30% of the LOQ.

B2. Analytical Method

Analysis of the samples was performed according to analytical method GRM005.05.A, renamed as method AGR/MOA/CHL-14 at intervals of 0, 1, 3, 6, 12 and 18 months.

The method involved extraction of the samples of muscle and liver with acetone/5M sulphuric acid followed by centrifugation. Samples of milk were extracted with acetonitrile and centrifuged. Samples of egg were extracted with acetonitrile/water and centrifuged. Aliquots of the extracts were taken and diluted in water/ hydrochloric acid. Final determination was by LC-MS/MS, monitoring for the primary transition (m/z 245→182) and the confirmatory transition (m/z 245→209). The LOQ was 0.01 mg/kg.

II. RESULTS AND DISCUSSION

Method Validation

Procedural recoveries were determined using freshly fortified samples at each interval. Samples were fortified with R182281 at 0.5 mg/kg. Individual recoveries, mean recoveries and %RSD are summarised in Table 6.1-30.

Table 6.1-30: Summary of procedural recoveries for R182281 in animal matrices

Recovery at zero time (%)	Recovery at 1 month (%)	Recovery at 3 months (%)	Recovery at 6 months (%)	Recovery at 12 months (%)	Recovery at 18 months (%)	Mean recovery (%)	RSD (%)
Bovine milk							
88, 85	90, 82	87, 86	83, 84	89, 90	101,102	89	7
Bovine liver							
85, 85	83, 83	84, 97	87, 85	86, 85	99, 100	88	7
Bovine muscle							
83, 82	80, 77	98, 92	86, 86	82, 85	98, 100	87	9
Poultry eggs							
87, 90	86, 85	85, 84	85, 85	86, 85	103, 99	88	7

Storage Stability of Residues

The recoveries of R182281 in various crops stored at -20°C are summarised in Table 6.1-31 below. The results are not corrected for freshly fortified recoveries.

Table 6.1-31: Freezer storage stability for R182281 at 0.5 mg/kg in animal matrices

Sampling interval (nominal months)	Sampling interval (actual days)	Uncorrected residue (mg/kg, mg/L for milk)	Mean uncorrected residue (mg/kg, mg/L for milk)	Mean procedural recovery (%)	Mean recovered uncorrected residue (%)
Bovine milk					
0	0	0.41, 0.44, 0.42	0.42	87	100
1	32	0.41, 0.40	0.40	86	95
3	95	0.43, 0.46	0.45	87	105
6	180	0.35, 0.37	0.36	83	85
12	364	0.45, 0.43	0.44	89	104
18	544	0.51, 0.50	0.51	101	119
Bovine Liver					
0	0	0.43, 0.43, 0.43	0.43	85	100
1	32	0.39, 0.39	0.39	83	92
3	95	0.46, 0.44	0.45	91	105
6	180	0.38, 0.39	0.39	86	90
12	364	0.42, 0.44	0.43	86	101
18	544	0.51, 0.50	0.50	99	117
Bovine Muscle					
0	0	0.42, 0.42, 0.42	0.42	83	100
1	32	0.39, 0.40	0.40	78	94
3	95	0.47, 0.46	0.47	95	110
6	180	0.37, 0.38	0.38	86	89
12	364	0.42, 0.46	0.44	84	104
18	544	0.50, 0.48	0.49	99	117
Poultry Eggs					
0	0	0.44, 0.43, 0.42	0.43	89	100
1	32	0.41, 0.42	0.42	86	97
3	95	0.41, 0.43	0.42	84	95
6	180	0.38, 0.38	0.38	85	88
12	364	0.43, 0.42	0.43	85	99
18	544	0.50, 0.50	0.50	101	116

Percentage recovered residue = residue concentration / initial residue concentration using uncorrected residues x 100.
Calculations performed on unrounded values.
No residues were present above the LOQ in control samples.

III. CONCLUSIONS

There was no significant decrease (>30% as compared to the zero-time value) in the observed residue levels of R182281 after deep frozen storage for 18 months.

(Amic S, 2014)

Report:	KCA 6.1/08. Amic S. (2015), Chlorothalonil - Storage stability of chlorothalonil metabolite R182281 in animal matrices under freezer storage conditions for up to two years. Eurofins Agroscience Service Chem SAS, Vergèze, France. Report Number S12-04421. Syngenta Regulatory Document No: R182281_10047.

Guidelines

OECD Guideline for Testing of Chemicals No. 506, Stability of Pesticide Residues in Stored Commodities, adopted 16 October 2007

EPA Residue Chemistry Test Guidelines, OPPTS 860.1380, Storage Stability Data, August 1996

Commission of the European Communities: Storage Stability of Residue Samples (**SANCO 7032/V1/95 rev. 5 22/7/1997**).

GLP

The study was carried out according to the principles of Good Laboratory Practice.

EXECUTIVE SUMMARY

Samples of bovine tissues (liver and muscle), bovine milk and poultry eggs were fortified at 0.5 mg/kg with R182281. Duplicate samples were stored under frozen conditions (-20°C) and analysed at intervals up to 24 months (six sampling points). The LOQ for R182281was 0.01 mg/kg.

There was no significant decrease (>30% compared to the zero time value) in the levels of R182281 in bovine liver tested over 24 months when stored at -20°C. There was no significant decrease (>30% compared to the zero time value) in the levels of R182281 in bovine milk and muscle and poultry eggs tested over 18 months when stored at -20°C.

Residues of R182281 were found to be stable in bovine liver for at least 24 months and in bovine muscle, milk and hen's eggs for at least 18 months when stored in the freezer at -20°C.

I. MATERIALS AND METHODS

A. MATERIALS

A1. Test Materials

The purity of the analytical standard used in this study is listed in Table 6.1-29.

Table 6.1-29: Purity of analytical standards

Analyte	Standard reference no.	Purity (wt. %)
R 182281	P2	98.7

A2. Test Commodity

The test commodities were untreated homogenised bovine tissues (liver and muscle), bovine milk and poultry eggs purchased from a local supermarket.

A3. Test Facilities

This study was performed at Eurofins Agroscience Services Chem SAS, 75 Chemin de Sommières, 30310 Vergèze, France.

B. STUDY DESIGN AND METHODS

B1. Fortification and Storage of Samples

Homogenised samples were fortified at 0.5 mg/kg with R182281 in acetone/ hydrochloric acid (100:5 v/v). Duplicate samples were stored under frozen conditions (-20°C) and analysed at intervals up to 24 months (six sampling points). Control samples were analysed at zero time and at all other time points to ensure that no residues of R182281 were present at levels above 30% of the LOQ.

B2. Analytical Method

Analysis of the samples was performed according to analytical method GRM005.05.A, renamed as method AGR/MOA/CHL-14 at intervals of 0, 1, 3, 6, 12, 18 and 24 months.

The method involved extraction of the samples of muscle and liver with acetone/5M sulphuric acid followed by centrifugation. Samples of milk were extracted with acetonitrile and centrifuged. Samples of egg were extracted with acetonitrile/water and centrifuged. Aliquots of the extracts were taken and diluted in water/ hydrochloric acid. Final determination was by LC-MS/MS, monitoring for the primary transition (m/z 245→182) and the confirmatory transition (m/z 245→209). The LOQ was 0.01 mg/kg.

II. RESULTS AND DISCUSSION

Method Validation

Procedural recoveries were determined using freshly fortified samples at each interval. Samples were fortified with R182281 at 0.5 mg/kg. Individual recoveries, mean recoveries and %RSD are summarised in Table 6.1-30.

Table 6.1-30: Summary of procedural recoveries for R182281 in animal matrices

Recovery at zero time (%)	Recovery at 1 month (%)	Recovery at 3 months (%)	Recovery at 6 months (%)	Recovery at 12 months (%)	Recovery at 18 months (%)	Recovery at 24 months (%)	Mean recovery (%)	RSD (%)
Bovine milk								
88, 85	90, 82	87, 86	83, 84	89, 90	101,102	76, 73, 76, 79	86	9
Bovine liver								
85, 85	83, 83	84, 97	87, 85	86, 85	99, 100	74, 72	86	9
Bovine muscle								
83, 82	80, 77	98, 92	86, 86	82, 85	98, 100	76, 76	86	10
Poultry eggs								
87, 90	86, 85	85, 84	85, 85	86, 85	103, 99	79, 73, 73, 79	85	9

Storage Stability of Residues

The recoveries of R182281 in various crops stored at -20°C are summarised in Table 6.1-31 below. The results are not corrected for freshly fortified recoveries.

Table 6.1-31: Freezer storage stability for R182281 at 0.5 mg/kg in animal matrices

Sampling interval (nominal months)	Sampling interval (actual days)	Uncorrected residue (mg/kg, mg/L for milk)	Mean uncorrected residue (mg/kg, mg/L for milk)	Mean procedural recovery (%)	Mean recovered uncorrected residue (%)
Bovine milk					
0	0	0.41, 0.44, 0.42	0.42	87	100
1	32	0.41, 0.40	0.40	86	95
3	95	0.43, 0.46	0.45	87	105
6	180	0.35, 0.37	0.36	83	85
12	364	0.45, 0.43	0.44	89	104
18	544	0.51, 0.50	0.51	101	119
24	731, 843	0.21, 0.27, 0.24, 0.22	0.24	76	57
Bovine Liver					
0	0	0.43, 0.43, 0.43	0.43	85	100
1	32	0.39, 0.39	0.39	83	92
3	95	0.46, 0.44	0.45	91	105
6	180	0.38, 0.39	0.39	86	90
12	364	0.42, 0.44	0.43	86	101
18	544	0.51, 0.50	0.50	99	117
24	731	0.51, 0.50	0.51	73	118
Bovine Muscle					
0	0	0.42, 0.42, 0.42	0.42	83	100
1	32	0.39, 0.40	0.40	78	94
3	95	0.47, 0.46	0.47	95	110
6	180	0.37, 0.38	0.38	86	89
12	364	0.42, 0.46	0.44	84	104
18	544	0.50, 0.48	0.49	99	117
24	843	0.27, 0.25	0.27	76	64
Poultry Eggs					
0	0	0.44, 0.43, 0.42	0.43	89	100
1	32	0.41, 0.42	0.42	86	97
3	95	0.41, 0.43	0.42	84	95
6	180	0.38, 0.38	0.38	85	88
12	364	0.43, 0.42	0.43	85	99
18	544	0.50, 0.50	0.50	101	116
24	731, 843	0.31, 0.27, 0.25, 0.23	0.27	76	63

Percentage recovered residue = residue concentration / initial residue concentration using uncorrected residues x 100.
Calculations performed on unrounded values.
No residues were present above the LOQ in control samples.

III. CONCLUSIONS

There was no significant decrease (>30% as compared to the zero-time value) in the observed residue levels of R182281 after deep frozen storage for 18 months. A decrease >30% was observed in residue levels in bovine milk, muscle and poultry eggs after 24 months.

Residues of R182281 were found to be stable in bovine liver for at least 24 months and in bovine muscle, bovine milk and hen's eggs for at least 18 months when stored in the freezer at -20°C.

(Amic S, 2015)

Summary of stability of residues during storage

A summary of storage stability results for chlorothalonil and R182281 in plant and animal commodities is presented in Table 6.1.1-32. A summary of storage stability results for R611965 in plant commodities is presented in Table 6.1.1-33 and a summary of storage stability results for R613636 in processed commodities is presented in Table 6.1.1-34.

Chlorothalonil was stable in crops representing the high water, high oil, high starch, high protein and high acid crop groups for 24 months when samples were homogenised in the presence of acid before storage.

R182281 was stable in crops representing the high water, high oil, high starch, high protein and high acid crop groups for 24 months when samples were homogenised in the presence of acid before storage. Residues of R182281 in onions and grapes were found to be stable for 3 months.

Chlorothalonil was stable in crops representing the high water, high oil, high starch and high acid crop groups ~~when samples were stored in the absence of acid for whole commodities or as homogenised samples prior to storage~~ for 48 ~~and 24~~ months when samples were homogenised without acid before storage ~~, respectively~~.

R182281 was stable in crops representing the high oil, high starch, high protein and high acid crop groups for 24 months when samples were homogenised without acid.

R611965 was stable in crops representing the high water, high acid, high starch, high protein and high oil crop groups for ~~12~~ 30 months.

R613636 was stable in a range of commodities processed from barley, wheat, peanut, beans with pods and tomato for 24 months

Residues of R182281 were stable in products of animal origin for 18 months.

Of the commodities tested in freezer stability studies, the results in tomato, cereals, potato and the animal commodities are directly relevant to the representative crops in this submission.

Chlorothalonil is stable in tomatoes (prepared both with and without the presence of acid) and cereal grain for 24 months and in cereal straw and potatoes for 12 months. R182281 is stable in tomatoes, potatoes (prepared in the presence of acid), cereal grain and cereal straw for 24 months and in animal products, muscle, liver, milk and eggs for 18 months and 12 months for kidney.

Table 6.1.1-32: Stability of chlorothalonil and R182281 in plant and animal commodities following freezer storage

Commodity Catergories[1]	Commodity	Period of Stability (months)		Study Reference	
		Chlorothalonil	R182281	Author, Year, File no	Dossier Reference
High water content	Celery stalks	48	--	King C; 1995 3064-88-0136-CR-003	--[2]
	Cherry fruit	48	--	King C; 1995 3064-88-0068-CR-003	--[2]
	Cucumber fruit	48	--	King C, Wiedmann JL; 1996 3064-88-0093-CR-003	--[2]
	Cucumber fruit	24	-	Anderson L, Chaggar S; 2007 R182281_0023	K-CA 6.1/01
	Cucumber fruit (prepared with acid)	24	24	Anderson L; 2007 R44686_4298	K-CA 6.1/02
	Melon whole fruit	24	-	Anderson L, Chaggar S; 2007 R182281_0023	K-CA 6.1/01
	Melon whole fruit (prepared with acid)	24	24	Anderson L; 2007 R44686_4298	K-CA 6.1/02
	Onion bulbs (prepared with acid)	24	<3	Anderson L; 2007 R44686_4298	K-CA 6.1/02
	Tomato fruit	48	--	Hayes PC Jr, Kenyon RG; 1996 3064-88-0083-CR-003	--[2]
	Tomato fruit	24	-	Anderson L, Chaggar S; 2007 R182281_0023	K-CA 6.1/01
	Tomato fruit (prepared with acid)	24	24	Anderson L; 2007 R44686_4298	K-CA 6.1/02
	Apple fruit (prepared with acid)	24	24	Anderson L; 2007 R44686_4298	K-CA 6.1/02
	broccoli (prepared with acid)	24	24	Anderson L; 2007 R44686_4298	K-CA 6.1/02
	Brussels sprout (prepared with acid)	24	24	Anderson L; 2007 R44686_4298	K-CA 6.1/02
	cabbage (prepared with acid)	24	24	Anderson L; 2007 R44686_4298	K-CA 6.1/02
	cauliflower (prepared with acid)	24	24	Anderson L; 2007 R44686_4298	K-CA 6.1/02
	French bean (prepared with acid)	24	24	Anderson L; 2007 R44686_4298	K-CA 6.1/02
	leek (prepared with acid)	24	24	Anderson L; 2007 R44686_4298	K-CA 6.1/02
	peas (prepared with acid)	24	24	Anderson L; 2007 R44686_4298	K-CA 6.1/02
	plum (fruit minus stone) (prepared with acid)	24	24	Anderson L; 2007 R44686_4298	K-CA 6.1/02
	Banana whole fruit (prepared with acid)	24	24	Anderson L; 2007 R44686_4298	K-CA 6.1/02

Commodity Catergories[1]	Commodity	Period of Stability (months)		Study Reference	
		Chlorothalonil	R182281	Author, Year, File no	Dossier Reference
High oil content	Almond nutmeat and hulls	24	--	King C, Wiedmann JL; 1995 3064-88-0158-CR-003	--[2]
	Peanut nutmeat	18	--	King, C; 1995 3064-88-160CR-003	--[2]
	Soya beans	48	--	Dvorak RS, Kenyon RG; 1995 3064-88-0097-CR-003	--[2]
	Soya beans	27	27	Anderson L, Chaggar S; 2007 R182281_0023	K-CA 6.1/01
	Olive (fruit minus stone) (prepared with acid)	24	24	Anderson L; 2007 R44686_4298	K-CA 6.1/02
High starch content/ High protein content	Carrot root	48	--	Rose C; 1995 3064-88-0096-CR-003	--[2]
	Carrot root and top	24	24	Anderson L, Chaggar S; 2007 R182281_0023	K-CA 6.1/01
	Carrot root (prepared with acid)	24	24	Anderson L; 2007 R44686_4298	K-CA 6.1/02
	Potato tuber	12	--	Rose C; 1995 3064-88-0095-CR-003	--[2]
	Potato tuber (prepared with acid)	24	24	Anderson L; 2007 R44686_4298	K-CA 6.1/02
	Sugar beet root (prepared with acid)	24	24	Anderson L; 2007 R44686_4298	K-CA 6.1/02
	Barley grain	24	24	Anderson L, Chaggar S; 2007 R182281_0023	K-CA 6.1/01
	Barley straw	12	27	Anderson L, Chaggar S; 2007 R182281_0023	K-CA 6.1/01
	Wheat grain	48	--	Kenyon RG; 1995 3064-88-0070-CR-003	--[2]
	Wheat grain	3	-	Krainz A; 2007 A71256	K-CA 6.1/05
	Wheat straw	3	-	Krainz A; 2007 A71256	K-CA 6.1/05
	Cereal straw	9	12	Brown D; 2014 R44383_11076.	K-CA 6.1/03
High acid content	Orange whole fruit	24	24	Anderson L, Chaggar S; 2007 R182281_0023	K-CA 6.1/01
	Strawberry fruit (prepared with acid)	24	24	Anderson L; 2007 R44686_4298	K-CA 6.1/02
	Grape berries (prepared with acid)	24	3	Anderson L; 2007 R44686_4298	K-CA 6.1/02

Commodity Catergories[1]	Commodity	Period of Stability (months)		Study Reference	
		Chlorothalonil	R182281	Author, Year, File no	Dossier Reference
Products of animal origin	Bovine milk, liver, muscle, fat	-	12	King C, Prince P; 1995 5927-93-0329-CR-001	--[2]
	Bovine muscle, fat, liver, kidney	-	3	Krainz A; 2007 A71278	K-CA 6.1/07
	Cow's milk	-	3	Krainz A; 2007 A71278	K-CA 6.1/07
	Bovine muscle and liver	-	18	Amic S; (2014) R182281_10008	K-CA 6.1/08
	Bovine milk	-	18	Amic S; (2014) R182281_10008	K-CA 6.1/08
	Poultry eggs	-	18	Amic S; (2014) R182281_10008	K-CA 6.1/08

[1] Crop commodities according to the categories described in OECD 506.
[2] Report submitted previously for Annex I listing and not presented in full in this dossier.

Table 6.1.1-33: Stability of R611965 in plant commodities following freezer storage

Commodity Catergories[1]	Commodity	Period of Stability (months)	Study Reference	
			Author, Year, File no	Dossier Reference
High water content	Tomato	~~12~~ 30	~~Watson G; 2014~~ Gasso-Brown D; 2015 S12-04611	K-CA 6.1/04
High oil content	Soybean seed	~~12~~ 30		
High starch content	Wheat grain	~~12~~ 30		
High acid content	Whole orange	~~12~~ 30		
High protein content	Lentil	~~12~~ 30		

[1] Crop commodities according to the categories described in OECD 506.

Table 6.1.1-34: Stability of R613636 in processed commodities following freezer storage

Commodity	Period of Stability (months)	Study Reference	
		Author, Year, File no	Dossier Reference
Pearl barley	24	Heillaut C and Anderson L; 2007 T007198-04-REG	K-CA 6.1/06
Beer	24		
Wheat bran	24		
Wheat flour	24		
Peanut meal	24		
Peanut oil	24		
Cooked beans with pods	24		
Tomato juice	24		
Tomato paste	24		
Tomato puree	24		

Stability of residues in sample extracts

Procedural recoveries obtained during residue analysis demonstrate the stability of residues of chlorothalonil, R182281, R611965 and R613636 in sample extracts. In addition, stability of residues in sample extracts studies that were not submitted for Annex I listing of chlorothalonil are also available. Summaries are presented below.

Report:	K-CA 6.1/09. Lister, N. (2000), Chlorothalonil: Validation of SOP RAM 320/01 for the determination of residues in crops. Syngenta, Jealott's Hill International Research Centre, Bracknell, United Kingdom. Syngenta Report Number RJ2872B. Syngenta File No: R44686/0099.

Guidelines

Not applicable.

GLP

The study was carried out according to the principles of Good Laboratory Practice.

EXECUTIVE SUMMARY

The storage stability of sample extracts was determined as part of the validation of method SOP RAM 320/01. Extracts of homogenised pear fruit, soya bean seed, barley grain and barley straw that were fortified at 0.01, 0.1 and 1.0 mg/kg with chlorothalonil were stored at < 7°C and analysed at intervals up to 35 days after extraction. The final measurement extracts were stored at < -18°C and reanalysed 1, 3 and 7 days after the initial analysis.

Extracts of representative crop matrices stored in extraction solvent at temperatures of < 7°C were shown to be stable for a period of 35 days. The final extracts in toluene were shown to be stable for a period of at least 7 days when stored at < -18°C.

I. MATERIALS AND METHODS

A. MATERIALS

A1. Test Materials

The purity of the analytical standards used in this study is listed in Table 6.1-35.

Table 6.1-35: Purity of analytical standards

Analyte	Standard reference no.	Purity (wt. %)
Chlorothalonil	ASJ10125-03S	99.6

A2. Test Commodity

The test commodities were pear fruit, soya bean seed, barley grain and barley straw. Samples were purchased from a local supermarket with the exception of the barley samples which were taken from a Syngenta field trial.

A3. Test Facilities

This study was performed at Syngenta, Jealott's Hill International Research Centre, Bracknell, Berkshire, RG42 6EY, UK.

B. STUDY DESIGN AND METHODS

B1. Fortification and Storage of extracts

Samples were fortified at 0.01, 0.10 and 1.0 mg/kg with chlorothalonil in acetone and extracted according to method RAM 320/01. Sample extracts in acetone/5M sulphuric acid taken immediately after homogenisation were stored at < 7°C and analysed at interval up to 35 days. The stability of the final measurement extracts in toluene was assessed by retaining the samples in the vials at temperatures <-18°C and reanalysing them 1, 3 and 7 days after the initial analysis.

B2. Analytical Method

Analysis of the samples was performed according to analytical method SOP RAM 365/01. A full method description and validation data are presented in document M-CA Section 4, CA 4.1.2.

II. RESULTS AND DISCUSSION

Storage Stability of Extracts

The recoveries of chlorothalonil in sample extracts stored at < 7°C and ≤ -18°C are summarised in Table 6.1-36 and Table 6.1-37, respectively.

Table 6.1-36: Storage stability of chlorothalonil in crop extraction solvent stored at <7°C

Crop Matrix	Recovery level (mg/kg)	Average Chlorothalonil recovery (mg/kg)			
		Day 0	Day 7-10	Day 13-17	Day 28-35
Pear fruit	0.01	0.010	0.010	0.009	nd
	0.1	0.091	0.090	0.081	nd
	1.0	0.98	0.94	0.82	nd
Pear fruit	0.01	0.008	nd	nd	0.009
	0.1	0.077	nd	nd	0.095
	1.0	0.86	nd	nd	1.05
Soya bean seed	0.01	0.009	0.008	0.008	0.008
	0.1	0.093	0.076	0.080	0.070
	1.0	1.02	0.82	0.83	0.81
Barley grain	0.01	0.008	0.009	0.008	0.008
	0.1	0.074	0.079	0.076	0.084
	1.0	0.86	0.89	0.80	1.01
Barley straw	0.01	0.009	0.009	0.009	0.009
	0.1	0.073	0.088	0.091	0.092
	1.0	0.79	0.88	1.00	0.90

nd = not determined

Table 6.1-37: Storage stability of chlorothalonil in toluene stored at <-18°C

Crop Matrix	Recovery level (mg/kg)	Average Chlorothalonil recovery (mg/kg)			
		Day 0	Day 1	Day 3	Day 7
Pear fruit	0.01	0.01	0.010	0.009	0.010
	0.1	0.091	0.089	0.081	0.089
	1.0	0.98	0.99	0.88	0.96
Soya bean seed	0.01	0.009	0.009	0.009	0.009
	0.1	0.091	0.088	0.089	0.091
	1.0	1.02	1.04	1.00	1.07
Barley grain	0.01	0.008	0.008	0.008	0.008
	0.1	0.074	0.073	0.072	0.070
	1.0	0.86	0.83	0.82	0.87
Barley straw	0.01	0.009	0.008	nd	0.010
	0.1	0.073	0.073	nd	0.085
	1.0	0.79	0.79	nd	0.93

nd = not determined

III. CONCLUSIONS

Extracts of representative crop matrices stored in extraction solvent at temperatures of < 7°C were shown to be stable for a period of 35 days. The final extracts in toluene were shown to be stable for a period of at least 7 days when stored at < -18°C.

(Lister N, 2000)

Report:	K-CA 6.1/10. McGill, C. and Robinson, N. (2002), Chlorothalonil metabolite R182281 (SDS-3701): Validation of analytical method 384/01 for the determination of residues in bovine muscle, fat, kidney, liver, milk and hen's eggs. Syngenta, Jealott's Hill International Research Centre, Bracknell, United Kingdom. Syngenta Report Number RJ3312B. Syngenta File No: R44686/3317

Guidelines

Not applicable.

GLP

The study was carried out according to the principles of Good Laboratory Practice.

EXECUTIVE SUMMARY

The storage stability of sample extracts was determined as part of the validation of method SOP RAM 384/01. Extracts of homogenised muscle, fat, liver, kidney, milk and egg that were fortified at 1.0 mg/kg with R182281 were stored at < 7°C and analysed at intervals up to 35 days after extraction. The final measurement extracts were stored at < 7°C and reanalysed 7 days after the initial analysis.

Extracts of representative matrices stored in extraction solvent at temperatures of < 7°C were shown to be stable for 30-35 days. The final extracts in acetone/water were shown to be stable for 7 days.

I. MATERIALS AND METHODS

A. MATERIALS

A1. Test Materials

The purity of the analytical standards used in this study is listed in Table 6.1-38.

Table 6.1-38: Purity of analytical standards

Analyte	Standard reference no.	Purity (wt. %)
R182281	ASJ10209-02	Not stated

A2. Test Commodity

The test commodities were bovine muscle, fat, kidney, liver, milk and hen's eggs. Samples were taken from pre-prepared control samples available at Syngenta with the exception of hen's eggs which were purchased from a local supermarket.

A3. Test Facilities

This study was performed at Syngenta, Jealott's Hill International Research Centre, Bracknell, Berkshire, RG42 6EY, UK.

B. STUDY DESIGN AND METHODS

B1. Fortification and Storage of extracts

Samples were fortified at 1.0 mg/kg with R182281 in acidified acetone and extracted according to method RAM 384/01. Sample extracts taken immediately after homogenisation were stored at < 7°C and analysed 30 to 35 days after extraction. The stability of the final measurement extracts in acetonitrile/water (50:50) was assessed by retaining the samples in the vials at temperatures < 7°C and reanalysing 7 days after the initial analysis.

B2. Analytical Method

Analysis of the samples was performed according to analytical method RAM 384/01. A full method description and validation data are presented in document M-CA Section 4, CA 4.2.

II. RESULTS AND DISCUSSION

Storage Stability of Extracts

The recoveries of chlorothalonil in sample extracts stored at < 7°C are summarised in Table 6.1-39 and Table 6.1-40 below.

Table 6.1-39: Storage stability of R182281 in extraction solvent stored at <7°C[a]

Matrix	Recovery level (mg/kg)	Storage interval (days)	R182281 recovery (mean of 5 replicates)	
			mg/kg	%*
Muscle	0.01	0	0.010	100
		30	0.009	90
	0.1	0	0.094	100
		30	0.092	98
Fat	0.01	0	0.009	100
		35	0.009	100
	0.1	0	0.086	100
		35	0.084	98
Kidney	0.01	0	0.010	100
		34	0.010	100
	0.1	0	0.097	100
		34	0.096	99
Liver	0.01	0	0.009	100
		34	0.010	111
	0.1	0	0.091	100
		34	0.083	91
Milk	0.01	0	0.008	100
		30	0.011	138#
	0.1	0	0.090	100
		30	0.100	109
Egg	0.01	0	0.008	100
		31	0.007	88
	0.1	0	0.081	100
		31	0.094	116

*Based on Day 0 result

[a] For muscle, fat, liver and kidney the extraction solvent used was acetone/5 M H_2SO_4 95:5 (v/v), for milk acetonitrile was the extraction solvent and for egg the extraction solvent was acetonitrile/water, 3:1 (v/v).

[#] The mean recovery is greater than 110%, however, the relative standard deviation in this analysis was less than 10% and so the data was accepted on that criterion

Table 6.1-40: Storage stability of R182281 in acetone/water 50/50 v/v stored at <7°C

Matrix	Recovery level (mg/kg)	Storage interval (days)	R182281 recovery (mean of 5 replicates)	
			mg/kg	%*
Muscle	0.01	0	0.010	100
		7	0.011	110
	0.10	0	0.094	100
		7	0.095	101
Fat	0.01	0	0.009	100
		7	0.009	100
	0.10	0	0.086	100
		7	0.084	98
Kidney	0.01	0	0.010	100
		7	0.010	100
	0.10	0	0.097	100
		7	0.097	100
Liver	0.01	0	0.009	100
		7	0.008	89
	0.10	0	0.091	100
		7	0.079	87
Milk	0.01	0	0.008	100
		7	0.008	100
	0.10	0	0.092	100
		7	0.085	92
Egg	0.01	0	0.008	100
		7	0.008	100
	0.10	0	0.081	100
		7	0.088	109

*Based on Day 0 result

III. CONCLUSIONS

R182281 stored in extraction solvent at temperatures of < 7°C was shown to be stable for 30-35 days. The final extracts in acetone /water (50/50 v/v) were shown to be stable for 7 days for all matrices.

(McGill C and Robinson N, 2002)

CA 6.2 Metabolism, Distribution and Expression of Residues

CA 6.2.1 Metabolism, distribution and expression of residues in plants

The metabolism of chlorothalonil has been studied in lettuce, tomato, carrot, celery, snap beans (French beans), wheat and peas using ^{14}C-chlorothalonil labelled in the phenyl position.

The studies were evaluated under Council Directive 91/414/EEC and are presented in the chlorothalonil monograph (**Vol.3, Annex B, Section B.7.1, January 2000**).

Crop	Author/s	Issue Year	Report Number
Lettuce	Nelsen TR	1985	672-3EF-84-0014-001
Tomatoes	Nelsen TR, Duane WC	1988	1184-85-0052-EF-001
Carrots	Nelsen TR	1987	1186-86-0026-EF-001
Celery	Huhtanen KL	1992	3503-90-0184-EF-001
Snap beans	Huhtanen KL	1993	5216-92-0063-EF-001
Tomatoes	Mayo B	1996	VCM 44/950175
Wheat	Mayo B	1996	VCM 38/950767
Peas	Vischim, McEwen	1997	VCM 68/962010

An executive summary of the studies submitted for Annex I listing is presented below. Discussion of the definition of the residue is presented in the 'Summary of metabolism, distribution and expression of residues in crops' at the end of the plant metabolism section.

EXECUTIVE SUMMARY OF PLANT METABOLISM STUDIES SUBMITTED FOR ANNEX I LISTING OF CHLOROTHALONIL

Chlorothalonil (R44686) is a non- systemic broad spectrum fungicide formulated either alone or with other fungicidal active substances for use on a wide range of crops including cereals, fruits and vegetables.

Plant uptake, distribution and metabolism of ^{14}C labelled chlorothalonil was investigated in leafy vegetables (lettuce, celery), root vegetables (carrot), fruiting vegetables (tomato), fresh legumes (peas, snap beans) and cereals (wheat).

An overview of the studies in which the metabolism and distribution of chlorothalonil has been investigated in plants for inclusion in Annex I of Council Directive 91/414/EEC is summarised in Table 6.2.1-1 below:

Table 6.2.1-1: Overview of plant metabolism studies evaluated for inclusion of chlorothalonil in Annex I of EU Directive 91/414/EEC

Crop	^{14}C-Radiolabel	Growth conditions	Application	Report
Lettuce	Phenyl	Greenhouse	Foliar by syringe; 4 applications equivalent to 1.75 kg as/ha per application. 4-5 days between applications	672-3EF-84-0014-001
Tomato	Phenyl	Greenhouse	Foliar; 3 applications equivalent to 2.3 kg as/ha per application. 7 days between applications	1184-85-0052-EF-001
Carrot	Phenyl	Greenhouse	Foliar; 3 applications equivalent to 1.6 kg as/ha per application. 7 days between applications	1186-86-0026-EF-001
Celery	Phenyl	Field	Spray on foliage, stalks and soil; 12 applications equivalent to 2.5 kg as/ha per application. 6-8 days between applications	3503-90-0184-EF-001
Snap beans	Phenyl	Field	Foliar; 4 applications equivalent to 2.46 kg as/ha per application. 7 days between applications	5216-92-0063-EF-001
Tomato	Phenyl	Greenhouse	Foliar; 1 application equivalent to 1.6 kg as/ha.	VCM 44/950175
Wheat	Phenyl	Field	Foliar; 1 application equivalent to 1.0 kg as/ha.	VCM 38/950767
Peas	Phenyl	Field	Foliar; 1 application equivalent to 1.4 kg as/ha.	VCN 68/962010

Lettuce plants received four foliar applications of [phenyl-U-^{14}C]-chlorothalonil at a rate equivalent to 1.75 kg a.s./ha (in total 7.0 kg a.s./ha). Plants were harvested at 1, 3, 7, 10, 14 and 21 days after the last treatment. Total radioactive residue (TRR) levels in lettuce varied from 118 to 170 mg/kg and were independent of the PHI. Approximately 90% of the total residue was identified and only 4.5% remained un-extracted. The major identified residue in lettuce was chlorothalonil, accounting for over 85% TRR. Metabolism resulted in a single, identifiable and quantifiable metabolite, R182281 (2,5,6-trichloro-4-hydroxyphtalonitrile, also known as SDS-3701) , accounting for a maximum of 2% TRR.

Two studies were submitted on tomatoes: In the first, tomato plants were treated with a single application of [phenyl-U-^{14}C]-chlorothalonil at a rate of 1.6 kg a.s./ha. Samples of fruit and leaves were taken 2 h and at two, three and four weeks after treatment. Total residue levels in fruit declined from 3.8 mg/kg two weeks after treatment to 1.8 mg/kg four weeks after treatment. More than 90% of the total residue in the fruit and leaves was present in surface washes at all sampling times, and more than 88% of the surface washes consisted of unchanged chlorothalonil. Although no metabolites were identified in this study, the overall results with respect to characterisation were found to be comparable to those of a second tomato study discussed below.

In the second study, tomato plants were treated with three applications of [phenyl-U-^{14}C] -chlorothalonil at a rate of 2.33 kg a.s./ha (in total 7.0 kg/ha). Tomato fruit and vines were harvested 1, 7 and 14 days after the last treatment. TRR in tomato fruit decreased from 2.6 mg/kg one day after treatment to 0.6 mg/kg 14 days after treatment. Less than 10 and less than 15% of the TRR was un-extracted for tomato fruit and vines, respectively. The major identified component of the residue was chlorothalonil, accounting for 50-76% and 41-73% TRR in fruit and vines, respectively. The second major identified residue component was R182281, accounting for less than 5% TRR in fruit and a maximum of 8% TRR in tomato vines. In total, approximately 50% or more of the total residue was identified. Polar, water-soluble residues in tomato fruit represented up to 32% TRR at 7 and 14 days PHI; considerable additional effort was made in an attempt to characterize/identify these residues. Attempts to further identify the water-soluble residue were only partly successful.

Carrot plants received three applications of [phenyl-U-^{14}C]-chlorothalonil at a rate of 1.6 kg a.s./ha. Plants were harvested 1, 7, 14 and 21 days after the last treatment, and separated into tops and roots. TRR in roots were 0.07 mg/kg and 0.04 mg/kg 1 and 21 days after treatment respectively. TRR in foliage were 36 mg/kg and 13 mg/kg 1 and 21 days after treatment, respectively. The only compounds identified were chlorothalonil (79% of surface rinse and organosoluble residue in roots) and R188281 (6.2% of surface rinse and organosoluble residue in roots). The levels at 21 days PHI were approximately 0.019 and 0.0015 mg/kg for chlorothalonil and R188281, respectively. Some minor, not completely identified compounds were found at very low levels. Translocation of ^{14}C-residue from the site of application (foliage) to the edible portion (root) was limited. The residue levels in the water-soluble and un-extracted fractions were at or below 0.01 mg/kg.

Celery plants were treated with 12 applications of [phenyl-U-^{14}C]-chlorothalonil at a rate of 2.5 kg a.s./ha (total of 30 kg a.s./ha). Plants were harvested at 7 and 21 days after the last treatment and separated into foliage and stalks. TRR for samples of stalks and foliage taken 7 days after treatment were 1.0-4.6 mg/kg and 161-263 mg/kg, respectively. On day 21, TRR levels in stalk were in the range 0.7-1.4 mg/kg and for foliage were in the range 52-78 mg/kg. Chlorothalonil was the only identifiable constituent in celery stalks (0.08-2.57 mg/kg) and foliage (22- 210 mg/kg) and accounted for up to 72-80% TRR. Neither R182281 nor R611965 (3-carboxy-2,5,6-trichloro benzamide, or SDS-46851) was detected. Up to 0.95 mg/kg and 34 mg/kg in stalk and foliage, respectively, was unidentified water-soluble and un-extracted residue. The water soluble and un-extracted fractions were treated by acid hydrolysis and hydrolytic enzymes, however, none of the many minor components in the aqueous soluble fractions of stalks or foliar samples could be identified. Further chemical and enzymatic hydrolysis of foliar samples did not release identifiable organo soluble components.

Snap bean plants were treated with four applications of [phenyl-U-^{14}C]-chlorothalonil at the rate of 2.46 kg a.s./ha. The plants were harvested 7 and 28 days after the last treatment. TRR in beans and leaves 7 days after treatment were in the range 0.90-1.2 mg/kg and 110-220 mg/kg, respectively. At 28 days PHI, these levels were in the range 1.0-3.1 mg/kg and 31-160 mg/kg, respectively. The major component of the organosoluble fraction in beans was identified as chlorothalonil, accounting for 20-31%TRR (0.18-0.30 mg/kg) and 3.3-14% TRR (0.03-0.43 mg/kg), at 7 and 28 days PHI, respectively. In the foliar samples, these values were 77-80% (82-170 mg/kg) and 33-70 (10-110 mg/kg), at 7 and 28 days PHI, respectively. R182281 and R611965 were also identified but not at quantifiable levels. Water-soluble and un-extracted residues in beans accounted for between to 50-60%TRR (0.43-0.18 mg/kg) and 14-28%TRR (0.12-0.75 mg/kg). Further analysis of the water-soluble fractions by a variety of techniques identified complex, multi-component mixtures. Each of these components was estimated to be <0.02 mg/kg. Similar efforts were applied to the un-extracted fraction in an attempt to characterise and identify these residues. Only small amounts were released, but appeared to be not organosoluble.

Pea plants were treated with a single spray application of [phenyl-U- ^{14}C]-chlorothalonil at a rate of 1.4 kg a.s./ha. Vines, pods and seeds (peas) were harvested one hour, and 7, 14, 30 and 41 days after

application. Total residues at 14 days after application were up to 0.04 mg /kg in peas, 10 mg/kg in pods, and 56 mg/kg in vines. TRR at maturity were up to 0.07 mg/kg in peas, 28 mg /kg in pods, and 71 mg/kg in vines. Peas contained 0.003 mg/kg of chlorothalonil and several other minor components at levels <0.01 mg/kg. About 80% TRR for mature vines and pods was removed by organic surface washes. Chlorothalonil accounted for 75% (21 mg/kg) to 78% (55 mg /kg) of the TRR in the surface washes, for vines and pods respectively. R182281 and a diglutathione conjugate accounted for 1.5 and 0.9 mg/kg, respectively, in pods and for 3.1 and 2.0 mg/kg, respectively in vines. The data indicated that systemic transport to the pods is very limited (<10% of the levels observed upon whole plant application) whereas transport to peas is significant.

Winter wheat was treated with a single spray application of [phenyl-U- ^{14}C]-chlorothalonil at a rate of 1.0 kg a.s./ha. Samples of immature wheat were taken 2 h after application and after 4 weeks. A further sample of wheat was taken 4 weeks prior to harvest with the remaining mature wheat taken at harvest. Mature wheat samples were separated into grain and straw. The mean total level of radioactive residues (TRR) amounted to 0.10 mg/kg in immature ears 4 weeks after treatment, to 0.05 mg/kg one month before harvest, and decreased to <0.01 mg/kg in mature grain at harvest. Characterisation and identification of residues in mature grain were not performed because of the low total residue levels. In forage, mean TRR levels were 51 mg/kg 2 h after application. In wheat straw, mean TRR levels varied from 6.8 mg/kg 4 weeks after application, to 1.7 mg/kg one month before maturity and 8.4 mg/kg at maturity due to growth and loss of moisture on ripening. The proportion of extractable residue decreased from 93% in forage to 48% for wheat straw at maturity. Chlorothalonil represented 89% TRR (45 mg/kg) in immature wheat 2 h after application, and 2.1% TRR (<0.1 mg/kg) 1 month before maturity. Chlorothalonil and R182281 appeared to be minor components in mature straw at levels of 0.02 mg/kg (0.2% TRR) and 0.04 mg/kg (0.5% TRR), respectively. The major component appeared to be a (di- and/or tri) glutathione conjugate of chlorothalonil at levels of 0.73 mg/kg (9.3% TRR). In addition, a large number of other components were present, none of which represented more than 8.1% TRR.

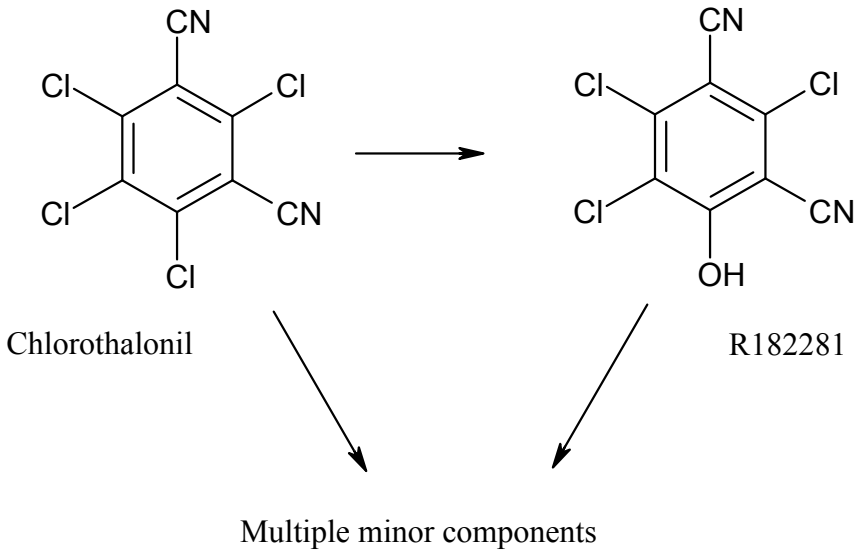
A comparison of the data in the different crops indicates that the biotransformation of chlorothalonil is qualitatively similar and chlorothalonil represents the major residue component. In general, this compound accounted for at least 50% of the total residue and over 90% of the identified residue components in edible parts. Other identified residue components generally accounted for less than 5% of the total residue in edible portions and frequently remained below the LOQ.

Two metabolites (R182281 and R611965) were identified. The major identified metabolite in primary crops, R182281, never reached a level higher than 10% of the level of the parent compound in edible parts. Only in carrot foliage at longer post-harvest intervals did R182281 represent the major identified residue component. The relative R182281 levels in carrot foliage increased from 14% of the identified residue at a PHI of 7 days to 75% at a PHI of 21 days. The level of R611965 always remained below the LOQ. There were some indications for the existence of other metabolites but all were considered to be toxicologically not relevant as they were water-soluble and assumed to be glutathione conjugates.

Parent chlorothalonil was the most important compound in all crops. The metabolism of chlorothalonil in plants was not highly extensive. It involves the substitution of chlorine by a hydroxyl group, leading to metabolite R182281.

The proposed metabolic pathway for chlorothalonil is given in Figure 6.2.1-1. The implications of the studies for the definition of the residue in plants are discussed in Point CA 6.7.1.

Figure 6.2.1-1: Proposed metabolic pathway for chlorothalonil in plants



CA 6.2.2 Poultry

The metabolism of chlorothalonil and R182281 has been studied in laying hens using ^{14}C-chlorothalonil and ^{14}C-R182281 labelled uniformly in the phenyl ring.

The studies were evaluated under Council Directive 91/414/EEC and are presented in the chlorothalonil monograph (**Vol.3, Annex B, Section B.7.2, January 2000**).

Species	Author/s	Issue Year	Report Number
Hen – Chlorothalonil	Capps TM	1983	596-4AM-82-0122-002
Hen – R182281	Capps TM	1983	593-4AM-82-0123-002

An executive summary of the studies submitted for Annex I listing is presented below. Since Annex I listing, a new metabolism study has been carried out in hens. This study is summarised in detail below after the Executive summary of the studies submitted for Annex I listing. An overall summary of all livestock metabolism studies is presented in Section CA 6.2.6.

EXECUTIVE SUMMARY OF HEN METABOLISM STUDIES SUBMITTED FOR ANNEX I LISTING OF CHLOROTHALONIL

The metabolism of chlorothalonil in laying hens was investigated in a study with [phenyl-U-^{14}C]-labelled chlorothalonil

Groups of laying hens (leghorn) were treated at dose rates of 0.22, 0.65 and 2.18 mg/kg bw/day ^{14}C-chlorothalonil by capsule for 21 consecutive days.

The animals were sacrificed 6 hours, 3 days and 7 days after the last dose. Eggs were collected daily. Liver, muscle, skin and fat were collected at sacrifice.

Total radioactive residues in tissues, egg yolk and egg white samples were measured by combustion and LSC. Extraction and characterisation of radioactive residues was not performed.

The transfer of residues to eggs and tissues was limited. Total radioactive residues were below the LOD in egg white for all dose levels and in egg yolk at all dose levels except the highest. At the highest dose level the total radioactivity in egg yolk accounted for 0.05 mg/kg.

Total residue levels in tissue were all below the LOD except in liver for the middle and highest dose levels. The highest residues found were for the group sacrificed 6 hours after the final dosing (0.098 mg/kg and 0.05 mg/kg for the medium and highest dose levels respectively). The residue levels at other depuration periods were below the LOD.

A second study was conducted with laying hens using ^{14}C- R182281 labelled uniformly in phenyl ring.

In this study, groups of laying hens (white Leghorn) were treated orally with a daily dose at 0.01, 0.03 and 0.1 mg/kg bw/day ^{14}C-R182281 via capsule for 21 consecutive days. The animals were sacrificed 6 hours, 3 days and 7 days after the last dose. Eggs were collected daily. Liver, muscle, skin and fat were collected at sacrifice.

Total radioactive residues in tissues, egg yolk and egg white were measured by combustion and LSC. Extraction and characterisation of radioactive residues was not performed.

At the lowest dose level of 0.01 mg/kg bw/day, residue levels were close to or below the LOD in eggs and tissue samples. At the dose level of 0.03 mg/kg bw/day, significant residues were only found in egg yolk (0.05-0.12 mg /kg) and liver (0.05-0.27 mg/kg). At the highest dose level, significant residues were found in egg yolk (0.06-0.42 mg/kg), cardiac muscle (0.15 mg/kg), liver (0.12-0.78 mg kg) and skin (0.37 mg/kg). In egg yolk, the plateau was reached after 11, 6 and 4 days in 0.01, 0.03 and 0.1 mg/kg bw/day dose groups, respectively.

Additional hen metabolism study

An additional metabolism study with chlorothalonil in hen has been conducted. This study was not available during the first EU evaluation of chlorothalonil. The study was conducted in order to characterise and identify metabolites as the studies considered in the original EU evaluation did not include any metabolite identification.

Report:	K-CA 6.2.2/01. Hardwick T (2014). [^{14}C]-Chlorothalonil - metabolism of [^{14}C]-chlorothalonil in the laying hen. Report number: 8243812. Covance Laboratories Limited, Otley Road, Harrogate, North Yorkshire, HG3 1PY, UK. Unpublished. Syngenta Task No TK0046447.Syngenta Report Number 8243812. (Syngenta File No: R044686_11082)

Guidelines

OECD Guideline for the Testing of Chemicals, 503, Metabolism in Livestock (January 2007).

EPA Residue Chemistry Test Guideline OCSPP 860.1300, Nature of the Residue in Plants, Livestock (August 1996).

Regulation (EC) No 1107/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market.

Commission Regulation (EU) No 283/2013 of 1 March 2013 setting out the data requirements for active substances, in accordance with Regulation (EC) No 1107/2009 of the European Parliament and of the Council concerning the placing of plant protection products on the market.

GLP

The study was carried out according to the principles of Good Laboratory Practice.

EXECUTIVE SUMMARY

Six laying hens were dosed orally with [phenyl-U- ^{14}C]-chlorothalonil for 14 days at a nominal rate of 15 mg/kg, based on dietary dry matter intake. The actual dose rate achieved, based on measured food consumption, was approximately 24.5 mg/kg. Excreta and eggs were collected daily. Eggs were separated into yolk and white. The hens were sacrificed approximately 12 hours after the administration of the final dose and tissues taken post mortem for quantification and analysis.

The radioactive residue was determined in all samples by solubilisation and LSC counting. Excreta were homogenised in water. All other samples were macerated to a homogenous consistency.

Liver, egg yolk and skin samples, which contained radioactive residues greater than 0.01 mg/kg, were subjected to further analysis to determine the metabolic profile.

Samples were extracted with organic solvents, extracted residues were further fractionated and characterised. Residues present in the principal fractions were subject to high performance liquid chromatograph and thin layer chromatography/bio-image analysis for quantification and identification/characterisation by comparison with authentic reference standards of parent chlorothalonil and its metabolites.

The mean radioactive balance for all hens was greater than 93% with the majority of the radioactivity (91%) accountable in the excreta.

Residues, determined by solubilisation, were found in liver (0.139 mg/kg), skin plus subcutaneous fat (0.100 mg/kg), perirenal fat (0.035 mg/kg) and peritoneal fat (<0.1 mg/kg). Residues in muscle and egg white were below the LOQ (<0.010 mg/kg). In egg yolk, mean residues reached a maximum of 0.087 mg/kg after 13 days dosing. Sub samples of liver skin and egg yolk were analysed further to determine the nature of the residue. Following extraction with organic solvents 32.3 to 58.3% of the TRR was solubilised.

Chlorothalonil was not detected in any of the samples. The phenolic metabolite, R182281, was the only identified residue and was found at levels of up to 35.9% TRR and 0.050 mg/kg (see table below).

Identified Components	Egg yolk		Whole egg		Liver		Skin	
	%TRR	mg/kg	%TRR	mg/kg	%TRR	mg/kg	%TRR	mg/kg
R182281	12.5	0.011	13.0	0.003	35.9	0.050	3.2	0.004

In excreta, 91% of the administered dose was recovered. The major identified component was chlorothalonil (43.2% TRR) with R182281 (2.3% TRR) the only other identified metabolite.

Unextractable residues were characterised following extraction with aqueous solvents, treatment with SDS with subsequent protein precipitation, acidic and basic hydrolysis and protease digestion. Where residue and radioactive levels were sufficient, these matrices were subjected to HPLC and TLC to

determine the nature of the residues. In the unextractable residues only R182281 was tentatively identified in eggs; in all other samples, HPLC and TLC analysis were inconclusive.

During TLC analysis, a proportion of radioactivity did not elute from the origin. This region accounted for 23.8% TRR (0.022 mg/kg) in egg yolk, 10.1% TRR (0.014 mg/kg) in liver and 4.2% TRR (0.004 mg/kg) in skin plus subcutaneous fat.

In order to demonstrate the storage stability in liver and egg yolk, chromatographic profiles obtained initially (within 6 months of sampling) were compared with profiles of the same extracts obtained on completion of the analysis.

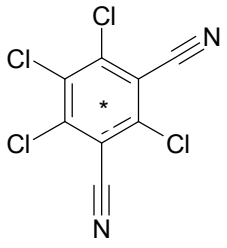
Following 14 consecutive daily doses of [phenyl-U-^{14}C]-chlorothalonil to laying hens at a nominal rate of 15 mg chlorothalonil equivalents/kg dry matter in the feed it was concluded that:

- [^{14}C]-chlorothalonil and/or its biotransformation products are readily excreted, as ≥91% of the dosed radioactivity was accounted for in the excreta and cagewash.
- Radioactive residues reached a plateau total in eggs after 10 days.
- Radioactive residues were ≤0.207 mg/kg in eggs and tissues.
- R182281 was the only residue identified in liver, eggs and skin plus subcutaneous fat.
- In excreta, chlorothalonil was the major extractable residue with R182281 being the only other residue identified.

I. MATERIALS AND METHODS

A. MATERIALS

A1. Test Materials

Structure/Label:	[Phenyl-U-^{14}C]-Chlorothalonil
Common name	Chlorothalonil
Syngenta code	R044686
CAS Number:	1897-45-6
Batch Number:	ILA-302.1B
Specific Activity:	57.1 µCi/mg (2.113 MBq/mg)
Radiochemical Purity:	97.8%
Structure: (* marks position of radiolabel)	

A2. Test Animals

Species	Hen
Gender	Female
Weight at first dosing	1.8 to 2.0 kg
Number of animals	6
Acclimatisation Period	14 days
Diet	Measured ration of commercially available non-medicated ground concentrate and offered grit *ad libitum*

Water	Tap water, *ad libitum*
Housing	Individual metabolism cages
Environmental Conditions:	
Temperature	14-22ºC
Humidity	23-98%
Photoperiod	Alternating 16-hour light and 8 h dark cycles.

B. STUDY DESIGN AND METHODS

B1. Dosing Regime

Nominal Dose Rate:	15.0 mg/kg (dry weight)
Actual Dose Rates	18.7-30 mg/kg (dry weight)
Mean Food consumption on Days 1 to 14 of dosing period (kg feed as received/day):	0.118-0.161 kg
Vehicle:	Gelatin capsule
Timing:	Once daily
Duration:	14 days
Interval from last dose to sacrifice:	11-12 hours after final dose

B2. Sample Collection

Egg collection:	Twice daily, separated into yolk and white
Excreta collection:	Once daily
Samples taken post mortem:	Liver, fat, skin (including subcutaneous fat), muscle, blood, GI tract, bile, carcass

B3. Extraction and Fractionation of Residues

Tissue samples were homogenised using standard food preparation units whilst frozen on dry ice. Radioactivity in samples was quantified by combustion and subsequent LSC analysis.

Sub-samples of liver were sequentially extracted with acetonitrile: water (4:1 v/v) followed by 2% w/v sodium dodecyl sulphate solution and acetonitrile water (4:1 v/v). The extraction solids were subjected to acid hydrolysis in 1M HCl followed by base hydrolysis in 1M ammonia solution. The residue following base hydrolysis was subjected to protease digestion hydrolysis by incubation for *ca* 18 hours at *ca* 37°C.

Samples of egg yolk, from Day 14, were pooled from all animals and sequentially extracted with hexane, ethyl acetate, acetonitrile, 1% formic acid in acetonitrile, water, 1M HCl and 1M ammonia. The ethyl acetate, acetonitrile and 1% formic acid in acetonitrile extracts were pooled, concentrated and partitioned against hexane. The hexane was then partitioned against 1% formic acid in acetonitrile and acetonitrile:water (9:1 v:v). The residue from the organic and aqueous extractions was sequentially extracted with aliquots of 2% w/v sodium dodecyl sulphate solution. The extraction solids were subjected to base hydrolysis in 0.1M ammonia solution followed by acid hydrolysis in 0.1M HCl. The residue following acid hydrolysis was subjected to protease digestion hydrolysis by incubation for *ca* 18 hours at *ca* 37°C.

Composite fat with skin samples were initially homogenised in hexane then sequentially extracted with ethyl acetate, acetonitrile, 1% formic acid in acetonitrile, water, 1M HCl and 1M ammonia. The ethyl acetate, acetonitrile and 1% formic acid in acetonitrile extracts were pooled as were the water, 1M HCl and 1M ammonia extracts. The residue from the organic and aqueous extract was sequentially extracted

with aliquots of 2% w/v sodium dodecyl sulphate solution. The extraction solids were subjected to base hydrolysis in 0.1M ammonia solution followed by acid hydrolysis in 0.1M HCl. The residue following acid hydrolysis was subjected to protease digestion hydrolysis by incubation for *ca* 18 hours at *ca* 37°C.

Portions of the samples extracts were analysed by HPLC and TLC to determine the metabolite profile.

II. RESULTS AND DISCUSSION

Total Radioactive Residues and Extractability

The distribution of radioactivity found in hens treated with [phenyl-U- ^{14}C]-chlorothalonil is presented in Table 6.2.2-1. The mean radioactive balance for all hens was greater than 93% with the majority of the radioactivity (91%) accountable in the excreta.

Table 6.2.2-1: Distribution of radioactivity and material balance from laying hens treated with [phenyl-U- ^{14}C]-chlorothalonil

Sample	% of dosed radioactivity recovered in sample
Excreta	90.97
Cage Wash	1.314
Egg White	<0.001
Egg Yolk	0.028
Liver	0.017
Breast Muscle	<0.001
Leg Muscle	<0.001
Peritoneal Fat	<0.001
Perirenal Fat	<0.001
Skin	0.002
Gastrointestinal tract contents	0.954
Material Balance	93.28

NS = Not Sampled
NA – Not Applicable

The mean total radioactive residues (TRRs) in egg white and yolk samples are presented in Table 6.2.2-2 along with calculated TRR values for whole egg. Residues in eggs white were below the LOQ (0.004 mg/kg) in all samples. Residues in egg yolk reached with a plateau concentration after 10 days dosing. In whole eggs, a plateau concentration of approximately 0.024 mg/kg was reached 10 days after the start of dosing.

Table 6.2.2-2: Total radioactive residues in eggs from laying hens treated with [phenyl-U- ^{14}C]-chlorothalonil

Sampling time	Mean total radioactive residue, TRR (mg/kg)		
	Egg white	Egg yolk	Whole egg[1]
Day 1	< 0.004	<0.004	<0.005
Day 2	< 0.004	0.007	0.002
Day 3	< 0.004	0.014	0.004
Day 4	< 0.004	0.029	0.008
Day 5	< 0.004	0.040	0.012
Day 6	< 0.004	0.057	0.018
Day 7	< 0.004	0.063	0.017
Day 8	< 0.004	0.074	0.015
Day 9	< 0.004	0.075	0.021
Day 10	< 0.004	0.083	0.024
Day 11	< 0.004	0.083	0.020
Day 12	< 0.004	0.086	0.026
Day 13	< 0.004	0.087	0.024
Day 14	< 0.004	0.084	0.019

[1] calculated on the basis of the weight of egg white and egg yolk.
NS = Not Sampled
NA – Not Applicable

TRR were 0.148 mg/kg in liver, 0.101 mg/kg in skin, 0.035 mg/kg in perirenal fat and 0.003 mg/kg in peritoneal fat. Residues in breast and leg muscle were below the LOQ. Concentrations of radioactivity in blood and plasma were 0.146 and 0.145 mg/kg, respectively. A summary of the total radioactive residues and extractability of residues is presented in Table 6.2.2-3.

Table 6.2.2-3: Summary of total radioactive residues and extractability in tissue and egg samples from laying hens treated with ^{14}C-chlorothalonil

Sample	TRR [1]	Extractable Radioactivity		Non-extractable Radioactivity	
	mg/kg	%TRR	mg/kg	%TRR	mg/kg
Peritoneal fat	0.003	NA	NA	NA	NA
Perirenal fat[2]	0.035	NA	NA	NA	NA
Breast muscle	<0.009	NA	NA	NA	NA
Leg/thigh muscle	<0.010	NA	NA	NA	NA
Liver	0.139	58.3	0.081	41.7	0.058
Egg yolk	0.091	44.4	0.040	55.3	0.050
Whole egg[4]	0.174	-	-	-	-
Skin and Fat [3]	0.100	32.3	0.032	67.7	0.068

[1] mg/kg calculated directly from radioactivity extracted, radioactivity in the debris and specific activity.
[2] There was insufficient sample to extract perirenal fat further.
[3] Composite skin with fat samples (excludes peritoneal fat).
[4] Calculated based on TRR in egg white and yolk and corrected for weight of whole eggs. See Table 6.2.2-5.
ND Not detected.
NA Not extracted.

Characterisation and Identification of Residues

The extracted radioactivity was analysed by TLC with UV and bio-imaging detection. Further analysis was conducted by HPLC. Metabolites were identified by comparison with reference standards and by HPLC-MS. Identification of radioactive residues is summarised in Table 6.2.2-4.

A sub-sample of **excreta** was sequentially extracted with ethyl acetate, acetonitrile, 1% formic acid in acetonitrile and methanol. Significant residues were extracted into the organic extracts corresponding to 55.6% TRR. Analysis by HPLC showed the presence of the parent molecule, chlorothalonil, as the major residue, accounting for 77.7% of the injected activity (43.2% TRR). Two minor metabolites were detected, one accounting for 1.3% of the injected radioactivity and the other corresponded to R182281, accounting for 4.2% of the injected radioactivity (2.3% TRR).

Table 6.2.2-4: Summary of the characterisation and identification of components in tissues and eggs from laying hens treated with ^{14}C-chlorothalonil

		Liver		Egg Yolk		Skin and fat	
TRR		0.139		0.091		0.100	
Extract for chromatography (% TRR)		49.1		42.5		32.3	
Origin of component	**Component**	**% TRR**	**Residue (mg/kg)**	**% TRR**	**Residue (mg/kg)**	**% TRR**	**Residue (mg/kg)**
Chromatographed [1]	R182281	35.9	0.050	12.5	0.011	3.2	0.001
	Unassigned [2]	1.3	0.002	5.0	0.004	1.1	0.001
	Baseline [3]	10.1	0.014	23.8	0.022	4.2	0.004
	Remainder [4]	0.9	<0.001	2.7	0.002	0.5	<0.001
	Other fractions[5]	-	-	-	-	13.3	0.13
	Losses on fractionation [6]	9.2	0.013	1.9	0.001	2.1	0.002
	Un-extracted [7]	41.7	0.058	55.3	0.050	67.7	0.068
	Total	99.1	0.137	101.2	0.090	92.1	0.092

[1] The components of the TRR that were derived from chromatographic analysis.
[2] Components resolved away from the origin in TLC. In all matrices this comprised at least three discrete components, none of which ≥2.3% TRR.
[3] Polar material on origin (TLC).
[4] Diffuse areas of radioactivity not assigned to discrete radioactive components.
[5] Extractable residues that were not analysed or gave no result in TLC analysis. No single fraction comprised ≥17.8% TRR (≥0.013 mg/kg).
[6] The net cumulative incremental losses during analysis. Calculation: 100 % - sum of all components.
[7] Radioactivity remaining in the debris after extraction with organic solvents.

In **egg yolk,** significant residues were extracted into the organic solvents corresponding to a total of 34.4% TRR (0.031 mg/kg). Only 10.0% TRR (0.009 mg/kg) was extracted by the aqueous solvents. Un-extracted radioactivity accounted for 55.3% TRR (0.050 mg/kg).

HPLC analysis of the organic egg yolk extract indicated that the largest region of radioactivity was R182281. TLC analysis with co-chromatography confirmed the presence of R182281 which accounted for 12.0% TRR (0.011 mg/kg). There were three other components each accounting for < 4.4% TRR (0.004 mg/kg). HPLC analysis of the aqueous egg yolk extract was inconclusive, with no region above the limit of quantification. TLC analysis with co-chromatography indicated the presence of R182281. During TLC analysis, a proportion of radioactivity did not elute from the origin accounting for 15.0% TRR (0.014 mg/kg).

Base hydrolysis of the un-extracted radioactivity released 26.3% TRR (0.024 mg/kg), acid hydrolysis released 6.2% TRR (0.006 mg/kg) and enzyme hydrolysis released 37.5% TRR (0.034 mg/kg). HPLC analysis of these extracts was inconclusive. There were no regions above the LOQ. TLC analysis of the extracts indicated tentative identification of R182281.

Levels of R182281 identified in egg yolk were adjusted to take into account the whole egg based on the weight of egg white and yolk determined during the study. These data are summarised in Table 6.2.2-5. The residue level of R182281 in whole egg was calculated to be equivalent to 0.003 mg/kg on this basis.

Table 6.2.2-5: Calculation of residues in whole egg samples from laying hens treated with ^{14}C-chlorothalonil

	Egg Yolk			Egg White			Total Egg	
	TRR: 0.083 mg/kg			TRR: 0 mg/kg			TRR: 0.023 mg/kg	
	1.395 µg equiv			0.000 µg equiv			1.395 µg equiv	
Radiocomponent	%TRR	mg/kg	µg equiv	%TRR	mg/kg	µg equiv	µg equiv	mg/kg
R182281	12.5	0.011	0.174	0	0.000	0.000	0.174	0.003

Average weight of **yolks** that were combined for nature of residue analysis	16.802 g
Average weight of **whites** that were combined for nature of residue analysis	43.367 g
Average weight of **whole egg** (calculated from above values)	60.169 g

In **liver**, 58.3% TRR (0.081 mg/kg) was extracted in aqueous acetonitrile. The un-extracted residue accounted for 41.7% TRR (0.058 mg/kg). HPLC analysis of the organic extract indicated that the major region (34.7% TRR, 0.048 mg/kg) was R182281. There was one other component present which accounted for <7% TRR. TLC analysis with co-chromatography supported the presence of R182281 (35.9%TRR, 0.050 mg/kg). Three other regions were separated, but each accounted for <1.0% TRR. During TLC analysis, a proportion of radioactivity did not elute from the origin accounting for 10.1% TRR (0.014 mg/kg). Confirmation of the identity of R182281 was achieved by LC-MS.

Initial levels of un-extracted radioactivity accounted for 41.7% TRR (0.058 mg/kg). Following repeated extraction with 2% SDS solution, 2.9% (0.004 mg/kg) was released. The remaining residue associated to protein released further radioactivity when hydrolysed with acid (3.4% TRR, 0.005 mg/kg), base (7.4% TRR, 0.010 mg/kg) and enzyme (17.1% TRR, 0.024 mg/kg).

The base hydrolysate and the protease digest were taken for chromatographic analysis. No regions above the limit of quantification were observed following HPLC analysis. TLC analysis yielded no regions that could be quantified with the majority of the radioactivity remaining at the origin.

In **fat with skin**, total of 11.1% TRR (0.011 mg/kg) was extracted into the organic solvents (ethyl acetate, acetonitrile, 1% formic acid in acetonitrile) and 13.3% TRR (0.013 mg/kg) was extracted into the aqueous solvents (water, 1M HCl and 1M ammonia solution). Un-extracted radioactivity accounted for 67.7% TRR (0.068 mg/kg).

HPLC analysis of the organic extract indicated that the major region (4.8% TRR, 0.005 mg/kg) was R182281. A second minor component at was also found (0.5% TRR, <0.001 mg/kg). TLC analysis with co-chromatography confirmed the presence of R182281 (3.2% TRR, 0.003 mg/kg) in addition to two unassigned regions each accounting for <1.0% TRR. During TLC analysis, a proportion of radioactivity did not elute from the origin accounting for 4.2% TRR (0.004 mg/kg).

SDS extracts were pooled and subjected to protein precipitation with diethyl ether/ethanol followed by basic, acidic and enzyme hydrolysis. The diethyl ether/ethanol extracted 4.8% TRR (0.005 mg/kg). Basic hydrolysis of the protein precipitate contained 1.3% TRR (0.001 mg/kg). Acidic hydrolysis of the protein precipitate contained 0.5% TRR (0.001 mg/kg). Enzyme hydrolysis of the protein precipitate contained 7.5% TRR (0.008 mg/kg).

Basic, acid and enzyme hydrolysis of the un-extracted residues released a further 2.2% TRR (0.002 mg/kg), 1.2% TRR (0.001 mg/kg) and 9.2% TRR (0.009 mg/kg) respectively. These extracts were not analysed further due to the low levels found.

Storage Stability Analysis

Initial analysis of the egg yolk and liver organic fractions took place 107 days after egg yolk collection or 85 days after necropsy. The original extracts were then re-analysed 305 days later. Comparison of the initial and final radio-profiles obtained showed no significant change in the profiles had occurred during the period of storage.

III. CONCLUSION

Following 14 consecutive daily doses of [phenyl-U-^{14}C]-chlorothalonil to laying hens at a nominal rate of 15 mg chlorothalonil equivalents/kg dry matter in the feed it was concluded:

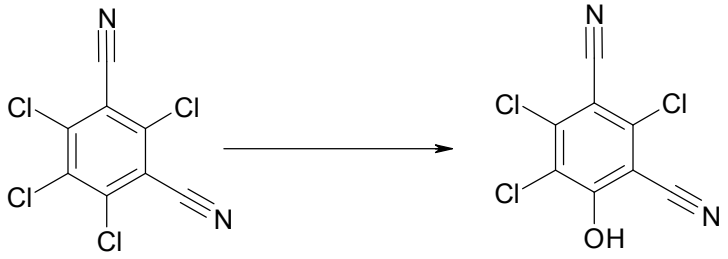
- [^{14}C]-chlorothalonil and/or its biotransformation products are readily excreted, as ≥91% of the dosed radioactivity was accounted for in the excreta and cagewash.
- Radioactive residues reached a plateau total in eggs after 10 days
- Radioactive residues were ≤0.207 mg/kg in eggs and tissues
- R182281 was the only residue identified in liver, eggs and skin plus subcutaneous fat.
- In excreta, chlorothalonil was the major extractable residue with R182281 being the only other residue identified.

(Hardwick T, 2014)

Proposed Metabolic Pathway

A metabolic pathway for chlorothalonil in the laying hen is proposed.

Figure 6.2.2-1: Proposed metabolic pathway for chlorothalonil in laying hens



Chlorothalonil R182281

CA 6.2.3 Lactating ruminants

The metabolism of chlorothalonil and R182281 has been studied in lactating ruminants using ^{14}C-chlorothalonil and ^{14}C-R182281 labelled uniformly in the phenyl ring.

The studies were evaluated under Council Directive 91/414/EEC and are presented in the chlorothalonil monograph (**Vol.3, Annex B, Section B.7.2, January 2000**).

Species	Author/s	Issue Year	Report Number
Goat – Chlorothalonil	Duane WC, Doran TJ	1990	1067-85-0080-EF-001
Goat – R182281	Ku HS	1990	1183-87-0024-EF-001
Goat – Chlorothalonil	Shaw D	1997	VCM 73/961389

An executive summary of the studies submitted for Annex I listing is presented below. An overall summary of all livestock metabolism studies is presented in section CA 6.2.6.

EXECUTIVE SUMMARY OF RUMINANT METABOLISM STUDIES SUBMITTED FOR ANNEX I LISTING OF CHLOROTHALONIL

Lactating goats (2 per dose level) were administered [phenyl-U-^{14}C]-chlorothalonil at a rate of 6 or 60 mg/day in capsules for 8 consecutive days, equivalent to 0.115 and 1.15 mg/kg bw/day. During the dosing period, milk was collected twice a day and pooled. Urine and faeces were collected daily. Blood was sampled prior to the last dose and on the day of sacrifice. At sacrifice, 10 hours after the last dosing, tissue samples of kidney, liver, muscle and fat were taken for analysis.

Radioactive residues were determined directly by LSC or by combustion and LSC.

Milk and tissue samples were derivatised, extracted by several solvents, and analysed by HPLC, GC-MS, and GPC.

The majority of the radioactivity was excreted via faces (61-63% applied radioactivity) and urine (approx. 7% applied radioactivity). At sacrifice, not more than 0.1-0.2% of the dose was recovered from each edible organ. The total radioactivity recovered was around 70% of the dose for both dose levels. Total residue levels in milk were 0.005-0.015 and 0.03-0.19 mg/kg in the low and high dose group, respectively, throughout the study. Highest total residue levels were detected in kidneys, (0.22 and 2.2 mg/kg in the low and high dose groups, respectively), followed by liver (0.08 and 0.7 mg/kg) and muscle and fat (<0.01 and 0.03 mg/kg, respectively, in both dose groups).

Parent chlorothalonil was not detected in milk and edible tissue samples (<0.01 mg/kg). R182281was the only identified metabolite in milk and tissue samples. Levels of this metabolite were < 0.01 mg/kg in milk and tissues for the low dose group. In the high dose group, R182281 levels were <0.01-0.05 in milk (25% TRR), 0.03-0.04 in liver (10% TRR), and 0.05-0.07 mg/kg in kidneys (3% TRR).

Despite several attempts to characterise more of the residue in milk, no other compounds were identified. The residues in the non-extractable fraction (<0.01 and 0.01-0.07 mg/kg in milk from low and high dose goats, respectively) were suggested to be covalent adducts to low or moderate molecular weight proteins as determined by GPC. The unidentified residues in milk from low and high dose goats were respectively <0.01 and 0.1 mg/kg in the organosoluble fraction, and <0.01 mg/kg for both dose levels in the water soluble fraction.

In liver, between 17 and 37% of the residue was characterised as organosoluble and 20-30% of this fraction consisted of multiple non-polar residues. Between 21 and 31% TRR was characterised as water soluble, presumably representing mono-, di-, and triglutathione conjugates. Between 30 and 45% of the liver residue remained not extracted. The levels of unidentified residues in liver from the low and high dose rates were <0.01 and <0.1 mg/kg in the organosoluble fraction, 0.02 and 0.2 mg/kg in the watersoluble fraction, and 0.03 and 0.3 mg/kg in the not extracted fraction.

In kidneys, about 10-15% of the total residue was organosoluble (low and high dose group), and 19-26% and 30-48% of the radiolabel was water soluble in the low and high dose group, respectively. The water soluble residues mainly consisted of protein bound and smaller conjugated residue compounds. The level of non-extractable radiolabel in solids was 43-44% TRR (0.1 mg/kg) and 35-38% TRR (0.8 mg/kg) in low dose and high dose goats, respectively, and was not analysed further. The levels of unidentified residues in low and high dose goats were approx. 0.02 and 0.15 mg/kg in the organosoluble fraction and 0.07 and 0.7 mg/kg in the water soluble fraction, respectively.

Residues in muscle and fat were not characterised or identified further.

In a second study, lactating goats were administered ^{14}C- R182281, labelled uniformly in the phenyl ring at rates of 0.4 and 4 mg daily for 9 consecutive days via capsule. During the dosing period, milk was collected twice a day and pooled, and urine and faeces were collected daily. Blood was sampled prior to

the last dose, before the final milking and on the day of sacrifice. At sacrifice, 8 hours after the last dosing, tissue samples of kidney, liver, muscle and fat were taken for analysis.

Radioactive residues were determined directly by LSC or by combustion and LSC.

Milk and tissue samples were derivatised, extracted by several solvents, and analysed by HPLC, GC-MS, and GPC.

Radioactivity excreted via urine and faeces accounted for 6-10 % and 17-19 % of the total radioactive residue, respectively. Between 13-23 % of the total radioactivity was excreted via milk. Residue levels in milk reached a plateau after 5 to 7 days and accounted for up to 0.15 and 1.0 mg/kg for the low and high dose group, respectively.

The highest total residues were detected in kidney (0.17-0.26 and 0.82-1.33 mg/ kg for the low and high dose group, respectively), followed by liver (0.07 and 0.57-0.77 mg/kg, respectively), muscle and fat (0.01-0.02 and 0.07-0.14 mg/kg in the low and high does groups, respectively). In total, over 90% of the total residues in milk and tissue samples were identified and less than 4% remained not extracted.

Over 90 % of the total residue in milk and tissues samples was characterised as organosoluble and over 90 % of this fraction was attributable to unchanged R182281. No other identifiable metabolites were detected in the milk or tissue samples.

In urine, the metabolite 2,4,5-trichloro-6-hydroxy-3-cyanobenzamide (R611968, SDS-47525) was identified and accounted for 3.6% of the total residue present in urine. One unidentified urinary metabolite accounted for about 5-20% of the urinary label but was not detected in any other matrix.

A third goat metabolism study was also conducted; however it was not considered suitable for inclusion in the overall evaluation as the health of the test animal was questioned and a large proportion of the radioactivity extracted in kidney was not characterised or identified. The results of this study were similar to those found in the other two goat metabolism studies.

Based on the structures identified, the degradation of chlorothalonil in lactating goats proceeds primarily via the following pathway:

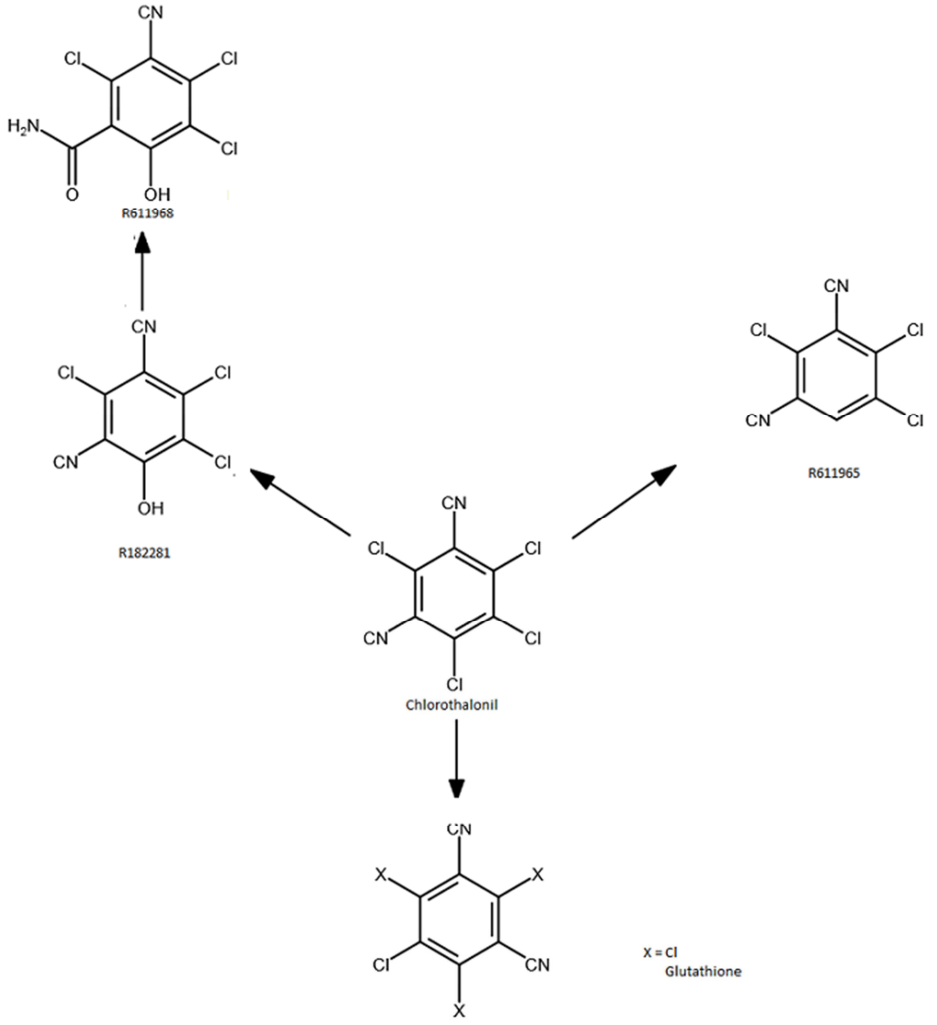
- Oxidation of chlorothalonil to 4-hydroxy-2, 5, 6-trichloroisophthalonitrile (R182281).

Chlorothalonil and phase 1 metabolism products are then presumed to under further metabolism to form glutathione conjugates.

Upon administration of the chlorothalonil metabolite R182281 to lactating goats, 2,4,5-trichloro-6-hydroxy-3-cyanobenzamide (R611968) was found as urinary metabolite (responsible for up to 3.6% of urinary radiolabel).

The biotransformation pathway is provided in Figure 6.2.3-1.

Figure 6.2.3-1: Proposed metabolic pathway for chlorothalonil in lactating goats



CA 6.2.4 Pigs

The metabolism of chlorothalonil in ruminants was similar to that seen in the rat and therefore a metabolism study in pigs is not required.

CA 6.2.5 Fish

No guideline is currently available for the estimation of the dietary burden of pesticide residues for farmed fish or for the design and conduct of fish-metabolism studies. Therefore, no fish metabolism studies have been conducted.

CA 6.2.6 Summary of metabolism, distribution and expression of residues in livestock

The metabolism of chlorothalonil in laying hens was investigated in three studies.

In the first study, groups of laying hens (leghorn) were treated with [phenyl-U-^{14}C]-labelled chlorothalonil at dose rates of 0.22, 0.65 and 2.18 mg/kg bw/day by capsule for 21 consecutive days. The animals were sacrificed 6 hours, 3 days and 7 days after the last dose. Eggs were collected daily. Liver, muscle, skin and fat were collected at sacrifice.

Total radioactive residues in tissues, egg yolk and egg white samples were measured by combustion and LSC. Extraction and characterisation of radioactive residues was not performed. The transfer of residues to eggs and tissues was limited. Total radioactive residues were below the LOD in egg white for all dose levels and in egg yolk at all dose levels except the highest. At the highest dose level the total radioactivity in egg yolk accounted for 0.05 mg/kg.

Total residue levels in tissue were all below the LOD except in liver for the middle and highest dose levels. The highest residues found were for the group sacrificed 6 hours after the final dosing (0.098 mg/kg and 0.05 mg/kg for the medium and highest dose levels respectively). The residue levels at other depuration periods were below the LOD.

In the second study laying hens were dosed daily with ^{14}C- R182281 labelled uniformly in the phenyl ring at 0.01, 0.03 and 0.1 mg/kg bw/day via capsule for twenty one consecutive days. The animals were sacrificed 6 hours, 3 days and 7 days after the last dose. Eggs were collected daily. Liver, muscle, skin and fat were collected at sacrifice.

Total radioactive residues in tissues, egg yolk and egg white were measured by combustion and LSC. Extraction and characterisation of radioactive residues was not performed. At the lowest dose level residue levels were close to or below the LOD in all samples. For the middle dose level of 0.03 mg/kg bw/day, significant residues were only found in egg yolk and liver. At the highest dose level, significant residues were found in egg yolk (0.06-0.42 mg/kg), cardiac muscle (0.15 mg/kg), liver (0.12-0.78 mg kg) and skin (0.37 mg/kg).

In a third study laying hens were dosed orally with [phenyl-U- ^{14}C]-chlorothalonil for 14 days at a nominal rate of 15 mg/kg. Excreta and eggs were collected daily. Eggs were separated into yolk and white. The hens were sacrificed approximately 12 hours after the administration of the final dose and tissues taken post mortem for quantification and analysis.

The radioactive residue was determined in all samples by solubilisation and LSC counting. Liver, egg yolk and skin samples, which contained radioactive residues greater than 0.01 mg/kg were subjected to extraction and analysis to determine the metabolic profile.

In excreta, 91% of the administered dose was recovered. The major identified component was chlorothalonil (43.2% TRR) with R182281 (2.3% TRR) the only other identified metabolite.

Chlorothalonil was not detected in any of the tissue and egg samples. The metabolite R182281 was the only identified residue and was found in significant levels in liver (35.9% TRR, 0.05 mg/kg) and egg yolk (12.5% TRR, 0.011 mg/kg).

The metabolism of chlorothalonil and R182281 has been studied in lactating ruminants using ^{14}C-chlorothalonil and ^{14}C-R182281 labelled uniformly in the phenyl ring.

Lactating goats were dosed with [phenyl-U-^{14}C]-chlorothalonil at a rate of 6 or 60 mg/day (equivalent to 0.115 and 1.15 mg/kg bw/day). Milk and tissue samples were derivatised, extracted by several solvents, and analysed by HPLC, GC-MS, and GPC. Radioactive residues were determined directly by LSC or by combustion and LSC.

The majority of the radioactivity was excreted. Parent chlorothalonil was not detected in milk and edible tissue samples. R182281was the only identified metabolite in milk and tissue samples. No other compounds were identified. In liver, between 17 and 37% of the residue was characterised as organosoluble and 20-30% of this fraction consisted of multiple non-polar residues. Between 21 and 31% TRR was characterised as water soluble. In kidneys, about 10-15% of the total residue was organosoluble,

and 19-26% and 30-48% of the radiolabel was water soluble. The water soluble residues mainly consisted of protein bound and smaller conjugated residue compounds.

In a second study, lactating goats were administered ^{14}C- R182281, labelled uniformly in the phenyl ring at rates of 0.4 and 4 mg daily for 9 consecutive days via capsule Radioactive residues were determined directly by LSC or by combustion and LSC. Milk and tissue samples were derivatised, extracted by several solvents, and analysed by HPLC, GC-MS, and GPC.

Radioactivity excreted via urine and faeces accounted for 6-19 % of the total radioactive residue. Residue levels in milk reached a plateau after 5 to 7 days. The highest total residues were detected in kidney, followed by liver, muscle and fat.

Over 90 % of the total residue in milk and tissues samples was characterised as organosoluble and over 90 % of this fraction was attributable to unchanged R182281. No other identifiable metabolites were detected in the milk or tissue samples.

In urine, the metabolite 2,4,5-trichloro-6-hydroxy-3-cyanobenzamide (R611968) was identified and accounted for 3.6% of the total residue present in urine.

A third goat metabolism study was also conducted; however it was not considered suitable for inclusion in the overall evaluation due to shortcomings in the conduct of the study and limited identification of metabolites.

Based on the structures identified, the degradation of chlorothalonil in both laying hens and lactating goats proceeds primarily via the following pathway:

- Oxidation of chlorothalonil to 4-hydroxy-2, 5, 6-trichloroisophthalonitrile (R182281).

The proposed residue definitions in commodities of animal origin are discussed in CA 6.7.1.

CA 6.3 Magnitude of Residues Trials in Plants

The use pattern for evaluation for renewal of approval of chlorothalonil is provided in **Document D1** for each representative product and is summarised below (Table 6.3-1).

Table 6.3-1: Chlorothalonil representative use patterns

Crop	Outdoor/ Protected	Growth stage	Max. No. of Applications	Minimum Application Interval (days)	Max. Application		Minimum PHI (days)
					Rate (kg a.s./ha)	Water (L/ha)	
Tomato	Outdoor (NEU)	BBCH 51-89	2	7	1.000	500 - 1500	3
	Outdoor (SEU)	BBCH 51-89	2	7	1.000	500 - 1500	3
Barley	Outdoor (NEU)	BBCH 30-59	2	14	0.750	100 - 400	NR
	Outdoor (SEU)	BBCH 30-59	2	14	0.750	100 - 400	NR
Wheat	Outdoor (NEU)	BBCH 30-69	2	14	0.750	100 - 400	NR
	Outdoor (SEU)	BBCH 30-69	2	14	0.750	100 - 400	NR
Potato	Outdoor (NEU)	BBCH 40-85	1	-	750	300-500	28
	Outdoor (SEU)	BBCH 40-85	1	-	750	300-500	28

NR – not relevant. Application is growth stage dependent and crops are harvested at maturity.

The representative crops included in the original EU review of chlorothalonil included tomato, barley, wheat and potato (and other crops) but at more critical GAPs (four applications to tomato, five applications to potato and two applications to cereals at similar timings but at a higher application rate). New trials are therefore available for tomato, barley, wheat and potato to support the new proposed critical GAP.

Residue trials in tomato, barley, wheat and potato conducted in the EU to support the proposed EU GAP are presented in Sections CA 6.3.1, CA 6.3.2, CA 6.3.3 and CA 6.3.4 respectively, below.

CA 6.3.1 Tomato

~~Chlorothalonil is proposed for use on tomato according to the following EU critical GAP, detailed in Table 6.3.1-1.~~
~~With regards to the number of applications on tomatoes this GAP deviates from the GAP presented in document D-1. Latest modelling results (as presented in the MCP section 9) have shown that the use on tomatoes can only be supported with 1 application. The presented residue trials address 2 applications, although a safe use for the 2 apps can be demonstrated from a dietary safety perspective. So the risk envelope approach can be applied.~~

~~Nevertheless trials to address one application on tomatoes are ongoing and can be presented in the course of the EU-evaluation.~~

Table 6.3.1–1: Proposed EU critical GAPs for chlorothalonil on tomato

Region	Outdoor/ Protected	Growth stage	Max. No. of Applications	Minimum Application Interval (days)	Maximum		Minimum PHI (days)
					Rate (g a.s./ha)	Water (L/ha)	
Northern EU	Outdoor	BBCH 51-89	2	7	1000	500-1500	3
Southern EU	Outdoor	BBCH 51-89	2	7	1000	500-1500	3

The residue reports supporting the proposed EU critical GAP for chlorothalonil on tomato are referenced in Table 6.3.1-2 and the data are presented in Table 6.3.1-5.

Table 6.3.1-2: Report references for trials supporting the proposed EU critical GAP for chlorothalonil on tomato

Annex Pt.	Number.	Author/s	Issue Year	Report Title
K-CA 6.3.1/01	(1 of 4)	L North	2012	Chlorothalonil and azoxystrobin - residue study on field tomato in Germany and northern France in 2011 Syngenta File No. A14111B_10063, Report No. S11-00520-REG
K-CA 6.3.1/02	(2 of 4)	D Schultz N Breyer	2013	Chlorothalonil – residue study on tomatoes in northern France and Hungary in 2012 Syngenta File No. A14111B_10825, Report No. S12-01285
K-CA 6.3.1/03	(3 of 4)	L North	2012a	Chlorothalonil and azoxystrobin - residue study on field tomato in Italy, Spain and southern France in 2011 Syngenta File No. A14111B_10060, Report No. S11-00521
K-CA 6.3.1/04	(4 of 4)	D Schultz N Breyer	2013a	Chlorothalonil – residue study on tomatoes in southern France, Italy and Spain in 2012 Syngenta File No. A14111B_10823, Report No. S12-01286

Guidelines

The studies meet the requirements of the Commission of the European Communities: General Recommendations for the Design, Preparation and Realization of Residue Trials (**7029/V1/95 rev. 5, 22/7/1997**), and are designed to comply with **Regulation (EC) 1107/2009**.

GLP

All trials (field and analytical phases) were carried out in compliance with the principles of Good Laboratory Practice.

Materials and Methods

Sixteen supervised residue trials were conducted on field grown tomato in 2011 and 2012, in northern or southern Europe. A summary of the trials conducted is presented in Table 6.3.1-3.

Table 6.3.1-3: Summary of chlorothalonil residue trials on tomato

Country	2011	2012
Northern Europe		
France (north)	3 Decline	2 Harvest
Germany	1 Decline	-
Hungary	-	2 Harvest
Southern Europe		
France (south)	1 Decline	3 Harvest
Spain	1 Decline	1 Harvest
Italy	1 Decline	1 Harvest

Decline trials are those with three or more sampling times.

Tomatoes are a major crop in northern and southern Europe and therefore generally require eight trials in each residue region.

Treatments with chlorothalonil were conducted as post emergence (BBCH 69-89) spray applications utilising the formulation as detailed in Table 6.3.1-4 at a nominal application rate of 1000 g a.s./ha (actual rates 917-1091 g a.s./ha) with an interval of 7 days between applications. The water volumes during application ranged from 380 to 808 L/ha.

Table 6.3.1-4: Summary of chlorothalonil formulations used in the presented trials

Product code	Formulation type	Composition	
		2011	2012
A14111B	SC	385 g/L chlorothalonil 78.4 g/L azoxystrobin	384 g/L chlorothalonil 74.7 g/L azoxystrobin

Samples of whole fruits were taken and analysed for residues of parent chlorothalonil and the metabolite R182281 using analytical method GRM005.01A with an LOQ of 0.01 mg/kg for both compounds. Full method descriptions and validation data are presented in document M-CA Section 4, CA 4.1.2. Procedural recovery data are presented with the results of the residues trials in Table 6.3.1-5.

Allowing for a 25% deviation from the proposed maximum application rate, rates and application timings in all trials cover the critical EU GAP.

Samples were stored up to a maximum of 8 months from sampling to extraction. Samples were homogenised in the presence of acid before freezing. Residues of chlorothalonil and R18221 are stable in acidified homogenised tomatoes for at least 24 months (see section CA 6.1) and therefore no degradation will have occurred between sampling and analysis.

The available trials are sufficient to support the EU critical GAP for tomato. 8 acceptable trials are available for northern Europe and 8 acceptable trials are available for southern Europe. Residues found in the trials from northern and southern Europe are comparable, leading to the same STMR value and similar HR values. The data sets can therefore be combined and give sufficient data to propose MRLs and conduct the consumer risk assessment.

The results of the residue trials for chlorothalonil and R182281 are presented in Table 6.3.1-5.

Table 6.3.1-5: Summary of residue data supporting the EU critical GAP for chlorothalonil on tomato

GLP and Trial Details	Crop (Variety)	Country (Region)	Application Rate Product Code	Growth Stage at application	PHI (days)	Crop Part (Growth stage at sampling)	Residue Found (Uncorrected) chlorothalonil mg/kg	 R182281 (mg/kg)	Recovery Data
Northern Europe									
Report: S11-00520 Study: : S11-00520 Trial: S11-00520-01 - Study to GLP - Study carried out in 2011	Tomato (Vanessa)	GERMANY (Europe North)	936 g a.s./ha 957 g a.s./ha A14111B	BBCH 81 BBCH 81-82	0	Fruit (BBCH 81-82)	1.6	<0.01	Chlorothalonil Whole fruit: mean = 93% RSD = 11.9% (n = 8 in 0.01 – 10.0 mg/kg spiking range) R182281 Whole fruit: mean = 99% RSD = NA (n = 2 in 0.01 – 0.20 mg/kg spiking range)
					1	Fruit (BBCH 83-85)	1.4	<0.01	
					3	Fruit (BBCH 85-89)	1.1	<0.01	
Report: S11-00520 Study: : S11-00520 Trial: S11-00520-03 - Study to GLP - Study carried out in 2011	Tomato (Brillante)	FRANCE (Europe North)	1042 g a.s./ha 950g a.s./ha A14111B	BBCH 81-82 BBCH 81-82	0	Fruit (BBCH 81-82)	0.23	<0.01	
					1	Fruit (BBCH 82-83)	0.13	<0.01	
					3	Fruit (BBCH 83-84)	0.07 ±	<0.01	
Report: S11-00520 Study: : S11-00520 Trial: S11-00520-04 - Study to GLP - Study carried out in 2011	Tomato (Topkapi)	FRANCE (Europe North)	997 g a.s./ha 1004 g a.s./ha A14111B	BBCH 81-82 BBCH 85	0	Fruit (BBCH 85)	3.0	<0.01	
					1	Fruit (BBCH 85)	1.5	<0.01	
					3	Fruit (BBCH 85)	1.4	<0.01	
Report: S11-00520 Study: : S11-00520 Trial: S11-00520-05 - Study to GLP - Study carried out in 2011	Tomato (Maestro)	FRANCE (Europe North)	1008 g a.s./ha 1000 g a.s./ha A14111B	BBCH 72-75 BBCH 73-76	0	Fruit (BBCH 73-76)	6.4	0.01	
					1	Fruit (BBCH 74-77)	9.7	0.02	
					3	Fruit (BBCH 74-77)	4.1	<0.01	
Report: S12-01285 Study: S12-01285 Trial: S12-01285-01 - Study to GLP - Study carried out in 2012	Tomato (Medina)	FRANCE (Europe North)	1002 g a.s./ha 998 g a.s./ha A14111B	BBCH 73-74 BBCH 83-84	3	Fruit (BBCH 84-85)	2.8	0.01	Chlorothalonil Whole fruit: mean = 87% RSD = 8.3% (n = 4 in 0.01 – 4.00 mg/kg spiking range)

GLP and Trial Details	Crop (Variety)	Country (Region)	Application Rate Product Code	Growth Stage at application	PHI (days)	Crop Part (Growth stage at sampling)	Residue Found (Uncorrected) chlorothalonil mg/kg	 R182281 (mg/kg)	Recovery Data
Report: S12-01285 Study: S12-01285 Trial: S12-01285-02 - Study to GLP - Study carried out in 2012	Tomato (Brillante)	FRANCE (Europe North)	1000 g a.s./ha 1058 g a.s./ha A14111B	BBCH 81-89 BBCH 81-89	3	Fruit (BBCH 81-89)	0.49	<0.01	R182281 Whole fruit: mean = 94% RSD = NA (n = 2 in 0.01 – 0.10 mg/kg spiking range)
Report: S12-01285 Study: S12-01285 Trial: S12-01285-03 - Study to GLP - Study carried out in 2012	Tomato (K-262)	HUNGARY (Europe North)	996 g a.s./ha 917 g a.s./ha A14111B	BBCH 71-73 BBCH 85-87	3	Fruit (BBCH 85-89)	0.58	<0.01	
Report: S12-01285 Study: S12-01285 Trial: S12-01285-04 - Study to GLP - Study carried out in 2012	Tomato (Lucullus)	HUNGARY (Europe North)	994 g a.s./ha 917 g a.s./ha A14111B	BBCH 83-85 BBCH 85-87	3	Fruit (BBCH 85-89)	0.21	<0.01	
Southern Europe									
Report: S11-00521 Study: S11-00521 Trial: S11-00521-02 - Study to GLP - Study carried out in 2011	Tomato (Beef Master)	FRANCE (Europe South)	1032 g a.s./ha 1039 g a.s./ha A14111B	BBCH 88-89 BBCH 89	0	Fruit (BBCH 89)	2.2	0.01	Chlorothalonil Whole fruit: mean = 93% RSD = 10.4% (n = 6 in 0.01 – 10.0 mg/kg spiking range) R182281 Whole fruit: mean = 95% RSD = NA (n = 2 in 0.01 – 0.2 mg/kg spiking range)
					1	Fruit (BBCH 89)	1.7	<0.01	
					3	Fruit (BBCH 89)	1.4	<0.01	
Report: S11-00521 Study: S11-00521 Trial: S11-00521-03 - Study to GLP - Study carried out in 2011	Tomato (Kero)	ITALY (Europe South)	1028 g a.s./ha 1026 g a.s./ha A14111B	BBCH 83-89 BBCH 83-89	0	Fruit (BBCH 85-89)	1.1	<0.01	
					1	Fruit (BBCH 87-89)	1.1	<0.01	
					3	Fruit (BBCH 87-89)	0.22	<0.01	
Report: S11-00521 Study: S11-00521 Trial: S11-00521-04 - Study to GLP - Study carried out in 2011	Tomato (Albatro)	SPAIN (Europe South)	994 g a.s./ha 1053 g a.s./ha A14111B	BBCH 82-83 BBCH 84-85	0	Fruit (BBCH 84-85)	2.2	<0.01	
					1	Fruit (BBCH 85)	2.7	<0.01	
					3	Fruit	0.47	<0.01	

GLP and Trial Details	Crop (Variety)	Country (Region)	Application Rate Product Code	Growth Stage at application	PHI (days)	Crop Part (Growth stage at sampling)	Residue Found (Uncorrected) chlorothalonil mg/kg	 R182281 (mg/kg)	Recovery Data
						(BBCH 85)			
Report: S12-01286 Study: S 12-01286 Trial: S12-01286-01 - Study to GLP - Study carried out in 2012	Tomato (Saint Pierre)	FRANCE (Europe South)	1091 g a.s./ha 1069 g a.s./ha A14111B	BBCH 69-87 BBCH 69-89	3	Fruit (BBCH 88-89)	1.4	<0.01	Chlorothalonil Whole fruit: mean = 109% RSD = 6.9% (n = 3 in 0.01 – 2.00 mg/kg spiking range) R182281 Whole fruit: mean = 107% RSD = NA (n = 2 in 0.01 – 0.10 mg/kg spiking range)
Report: S12-01286 Study: S 12-01286 Trial: S12-01286-02 - Study to GLP - Study carried out in 2012	Tomato (Ondina)	FRANCE (Europe South)	1020 g a.s./ha 1031 g a.s./ha A14111B	BBCH 85-86 BBCH 86-89	3	Fruit (BBCH 89)	0.82	<0.01	
Report: S12-01286 Study: S 12-01286 Trial: S12-01286-03 - Study to GLP - Study carried out in 2012	Tomato (Fokker)	ITALY (Europe South)	1006 g a.s./ha 994 g a.s./ha A14111B	BBCH 77-83 BBCH 77-85	3	Fruit (BBCH 88)	0.33	<0.01	
Report: S12-01286 Study: S 12-01286 Trial: S12-01286-04 - Study to GLP - Study carried out in 2012	Tomato (H-97)	SPAIN (Europe South)	1008 g a.s./ha 1080 g a.s./ha A14111B	BBCH 85-87 BBCH 87-89	3	Fruit (BBCH 87-89)	0.58	<0.01	
Report: S12-01286 Study: S 12-01286 Trial: S12-01286-05 - Study to GLP - Study carried out in 2012	Tomato (Hector)	FRANCE (Europe South)	998 g a.s./ha 1039 g a.s./ha A14111B	BBCH 85-87 BBCH 87-89	3	Fruit (BBCH 89)	0.49	<0.01	

Unless otherwise stated residues of chlorothalonil and R182281 in untreated samples were less than the LOQ.

‡ Residues of chlorothalonil 0.04 – 0.08 mg/kg found in control samples for PHI of 3 days

NA = not applicable

Findings

For MRL setting and risk assessment, the definition of the residue for chlorothalonil is parent chlorothalonil only. In addition a separate residue definition for 2,5,6-trichloro-4-hydroxyphtalonitrile (R182281) is also proposed. Separate calculations for both chlorothalonil and R182281 are presented below.

Chlorothalonil residue calculations for MRL setting and risk assessment

MRLs, STMR and HR values for tomatoes have been calculated for northern and southern Europe for chlorothalonil. The STMR is the median residue and the HR is the highest residue value found. MRLs are calculated according to the OECD calculator (**OECD Series on pesticides No. 56, ENV/JM/MONO (2011)2, 1 March 2011**). In these calculations a single data point from each trial supporting the EU critical GAP has been considered. The chlorothalonil residue values used in the MRL, STMR and HR calculations are underlined in Table 6.3.1-5. The calculated outputs are presented in Table 6.3.1-6.

Table 6.3.1-6: MRL, STMR and HR calculations for chlorothalonil on tomato (fruit) – proposed EU GAPs

Region	Outdoor / Protected	Residue Data (mg/kg)	MRL OECD Method (mg/kg)	MRL OECD Rounded (mg/kg)	STMR (mg/kg)	HR (mg/kg)
Northern EU	Outdoor	0.07, 0.21, 0.49, 0.58, 1.1, 1.4, 2.8, 4.1	7.00	7	0.84	4.1
Southern EU	Outdoor	0.22, 0.33, 0.47, 0.49, 0.58, 0.82, 2 x 1.4	2.55	3	0.54	1.4
Combined EU	Outdoor	0.07, 0.21, 0.22, 0.33, 0.47, 2 x 0.49, 2 x 0.58, 0.82, 1.1, 3 x 1.4, 2.8, 4.1	5.30	6	0.58	4.1

There is an existing EU MRL of 2.0 mg/kg for chlorothalonil on tomatoes (parent chlorothalonil). A recent proposal currently being considered (SANCO 12240/2013) has proposed a MRL of 6 mg/kg. The data presented in Table 6.3.1-6 from trials supporting the proposed EU critical GAP indicate that residues will be within the recently proposed EU MRL of 6 mg/kg; however the MRL calculated for northern Europe data alone according to the OECD method gives a value of 7 mg/kg. 8 acceptable trials are available for northern Europe and 8 acceptable trials are available for southern Europe. Taking into account the data from both northern and southern Europe the MRL of 6 mg/kg will not be exceeded.

R182281 residue calculations for MRL setting and risk assessment

MRLs, STMR and HR values for tomatoes have been calculated for northern and southern Europe for R182281. The STMR is the median residue and the HR is the highest residue value found. MRLs are calculated according to the OECD calculator (**OECD Series on pesticides No. 56, ENV/JM/MONO (2011)2, 1 March 2011**). In these calculations a single data point from each trial supporting the EU critical GAP has been considered. The R182281 residue values used in the MRL, STMR and HR calculations are underlined in Table 6.3.1-5. The calculated outputs are presented in Table 6.3.1-7.

Table 6.3.1-7: MRL, STMR and HR calculations for R182281 on tomato (fruit) – proposed EU GAPs

Region	Outdoor / Protected	Residue Data (mg/kg)	MRL OECD Method (mg/kg)	MRL OECD Rounded (mg/kg)	STMR (mg/kg)	HR (mg/kg)
Northern EU	Outdoor	7 x <0.01, 0.01	0.013	0.015	0.01	0.01
Southern EU	Outdoor	8 x <0.01	0.010	0.01	0.01	0.01
Combined	Outdoor	15 x <0.01, 0.01	0.011	0.015	0.01	0.01

Region	Outdoor / Protected	Residue Data (mg/kg)	MRL OECD Method (mg/kg)	MRL OECD Rounded (mg/kg)	STMR (mg/kg)	HR (mg/kg)
EU						

There are currently no EU MRLs for R182281. The data presented in Table 6.3.1-7 from trials supporting the proposed EU critical GAP indicate that an MRL of 0.03 mg/kg is appropriate.

Conclusions

The proposed EU MRLs for chlorothalonil and R182281 together with the corresponding STMR and HR for risk assessment for tomatoes are presented in Table 6.3.1-8 and Table 6.3.1-9, respectively.

Table 6.3.1-8: Proposed EU MRL and proposed STMR and HR for chlorothalonil on tomatoes

Commodity (code)	Existing EU MRL (mg/kg)	Proposed EU MRL (mg/kg)	STMR (mg/kg)	HR (mg/kg)
Tomatoes (0231010)	2/6‡	6	0.54	4.1

‡ proposal currently being considered (SANCO 12240/2013)

Table 6.3.1-9: Proposed EU MRL and proposed STMR and HR for R182281 on tomatoes

Commodity (code)	Existing EU MRL (mg/kg)	Proposed EU MRL (mg/kg)	STMR (mg/kg)	HR (mg/kg)
Tomatoes (0231010)	-	0.015	0.01	0.01

Following communications with the RMS it was agreed the new tomato residue trials conducted a reduced critical GAP could be included in the M-CA Section 6 under specified conditions in the presentation of the trial data.

Chlorothalonil is proposed for use on tomato according to the following EU critical GAP, detailed in Table 6.3.1-1.

Table 6.3.1–1: Proposed EU critical GAPs for chlorothalonil on tomato

Region	Outdoor/ Protected	Growth stage	Max. No. of Applications	Minimum Application Interval (days)	Maximum		Minimum PHI (days)
					Rate (g a.s./ha)	Water (L/ha)	
Northern EU	Outdoor	BBCH 51-89	1	-	1000	500-1500	3
Southern EU	Outdoor	BBCH 51-89	1	-	1000	500-1500	3

The residue reports supporting the proposed EU critical GAP for chlorothalonil on tomato are referenced in Table 6.3.1-2 and the data are presented in Table 6.3.1-5.

Table 6.3.1-2: Report references for trials supporting the proposed EU critical GAP for chlorothalonil on tomato

Annex Pt.	Number.	Author/s	Issue Year	Report Title
K-CA 6.3.1/01	(1 of 3)	D Schulz, C Trumper	2016	Chlorothalonil - Residue study on Field Tomatoes in Southern France, Spain and Italy in 2014 Syngenta File No. A7867A_11391, Syngenta Report No. S14-02773
K-CA 6.3.1/02	(2 of 3)	D Schultz C Trumper	2015	Chlorothalonil - Residue study on Field Tomatoes in Northern France, Poland and Hungary in 2014 Syngenta File No. A7867A_11386, Report No. S14-02774
K-CA 6.3.1/03	(3 of 3)	D Schultz C Trumper	2016a	Chlorothalonil – Residue study on Field Tomato in Northern France and Germany in 2015 Syngenta File No. A7867A_11403, Report No. S15-02003

Guidelines

The studies meet the requirements of the Commission of the European Communities: General Recommendations for the Design, Preparation and Realization of Residue Trials (**7029/V1/95 rev. 5, 22/7/1997**), and are designed to comply with **Regulation (EC) 1107/2009**.

GLP

All trials (field and analytical phases) were carried out in compliance with the principles of Good Laboratory Practice.

Materials and Methods

Sixteen supervised residue trials were conducted on field grown tomato in 2014 and 2014, in northern or southern Europe. A summary of the trials conducted is presented in Table 6.3.1-3.

Table 6.3.1-3: Summary of chlorothalonil residue trials on tomato

Country	2014	2015
Northern Europe		
France (north)	1 Decline	1 Decline; 1 Harvest
Germany	-	1 Decline; 1 Harvest
Hungary	1 Harvest	-
Poland	1 Decline; 1 Harvest	
Southern Europe		
France (south)	1 Harvest	-
Spain	2 Decline; 3 Harvest	-
Italy	2 Decline	-

Decline trials are those with three or more sampling times.

Tomatoes are a major crop in northern and southern Europe and therefore generally require eight trials in each residue region.

Treatments with chlorothalonil were conducted as post emergence (BBCH 81-89) spray applications utilising the formulation as detailed in Table 6.3.1-4 at a nominal application rate of 1000 g a.s./ha (actual rates 959-1086 g a.s./ha). The water volumes during application ranged from 437 to 594 L/ha.

Table 6.3.1-4: Summary of chlorothalonil formulations used in the presented trials

Product code	Formulation type	Composition	
		2014	2015
A7867A	SC	498 g/L chlorothalonil	510 g/L chlorothalonil

Samples of whole fruits were taken and analysed for residues of parent chlorothalonil and the metabolite R182281 using analytical method GRM005.01A with an LOQ of 0.01 mg/kg for both compounds. Full method descriptions and validation data are presented in document M-CA Section 4, CA 4.1.2. Procedural recovery data are presented with the results of the residues trials in Table 6.3.1-14.

Allowing for a 25% deviation from the proposed maximum application rate, rates and application timings in all trials cover the critical EU GAP.

Samples were stored up to a maximum of 9 months from sampling to extraction. Samples were homogenised in the presence of acid before freezing. Residues of chlorothalonil and R18221 are stable in acidified homogenised tomatoes for at least 24 months (see section CA 6.1) and therefore no degradation will have occurred between sampling and analysis.

The available trials are sufficient to support the EU critical GAP for tomato. 8 acceptable trials are available for northern Europe and 8 acceptable trials are available for southern Europe. Residues found in the trials from northern and southern Europe are comparable, leading to the same STMR value and similar HR values. The data sets can therefore be combined and give sufficient data to propose MRLs and conduct the consumer risk assessment.

The results of the residue trials for chlorothalonil and R182281 are presented in Table 6.3.1-5.

Table 6.3.1-5: Summary of residue data supporting the EU critical GAP for chlorothalonil on tomato

GLP and Trial Details	Crop (Variety)	Country (Region)	Application Rate Product Code	Growth Stage at application	PHI (days)	Crop Part (Growth stage at sampling)	Residue Found (Uncorrected) chlorothalonil mg/kg	 R182281 (mg/kg)	Recovery Data
Northern Europe									
Report: S14-02774 Study: : S14-02774 Trial: S14-02774-01 - Study to GLP - Study carried out in 2014	Tomato (Topkapi)	FRANCE (Europe North) Varennes Sur Loire Pays de la Loire Maine et Loire	1039 g a.s./ha A7867A	BBCH 83 09/09/2014	0	Fruit (BBCH 83)	0.69	< 0.01	Chlorothalonil Whole fruit: mean = 84% RSD = 7.9% (n = 3 in 0.01 – 2.0 mg/kg spiking range) R182281 Whole fruit: mean = 105% RSD = NA (n = 2 in 0.01 – 0.10 mg/kg spiking range) Chlorothalonil (Fruit) GRM005.01A R182281 (Fruit) GRM005.01A
					1	Fruit (BBCH 83)	0.27	< 0.01	
					3	Fruit (BBCH 83)	0.63	< 0.01	
Report: S14-02774 Study: : S14-02774 Trial: S14-02774-03 - Study to GLP - Study carried out in 2014	Tomato (Galilea)	POLAND (Europe North) Gaj Maly Wielkopolska Szamotulski 64-520	987 g a.s./ha A7867A	BBCH 84-85 19/08/2014	0	Fruit (BBCH 84-85)	0.46	< 0.01	Chlorothalonil Whole fruit: mean = 84% RSD = 7.9% (n = 3 in 0.01 – 2.0 mg/kg spiking range) R182281 Whole fruit: mean = 105% RSD = NA (n = 2 in 0.01 – 0.10 mg/kg spiking range) Chlorothalonil (Fruit) GRM005.01A R182281 (Fruit) GRM005.01A
					1	Fruit (BBCH 84-85)	0.34	< 0.01	
					3	Fruit (BBCH 85-86)	0.15	<.0.01	
Report: S14-02774 Study: : S14-02774 Trial: S14-02774-06 - Study to GLP - Study carried out in 2014	Tomato (Benito)	POLAND (Europe North) Chrzypsko Wielkie Wielkopolskie Miedzychodzki 64-412	1038 g a.s./ha A7867A	BBCH 84-85 22/08/2014	3	Fruit (BBCH 85-86)	0.44	< 0.01	Chlorothalonil Whole fruit: mean = 84% RSD = 7.9% (n = 3 in 0.01 – 2.0 mg/kg spiking range) R182281 Whole fruit: mean = 105% RSD = NA (n = 2 in 0.01 – 0.10 mg/kg spiking range) Chlorothalonil (Fruit) GRM005.01A R182281 (Fruit) GRM005.01A
Report: S14-02774 Study: : S14-02774 Trial: S14-02774-07 - Study to GLP - Study carried out in 2014	Tomato (Alfréd F1)	HUNGARY (Europe North) Szatymaz Dél-Alföd Csongrád 6763	1049 g a.s./ha A7867A	BBCH 85 09/09/2014	3	Fruit (BBCH 87)	0.26	< 0.01	Chlorothalonil Whole fruit: mean = 84% RSD = 7.9% (n = 3 in 0.01 – 2.0 mg/kg spiking range) R182281 Whole fruit: mean = 105% RSD = NA (n = 2 in 0.01 – 0.10 mg/kg spiking range) Chlorothalonil (Fruit) GRM005.01A

GLP and Trial Details	Crop (Variety)	Country (Region)	Application Rate Product Code	Growth Stage at application	PHI (days)	Crop Part (Growth stage at sampling)	Residue Found (Uncorrected) chlorothalonil mg/kg	 R182281 (mg/kg)	Recovery Data
									R182281 (Fruit) GRM005.01A
Report: S15-02003 Study: : S15-02003 Trial: S15-02003-01 - Study to GLP - Study carried out in 2015	Tomato (Petula)	FRANCE (Europe North) Varennes Sur Loire Pays de la Loire Maine-et-Loire 49730	1013 g a.s./ha A7867A	BBCH 85-86 28/08/2015	0	Fruit (BBCH 85-86)	0.49	< 0.01	Chlorothalonil Whole fruit: mean = 94% RSD = 8.4% (n = 4 in 0.01 – 1.0 mg/kg spiking range) R182281 Whole fruit: mean = 101% RSD = NA (n = 2 in 0.01 – 0.10 mg/kg spiking range) Chlorothalonil (Fruit) GRM005.01A R182281 (Fruit) GRM005.01A
					1	Fruit (BBCH 85-86)	0.43	< 0.01	
					3	Fruit (BBCH 85-86)	0.13	< 0.01	
Report: S15-02003 Study: : S15-02003 Trial: S15-02003-02 - Study to GLP - Study carried out in 2015	Tomato (Phantasia)	GERMANY (Europe North) Kirchheim Baden-Württemberg Heidelberg, Stadtkreis 69124	988 g a.s./ha A7867A	BBCH 61-83 27/07/2015	0	Fruit (BBCH 61-89)	0.43	< 0.01	Chlorothalonil Whole fruit: mean = 94% RSD = 8.4% (n = 4 in 0.01 – 1.0 mg/kg spiking range) R182281 Whole fruit: mean = 101% RSD = NA (n = 2 in 0.01 – 0.10 mg/kg spiking range) Chlorothalonil (Fruit) GRM005.01A R182281 (Fruit) GRM005.01A
					1	Fruit (BBCH 61-89)	0.56	< 0.01	
					3	Fruit (BBCH 61-89)	0.36	< 0.01	
Report: S15-02003 Study: : S15-02003 Trial: S15-02003-03 - Study to GLP - Study carried out in 2015	Tomato (Monafavet)	FRANCE (Europe North) St Hilaire St Mesmin Loiret 45160	986 g a.s./ha A7867A	BBCH 72-81 03/08/2015	3	Fruit (BBCH 81-85)	0.25	< 0.01	Chlorothalonil Whole fruit: mean = 94% RSD = 8.4% (n = 4 in 0.01 – 1.0 mg/kg spiking range) R182281 Whole fruit: mean = 101% RSD = NA (n = 2 in 0.01 – 0.10 mg/kg spiking range) Chlorothalonil (Fruit) GRM005.01A R182281 (Fruit) GRM005.01A
Report: S15-02003 Study: : S15-02003 Trial: S15-02003-04 - Study to GLP - Study carried out in 2015	Tomato (Pannovy)	GERMANY (Europe North) Markgröningen Baden-Württemberg Ludwigsburg 71706	977 g a.s./ha A7867A	BBCH 74-81 18/08/2015	3	Fruit (BBCH 75-85)	0.83	< 0.01	Chlorothalonil Whole fruit: mean = 94% RSD = 8.4% (n = 4 in 0.01 – 1.0 mg/kg spiking range) R182281 Whole fruit: mean = 101% RSD = NA (n = 2 in 0.01 – 0.10 mg/kg spiking range) Chlorothalonil (Fruit) GRM005.01A R182281 (Fruit) GRM005.01A

GLP and Trial Details	Crop (Variety)	Country (Region)	Application Rate Product Code	Growth Stage at application	PHI (days)	Crop Part (Growth stage at sampling)	Residue Found (Uncorrected) chlorothalonil mg/kg	 R182281 (mg/kg)	Recovery Data
Southern Europe									
Report: S14-02773 Study: S14-02773 Trial: S14-02773-02 - Study to GLP unchecked - Study carried out in 2014 (Field)	Tomato (H-9036)	SPAIN (Europe South) Remolinos Zaragoza Aragon 50635	959 g ai/ha (A7867A) (-)	BBCH 85 - 87 25/08/2014	0	Fruit (BBCH 87-89)	0.80	< 0.01	Chlorothalonil Fruit Mean = 93% RSD = 7% (n = 5 in 0.01 - 2 mg/kg spiking range) R182281 Fruit Mean = 103% RSD = 14% (n = 4 in 0.01 - 0.1 mg/kg spiking range) Chlorothalonil (Fruit) GRM005.01A R182281 (Fruit) GRM005.01A
					1	Fruit (BBCH 87-89)	0.39	< 0.01	
					3	Fruit (BBCH 87-89)	0.36	< 0.01	
Report: S14-02773 Study: S14-02773 Trial: S14-02773-03 - Study to GLP unchecked - Study carried out in 2014 (Field)	Tomato (Gamlex)	ITALY (Europe South) Lagosanto Emilia Romagna Ferrara 44023	1086g ai/ha (A7867A) (-)	BBCH 87 18/08/2014	0	Fruit (BBCH 87-89)	1.64	< 0.01	Chlorothalonil Fruit Mean = 93% RSD = 7% (n = 5 in 0.01 - 2 mg/kg spiking range) R182281 Fruit Mean = 103% RSD = 14% (n = 4 in 0.01 - 0.1 mg/kg spiking range) R182281 Fruit Mean = 103% RSD = 14% (n = 4 in 0.01 - 0.1 mg/kg spiking range) Chlorothalonil (Fruit) GRM005.01A R182281 (Fruit) GRM005.01A
					1	Fruit (BBCH 87-89)	0.87	< 0.01	
					3	Fruit (BBCH 87-89)	0.58	< 0.01	
Report: S14-02773 Study: S14-02773 Trial: S14-02773-04 - Study to GLP unchecked - Study carried out in 2014 (Field)	Tomato (Littano)	ITALY (Europe South) Crevalcore Emilia Romagna Bologna 40014	1003 g ai/ha (A7867A) (-)	BBCH 85 – 87 01/08/2014	0	Fruit (BBCH 87-89)	1.02	0.02	Chlorothalonil Fruit Mean = 93% RSD = 7% (n = 5 in 0.01 - 2 mg/kg spiking range) R182281 Fruit Mean = 103% RSD = 14% (n = 4 in 0.01 - 0.1 mg/kg spiking range) Chlorothalonil (Fruit) GRM005.01A R182281 (Fruit) GRM005.01A
					1	Fruit (BBCH 87-89)	0.86	< 0.01	
					3	Fruit (BBCH 87-89)	0.59	< 0.01	
Report: S14-02773 Study: S14-02773 Trial: S14-02773-05 - Study to GLP unchecked - Study carried out in 2014 (Field)	Tomato (Hector)	FRANCE (Europe South) (-) Saint Laurent de la Salanque Languedoc-Roussillon Pyrénées-Orientales 66250	1016 g ai/ha (A7867A) (-)	BBCH 87 04/08/2014	3	Fruit (BBCH 89)	0.06	< 0.01	Chlorothalonil Fruit Mean = 93% RSD = 7% (n = 5 in 0.01 - 2 mg/kg spiking range) R182281 Fruit Mean = 103% RSD = 14% (n = 4 in 0.01 - 0.1 mg/kg spiking range) Chlorothalonil (Fruit) GRM005.01A R182281 (Fruit) GRM005.01A

GLP and Trial Details	Crop (Variety)	Country (Region)	Application Rate Product Code	Growth Stage at application	PHI (days)	Crop Part (Growth stage at sampling)	Residue Found (Uncorrected) chlorothalonil mg/kg	 R182281 (mg/kg)	Recovery Data
Report: S14-02773 Study: S14-02773 Trial: S14-02773-06 - Study to GLP unchecked - Study carried out in 2014 (Field)	Tomato (H-9036)	SPAIN (Europe South) Ribaforada Comunidad Foral de Navarra Navarra 31550	1085 g ai/ha (A7867A) (-)	BBCH 85 – 87 07/10/2014	3	Fruit (BBCH 87-89)	0.58	< 0.01	Chlorothalonil Fruit Mean = 93% RSD = 7% (n = 5 in 0.01 - 2 mg/kg spiking range) R182281 Fruit Mean = 103% RSD = 14% (n = 4 in 0.01 - 0.1 mg/kg spiking range) Chlorothalonil (Fruit) GRM005.01A R182281 (Fruit) GRM005.01A
Report: S14-02773 Study: S14-02773 Trial: S14-02773-07 - Study to GLP unchecked - Study carried out in 2014 (Field)	Tomato (Albatros)	SPAIN (Europe South) Las Marismillas (Lebrija) Andalucia Sevilla 41740	983 g ai/ha (A7867A) (-)	BBCH 87 – 89 15/07/2014	3	Fruit (BBCH 88-89)	0.12	< 0.01	Chlorothalonil Fruit Mean = 93% RSD = 7% (n = 5 in 0.01 - 2 mg/kg spiking range) R182281 Fruit Mean = 103% RSD = 14% (n = 4 in 0.01 - 0.1 mg/kg spiking range) Chlorothalonil (Fruit) GRM005.01A R182281 (Fruit) GRM005.01A
Report: S14-02773 Study: S14-02773 Trial: S14-02773-09 - Study to GLP unchecked - Study carried out in 2014 (Field)	Tomato (Matias)	SPAIN (Europe South) Conil de la Frontera Andalucia Cádiz	960 g ai/ha (A7867A) (-)	BBCH 81 – 82 15/09/2014	0	Fruit (BBCH 82-83)	0.37	< 0.01	Chlorothalonil Fruit Mean = 93% RSD = 7% (n = 5 in 0.01 - 2 mg/kg spiking range) R182281 Fruit Mean = 103% RSD = 14% (n = 4 in 0.01 - 0.1 mg/kg spiking range) Chlorothalonil (Fruit) GRM005.01A R182281 (Fruit) GRM005.01A
					1	Fruit (BBCH 82-83)	0.36	< 0.01	
					3	Fruit (BBCH 82-83)	0.17	< 0.01	
Report: S14-02773 Study: S14-02773 Trial: S14-02773-10 - Study to GLP unchecked - Study carried out in 2014 (Field)	Tomato (Bosca)	SPAIN (Europe South) La Palma del Condado Andalucia Huelva	1026 g ai/ha (A7867A) (-)	BBCH 88 – 89 15/09/2014	3	Fruit (BBCH 88-89)	0.46	< 0.01	Chlorothalonil Fruit Mean = 93% RSD = 7% (n = 5 in 0.01 - 2 mg/kg spiking range) R182281 Fruit Mean = 103% RSD = 14% (n = 4 in 0.01 - 0.1 mg/kg spiking range) Chlorothalonil (Fruit) GRM005.01A R182281 (Fruit) GRM005.01A
Unless otherwise stated residues of chlorothalonil and R182281 in untreated samples were less than the LOQ.									

Findings

For MRL setting and risk assessment, the definition of the residue for chlorothalonil is parent chlorothalonil only. In addition a separate residue definition for 2,5,6-trichloro-4-hydroxyphtalonitrile (R182281) is also proposed. Separate calculations for both chlorothalonil and R182281 are presented below.

Chlorothalonil residue calculations for MRL setting and risk assessment

MRLs, STMR and HR values for tomatoes have been calculated for northern and southern Europe for chlorothalonil. The STMR is the median residue and the HR is the highest residue value found. MRLs are calculated according to the OECD calculator (**OECD Series on pesticides No. 56, ENV/JM/MONO (2011)2, 1 March 2011**). In these calculations a single data point from each trial supporting the EU critical GAP has been considered. The chlorothalonil residue values used in the MRL, STMR and HR calculations are underlined in Table 6.3.1-5. The calculated outputs are presented in Table 6.3.1-6.

Table 6.3.1-6: MRL, STMR and HR calculations for chlorothalonil on tomato (fruit) – proposed EU GAPs

Region	Outdoor / Protected	Residue Data (mg/kg)	MRL OECD Method (mg/kg)	MRL OECD Rounded (mg/kg)	STMR (mg/kg)	HR (mg/kg)
Northern EU	Outdoor	0.13, 0.15, 0.25, 0.26, 0.36, 0.44, 0.63, 0.83	1.356	1.5	0.31	0.83
Southern EU	Outdoor	0.06, 0.12, 0.17, 0.36, 0.46, 2 x 0.58, 0.59	1.251	1.5	0.41	0.59
Combined EU	Outdoor	0.13, 0.15, 0.25, 0.26, 0.36, 0.44, 0.63, 0.83, 0.06, 0.12, 0.17, 0.36, 0.46, 2 x 0.58, 0.59	1.294	1.5	0.36	0.83

There is an existing EU MRL of 2.0 mg/kg for chlorothalonil on tomatoes (parent chlorothalonil). A recent proposal currently being considered (SANCO 12240/2013) has proposed a MRL of 6 mg/kg. The data presented in Table 6.3.1-6 from trials supporting the proposed EU critical GAP indicate that residues will be within the recently proposed EU MRL of 6 mg/kg. 8 acceptable trials are available for northern Europe and 8 acceptable trials are available for southern Europe. Taking into account the data from both northern and southern Europe the MRL of 6 mg/kg will not be exceeded.

R182281 residue calculations for MRL setting and risk assessment

MRLs, STMR and HR values for tomatoes have been calculated for northern and southern Europe for R182281. The STMR is the median residue and the HR is the highest residue value found. MRLs are calculated according to the OECD calculator (**OECD Series on pesticides No. 56, ENV/JM/MONO (2011)2, 1 March 2011**). In these calculations a single data point from each trial supporting the EU critical GAP has been considered. The R182281 residue values used in the MRL, STMR and HR calculations are underlined in Table 6.3.1-5. The calculated outputs are presented in Table 6.3.1-7.

Table 6.3.1-7: MRL, STMR and HR calculations for R182281 on tomato (fruit) – proposed EU GAPs

Region	Outdoor / Protected	Residue Data (mg/kg)	MRL OECD Method (mg/kg)	MRL OECD Rounded (mg/kg)	STMR (mg/kg)	HR (mg/kg)
Northern EU	Outdoor	8 x <0.01	0.010	0.010	0.01	0.01
Southern EU	Outdoor	8 x <0.01	0.010	0.010	0.01	0.01
Combined EU	Outdoor	16 x <0.01	0.010	0.010	0.01	0.01

There are currently no EU MRLs for R182281. The data presented in Table 6.3.1-7 from trials supporting the proposed EU critical GAP indicate that an MRL of 0.01 mg/kg is appropriate.

Conclusions

The proposed EU MRLs for chlorothalonil and R182281 together with the corresponding STMR and HR for risk assessment for tomatoes are presented in Table 6.3.1-8 and Table 6.3.1-9, respectively.

Table 6.3.1-8: Proposed EU MRL and proposed STMR and HR for chlorothalonil on tomatoes

Commodity (code)	Existing EU MRL (mg/kg)	Proposed EU MRL (mg/kg)	STMR (mg/kg)	HR (mg/kg)
Tomatoes (0231010)	2/6†	6	0.41	0.83

† proposal currently being considered (SANCO 12240/2013)

Table 6.3.1-9: Proposed EU MRL and proposed STMR and HR for R182281 on tomatoes

Commodity (code)	Existing EU MRL (mg/kg)	Proposed EU MRL (mg/kg)	STMR (mg/kg)	HR (mg/kg)
Tomatoes (0231010)	-	0.01	0.01	0.01

CA 6.3.2 Barley

Following communications with the RMS with regards to the typographical error in the Doc D-1 for the barley GAP, which stated that the application growth stages were BBCH 30-69, which was incorrect. The RMS has agreed to amend the residue evaluation on the barley BBCH scale 30-59 instead of 30-69.

Chlorothalonil is proposed for use on barley according to the following EU critical GAP, detailed in Table 6.3.2-1.

Table 6.3.2–1: Proposed EU critical GAPs for chlorothalonil on barley

Region	Outdoor/ Protected	Growth stage	Max. No. of Applications	Minimum Application Interval (days)	Maximum		Minimum PHI (days)
					Rate (g a.s./ha)	Water (L/ha)	
Northern EU	Outdoor	BBCH 30-59	2	14	750	100-400	NR
Southern EU	Outdoor	BBCH 30-59	2	14	750	100-400	NR

NR – not relevant. Application is growth stage dependent and crops are harvested at maturity.

The residue reports supporting the proposed EU critical GAP for chlorothalonil on barley are referenced in Table 6.3.2-2 and the data are presented in Table 6.3.2-5.

Table 6.3.2-2: Report references for trials supporting the proposed EU critical GAP for chlorothalonil on barley

Annex Pt.	Number.	Author/s	Issue Year	Report Title
K-CA 6.3.2/01	(1 of 9)	T White	2013	Chlorothalonil – residue study on barley in northern France and the United Kingdom in 2011 Syngenta File No. A14111B_10905, Report No. S11-00522
K-CA 6.3.2/02	(2 of 9)	T White	2014	Chlorothalonil – residue study on barley in Germany, Poland and the United Kingdom in 2012 Syngenta File No. A14111B_10908, Report No. S11-01274

Annex Pt.	Number.	Author/s	Issue Year	Report Title
K-CA 6.3.2/03	(3 of 9)	T White	2014a	Chlorothalonil – residue study on barley in Spain, Italy and southern France in 2011 Syngenta File No. A14111B_11144, Report No. S11-00523
K-CA 6.3.2/04	(4 of 9)	T White	2014b	Chlorothalonil – residue study on barley in southern France, Italy and Spain in 2012, Final Report Amendment 1, Syngenta File No. A14111B_10899, Report No. S12-01275
K-CA 6.3.2/05	(5 of 9)	T White	2013a	Chlorothalonil – residue study on barley in southern France in 2013, Syngenta File No. A14111B_10861, Report No. S13-01041
K-CA 6.3.2/06	(6 of 9)	A Sala	2014	Determination of chlorothalonil and its metabolite SDS3701 residues in raw agricultural commodity barley (grain, straw), following two applications of chlorothalonil 500 SC, 2 trials, northern Europe, year 2013, Syngenta File No R044686_11190, Report No. RAU-020-13
K-CA 6.3.2/07	(7 of 9)	A Sala	2014a	Determination of chlorothalonil and its metabolite SDS3701 residues in raw agricultural commodity barley (grain, straw), following two applications of chlorothalonil 500 SC, 2 trials, southern Europe, year 2013, Syngenta File No. R044686_11181, Report No. RAU-018-13
K-CA 6.3.2/08	(8 of 9)	F Mazzi	2014	Determination of chlorothalonil and its metabolite SDS3701 residues in raw agricultural commodity barley (plant, silage, hay, grain, straw) following two applications of Clortosip 500 SC (northern Europe – 6 trials year 2014), Syngenta File No. R044686_11180, Report No. BIU-017-14
K-CA 6.3.2/09	(9 of 9)	F Mazzi	2014a	Determination of chlorothalonil and its metabolite SDS3701 residues in raw agricultural commodity barley (plant, silage, hay, grain, straw) following two applications of Clortosip 500 SC (south Europe – 6 trials year 2014), Syngenta File No. R044686_11182, Report No. BIU-016-14

Guidelines

The studies meet the requirements of the Commission of the European Communities: General Recommendations for the Design, Preparation and Realization of Residue Trials (**7029/V1/95 rev. 5, 22/7/1997**), and are designed to comply with **Regulation (EC) 1107/2009**.

GLP

All trials (field and analytical phases) were carried out in compliance with the principles of Good Laboratory Practice.

Materials and Methods

Thirty-two supervised residue trials were conducted on barley in 2011, 2012, 2013 and 2014 in northern or southern Europe. A summary of the trials conducted is presented in Table 6.3.2-3.

Table 6.3.2-3: Summary of chlorothalonil residue trials on barley

Country	2011	2012	2013	2014
Northern Europe				
United Kingdom	2 Harvest	1 Harvest	-	-
France (north)	1 Harvest	2 Harvest	1 Harvest	3 Harvest
Germany	1 Harvest	-	-	-
Poland	-	1 Harvest	-	3 Harvest
Belgium	-	-	1 Harvest	-
Southern Europe				
France (south)	-	2 Harvest	2 Harvest	1 Harvest
Spain	1 Harvest	1 Harvest	-	-
Italy	2 Harvest	1 Harvest	1 Harvest	5 Harvest

Decline trials are those with five or more sampling times.

Barley is a major crop in northern and southern Europe and therefore generally requires eight trials in each residue region.

Treatments with chlorothalonil were conducted as post emergence (BBCH 30-32 and BBCH 59 [up to BBCH 61-69 for some trials]) spray applications utilising the formulation as detailed in Table 6.3.2-4 at a nominal application rate of 750 g a.s./ha (actual rates 682-808 g a.s./ha). The water volumes during application ranged from 94 to 413 L/ha.

Table 6.3.2-4: Summary of chlorothalonil formulations used in the presented trials

Product code	Formulation type	Composition			
		2011	2012	2013	2014
A14111B	SC	385 g/L chlorothalonil 78.4 g/L azoxystrobin	384 g/L chlorothalonil 74.7 g/L azoxystrobin	384 g/L chlorothalonil 74.7 g/L azoxystrobin	-
Chlorothalonil 500 SC	SC	-	-	502 g/L chlorothalonil (batch O232)	507 g/L chlorothalonil (batch PN1911)

Samples of various parts of mature and immature barley plants were taken and analysed for residues of chlorothalonil and R182281 using either analytical method GRM005.01A with an LOQ of 0.01 mg/kg for both compounds in all commodities analysed, or by analytical methods described in study BIU-016-14, with an LOQ of 0.01 mg/kg in grain and 0.05 mg/kg for other commodities for chlorothalonil and 0.02 mg/kg for all commodities for R182281. Full method descriptions and validation data are presented in document M-CA Section 4, CA 4.1.2. Procedural recovery data are presented with the results of the residues trials in Table 6.3.2-5.

Allowing for a 25% deviation from the proposed maximum application rate, rates and application timings in all trials cover the critical EU GAP. No PHI is proposed in the critical EU GAP since the application is growth stage dependent and the barley is harvested at maturity. Most of the trials were treated at the latest growth stage consistent with the proposed GAP. For some of the trials applications were made at later growth stages than the proposed GAP, however this is considered to represent a worst case and the trials are representative of the proposed EU GAP.

Samples were stored up to a maximum of 12 months from sampling to extraction. Samples of whole plant only were homogenised in the presence of acid before freezing. Residues of chlorothalonil and R18221 are stable in acidified homogenised high water crops for at least 24 months and in samples of cereal grains and straw for up to 24 months (see CA 6.1) and therefore no degradation will have occurred between sampling and analysis.

The available trials are sufficient to support the EU critical GAP for barley.

The results of the residue trials for chlorothalonil and R182281 are presented in Table 6.3.2-5.

Where two or more values are available from duplicate analysis for the same trial following applications according to the GAP, the mean has been used. Where two or more values are available from duplicate sampling for the same trial following applications according to the GAP, the highest has been used.

Table 6.3.2-5: Summary of residue data supporting the EU critical GAP for chlorothalonil on barley

GLP and Trial Details	Crop (Variety)	Country (Region)	Application Rate Product Code	Growth Stage at application	PHI (days)	Crop Part (Growth stage at sampling)	Residue Found (Uncorrected)		Recovery Data
							chlorothalonil mg/kg	R182281 (mg/kg)	
Northern Europe									
Report: S11-00522 Study: S11-00522 Trial: S11-00522-01 - Study to GLP - Study carried out in 2011	Barley (Waggon)	UNITED KINGDOM (Europe North)	741 g a.s./ha 758 g a.s./ha A14111B	BBCH 32 BBCH 59-63	0 DAA1	Whole plant (BBCH 32)	30	0.42	**Chlorothalonil** Whole plant (immature): mean = 104% RSD = 10.9% (n = 6 in 0.01 – 50.0 mg/kg spiking range) Whole plant (silage): mean =100% RSD = 10.5% (n = 6 in 0.01 – 5.00 mg/kg spiking range) Whole plant (hay): mean = 104% RSD = 3.5% (n = 4 in 0.01 – 10.0 mg/kg spiking range) Grain: mean = 98% RSD = 4.7% (n = 6 in 0.01 -0.10 mg/kg spiking range) Straw: mean = 101% RSD = 8.4% (n = 6 in 0.01 –10.0 mg/kg spiking range) **R182281** Whole plant (immature): mean = 98% RSD = 13.1% (n = 4 in 0.01 – 1.00 mg/kg spiking range) Whole plant (silage): mean = 97% RSD = 14.1% (n = 4 in 0.01 – 1.00 mg/kg spiking range) Whole plant (hay): mean = 101% RSD = 13.0% (n = 6 in 0.01 – 5.00 mg/kg spiking range) Grain: mean = 100% RSD = 5.0% (n = 6 in 0.01- 0.10 mg/kg spiking range) Straw: mean = 87% RSD = 11.3% (n = 6 in 0.01 – 10.0 mg/kg spiking range)
					28/31†	Whole plant/ silage (BBCH 77-83)	5.0	0.08	
					28/37†	Whole plant/ hay (BBCH 77-83)	4.5	0.11	
					62	Grain (BBCH 89)	<0.01	<0.01	
					62	Straw (BBCH 89)	5.7	0.30	
Report: S11-00522 Study: S11-00522 Trial: S11-00522-02 - Study to GLP - Study carried out in 2011	Barley (Waggon)	UNITED KINGDOM (Europe North)	759 g a.s./ha 745 g a.s./ha A14111B	BBCH 32 BBCH 59	0 DAA1	Whole plant (BBCH 32)	21	0.27	
					33/41†	Whole plant/silage (BBCH 77-83)	2.1	0.08	
					33/46†	Whole plant/ hay (BBCH 77-83)	1.5	0.06	
					73	Grain (BBCH 89)	0.02, 0.02, 0.01 Mean = 0.02	<0.01	
					73	Grain (BBCH 89)	0.01, 0.04 Mean = 0.03	<0.01	
					73	Straw (BBCH 89)	2.2	0.09	
Report: S11-00522 Study: S11-00522 Trial: S11-00522-03 - Study to GLP - Study carried out in 2011	Barley (Highlight)	GERMANY (Europe North)	755 g a.s./ha 753 g a.s./ha A14111B	BBCH 31-32 BBCH 59	0 DAA1	Whole plant (BBCH 31-32)	45	0.47	
					22/28†	Whole plant/silage (BBCH 81-83)	1.7	0.07	
					22/40†	Whole plant/ hay (BBCH 81-83)	0.83	0.06	
					49	Grain (BBCH 89)	<0.01	<0.01	

GLP and Trial Details	Crop (Variety)	Country (Region)	Application Rate Product Code	Growth Stage at application	PHI (days)	Crop Part (Growth stage at sampling)	Residue Found (Uncorrected)		Recovery Data
							chlorothalonil mg/kg	R182281 (mg/kg)	
					49	Straw (BBCH 89)	1.7	0.09	
Report: S11-00522 Study: S11-00522 Trial: S11-00522-04 - Study to GLP - Study carried out in 2011	Barley (Sunshine)	FRANCE (Europe North)	757 g a.s./ha 733 g a.s./ha A14111B	BBCH 31-32 BBCH 59	0 DAA1	Whole plant (BBCH 31-32)	27	0.48	
					21/21†	Whole plant/silage (BBCH 75-77)	1.8	0.01	
					21/22†	Whole plant/ hay (BBCH 75-77)	2.3	0.03	
					49	Grain (BBCH 89)	<0.01	<0.01	
					49	Straw (BBCH 89)	0.72	0.03	
Report: S12-01274 Study: S12-01274 Trial: S12-01274-01 - Study to GLP - Study carried out in 2012	Barley (Westminster)	UNITED KINGDOM (Europe North)	750 g a.s./ha 727 g a.s./ha A14111B	BBCH 30-32 BBCH 59	0 DAA1	Whole plant (BBCH 30-32)	33	0.43	**Chlorothalonil** Whole plant (immature): mean = 98% RSD = 7.7% (n = 5 in 0.01 – 50.0 mg/kg spiking range) Whole plant (silage): mean = 92% RSD = 6.5% (n = 4 in 0.01 – 5.00 mg/kg spiking range) Whole plant (hay): mean = 94% RSD = 3.4% (n = 4 in 0.01 – 5.00 mg/kg spiking range) Grain: mean = 86% RSD = 7.8% (n = 6 in 0.01 - 0.10 mg/kg spiking range) Straw: mean = 92% RSD = 2.3% (n = 4 in 0.01 – 5.00 mg/kg spiking range) **R182281** Whole plant (immature): mean = 100% RSD = 2.9% (n = 4 in 0.01 – 1.00 mg/kg spiking range) Whole plant (silage): mean = 103% RSD = 1.7% (n = 4 in 0.01 – 1.00 mg/kg spiking range) Whole plant (hay): mean = 101% RSD = 11.4% (n = 4 in 0.01 – 1.00 mg/kg spiking range) Grain: mean = 107% RSD = 5.4% (n = 6
					35/38†	Whole plant/silage (BBCH 85)	0.80	0.03	
					35/43†	Whole plant/ hay (BBCH 85)	0.83	0.06	
					64	Grain (BBCH 89)	0.04	<0.01	
					64	Straw (BBCH 89)	0.44	0.03	
Report: S12-01274 Study: S12-01274 Trial: S12-01274-02 - Study to GLP - Study carried out in 2012	Barley (Quench)	GERMANY (Europe North)	730 g a.s./ha 771 g a.s./ha A14111B	BBCH 30-31 BBCH 59	0 DAA1	Whole plant (BBCH 30-31)	17	0.09	
					20/22†	Whole plant/silage (BBCH 79)	0.46	0.02	
					20/25†	Whole plant/hay (BBCH 79)	0.59	0.03	
					40	Grain (BBCH 89)	0.01	<0.01	
					40	Straw (BBCH 89)	0.68	0.10	
Report: S12-01274	Barley	GERMANY	808 g a.s./ha	BBCH 32	0 DAA1	Whole plant	7.9	0.10	

GLP and Trial Details	Crop (Variety)	Country (Region)	Application Rate Product Code	Growth Stage at application	PHI (days)	Crop Part (Growth stage at sampling)	Residue Found (Uncorrected) chlorothalonil mg/kg	 R182281 (mg/kg)	Recovery Data
Study: S12-01274 Trial: S12-01274-03 - Study to GLP - Study carried out in 2012	(Lomerit)	(Europe North)	778 g a.s./ha A14111B	BBCH 59		(BBCH 32)			in 0.01- 0.10 mg/kg spiking range) Straw: mean = 100% RSD = 4.7% (n = 4 in 0.01 – 1.00 mg/kg spiking range)
					29/34†	Whole plant/silage (BBCH 77-83)	4.5	0.03	
					29/48†	Whole plant/hay (BBCH 77-83)	6.3	0.13	
					62	Grain (BBCH 89)	0.01	<0.01	
					62	Straw (BBCH 89)	2.8	0.11	
Report: S12-01274 Study: S12-01274 Trial: S12-01274-04 - Study to GLP - Study carried out in 2012	Barley (Frontier)	POLAND (Europe North)	753 g a.s./ha 723 g a.s./ha A14111B	BBCH 30-32 BBCH 59	0 DAA1	Whole plant (BBCH 30-32)	23	0.40	
					17/18†	Whole plant/silage (BBCH 75-77)	1.3	<0.01	
					17/27†	Whole plant/ hay (BBCH 75-77)	1.4	0.04	
					47	Grain (BBCH 89)	<0.01	<0.01	
					47	Straw (BBCH 89)	0.45	0.02	
Report: RAU-020-13 Study: RAU-020-13 Trial: F/CH13/BA03 - Study to GLP - Study carried out in 2013	Barley (Cervoise)	FRANCE (Europe North)	722 g a.s./ha 722 g a.s./ha 500 g/L SC	BBCH 32 BBCH 61	52 52	Grain (BBCH 89)	0.03	<0.02	**Chlorothalonil** Grain: mean = 97% RSD = NA (n = 2 in 0.01 -0.10 mg/kg spiking range) Straw: mean = 100% RSD = 4.7% (n = 4 in 0.05 –2.0 mg/kg spiking range) **R182281** Grain: mean = 98% RSD = 3.4% (n = 3 in 0.02- 0.20 mg/kg spiking range) Straw: mean = 105% RSD = NA (n = 2 in 0.02– 0.20 mg/kg spiking range)
						Straw (BBCH 89)	0.74	0.06	
Report: RAU-020-13 Study: RAU-020-13 Trial: B/CH13/BA04 - Study to GLP - Study carried out in 2013	Barley (Meridian)	BELGIUM (Europe North)	743 g a.s./ha 758 g a.s./ha 500 g/L SC	BBCH 31 BBCH 61	44 44	Grain (BBCH 89)	0.04	<0.02	
						Straw (BBCH 89)	1.0	<0.02	
Report: BIU-017-14 Study: BIU-017-14 Trial: F/CH14/BA07 - Study to GLP	Barley (Cervoise)	FRANCE (Europe North)	791 g a.s./ha 804 g a.s./ha 500 g/L SC	BBCH 63 BBCH 69	0	Whole plant (BBCH 69)	18	0.49	**Chlorothalonil** Grain: mean = 91% RSD = 7.6% (n = 4 in 0.01 -0.10 mg/kg spiking range) Hay: mean = 94% RSD = NA
					18/26†	Whole plant/silage (BBCH 77)	0.38	0.36	

GLP and Trial Details	Crop (Variety)	Country (Region)	Application Rate Product Code	Growth Stage at application	PHI (days)	Crop Part (Growth stage at sampling)	Residue Found (Uncorrected)		Recovery Data
							chlorothalonil mg/kg	R182281 (mg/kg)	
- Study carried out in 2014					18/33†	Whole plant/hay (BBCH 77)	5.1	0.50	(n = 2 in 0.05 –20 mg/kg spiking range) Straw: mean = 101% RSD = 8.4% (n = 4 in 0.05 –20 mg/kg spiking range) **R182281** Grain: mean = 87% RSD = NA (n = 2 in 0.02- 0.20 mg/kg spiking range) Whole plant : mean = 88% RSD = NA (n = 2 in 0.05 –1.0 mg/kg spiking range) Straw: mean = 102% RSD = NA (n = 2 in 0.02– 2.0 mg/kg spiking range)
					42	Grain (BBCH 89)	0.02	<0.02	
					42	Straw (BBCH 89)	2.3	0.61	
Report: BIU-017-14 Study: BIU-017-14 Trial: F/CH14/BA08 - Study to GLP - Study carried out in 2014	Barley (Esterel)	FRANCE (Europe North)	797 g a.s./ha 797 g a.s./ha 500 g/L SC	BBCH 61 BBCH 69	47	Grain (BBCH 89)	0.04	<0.02	
					47	Straw (BBCH 89)	1.2	0.38	
Report: BIU-017-14 Study: BIU-017-14 Trial: F/CH14/BA09 - Study to GLP - Study carried out in 2014	Barley (Esterel)	FRANCE (Europe North)	773 g a.s./ha 794 g a.s./ha 500 g/L SC	BBCH 57 BBCH 69	49	Grain (BBCH 89)	0.04	<0.02	
					49	Straw (BBCH 89)	1.3	0.07	
Report: BIU-017-14 Study: BIU-017-14 Trial: P/CH14/BA10 - Study to GLP - Study carried out in 2014	Barley (Lomerit)	POLAND (Europe North)	777 g a.s./ha 769 g a.s./ha 500 g/L SC	BBCH 55 BBCH 61	53	Grain (BBCH 89)	<0.01	<0.02	
					53	Straw (BBCH 89)	4.9	1.1	
Report: BIU-017-14 Study: BIU-017-14 Trial: P/CH14/BA11 - Study to GLP - Study carried out in 2014	Barley (Maybrit)	POLAND (Europe North)	752 g a.s./ha 760 g a.s./ha 500 g/L SC	BBCH 55 BBCH 61	58	Grain (BBCH 89)	0.03	<0.02	
					58	Straw (BBCH 89)	2.0	0.19	
Report: BIU-017-14 Study: BIU-017-14 Trial: P/CH14/BA12 - Study to GLP - Study carried out in 2014	Barley (Souleika)	POLAND (Europe North)	750 g a.s./ha 741 g a.s./ha 500 g/L SC	BBCH 39 BBCH 61	54	Grain (BBCH 89)	<0.01	<0.02	
					54	Straw (BBCH 89)	2.3	0.23	

GLP and Trial Details	Crop (Variety)	Country (Region)	Application Rate Product Code	Growth Stage at application	PHI (days)	Crop Part (Growth stage at sampling)	Residue Found (Uncorrected)		Recovery Data
							chlorothalonil mg/kg	R182281 (mg/kg)	
Southern Europe									
Report: S11-00523 Study: S11-00523 Trial: S11-00523-02 - Study to GLP - Study carried out in 2011	Barley (Prestige)	SPAIN (Europe South)	695 g a.s./ha 742 g a.s./ha A14111B	BBCH 30-32 BBCH 59	0 DAA1	Whole plant (BBCH 30-32)	32	0.51	**Chlorothalonil** Whole plant (immature): mean = 98% RSD = 13% (n = 5 in 0.01 – 50 mg/kg spiking range) Whole plant (silage): mean = 105% RSD = 9.6% (n = 5 in 0.01 – 10 mg/kg spiking range) Whole plant (hay): mean = 97% RSD = 9.0% (n = 4 in 0.01 – 5.0 mg/kg spiking range) Grain: mean = 95% RSD = 3.6% (n =4 in 0.01 -0.10 mg/kg spiking range) Straw: mean = 101% RSD = 12% (n = 7 in 0.01 – 50 mg/kg spiking range) **R182281** Whole plant (immature): mean = 93% RSD = 6.5% (n = 4 in 0.01 – 1.0 mg/kg spiking range) Whole plant (silage): mean = 103% RSD = 5.1% (n = 4 in 0.01 – 1.0 mg/kg spiking range) Whole plant (hay): mean = 97% RSD = 1.7% (n = 4 in 0.01 – 1.0 mg/kg spiking range) Grain: mean = 107% RSD = 5.3% (n = 4 in 0.01- 0.10 mg/kg spiking range) Straw: mean = 99% RSD = 7.7% (n = 7 in 0.01 – 10 mg/kg spiking range)
					22/25†	Whole plant/silage (BBCH 75-85)	0.58	<0.01	
					22/28†	Whole plant/hay (BBCH 75-85)	0.44	0.01	
					58	Grain (BBCH 89)	<u><0.01</u>	<u><0.01</u>	
					58	Straw (BBCH 89)	<u>0.20</u>	<u><0.01</u>	
Report: S11-00523 Study: S11-00523 Trial: S11-00523-03 - Study to GLP - Study carried out in 2011	Barley (Amorosa)	ITALY (Europe South)	758 g a.s./ha 751 g a.s./ha A14111B	BBCH 32 BBCH 59	0 DAA1	Whole plant (BBCH 32)	22	0.31	
					27/36†	Whole plant/silage (BBCH 77)	0.07	<0.01	
					27/39†	Whole plant/hay (BBCH 77)	0.04	<0.01	
					41	Grain (BBCH 89)	<u><0.01</u>	<u><0.01</u>	
					41	Straw (BBCH 89)	<u>0.15</u>	<u>0.02</u>	
Report: S11-00523 Study: S11-00523 Trial: S11-00523-04 - Study to GLP - Study carried out in 2011	Barley (Atomo)	ITALY (Europe South)	727 g a.s./ha 806 g a.s./ha A14111B	BBCH 30-32 BBCH 59	0 DAA1	Whole plant (BBCH 30-32)	18	0.27	
					23/30†	Whole plant/silage (BBCH 77-83)	7.3	0.10	
					23/36†	Whole plant/hay (BBCH 77-83)	4.8	0.15	
					40	Grain (BBCH 89)	<u><0.01</u>	<u><0.01</u>	
					40	Straw (BBCH 89)	<u>0.64</u>	<u>0.12</u>	
Report: S12-01275 Study: S12-01275	Barley (Azurel)	FRANCE (Europe South)	764 g a.s./ha 725 g a.s./ha	BBCH 32 BBCH 59	0 DAA1	Whole plant (BBCH 32)	18	0.19	**Chlorothalonil** Whole plant (immature): mean = 93%

GLP and Trial Details	Crop (Variety)	Country (Region)	Application Rate Product Code	Growth Stage at application	PHI (days)	Crop Part (Growth stage at sampling)	Residue Found (Uncorrected) chlorothalonil mg/kg	 R182281 (mg/kg)	Recovery Data
Trial: S12-01275-01 - Study to GLP - Study carried out in 2012			A14111B		22/22†	Whole plant/silage (BBCH 75-85)	2.0	0.02	RSD = 8.5% (n = 7 in 0.01 – 50 mg/kg spiking range) Whole plant (silage): mean = 92% RSD = 5.8% (n = 4 in 0.01 – 5.0 mg/kg spiking range) Whole plant (hay): mean = 95% RSD = 5.2% (n = 4 in 0.01 – 10 mg/kg spiking range) Grain: mean = 92% RSD = 10.3% (n = 6 in 0.01 - 5.0 mg/kg spiking range) Straw: mean = 90% RSD = 5.3% (n = 4 in 0.01 – 5.0 mg/kg spiking range) **R182281** Whole plant (immature): mean = 103% RSD = 5.6% (n = 3 in 0.01 – 1.0 mg/kg spiking range) Whole plant (silage): mean = 93% RSD = 5.7% (n = 4 in 0.01 – 5.0 mg/kg spiking range) Whole plant (hay): mean = 95% RSD = 16.5% (n = 5 in 0.01 – 10 mg/kg spiking range) Grain: mean = 100% RSD = 5.1% (n = 6 in 0.01- 1.0 mg/kg spiking range) Straw: mean = 102% RSD = 5.2% (n = 4 in 0.01 – 1.0 mg/kg spiking range)
					22/30†	Whole plant/hay (BBCH 75-85)	3.9	0.11	
					37	Grain (BBCH 89)	0.14, 0.22, 0.20 Mean = 0.19	<0.01, <0.01, 0.01 Mean = 0.01	
					37	Straw (BBCH 89)	3.1	0.27	
Report: S12-01275 Study: S12-01275 Trial: S12-01275-02 - Study to GLP - Study carried out in 2012	Barley (Campagnill)	FRANCE (Europe South)	704 g a.s./ha 750 g a.s./ha A14111B	BBCH 31-32 BBCH 59	0 DAA1	Whole plant (BBCH 31-32)	18	0.17	
					20/21†	Whole plant/silage (BBCH 75-85)	3.6	0.04	
					20/28†	Whole plant/hay (BBCH 75-85)	2.1	0.37	
					46	Grain (BBCH 89)	<0.01	<0.01	
					46	Straw (BBCH 89)	0.45	0.03	
Report: S12-01275 Study: S12-01275 Trial: S12-01275-03 - Study to GLP - Study carried out in 2012	Barley (Atomo)	ITALY (Europe South)	764 g a.s./ha 725 g a.s./ha A14111B	BBCH 30-32 BBCH 59	0 DAA1	Whole plant (BBCH 30-32)	16	0.24	
					25/30†	Whole plant/silage (BBCH 75-85)	4.2	0.05	
					25/32†	Whole plant/hay (BBCH 75-85)	5.2	0.07	
					45	Grain (BBCH 89)	0.12, 0.16, 0.26 Mean = 0.18	<0.01, <0.01, <0.01 Mean = <0.01	
					45	Straw (BBCH 89)	1.8	0.06	
Report: S12-01275 Study: S12-01275 Trial: S12-01275-04 - Study to GLP	Barley (Volley)	SPAIN (Europe South)	682 g a.s./ha 742 g a.s./ha A14111B	BBCH 30-32 BBCH 59	0 DAA1	Whole plant (BBCH 30-32)	24	0.39	
					18/19†	Whole plant/silage (BBCH 75-85)	1.7	0.05	

GLP and Trial Details	Crop (Variety)	Country (Region)	Application Rate Product Code	Growth Stage at application	PHI (days)	Crop Part (Growth stage at sampling)	Residue Found (Uncorrected) chlorothalonil mg/kg	 R182281 (mg/kg)	Recovery Data
- Study carried out in 2012					18/24†	Whole plant/hay (BBCH 75-85)	1.5	0.06	
					34	Grain (BBCH 89)	<0.01	<0.01	
					34	Straw (BBCH 89)	0.67	0.07	
Report: S13-01041 Study: S13-01041 Trial: S13-01041-01 - Study to GLP - Study carried out in 2013	Barley (Prestige)	FRANCE (Europe South)	745 g a.s./ha 756 g a.s./ha A14111B	BBCH 32 BBCH 59	0 DAA1	Whole plant (BBCH 32)	26	0.07	**Chlorothalonil** Whole plant (immature): mean = 87% RSD = 2.4% (n = 3 in 0.01 – 50 mg/kg spiking range) Grain: mean = 87% RSD = NA (n =2 in 0.01 -0.1 mg/kg spiking range) Straw: mean = 82% RSD = NA (n = 2 in 0.01 – 1.0 mg/kg spiking range) **R182281** Whole plant (immature): mean = 84% RSD = NA (n = 2 in 0.01 – 0.1 mg/kg spiking range) Grain: mean = 104% RSD = NA (n = 2 in 0.01- 0.1 mg/kg spiking range) Straw: mean = 98% RSD = NA (n = 2 in 0.01 – 0.1 mg/kg spiking range)
					50	Grain (BBCH 89)	<0.01	<0.01	
					50	Straw (BBCH 89)	0.30	0.19	
Report: RAU-018-13 Study: RAU-018-13 Trial: I/CH13/BA01 - Study to GLP - Study carried out in 2013	Barley (Arda)	ITALY (Europe South)	766 g a.s./ha 757 g a.s./ha 500 g/L SC	BBCH 33 BBCH 61-65	50 50	Grain (BBCH 89)	<0.01	<0.02	**Chlorothalonil** Grain: mean = 95% RSD = NA (n = 2 in 0.01 -0.10 mg/kg spiking range) Straw: mean = 101% RSD = NA (n = 2 in 0.05 –0.5 mg/kg spiking range) **R182281** Grain: mean = 90% RSD =NA (n = 2 in 0.02- 0.20 mg/kg spiking range) Straw: mean = 98% RSD = NA (n = 2 in 0.02– 0.20 mg/kg spiking range)
						Straw (BBCH 89)	0.25	0.05	
Report: RAU-018-13 Study: RAU-018-13 Trial: F/CH13/BA02 - Study to GLP - Study carried out in 2013	Barley (Sebastian)	FRANCE (Europe South)	753 g a.s./ha 773 g a.s./ha 500 g/L SC	BBCH 31 BBCH 61	39	Grain (BBCH 89)	<0.01	<0.02	
					39	Straw (BBCH 89)	0.34	0.05	

GLP and Trial Details	Crop (Variety)	Country (Region)	Application Rate Product Code	Growth Stage at application	PHI (days)	Crop Part (Growth stage at sampling)	Residue Found (Uncorrected) chlorothalonil mg/kg	 R182281 (mg/kg)	Recovery Data
Report: BIU-016-14 Study: BIU-016-14 Trial: I/CH14/BA01 - Study to GLP - Study carried out in 2014	Barley (Arda)	ITALY (Europe South)	750 g a.s./ha 741 g a.s./ha 500 g/L SC	BBCH 47-49 BBCH 65-69	42 42	Grain (BBCH 89)	<0.01	<0.02	**Chlorothalonil** Grain: mean = 100% RSD = 20% (n = 6 in 0.01 -0.10 mg/kg spiking range) Whole plant: mean = 100% RSD = 12% (n = 6 in 0.05 –50 mg/kg spiking range) Straw: mean = 87% RSD = 7.1% (n = 8 in 0.05 –1.0 mg/kg spiking range) **R182281** Grain: mean = 82% RSD = 11% (n = 6 in 0.02- 0.20 mg/kg spiking range) Whole plant : mean = 102% RSD = 8.9% (n = 6 in 0.02 –1.0 mg/kg spiking range) Straw: mean = 95% RSD = 11% (n = 6 in 0.02– 2.0 mg/kg spiking range)
						Straw (BBCH 89)	0.15	0.10	
Report: BIU-016-14 Study: BIU-016-14 Trial: I/CH14/BA02 - Study to GLP - Study carried out in 2014	Barley (Etincel)	ITALY (Europe South)	756 g a.s./ha 753 g a.s./ha 500 g/L SC	BBCH 33 BBCH 61	45	Grain (BBCH 89)	<0.01	<0.02	
					45	Straw (BBCH 89)	0.06	0.03	
Report: BIU-016-14 Study: BIU-016-14 Trial: I/CH14/BA03 - Study to GLP - Study carried out in 2014	Barley (Cometa)	ITALY (Europe South)	745 g a.s./ha 755 g a.s./ha 500 g/L SC	BBCH 54 BBCH 61	49	Grain (BBCH 89)	<0.01	<0.02	
					49	Straw (BBCH 89)	0.06	0.06	
Report: BIU-016-14 Study: BIU-016-14 Trial: I/CH14/BA04 - Study to GLP - Study carried out in 2014	Barley (Tuareg)	ITALY (Europe South)	734 g a.s./ha 775 g a.s./ha 500 g/L SC	BBCH 56 BBCH 61	0	Whole plant (BBCH 61)	27	0.54	
					16	Whole plant/silage (BBCH 75)	4.2	0.10	
					17	Whole plant/hay (BBCH 75)	4.7	0.14	
					49	Grain (BBCH 89)	<0.01	<0.02	
					49	Straw (BBCH 89)	0.43	0.11	
Report: BIU-016-14 Study: BIU-016-14 Trial: I/CH14/BA05 - Study to GLP - Study carried out in 2014	Barley (Cometa)	ITALY (Europe South)	755 g a.s./ha 755 g a.s./ha 500 g/L SC	BBCH 54 BBCH 61	49	Grain (BBCH 89)	<0.01	<0.02	
					49	Straw (BBCH 89)	0.48	0.13	
Report: BIU-016-14 Study: BIU-016-14 Trial: F/CH14/BA06 - Study to GLP - Study carried out in 2014	Barley (Sebastian)	FRANCE (Europe South)	725 g a.s./ha 750 g a.s./ha 500 g/L SC	BBCH 59 BBCH 61	47	Grain (BBCH 89)	0.02	<0.02	
					47	Straw (BBCH 89)	0.66	0.13	
Residues in all untreated samples were less than the LOQ.									

GLP and Trial Details	Crop (Variety)	Country (Region)	Application Rate Product Code	Growth Stage at application	PHI (days)	Crop Part (Growth stage at sampling)	Residue Found (Uncorrected)		Recovery Data
							chlorothalonil mg/kg	R182281 (mg/kg)	
DAA1 = days after first application. All other PHI values are days after the second application. †For silage and hay samples were cut at various growth stages between BBCH 75 and 85 then left in the field to dry until the moisture content reached the typical moisture content of silage and hay respectively. For these crops there are therefore two PHI values reported: the PHI when the crop was cut and the PHI when the sample was taken from the field (i.e. including drying). NA = not applicable									

Findings

For MRL setting and risk assessment, the definition of the residue for chlorothalonil is parent chlorothalonil only. In addition a separate residue definition for 2,5,6-trichloro-4-hydroxyphtalonitrile (R182281) is also proposed. Separate calculations for both chlorothalonil and R182281 are presented below.

Chlorothalonil residue calculations for MRL setting and risk assessment

MRLs, STMR and HR values for barley grain have been calculated for northern and southern Europe for chlorothalonil. The STMR is the median residue and the HR is the highest residue value found. MRLs are calculated according to the OECD calculator (**OECD Series on pesticides No. 56, ENV/JM/MONO (2011)2, 1 March 2011**). In these calculations a single data point from each trial supporting the EU critical GAP has been considered. The chlorothalonil residue values used in the MRL, STMR and HR calculations are underlined in Table 6.3.2-5. The calculated outputs are presented in Table 6.3.2-6.

Table 6.3.2-6: MRL, STMR and HR calculations for chlorothalonil on barley (grain) – proposed EU GAPs

Region	Outdoor / Protected	Residue Data (mg/kg)	MRL OECD Method (mg/kg)	MRL OECD Rounded (mg/kg)	STMR (mg/kg)	HR (mg/kg)
Northern EU	Outdoor	6 x <0.01, 2 x 0.01, 0.02, 3 x 0.03, 4 x 0.04	0.075	0.08	0.015	0.04
Southern EU	Outdoor	13 x <0.01, 0.02, 0.18, 0.19	0.271	0.3	0.01	0.19
Combined EU	Outdoor	19 x < 0.01, 2 x 0.01, 2 x 0.02, 3 x 0.03, 4 x 0.04, 0.18, 0.19	0.198	0.2	0.01	0.19

There is an existing EU MRL of 0.3 mg/kg for chlorothalonil on barley grain (parent chlorothalonil). A recent proposal currently being considered (SANCO 12240/2013) has proposed a MRL of 0.4 mg/kg. The data presented in Table 6.3.2-6 from trials supporting the proposed EU critical GAP suggest that a MRL value of 0.3 mg/kg is appropriate based on the southern EU residues trials data.

STMR and HR values for barley straw as potential livestock feed items have also been calculated for northern and southern Europe. Barley forage and silage are not considered relevant crops as the proposed use is for on cereals for grain production only. It was agreed by EFSA and the MS that uses proposed for cereal grains would not be relevant to derive residues in forage or silage as the GAP is different when cereals are grown for forage and silage. Therefore it was agreed, by default that uses on cereals should be understood as "on cereal for grain production" and only residues in grains and straw should be considered for the animal burden calculation. (Minutes of the 1st meeting on MRL procedures held on 19.06 – 20.06.2014, EFSA Parma). The residue values for straw used in the HR and STMR calculations are underlined in Table 6.3.2-5. The calculated outputs are presented in Table 6.3.2-7.

Table 6.3.2-7: STMR and HR calculations for chlorothalonil on barley (straw) – proposed EU GAPs

Region	Outdoor / Protected	Residue Data (mg/kg)	STMR (mg/kg)	HR (mg/kg)
Straw				
Northern EU	Outdoor	0.44, 0.45, 0.68, 0.72, 0.74, 1.0, 1.2, 1.3, 1.7, 2.0, 2.2, 2 x 2.3, 2.8, 4.9, 5.7	1.5	5.7
Southern EU	Outdoor	2 x 0.06, 2 x 0.15, 0.20, 0.25, 0.30, 0.34, 0.43, 0.45, 0.48, 0.64, 0.66, 0.67, 1.8, 3.1	0.39	3.1
Combined EU	Outdoor	2 x 0.06, 2 x 0.15, 0.20, 0.25, 0.30, 0.34, 0.43, 0.44, 2 x 0.45, 0.48, 0.64, 0.66, 0.67, 0.68, 0.72, 0.74, 1.0, 1.2, 1.3, 1.7, 1.8, 2.0, 2.2, 2 x 2.3, 2.8, 3.1, 4.9, 5.7	0.68	5.7

R182281 residue calculations for MRL setting and risk assessment

MRLs, STMR and HR values for barley grain have been calculated for northern and southern Europe for R182281. The STMR is the median residue and the HR is the highest residue value found. MRLs are calculated according to the OECD calculator (**OECD Series on pesticides No. 56, ENV/JM/MONO (2011)2, 1 March 2011**). In these calculations a single data point from each trial supporting the EU critical GAP has been considered. The R182281 residue values used in the MRL, STMR and HR calculations are underlined in Table 6.3.2-5. The calculated outputs are presented in Table 6.3.2-8.

Table 6.3.2-8: MRL, STMR and HR calculations for R182281 on barley (grain) – proposed EU GAPs

Region	Outdoor / Protected	Residue Data (mg/kg)	MRL OECD Method (mg/kg)	MRL OECD Rounded (mg/kg)	STMR (mg/kg)	HR (mg/kg)
Northern EU	Outdoor	8 x <0.01, 8 x <0.02	0.020	0.02	0.015	0.02
Southern EU	Outdoor	7 x <0.01, 0.01, 8 x <0.02	0.036	0.04	0.015	0.02
Combined EU	Outdoor	15 x <0.01, 0.01, 16 x <0.02	0.035	0.04	0.015	0.02

There are currently no EU MRLs for R182281. The data presented in Table 6.3.2-8 from trials supporting the proposed EU critical GAP indicate that a MRL of 0.04 mg/kg is appropriate.

STMR and HR values for barley straw as potential livestock feed items have also been calculated for northern and southern Europe. Barley forage and silage are not considered relevant crops as the proposed use is for on cereals for grain production only. The residue values for straw used in the HR and STMR calculations are underlined in Table 6.3.2-5. The calculated outputs are presented in Table 6.3.2-9.

Table 6.3.2-9: STMR and HR calculations for R182281 on barley (straw) – proposed EU GAPs

Region	Outdoor / Protected	Residue Data (mg/kg)	STMR (mg/kg)	HR (mg/kg)
Straw				
Northern EU	Outdoor	<0.02, 0.02, 2 x 0.03, 0.06, 0.07, 2 x 0.09, 0.10, 0.11, 0.19, 0.23, 0.30, 0.38, 0.61, 1.1	0.10	1.1
Southern EU	Outdoor	<0.01, 0.02, 2 x 0.03, 2 x 0.05, 2 x 0.06, 0.07, 0.10, 0.11, 0.12, 2 x 0.13 0.19, 0.27	0.07	0.27
Combined EU	Outdoor	<0.01, <0.02, 2 x 0.02, 4 x 0.03, 0.05, 3 x 0.06, 2 x 0.07, 2 x 0.09, 3 x 0.10, 2 x 0.11, 0.12, 2 x 0.13, 2 x 0.19, 0.23, 0.27, 0.30, 0.38, 0.61, 1.1	0.10	1.1

Conclusions

The proposed EU MRLs for chlorothalonil and R182281 together with the corresponding STMR and HR values for risk assessment for barley grain are presented in Table 6.3.2-10 and Table 6.3.2-11. For use in dietary burden estimations, STMR and HR values for barley straw are also presented in Table 6.3.2-10 and Table 6.3.2-11.

Table 6.3.2-10: Proposed EU MRL and proposed STMR and HR for chlorothalonil on barley

Commodity (code)	Existing EU MRL (mg/kg)	Proposed EU MRL (mg/kg)	STMR (mg/kg)	HR (mg/kg)
Barley grain (500010)	0.3/0.4	0.3	0.01	0.19
Barley straw (not applicable)	-	-	1.5	5.7

Table 6.3.2-11: Proposed EU MRL and proposed STMR and HR for R182281 on barley

Commodity (code)	Existing EU MRL (mg/kg)	Proposed EU MRL (mg/kg)	STMR (mg/kg)	HR (mg/kg)
Barley grain (500010)	-	0.04	0.015	0.02
Barley straw (not applicable)	-	-	0.10	1.1

CA 6.3.3 Wheat

Chlorothalonil is proposed for use on wheat according to the following EU critical GAP, detailed in Table 6.3.3-1.

Table 6.3.3–1: Proposed EU critical GAPs for chlorothalonil on wheat

Region	Outdoor/ Protected	Growth stage	Max. No. of Applications	Minimum Application Interval (days)	Maximum		Minimum PHI (days)
					Rate (g a.s./ha)	Water (L/ha)	
Northern EU	Outdoor	BBCH 30-69	2	14	750	100-400	NR
Southern EU	Outdoor	BBCH 30-69	2	14	750	100-400	NR

NR – not relevant. Application is growth stage dependent and crops are harvested at maturity.

The residue reports supporting the proposed EU critical GAP for chlorothalonil on wheat are referenced in Table 6.3.3-2 and the data are presented in Table 6.3.3-5.

Table 6.3.3-2: Report references for trials supporting the proposed EU critical GAP for chlorothalonil on wheat

Annex Pt.	Number.	Author/s	Issue Year	Report Title
K-CA 6.3.3/01	(1 of 6)	S Lakaschus A Gizler	2014	Chlorothalonil – residue study on wheat in northern France, Germany, Poland and the United Kingdom in 2012 Syngenta File No. A14111B_11147, Report No. S12-01272
K-CA 6.3.3/02	(2 of 6)	S Lakaschus A Gizler	2014a	Chlorothalonil – residue study on wheat in southern France, Italy and Spain in 2012 Syngenta File No. A14111B_11149, Report No. S12-01273
K-CA 6.3.3/03	(3 of 6)	A Sala	2014b	Determination of chlorothalonil and its metabolite SDS3701 residues in raw agricultural commodity winter wheat (grain, straw) following two applications of chlorothalonil 500 SC, 4 trials, northern Europe, year 2013, Syngenta File No R044686_11186, Report No. RAU-019-13
K-CA 6.3.3/04	(4 of 6)	A Sala	2014c	Determination of chlorothalonil and its metabolite SDS3701 residues in raw agricultural commodity winter wheat (grain, straw) following two applications of chlorothalonil 500 SC, 4 trials, southern Europe, year 2013, Syngenta File No R044686_11188. Report No. RAU-017-13
K-CA 6.3.3/05	(5 of 6)	F Mazzi	2014b	Determination of chlorothalonil and its metabolite SDS3701 residues in raw agricultural commodity winter wheat (plant, silage, hay, grain, straw) following two applications of Clortosip 500 SC (northern Europe – 4 trials year 2014), Syngenta File No. R044686_11187, Report No. BIU-015-14
K-CA 6.3.3/06	(6 of 6)	F Mazzi	2014c	Determination of chlorothalonil and its metabolite SDS3701 residues in raw agricultural commodity winter wheat (plant, silage, hay, grain, straw) following two applications of chlorothalonil 500 SC (south Europe – 4 trials year 2014), Syngenta File No. R044686_11185, Report No. BIU-014-14

Guidelines

The studies meet the requirements of the Commission of the European Communities: General Recommendations for the Design, Preparation and Realization of Residue Trials (**7029/V1/95 rev. 5, 22/7/1997**), and are designed to comply with **Regulation (EC) 1107/2009**.

GLP

All trials (field and analytical phases) were carried out in compliance with the principles of Good Laboratory Practice.

Materials and Methods

Thirty-two supervised residue trials were conducted on wheat in 2012, 2013 and 2014, in northern or southern Europe. A summary of the trials conducted is presented in Table 6.3.3-3.

Table 6.3.3-3: Summary of chlorothalonil residue trials on wheat

Country	2012	2013	2014
Northern Europe			
France (north)	2 Harvest	1 Harvest	3 Harvest
Germany	3 Harvest	2 Harvest	-
Poland	1 Harvest	-	1 Harvest
United Kingdom	2 Harvest	-	-
Belgium	-	1 Harvest	-
Southern Europe			
France (south)	3 Harvest	1 Harvest	1 Harvest
Spain	3 Harvest	-	-
Italy	2 Harvest	3 Harvest	3 Harvest

Decline trials are those with five or more sampling times.

Wheat is a major crop in northern and southern Europe and therefore generally requires eight trials in each residue region.

Treatments with chlorothalonil were conducted as post emergence (BBCH 30-32 [up to BBCH 41 in three trials] and BBCH 69 [up to 70/73 in two trials]) spray applications utilising the formulations as detailed in Table 6.3.3-4 at a nominal application rate of 750 g a.s./ha (actual rates 681-791 g a.s./ha). The water volumes during application ranged from 100 to 420 L/ha. Trials were widespread across the northern and southern EU regions.

Table 6.3.3-4: Summary of chlorothalonil formulation used in the presented trials

Product code	Formulation type	Composition		
		2012	2013	2014
A14111B	SC	384 g/L chlorothalonil 74.7 g/L azoxystrobin	-	-
Chlorothalonil 500 SC	SC	-	502 g/L chlorothalonil (batch O232)	507 g/L chlorothalonil (batch PN1911)

Samples of various parts of mature and immature wheat plants were taken and analysed for residues of chlorothalonil and R182281 using either analytical method GRM005.01A with an LOQ of 0.01 mg/kg for both compounds in all commodities analysed, or by analytical methods described in study BIU-016-14, with an LOQ of 0.01 mg/kg in grain and 0.05 mg/kg for other commodities for chlorothalonil and 0.02 mg/kg for all commodities for R182281. Full method descriptions and validation data are presented in document M-CA Section 4, CA 4.1.2. Procedural recovery data are presented with the results of the residues trials in Table 6.3.3-5.

Allowing for a 25% deviation from the proposed maximum application rate, rates and application timings in all trials cover the critical EU GAP. No PHI is proposed in the critical EU GAP since the application is growth stage dependent and the wheat is harvested at maturity. All trials were treated at the latest growth stage consistent with the proposed GAP.

Samples were stored up to a maximum of 16 months from sampling to extraction. Samples of whole plant only were homogenised in the presence of acid before freezing. Residues of chlorothalonil and R18221 are stable in acidified homogenised high water content crops for at least 24 months and in samples of cereal grains and straw for up to 24 months (see CA 6.1) and therefore no degradation will have occurred between sampling and analysis.

The available trials are sufficient to support the EU critical GAP for wheat.

The results of the residue trials for chlorothalonil and R182281 are presented in Table 6.3.3-5.

Table 6.3.3-5: Summary of residue data supporting the EU critical GAP for chlorothalonil on wheat

GLP and Trial Details	Crop (Variety)	Country (Region)	Application Rate Product Code	Growth Stage at application	PHI (days)	Crop Part (Growth stage at sampling)	Residue Found (Uncorrected) chlorothalonil mg/kg	 R182281 (mg/kg)	Recovery Data
Northern Europe									
Report: S12-01272 Study: S12-01272 Trial: S12-01272-01 - Study to GLP - Study carried out in 2012	Wheat (Granary)	UNITED KINGDOM (Europe North)	750 g a.s./ha 738 g a.s./ha A14111B	BBCH 30-32 BBCH 69	0 DAA1	Whole plant (BBCH 30-32)	19	0.38	**Chlorothalonil** Whole plant (immature): mean = 83% RSD = 17% (n = 8 in 0.01 – 60 mg/kg spiking range) Whole plant (silage): mean = 108% RSD = 6.0% (n = 7 in 0.01 – 10 mg/kg spiking range) Whole plant (hay): mean = 105% RSD = 7.8% (n = 7 in 0.01 – 10 mg/kg spiking range) Grain: mean = 89% RSD = 8.7% (n =13 in 0.01 - 0.1 mg/kg spiking range) Straw: mean = 93% RSD = 8.5% (n = 12 in 0.01 – 10 mg/kg spiking range) **R182281** Whole plant (immature): mean = 99% RSD = 9.3% (n = 8 in 0.01 – 0.5 mg/kg spiking range) Whole plant (silage): mean = 108% RSD = 13% (n = 6 in 0.01 – 0.1 mg/kg spiking range) Whole plant (hay): mean = 109% RSD = 5.5% (n = 6 in 0.01 – 0.1 mg/kg spiking range) Grain: mean = 112% RSD = 5.6% (n = 12 in 0.01- 0.1 mg/kg spiking range) Straw: mean = 107% RSD = 11% (n = 12 in 0.01 – 0.1 mg/kg spiking range)
					49/52†	Whole plant/silage (BBCH 83)	13	0.05	
					49/56†	Whole plant/hay (BBCH 83)	0.56	0.05	
					64	Grain (BBCH 89-92)	<0.01	<0.01	
					64	Straw (BBCH 89-92)	0.18	0.03	
Report: S12-01272 Study: S12-01272 Trial: S12-01272-02 - Study to GLP - Study carried out in 2012	Wheat (Granary)	UNITED KINGDOM (Europe North)	769 g a.s./ha 734 g a.s./ha A14111B	BBCH 37-39 BBCH 69	0 DAA1	Whole plant (BBCH 37-39)	12	0.10	
					22/26†	Whole plant/silage (BBCH 75-79)	12	0.12	
					22/30†	Whole plant/hay (BBCH 75-79)	12	0.13	
					72	Grain (BBCH 89)	<0.01	<0.01	
					72	Straw (BBCH 89)	1.2	0.07	
Report: S12-01272 Study: S12-01272 Trial: S12-01272-03 - Study to GLP - Study carried out in 2012	Wheat (Tabasco)	GERMANY (Europe North)	756 g a.s./ha 729 g a.s./ha A14111B	BBCH 31-32 BBCH 69	0 DAA1	Whole plant (BBCH 31-32)	40	0.66	
					23/24†	Whole plant/silage (BBCH 81-83)	2.5	0.01	
					23/36†	Whole plant/hay (BBCH 81-83)	4.7	0.09	
					56	Grain (BBCH 89)	<0.01	<0.01	
					56	Straw (BBCH 89)	0.79	0.06	

GLP and Trial Details	Crop (Variety)	Country (Region)	Application Rate Product Code	Growth Stage at application	PHI (days)	Crop Part (Growth stage at sampling)	Residue Found (Uncorrected) chlorothalonil mg/kg	 R182281 (mg/kg)	Recovery Data
Report: S12-01272 Study: S12-01272 Trial: S12-01272-04 - Study to GLP - Study carried out in 2012	Wheat (Asano)	GERMANY (Europe North)	733 g a.s./ha 750 g a.s./ha A14111B	BBCH 30-32 BBCH 67-69	0 DAA1	Whole plant (BBCH 30-32)	23	0.27	
					29/31†	Whole plant/silage (BBCH 75-85)	0.94	0.02	
					29/35†	Whole plant/hay (BBCH 75-85)	1.4	0.04	
					52	Grain (BBCH 89)	<0.01	<0.01	
					52	Straw (BBCH 89)	1.0	0.09	
Report: S12-01272 Study: S12-01272 Trial: S12-01272-05 - Study to GLP - Study carried out in 2012	Wheat (Magister)	GERMANY (Europe North)	738 g a.s./ha 744 g a.s./ha A14111B	BBCH 31-32 BBCH 69	0 DAA1	Whole plant (BBCH 31-32)	29	0.61	
					15/22†	Whole plant/silage (BBCH 79-83)	8.0	0.07	
					15/33†	Whole plant/hay (BBCH 79-83)	8.7	0.18	
					49	Grain (BBCH 89)	<0.01	<0.01	
					49	Straw (BBCH 89)	0.88	0.03	
Report: S12-01272 Study: S12-01272 Trial: S12-01272-06 - Study to GLP - Study carried out in 2012	Wheat (Arrezzo)	FRANCE (Europe North)	742 g a.s./ha 763 g a.s./ha A14111B	BBCH 31-32 BBCH 69-73	0 DAA1	Whole plant (BBCH 31-32)	38	0.52	
					18/19†	Whole plant/silage (BBCH 75-77)	3.1	0.03	
					18/21†	Whole plant/hay (BBCH 75-77)	4.5	0.14	
					40	Grain (BBCH 89)	0.01	<0.01	
					40	Straw (BBCH 89)	1.1	0.04	

GLP and Trial Details	Crop (Variety)	Country (Region)	Application Rate Product Code	Growth Stage at application	PHI (days)	Crop Part (Growth stage at sampling)	Residue Found (Uncorrected)		Recovery Data
							chlorothalonil mg/kg	R182281 (mg/kg)	
Report: S12-01272 Study: S12-01272 Trial: S12-01272-07 - Study to GLP - Study carried out in 2012	Wheat (Campero)	FRANCE (Europe North)	725 g a.s./ha 770 g a.s./ha A14111B	BBCH 32 BBCH 69	0 DAA1	Whole plant (BBCH 32)	33	0.22	
					31/31†	Whole plant/silage (BBCH 77)	1.4	0.02	
					31/47†	Whole plant/hay (BCH 77)	2.1	0.05	
					53	Grain (BBCH 89)	<0.01	<0.01	
					53	Straw (BBCH 89)	0.58	0.02	
Report: S12-01272 Study: S12-01272 Trial: S12-01272-08 - Study to GLP - Study carried out in 2012	Wheat (Tybalt)	POLAND (Europe North)	752 g a.s./ha 711 g a.s./ha A14111B	BBCH 30-32 BBCH 69	0 DAA1	Whole plant (BBCH 30-32)	21	0.34	
					15/15†	Whole plant/silage (BBCH 75)	1.4	0.01	
					15/29†	Whole plant/hay (BBCH 75)	3.6	0.08	
					60	Grain (BBCH 89)	<0.01	<0.01	
					60	Straw (BBCH 89)	0.07	0.02	
Report: RAU-019-13 Study: RAU-019-13 Trial: F/CH13/WW05 - Study to GLP - Study carried out in 2013	Wheat (Pakito)	FRANCE (Europe North)	742 g a.s./ha 742 g a.s./ha 500 g/L SC	BBCH 31 BBCH 69	68	Grain (BBCH 89)	<0.01	<0.02	**Chlorothalonil** Grain: mean = 98% RSD = 4.7% (n = 4 in 0.01 -0.10 mg/kg spiking range) Straw: mean = 96% RSD = 3.6% (n = 6 in 0.05 –5.0 mg/kg spiking range) **R182281** Grain: mean = 103% RSD = 11% (n = 4 in 0.02- 0.20 mg/kg spiking range) Straw: mean = 102% RSD = 5.9% (n = 4 in 0.02– 0.20 mg/kg spiking range)
					68	Straw (BBCH 89)	0.85	0.10	
Report: RAU-019-13 Study: RAU-019-13 Trial: G/CH13/WW06 - Study to GLP - Study carried out in 2013	Wheat (Genius)	GERMANY (Europe North)	764 g a.s./ha 727 g a.s./ha 500 g/L SC	BBCH 31 BBCH 69	43	Grain (BBCH 89)	<0.01	<0.02	
					43	Straw (BBCH 89)	0.77	0.06	

GLP and Trial Details	Crop (Variety)	Country (Region)	Application Rate Product Code	Growth Stage at application	PHI (days)	Crop Part (Growth stage at sampling)	Residue Found (Uncorrected) chlorothalonil mg/kg	 R182281 (mg/kg)	Recovery Data
Report: RAU-019-13 Study: RAU-019-13 Trial: G/CH13/WW07 - Study to GLP - Study carried out in 2013	Wheat (Cubus)	GERMANY (Europe North)	727 g a.s./ha 791 g a.s./ha 500 g/L SC	BBCH 31 BBCH 69	33	Grain (BBCH 89)	<0.01	<0.02	
					33	Straw (BBCH 89)	1.9	0.07	
Report: RAU-019-13 Study: RAU-019-13 Trial: B/CH13/WW08 - Study to GLP - Study carried out in 2013	Wheat (Matrix)	BELGIUM (Europe North)	748 g a.s./ha 723 g a.s./ha 500 g/L SC	BBCH 31 BBCH 69	43	Grain (BBCH 89)	<0.01	<0.02	
					43	Straw (BBCH 89)	0.44	0.07	
Report: BIU-015-14 Study: BIU-015-14 Trial: F/CH14/WW05 - Study to GLP - Study carried out in 2014	Wheat (Lear)	FRANCE (Europe North)	729 g a.s./ha 774 g a.s./ha 500 g/L SC	BBCH 37 BBCH 69	42	Grain (BBCH 89)	<0.01	<0.02	**Chlorothalonil** Grain: mean = 82% RSD = 2.3% (n = 4 in 0.01 -0.10 mg/kg spiking range) Whole plant: mean = 89% RSD = 5.0% (n = 4 in 0.05 –20 mg/kg spiking range) Straw: mean = 86% RSD = 16% (n = 4 in 0.05 –12 mg/kg spiking range) **R182281** Grain: mean = 85% RSD = NA (n = 2 in 0.02- 0.20 mg/kg spiking range) Whole plant: mean = 100% RSD = NA (n = 2 in 0.02 –1.0 mg/kg spiking range) Straw: mean = 91% RSD = NA (n = 2 in 0.02– 0.2 mg/kg spiking range)
					42	Straw (BBCH 89)	1.1	0.07	
Report: BIU-015-14 Study: BIU-015-14 Trial: F/CH14/WW06 - Study to GLP - Study carried out in 2014	Wheat (Rubisko)	FRANCE (Europe North)	764 g a.s./ha 771 g a.s./ha 500 g/L SC	BBCH 41 BBCH 69	0	Whole plant (BBCH 69)	12	0.16	
					11/19†	Whole plant/silage (BBCH 75-77)	1.6	0.11	
					11/28†	Whole plant/hay (BBCH 75-77)	2.7	0.15	
					41	Grain (BBCH 89)	<0.01	<0.02	
					41	Straw (BBCH 89)	1.1	0.04	
Report: BIU-015-14 Study: BIU-015-14 Trial: F/CH14/WW07 - Study to GLP - Study carried out in 2014	Wheat (JB Diego)	FRANCE (Europe North)	744 g a.s./ha 735 g a.s./ha 500 g/L SC	BBCH 32 BBCH 62	53	Grain (BBCH 89)	<0.01	<0.02	
					53	Straw (BBCH 89)	0.50	0.03	

GLP and Trial Details	Crop (Variety)	Country (Region)	Application Rate Product Code	Growth Stage at application	PHI (days)	Crop Part (Growth stage at sampling)	Residue Found (Uncorrected)		Recovery Data
							chlorothalonil mg/kg	R182281 (mg/kg)	
Report: BIU-015-14 Study: BIU-015-14 Trial: P/CH14/WW08 - Study to GLP - Study carried out in 2014	Wheat (Jantarka)	POLAND (Europe North)	756 g a.s./ha 763 g a.s./ha 500 g/L SC	BBCH 37 BBCH 69	0	Whole plant (BBCH 69)	13	0.20	
					13/14†	Whole plant/silage (BBCH 77)	12	0.19	
					13/22†	Whole plant/hay (BBCH 77)	11	0.15	
					55	Grain (BBCH 89)	<0.01	<0.02	
					55	Straw (BBCH 89)	0.06	0.02	
Southern Europe									
Report: S12-01273 Study: S12-01273 Trial: S12-01273-01 - Study to GLP - Study carried out in 2012	Wheat (Ingenio)	FRANCE (Europe South)	755 g a.s./ha 727 g a.s./ha A14111B	BBCH 31-32 BBCH 69	0 DAA1	Whole plant (BBCH 31-32)	20	0.19	**Chlorothalonil** Whole plant (immature): mean = 96% RSD = 14% (n = 7 in 0.01 – 60 mg/kg spiking range) Whole plant (silage): mean = 106% RSD = 6.0% (n = 7 in 0.01 – 10 mg/kg spiking range) Whole plant (hay): mean = 104% RSD = 15% (n = 7 in 0.01 – 10 mg/kg spiking range) Grain: mean = 87% RSD = 8.2% (n =11 in 0.01 - 0.1 mg/kg spiking range) Straw: mean = 99% RSD = 10% (n = 11 in 0.01 – 10 mg/kg spiking range) **R182281** Whole plant (immature): mean = 99% RSD = 4.0% (n = 6 in 0.01 – 0.1 mg/kg spiking range) Whole plant (silage): mean = 106% RSD = 12% (n = 6 in 0.01 – 0.1 mg/kg spiking range) Whole plant (hay): mean = 111% RSD = 9.3% (n = 6 in 0.01 – 0.1 mg/kg spiking
					29/29†	Whole plant/silage (BBCH 83-85)	1.5	0.02	
					29/33†	Whole plant/hay (BBCH 83-85)	1.7	0.08	
					41	Grain (BBCH 89)	<0.01	<0.01	
					41	Straw (BBCH 89)	0.92	0.07	
Report: S12-01273 Study: S12-01273 Trial: S12-01273-02 - Study to GLP - Study carried out in 2012	Wheat (Sirtaki)	FRANCE (Europe South)	784 g a.s./ha 750 g a.s./ha A14111B	BBCH 32 BBCH 69	0 DAA1	Whole plant (BBCH 32)	20	0.24	
					26/27†	Whole plant/silage (BBCH 75)	1.4	0.03	
					26/30†	Whole plant/hay (BBCH 75)	0.44	0.02	
					47	Grain (BBCH 89)	<0.01	<0.01	
					47	Straw (BBCH 89)	0.62	0.04	

GLP and Trial Details	Crop (Variety)	Country (Region)	Application Rate Product Code	Growth Stage at application	PHI (days)	Crop Part (Growth stage at sampling)	Residue Found (Uncorrected) chlorothalonil mg/kg	 R182281 (mg/kg)	Recovery Data
Report: S12-01273 Study: S12-01273 Trial: S12-01273-03 - Study to GLP - Study carried out in 2012	Wheat (Arezzo)	FRANCE (Europe South)	716 g a.s./ha 749 g a.s./ha A14111B	BBCH 32 BBCH 69	0 DAA1	Whole plant (BBCH 32)	18	0.17	
					13/14†	Whole plant/silage (BBCH 75-85)	3.1	0.05	
					13/18†	Whole plant/hay (BBCH 75-85)	0.70	0.22	
					40	Grain (BBCH 89)	<0.01	<0.01	
					40	Straw (BBCH 89)	0.40	0.04	
Report: S12-01273 Study: S12-01273 Trial: S12-01273-04 - Study to GLP - Study carried out in 2012	Wheat (Dylan)	ITALY (Europe South)	780 g a.s./ha 727 g a.s./ha A14111B	BBCH 30-32 BBCH 69	0 DAA1	Whole plant (BBCH 30-32)	38	0.16	
					33/36†	Whole plant/silage (BBCH 79-83)	2.7	0.04	
					33/40†	Whole plant/hay (BBCH 79-83)	1.0	0.08	
					46	Grain (BBCH 89)	<0.01	<0.01	
					46	Straw (BBCH 89)	0.99	0.08	
Report: S12-01273 Study: S12-01273 Trial: S12-01273-05 - Study to GLP - Study carried out in 2012	Wheat (Simeto)	ITALY (Europe South)	750 g a.s./ha 755 g a.s./ha A14111B	BBCH 30-32 BBCH 69	0 DAA1	Whole plant (BBCH 30-32)	35	0.55	
					27/30†	Whole plant/silage (BBCH 79-83)	2.0	0.12	
					27/33†	Whole plant/hay (BBCH 79-83)	0.68	0.15	
					43	Grain (BBCH 89)	<0.01	<0.01	
					43	Straw (BBCH 89)	1.1	0.32	

GLP and Trial Details	Crop (Variety)	Country (Region)	Application Rate Product Code	Growth Stage at application	PHI (days)	Crop Part (Growth stage at sampling)	Residue Found (Uncorrected)		Recovery Data
							chlorothalonil mg/kg	R182281 (mg/kg)	
Report: S12-01273 Study: S12-01273 Trial: S12-01273-06 - Study to GLP - Study carried out in 2012	Wheat (Marius)	SPAIN (Europe South)	784 g a.s./ha 733 g a.s./ha A14111B	BBCH 30-32 BBCH 69	0 DAA1	Whole plant (BBCH 30-32)	29	0.43	
					13/14†	Whole plant/silage (BBCH 75-85)	9.4	0.04	
					13/18†	Whole plant/hay (BBCH 75-85)	4.9	0.15	
					48	Grain (BBCH 89)	<0.01	<0.01	
					48	Straw (BBCH 89)	9.9	0.43	
Report: S12-01273 Study: S12-01273 Trial: S12-01273-07 - Study to GLP - Study carried out in 2012	Wheat (Bastide)	SPAIN (Europe South)	773 g a.s./ha 781 g a.s./ha A14111B	BBCH 30-32 BBCH 68-70	0 DAA1	Whole plant (BBCH 30-32)	34	0.46	
					11/12†	Whole plant/silage (BBCH 75-85)	6.6	0.40	
					11/14†	Whole plant/hay (BBCH 75-85)	2.9	0.37	
					26	Grain (BBCH 89)	0.02	<0.01	
					26	Straw (BBCH 89)	4.1	0.58	
Report: S12-01273 Study: S12-01273 Trial: S12-01273-08 - Study to GLP - Study carried out in 2012	Wheat (Marius)	SPAIN (Europe South)	681 g a.s./ha 776 g a.s./ha A14111B	BBCH 30-32 BBCH 69	0 DAA1	Whole plant (BBCH 30-32)	34	0.28	
					14/16†	Whole plant/silage (BBCH 75-85)	5.6	0.51	
					14/18†	Whole plant/hay (BBCH 75-85)	2.6	0.30	
					31	Grain (BBCH 89)	0.01	<0.01	
					31	Straw (BBCH 89)	6.8	0.38	

GLP and Trial Details	Crop (Variety)	Country (Region)	Application Rate Product Code	Growth Stage at application	PHI (days)	Crop Part (Growth stage at sampling)	Residue Found (Uncorrected) chlorothalonil mg/kg	 R182281 (mg/kg)	Recovery Data
Report: RAU-017-13 Study: RAU-017-13 Trial: I/CH13/WW01 - Study to GLP - Study carried out in 2013	Wheat (Levante)	ITALY (Europe South)	786 g a.s./ha 791 g a.s./ha 500 g/L SC	BBCH 31 BBCH 69	58	Grain (BBCH 89)	<0.01	<0.02	**Chlorothalonil** Grain: mean = 97% RSD = 1.5% (n = 6 in 0.01 -0.10 mg/kg spiking range) Straw: mean = 100% RSD = 2.6% (n = 8 in 0.05 –5.0 mg/kg spiking range) **R182281** Grain: mean = 95% RSD =4.6% (n = 4 in 0.02- 0.20 mg/kg spiking range) Straw: mean = 87% RSD = 5.8% (n = 4 in 0.02– 0.50 mg/kg spiking range)
					58	Straw (BBCH 89)	0.22	0.08	
Report: RAU-017-13 Study: RAU-017-13 Trial: I/CH13/WW02 - Study to GLP - Study carried out in 2013	Wheat (PR 058)	ITALY (Europe South)	745 g a.s./ha 745 g a.s./ha 500 g/L SC	BBCH 31 BBCH 69	42	Grain (BBCH 89)	<0.01	<0.02	
					42	Straw (BBCH 89)	0.08	0.03	
Report: RAU-017-13 Study: RAU-017-13 Trial: I/CH13/WW03 - Study to GLP - Study carried out in 2013	Wheat (Arrocco)	ITALY (Europe South)	761 g a.s./ha 740 g a.s./ha 500 g/L SC	BBCH 31 BBCH 69	40	Grain (BBCH 89)	<0.01	<0.02	
					40	Straw (BBCH 89)	0.07	0.04	
Report: RAU-017-13 Study: RAU-017-13 Trial: F/CH13/WW04 - Study to GLP - Study carried out in 2013	Wheat (Quality)	FRANCE (Europe South)	779 g a.s./ha 764 g a.s./ha 500 g/L SC	BBCH 41 BBCH 69	63	Grain (BBCH 89)	<0.01	<0.02	
					63	Straw (BBCH 89)	2.1	0.12	
Report: BIU-014-14 Study: BIU-014-14 Trial: I/CH14/WW01 - Study to GLP - Study carried out in 2014	Wheat (Salgemma)	ITALY (Europe South)	759 g a.s./ha 763 g a.s./ha 500 g/L SC	BBCH 39 BBCH 69	58	Grain (BBCH 89)	<0.01	<0.02	**Chlorothalonil** Grain: mean = 100% RSD = 15% (n = 4 in 0.01 -0.10 mg/kg spiking range) Silage: mean = 97% RSD = 5.6% (n = 9 in 0.05 –28 mg/kg spiking range)
					58	Straw (BBCH 89)	0.08	<0.02	

GLP and Trial Details	Crop (Variety)	Country (Region)	Application Rate Product Code	Growth Stage at application	PHI (days)	Crop Part (Growth stage at sampling)	Residue Found (Uncorrected) chlorothalonil mg/kg	 R182281 (mg/kg)	Recovery Data
Report: BIU-014-14 Study: BIU-014-14 Trial: I/CH14/WW02 - Study to GLP - Study carried out in 2014	Wheat (Levante)	ITALY (Europe South)	746 g a.s./ha 756 g a.s./ha 500 g/L SC	BBCH 33 BBCH 69	0	Whole plant (BBCH 69)	21	0.74	
					12	Whole plant/silage (BBCH 75)	5.8	0.06	
					13	Whole plant/hay (BBCH 75)	6.8	<0.02	
					48	Grain (BBCH 89)	<0.01	<0.02	
					48	Straw (BBCH 89)	0.08	<0.02	
Report: BIU-014-14 Study: BIU-014-14 Trial: I/CH14/WW03 - Study to GLP - Study carried out in 2014	Wheat (Aubusson)	ITALY (Europe South)	739 g a.s./ha 756 g a.s./ha 500 g/L SC	BBCH 32 BBCH 69	0	Whole plant (BBCH 69)	20	0.36	
					21	Whole plant/silage (BBCH 77)	2.5	0.02	
					22	Whole plant/hay (BBCH 77)	2.7	<0.02	
					40	Grain (BBCH 89)	<0.01	<0.02	
					40	Straw (BBCH 89)	0.33	<0.02	
Report: BIU-014-14 Study: BIU-014-14 Trial: F/CH14/WW04 - Study to GLP - Study carried out in 2014	Wheat (Solveig)	FRANCE (Europe South)	764 g a.s./ha 782 g a.s./ha 500 g/L SC	BBCH 61 BBCH 69	46	Grain (BBCH 89)	<0.01	<0.02	
					46	Straw (BBCH 89)	0.69	0.03	

Residues in all untreated samples were < 0.01 mg/kg with the following exceptions:

- Trial S12-0172-02 – residues of chlorothalonil were found in untreated samples of whole plant (0.03 mg/kg).
- Trial S12-0172-05 – residues of chlorothalonil were found in untreated samples of hay (0.02 mg/kg).
- Trial S12-0173-02 – residues of chlorothalonil were found in untreated samples of whole plant (0.27 mg/kg), silage (0.17 mg/kg) and hay (0.15 mg/kg).

DAA1 = days after first application. All other PHI values are days after the second application

†For silage and hay samples were cut at various growth stages between BBCH 75 and 85 then left in the field to dry until the moisture content reached the typical moisture content of silage and hay respectively. For these crops there are therefore two PHI values reported: the PHI when the crop was cut and the PHI when the sample was taken from the field (i.e. including drying).

Findings

For MRL setting and risk assessment, the definition of the residue for chlorothalonil is parent chlorothalonil only. In addition a separate residue definition for 2,5,6-trichloro-4-hydroxyphtalonitrile (R182281) is also proposed. Separate calculations for both chlorothalonil and R182281 are presented below.

Chlorothalonil residue calculations for MRL setting and risk assessment

MRLs, STMR and HR values for wheat grain have been calculated for northern and southern Europe for chlorothalonil. The STMR is the median residue and the HR is the highest residue value found. MRLs are calculated according to the OECD calculator (**OECD Series on pesticides No. 56, ENV/JM/MONO (2011)2, 1 March 2011**). In these calculations a single data point from each trial supporting the EU critical GAP has been considered. The chlorothalonil residue values used in the MRL, STMR and HR calculations are underlined in Table 6.3.3-5. The calculated outputs are presented in Table 6.3.3-6.

Table 6.3.3-6: MRL, STMR and HR calculations for chlorothalonil on wheat (grain) – proposed EU GAPs

Region	Outdoor / Protected	Residue Data (mg/kg)	MRL OECD Method (mg/kg)	MRL OECD Rounded (mg/kg)	STMR (mg/kg)	HR (mg/kg)
Northern EU	Outdoor	15 x <0.01, 0.01	0.011	0.015	0.01	0.01
Southern EU	Outdoor	14 x <0.01, 0.01, 0.02	0.021	0.02	0.01	0.02
Combined EU	Outdoor	29 x <0.01, 2 x 0.01, 0.02	0.020	0.02	0.01	0.02

There is an existing EU MRL of 0.1 mg/kg for chlorothalonil on wheat grain (parent chlorothalonil). A recent proposal currently being considered (SANCO 12240/2013) has also proposed an MRL of 0.1 mg/kg. The data presented in Table 6.3.3-6 from trials supporting the proposed EU critical GAP indicate that residues will be within the existing EU MRL.

STMR and HR values for wheat straw as a potential livestock feed items have also been calculated for northern and southern Europe. Wheat forage and silage are not considered relevant crops as the proposed use is for on cereals for grain production only. The residue values for straw used in the HR and STMR calculations are underlined in Table 6.3.3-5. The calculated outputs are presented in Table 6.3.3-7.

Table 6.3.3-7: STMR and HR calculations for chlorothalonil on wheat (straw) – proposed EU GAPs

Region	Outdoor / Protected	Residue Data (mg/kg)	STMR (mg/kg)	HR (mg/kg)
Straw				
Northern EU	Outdoor	0.06,0.07, 0.18, 0.44, 0.50, 0.58, 0.77, 0.79, 0.85, 0.88, 1.0, 3 x 1.1, 1.2, 1.9	0.82	1.9
Southern EU	Outdoor	0.07, 3 x 0.08, 0.22, 0.33, 0.40, 0.62, 0.69, 0.92, 0.99, 1.1, 2.1, 4.1, 6.8, 9.9	0.66	9.9
Combined EU	Outdoor	0.06, 2 x 0.07, 3 x 0.08, 0.18, 0.22, 0.33, 0.40, 0.44, 0.50, 0.58, 0.62, 0.69, 0.77, 0.79, 0.85, 0.88, 0.92, 0.99, 1.0, 4 x 1.1, 1.2, 1.9, 2.1, 4.1, 6.8, 9.9	0.78	9.9

R182281 residue calculations for MRL setting and risk assessment

MRLs, STMR and HR values for wheat grain have been calculated for northern and southern Europe fro R182281. The STMR is the median residue and the HR is the highest residue value found. MRLs are calculated according to the OECD calculator (**OECD Series on pesticides No. 56, ENV/JM/MONO (2011)2, 1 March 2011**). In these calculations a single data point from each trial supporting the EU critical GAP has been considered. The R182281residue values used in the MRL calculations are underlined in Table 6.3.3-5. The calculated outputs are presented in Table 6.3.3-8.

Table 6.3.3-8: MRL, STMR and HR calculations for R182281 on wheat (grain) – proposed EU GAPs

Region	Outdoor / Protected	Residue Data (mg/kg)	MRL OECD Method (mg/kg)	MRL OECD Rounded (mg/kg)	STMR (mg/kg)	HR (mg/kg)
Northern EU	Outdoor	8 x < 0.01, 8 x < 0.02	0.02	0.02*	0.015	0.02
Southern EU	Outdoor	8 x < 0.01, 8 x < 0.02	0.02	0.02*	0.015	0.02
Combined EU	Outdoor	16 x < 0.01, 16 x <0.02	0.02	0.02*	0.015	0.02

There are currently no EU MRLs for R182281. The data presented in Table 6.3.3-9 from trials supporting the proposed EU critical GAP indicate that an MRL of 0.02 mg/kg (LOQ) is appropriate

STMR and HR values for wheat straw as a potential livestock feed items have also been calculated for northern and southern Europe. Wheat forage and silage are not considered relevant crops as the proposed use is for on cereals for grain production only. It was agreed by EFSA and the MS that uses proposed for cereal grains would not be relevant to derive residues in forage or silage as the GAP is different when cereals are grown for forage and silage. Therefore it was agreed, by default that uses on cereals should be understood as "on cereal for grain production" and only residues in grains and straw should be considered for the animal burden calculation. (Minutes of the 1st meeting on MRL procedures held on 19.06 – 20.06.2014, EFSA Parma). The residue values for straw used in the HR and STMR calculations are underlined in Table 6.3.3-5. The calculated outputs are presented in Table 6.3.3-9.

Table 6.3.3-9: STMR and HR calculations for R182281 on wheat (straw) – proposed EU GAPs

Region	Outdoor / Protected	Residue Data (mg/kg)	STMR (mg/kg)	HR (mg/kg)
Straw				
Northern EU	Outdoor	3 x 0.02, 3 x 0.03, 2 x 0.04, 2 x 0.06, 4 x 0.07, 0.09, 0.10	0.05	0.10
Southern EU	Outdoor	3 x < 0.02, 2 x 0.03, 3 x 0.04, 0.07, 2 x 0.08, 0.12, 0.32, 0.38, 0.43, 0.58	0.06	0.58
Combined EU	Outdoor	3 x < 0.02, 3 x 0.02, 5 x 0.03, 5 x 0.04, 2 x 0.06, 5 x 0.07, 2 x 0.08, 0.09, 0.10, 0.12, 0.32, 0.38, 0.43, 0.58	0.05	0.58

Conclusions

The proposed EU MRLs for chlorothalonil and R182281 together with the corresponding STMR and HR for risk assessment for wheat grain are presented in Table 6.3.3-9 and Table 6.3.3-10. For use in dietary burden estimations, STMR and HR values for wheat straw are also presented in Table 6.3.3-10 and Table 6.3.3-11

Table 6.3.3-10: Proposed EU MRL and proposed STMR and HR for chlorothalonil on wheat

Commodity (code)	Existing EU MRL (mg/kg)	Proposed EU MRL (mg/kg)	STMR (mg/kg)	HR (mg/kg)
Wheat grain (0500090)	0.1	0.1	0.01	0.02
Wheat straw (not applicable)	-	-	0.82	9.9

Table 6.3.3-11: Proposed EU MRL and proposed STMR and HR for R182281 on wheat

Commodity (code)	Existing EU MRL (mg/kg)	Proposed EU MRL (mg/kg)	STMR (mg/kg)	HR (mg/kg)
Wheat grain (0500090)	-	0.02*	0.015	0.02
Wheat straw (not applicable)	-	-	0.06	0.58

CA 6.3.4 Potato

Chlorothalonil is proposed for use on potato according to the following EU critical GAP, detailed in Table 6.3.4-1.

With regards to the number of applications on potatoes, the latest modelling results (as presented in the MCP section 9) have shown that the use on potatoes can only be supported with 1 application. The presented residue trials address 2 applications, although a safe use for the 2 apps can be demonstrated from a dietary safety perspective. So the risk envelope approach can be applied.

Nevertheless trials to address one application on potatoes are ongoing and can be presented in the course of the EU-evaluation.

Table 6.3.4–1: Proposed EU critical GAPs for chlorothalonil on potato

Region	Outdoor/ Protected	Growth stage	Max. No. of Applications	Minimum Application Interval (days)	Maximum		Minimum PHI (days)
					Rate (g a.s./ha)	Water (L/ha)	
Northern EU	Outdoor	BBCH 40-85*	1	-	750	200-800	28
Southern EU	Outdoor	BBCH 40-85*	1	-	750	200-800	28

* Growth stage based on foliage. This is equivalent to BBCH 39 – 47 for the tubers

The residue reports supporting the proposed EU critical GAP for chlorothalonil on potato are referenced in Table 6.3.4-2 and the data are presented in Table 6.3.4-5.

Table 6.3.4-2: Report references for trials supporting the proposed EU critical GAP for chlorothalonil on potato

Annex Pt.	Number.	Author/s	Issue Year	Report Title
K-CA 6.3.4/01	(1 of 4)	A Sala	2014d	Determination of chlorothalonil and its metabolite SDS3701 residues in raw agricultural commodity potato following three applications of chlorothalonil 500SC, 2 trials, northern Europe, year 2013, Syngenta File No. R044636_11232, Report No. RAU-022-13

Annex Pt.	Number.	Author/s	Issue Year	Report Title
K-CA 6.3.4/02	(2 of 4)	A Sala	2014e	Determination of chlorothalonil and its metabolite SDS3701 residues in raw agricultural commodity potato following three applications of chlorothalonil 500SC (2 trials, northern Europe, year 2014), Syngenta File No. R044636_11234, Report No. RAU-011-14
K-CA 6.3.4/03	(3 of 4)	A Sala	2014f	Determination of chlorothalonil and its metabolite SDS3701 residues in raw agricultural commodity potato following three applications of chlorothalonil 500SC, 2 trials, southern Europe, year 2013, Syngenta File No. R044636_11231, Report No. RAU-021-13
K-CA 6.3.4/04	(4 of 4)	A Sala	2014g	Determination of chlorothalonil and its metabolite SDS3701 residues in raw agricultural commodity potato following three applications of chlorothalonil 500SC (2 trials, southern Europe, year 2014), Syngenta File No. R044636_11233, Report No. RAU-022-14

Guidelines

The studies meet the requirements of the Commission of the European Communities: General Recommendations for the Design, Preparation and Realization of Residue Trials (**7029/V1/95 rev. 5, 22/7/1997**), and are designed to comply with **Regulation (EC) 1107/2009**.

GLP

All trials (field and analytical phases) were carried out in compliance with the principles of Good Laboratory Practice.

Materials and Methods

Eight supervised residue trials were conducted on field grown potato in 2013 and 2014, in northern or southern Europe. A summary of the trials conducted is presented in Table 6.3.4-3.

Table 6.3.4-3: Summary of chlorothalonil residue trials on potato

Country	2013	2014
Northern Europe		
France (north)	1 Harvest	2 Harvest
Belgium	1 Harvest	-
Southern Europe		
France (south)	1 Harvest	1 Harvest
Italy	1 Harvest	1 Harvest

Decline trials are those with three or more sampling times.

Potatoes are a major crop in northern and southern Europe and therefore generally require eight trials in each residue region.

Treatments with chlorothalonil were conducted as post emergence (BBCH 39-47 based on growth stages of the tuber) spray applications utilising the formulation as detailed in Table 6.3.4-4 at a nominal application rate of 750 g a.s./ha (actual rates 697-812 g a.s./ha) with an interval of 7 days between applications. The water volumes during application ranged from 346 to 510 L/ha.

Table 6.3.4-4: Summary of chlorothalonil formulations used in the presented trials

Product code	Formulation type	Composition	
		2013	2014
Chlorothalonil 500 SC	SC	502 g/L chlorothalonil (batch O232)	507 g/L chlorothalonil (batch PN1911)

Samples of whole tubers were taken and analysed for residues of parent chlorothalonil and the metabolite R182281 (SDS3701) by analytical methods described in study RAU-022-14. The LOQ is 0.01 mg/kg for chlorothalonil and 0.02 mg/kg for R182281. Full method descriptions and validation data are presented in document M-CA Section 4, CA 4.1.2. Procedural recovery data are presented with the results of the residues trials in Table 6.3.4-5.

Allowing for a 25% deviation from the proposed maximum application rate, rates and application timings in all trials cover the critical EU GAP. The proposed GAP is for one application; however the trials were treated with three applications. Residues of both chlorothalonil and R182281 were below the LOQ in tubers in all the trials, indicating that the number of applications did not impact on residues at harvest. Therefore the trials conducted with three applications can be considered to support the proposed GAP.

Samples were stored up to a maximum of 5 months from sampling to extraction. Samples were homogenised in without acid before freezing. Residues of chlorothalonil and R18221 are stable in homogenised high starch commodities for at least 24 months (see section CA 6.1) and therefore no degradation will have occurred between sampling and analysis.

The available trials are sufficient to support the EU GAP for potato. 4 acceptable trials are available for northern Europe and 4 acceptable trials are available for southern Europe. Although generally a minimum of 8 trials are required in each region the residues of both chlorothalonil and R182281 were below the LOQ in all trials conducted at a more critical GAP therefore a reduced data set of 4 trials for each region is acceptable.

The results of the residue trials for chlorothalonil and R182281 are presented in Table 6.3.4-5.

Table 6.3.4-5: Summary of residue data supporting the EU critical GAP for chlorothalonil on potato

GLP and Trial Details	Crop (Variety)	Country (Region)	Application Rate Product Code	Growth Stage at application	PHI (days)	Crop Part (Growth stage at sampling)	Residue Found (Uncorrected)		Recovery Data
							chlorothalonil mg/kg	R182281 (mg/kg)	
Northern Europe									
Report: RAU-022-13 Study : RAU-022-13 Trial: F/CH13/PO03 Study to GLP - Study carried out in 2013	Potato (Marabel)	FRANCE (Europe North)	715 g a.s./ha 778 g a.s./ha 766 g a.s./ha 500 g/L SC	Tuber growth stages BBCH 39-40 BBCH 40 BBCH 40-43	28	Tuber (BBCH 49)	<0.01	<0.02	Chlorothalonil Whole tubers: mean = 96% RSD = NA (n = 2 in 0.01 – 0.1 mg/kg spiking range) R182281 (SDS3701) Whole tubers: mean = 101% RSD = NA (n = 2 in 0.02 – 0.20 mg/kg spiking range)
Report: RAU-022-13 Study : RAU-022-13 Trial: B/CH13/PO04 Study to GLP - Study carried out in 2013	Potato (Bintje)	BELGIUM (Europe North)	759 g a.s./ha 747 g a.s./ha 697 g a.s./ha 500 g/L SC	Tuber growth stages BBCH 45† BBCH 47-48† BBCH 47-48†	28	Tuber (BBCH 49)	<0.01	<0.02	
Report: RAU-011-14 Study : RAU-011-14 Trial: F/CH14/PO03 Study to GLP - Study carried out in 2014	Potato (Samba)	FRANCE (Europe North)	786 g a.s./ha 786 g a.s./ha 812 g a.s./ha 500 g/L SC	Tuber growth stages BBCH 43 BBCH 43 BBCH 45	28	Tuber (BBCH 49)	<0.01	<0.02	Chlorothalonil Whole tubers: mean = 97% RSD = NA (n = 2 in 0.01 – 0.1 mg/kg spiking range) R182281 (SDS3701) Whole tubers: mean = 90% RSD = NA (n = 2 in 0.02 – 0.20 mg/kg spiking range)
Report: RAU-011-14 Study : RAU-011-14 Trial: F/CH14/PO04 Study to GLP - Study carried out in 2014	Potato (Bintje)	FRANCE (Europe North)	751 g a.s./ha 766 g a.s./ha 766 g a.s./ha 500 g/L SC	Tuber growth stages BBCH 45 BBCH 45 BBCH 46	28	Tuber (BBCH 49)	<0.01	<0.02	
Southern Europe									
Report: RAU-021-13 Study : RAU-021-13 Trial: F/CH13/PO01 Study to GLP - Study carried out in 2013	Potato (Ermes)	ITALY (Europe South)	764 g a.s./ha 753 g a.s./ha 740 g a.s./ha 500 g/L SC	Tuber growth stages BBCH 43† BBCH 43† BBCH 43†	27	Tuber (BBCH 47-48†)	<0.01	<0.02	Chlorothalonil Whole tubers: mean = 95% RSD = NA (n = 2 in 0.01 – 0.1 mg/kg spiking range) R182281 (SDS3701) Whole tubers: mean = 99% RSD = NA

GLP and Trial Details	Crop (Variety)	Country (Region)	Application Rate Product Code	Growth Stage at application	PHI (days)	Crop Part (Growth stage at sampling)	Residue Found (Uncorrected) chlorothalonil mg/kg	 R182281 (mg/kg)	Recovery Data
Report: RAU-021-13 Study : RAU-021-13 Trial: F/CH13/PO02 Study to GLP - Study carried out in 2013	Potato (Agatha)	FRANCE (Europe South)	766 g a.s./ha 777 g a.s./ha 766 g a.s./ha 500 g/L SC	Tuber growth stages BBCH 41-43 BBCH 43 BBCH 43	28	Tuber (BBCH 49)	<0.01	<0.02	(n = in 0.02 – 0.20 mg/kg spiking range)
Report: RAU-022-14 Study : RAU-022-14 Trial: F/CH14/PO01 Study to GLP - Study carried out in 2014	Potato (Kennebec)	ITALY (Europe South)	776 g a.s./ha 776 g a.s./ha 761 g a.s./ha 500 g/L SC	Tuber growth stages BBCH 41 BBCH 44 BBCH 47	28	Tuber (BBCH 49)	<0.01	<0.02	Chlorothalonil Whole tubers: mean = 96% RSD = 6.2% (n = 10 in 0.01 – 0.1 mg/kg spiking range) R182281 (SDS3701) Whole tubers: mean = 97% RSD = 6.4% (n = 10 in 0.02 –0.20 mg/kg spiking range)
Report: RAU-022-14 Study : RAU-022-14 Trial: F/CH14/PO02 Study to GLP - Study carried out in 2014	Potato (Bintje)	FRANCE (Europe South)	788 g a.s./ha 794 g a.s./ha 788 g a.s./ha 500 g/L SC	Tuber growth stages BBCH 42 BBCH 43† BBCH 43	28	Tuber (BBCH 48†)	<0.01	<0.02	

Unless otherwise stated residues of chlorothalonil and R182281 in untreated samples were < LOQ of 0.01 and 0.02 mg/kg respectively.

†Growth stages were expressed in terms of the foliage in the report. These have been expressed in the terms of the tuber for consistency across all trials.

NA = not applicable

Findings

For MRL setting and risk assessment, the definition of the residue for chlorothalonil is parent chlorothalonil only. In addition a separate residue definition for 2,5,6-trichloro-4-hydroxyphtalonitrile (R182281 or SDS3701) is also proposed. Separate calculations for both chlorothalonil and R182281 are presented below.

Chlorothalonil residue calculations for MRL setting and risk assessment

MRLs, STMR and HR values for potatoes have been calculated for northern and southern Europe for chlorothalonil. The STMR is the median residue and the HR is the highest residue value found. MRLs are calculated according to the OECD calculator (**OECD Series on pesticides No. 56, ENV/JM/MONO (2011)2, 1 March 2011**). In these calculations a single data point from each trial supporting the EU critical GAP has been considered. The chlorothalonil residue values used in the MRL, STMR and HR calculations are underlined in Table 6.3.4-5. The calculated outputs are presented in Table 6.3.4-6.

Table 6.3.4-6: MRL, STMR and HR calculations for chlorothalonil on potato (tubers) – proposed EU GAPs

Region	Outdoor / Protected	Residue Data (mg/kg)	MRL OECD Method (mg/kg)	MRL OECD Rounded (mg/kg)	STMR (mg/kg)	HR (mg/kg)
Northern EU	Outdoor	4 x < 0.01	0.01	0.01*	0.01	0.01
Southern EU	Outdoor	4 x < 0.01	0.01	0.01*	0.01	0.01
Combined EU	Outdoor	8 x < 0.01	0.01	0.01*	0.01	0.01

There is an existing EU MRL of 0.02 mg/kg for chlorothalonil on potatoes (parent chlorothalonil). A recent proposal currently being considered (SANCO 12240/2013) has proposed a MRL of 0.01* mg/kg. The data presented in Table 6.3.4-6 from trials supporting the proposed EU critical GAP indicate that residues will be within the recently proposed EU MRL of 0.01* mg/kg.

R182281 residue calculations for MRL setting and risk assessment

MRLs, STMR and HR values for potatoes have been calculated for northern and southern Europe for R182281. The STMR is the median residue and the HR is the highest residue value found. MRLs are calculated according to the OECD calculator (**OECD Series on pesticides No. 56, ENV/JM/MONO (2011)2, 1 March 2011**). In these calculations a single data point from each trial supporting the EU critical GAP has been considered. The R182281 residue values used in the MRL, STMR and HR calculations are underlined in Table 6.3.4-5. The calculated outputs are presented in Table 6.3.4-7.

Table 6.3.4-7: MRL, STMR and HR calculations for R182281 on potato (tubers) – proposed EU GAPs

Region	Outdoor / Protected	Residue Data (mg/kg)	MRL OECD Method (mg/kg)	MRL OECD Rounded (mg/kg)	STMR (mg/kg)	HR (mg/kg)
Northern EU	Outdoor	4 x < 0.02	0.02	0.02*	0.02	0.02
Southern EU	Outdoor	4 x < 0.02	0.02	0.02*	0.02	0.02
Combined EU	Outdoor	8 x < 0.02	0.02	0.02*	0.02	0.02

There are currently no EU MRLs for R182281. The data presented in Table 6.3.4-7 from trials supporting the proposed EU critical GAP indicate that an MRL of 0.02 mg/kg is appropriate.

Conclusions

The proposed EU MRLs for chlorothalonil and R182281 together with the corresponding STMR and HR for risk assessment for potatoes are presented in Table 6.3.4-8 and Table 6.3.4-9, respectively.

Table 6.3.4-8: Proposed EU MRL and proposed STMR and HR for chlorothalonil on potatoes

Commodity (code)	Existing EU MRL (mg/kg)	Proposed EU MRL (mg/kg)	STMR (mg/kg)	HR (mg/kg)
Potatoes (0211000)	0.02/0.01*†	0.01*	0.01	0.01

† proposal currently being considered (SANCO 12240/2013)

Table 6.3.4-9: Proposed EU MRL and proposed STMR and HR for R182281 on potatoes

Commodity (code)	Existing EU MRL (mg/kg)	Proposed EU MRL (mg/kg)	STMR (mg/kg)	HR (mg/kg)
Potatoes (0211000)	-	0.02	0.02	0.02

CA 6.4 Feeding Studies

Dietary burden calculations

It is an EU data requirement (**Commission Regulation (EU) No 283/2013, 1 March 2013**) and guideline requirement (**OECD 505, Residues in Livestock**) to estimate the dietary intakes for poultry, dairy cattle, beef cattle and pigs if residues are likely in crops or part of crops fed to animals.

The potential dietary exposure to chlorothalonil and R182281 residues in the supported representative crops of tomato, barley, wheat and potato or their processed products has been calculated using the EU methodologies described. According to available OECD guidance, for the crops considered in this document, products from tomato, barley, wheat and potato may form a part of global livestock diets. However, on the basis of the OECD feeding tables only the following commodities form part of the dietary burden for livestock species in the EU:

Barley straw and grain; wheat straw and grain; distillers grain, brewers grain, wheat meal; wheat milled by-products; potato culls; potato process waste and potato dried pulp.

Barley and wheat forage and silage are not considered relevant crops as the proposed uses for chlorothalonil are on cereals for grain production only.

The dietary inputs into the calculation are summarised in Table 6.4-1 and 6.4-2. The highest residues in supervised trials (HR) are used to calculate the maximum potential dietary intake except for feed commodities that are bulked, where the STMR is used, or processed, where the STMR-P is used, as detailed in Table 6.4-1. The STMR values in supervised trials have been used to calculate the median potential dietary intake.

The residue definition for risk assessment is defined as chlorothalonil alone and R182281 alone. Dietary burdens have been calculated on the basis of the combined residue of chlorothalonil and R182281 as residues found in treated crops feed to animals will potentially be comprised of both chlorothalonil and R182281. The exposure to livestock will therefore be for the combined residue rather than the two

compounds individually. Livestock metabolism data indicate that residues in animal products will comprise of R182281 when animals are dosed with either chlorothalonil or R182281.

The combined residue has been calculated as follows:

Combined residue = Residue of chlorothalonil + (residue R182281 x 0.931)

[Conversion of R182281 residues to chlorothalonil based on molecular weight]

Table 6.4-1: Chlorothalonil and R182281 residue values used for calculation of livestock dietary burdens

Commodity	Commodity category[1]	STMR (mg/kg)	Processing factor	STMR-P (mg/kg)	HR (mg/kg)	Origin
Chlorothalonil						
Barley straw	Forages	1.5	--	--	5.7	Residue data in CA 6.3.2
Wheat straw		0.82	--	--	9.9	Residue data in CA 6.3.3
Barley grain	Cereal grains/ Crops seeds	0.01	--	--	--	Residue data in CA 6.3.2
Wheat grain		0.01	--	--	--	Residue data in CA 6.3.3
Potato culls	Roots and Tubers	0.01	5.0	0.05	0.05	Residue data in CA 6.3.4 Theoretical processing factor used[2]
Distillers grain[2]	By-products	0.01	0.02	0.0002	--	Residue data in CA 6.3.2 Mean processing factor for spent grain used.
Brewers grain		0.01	0.02	0.0002	--	Residue data in CA 6.3.2 Mean processing factor for spent grain used.
Wheat meal		0.01	0.18	0.0018	--	Residue data in CA 6.3.3 Mean processing factor for gluten used.
Wheat milled by-products		0.01	2.2	0.022	--	Residue data in CA 6.3.3 Mean processing factor for bran used.
Potato process waste		0.01	4.0	0.04	--	Residue data in CA 6.3.4 Theoretical processing factor used[2]
Potato dried pulp		0.01	4.4	0.044	--	Residue data in CA 6.3.4 Theoretical processing factor used[2]
R182281						
Barley straw	Forages	0.10	--	--	1.1	Residue data in CA 6.3.2
Wheat straw		0.06	--	--	0.58	Residue data in CA 6.3.3
Barley grain	Cereal grains/ Crops seeds	0.015	--	--	--	Residue data in CA 6.3.2
Wheat grain		0.015	--	--	--	Residue data in CA 6.3.3
Potato culls	Roots and Tubers	0.02	5.0	0.10	0.10	Residue data in CA 6.3.4 Theoretical processing factor used[2]
Distillers grain	By-products	0.015	0.38	0.006	--	Residue data in CA 6.3.2 Mean processing factor for spent grain used.
Barley - Brewers grain		0.015	0.38	0.006	--	Residue data in CA 6.3.2 Mean processing factor for spent grain used.
Wheat meal		0.015	0.8	0.012	--	Residue data in CA 6.3.3 Mean processing factor for gluten used.
Wheat milled by-products		0.015	4.5	0.07	--	Residue data in CA 6.3.3 Mean processing factor for bran used.
Potato process waste		0.02	4.0	0.08	--	Residue data in CA 6.3.4 Theoretical processing factor used[2]
Potato dried pulp		0.02	4.4	0.088	--	Residue data in CA 6.3.4 Theoretical processing factor used[2]

[1] - As defined in ENV/JM/MONO(2009)31
[2] - As defined in US EPA Residue Chemistry Test Guidelines, OPPTS 860.1520, Processed Food/Feed, 1996
For the purposes of calculation values stated to be "<"are assumed to be at that value e.g. < 0.01 is assumed to be 0.01

Table 6.4-2: Combined chlorothalonil and R182281 residue values used for calculation of livestock dietary burdens

Commodity	Commodity category	STMR or STMR-P (mg/kg)			HR (mg/kg)		
		Chlorothalonil	R182281	Total	Chlorothalonil	R182281	Total
Barley straw	Forages	1.5	0.10	1.59[1]	5.7	1.1	6.72
Wheat straw		0.82	0.06	0.87	9.9	0.58	10.44
Barley grain	Cereal grains/ Crops seeds	0.01	0.015	0.024	--	--	--
Wheat grain		0.01	0.015	0.024	--	--	--
Potato culls	Roots and Tubers	0.05	0.10	0.143	0.05[2]	0.10[2]	0.143
Distillers grain	By-products	0.0002	0.006	0.0058	--	--	--
Brewers grain		0.0002	0.006	0.0058	--	--	--
Wheat meal		0.0018	0.012	0.014	--	--	--
Wheat milled by-products		0.022	0.07	0.092	--	--	--
Potato process waste		0.04[1]	0.08[1]	0.114	--	--	--
Potato dried pulp		0.044[2]	0.088[2]	0.126	--	--	--

[1] Total Residue = Residue of chlorothalonil + (residue R182281 x 0.931).
[2] STMR-P used

Table 6.4-3 presents a summary of the dietary burden calculations calculated for combined residues of chlorothalonil and R182281 in each livestock species.

Table 6.4-3: Maximum and median dietary intakes of combined residues of chlorothalonil and R182281 in livestock species

Livestock species	Maximum Residue intake (mg a.s./kg bw/day)	Median Residue intake (mg a.s./kg bw/day)
Beef cattle	0.071	0.027
Dairy cattle	0.111	0.040
Rams/Ewes	0.176	0.049
Lambs	0.216	0.060
Breeding Swine	0.013	0.013
Finishing Swine	0.012	0.012
Broiler hens	0.008	0.008
Laying hens	0.089	0.014
Turkey	0.013	0.013

CA 6.4.1 Poultry

Calculated only for the supported crop uses in this submission, the maximum dietary burden of combined chlorothalonil and R182281 residues in poultry is shown to be 0.089 mg/kg bw/day for laying hens.

No feeding studies were submitted for Annex I listing of chlorothalonil. Derivation of appropriate residue levels in poultry products on the basis of the proposed uses of chlorothalonil is discussed in CA 6.4.3.

CA 6.4.2 Ruminants

Calculated only for the supported crop uses in this submission, the maximum dietary burden combined chlorothalonil and R182281 in ruminants is shown to be 0.216 mg/kg bw/day for lambs.

No feeding studies were submitted for Annex I listing of chlorothalonil. New studies are available, and full summaries are presented here. Derivation of appropriate residue levels in ruminant products on the basis of the proposed uses of chlorothalonil is discussed in CA 6.4.3.

Report:	K-CA 6.4.2/01. Wiedmann JL and Kenyon RG. (1995), Meat and milk magnitude of residue study in lactating dairy cows dosed with chlorothalonil and SDS-3701. Ricerca Inc, Syngenta Report No. 6007-94-0120-CR-003 (Syngenta File No. R44686/1598).

Guidelines

US EPA Guideline 171-4

GLP

The study was carried out according to the principles of Good Laboratory Practice.

EXECUTIVE SUMMARY

Lactating Holstein cattle were dosed for 28 consecutive days with a mixture of chlorothalonil and R182281 by gelatin capsules at a dietary concentration of 0.5X, 1X, 3X or 10X (four animals per group) where the 1X dose was 3 mg/kg chlorothalonil and 0.2 mg/kg R182281 in the diet. Four additional cows served as controls.

Milk samples were collected twice daily and on days 9, 15, 21 and 27 extra composite samples of milk were made and separated into skimmed milk and cream fractions. Within 24 hours of the final dose all animals were sacrificed and samples of round muscle, loin muscle, liver, kidney, perirenal fat and omental fat were taken. Samples were analysed for residues of R182281.

Residues of R182281 were found in all tissues and milk for all dose levels with the exception of muscle samples from the lowest dose level. Residues of R182281 in milk reached plateau levels after approximately 10 days at all dosing levels, and did not concentrate into either cream or skimmed milk.

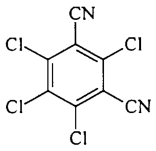
Maximum residues of R182281 in milk were 0.04, 0.10, 0.31 and 0.65 mg/kg, respectively, for the 0.5X, 1X, 3X and 10X dose levels. Highest residues of R182281 were found in kidney and liver; respectively ranging from 0.14 to 1.19 mg/kg and 0.03 to 0.55 mg/kg, depending on the dose level.

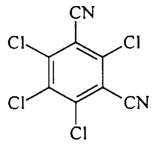
Residues of R182281 showed a broadly linear relationship to dosing level in milk and animal tissues.

I. MATERIALS AND METHODS

A. MATERIALS

A1. Test Materials

Structure	
Common name	Chlorothalonil
Syngenta code	R044686
CAS Number	1897-45-6
Batch number	SDS-2787-1501 (99.6%)
Stability of test compound	The test substance is assumed to be stable for the duration of the dosing period

Structure	
Common name	2,5,6-trichloro-4-hydroxyisophthalonitrile
Syngenta code	R182281
CAS Number	28343-61-5
Batch number	SDS-3701-0201 (100%) SDS-3701-0301 (99.2%)
Stability of test compound	The test substance is assumed to be stable for the duration of the dosing period

A2. Test Facilities

In-life phase	Bio-Life Associates Ltd, Neillsville, Wisconsin, USA.
Analytical phase	Ricerca Inc., Department of Residues Analysis, Painesville, Ohio, USA

A2. Test Animals

Species	Holstein cows
Age	3-5 years old
Weight at dosing	407-636 kg
Number of animals	20 (four groups of 4 per treatment, 4 control)
Acclimation period	15 days
Diet and water	4.6 kg commercial dairy ration during a.m. and p.m. milking, 15 kg alfalfa hay cubes, 2 kg hay per day. Fresh drinking water *ad libitum*
Housing	Indoors, in individual stalls

Environmental conditions	Average temp 23°C; Rel. Humid 83%; 14 hours light per 24 hours

B. STUDY DESIGN

B1. Experimental conditions

Dosing regime	**Group**	**Treatment**	**Dietary concentration (mg/kg)**	**Dose rate (mg/day)**
	Control	Control	0	0
	0.5X	Chlorothalonil	1.5	39.3
		R182281	0.1	2.62
	1X	Chlorothalonil	3	78.6
		R182281	0.2	5.24
	3X	Chlorothalonil	9	235.8
		R182281	0.6	15.72
	10X	Chlorothalonil	30	786
		R182281	2	52.4
Timing	Once per day after morning milking			
Duration	28 consecutive days			
Method	Gelatine capsules via bolus			

B2. Sample Collection

Milk samples for analysis were collected twice daily and pooled. On days 9, 15, 21 and 27 aliquots of the pooled milk samples were separated into skimmed milk and cream fractions. Within 24 hours of the final dose all animals were sacrificed and samples of round muscle, loin muscle, liver, kidney, perirenal fat and omental fat were taken.

All tissue and milk samples were stored frozen until analysis. Tissue samples were stored for up to three months before extraction, and milk and cream samples for up to seven months.

B3. Analytical Phase

Residues of R182281 were determined by analytical method 6007-94-0120-CR000:

The method involved extraction of the samples with acetone/sulphuric acid followed by filtration. An aliquot of the extract was taken, evaporated into dryness and re-dissolved in sodium hydrogen carbonate solution. The extract was partitioned initially with petroleum ether and then into diethyl ether. Residues of R182281 were derivatised with trimethylsilyl diazomethane to produce methyl R182281 (R619464). The extract was then passed through an alumina column clean-up before analysis by GC-ECD. The LOQ was 0.01 mg/kg. Procedural recovery data are presented in Table 6.4.2.-1.

II. RESULTS AND DISCUSSION

Table 6.4.2-1: Summary of procedural recoveries for R182281 in product of animal origin

Commodity	Fortification Range (mg/kg)	No samples	Recovery range (%)	Mean recovery (%)	RSD (%)
Milk	0.01-1.0	116	70-120	99	9.6
Skimmed milk	0.01-0.80	16	86-112	97	6.9
Butterfat	0.01-0.50	16	84-110	97	6.9
Omental fat	0.01-0.50	3	82-100	91	9.0
Perirenal fat	0.01-0.50	4	71-96	83	10
Loin muscle	0.01-0.20	4	78-103	89	12
Round Muscle	0.01-0.50	4	90-110	102	8.7
Liver	0.01-0.50	4	76-106	94	14
Kidney	0.01-5.0	4	94-120	101	13

The R182281 residue levels in milk reached plateau levels after approximately 10 days in all dose groups, and based on the residue levels from the 1X dose group, the residue levels in milk from the other dose groups bear a reasonably linear relationship. Maximum residues of R182281 in milk were 0.04, 0.10, 0.31 and 0.65 mg/kg for the 0.5X, 1X, 3X and 10 X dose levels, respectively.

The maximum levels of R182281 in the butterfat and skimmed milk samples were equivalent indicating no significant concentration of residues into either of the fractions.

The results in milk are summarised in Table 6.4.2-2.

Table 6.4.2-2: R182281 residue levels in whole milk, skimmed milk and butterfat of lactating cows

	0.5 X dose: 1.5 mg chlorothalonil/kg 0.1 mg R182281/kg	1 X dose: 3 mg chlorothalonil/kg 0.2 mg R182281/kg	3 X dose: 9 mg chlorothalonil/kg 0.6 mg/kg R182281	10 X dose: 30 mg chlorothalonil/kg 2.0 mg R182281/kg
R182281 Residue Levels in Whole Milk (mg/kg)				
Range*	0.02 – 0.04	0.02 – 0.10	0.11 – 0.31	0.37 – 0.65
Mean*	0.03	0.06	0.20	0.48
Maximum	0.04	0.10	0.31	0.65
R182281 Residue Levels in Skimmed Milk (mg/kg)				
Range	0.02 – 0.04	0.03 – 0.08	0.13 – 0.28	0.33 – 0.59
Mean	0.03	0.05	0.19	0.42
Maximum	0.04	0.08	0.28	0.59
R182281 Residue Levels in Butterfat (mg/kg)				
Range	0.03 – 0.06	0.04 – 0.09	0.12 – 0.26	0.30 – 0.58
Mean	0.04	0.06	0.19	0.44
Maximum	0.06	0.09	0.26	0.58

* Data refer to values after plateau was reached.

No residues of R182281 at or above 0.01 mg/kg were found in muscle samples for the lowest dose level. Maximum residues of R182281 following the 1X, 3X and 10X dose levels were, respectively, 0.02, 0.09 and 0.15 mg/kg in round muscle and 0.02, 0.07 and 0.24 mg/kg in loin muscle.

Following the 0.5X and 1X dose levels, maximum residues of R182281 were, respectively, 0.14 and 0.28 mg/kg in kidney, 0.03 and 0.04 mg/kg in liver, 0.03 and 0.07 mg/kg in omental fat, and 0.02 and 0.05 mg/kg in perirenal fat.

Following the 3X and 10X dose levels, maximum residues of R182281 were, respectively, 0.55 and 1.19 mg/kg in kidney, 0.18 and 0.55 mg/kg in liver , 0.06 and 0.36 mg/kg in omental fat, and 0.08 and 0.85 mg/kg in perirenal fat.

As for the milk samples, based on the residue levels from the 1X dose group, the residue levels in animal tissues from the other dose groups bear a reasonably linear relationship.

The results in tissues are summarised in Table 6.4.2-3.

Table 6.4.2-3: Residues of R182281 in tissues of lactating cows

Tissue		R182281 Residue Levels in Tissues (mg/kg)			
		0.5 X dose: 1.5 mg chlorothalonil/kg 0.1 mg R182281/kg	**1 X dose: 3 mg chlorothalonil/kg 0.2 mg R182281/kg**	**3 X dose: 9 mg chlorothalonil/kg 0.6 mg R182281/kg**	**10 X dose: 30 mg chlorothalonil/kg 2.0 mg R182281/kg**
Round Muscle	Mean	<0.01	0.01	0.06	0.14
	Maximum	<0.01	0.02	0.09	0.15
Loin Muscle	Mean	<0.01	0.01	0.05	0.15
	Maximum	<0.01	0.02	0.07	0.24
Liver	Mean	0.02	0.03	0.16	0.45
	Maximum	0.03	0.04	0.18	0.55
Kidney	Mean	0.14	0.20	0.49	0.95
	Maximum	0.14	0.28	0.55	1.19
Perirenal Fat	Mean	0.02	0.04	0.06	0.67
	Maximum	0.02	0.05	0.08	0.85
Omental Fat	Mean	0.03	0.04	0.04	0.21
	Maximum	0.03	0.07	0.06	0.36

III. CONCLUSIONS

Residues of R182281 were found in all tissues and milk for all dose levels with the exception of muscle samples from the lowest dose level. Residues of R182281 in milk reached plateau levels after approximately 10 days at all dosing levels, and did not concentrate into either cream or skimmed milk.

Maximum residues of R182281 in milk were 0.04, 0.10, 0.31 and 0.65 mg/kg, respectively, for the 0.5X, 1X, 3X and 10X dose levels. Highest residues of R182281 were found in kidney and liver; respectively ranging from 0.14 to 1.19 and 0.03 to 0.55 mg/kg, depending on the dose level.

Residues of R182281 showed a broadly linear relationship to dosing level in milk and animal tissues.

(Wiedmann JL, Kenyon RG, 1995)

Report:	K-CA 6.4.2/02. Dever M (2008); The determination of tissue residues as measured by the major metabolite 4-hydroxy-2,5,6-trichloro-1,3-dicyanobenzene in liver, kidney, muscle and fat following daily ingestion by cattle of chlorothalonil over a 28 day period. Veterinary Health Research PTY Ltd. Report No SICB1880, Syngenta File No. R044686_11199.

Guidelines

Commission Directive 96/68/EC

US EPA Residue Chemistry Test Guidelines OPPTS 860.1480.

GLP

The study was carried out according to the principles of Good Laboratory Practice.

EXECUTIVE SUMMARY

Beef cattle were dosed for 28 consecutive days with chlorothalonil in the feed at a concentration of 0.1, 1.5 or 12.7 mg/kg chlorothalonil bw/day. Three additional cows served as controls.

Within 24 hours of the final dose animals were sacrificed and samples of muscle, liver, kidney, perirenal fat and subcutaneous fat were taken. Two animals from the highest dosing group were sacrificed 14 days after the last dose and samples of round muscle, loin muscle, liver, kidney, perirenal fat and sub-cutaneous fat were taken. Samples were analysed for residues of 4-hydroxy-2,5,6-trichloro-1,3-dicyanobenzene (R182281).

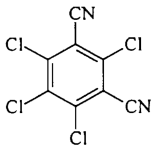
Residues of R182281 were found in all tissues for all dose levels with the exception of muscle and fat samples from the lowest dose level. Highest residues of R182281 were found in liver and kidney; respectively ranging from 0.008 to 1.04 mg/kg and 0.024 to 1.51 mg/kg, depending on the dose level.

Residues of R182281 decreased after a 14 day depuration period, although were still significant. Residues of R182281 showed a broadly linear relationship to dosing level in animal tissues.

I. MATERIALS AND METHODS

A. MATERIALS

A1. Test Materials

Structure	
Common name	Chlorothalonil
CAS Number	1897-45-6
Batch number	F343 (98.6%)
Stability of test compound	The test substance is assumed to be stable for the duration of the dosing period

A2. Test Facilities

In-life phase	Veterinary Health Research Pty Ltd, New South Wales, Australia.
Analytical phase	Veterinary Health Research Pty Ltd, New South Wales, Australia.

A2. Test Animals

Species	Angus and Angus cross male castrates
Age	18 months
Weight at dosing	400-452 kg
Number of animals	14 (3 for low and medium dose, 5 for high dose, 3 control)
Acclimation period	14 days
Diet and water	Mixed ration calculated daily. Residual feed weighed and discarded daily. Fresh drinking water *ad libitum*
Housing	Indoors, in individual stalls

B. STUDY DESIGN

B1. Experimental conditions

Dosing regime	**Group**	**Treatment**	**Dietary concentration (mg/kg)**	**Dose rate (mg/day)***
	Group 1	Control	0	0
	Group 2	Chlorothalonil	0.1	41.1-44.5
	Group 3	Chlorothalonil	1.5	635 - 698
	Group 4	Chlorothalonil	12	5136 - 5555
Timing	Once per day			
Duration	28 consecutive days			
Depuration	14 days			
Method	Mixed into feed			

*Animals were weighed on a weekly basis and the bodyweight data used to determine the actual dose rate in the following week. The average feed intake data were used to calculate the actual dose rate administered.

B2. Sample Collection

Within 24 hours of the final dose animals were sacrificed and samples of muscle, liver, kidney, perirenal fat and subcutaneous fat were taken. Two animals from the highest dosing group were sacrificed 14 days after the last dose and samples of round muscle, loin muscle, liver, kidney, perirenal fat and sub-cutaneous fat were taken.

All samples were stored frozen for up to 11 months before analysis.

B3. Analytical Phase

Residues of R182281 were determined by an analytical method based on the QuEChERS method:

The method involved extraction of the samples with acetonitrile containing 1% acetic acid, followed by the addition of anhydrous magnesium sulphate and sodium acetate and further homogenisation. The extracts were centrifuged and the supernatant removed. The supernatant was evaporated into dryness and re-dissolved in acetonitrile: water (1:1 v/v). Residues of R182281 were determined by LC-MS, using ion *m/z* 245 for quantification and *m/z* 247 for confirmation. The LOQ was 0.005 mg/kg.

II. RESULTS AND DISCUSSION

Recovery data for the method of analysis are presented in Table 6.4.2-4. Samples from the feeding study were analysed against matrix matched standards and linearity was demonstrated in liver, kidney, muscle and fat matrices over the concretion range equivalent to 0.005 - 0.075 mg/kg ($r^2 > 0.996$).

Table 6.4.2-4: Summary of recovery data for R182281 in products of animal origin

Commodity	Fortification concentration (mg/kg)	Quantified against solvent standards			Quantified against matrix matched standards		
		No. samples	Mean recovery (%)	RSD (%)	No samples	Mean recovery (%)	RSD (%)
Bovine liver	0.005	7	64	6	7	116	10
	0.01	7	57		7	101	10
	0.025	7	58		7	103	4
	0.075	7	57		7	107	6
Bovine kidney	0.005	7	116	6	7	114	4
	0.01	7	121		7	106	4
	0.025	7	107		7	89	7
	0.075	7	108		7	92	9
Bovine muscle	0.005	7	66	13	7	106	8
	0.01	7	57		7	90	9
	0.025	7	52		7	85	7
	0.075	7	51		7	89	6
Bovine fat	0.005	7	88	18	7	94	14
	0.01	7	80		7	87	7
	0.025	7	120		7	113	11
	0.075	7	96		7	99	11

No residues of R182281 at or above 0.005 mg/kg were found in muscle or fat samples for the lowest dose level.

Maximum residues of R182281 found in the medium and high dose levels were, respectively, 0.01 and 0.06 mg/kg in muscle and 0.026 and 0.078 mg/kg in fat.

Following the lowest dose, maximum residues of R182281 were 0.008 mg/kg in liver and 0.024 mg/g in kidney.

For the medium and highest dose levels, maximum residues of R182281 were, respectively, 0.087 and 1.04 mg/kg in liver, and 0.39 and 1.51 mg/kg in kidney.

For the highest dose level, residues of R182281 decreased after a 14 day depuration period, although were still significant. Based on the residue levels from the lowest dose group, the residue levels in animal tissues from the other dose groups show a reasonably linear relationship.

The results in tissues are summarised in Table 6.4.2-5.

Table 6.4.2-5: Residues of R182281 in tissues of beef cows

Tissue		R182281 Residue Levels in Tissues (mg/kg)			
		0.1 mg/kg	1.5 mg/kg	12 mg/kg	12 mg/kg (after depuration)
Muscle		3 x <0.005	0.006, <0.005, 0.01	0.051, 0.061, 0.043	0.021, 0.034
	Mean	<0.005	0.007	0.052	0.028
Liver		0.008, <0.005, 0.006	0.071, 0.058, 0.087	0.881, 1.04, 0.323	0.460, 0.486
	Mean	0.006	0.072	0.748	0.473
Kidney		0.024, 0.015, 0.020	0.392, 0.273, 0.332	1.450, 1.510, 1.290	1.310, 1.080
	Mean	0.020	0.332	1.416	1.195
Perirenal Fat		3 x <0.005	0.014, <0.005, 0.008	0.078, 0.049, 0.061	0.020, 0.044
	Mean	<0.005	0.009	0.063	0.032
Sub-cutaneous Fat		3 x <0.005	0.026, 0.016, 0.025	0.052, 0.073, 0.070	0.050, 0.081
	Mean	<0.005	0.022	0.065	0.066

III. CONCLUSIONS

Residues of R182281 were found in all tissues for all dose levels with the exception of muscle and fat samples from the lowest dose level. Highest residues of R182281 were found in liver and kidney; respectively ranging from 0.008 to 1.04 mg/kg and 0.024 to 1.51 mg/kg, depending on the dose level.

Residues of R182281 decreased after a 14 day depuration period, although were still significant. Residues of R182281 showed a broadly linear relationship to dosing level in animal tissues.

(Dever M, 2008)

Report:	K-CA 6.4.2/03. Rogers G (2008); The determination of the major metabolite 4-hydroxy-2,5,6-trichloro-1,3-dicyanobenzene residues in bovine milk following daily ingestion of chlorothalonil by lactating dairy cows over a 28 day period. Veterinary Health Research PTY Ltd. Report No SICB1859, Syngenta File No. R044686_11200.

Guidelines

Commission Directive 96/68/EC

US EPA Residue Chemistry Test Guidelines OPPTS 860.1480.

GLP

The study was carried out according to the principles of Good Laboratory Practice.

EXECUTIVE SUMMARY

Dairy cattle were dosed for 28 consecutive days with chlorothalonil in the feed at a concentration of 0.1, 1.5 or 12.7 mg/kg chlorothalonil bw/day. Three additional cows served as controls.

Milk was collected each day in the morning and evening and combined to provide a daily sample for individual cows. The milk from two cows in the highest dose group was collected for a further 14 days

after dosing ceased. Samples were analysed for residues of 4-hydroxy-2,5,6-trichloro-1,3-dicyanobenzene (R182281).

Maximum residues of R182281 found in milk for the low, medium and high dose levels were, respectively, 1.2, 150 and 231 µg/L.

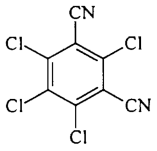
Maximum residues of R182281 found in cream for the low, medium and high dose levels were, respectively, 17.5, 247 and 336 µg/L.

For the highest dose level, residues of R182281 in whole milk decreased after a 14 day depuration period, although were still significant. Residues in cream increased during the depuration period.

I. MATERIALS AND METHODS

A. MATERIALS

A1. Test Materials

Structure	
Common name	Chlorothalonil
CAS Number	1897-45-6
Batch number	F343 (98.6%)
Stability of test compound	The test substance is assumed to be stable for the duration of the dosing period

A2. Test Facilities

In-life phase	A commercial dairy farm, Dayboro 4521, Queensland, Australia.
Analytical phase	Veterinary Health Research Pty Ltd, New South Wales, Australia.

A2. Test Animals

Species	Holstein/Friesian
Age	2 years
Weight at dosing	445-655 kg
Number of animals	14 (3 for low and medium dose, 5 for high dose, 3 control)
Acclimation period	14 days
Diet and water	Pasture, *ad libitum* (open grazing paddocks). High energy supplement offered during milking. Fresh drinking water *ad libitum.*
Housing	Open grazing paddocks

B. STUDY DESIGN

B1. Experimental conditions

Dosing regime	**Group**	**Treatment**	**Dietary concentration (mg/kg)***	**Dose rate (mg/kg bodyweight/day)****
	Group 1	Control	0	0
	Group 2	Chlorothalonil	2	0.1
	Group 3	Chlorothalonil	30	1.53
	Group 4	Chlorothalonil	250	12.7
Timing	Once per day			
Duration	28 consecutive days			
Depuration	14 days			
Method	Orally, via syringe			

* On the assumption of a 550 kg animal consuming 24 kg dry matter/28 kg fresh feed daily.
**Animals were weighed on a weekly basis and the bodyweight data used to determine the actual dose rate in the following week.

B2. Sample Collection

All cows were milked individually morning and evening. The morning and evening milk was amalgamated to give a composite daily sample for each cow. A sub-sample of each day's milk was refrigerated for 24 hours to allow separation of cream form milk. Milk samples from two cows from the highest dose group were collected for a further 14 days after the last dose was administered. Following the depuration period all cows were returned to the dairy herd.

All samples were stored frozen for up to 10 months before analysis.

B3. Analytical Phase

Residues of R182281 were determined by an analytical method based on the QuEChERS method:

The method involved extraction of the samples with acetonitrile containing 1% acetic acid, followed by the addition of anhydrous magnesium sulphate and sodium acetate and further homogenisation. The extracts were centrifuged and the supernatant removed. The supernatant was evaporated into dryness and re-dissolved in acetonitrile: water (1:1 v/v). Residues of R182281 were determined by LC-MS, using ion *m/z* 245 for quantification and *m/z* 247 for confirmation. The LOQ was 5 µg/L in both milk and cream.

II. RESULTS AND DISCUSSION

Recovery data for the method of analysis are presented in Table 6.4.2-6. Samples from the feeding study were analysed against matrix matched standards and linearity was demonstrated in milk and cream matrices over the concentration range equivalent to 5 - 250 µg/L ($r^2 > 0.999$).

Table 6.4.2-6: Summary of recovery data for R182281 in milk and cream

Commodity	Fortification concentration (µg/L)	No. samples	Recovery (%)	Mean (%)	RSD (%)
Milk	5	6	105, 104, 105, 102, 103, 95	102	3.7
	10	5	100, 101, 98, 92, 96	97	3.7
	25	6	100, 99, 95, 95, 95, 93	96	2.8
	75	5	89, 84, 86, 87, 84	86	2.5
	250	6	93, 88, 97, 93, 95, 89	93	3.7
	Overall	28	-	95	6.5
Cream	5	6	98, 76, 85, 86, 86, 90	87	8.6
	10	6	99, 96, 90, 97, 98, 97	96	3.3
	25	6	102, 102, 97, 95, 96, 96	98	3.2
	75	6	100, 98, 93, 92, 92, 92	95	3.8
	250	6	87, 97, 92, 99, 96, 97	95	4.7
	Overall	30	-	94	6.2

No residues of R182281 above 5 µg/L were found in control samples.

Maximum residues of R182281 found in milk for the low, medium and high dose levels were, respectively, 1.2, 150 and 231 µg/L.

Maximum residues of R182281 found in cream for the low, medium and high dose levels were, respectively, 17.5, 247 and 336 µg/L.

For the highest dose level, residues of R182281 in whole milk decreased after a 14 day depuration period, although were still significant. Residues in cream increased during the depuration period.

The results are summarised in Table 6.4.2-7.

Table 6.4.2-7: Residues of R182281 in milk and cream

Day		Milk residues (µg/L)			Cream residues (µg/L)		
		0.1 mg/kg bw/day	1.5 mg/kg bw/day	12 mg/kg bw/day	0.1 mg/kg bw/day	1.5 mg/kg bw/day	12 mg/kg bw/day
0	Range	3 x <0.2	3 x <0.2	<0.2 – 0.6	3 x < 0.2	3 x <0.2	5 x <0.2
	Mean	<0.2	<0.2	0.3	<0.2	<0.2	<0.2
3	Range	-	-	44.0 – 117	-	-	56.3 – 130
	Mean	-	-	69.8	-	-	107.8
4	Range	<0.2 – 1.2	4.8 – 36.1	46.8 – 136	-	-	-
	Mean	0.6	14.4	86.6	-	-	-
7	Range	<0.2 – 0.3	8.9 – 46.6	67.5 – 216	-	-	33.2 – 210
	Mean	0.3	21.7	126.2	-	-	127.7
11	Range	-	-	58.8 – 231	-	-	66.7 – 233
	Mean	-	-	149.4	-	-	157.7
12	Range	<0.2 – 1.2	14.0 - 150	85.3 – 179	-	-	-
	Mean	0.8	59.5	136.1	-	-	-
14	Range	-	-	-	5.1 – 17.5	18.0 - 205	69.6 – 214
	Mean	-	-	-	10.2	99.7	156.1
15	Range	-	-	95.9 – 192	-	-	83.2 – 212
	Mean	-	-	157.2	-	-	173.6
17	Range	<0.2-0.5	11.6 – 37.0	107 – 191	-	-	-
	Mean	0.3	21.8	148.4	-	-	-
19	Range	-	-	106 – 182	-	-	119 – 202
	Mean	-	-	144.8	-	-	169.0
21	Range	<0.2 – 0.4	14.3 – 57.0	107 – 198	-	-	-
	Mean	0.3	29.6	151.6	-	-	-
23	Range	-	-	99.3 – 180	-	-	46.4 – 226
	Mean	-	-	133.7	-	-	172.1
24	Range	<0.2 - 0.3	18.7 – 46.9	79.1 – 176	-	-	-
	Mean	0.2	29.2	119.7	-	-	-
26	Range	<0.2 – 0.6	13.2 – 55.6	22.9 – 187	-	-	-
	Mean	0.3	29.1	105.1	-	-	-
27	Range	-	-	2.3-215	-	-	62.4 – 232
	Mean	-	-	114	-	-	145.6
28	Range	<0.2 – 0.8	15.9 – 52.9	7.9 – 183	<0.2 – 16.7	29.4 - 247	124 – 237
	Mean	0.5	29.3	119.6	5.7	127.5	167.8
29	Range	-	-	83.0 – 195	-	-	186 – 199
	Mean	-	-	139	-	-	192.5
30	Range	-	-	74.6 – 165	-	-	203 – 269
	Mean	-	-	119.8	-	-	236.0
31	Range	-	-	76.2 – 168	-	-	236 – 282
	Mean	-	-	122.1	-	-	259.0
32	Range	-	-	54.0 – 124	-	-	178 – 323
	Mean	-	-	89.0	-	-	250.5
33	Range	-	-	54.5 -92.2	-	-	245 – 336

Day		Milk residues (µg/L)			Cream residues (µg/L)		
		0.1 mg/kg bw/day	1.5 mg/kg bw/day	12 mg/kg bw/day	0.1 mg/kg bw/day	1.5 mg/kg bw/day	12 mg/kg bw/day
	Mean	-	-	73.4	-	-	290.5
34	Range	-	-	41.6 – 90.7	-	-	-
	Mean	-	-	66.2	-	-	-
37	Range	-	-	22.3 – 57.8	-	-	-
	Mean	-	-	40.1	-	-	-
40	Range	-	-	12.4 – 27.9	-	-	-
	Mean	-	-	20.2	-	-	-
42	Range	-	-	8.6 – 18.9	-	-	-
	Mean	-	-	13.8	-	-	-

III. CONCLUSIONS

Maximum residues of R182281 found in milk for the low, medium and high dose levels were, respectively, 1.2, 150 and 231 µg/L.

Maximum residues of R182281 found in cream for the low, medium and high dose levels were, respectively, 17.5, 247 and 336 µg/L.

For the highest dose level, residues of R182281 in whole milk decreased after a 14 day depuration period, although were still significant. Residues in cream increased during the depuration period.

(Rogers G, 2008)

Summary of residue levels in products of animal origin

Poultry

The maximum and median estimated intakes for poultry are summarised in Table 6.4.2-8.

Table 6.4.2-8: Intake of combined chlorothalonil and R182281 residues in poultry

	Maximum residue intake (mg a.s./kg bw/day)	Median Residue intake (mg a.s./kg bw/day)
Broiler	0.008	0.008
Laying hen	0.089	0.014
Turkey	0.013	0.013

No feeding studies were submitted. Hen metabolism data have been submitted (section CA 6.2.2).

In metabolism studies, laying hens were treated at dose rates of 0.22, 0.65 and 2.18 mg/kg bw/day ^{14}C-chlorothalonil by capsule for 21 consecutive days. These dose rates are equivalent to 2.5, 7.3 and 24 times the estimated maximum intake of total chlorothalonil for laying hens based on the proposed uses. Therefore the lowest dose rate is the most relevant. Total radioactive residues were below the LOD in egg white, egg yolk and all tissues at this dose level.

In a recent study (2014), hens were dosed with [phenyl-U- ^{14}C]-chlorothalonil at a rate of 15 mg/kg, based on dietary dry matter intake (*ca* equivalent to 1.0 mg/kg bw/day[1] i.e. equivalent to 11 times the estimated maximum intake based on the proposed uses.) Total radioactive residues were 0.026 mg/kg in whole eggs, 0.148 mg/kg in liver, 0.101 mg/kg in skin and 0.035 mg/kg in perirenal fat. Residues in breast and leg muscle were below the limit of quantification.

Residues of R182281 (the residue definition for animal products) were 0.01 mg/kg in egg yolk, 0.003 mg/kg in whole egg, 0.05 mg/kg in liver and 0.004 mg/kg in skin with fat. Residues in muscle were < 0.001 mg/kg. Residues in eggs and tissues at the maximum and median estimated intakes of chlorothalonil (0.089 mg/kg) are therefore expected to be < 0.01 mg/kg.

It can be concluded that residues of R182281 will not occur in poultry products at levels above 0.01 mg/kg on the basis of livestock intakes of chlorothalonil or R182281. MRLs for poultry products are not required.

Lactating ruminants

The maximum and median estimated intakes for ruminants are summarised in Table 6.4.2-9.

Table 6.4.2-9: Intake of combined chlorothalonil and R182281 residues in ruminants

	Maximum residue intake (mg a.s./kg bw/day)	Median Residue intake (mg a.s./kg bw/day)
Beef cattle	0.071	0.027
Dairy cattle	0.111	0.040
Rams/Ewes	0.176	0.049
Lambs	0.216	0.060

Feeding studies were conducted in the cow (Wiedmann and Kenyan, 1995). Full summaries of the studies are given in section CA 4.2 above. The feeding studies where a combined dose of chlorothalonil and R182281 was used were chosen as being most relevant to derive residue levels in products of animal origin. Groups of cattle were dosed with a mixture of chlorothalonil and R182281 (ratio of 15:1) at 1.5, 3, 9 and 30 mg/kg chlorothalonil in the diet for 27/28 days.

The combined dose rates of both chlorothalonil were calculated to be 1.59, 3.19, 9.56 and 31.86 mg/kg in the diet.

Combined dose rate = dose rate CTN + (dose rate R182281 x 0.931)

The highest estimated livestock intake of combined chlorothalonil and R182281 residues is 0.216 mg/kg bw/day for lambs. The highest estimated livestock intake of combined chlorothalonil and R182281 residues for dairy cattle is 0.111 mg/kg bw/day and for beef cattle is 0.071 mg/kg bw/day. These intakes are comparable to between the middle two dose rates applied in the feeding study (3.19 and 9.56 mg/kg combined residue equivalent to 0.12 and 0.37 mg/kg bw/day).

The median estimated livestock intake of combined chlorothalonil and R182281 residues is 0.060 mg/kg bw/day for lambs. The median estimated livestock intake of combined chlorothalonil and R182281 residues for dairy cattle is 0.040 mg/kg bw/day and for beef cattle is 0.027 mg/kg bw/day. These intakes

[1] Calculated on basis of body weight of 1.9 kg and daily intake of 0.12 kg DM e.g.(15 x 0.12) /1.9

are comparable to the lowest dose rate applied in the feeding study (1.59 mg/kg combined residue equivalent to 0.06 mg/kg bw/day).

Table 6.4.2-10: Residue levels in bovine commodities based on combined dietary livestock burdens of chlorothalonil and R182281

Commodity	Dose level (mg/kg diet) Total residue	Dose level (mg/kg bw/day) Total residue	Mean residue R182281 (mg/kg)	Highest residue R182281 (mg/kg)
Muscle	1.59	0.060	<0.01	<0.01
	3.19	0.123	0.01	0.02
	9.56	0.368	0.06	0.09
Fat	1.59	0.060	0.03	0.03
	3.19	0.123	0.04	0.07
	9.56	0.368	0.06	0.08
Liver	1.59	0.060	0.02	0.03
	3.19	0.123	0.03	0.04
	9.56	0.368	0.16	0.18
Kidney	1.59	0.060	0.14	0.14
	3.19	0.123	0.20	0.28
	9.56	0.368	0.49	0.55
Milk	1.59	0.060	0.03	0.04
	3.19	0.123	0.06	0.10
	9.56	0.368	0.20	0.31

On the basis of the results above, MRL, STMR and HR values for products of animal origin have been proposed. These values have been calculated by interpolation between the maximum or mean residues measured at the relevant dose levels for the estimated combined maximum or median chlorothalonil and R182281 intake values.

There are existing MRLs for chlorothalonil for products of animal origin (residue definition of R182281) as published in Reg. (EC) No 441/2012. Recent proposals currently being considered (SANCO 12240/2013) also propose MRLs for products of animal origin. The data presented in Table 6.4.4-4 gives an overview of the current EU MRLs and proposals made in this document

CA 6.4.3 Pigs

The maximum and median estimated intakes for pigs are summarised in Table 6.4.3-1.

Table 6.4.3-1: Intake of combined chlorothalonil and R182281 residues in pigs

	Maximum residue intake (mg a.s./kg bw/day)	Median Residue intake (mg a.s./kg bw/day)
Breeding Swine	0.013	0.013
Finishing Swine	0.012	0.012

Calculated only for the supported crop use in this submission, the maximum dietary burden of combined residues of chlorothalonil and R182281in pigs is 0.013 mg/kg bw/day for breeding swine. The metabolism of chlorothalonil in ruminants was similar to that seen in the rat. Metabolism and feeding studies in pigs are not required, as data for ruminants can be used to address the potential for residues in pigs.

Feeding studies were conducted in the cow (Wiedmann and Kenyan, 1995). Full summaries of the studies are given in section CA 4.2 above. The feeding studies where a combined dose of chlorothalonil and R182281 was used were chosen as being most relevant to derive residue levels in products of animal origin. Groups of cattle were dosed with a mixture of chlorothalonil and R182281 (ratio of 15:1) at 1.5, 3, 9 and 30 mg/kg chlorothalonil in the diet for 27/28 days.

The combined dose rates of both chlorothalonil were calculated to be 1.59, 3.19, 9.56 and 31.86 mg/kg in the diet.

Combined dose rate = dose rate CTN + (dose rate R182281 x 0.931)

The highest estimated livestock intake of combined chlorothalonil and R182281 residues is 0.013 mg/kg bw/day for breeding swine. The lowest dose rate applied in the feeding study was 1.59 mg/kg (equivalent to 0.061mg/kg bw/day i.e. 5 times the maximum intake). This dose level is applicable to both the maximum and median dietary intakes for swine.

Table 6.4.3-2: Residue levels in swine commodities based on dietary livestock burdens of chlorothalonil and R182281

Commodity	Dose level (mg/kg diet) Total residue	Dose level (mg/kg bw/day) Total residue	Mean residue R182281 (mg/kg)	Highest residue R182281 (mg/kg)
Muscle	1.59	0.061	<0.01	<0.01
Fat	1.59	0.061	0.02	0.03
Liver	1.59	0.061	0.02	0.03
Kidney	1.59	0.061	0.14	0.14

On the basis of the results above, it can be seen that significant residues in swine muscle, fat and liver above the LOQ of 0.01 mg/kg would not be expected. An MRL value for kidney has been calculated by extrapolation from the lowest dose level of 0.061 mg/kg bw/day for an estimated combined chlorothalonil and R182281 intake value of 0.013 mg/kg bw/day. There are existing MRLs for chlorothalonil for products of animal origin (residue definition of R182281) as published in Reg. (EC) No 441/2012. Recent proposals currently being considered (SANCO 12240/2013) also propose MRLs for products of animal origin. The data presented in Table 6.4.3-3 gives an overview of the current EU MRLs and proposals made in this document.

Table 6.4.3-3: Proposed EU MRL and proposed STMR and HR for residues in products of animal origin

Commodity (code)	Existing EU MRL (mg/kg)	Proposed EU MRL (mg/kg)[1]	Proposed MRL (this application)	STMR[2] (mg/kg)	HR[3] (mg/kg)
Muscle (bovine)	0.02	0.02	0.02	<0.01	0.02
Muscle (sheep, goat, equine)	0.02	0.02	0.04	<0.01	0.04
Muscle (swine)	0.02	0.02	0.01*	<0.01	<0.01
Fat tissue (bovine)	0.07	0.07	0.02	0.01	0.02
Fat tissue (sheep, goat, equine)	0.07	0.07	0.07	0.01	0.07
Fat tissue (swine)	0.07	0.07	0.01*	<0.01	<0.01
Liver (bovine)	0.2	0.2	0.1	<0.01	0.05
Liver (sheep, goat, equine)	0.2	0.2	0.1	0.02	0.08
Liver (swine)	0.2	0.2	0.01*	<0.01	<0.01
Kidney (bovine)	0.3	0.7	0.3	0.14	0.25
Kidney (sheep, goat, equine)	0.3	0.7	0.3	0.14	0.31
Kidney (swine)	0.3	0.7	0.03	0.03	0.03
Other edible offal (bovine)	0.2	0.2	0.2	<0.01	0.08
Other edible offal (sheep, goat, equine)	0.2	0.2	0.2	0.02	0.08
Other edible offal (swine)	0.2	0.2	0.03	0.03	0.03
Poultry muscle	0.01*	0.01*	0.01*	<0.01	<0.01
Poultry fat	0.07	0.01*	0.01*	<0.01	<0.01
Poultry liver	0.07	0.01*	0.01*	<0.01	<0.01
Poultry kidney	0.07	0.07	0.01*	<0.01	<0.01
Poultry, edible offals	0.01*	0.01*	0.01*	<0.01	<0.01
Milk	0.07	0.1	0.05	0.03	0.14
Eggs	0.01*	0.01*	0.01*	<0.01	<0.01

[1] proposal currently being considered (SANCO 12240/2013)

[2] derived by interpolation/extrapolation of the median dietary burden between the relevant feeding groups of the study (FAO, 2009, EFSA RO on review of existing MRLS for chlorothalonil, EFSA Journal 2012; 10 (10):2940).

[3] derived by interpolation/extrapolation of the maximum dietary burden between the relevant feeding groups of the study (FAO, 2009, EFSA RO on review of existing MRLS for chlorothalonil, EFSA Journal 2012; 10 (10):2940).

CA 6.4.4 Fish

No guideline is currently available for the estimation of the dietary burden of pesticide residues for farmed fish or for the design and conduct of fish-metabolism studies. No fish metabolism studies have been conducted.

CA 6.5 Effects of Processing

CA 6.5.1 Nature of the residue

A new study not previously submitted is now available and is summarised below.

Report:	K-CA 6.5.1/01. Grout, SJ. (2007), Chlorothalonil – aqueous hydrolysis at 90, 100 and 120ºC. Syngenta, Jealott's Hill International Research Centre, Bracknell, United Kingdom. Syngenta Report No. RJ3331B (Syngenta File No. R44686/3564).

Guidelines

Commission of the European Communities. Processing Studies (**SANCO 7035/V1/95 rev. 5 22/7/1997**).

GLP

The study was carried out according to the principles of Good Laboratory Practice.

EXECUTIVE SUMMARY

The hydrolytic stability of [phenyl-U-^{14}C]-labelled chlorothalonil was investigated in aqueous buffer solutions at three pH values and temperatures to simulate processing practices.

The study was performed at pH 4 and 90ºC to simulate pasteurisation, pH 5 and 100ºC to simulate baking/brewing/boiling, and at pH 6 and 120ºC to simulate sterilisation. Additional experiments were also performed at pH 4 at 120°C and pH 6 at 90°C for 20 minutes to investigate whether pH or temperature was the key variable in hydrolytic degradation of chlorothalonil

Buffer solutions containing [phenyl-U-^{14}C]-chlorothalonil at an initial concentration of 5 µg/mL were incubated in closed high-pressure glass vessels. The temperatures were maintained constant throughout incubation time and no significant variation of the pH values were observed in the buffered solutions.

At time 0 and after 20 or 60 minutes incubation, duplicate samples per pH value (except at time 0) were taken, measured for total radioactivity by LSC, and analysed to determine the nature of degradates by HPLC and by two-dimensional thin layer chromatography (2D-TLC). Identification of unknowns was by LC-MS/MS.

Recoveries of applied radioactivity ranged from 85.4 to 96.5 %.

A summary of the results is given in Table 6.5.1-1. Chlorothalonil undergoes hydrolysis at two positions in the molecule:

a) Nucleophilic substitution of a chloride ion by a hydroxyl group to give R182281

b) Hydrolysis of the cyano functionality to give the amide R613636

Both temperature and pH are determining factors in the hydrolysis of chlorothalonil.

Table 6.5.1-1: Summary of radioactive residues in reaction mixtures treated with ^{14}C-phenyl labelled chlorothalonil

Hydrolysis conditions (buffer, pH, temperature, time)	Mean % applied			Radioactive recovery (%)
	Chlorothalonil	R182281	R613636	
Ammonium citrate, pH 4, 90°C, 20 minutes	105.0	1.9	0.0	108.5
Ammonium citrate, pH 6, 120°C, 20 minutes [1]	3.1	47.5	23.1	109.9
Sodium acetate, pH 6, 120°C, 20 minutes	26.1	58.7	15.2	102.5
Ammonium citrate, pH 6, 90°C, 20 minutes	85.0	5.3	2.8	96.6
Ammonium citrate, pH 5, 100°C, 60 minutes	80.5	19.2	3.4	106.7
Ammonium citrate, pH 4, 120°C, 20 minutes	73.4	17.1	2.3	95.0

[1] - data not used due to the presence of the artefact in the buffer solution

I. MATERIALS AND METHODS

A. MATERIALS

A1. Test Materials

Test item	[phenyl-U-^{14}C]-chlorothalonil	
Lot No.	98-54.1	98-54.2
Radiochemical purity	98.0%	98.2%
Specific radioactivity	7296 Bq/µg, 1.94 GBq/mmol	6749 Bq/µg, 1.79 GBq/mmol

A2. Test Facilities

The study was performed at Syngenta, Jealott's Hill International Research Centre, Bracknell, Berkshire, RG42 6EY, UK.

B. STUDY DESIGN AND METHODS

B1. Hydrolysis phase

0.1M tri-ammonium citrate /citric acid buffer solutions were prepared at pH 4, 5 and 6. An acetonitrile solution of [phenyl-^{14}C]-chlorothalonil was added to each buffer solution at a nominal concentration of 5 µg/mL; the solutions were then incubated in the dark at 90°C for 20 minutes (pH 4), 100°C for 60 minutes (pH 5) and 120°C for 20 minutes (pH 6). The experiment at 120°C for 20 minutes (pH 6) was repeated using sodium acetate buffer to assess whether a compound identified in the ammonium citrate experiment was a true hydrolysis product or an artefact.

Additional experiments were carried out at pH 4 (120°C for 20 minutes) and pH 6 (90°C for 20 minutes) to assess whether pH or temperature was the major factor affecting chlorothalonil hydrolysis.

B2. Analytical Phase

Radioactivity in buffer solutions was quantified by LSC. Samples were analysed by 2D-TLC on silica gel plates against a reference standards using four solvent systems, with detection by phosphor- imaging. Identification of unknowns was confirmed by HPLC with UV and ^{14}C detection or LC-MS/MS.

II. RESULTS AND DISCUSSION

Recoveries of applied radioactivity ranged from 82.6% to 124.1%.

The results from analysis of the buffer solutions following incubation are summarised in Table 6.5.1-2.

Analysis of the control samples indicated no significant hydrolysis of chlorothalonil at room temperature at any pH. The samples incubated at pH 4 and 90°C for 20 minutes indicated a small amount of hydrolysis had occurred. The only metabolite identified was R182281 (1.9% TRR).

The samples incubated at pH 5 and 100°C for 60 minutes showed a greater level of hydrolysis occurring. TLC analysis indicated chlorothalonil was still the major component of the residue (80.5% TRR). Other identified metabolites were R182281 (19.2% TRR) and R613636 (3.4% TRR).

The greatest degree of chlorothalonil degradation was observed in the samples incubated at pH 6 and 120°C for 20 minutes. In the ammonium citrate buffer solution, four main components of the residue were identified; chlorothalonil (3.1% TRR), R182281 (47.5% TRR), R613636 (23.1% TRR) and a fourth component (27.7% TRR). Unidentified unknowns which consisted of at least six discrete components amounted to 5.9% TRR. Mass spectroscopic analysis of the fourth component identified indicated it was 4-amino-2,5,6-trichloroisophthalonitrile.

On repeating the experiment at pH 6 and 120°C using a sodium acetate buffer, three main components of the residue were identified: chlorothalonil (26.1% TRR), R182281 (58.7% TRR) and R613636 (15.2% TRR). None of the fourth component was observed. This suggests it is an artefact of the conditions and the ammonium acetate buffer system used and is likely formed by a nucleophilic substitution of a chloride ion with an amino moiety from the buffer system.

In the additional experiment conducted at pH 4, 120°C the levels of the main degradation products were 17.1% and 2.3% for R182281 and R613636 and at pH 6, 90°C the levels were 5.3% and 2.8% respectively. These data suggest that both temperature and pH are determining factors in the hydrolysis of chlorothalonil.

Table 6.5.1-2: Summary of chlorothalonil degradation under high temperature hydrolysis conditions

Conditions	Reaction Vessel	Radioactive recovery (%)[1]	Residue (%)					
			Chlorothalonil	R182281	R613636	Artefact	Unknowns	Remainder
pH 4 90°C	1	92.8	89.4	2.0	-	-	-	1.6
	2	124.1	120.6	1.8	-	-	-	1.7
	Mean	**108.5**	**105.0**	**1.9**	**-**	**-**	**-**	**1.7**
pH 5 100°C	4	111.0	82.9	20.9	3.9	1.1	-	2.3
	5	102.3	78.1	17.4	2.9	1.6	-	2.3
	Mean	**106.7**	**80.5**	**19.2**	**3.4**	**1.4**	**-**	**2.3**
pH 6 120°C	10	109.5	3.1	46.2	23.9	26.7	5.8[3]	3.8
	11	110.3	3.0	48.7	22.2	28.6	5.9[4]	1.9
	Mean	**109.9**	**3.1**	**47.5**	**23.1**	**27.7**	**5.9**	**2.9**
pH 4 120°C	12	95.0	73.4	17.1	2.3	0.4	0.4	1.3
pH 6 90°C	15	96.6	85.0	5.3	2.8	2.1	0.4	1.0
pH 6 120°C[2]	16	102.2	20.9	62.9	51.8	-	1.8[5]	0.5
	17	102.8	31.2	54.4	14.5	-	1.6[6]	0.5
	Mean	**102.5**	**26.1**	**58.7**	**15.2**	**-**	**1.7**	**0.5**

[1] due to rounding total mean may not equal the sum of the components indicated
[2] acetate buffer instead of citrate buffer
[3] consists of at least 6 discrete components, none greater than 2.4%
[4] consists of at least 6 discrete components, none greater than 1.9%
[5] consists of at least 3 discrete components, none greater than 0.9%
[6] consists of at least 3 discrete components, none greater than 1.0%

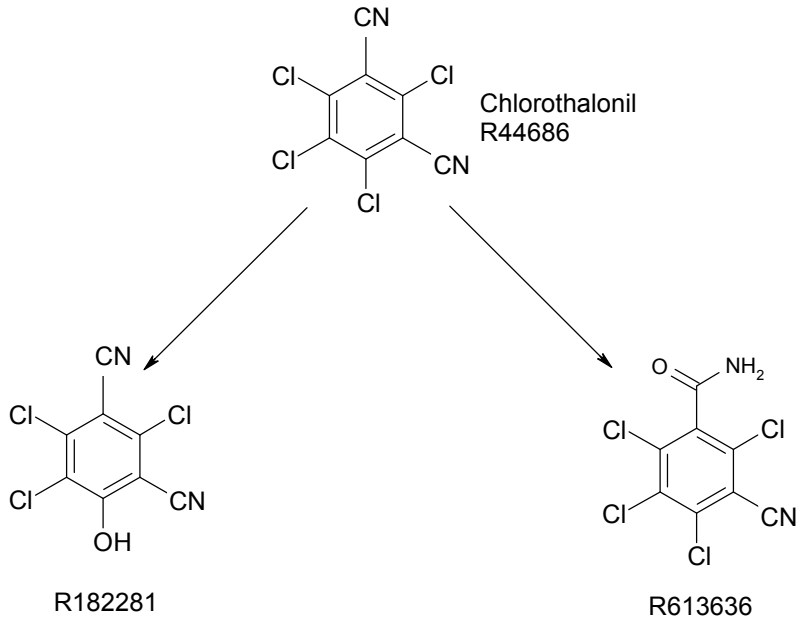
III. CONCLUSIONS

Chlorothalonil is relatively stable under conditions representing pasteurisation (pH 4, 90°C), but becomes increasingly unstable under more rigorous conditions e.g. sterilisation (pH 6, 120°C). Further investigations indicated that both temperature and pH are determining factors in the rate of chlorothalonil hydrolysis.

The mechanism of degradation is by either nucleophilic substitution of a chloride ion with a hydroxyl group to give R182281, or hydrolysis of the cyano group to give R613636 as shown in Figure 6.5.1-1.

(Grout SJ, 2007)

Figure 6.5.1-1: Proposed hydrolytic breakdown of chlorothalonil



CA 6.5.2 Distribution of the residue in inedible peel and pulp

The distribution of the residues in peel/pulp is not relevant for barley and wheat. Tomato is separated into peel and pulp during processing. Studies in tomato, including measurements of distribution of the residue in peel and pulp, are presented in Point IIA 6.5.3. Potatoes can be peeled during processing, however as residues in whole tubers were < LOQ for both chlorothalonil and R182281, processing data are not required.

CA 6.5.3 Magnitude of residues in processed commodities

The magnitude of chlorothalonil residues in processed crops was investigated in field trials. The studies were evaluated under Council Directive 91/414/EEC and are presented in the chlorothalonil monograph (**Vol.3, Annex B, Section B.7.7.1 and B.7.7.2, January2000**).

Commodity	Author/s	Issue Year	Report Number
Tomato	SzalkpowskiMB	1980	411-3CR-80-0054-001
Vegetables	Marks AF	1983	372-3EF-83-0004-001
Tomato	Dillon	1986	728-3CR-85-0008-001
Wheat	Stallard DE, Marks, AF	1983	573-3CR-82-0036-002

The processing of tomatoes into various products resulted in lower chlorothalonil levels compared to the raw (unwashed) agricultural product. Chlorothalonil levels in tomatoes in packing houses had decreased to <0.69-3.6% of the field tomato levels. Tomatoes in groceries and restaurants contained <1.9% of the initial chlorothalonil.

In wheat, no chlorothalonil or R182281 were detected in grain samples (LOD: 0.01 mg/kg for both compounds) or in any processed product (reduction flour, break flour, bran, shorts); LOD: 0.03 mg/kg for both compounds).

New processing studies not submitted for Annex I listing of chlorothalonil in tomato, barley and wheat are now available and summaries are presented below. Processing studies for potatoes are not required due to the low residues in the whole tuber arising from the proposed use rate.

Tomatoes

Report:	K-CA 6.5.3/01. Gardinal P. (2007), Chlorothalonil (R44686): Residue study on outdoor tomatoes and processed tomato products in southern France. Syngenta, Jealott's Hill International Research Centre, Bracknell, United Kingdom. Syngenta Report Number 05-6039. (Syngenta File No: R44686/4093).

Guidelines

FAO Guidelines on Producing Pesticide Residues Data from Supervised Trials (Rome, 1990).

Commission of the European Communities. General Recommendations for the Design, Preparation and Realization of Residue Trials (**SANCO 7029/V1/95 rev. 5 22/7/1997**).

Guidelines and Criteria for the Preparation and Presentation of Complete Dossiers and of Summary Dossiers for the Inclusion of Active Substances in Annex I of Directive 91/414/EEC (Article 5.3 and 8.2), 1996.

GLP

The study was carried out according to the principles of Good Laboratory Practice

Executive Summary

Outdoor tomatoes grown in Southern France were treated with A7867A, a SC formulation containing chlorothalonil. The plot was sprayed three times with nominal application rates of 7.5 kg chlorothalonil/ha. Samples were harvested 3 days after the last application of A7867A and a sub-sample analysed to determine residues of chlorothalonil and R182281. An additional sample of tomatoes taken at 3 days from the treated plot was used for the production of tomato juice, tomato puree and canned tomatoes and samples of various processed commodities analysed for chlorothalonil, R182281 and R613636. A full mass balance study was conducted to determine the accountability of the chlorothalonil residue, and three follow-up studies were conducted to determine residue transfer into the processed commodities.

The % residue recovered (mass balance) for tomato juice was 45%, for tomato puree was 20% and for canned tomatoes was 39%.The average transfer factors for chlorothalonil determined for the various process fractions were as follows:

$$\text{Transfer Factor} = \frac{\text{Residue in processed commodity}}{\text{Residue in raw agricultural commodity}}$$

Unwashed fruit to washed fruit:	0.3
Unwashed fruit to wet pomace	0.3
Unwashed fruit to dry pomace	1.2
Unwashed fruit to bottled juice	0.11
Unwashed fruit to sterilised puree	0.001
Unwashed fruit to solid portion for sterilised canned tomatoes	0.001
Unwashed fruit to liquid portion for sterilised canned tomatoes	0.002

From these results it can be concluded chlorothalonil would tend to concentrate in dry pomace but would not be expected to concentrate in wet pomace, tomato juice, tomato puree or canned tomatoes. Approximately 70% of the residue can be removed from the fruit by washing.

For R182281 it can be concluded that residues would be expected to concentrate in dry pomace and tomato puree. Transfer factors greater than 1 were also obtained for wet pomace, tomato juice and canned tomatoes; although there is some uncertainty as to whether these results indicate concentration of residues given that the levels of R182281 in the initial raw tomatoes were low. Residues of R182281 were reduced by washing.

R613636 was below the LOQ (0.01 mg/kg) in all of the tomato commodities subjected to high temperature processing. This indicates exposure to this metabolite through the consumption of processed tomatoes is likely to be negligible.

I. MATERIALS AND METHODS

A. MATERIALS

A1. Test Materials

Test Material	A7857A
Description	Suspension concentrate formulation containing chlorothalonil
Purity	506 g/L
Batch number	SIP4C40916
Stability of test compound	The test substance has been shown to be stable under the storage and test conditions of the study

A2. Test Facilities

The field trial was performed at Agrisearch France SARL, Les Herbonnes, 82290, Meauzac, France

The processing phase was performed at VITI RD, 101 Impasse des Capitelles, F-34400 Villetelle, France

The analytical phase was performed at Syngenta, Jealott's Hill International Research Centre, Bracknell, Berkshire, RG42 6EY, UK.

B. STUDY DESIGN AND METHODS

B1. Processing phase

Tomatoes plants were treated three times with a foliar spray of the formulation A7867A, at nominal rates of 7.5 kg chlorothalonil/ha. The interval between the applications was 7 days.

Tomatoes were harvested 3 days after the last application and were used for the production of tomato puree, tomato juice and canned tomatoes.

The washed tomatoes were produced by washing the fruits with water from a constant pressure sprayer.

Tomato juice was produced by crushing the washed tomatoes followed by sieving to remove the peel and seeds (wet pomace). Cooking salt was added to the resultant puree at a level of 4g/kg and the pH adjusted to 3.37 by the addition of citric acid, prior to pasteurisation. A sample of the wet pomace was dried to constant weight to produce dry pomace.

Tomato puree was produced by crushing washed tomatoes and the resultant pulp reduced by heating before sieving to remove peel and seeds. Cooking salt was added to the resultant juice and the pH adjusted to 3.59 before sterilisation.

Canned tomatoes were produced by blanching washed tomatoes to remove the peel. The peeled tomatoes and portion of tomato juice from the juicing process were then sterilised in glass jars.

B2. Analytical Phase

Samples of the raw agricultural commodity (tomatoes) and various processed fractions were analysed for chlorothalonil and R182281 using method GRM005.01A. Selected processed fractions were also analysed for R613636 using method RAM 464/01. The LOQ was 0.01 mg/kg for all analytes in all commodities. Full method descriptions and validation data are presented in document M-CA Section 4, CA 4.1.2.

The chlorothalonil residue accountability for each individual process was calculated from a mass balance study, and transfer factors from the washed fruit into various processed commodities determined from this and three additional follow up studies.

II. RESULTS AND DISCUSSION

A summary of the measured residues from the various fractions for each of the separate processed fractions is given in Table 6.5.3-1.

Table 6.5.3-1: Summary of chlorothalonil, R182281 and R613636 residues in tomato and processed commodities from a trial conducted in southern France

Commodity	Residues (mg/kg)											
	Balance			Follow-up 1			Follow-up 2			Follow-up 3		
	chlorothalonil	R182281	R613636	chlorothalonil	R182281	R613636	chlorothalonil	R182281	R613636	chlorothalonil	R182281	R613636
Field samples												
Mean Tomato Residue Prior to processing	9.6	0.02	n.a.	-	-	-	-	-	-	-	-	-
Tomato juice production												
Crushed tomato	2.5	<0.01	n.a.	-	-	-	-	-	-	-	-	-
Wet pomace	3.1	0.03	n.a.	-	-	-	-	-	-	-	-	-
Raw juice	2.9	0.01	n.a.	-	-	-	-	-	-	-	-	-
Dry pomace	12	0.25	<0.01	13	0.31	<0.01	10	0.28	<0.01	12	0.36	<0.01
Bottled juice	1.1	0.02	<0.01	1.0	0.02	<0.01	0.87	0.02	<0.01	1.2	0.03	<0.01
Tomato puree production												
Crushed tomato	3.5	<0.01	n.a.	-	-	-	-	-	-	-	-	-
Reduced tomato	0.05	0.24	<0.01	-	-	-	-	-	-	-	-	-
Sieved tomato	<0.01	0.15	<0.01	-	-	-	-	-	-	-	-	-
Wet pomace	0.09	0.38	<0.01	-	-	-	-	-	-	-	-	-
Puree pre-sterilisation	<0.01	0.14	<0.01	-	-	-	-	-	-	-	-	-
Puree post-sterilisation	<0.01	0.15	<0.01	<0.01	0.13	<0.01	<0.01	0.12	<0.01	<0.01	0.11	<0.01
Canned Tomato Production												
Blanching water	1.0	0.03	0.07	-	-	-	-	-	-	-	-	-
Cooling water	0.17	<0.01	0.01	-	-	-	-	-	-	-	-	-
Peeled tomato	0.24	<0.01	<0.01	-	-	-	-	-	-	-	-	-
Peels	28	0.03	<0.01	-	-	-	-	-	-	-	-	-
Solid portion pre-sterilisation	0.43	<0.01	<0.01	-	-	-	-	-	-	-	-	-
Liquid portion pre-sterilisation	2.0	<0.01	<0.01	-	-	-	-	-	-	-	-	-
Solid portion post-sterilisation	<0.01	0.02	<0.01	<0.01	0.04	<0.01	<0.01	0.04	<0.01	<0.01	0.05	<0.01
Liquid portion post-sterilisation	0.04	0.04	<0.01	<0.01	0.02	<0.01	<0.01	0.02	<0.01	<0.01	0.02	<0.01

n.a.: not analysed. The residue analysis of R613636 was carried out only on samples which have been through high temperature processing.

The mean transfer factors of chlorothalonil and R182281 for each commodity are calculated and presented in Table 6.5.3-2 and Table 6.5.3-3, respectively.

Table 6.5.3-2: Summary of chlorothalonil transfer factors into processed tomato products

Commodity	Transfer Factor	Mean Transfer Factor
Washed Tomatoes	0.35, 0.32, 0.24, 0.27	0.3
Wet Pomace	0.32	0.3
Dry Pomace	1.25, 1.35, 1.04, 1.25	1.2
Tomato Juice	0.11, 0.10, 0.91, 0.13	0.3
Tomato Puree	<0.001, <0.001, <0.001, <0.001	<0.001
solid portion for sterilised canned tomatoes	<0.001, <0.001, <0.001, <0.001	<0.001
liquid portion for sterilised canned tomatoes	0.004, <0.001, <0.001, <0.001	<0.002

Transfer factor = residue in processed commodity/mean residue prior to processing (e.g. for wet pomace 3.1/9.6 = 0.32)

Table 6.5.3-3: Summary of R182281 transfer factors into processed tomato products

Commodity	Transfer Factor	Mean Transfer Factor
Washed Tomatoes	-*	-*
Wet Pomace	1.5	1.5
Dry Pomace	12.5, 15.5, 14, 18	15
Tomato Juice	1, 1, 1, 1.5	1.13
Tomato Puree	7.5, 6.5, 6, 5.5	6.38
solid portion for sterilised canned tomatoes	1, 2, 2, 2.5	1.88
liquid portion for sterilised canned tomatoes	2, 1, 1, 1	1.25

Transfer factor = residue in processed commodity/mean residue prior to processing (e.g. for wet pomace 0.03/0.02 =1.5)
*Residues of R182281 in washed tomatoes were not analysed

A mass balance study was conducted to determine the accountability of the chlorothalonil residue. The results are not reported in detail here, however the % residue recovered (mass balance) for tomato juice was 45%, for tomato puree was 20% and for canned tomatoes was 39%.

III. CONCLUSIONS

Sufficient data is available to allow transfer factors to be calculated for chlorothalonil residues from raw tomatoes into tomato puree, canned tomatoes and tomato juice. For chlorothalonil, it can be concluded that chlorothalonil residues would be expected to concentrate in dry pomace, although it would not be expected to concentrate in wet pomace, juice, puree or canned tomatoes. Approximately 70% of the chlorothalonil residue can be removed from the fruit by washing. During the heating stages of the process, the levels of chlorothalonil decline significantly as may be expected due to its behaviour under high temperature hydrolytic conditions already demonstrated. Hence the achieved residue mass balance is less than 100%.

For R182281 it is concluded that residues would be expected to concentrate in dry pomace and tomato puree. Transfer factors greater than 1 were also obtained for wet pomace, tomato juice and canned tomatoes; although there is some uncertainty as to whether these results indicate concentration of residues given that the levels of R182281 in the initial raw tomatoes were low. Residues of R182281 were reduced by washing.

R613636 was below the LOQ (0.01 mg/kg) in all of the tomato commodities subjected to high temperature processing. This indicates exposure to this metabolite through the consumption of processed tomatoes is likely to be negligible.

(Gardinal P, 2007)

Barley

Report:	K-CA 6.5.3/02. Simon P. (2007), Chlorothalonil: Residue study on barley and processed barley products in Germany. Syngenta Agro GmbH, Technologiepark 1-5, D-63477 Maintal, Germany. Syngenta Report Number gba243004. (Syngenta File No: R44686/4112).

Guidelines

Grundsätze der Guten Laborpraxis, Chemikaliengesetz: veröffentlicht in der Neufassung des Gesetzes über den Schutz vor gefährlichen Stoffen (ChemG) vom 20.06.2002 (BGBL Teil I, Nr. 40,S. 2290-2310)

"OECD Principles of Good Laboratory Practice (as revised in 1997)", ENV/MC/CHEM (98)17, Paris 1998

OECD GLP Consensus Document: "The application of the GLP Principles to field studies", ENV/JM/MONO (99)22 (as revised in 1999), Paris

GLP

The study was carried out according to the principles of Good Laboratory Practice.

Executive Summary

Outdoor barley grown in Germany was treated with A7867A, a SC formulation containing chlorothalonil. The plot was sprayed twice with nominal application rates of 3.0 kg chlorothalonil/ha. Samples of mature barley grain were harvested 35 days after the last application of A7867A and then analysed to determine residues of chlorothalonil and R182281

An additional sample of mature barley grain, taken at 35 days from the treated plot was used for the production of pot barley and beer. A full mass balance study was conducted to determine the accountability of the chlorothalonil residue, and three follow-up studies were conducted to determine residue transfer into the processed commodity.

The % residue recovered (mass balance) for brewing was 36 % and for pot barley was 52 %. The average transfer factors determined for the various process fractions were as follows:

$$\text{Transfer Factor} = \frac{\text{Residue in processed commodity}}{\text{Residue in raw agricultural commodity}}$$

	Chlorothalonil	R182281
Un-cleaned grain to malt	0.04	0.44
Un-cleaned Sieved grain to malt sprouts	0.08	0.35
Un-cleaned grain to spent grain	0.04	0.39
Un-cleaned grain to malt flocs	0.04	1.04
Un-cleaned grain to malt spent yeast	0.04	1.35

Un-cleaned grain to young beer	0.04	0.04
Un-cleaned grain to beer	0.04	0.04
Un-cleaned grain to abrasion dust	2.61	5.18
Un-cleaned grain to pot barley	0.25	0.08

From these results it can be concluded that residues of chlorothalonil and R182281 would tend not to concentrate in barley commodities.

Residues of R613636 were below the LOQ (0.01 mg/kg) in the commodities subjected to high temperature processing. This indicates exposure to this metabolite through the consumption of processed barley fractions is likely to be negligible.

I. MATERIALS AND METHODS

A. MATERIALS

A1. Test Materials

Test Material	A7857A	
Description	Suspension concentrate formulation containing chlorothalonil	
Purity	505 g/L	512 g/L
Batch number	YAL-2-A23-A	YAL-3-C24-A
Stability of test compound	The test substance has been shown to be stable under the storage and test conditions of the study	

A2. Test Facilities

Field trial	Saxonia, Germany
Cleaning of grain	BioChem agrar GmbH, Kupferstrasse, D-04827, Gerichshain, Germany
Malting, Brewing and pot barley production	Fachhochschule Anhalt (FH), Fachbereich Lebensmitteltechnologie, Bernburger Strasse, D-06366 Köthen, Germany
Malting	Wersuch und Lehranstalt für Brauerei, Forschunginstitut für Rohstoffe, Seestrasse 13, D-13353, Berlin, Germany
Brewing	Fermtech GmbH, Invalidenstrasse 42, D-10115, Berlin, Germany
Pot barley production	Technische Universität Berlin, Institu für Lebensmitteltechnologie II, Seestreasse 11, D-13353, Berlin, Germany
Analytical phase	Syngenta, Jealott's Hill International Research Centre, Bracknell, Berkshire, RG42 6EY, UK

B. STUDY DESIGN AND METHODS

B1. Processing phase

Spring barley plants were treated twice with a foliar spray of the formulation A7867A, at nominal application rates of 3.0 kg chlorothalonil/ha. The interval between the applications was 29 days.

Mature barley grains were harvested 35 days after the last application and were used for the production of beer and pot barley.

The grains were prepared by sieving to retain grains with a minimum diameter of 2.5 mm. The sieved grain was steeped to raise the water content to 42-45%; the grains were then germinated in aerobic conditions within a temperature range of 14-16^{o}C and a relative humidity of 85-92% for approximately 5 days. The germination process was stopped by drying to approximately 4% water content within 24 hours.

The malt was milled before mashing. The mashing process attained temperatures of 76-77^{o}C. Mashing was followed by lautering, where hops were added and the wort was cooked at normal pressure for approximately 1.5 hours. After a rest period, yeast was added and left to ferment at 3°C for 8-9 days. The yeast was then decanted and the young beer matured at temperatures of 0-2°C over a period of 19-21 days.

B2. Analytical Phase

Samples of the raw agricultural commodity (grain) and various processed fractions were analysed for chlorothalonil and R182281 using methods RAM365/02 or GRM005.01A. Selected processed fractions were also analysed for R613636 using method RAM 464/01. The LOQ was 0.01 mg/kg for all analytes in all commodities. Full method descriptions and validation data are presented in document M-CA Section 4, CA 4.1.2.

Samples to be analysed for chlorothalonil require the addition of acid during preparation. In this processing study the use of acid was omitted in error hence this may have resulted in some loss of chlorothalonil during sample preparation. This is considered not to have impacted the integrity of the study since all samples (pre-processed and processed commodities) were prepared in the same manner, and therefore the resulting transfer factors are representative.

The chlorothalonil residue accountability for the brewing process was calculated from a mass balance study, and transfer factors for the processed commodities were determined from this and the additional follow up studies.

II. RESULTS AND DISCUSSION

A summary of the measured residues from the various fractions for the processed fraction is given in Table 6.5.3-4.

Table 6.5.3-4: Summary of chlorothalonil, R182281 and R613636 residues in barley and processed commodities from a trial conducted in Germany

Commodity	Residues (mg/kg)											
	Balance 1			Follow-up 1			Follow-up 2			Follow-up 3		
	chlorothalonil	R182281	R613636	chlorothalonil	R182281	R613636	chlorothalonil	R182281	R613636	chlorothalonil	R182281	R613636
Grain before processing*												
Mean Barley Residue	0.24	0.23	n.a.	0.24	0.23	n.a.	0.24	0.23	n.a.	0.24	0.23	n.a.
Brewing and Pot Barley Process												
Malt after drying	<0.01	0.10		<0.01	0.12	n.a	<0.01	0.09	<0.01	<0.01	0.10	<0.01
Malt Sprouts	0.02	0.07	<0.01	-	-	-	-	-	-	-	-	
Malt before Brewing	<0.01	0.07	<0.01	<0.01	0.09	<0.01	<0.01	0.08	<0.01	<0.01	0.08	<0.01
Spent Grain	<0.01	0.09	<0.01	-	-	-	-	-	-	-	-	-
Wort before cooking	<0.01	0.01	<0.01	-	-	-	-	-	-	-	-	-
Flocs	<0.01	0.24	<0.01	-	-	-	-	-	-	-	-	-
Wort after cooking	<0.01	0.02	<0.01	-	-	-	-	-	-	-	-	-
Spent Yeast	<0.01	0.31	<0.01	-	-	-	-	-	-	-	-	-
Beer	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01
Abrasion Dust	0.54	1.2	<0.01	0.59	1.3	<0.01	0.62	0.97	<0.01	0.75	1.3	<0.01
Pot Barley	0.06	0.02	<0.01	0.06	<0.01	<0.01	0.05	0.02	<0.01	0.07	0.02	<0.01

* Mean residues in grain taken at harvest: 0.9 mg/kg chlorothalonil and 0.06 mg/kg R182281. Grain was stored at ambient temperature prior to processing and reanalysed. The values given in the table are the mean results of triplicate analysis of three different samples reanalysed prior to processing.

n.a. : not analysed. The residue analysis of R613636 was carried out only on samples which have been through high temperature processing.

The mean transfer factors for each commodity for chlorothalonil and R182281 were calculated and are presented in Table 6.5.3-5 and Table 6.5.3-6.

Table 6.5.3-5: Summary of chlorothalonil transfer factors into processed barley products

Commodity	Transfer Factor	Mean Transfer Factor
Un-cleaned grain to malt	<0.04,<0.04,<0.04,<0.04	<0.04
Un-cleaned grain to malt sprouts	0.08	0.08
Un-cleaned grain to spent grain	0.04	0.04
Un-cleaned grain to flocs	0.04	0.04
Un-cleaned grain to spent yeast	0.04	0.04
Un-cleaned grain to young beer	0.04	0.04
Un-cleaned grain to beer	<0.04, <0.04,<0.04, <0.04	<0.04
Un-cleaned grain to abrasion dust	2.25, 2.46, 2.58, 3.13	2.61
Un-cleaned grain to pot barley	0.25, 0.25, 0.21, 0.29	0.25

Transfer factor = residue in processed commodity/mean residue in uncleaned grain (e.g. for malt sprouts 0.02/0.24 = 0.08)

Table 6.5.3-6: Summary of R182281 transfer factors into processed barley products

Commodity	Transfer Factor	Mean Transfer Factor
Un-cleaned grain to malt	0.43, 0.52, 0.39, 0.43	0.44
Un-cleaned grain to malt sprouts	0.35	0.35
Un-cleaned grain to spent grain	0.39	0.39
Un-cleaned grain to flocs	1.04	1.04
Un-cleaned grain to spent yeast	1.35	1.35
Un-cleaned grain to young beer	0.04	0.04
Un-cleaned grain to beer	<0.04, <0.04, <0.04, <0.04	<0.04
Un-cleaned grain to abrasion dust	5.22, 5.65, 4.22, 5.65	5.18
Un-cleaned grain to pot barley	0.09, <0.04, 0.09, 0.09	<0.08

Transfer factor = residue in processed commodity/mean residue in uncleaned grain (e.g. for malt sprouts 0.07/0.23 = 0.35)

Final measured residues of chlorothalonil in beer were less than the limit of quantification (0.01 mg/kg) which is consistent with the instability observed in the high-temperature hydrolysis study. The derived mass balance is significantly less than 100% for the same reason. Residues of chlorothalonil were found to concentrate in the abrasion dust but did not concentrate in pot barley.

III. CONCLUSIONS

Sufficient data is available to allow transfer factors to be calculated for chlorothalonil residues from barley into beer, pot barley and other barley processed commodities. It can be concluded that residues of chlorothalonil would tend to concentrate in the abrasion dust but would not be expected to concentrate in beer or pot barley. During the heating stages of the process, the levels of chlorothalonil declined significantly as may be expected due to its behaviour under high temperature hydrolytic conditions already demonstrated. Hence the achieved residue mass balance is less than 100%.

Residues of R182281 were also concentrated in abrasion dust but would not expect to concentrate in beer or pot barley.

Residues of R613636 were below the LOQ (0.01 mg/kg) in abrasion dust, pot barley and beer i.e. the commodities subjected to high temperature processing. This indicates exposure to this metabolite through the consumption of processed barley fractions is likely to be negligible.

(Simon P, 2007)

Report:	K-CA 6.5.3/03. North N. (2014), Chlorothalonil – Residue study on barley and processed products in Germany and Southern France in 2011. Syngenta Report Number S11-00524-REG, File No: A7867A_11251)

Guidelines

FAO Guidelines on Producing Pesticide Residues Data from Supervised Trials (Rome, 1990).

Commission of the European Communities: General Recommendations for the Design, Preparation and Realization of Residue Trials (**SANCO 7029/V1/95 rev. 5 22/7/1997**).

Commission of the European Communities, Processing Studies; (**SANCO 7035/V1/95 rev. 5 22/7/1997**)

OECD Guidelines for the Testing of Chemicals: OECD Test Guideline 508: Magnitude of the Pesticide Residues in Processed Commodities.

European Commission Guidance Document on Residue Analytical Method (**SANCO/825/00 revision 8.1, 16 Nov 2010**).

Guidelines and Criteria for the Preparation and Presentation of Complete Dossiers and of Summary Dossiers for the Inclusion of Active Substances in Annex I of Directive 91/414/EEC (Article 5.3 and 8.2), 1996

GLP

The study was carried out according to the principles of Good Laboratory Practice.

Executive Summary

Two residue trials on barley were conducted in Germany and southern France during 2011. Two applications of chlorothalonil were applied to each plot as A7867A, a suspension concentrate (SC) formulation at a nominal rate of 3 kg a.s./ha separated by a 10 or 17 day interval. Samples of mature barley grain were harvested 42 days after the last application of A7867A and analysed to determine residues of chlorothalonil and R182281.

Samples of mature barley grain were processed into pearl barley, brewing malt, beer, pot barley and barley flour. One balance study and three follow-up studies were carried out for each process. The processed samples were analysed for chlorothalonil and R182281.

Separate mass balances and transfer factors for chlorothalonil and for R182281 were calculated.

Sufficient data is available to allow transfer factors to be calculated for chlorothalonil and R182281 residues from barley into beer, pot barley and other barley processed commodities. It is concluded that residues of chlorothalonil and R182281 would not be expected to concentrate in beer, pearl barley, pot barley or flour.

I. MATERIALS AND METHODS

A. MATERIALS

A1. Test Materials

Test Material	A7867A
Description	Suspension concentrate formulation containing chlorothalonil
Purity	495 g/L
Batch number	SAV0L00018
Stability of test compound	The test substance is assumed to be stable for the period of use in the study

A2. Test Facilities

Field trials	Niedersachen, Germany	Midi Pyrénnées, France
Processing phase	Eurofins Agroscience Services GmbH, Carl-Goerdeler-Weg 5, D-21684 Stade, Germany	
Analytical phase	Eurofins Agroscience Services Ltd., Slade Lane, Wilson, Melbourne, Derbyshire DE73 8AG, UK	

B. STUDY DESIGN AND METHODS

B1. Processing phase

In field trials, commercially grown barley was treated twice (at growth stage BBCH 55 and at BBCH 65-69) with a foliar spray of A7867A, at nominal application rates of 3.0 kg chlorothalonil/ha. The interval between the applications was 10 or 17 days.

Mature barley grain was harvested 42 days after the last application and used for the production of pearl barley, beer and pot barley.

Prior to each of the balance and follow-up processing studies, uncleaned barley grain from each trial was analysed to give a pre-processed residue value.

The uncleaned barley grain was cleaned using a ‘sample cleaner’ and samples of cleaned barley grain were taken (samples of shrivelled grain and impurities were also taken for the balance study).

<u>Pot barley, pearl barley and flour</u>

The moisture content of the grain was tested and found to be 15% therefore a conditioning step was not required. The cleaned barley grain was decorticated at different abrasion rates (8.2-12% for pot barley and 25-31% for pearl barley) and fractions of pot barley and bran, and pearl barley and ‘rub off’ were taken. Some of the pot barley fraction was milled to give flour.

<u>Malting</u>

Cleaned grain was stored cooled for 63-85 days. After dormancy the grain was steeped by covering with water for 23-24 hours, after which the water was removed. For the sprouting process which was conducted in a climatic exposure cabinet, the grains were turned by hand periodically and moistened with tap water. The temperature during sprouting was 10-14°C. The emergence period was 6-8 days. After sprouting, the green malt was kiln dried in a drying oven at 50-60°C for 6 hours. The drying temperature was then elevated for approximately 8 hours to 85-100°C, followed by a generally constant temperature of 85-100°C for another 9-11 hours. After kiln drying the malt sprouts were separated mechanically. Fractions of malt sprouts and brewing malt were taken.

Beer

The brewing malt was stored for 1-6 days at 4.5-7.0°C until brewing. The malt was ground and mixed with warm water to produce a mash. The mash temperature was slowly raised to 78°C with resting periods and then rinsed with water at 80-82°C. The wort was then cooked for 80 minutes during which hops were added. The deposited 'flocs' ('trub' or 'hops draff') were removed. The remaining wort was filtered and cooled. Fermentation was started by addition of yeast solubilised in wort and lasted for 7 days, after which the beer was stored in bottles for 14 days for a secondary fermentation.

The following samples were taken for analysis in order to determine the residue accountability from the mass balance:

Uncleaned grain, cleaning impurities, cleaned grain, cleaned grain after storage, 'rub-off', pearl barley, cleaned grain after dormancy, steeping water, malt with sprouts, malt sprouts, brewing malt, malt before brewing, spent grain, dried spent grain, wort, trub/flocs, brewer's yeast, young beer, beer, bran, pot barley and barley flour.

Transfer factors were determined from the mass balance and follow up studies for the following samples:

Cleaned grain, pearl barley, pot barley, barley flour, brewing malt, dried spent grain, brewer's yeast and beer.

The chlorothalonil and R182281 residue accountability for the brewing process was calculated from a mass balance study, and transfer factors for the processed commodities were determined from this and the additional follow up studies.

Samples were stored frozen for a maximum period of 14 months from sampling to analysis.

B2. Analytical Phase

Samples of the raw agricultural commodity (grain) and various processed fractions were analysed for chlorothalonil and R182281 using method GRM005.01A. The LOQ was 0.01 mg/kg for both analytes in all commodities. A full method description and validation data are presented in document M-CA Section 4, CA 4.1.2.

II. RESULTS AND DISCUSSION

A summary of the measured residues from the various processed fractions is given in Table 6.5.3-7. The mean transfer factors for each commodity for chlorothalonil and R182281 were calculated and are presented in Table 6.5.3-8 and Table 6.5.3-9, respectively.

Table 6.5.3-7: Summary of chlorothalonil and R182281 residues in barley processed commodities from trials in Germany and southern France

Commodity	Residues (mg/kg)							
	Balance 1		Follow-up 1		Follow-up 2		Follow-up 3	
	chloro-thalonil	R182281	chloro-thalonil	R182281	chloro-thalonil	R182281	chloro-thalonil	R182281
Cleaning								
Mean barley grain (RAC)	0.97	0.12	0.76	0.11	0.82	0.11	0.82	0.08
Cleaned grain	0.61	0.09	0.41	0.06	0.40	0.05	0.60	0.07
Impurities	3.99	0.83	-	-	-	-	-	-
Pearl barley								
Cleaned grain after storage	0.65	0.11	0.40	0.11	0.49	0.08	0.58	0.08
Rub- off	1.05	0.72	-	-	-	-	-	-
Pearl barley	0.11	0.02	0.13	0.02	0.04	<0.01	0.10	0.01
Malt								
Cleaned grain after dormancy	0.58	0.10	0.27	0.07	0.70	0.08	0.63	0.08
Steeping water	0.02	0.03	-	-	-	-	-	-
Malt with sprouts	0.02	0.07	-	-	-	-	-	-
Malt sprouts	0.06	0.12	0.06	0.12	0.06	0.16	0.09	0.23
Brewing malt	0.02	0.06	0.02	0.04	0.02	0.05	0.02	0.06
Beer								
Malt before brewing	0.01	0.05	<0.01	0.04	<0.01	0.05	0.01	0.06
Spent grain	<0.01	0.08	-	-	-	-	-	-
Dried spent grain	<0.01	0.04	<0.01	0.02	<0.01	0.04	<0.01	0.05
Wort	<0.01	0.02	-	-	-	-	-	-
Trub/flocs	<0.01	0.03	-	-	-	-	-	-
Brewer's yeast	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01
Young beer	<0.01	0.02	-	-	-	-	-	-
Beer	<0.01	0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01
Pot barley/flour								
Bran	2.21	1.10	-	-	-	-	-	-
Pot barley	0.23	0.05	0.16	0.05	0.11	0.03	0.10	0.02
Barley flour	0.07	0.07	0.06	0.07	0.05	0.03	0.06	0.04

--: not analysed in follow up study.

Table 6.5.3-8: Summary of chlorothalonil transfer factors into processed barley products

Commodity	Transfer Factor	Mean Transfer Factor
Cleaned grain	0.63, 0.54, 0.49, 0.73	0.60
Pearl barley	0.11, 0.17, 0.05, 0.12	0.11
Pot barley	0.24, 0.21, 0.13, 0.12	0.18
Barley flour	0.07, 0.08, 0.06, 0.07	0.07
Brewing malt	0.02, 0.03, 0.02, 0.02	0.02
Dried spent grain	<0.01, <0.01, <0.01, <0.01	<0.01
Brewer's yeast	<0.01, <0.01, <0.01, <0.01	<0.01
Beer	<0.01, <0.01, <0.01, <0.01	<0.01

Transfer factor = residue in processed commodity/mean residue in uncleaned grain (e.g. for cleaned grain 0.61/0.97 = 0.63)

Table 6.5.3-9: Summary of R182281 transfer factors into processed barley products

Commodity	Transfer Factor	Mean Transfer Factor
Cleaned grain	0.75, 0.55, 0.45, 0.88	0.66
Pearl barley	0.17, 0.18, <0.09, 0.13	<0.14
Pot barley	0.42, 0.45, 0.27, 0.25	0.35
Barley flour	0.58, 0.64, 0.27, 0.50	0.50
Brewing malt	0.50, 0.36, 0.45, 0.75	0.52
Dried spent grain	0.33, 0.18, 0.36, 0.63	0.38
Brewer's yeast	<0.08, <0.09, <0.09, <0.13	<0.10
Beer	0.08, <0.09, <0.09, <0.13	<0.10

Transfer factor = residue in processed commodity/mean residue in uncleaned grain (e.g. for cleaned grain 0.09/0.12 = 0.75)

Residues of chlorothalonil and R182281 in the pre-processed barley grain samples were 0.70 to 1.05 mg/kg and 0.07 to 0.12 mg/kg, respectively. No residues of chlorothalonil or R182281 were found at or above the LOQ (0.01 mg/kg) in any of the untreated barley grain or untreated processed commodities.

Processing into pearl barley

Residues of both chlorothalonil and R182281 were reduced during pearl barley production; residues of chlorothalonil in pearl barley were 0.04 to 0.13 mg/kg (mean transfer factor of 0.11) and residues of R182281 were <0.01 to 0.02 mg/kg (mean transfer factor of < 0.14). A mass balance of 100% was achieved; 72% of the initial chlorothalonil residue and 94% of the initial R182281 was recovered during the process.

Processing into pot barley and flour

For pot barley production residues of chlorothalonil and R182281 were also reduced; residues of chlorothalonil in pot barley were 0.10 to 0.23 mg/kg (mean transfer factor of 0.18) and residues of R182281 were 0.02 to 0.05 mg/kg (mean transfer factor of 0.35). For barley flour chlorothalonil residues were 0.05 to 0.07 mg/kg (mean transfer factor of 0.07) and residues of R182281 were 0.03 to 0.07 mg/kg (mean transfer factor of 0.50). The mass balance during pot barley and barley flour production was 100% of the initial barley grain mass; 73% of the initial chlorothalonil residue and 95% of the initial R182281 was recovered during the process.

Processing into beer

No residues of chlorothalonil were found above 0.01 mg/kg in the treated beer samples. Residues of R182281 in beer were <0.01 to 0.01 mg/kg. The mass balance during beer production was 102% of the initial barley grain mass; 66% of the initial chlorothalonil residue and 93% of the initial R182281 residue was recovered during the process.

III. CONCLUSIONS

Sufficient data is available to allow transfer factors to be calculated for chlorothalonil and R182281 residues from barley into beer, pot barley and other barley processed commodities. It is concluded that residues of chlorothalonil and R182281 would not be expected to concentrate in beer, pearl barley, pot barley or flour.

(North N, 2014)

Report:	K-CA 6.5.3/04. Sala A. (2014h), Determination of chlorothalonil and its metabolites SDS3701 and R613636 residues in raw agricultural commodity barley and processed commodity (pot barley, brewing malt, beer) following two applications of chlorothalonil 500 SC. Syngenta File No: R044686_11189. Report Number RAU-008-14.

Guidelines

Regulation (EC) No. 1107/2009 of the European Parliament and of the Council of 21 October 2009, concerning the placing of plant protection products on the market and repealing Council Directives 78/117/EEC and 91/414/EEC.

EU Guidance documents on residue analytical methods SANCO/3029/99, rev. 4 (11/07/2000)

EC guidance document 1607/VI/97 rev.2, 10/6/1999

GLP

The study was carried out according to the principles of Good Laboratory Practice.

Executive Summary

Outdoor barley grown in field trials in Italy and Poland was treated with Chlorothalonil 500 SC. The plots were sprayed twice with nominal application rates of 3.0 kg chlorothalonil/ha. Samples of mature barley grain were harvested 40 or 54 days after the last application and analysed to determine residues of chlorothalonil, R182281 and R613636.

Additional samples of the mature barley grain taken at 40 or 54 days from the treated plots were used for the production of pot barley, brewing malt and beer, and the processed samples were analysed for residues of chlorothalonil, R182281 and R613636.

Transfer factors for the various processed fractions were calculated. The study showed that residues of chlorothalonil and R182281 would not be expected to concentrate in beer, brewing malt or pot barley. Residues of R613636 were below the LOQ (0.01 mg/kg) in the grain before processing and all processed products.

I. MATERIALS AND METHODS

A. MATERIALS

A1. Test Materials

Test Material	Chlorothalonil 500 SC
Description	Suspension concentrate formulation containing chlorothalonil
Purity	507 g/L
Batch number	PN1911
Stability of test compound	The test substance has been shown to be stable under the storage and test conditions of the study

A2. Test Facilities

Field trial	Italy	Poland
Malting and brewing	Staphyt Processing, MAS la Paluzette, F-34590, France	
Pot barley production	INRA, 2 Place Viala, 34060 Montpellier, France	
Analytical phase	Biospheres Residues Analysis Unit, Via Vittoria Veneto, 26857 Salerano sul Lambro (LO), Italy	

B. STUDY DESIGN AND METHODS

B1. Processing phase

In two field trials, barley was treated twice with a foliar spray of the formulation at nominal application rates of 3.0 kg chlorothalonil/ha. The interval between the applications was 9-14 days.

Mature barley grain was harvested at the two sites 40 or 54 days after the last application and used for the production of beer, brewing malt and pot barley.

The grains were prepared by sieving to retain grains with a minimum diameter of 2.5 mm. The sieved grain was steeped at a temperature of 18°C for 47 hours then germinated at 16°C for approximately 5 days. The germinated grain was then dried by raising the temperature from 30° to 80°C over a period of 24 hours.

The malt was milled before mashing. Ground malt was mixed with water at 45°C and the PH was adjusted to 5.5 by the addition of lactic acid. The mashing process took place in three stages: firstly at 45°C for 20 minutes, secondly at 64°C for 20 minutes and thirdly at 74°C for 30 minutes. Hops were added and the wort was cooked at 100°C for approximately 1.5 hours. The wort was cooled, yeast was added and left to ferment at 12°C for 15-16 days until a stable density was obtained.

For pot barley, the grains were passed through a husker twice and the hulls were recovered.

B2. Analytical Phase

Samples of the raw agricultural commodity (grain) and various processed fractions were analysed for chlorothalonil, R182281 and R613636 using methods described in Section CA 4.1. The LOQ was 0.01 mg/kg for chlorothalonil and 0.02 mg/kg for R182281 in all commodities. Full method descriptions and validation data are presented in document M-CA Section 4, CA 4.1.2.

Transfer factors for the processed commodities were determined.

II. RESULTS AND DISCUSSION

A summary of the measured residues from the various fractions for the processed fraction is given in Table 6.5.3-10.

Table 6.5.3-10: Summary of chlorothalonil, R182281 and R613636 residues in barley and processed commodities from trials conducted in Italy and Poland

Trial:	Residues (mg/kg)					
	Italy			Poland		
Commodity	**Chlorothalonil**	**R182281**	**R613636**	**Chlorothalonil**	**R182281**	**R613636**
Grain (RAC)	0.39	0.04	<0.01	0.21	0.04	<0.01
Grain for processing	0.36	0.05	<0.01	0.11	0.04	<0.01
Pot barley	<0.01	<0.02	<0.01	0.04	<0.02	<0.01
Brewing malt	0.02	<0.02	<0.01	<0.01	<0.02	<0.01
Beer	<0.01	<0.02	<0.01	<0.01	<0.02	<0.01

The mean transfer factors for each commodity for chlorothalonil and R182281 were calculated and are presented in Table 6.5.3-11. Transfer factors for R613636 were not calculated as residues in the grain before processing and in all processed commodities were below the LOQ (0.01 mg/kg).

Table 6.5.3-11: Summary of transfer factors into processed barley products

	Chlorothalonil		R182281	
Commodity	**Transfer Factors**	**Mean Transfer Factor**	**Transfer Factors**	**Mean Transfer Factor**
Pot barley	<0.03, 0.36	0.20	<0.4, <0.5	<0.5
Brewing malt	0.06, <0.09	0.08	<0.4, <0.5	<0.5
Beer	<0.03, <0.09	0.06	<0.4, <0.5	<0.5

Transfer factor = residue in processed commodity/mean residue in grain for processing (e.g. for brewing malt 0.02/0.36 = 0.06).

Residues of chlorothalonil and R182281 did not concentrate in pot barley, brewing malt or beer.

III. CONCLUSIONS

Sufficient data is available to allow transfer factors to be calculated for chlorothalonil residues from barley into beer, pot barley and brewing malt. It can be concluded that residues of chlorothalonil and R182281 would not be expected to concentrate in beer, brewing malt or pot barley.

Residues of R613636 were below the LOQ (0.01 mg/kg) in the grain before processing and all processed products.

(Sala A, 2014h)

Wheat

Please note that for this study residues in the pre-processed grain were very low; a maximum residue of 0.01 mg/kg was found in the pre-processed grain and so the results of this study should be interpreted with caution. A more recent study has been conducted where residues in the pre-processed grain were higher (see CA 6.5.3/07); however the study below is presented for completeness.

Report:	K-CA 6.5.3/05. Gill JP and Sutra G. (2001), Residue levels in wheat and processed wheat products from trials carried out in France during 1999. Zeneca Study No 99JH076. Syngenta Report Number RJ3094B. (Syngenta File No: R44686/2186).

Guidelines

Commission of the European Communities, Processing Studies; (**SANCO 7035/V1/95 rev. 5 22/7/1997**)

GLP

The study was carried out according to the principles of Good Laboratory Practice.

Executive Summary

Three residue field trials were conducted on wheat where two applications of a suspension concentrate formulation containing 500 g/L chlorothalonil, were made at a rate of 1.1 kg a.s./ha. Grain sampled at harvest was milled into white flour and wholemeal flour. The wholemeal flour was then used to bake bread by two typical commercial processes (the Chorleywood Bread Process and the spiral-mixing process). Wholemeal flour, middlings, break flour, bran, offal, toppings, white flour, type 550 flour and bread were analysed for residues of chlorothalonil.

Residues of chlorothalonil were not found above the LOQ of 0.01 mg/kg in flour or bread and would therefore not be expected to concentrate in these processed commodities. Residues were found to concentrate in bran, leading to a transfer factor of 6. Residues in the pre-processed grain were very low; a maximum residue of 0.01 mg/kg was found in the pre-processed grain and so the results of this study should be interpreted with caution.

I. MATERIALS AND METHODS

A. MATERIALS

A1. Test Materials

Test Material	YF10934
Description	Suspension concentrate formulation containing chlorothalonil
Purity	523 g/l
Batch number	882
Stability of test compound	The test substance has been shown to be stable under the storage and test conditions of the study

A2. Test Facilities

Field trials	Northern and Southern France
Milling and bread production	Campden and Chorleywood Food Research Association, Chipping Campden, Gloucestershire, GL55 6LD, UK
Analytical phase	Syngenta, Jealott's Hill International Research Centre, Bracknell, Berkshire, RG42 6EY, UK

B. STUDY DESIGN AND METHODS

B1. Processing phase

Three residue field trials were conducted on wheat in France during 1999, 2 in northern France and 1 in southern France. In each trial two applications of a suspension concentrate formulation containing 500 g/L chlorothalonil, were made at a rate of 1.1 kg a.s./ha.

Grain sampled at harvest from the two northern France trials (39 and 52 days after final application) were milled into white flour and wholemeal flour.

The wholemeal flour was then used to bake bread by two typical commercial processes (the Chorleywood Bread Process and the spiral-mixing process). Samples of wholemeal flour, middlings, break flour, bran, offal, toppings, white flour, type 550 flour and bread were analysed for residues of chlorothalonil.

B2. Analytical Phase

Samples of the raw agricultural commodity (grain) and various processed fractions were analysed for chlorothalonil using method RAM 320/01. The LOQ was 0.01 mg/kg for all commodities. A full method description and validation data are presented in document M-CA Section 4, CA 4.1.2.

II. RESULTS AND DISCUSSION

A summary of the measured residues from the various processed fractions along with the calculated transfer factors are given in Table 6.5.3-12.

Table 6.5.3-12: Summary of Chlorothalonil Residues in Wheat and Processed Wheat Products

Commodity	Residues (mg/kg)			
	FR41-99-S761	Transfer Factor	FR61-99-S762	Transfer Factor[3]
Grain	<0.01	Not applicable	na[1]	Not applicable
Grain (Pre-milling)	<0.01	Not applicable	0.01	-
Wholemeal Flour	<0.01	Not applicable	<0.01	<1
Middlings	<0.01	Not applicable	<0.01	<1
Break Flour	<0.01	Not applicable	<0.01	<1
Bran	<0.01	Not applicable	0.06	6
White Flour	<0.01	Not applicable	<0.01	<1
Cleaned Course Bran	<0.01	Not applicable	0.06	6
Cleaned Offal	<0.01	Not applicable	<0.01	<1
Toppings	<0.01	Not applicable	<0.01	<1
Type 550 Flour	<0.01	Not applicable	<0.01	<1
Wholemeal Bread (CBP)[2]	<0.01	Not applicable	<0.01	<1
Wholemeal Bread (Spiral Mixed)	<0.01	Not applicable	<0.01	<1

[1] na – Not analysed
[2] CBP – Chorleywood Baking Process
[3] transfer factors based on the residue level of the pre-milling grain fraction

Residues of chlorothalonil in grain and processed wheat products were all below the LOQ of 0.01 mg/kg for one trial. In the second trial residues of chlorothalonil were reduced in flour and bread. Residues were shown to concentrate in bran leading to a transfer factor of 6.

III. CONCLUSIONS

Residues of chlorothalonil would not be expected to concentrate in flour and bread. Residues were found to concentrate in bran, leading to a transfer factor of 6. Residues in the pre-processed grain were very low; a maximum residue of 0.01 mg/kg was found in the pre-processed grain and so the results of this study should be interpreted with caution.

(Gill JP and Sutra G, 2001)

Report:	K-CA 6.5.3/06. Gill JP and Myles P. (2001), Residue levels in wheat and processed wheat products from trials carried out in the UK during 1999. Zeneca Study No 99JH077. Syngenta Report Number RJ3095B. (Syngenta File No: R44686/2187).

Please note that for this study residues in the pre-processed grain were very low; a maximum residue of 0.02 mg/kg was found in the pre-processed grain and so the results of this study should be interpreted with caution. A more recent study has been conducted where residues in the pre-processed grain were higher (see CA 6.5.3/07); however the study below is presented for completeness.

Guidelines

Commission of the European Communities, Processing Studies; (**SANCO 7035/V1/95 rev. 5 22/7/1997**)
GLP

The study was carried out according to the principles of Good Laboratory Practice.

Executive Summary

Three residue field trials were conducted on wheat where two applications of a suspension concentrate formulation containing 500 g/L chlorothalonil, were made at a rate of 1.1 kg a.s./ha. Grain sampled at harvest was milled into white flour and wholemeal flour. The wholemeal flour was then used to bake bread by two typical commercial processes (the Chorleywood Bread Process and the spiral-mixing process). Wholemeal flour, middlings, break flour, bran, offal, toppings, white flour, type 550 flour and bread were analysed for residues of chlorothalonil.

Residues of chlorothalonil were not found above the LOQ of 0.01 mg/kg in flour or bread and would therefore not be expected to concentrate in these processed commodities. Residues were found to concentrate in bran, leading to a transfer factor of 4. Residues in the pre-processed grain were very low; a maximum residue of 0.02 mg/kg was found in the pre-processed grain and so the results of this study should be interpreted with caution.

I. MATERIALS AND METHODS

A. MATERIALS

A1. Test Materials

Test Material	YF10934
Description	Suspension concentrate formulation containing chlorothalonil
Purity	523 g/l
Batch number	882
Stability of test compound	The test substance has been shown to be stable under the storage and test conditions of the study

A2. Test Facilities

Field trials	UK
Milling and bread production	Campden and Chorleywood Food Research Association, Chipping Campden, Gloucestershire, GL55 6LD, UK
Analytical phase	Syngenta, Jealott's Hill International Research Centre, Bracknell, Berkshire, RG42 6EY, UK

B. STUDY DESIGN AND METHODS

B1. Processing phase

Three residue field trials were conducted on wheat in the UK during 1999 consisting of two decline trials and one harvest trial. In each trial two applications of a suspension concentrate formulation containing 500 g/L chlorothalonil, were made at a rate of 1.1 kg a.s./ha.

Grain sampled at harvest from the two decline trials (67 and 54 days after final application) were milled into white flour and wholemeal flour.

The wholemeal flour was then used to bake bread by two typical commercial processes (the Chorleywood Bread Process and the spiral-mixing process). Samples of wholemeal flour, middlings, break flour, bran, offal, toppings, white flour, type 550 flour and bread were analysed for residues of chlorothalonil.

B2. Analytical Phase

Samples of the raw agricultural commodity (grain) and various processed fractions were analysed for chlorothalonil using method RAM 320/01. The LOQ was 0.01 mg/kg for all commodities. A full method description and validation data are presented in document M-CA Section 4, CA 4.1.2.

II. RESULTS AND DISCUSSION

A summary of the measured residues from the various processed fractions along with the calculated transfer factors are given in Table 6.5.3-13.

Table 6.5.3-13: Summary of chlorothalonil residues in wheat and processed wheat products

Commodity	Residues (mg/kg)			
	GB04-99-S078	Transfer Factor	GB04-99-S079	Transfer Factor
Grain	na[1]	Not applicable	0.02	-
Grain (Pre-milling)	<0.01		0.02	1
Wholemeal Flour	<0.01		0.01	0.5
Middlings	<0.01		<0.01	<0.5
Break Flour	<0.01		<0.01	<0.5
Bran	<0.01		0.08	4
White Flour	<0.01		<0.01	<0.5
Cleaned Course Bran	0.01	<1	0.06	3
Cleaned Offal	<0.01		0.03	1.5
Toppings	<0.01		<0.01	<0.5
Type 550 Flour	<0.01		<0.01	<0.5
Wholemeal Bread (CBP)[2]	<0.01		<0.01	<0.5
Wholemeal Bread (Spiral Mixed)	<0.01		<0.01	<0.5

[1] na – Not analysed
[2] CBP – Chorleywood Baking Process

Residues of chlorothalonil in grain and processed wheat products were all below the LOQ of 0.01 mg/kg for one trial. In the second trial residues of chlorothalonil were reduced in flour and bread. Residues were shown to concentrate in bran leading to a transfer factor of 4.

III. CONCLUSIONS

Residues of chlorothalonil would not be expected to concentrate in flour and bread. Residues were found to concentrate in bran, leading to a transfer factor of 4. Residues in the pre-processed grain were very low; a maximum residue of 0.02 mg/kg was found in the pre-processed grain and so the results of this study should be interpreted with caution.

(Gill JP and Myles P, 2001)

Report:	K-CA 6.5.3/07. North L., (2014a) Chlorothalonil – Residue study on wheat and processed products in Germany and northern France in 2011, Eurofins Agroscience Services Ltd, Report Number S11-00526-REG. (Syngenta File No. A7867A_11256)

Guidelines

FAO Guidelines on Producing Pesticide Residues Data from Supervised Trials (Rome, 1990).

Commission of the European Communities. General Recommendations for the Design, Preparation and Realization of Residue Trials (**SANCO 7029/V1/95 rev. 5 22/7/1997**).

Commission of the European Communities, Processing Studies; (**SANCO 7035/V1/95 rev. 5 22/7/1997**)

OECD Guidelines for the Testing of Chemicals : OECD Test Guideline 508: Magnitude of the Pesticide Residues in Processed Commodities.

European Commission Guidance Document on Residue Analytical Method (**SANCO/825/00 rev. 8.1, 16 Nov 2010**).

Guidelines and Criteria for the Preparation and Presentation of Complete Dossiers and of Summary Dossiers for the Inclusion of Active Substances in Annex I of Directive 91/414/EEC (Article 5.3 and 8.2), 1996

GLP

The study was carried out according to the principles of Good Laboratory Practice.

Executive Summary

Two residue trials on wheat were conducted in northern France and Germany during 2011. Two applications of chlorothalonil were applied to each plot as A7867A, a suspension concentrate (SC) formulation at a nominal rate of 3 kg a.s./ha separated by a 10 or 12 day interval. Samples of mature wheat grain were harvested 58 or 63 days after the last application of A7867A and analysed to determine residues of chlorothalonil and R182281.

Samples of mature wheat grain were processed into white flour (type 550), wholemeal flour, wholemeal bread, wheat germs, starch and gluten. One balance study and one follow-up study were carried out for each trial, for each process. Therefore, a total of two balance and two follow-up studies were performed. The processed samples were analysed for residues of chlorothalonil and R182281.

Separate transfer factors for chlorothalonil and for R182281 were calculated. Mass balances were calculated for chlorothalonil only, due to the low levels of R182281 found in the samples before processing.

Sufficient data are available to allow transfer factors to be calculated for chlorothalonil and R182281 residues for wheat processed products. It is concluded that residues of chlorothalonil and R182281 would not be expected to concentrate in flour, bread, wheat germ, dried starch, dried gluten and gluten feed meal. Residues of chlorothalonil and R182281 would be expected to concentrate in course bran.

I. MATERIALS AND METHODS

A. MATERIALS

A1. Test Materials

Test Material	A7867A
Description	Suspension concentrate formulation containing chlorothalonil
Purity	495 g/L
Batch number	SAV0L00018
Stability of test compound	The test substance is assumed to be stable for the period of use in the study

A2. Test Facilities

Field trials	Württemberg, Germany	Loiret, France
Processing phase	Eurofins Agroscience Services GmbH, Carl-Goerdeler-Weg 5, D-21684 Stade, Germany	
Analytical phase	Eurofins Agroscience Services Ltd., Slade Lane, Wilson, Melbourne, Derbyshire DE73 8AG, UK	

B. STUDY DESIGN AND METHODS

B1. Processing phase

In field trials, commercially grown wheat was treated twice (at growth stage BBCH 53-57 and at BBCH 67-69) with a foliar spray of A7867A, at nominal application rates of 3.0 kg chlorothalonil/ha. The interval between the applications was 10 or 12 days.

Mature wheat grain was harvested 58 or 63 days after the last application and used for the production of white flour (type 550), wholemeal flour, wholemeal bread, wheat germ, starch and gluten.

Prior to each of the balance and follow-up processing studies, uncleaned wheat grain from each trial was analysed in duplicate to give a pre-processed residue value.

The un-cleaned wheat grain was cleaned using a ‘sample cleaner’ and for the balance studies, samples of cleaned wheat grain, impurities and shrivelled grain were taken for analysis. Part of the cleaned wheat was stored for subsequent processing to germ, starch and gluten.

White flour (type 550)

The cleaned grain was moistened overnight with tap water at 13.1°C – 19.9°C and the resulting conditioned grain had a moisture content of 15.7 – 16.7%. The conditioned grain was milled, producing flour (type 550), fine bran and coarse bran. The coarse bran was purified into cleaned coarse bran and ‘toppings 2’. The fine bran was purified to produce cleaned fine bran, ‘toppings 1’ and ‘middlings’ fractions. The ‘middlings’ and coarse bran were then mixed at rate of 1:1 and the ‘toppings 1 and 2’ fractions were mixed to produce ‘toppings’. Part of remaining ‘toppings’ and flour (type 550) were mixed.

Wholemeal flour

The cleaned grain was moistened overnight with tap water at temperature 13.1°C – 19.9°C and the resulting conditioned grain had moisture content of 15.7 – 16.7%. The conditioned grain was milled to produce wholemeal flour.

Wholemeal bread

Wholemeal flour was mixed with salt, sugar, plant fat, ascorbic acid, yeast and water in the kneading machine for 10 minutes. The dough was placed in an environmental cabinet, with a controlled climate at 24-27 °C and a relative humidity of 70-80% for 25 minutes. After the first fermentation process the dough was kneaded for 1 minute and then taken through a second fermentation process. After 15 minutes of fermentation, the dough was kneaded for an extra minute and then divided into loaves. The loaves were transferred into baking forms and placed under the same environmental conditions for 20 minutes. The dough was baked at 182-213°C for 24-26 minutes.

Wheat germ

The cleaned grain was moistened in a counter current mixer for 30 minutes and the resulting conditioned grain had moisture content of 16.3 – 17.4%. The remaining conditioned grain was milled and the following fractions were produced: flour, fine bran, coarse bran. Only the coarse bran containing the germs was taken through the purification process. During the purification process cleaned coarse bran and 'toppings' were produced. The cleaned coarse bran fraction was cleaned again and the wheat germ fraction was taken.

Starch and gluten

Flour (type 550) was mixed with water in a kneading machine for 5-10 minutes and then the dough was sprayed with 3% table salt solution in 4-6 washing steps. After each step, the starch/gluten solution was drained into a vessel and retained for the starch/water centrifugation. The remaining fraction in the kneading machine, wet gluten, was sampled. The starch/water solution was centrifuged for 4 minutes and the fractions wet starch and process water were produced. Fractions of wet starch and wet gluten were dried to produce dried starch and dried gluten. Dried starch and dried gluten were mixed (ratio 1:1) to give gluten feed meal.

The following samples were taken for analysis in order to determine the residue accountability of chlorothalonil from the mass balance:

Uncleaned grain, cleaning impurities, shrivelled grain, cleaned grain, conditioned grain, fine bran, course bran, cleaned fine bran, 'middlings', coarse bran + 'middlings', cleaned coarse bran, 'toppings', flour type 550, wholemeal flour ,flour type 550 + toppings, dough, wholemeal bread, wheat germ, wet starch, wet gluten, starch washing water, dried starch, dried gluten and gluten feed meal.

Transfer factors were determined from the mass balance and follow up studies for the following samples:

Uncleaned grain, cleaned grain, conditioned grain, fine bran, course bran, flour type 550, wholemeal flour, dough, wholemeal bread, wheat germ, dried starch, dried gluten and gluten feed meal.

Samples were stored frozen for a maximum period of 12 months from sampling to analysis.

B2. Analytical Phase

Samples of the raw agricultural commodity (grain) and various processed fractions were analysed for chlorothalonil and R182281 using method GRM005.01A. The LOQ was 0.01 mg/kg for both analytes in all commodities. A full method description and validation data are presented in document M-CA Section 4, CA 4.1.2.

II. RESULTS AND DISCUSSION

A summary of the measured residues from the various processed fractions are given in Table 6.5.3-14.

Table 6.5.3-14: Summary of chlorothalonil and R182281 residues in wheat processed commodities from trials in Germany and northern France

Commodity	Residues (mg/kg)							
	Balance 1		Follow-up 1		Balance 2		Follow-up 2	
	chloro-thalonil	R182281	chloro-thalonil	R182281	chloro-thalonil	R182281	chloro-thalonil	R182281
Mean wheat grain (RAC)	0.07	0.02	0.04	0.01	0.04	<0.01	0.12	0.01
Cleaning								
Cleaned grain	0.07	0.02	0.05	0.02	0.03	<0.01	0.03	<0.01
Impurities	16.61	2.24	--	--	3.41	0.21	--	--
Shrivelled grain	0.16	0.04	--	--	0.13	0.02	--	--
White flour production								
Grain (conditioned)	0.04	0.02	0.03	0.02	0.01	<0.01	0.01	<0.01
Flour type 550	<0.01	<0.01	--	--	<0.01	<0.01	--	--
Fine bran	0.03	0.02	0.02	0.01	<0.01	<0.01	0.01	<0.01
Coarse bran	0.18	0.09	0.17	0.06	0.05	0.02	0.07	0.03
Cleaned fine bran	0.08	0.05	--	--	0.02	0.01	--	--
Middlings	0.03	0.02	--	--	<0.01	<0.01	--	--
Coarse bran + middlings	0.10	0.06	--	--	0.02	0.01	--	--
Cleaned coarse bran	0.12	0.07	--	--	0.04	0.02	--	--
Toppings	0.08	0.05	--	--	0.03	0.02	--	--
Flour type 550 + toppings	0.05	0.04	0.05	0.03	0.02	0.01	0.01	<0.01
Wholemeal flour and bread production								
Grain (conditioned)	0.05	0.02	0.03	0.02	0.01	<0.01	0.02	<0.01
Wholemeal flour	0.03	0.03	0.03	0.02	0.01	<0.01	<0.01	<0.01
Dough	<0.01	0.02	<0.01	0.01	<0.01	<0.01	<0.01	<0.01
Wholemeal bread	<0.01	0.02	<0.01	0.01	<0.01	<0.01	<0.01	<0.01
Wheat germ								
Grain (conditioned)	0.03	0.02	0.04	0.02	0.01	<0.01	0.02	<0.01
Fine bran	0.07	0.04	--	--	0.02	0.01	--	--
Coarse bran	0.13	0.06	--	--	0.06	0.02	--	--
Toppings	0.10	0.07	--	--	0.03	0.02	--	--
Cleaned coarse bran	0.13	0.07	--	--	0.04	0.02	--	--
Wheat germ	0.04	0.02	0.05	0.03	<0.01	<0.01	0.01	<0.01
Starch and gluten								
Grain (conditioned)	0.05	0.01	0.04	0.01	0.01	<0.01	0.02	<0.01
Wet starch	<0.01	<0.01	--	--	<0.01	<0.01	--	--
Wet gluten	<0.01	<0.01	--	--	<0.01	<0.01	--	--
Process water	<0.01	<0.01	--	--	<0.01	<0.01	--	--
Dried starch	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01
Dried gluten	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01
Gluten feed meal	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01

--: not analysed in follow up study.

Residues of chlorothalonil and R182281 in the pre-processed grain samples were in the range 0.02 to 0.14 mg/kg and <0.01 to 0.02 mg/kg, respectively. No residues of chlorothalonil or R182281 were found at or above the LOQ (0.01 mg/kg) in any of the untreated wheat grain or untreated processed commodities.

Processing into white flour (type 550)

Residues of chlorothalonil in cleaned wheat grain were 0.03 to 0.07 mg/kg, in fine bran were <0.01 to 0.03 mg/kg, in coarse bran were 0.05 to 0.18 mg/kg and in white flour type 550 including toppings were 0.01 to 0.05 mg/kg.

Residues of R182281 in cleaned wheat grain were <0.01 to 0.02 mg/kg, in fine bran were <0.01 to 0.03 mg/kg, in coarse bran were 0.02 to 0.09 mg/kg and in white flour type 550 including toppings were <0.01 to 0.04 mg/kg.

The mass balance during white flour type 550 including toppings production was 100% of the initial wheat grain mass; 80% of the initial chlorothalonil residue was recovered during the process.

Processing into wholemeal flour and bread

Residues of chlorothalonil in grain after conditioning were 0.01 to 0.05 mg/kg, were <0.01 to 0.03 mg/kg for wholemeal flour and were < 0.01 mg/kg in wholemeal bread.

Residues of R182281 in grain after conditioning were <0.01 to 0.02 mg/kg, were <0.01 to 0.03 mg/kg for wholemeal flour and were < 0.01 mg/kg to 0.02 mg/kg in wholemeal bread.

The mass balance during wholemeal flour production was 100% of the initial wheat grain mass; 77% to 104% of the initial chlorothalonil residue was recovered during the process. The mass balance during wholemeal bread production was 100% of the initial wheat grain mass; 76% to 103% of the initial chlorothalonil residue was recovered during the process.

Processing into wheat germ

Residues of chlorothalonil in grain after conditioning were 0.01 to 0.03 mg/kg and in wheat germ were <0.01 to 0.05 mg/kg. Residues of R182281 in grain after conditioning were <0.01 to 0.02 mg/kg and in wheat germ were <0.01 to 0.03 mg/kg.

The mass balance during wheat germ production was 99-100% of the initial wheat grain mass; 77-103% of the initial chlorothalonil residue was recovered during the process.

Processing into starch and gluten

Residues of both chlorothalonil and R182281 were < 0.01 mg/kg in all dried starch, dried gluten and gluten feed meal samples. The mass balance during gluten feed meal production was 99% of the initial wheat grain mass; 79- 105% of the initial chlorothalonil residue was recovered during the process.

The mean transfer factors for each commodity for chlorothalonil and R182281 were calculated and are presented in Table 6.5.3-15 and Table 6.5.3-16, respectively.

Table 6.5.3-15: Summary of chlorothalonil transfer factors into processed wheat products

Commodity	Transfer Factor	Mean Transfer Factor
Coarse bran	2.57, 1.25, 4.25, 0.58	2.2
Fine bran	0.43, <0.25, 0.50, 0.08	<0.32
White flour (550) + toppings	0.71, 0.50, 1.25, 0.08	0.64
Wholemeal flour	0.43, 0.25, 0.75, <0.08	<0.38
Wholemeal bread	<0.14, <0.25, <0.25, <0.08	<0.18
Wheat germs	0.57, <0.25, 1.25, 0.08	<0.54
Dried starch	<0.14, <0.25, <0.25, <0.08	<0.18
Dried gluten	<0.14, <0.25, <0.25, <0.08	<0.18
Gluten feed meal	<0.14, <0.25, <0.25, <0.08	<0.18

Transfer factor = residue in processed commodity/mean residue in grain (e.g. for coarse bran 0.18/0.07 = 2.57)

Table 6.5.3-16: Summary of R182281 transfer factors into processed wheat products

Commodity	Transfer Factor*	Mean Transfer Factor*
Coarse bran	4.5, 6, 3.0	4.5
Fine bran	1.0, 1.0, <1.0	<1.0
White flour (550) + toppings	2.0, 3.0, <1.0	<2.0
Wholemeal flour	1.5, 2.0, <1.0	<1.5
Wholemeal bread	1.0, 1.0, <1.0	<1.0
Wheat germs	1.0, 3.0, <1.0	<1.6
Dried starch	<0.5, <1.0, <1.0	<0.8
Dried gluten	<0.5, <1.0, <1.0	<0.8
Gluten feed meal	<0.5, <1.0, <1.0	<0.8

Transfer factor = residue in processed commodity/mean residue in grain (e.g. for coarse bran 0.09/0.02 = 4.5)
* Data from Balance study 2 were not used in the calculation of transfer factors as residues of R182281 were <0.01 in the grain before processing.

Residues of chlorothalonil in coarse bran were higher (maximum 0.17 mg/kg) than in the wheat grain samples prior to processing. The mean transfer factor was 2.2, indicating that residues of chlorothalonil are concentrated in coarse bran. Residues of chlorothalonil in fine bran were lower (maximum 0.07 mg/kg) than in the wheat grain samples prior to processing, leading to an overall mean transfer factor of <0.32.

Residues of R182281 in coarse bran were higher (maximum 0.09 mg/kg) than in the wheat grain samples prior to processing leading to an overall mean transfer factor of 4.5. Residues of R182281 in fine bran were the same as in the wheat grain samples prior to processing.

Residues of chlorothalonil in both white and wholemeal flour were lower than in the wheat grain samples prior to processing indicating that residues do not concentrate in flour. Residues of R182281 were higher in white flour (maximum 0.04 mg/kg) than in the wheat grain samples prior to processing in two studies, but were <0.01 mg/kg in one study leading to an overall mean transfer factor of <2.0. Residues of R182281 in wholemeal flour were the same as in the wheat grain samples prior to processing.

Residues of chlorothalonil were < 0.01 mg/kg in wholemeal bread leading to overall transfer factors < 1. Residues of R182281 were the same or lower than in the wheat grain samples prior to processing leading to a mean transfer factor of <1.

Residues of chlorothalonil in wheat germ were lower (maximum 0.05 mg/kg) then wheat grain samples prior to processing, leading to a mean transfer factor <0.54.

Residues of R182281 in wheat germ were higher (maximum 0.03 mg/kg) than wheat grain samples prior to processing in one study; however were lower or the same than in the wheat grain samples prior to processing in the other studies. Overall the mean transfer factor was <1.6.

Residues of chlorothalonil and R182281 in dried starch, dried gluten and gluten feed meal were all <0.01 mg/kg, leading to overall mean transfer factors <0.8.

III. CONCLUSIONS

Sufficient data are available to allow transfer factors to be calculated for chlorothalonil and R182281 residues for wheat processed products. It is concluded that residues of chlorothalonil and R182281 would not be expected to concentrate in flour, bread, wheat germ, dried starch, dried gluten and gluten feed meal. Residues of chlorothalonil and R182281 would be expected to concentrate in course bran.

(North L, 2014a)

Report:	K-CA 6.5.3/08. Sala A. (2015), Determination of chlorothalonil and its metabolites SDS3701 and R613636 residues in raw agricultural commodity winter wheat and processed commodity (grain, flour, total bran, wholemeal flour, wholemeal bread, wheat germ) following two applications of chlorothalonil 500 SC. Syngenta File No: R044686_11359. Report Number RAU-007-14.

Guidelines

Regulation (EC) No. 1107/2009 of the European Parliament and of the Council of 21 October 2009, concerning the placing of plant protection products on the market and repealing Council Directives 78/117/EEC and 91/414/EEC.

EU Guidance documents on residue analytical methods SANCO/3029/99, rev. 4 (11/07/2000)

EC guidance document 1607/VI/97 rev.2, 10/6/1999

GLP

The study was carried out according to the principles of Good Laboratory Practice.

Executive Summary

Outdoor wheat grown in field trials in Italy and Poland was treated with Chlorothalonil 500 SC. The plots were sprayed twice with nominal application rates of 3.0 kg chlorothalonil/ha. Samples of mature wheat grain were harvested 47 or 55 days after the last application and then analysed to determine residues of chlorothalonil, R182281 and R613636.

Additional samples of the mature wheat grain taken at 47 or 55 days from the treated plots were used for the production of white flour, wholemeal flour, bran, wheat germs and wholemeal bread, and the processed samples were analysed for residues of chlorothalonil, R182281 and R613636.

Residues in the pre-processed grain were very low; residues of R182281 and R613636 were below the LOQ in grain and all processed commodities meaning that transfer factors could not be determined. Transfer factors determined for the various process fractions were calculated for chlorothalonil only. The study showed that residues of chlorothalonil would not be expected to concentrate in white flour, wholemeal flour and wheat germs. Residues of chlorothalonil may be expected to concentrate in bran and wholemeal bread, although as residues in the pre-processed grain were very low the results of this study should be interpreted with caution.

I. MATERIALS AND METHODS

A. MATERIALS

A1. Test Materials

Test Material	Chlorothalonil 500 SC
Description	Suspension concentrate formulation containing chlorothalonil
Purity	507 g/L
Batch number	PN1911
Stability of test compound	The test substance has been shown to be stable under the storage and test conditions of the study

A2. Test Facilities

Field trial	Roccabianca (PR) Italy	Wielkopolska Poland
Milling and bread production	Biospheres Processing Laboratory, Via Vittoria Veneto, 26857 Salerano sul Lambro (LO), Italy	
Analytical phase	Biospheres Residues Analysis Unit, Via Vittoria Veneto, 26857 Salerano sul Lambro (LO), Italy	

B. STUDY DESIGN AND METHODS

B1. Processing phase

In two field trials, wheat was treated twice with a foliar spray of the formulation at nominal application rates of 3.0 kg chlorothalonil/ha. The interval between the applications was 9-25 days.

Mature wheat grain was harvested 47 or 55 days after the last application and used for the production of flour, bran, bread and wheat germ.

The grains were milled and sieved to give white flour (550 type) and bran. Separate aliquots of grains were milled to give wholemeal flour that was used to bake bread by a typical commercial process.

To obtain wheat germs, the grains were spread homogenously in a thin layer, covered with water and left to germinate for 11-12 days. The wheat germs were then removed and dried at room temperature.

B2. Analytical Phase

Samples of the raw agricultural commodity (grain) and various processed fractions were analysed for chlorothalonil and R182281 using the method described in study BIU-014-14, and for R613636 using analytical method RAM 464/01. The LOQ was 0.01 mg/kg for chlorothalonil and R613636, and 0.02 mg/kg for R182281 in all commodities. Full method descriptions and validation data are presented in document M-CA Section 4, CA 4.1.2.

Transfer factors for the processed commodities were determined.

II. RESULTS AND DISCUSSION

A summary of the measured residues from the various fractions for the processed fraction is given in Table 6.5.3-17.

Table 6.5.3-17: Summary of chlorothalonil, R182281 and R613636 residues in wheat and processed commodities from trials conducted in Italy and Poland

	Residues (mg/kg)					
Trial:	Italy			Poland		
Commodity	Chlorothalonil	R182281	R613636	Chlorothalonil	R182281	R613636
Grain (RAC)	0.02	<0.02	<0.01	0.01	<0.02	<0.01
Grain for processing	0.01	<0.02	<0.01	0.01	<0.02	<0.01
Bran	0.02	<0.02	<0.01	<0.01	<0.02	<0.01
Flour	<0.01	<0.02	<0.01	<0.01	<0.02	<0.01
Wholemeal flour	<0.01	<0.02	<0.01	<0.01	<0.02	<0.01
Wholemeal bread	0.02	<0.02	<0.01	<0.01	<0.02	<0.01
Wheat germ	<0.01	<0.02	<0.01	<0.01	<0.02	0.02

The mean transfer factors for each commodity for chlorothalonil were calculated and are presented in Table 6.5.3-18. Transfer factors for R182281 and R613636 were not calculated as residues in the grain before processing and in all processed commodities were below the LOQ (0.02 mg/kg and 0.01 mg/kg, respectively).

Table 6.5.3-18: Summary of transfer factors into processed wheat products

	Chlorothalonil	
Commodity	Transfer Factors	Mean Transfer Factor
Bran	2.0, <1.0	1.5
Flour	<1.0, <1.0	<1.0
Wholemeal flour	<1.0, <1.0	<1.0
Wholemeal bread	2.0, <1.0	1.5
Wheat germ	<1.0, <1.0	<1.0

Transfer factor = residue in processed commodity/mean residue in grain for processing (e.g. for bran 0.02/0.01 = 2.0).

III. CONCLUSIONS

Residues in the pre-processed grain were very low; residues of R182281 and R613636 were below the LOQ in grain and all processed products meaning that transfer factors could not be determined. Transfer factors determined for the various process fractions were calculated for chlorothalonil only.

Residues of chlorothalonil would not be expected to concentrate in white flour, wholemeal flour and wheat germs. Residues of chlorothalonil may be expected to concentrate in bran and wholemeal bread, although as residues in the pre-processed grain were very low the results of this study should be interpreted with caution.

(Sala A. 2015)

Summary of processing studies in crops

A summary of transfer factors for chlorothalonil and R182281 in processed tomato, wheat and barley commodities are presented in Table 6.5.3-17 and Table 6.5.3-18.

Residues of chlorothalonil would are not expected to concentrate in tomato or wheat and barley processed products with the exception of wheat bran and a slight increase in tomato pomace. Suitable transfer factors for these commodities have been derived.

Residues of R182281 are not expected to concentrate in wheat and barley processed products with the exception of wheat bran. Residues of R182281 are not expected to concentrate in tomato juice but were shown to concentrate in wet and dry tomato pomace, tomato puree and canned tomato.

Table 6.5.3-17: Summary of chlorothalonil transfer factors into processed tomato, barley and wheat products

Crop	Processed Commodity	Transfer Factor	Mean Transfer Factor
Tomato	Washed tomato	0.35, 0.32, 0.24, 0.27	0.30
	Wet pomace	0.32	0.32
	Dry pomace	1.3, 1.4, 1.0, 1.3	1.3
	Tomato juice	0.11, 0.10, 0.91, 0.13	0.3
	Tomato puree	<0.001, <0.001, <0.001, <0.001	<0.001
	Canned tomatoes (solid portion)	<0.001, <0.001, <0.001, <0.001	<0.001
	Canned tomatoes (liquid portion)	0.004, <0.001, <0.001, <0.001	<0.002
Barley	Malt	0.04, 0.04, 0.04, 0.04, 0.02, 0.03, 0.02, 0.02, 0.06, <0.09	0.04
	Malt sprouts	0.08	0.08
	Spent grain	<0.01, <0.01, <0.01, <0.01, 0.04	<0.02
	Brewer's yeast (spent yeast)	<0.01, <0.01, <0.01, <0.01, 0.04	<0.02
	Beer	<0.01, <0.01, <0.01, <0.01, < 0.03, 4 x <0.04, <0.09	<0.03
	Pot barley	0.25, 0.25, 0.21, 0.29, <0.03, 0.24, 0.21, 0.13, 0.12, 0.36	0.21
	Pearl barley	0.11, 0.17, 0.05, 0.12	0.11
	Barley flour	0.07, 0.08, 0.06, 0.07	0.07
Wheat[1]	Coarse bran	2.57, 1.25, 4.25, 0.58, 2.0, <1.0	~~2.2~~ 1.9
	Fine bran	0.43, <0.25, 0.50, 0.08	<0.32
	White flour (550)	0.71, 0.50, 1.25, 0.08, <1.0, <1.0	~~0.64~~ 0.76
	Wholemeal flour	0.43, 0.25, 0.75, <0.08, <1.0, <1.0	<0.38 0.59
	Wholemeal bread	<0.14, <0.25, <0.25, <0.08, 2.0, <1.0	~~<0.18~~ <0.62
	Wheat germs	0.57, <0.25, 1.25, 0.08, <1.0, <1.0	<0.54 <0.69
	Dried starch	<0.14, <0.25, <0.25, <0.08	<0.18
	Dried gluten	<0.14, <0.25, <0.25, <0.08	<0.18
	Gluten feed meal	<0.14, <0.25, <0.25, <0.08	<0.18

[1]Results from study CA 6.5.3/05 and CA 6.5.3/06 not included due to low residues in un-processed grain

Table 6.5.3-18: Summary of R182281 transfer factors into processed tomato, barley and wheat products

Crop	Processed Commodity	Transfer Factor	Mean Transfer Factor
Tomato	Washed tomato	*	*
	Wet pomace	1.5	1.5
	Dry pomace	13, 16, 14, 18	15
	Tomato juice	1.0, 1.0, 1.0, 1.5	1.1
	Tomato puree	7.5, 6.5, 6, 5.5	6.4
	Canned tomatoes (solid portion)	1, 2.0, 2.0, 2.5	1.9
	Canned tomatoes (liquid portion)	2.0, 1.0, 1.0, 1.0	1.3
Barley	Malt	0.43, 0.52, 0.39, 0.43, 0.50, 0.36, 0.45, 0.75, <0.4, <0.5	0.47
	Malt sprouts	0.35	0.35
	Spent grain	0.39, 0.33, 0.18, 0.36, 0.63	0.38
	Brewer's yeast (spent yeast)	<0.08, <0.09, <0.09, <0.13, 1.35	<0.40
	Beer	<0.04, <0.04, <0.04, <0.04, 0.08, <0.09, <0.09, <0.13, <0.4, <0.5	<0.15
	Pot barley	0.09, <0.04, 0.09, 0.09, 0.42, 0.45, 0.27, 0.25, <0.4, <0.5	0.26
	Pearl barley	0.17, 0.18, <0.09, 0.13	<0.14
	Barley flour	0.58, 0.64, 0.27, 0.50	0.50
Wheat	Coarse bran	4.5, 6.0, 3.0	4.5
	Fine bran	1.0, 1.0, <1.0	<1.0
	White flour (550)	2.0, 3.0, <1.0	<2.0
	Wholemeal flour	1.5, 2.0, <1.0	<1.5
	Wholemeal bread	1.0, 1.0, <1.0	<1.0
	Wheat germs	1.0, 3.0, <1.0	<1.7
	Dried starch	<0.5, <1.0, <1.0	<0.8
	Dried gluten	<0.5, <1.0, <1.0	<0.8
	Gluten feed meal	<0.5, <1.0, <1.0	<0.8

*Residues of R182281 in washed tomatoes not analysed

CA 6.6 Residues in Rotational Crops

CA 6.6.1 Metabolism in rotational crops

A confined rotational crop study was conducted using [phenyl-U-^{14}C]-chlorothalonil to address the potential uptake and metabolism of chlorothalonil residues into succeeding or rotated crops following an application to the primary crop.

The study was evaluated under Council Directive 91/414/EEC and is presented in the chlorothalonil monograph (**Vol.3, Annex B, Section B.7.9.1, January 2000**).

Confined/Outdoor	Author/s	Issue Year	Report Number
Confined	Nelson TR	1995	608-4EF-82-0169-001

At 30 and 80 days after soil treatment [phenyl-U-^{14}C]-chlorothalonil, the major soil residue was R611965 (almost 25% of the total soil residues), followed by the parent compound accounting for 11 and 5% of the total residue at the respective treatment days. R611965 was the major residue identified in rotational crop samples. R182281 was present at low levels. Parent compound was not detected in crop samples.

Additional confined crop rotation studies have also been conducted. These studies were not available during the first EU evaluation of chlorothalonil and full summaries are presented here.

Report:	K-CA 6.6.1/01. Rizzo F. and Ferrario F. (2005), Uptake, translocation and metabolism of 14C-Chlorthalonil in rotated crops of spring wheat, carrots and lettuce. Study number MEF.03.03. Syngenta File No. R044686_11201.

Guidelines

None

GLP

The study was carried out according to the principles of Good Laboratory Practice.

EXECUTIVE SUMMARY

A confined rotational crop metabolism study was conducted to provide information on the magnitude and nature of residues of chlorothalonil in following crops. [Phenyl-U-^{14}C]-chlorothalonil in acetonitrile/water was applied drop-wise at 7.5 kg a.s/ha to separate containers of soil prior to sowing. At each rotational interval of 30, 120 and 365 days after application (DAT), a representative cereal (spring wheat), leafy vegetable (lettuce) and root vegetable (carrot) were sown into the soil. All crops were grown under field conditions and harvested at maturity. Harvested crops were separated into commodities of representative food and feed items (wheat forage, straw and grain; mature lettuce; carrot foliage and roots). The total radioactive residue concentration (TRR, mg a.s. equivalents per kg of commodity, mg/kg) was quantified and characterised

Radioactivity was measured by combustion and LSC. Samples were extracted using various solvents. Sample extracts were analysed by normal and reverse-phase TLC, using two solvent systems for each stationary phase. Selected aqueous phases were submitted to enzymatic (β-glucosidase), hydrolysis. Post-extraction solids were refluxed successively with water, alkali (NaOH) and acid (HCl). Metabolite identification was performed using co-chromatography with certified reference compounds.

The TRR (mg/kg chlorothalonil equivalents) by combustion analysis in all rotational commodities were ≥0.05 mg/kg. The highest TRR were observed in 30 DAT mature lettuces (0.241 mg/kg), 120 DAT carrot leaves (1.516 mg/kg), carrot roots (0.431 mg/kg) and wheat straw (25.12 mg/kg), and 365 DAT wheat forage (1.407 mg/kg) and wheat grain (2.23 mg/kg). In general, TRR tended to remain at similar levels across all plant-back intervals. The majority of the radioactive residues were extractable, accounting for 65 to 95% TRR.

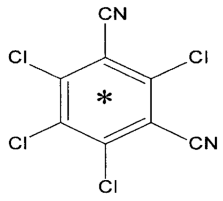
In all crops the majority of the radioactive residue was assigned to the metabolites R611965 and R417888. Up to 30% TRR in was assigned as conjugated as conjugated material. Enzyme hydrolysis this extract released radioactivity indicating that the conjugated material was made up of glucosyl conjugates of R611968, R613636 and “compound C15”. Other identified metabolites identified, including R611553, R182281 and R612636, represented minor percentages of the TRR. R611968 accounted for up to 10% TRR in grain.

The post-extraction solids (PES) were 8.9 - 23% TRR in carrot root, 21.4 – 32.7% TRR in carrot leaves and 22.4% TRR in lettuce. Post extraction solids for cereal samples were 7.8 – 10.5% TRR and 4.6 – 15.7% TRR for grain and straw, respectively. A large proportion of this radioactivity was released by aqueous reflux (ranging between 3.62 and 24.67% of TRR), with further radioactivity incorporated into the sodium hydroxide reflux fraction representing cellulose incorporation (ranging between 0.45 and 3.96% TRR) and into the acid reflux fraction, representing lignin incorporation (0.49 to 2.69% TRR).

I. MATERIALS AND METHODS

A. MATERIALS

A1. Test Materials

Structure/Label	[Phenyl-U-^{14}C]-chlorothalonil	
	 (* = ^{14}C position)	
Common name	Chlorothalonil	
Syngenta code	-	
CAS Number	1897-45-6	
Batch number	Lot #218	Lot #220
Specific Activity	2.087 MBq/mg 56.4122 µCi/mg 125235 dpm/µg	5.162 MBq/mg 139.5261 µCi/mg 309748 dpm/µg
Radiochemical Purity	>99%	>99%

A2. Test System

The crops used were:

Carrot (*Daucus carota*), variety Mezzalunga Nantese 3.

Lettuce (*Lactuca sativa*), variety Kagraner Sommer 2.

Spring Wheat (*Triticum spp.)*, variety Pandas.

A3. Test Soil

Soil texture	Sandy loam
Soil composition	51.75% sand, 68.50% silt, 4.25% clay
pH	6.41
Organic carbon	0.90%
Cation exchange capacity	12.65 meq/100 g

A4. Test Facilities

The study was performed at Isagro Ricerca Srl, Environmental Chemistry Department, Metabolism and Environmental Fate, Unit 1, Via Fauser 4, Novara, Italy.

B. STUDY DESIGN AND METHODS

B1. Field Phase

22 pots were filled with sandy loam soil and treated with a 2g/L solution of a mixture of ^{14}C-labelled and non- labelled chlorothalonil in acetonitrile/water (30/70 v/v) at an equivalent rate of 7.5 kg a.s./ha by drop-wise addition to the soil. Groups of 4 pots were aged for 30, 120 and 365 days after which crops of carrot, lettuce and spring wheat were sown. The crops were grown outdoors in accordance with usual agricultural practice and irrigated as necessary.

Test Samples

Samples of crops at harvest maturity were taken for each plant-back interval. Carrots were separated into tops (leaves) and roots after excess soil was removed. The roots were washed gently with water and the washing returned to the growing pots. Lettuce samples were cut and rinsed gently, with the washing returned to the growing pots. Immature and mature wheat samples were cut close to the soil surface. Mature wheat was separated into straw and grain. Duplicate soil cores (5 cm wide and 25 cm deep) were taken at treatment, at planting and at harvest for each plant-back interval.

All samples were stored frozen (approximately -20°C) until analysis.

B2. Analytical Phase

Homogenised samples were combusted and the total radioactive residue (TRR) was determined by liquid scintillation counting (LSC).

An aliquot of the homogenised plant material was extracted with acetone/water (50/50, v/v) using an Ultraturrax Homogenizer and concentrated to remove the acetone. The extracts were then partitioned with hexane or ethyl acetate. Selected aqueous phases were submitted to enzymatic (β-glucosidase) hydrolysis.

The remaining solids were further extracted with acetone by shaking, followed by centrifugation. After drying, the solids were refluxed successively with water, followed by 5% sodium hydroxide solution and then 6N hydrochloric acid to release any bound radioactivity.

The un-extracted residues (post-extraction solids, PES) were determined by combustion and LSC. Sample extracts were analysed by normal and reverse-phase TLC, using two solvent systems for each stationary phase, and metabolites identified by co-chromatography against reference standards.

Soil samples were extracted by shaking with successive aliquots of acetone / water (50/50 v/v) then acetone/ 0.1N HCl (50/50 v/v) followed by filtration. The extracts were concentrated to remove the acetone. Un-extracted residues were determined by combustion and LSC.

II. RESULTS AND DISCUSSION

Distribution of residues

All residue values quoted in this section are expressed as mg chlorothalonil equivalents/kg.

The TRR and extractability of residues in following crops are summarised in Table 6.6.1-1 and Table 6.6.1-2.

The highest TRR were observed in 30 DAT mature lettuces (0.24 mg/kg), 120 DAT carrot leaves (1.5 mg/kg), carrot roots (0.43 mg/kg) and wheat straw (25 mg/kg) and 365 DAT wheat forage (1.4 mg/kg) and wheat grain (2.2 mg/kg). In general, TRR tended to remain at similar levels across all plant-back intervals.

The majority of the radioactive residues were extractable, accounting for 65 to 95% TRR. For all plant-back intervals the majority of the extractable residue was partitioned into the aqueous phase with the exception of wheat grain where the majority of extractable radioactivity was associated with the organic ethyl acetate phase (50%, 65% and 73% TRR associated with ethyl acetate for the 30, 120 and 365 day plant-back intervals, respectively).

The radioactivity in soil was quantified at treatment, at sowing and at harvest of each crop; total residues ranged from 0.68 to 6.9 mg/kg. TLC analysis of soil extracts showed that chlorothalonil was present only in the shorter soil ageing periods; levels decreased over time. Chlorothalonil was extensively metabolised in soil and at least eight known metabolites were identified.

Table 6.6.1-1: Summary of total radioactive residues by combustion in rotational crop samples grown in soil treated with [Phenyl-U-^{14}C]-chlorothalonil

Crop	Crop Commodity	mg/kg chlorothalonil equivalents Plant Back Interval		
		30 DAT	120 DAT	365 DAT
Lettuce	Mature	0.24	0.24	0.12
Carrot	Leaves	0.78	1.52	0.82
	Roots	0.28	0.43	0.18
Wheat	Forage	1.4	1.4	1.4
	Straw	23	25	29
	Grain	1.3	1.5	2.2

Table 6.6.1-2: Summary of total radioactive residues and extractability in rotational crop samples grown in soil treated with [Phenyl-U-^{14}C]-chlorothalonil

Crop	Days after Treatment	Crop Commodity	Extractable Radioactivity		Non-extractable Radioactivity		TRR
			%TRR	mg/kg	%TRR	mg/kg	mg/kg
Lettuce	30	Mature	73	0.18	22	0.05	0.24
	120	Mature	92	0.22	8.7	0.02	0.24
	365	Mature	85	0.10	16	0.02	0.12
Carrot	30	Root	90	0.28	8.9	0.03	0.28
		Leaves	75	0.59	21	0.17	0.78
	120	Root	91	0.44	11	0.05	0.43
		Leaves	65	0.99	33	0.50	1.5
	365	Root	78	0.18	23	0.04	0.18
		Leaves	72	0.59	28	0.23	0.82
Wheat	30	Forage	89	1.2	14	0.19	1.4
		Straw	86	20	12	2.7	23
		Grain	90	1.2	10	0.13	1.3
	120	Forage	88	1.2	14	0.20	1.4
		Straw	85	21	16	3.9	25
		Grain	90	1.7	9.3	0.14	1.5
	365	Forage	95	1.3	8.7	0.12	1.4
		Straw	95	23	4.6	1.1	28
		Grain	91	2.03	7.8	0.17	2.23

Characterisation of residues

Tables 6.6.1-3 – 6.6.1-8 summarise the results of the characterisation of residues and metabolite levels found.

Chlorothalonil was not detected in any of the plant samples (limit of detection 0.02 mg/kg).

In carrot roots the majority of the radioactive residue was assigned to the metabolites R611965 and R417888, accounting for 59%, 66% and 51% TRR for the 30, 120 and 265 plant-back intervals, respectively. These metabolites co-eluted on the TLC systems used, however further TLC analysis of the sample extract from the 30 day plant-back interval indicated that the majority of the residue was due to metabolite R611965 (51% TRR, 0.14 mg/kg). 24 - 31% TRR was assigned as conjugated material. Enzyme hydrolysis of this extract released radioactivity indicating that the conjugated material was made up of glucosyl conjugates of R611968, R612636 and “compound C15” (11%, 13% and 6.4% TRR, respectively, for the 30 day plant-back interval).

The metabolic profile for carrot leaves and lettuce was similar, with the majority of the radioactive residue assigned to metabolites R611965, R417888 and to conjugated material. Other metabolites identified at lower levels included R611553 (1.1 – 3.3% TRR), R182281 (0.41 – 1.7% TRR), R611968 (0.41-1.8% TRR), and R612636 (0.66 -5.0% TRR). These metabolites were identified for all plant-back intervals.

Table 6.6.1-3: Summary of identification and characterisation of residues in mature carrot roots grown in soil treated with [pheny-U-^{14}C]-chlorothalonil

	30 DAT plant-back		120 DAT plant-back		365 DAT plant-back	
TRR (mg/kg)	0.28		0.43		0.18	
Component	%TRR	mg/kg	%TRR	mg/kg	%TRR	mg/kg
Chlorothalonil	N/D	N/D	N/D	N/D	N/D	N/D
R611965 + R417888	59	0.16	66	0.29	51	0.09
R611968	N/D	N/D	N/D	N/D	N/D	N/D
Compound C15	N/D	N/D	N/D	N/D	N/D	N/D
R182281	0.71	0.002	0.93	0.004	0.56	0.001
R611533	N/D	N/D	N/D	N/D	N/D	N/D
Compound VIS02	N/D	N/D	N/D	N/D	1.69	0.003
R612636	N/D	N/D	N/D	N/D	N/D	N/D
Conjugates	31	0.09	24	0.10	25	0.04
Total identified	90	0.25	91	0.39	78	0.14
Non-extractable	8.9	0.03	11	0.05	23	0.04

The figures in the table are the total radioactive residue for each metabolite reported expressed as mg/kg chlorothalonil equivalents.
N/D Not detected

Table 6.6.1-4: Summary of identification and characterisation of residues in mature carrot leaves grown in soil treated with [^{14}C]-chlorothalonil

	30 DAT plant-back		120 DAT plant-back		365 DAT plant-back	
TRR (mg/kg)	0.78		1.5		0.82	
Component	%TRR	mg/kg	%TRR	mg/kg	%TRR	mg/kg
Chlorothalonil	N/D	N/D	N/D	N/D	N/D	N/D
R611965 + R417888	41	0.32	35	0.52	30	0.25
R611968	1.5	0.01	1.8	0.03	1.2	0.01
Compound C15	N/D	N/D	N/D	N/D	N/D	N/D
R182281	0.90	0.007	0.92	0.01	0.98	0.008
R611533	2.2	0.02	1.4	0.02	1.1	0.009
Compound VIS02	0.38	0.003	0.20	0.003	1.6	0.01
R612636	0.77	0.006	0.66	0.01	1.4	0.01
Conjugates	29	0.22	26	0.39	36	0.30
Total identified	75	0.59	66	0.99	73	0.59
Non-extractable	21	0.17	33	0.50	28	0.23

The figures in the table are the total radioactive residue for each metabolite reported expressed as mg/kg chlorothalonil equivalents.
N/D Not detected

Table 6.6.1-5: Summary of identification and characterisation of residues in mature lettuce grown in soil treated with [^{14}C]-chlorothalonil

	30 DAT plant-back		120 DAT plant-back		365 DAT plant-back	
TRR (mg/kg)	0.24		0.24		0.12	
Component	%TRR	mg/kg	%TRR	mg/kg	%TRR	mg/kg
Chlorothalonil	N/D	N/D	N/D	N/D	N/D	N/D
R611965 + R417888	34	0.08	44	0.11	39	0.05
R611968	0.41	0.001	1.2	0.003	1.7	0.002
Compound C15	0.83	0.002	0.83	0.002	0.83	0.001
R182281	0.41	0.001	1.2	0.003	--	--
R611533	3.3	0.008	3.3	0.008	2.5	0.003
Compound VIS02	2.5	0.006	1.7	0.004	6.6	0.008
R612636	4.2	0.010	5.4	0.01	5.0	0.006
Conjugates	25	0.06	32	0.08	30	0.04
Unknown[1]	3.7	0.009	2.9	0.007	--	--
Total identified	73	0.18	92	0.22	85	0.10
Non-extractable	22	0.05	8.7	0.02	16	0.02

The figures in the table are the total radioactive residue for each metabolite reported expressed as mg/kg chlorothalonil equivalents.
N/D Not detected.
[1] Unassigned radiocomponents which chromatographed away from the origin using 2D-TLC.

In wheat forage, straw and grain the metabolite profile was similar for all three crop parts over the three plant-back intervals. The majority of the radioactive residue was assigned to metabolites R611965 and R417888 with further TLC analysis of the sample extracts from the 30 day plant-back interval indicating that the majority of the residue was due to metabolite R611965 (68% TRR, 0.87 mg/kg for grain and 26% TRR, 5.8 mg/kg for straw). Other identified metabolites represented minor percentages, including R182881 (1.2-1.5% TRR in forage, 0.84 – 7.7 % in straw and not found in grain) and R611968 (1.7-2.5% TRR in forage, 0.68-4.0 %TRR in straw and 4.3-9.8% TRR in grain). 11 - 41% TRR was assigned as conjugated material. Enzyme hydrolysis of this extract released radioactivity indicating that, as for carrot roots the conjugated material was made up of glucosyl conjugates of R611968, R613636 and "compound C15"

Table 6.6.1-6: Summary of identification and characterisation of residues in wheat forage grown in soil treated with [^{14}C]-chlorothalonil

	30 DAT plant-back		120 DAT plant-back		365 DAT plant-back	
TRR (mg/kg)	1.4		1.4		1.4	
Component	%TRR	mg/kg	%TRR	mg/kg	%TRR	mg/kg
Chlorothalonil	N/D	N/D	N/D	N/D	N/D	N/D
R611965 + R417888	61	0.84	62	0.87	67	0.94
R611968	2.2	0.03	1.7	0.02	2.5	0.04
Compound C15	1.2	0.02	0.85	0.01	1.2	0.02
R182281	1.4	0.02	1.2	0.02	1.5	0.02
R611533	N/D	N/D	N/D	N/D	N/D	N/D
Compound VIS02	N/D	N/D	N/D	N/D	N/D	N/D
R612636	N/D	N/D	N/D	N/D	N/D	N/D
Conjugates	23	0.31	22	0.31	23	0.33
Total identified	89	1.2	88	1.2	95	1.3
Non-extractable	14	0.19	14	0.20	8.	0.12

The figures in the table are the total radioactive residue for each metabolite reported expressed as mg/kg chlorothalonil equivalents.
N/D Not detected

Table 6.6.1-7: Summary of identification and characterisation of residues in wheat straw grown in soil treated with [^{14}C]-chlorothalonil

	30 DAT plant-back		120 DAT plant-back		365 DAT plant-back	
TRR (mg/kg)	23		25		24	
Component	%TRR	mg/kg	%TRR	mg/kg	%TRR	mg/kg
Chlorothalonil	N/D	N/D	N/D	N/D	N/D	N/D
R611965 + R417888	49	11	50	12	49	12
R611968	0.68	0.16	1.1	0.28	4.0	0.96
Compound C15	0.80	0.18	0.79	0.19	--	--
R182281	7.7	1.8	4.7	1.2	0.84	0.20
R611533	N/D	N/D	1.1	0.28	0.94	0.22
Compound VIS02	N/D	N/D	N/D	N/D	0.42	0.10
R612636	0.93	0.21	1.5	0.37	N/D	N/D
Conjugates	27	6.2	26	6.6	40	9.5
Total identified	86	20	86	21	95	23
Non-extractable	12	2.7	16	3.9	4.6	1.1

The figures in the table are the total radioactive residue for each metabolite reported expressed as mg/kg chlorothalonil equivalents.
N/D Not detected

Table 6.6.1-8: Summary of Identification and Characterisation of Residues in Wheat Grain Grown in Soil Treated with [^{14}C]-chlorothalonil

	30 DAT plant-back		120 DAT plant-back		365 DAT plant-back	
TRR (mg/kg)	1.3		1.5		2.2	
Component	%TRR	mg/kg	%TRR	mg/kg	%TRR	mg/kg
Chlorothalonil	N/D	N/D	N/D	N/D	N/D	N/D
R611965 + R417888	71	0.91	73	1.1	40	0.89
R611968	4.3	0.06	6.0	0.09	9.8	0.22
Compound C15	2.9	0.04	N/D	N/D	N/D	N/D
R182281	N/D	N/D	N/D	N/D	N/D	N/D
R611533	N/D	N/D	N/D	N/D	N/D	N/D
Compound VIS02	N/D	N/D	N/D	N/D	N/D	N/D
R612636	N/D	N/D	N/D	N/D	N/D	N/D
Conjugates	12	0.15	11	0.17	41	0.92
Total identified	90	1.2	90	1.4	91	2.0
Non-extractable	10	0.13	9.3	0.14	7.8	0.17

The figures in the table are the total radioactive residue for each metabolite reported expressed as mg/kg chlorothalonil equivalents.
N/D Not detected

The post-extraction solids (PES) residues ranged from 0.03 to 0.05 mg/kg (8.9 - 23% TRR) in carrot root, 0.17 to 0.50 mg/kg (21 – 33% TRR) in carrot leaves and 0.02 to 0.05 mg/kg (8.7 – 22% TRR) in lettuce. Post extraction solids for cereal samples ranged from 0.13 – 0.17 mg/kg (7.8 – 10% TRR) and 1.1 – 3.9 mg/kg (4.6 – 16% TRR) for grain and straw, respectively. Considerable amounts of this radioactivity were released by aqueous reflux (ranging between 3.6 and 25% of TRR); with further radioactivity incorporated into the sodium hydroxide reflux fraction representing cellulose incorporation (ranging between 0.45 and 4.0% TRR) and into the acid reflux fraction, representing lignin incorporation (0.49 to 2.7% TRR).

Proposed metabolic pathway for chlorothalonil in following crops

The proposed metabolic pathway for chlorothalonil in following crops is given in Figure 6.6.1-1.

III. CONCLUSIONS

Following application of [phenyl-U-^{14}C]-chlorothalonil to bare soil at 7.5 kg a.s/ha, lettuce, carrot, and wheat were sown in the treated soil after periods of 30, 120 and 365 days. Samples of mature lettuce, carrot root and leaves and wheat forage, straw and grain were taken after each ageing period.

The highest total radioactive residues (TRR, mg/kg chlorothalonil equivalents), were observed in 30 DAT mature lettuces (0.24 mg/kg), 120 DAT carrot leaves (1.5 mg/kg), carrot roots (0.43 mg/kg) and wheat straw (25 mg/kg), and 365 DAT wheat forage (1.4 mg/kg) and wheat grain (2.2 mg/kg). The majority of the radioactive residues were extractable, accounting for 65 to 95% TRR.

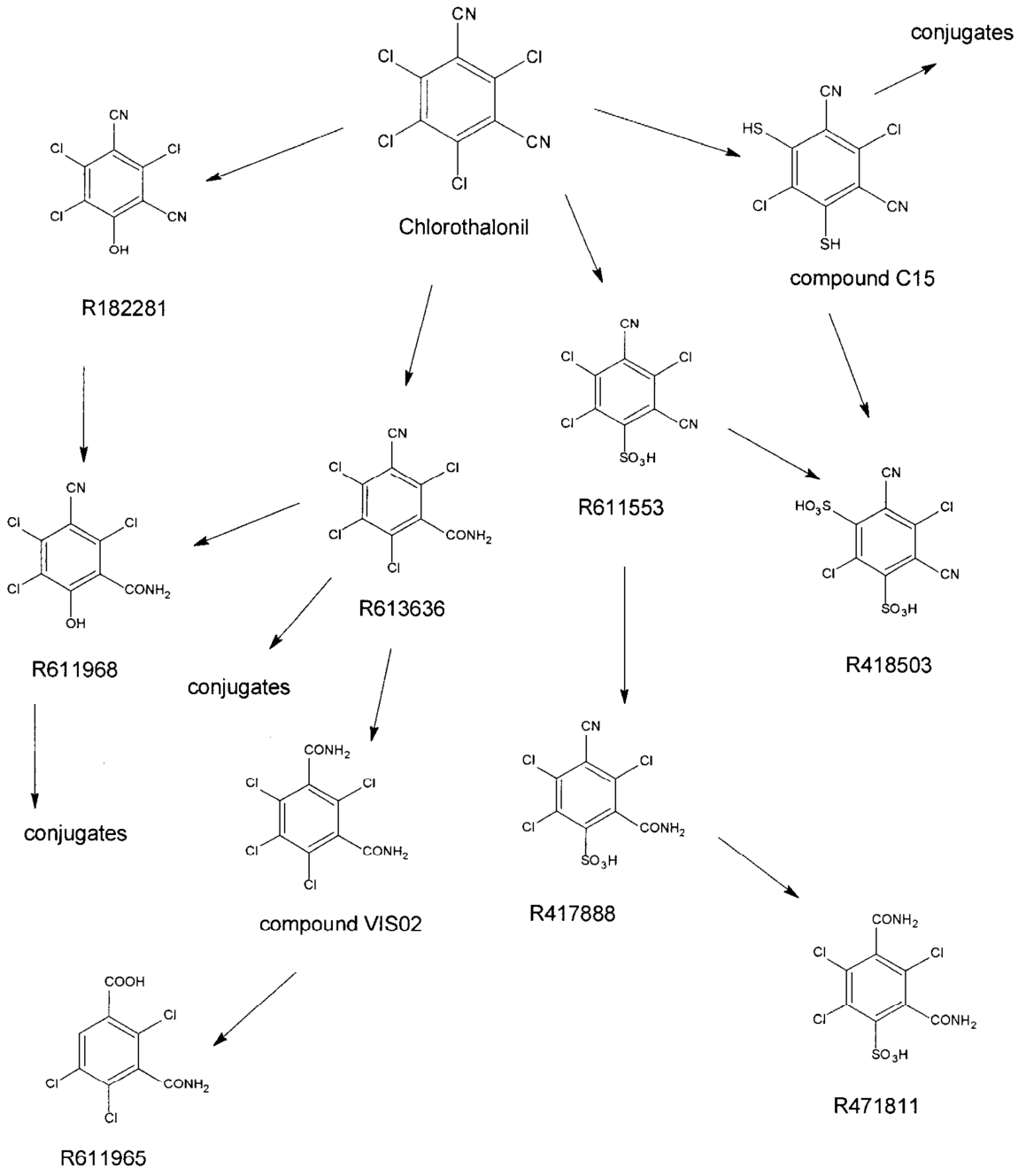
The results show that:

- In general, TRR remained at similar levels across all plant-back intervals.
- Levels of residues in crops grown in soil treated with chlorothalonil were ≥0.05 mg/kg for all plant-back intervals.
- Parent chlorothalonil is a minor residue (not detected) in rotational crops.
- R611965 and R417888 were significant metabolites in all crops. These metabolites are known soil metabolites with long DT_{50} values.
- Levels of R182281 were low (<5%TRR) in carrots, lettuce and wheat forage, and were not detected in wheat grain. Levels in wheat straw decreased from a maximum of 7% TRR with longer plant-back intervals.

Chlorothalonil is metabolised in soil initially to R613636 and R182281 and then to other multiple components which are available for uptake by crops. The metabolism in following crops is similar to that in primary crops.

(Rizzo F, Ferrario F, 2005)

Figure 6.6.1-1: Proposed metabolic pathway for chlorothalonil in following crops



Report:	K-CA 6.6.1/02. Mamouni A. (2009), ^{14}C-Chlorothalonil – Confined accumulation in rotational crops, Harlan Laboratories Ltd. Report number B34931. Syngenta File No. R044686_11194.

Guidelines

The study was performed according to the EU Commission Working Document 7524/VI/95 rev. 2: Appendix C - Testing of Plant Protection Products in Rotational Crops and under consideration of OPPTS Guideline 860.1850

GLP

The study was carried out according to the principles of Good Laboratory Practice.

EXECUTIVE SUMMARY

[Phenyl-U-^{14}C]-chlorothalonil formulated as a SC was applied as a single spray application at 1kg a.s./ha to separate containers of soil. The soil was aged for 30 days and representative crops of cereals (barley), leafy vegetable (spinach) and root vegetable (radish) were sown into the soil and grown under field conditions. Samples were taken soon after emergence and at immature and mature growth stages. Harvested crops were separated into commodities of representative food and feed items (barley forage, straw and grain; spinach leaves; radish leaves and roots). Samples were homogenised and the total radioactive residue concentration (TRR, mg chlorothalonil equivalents per kg of commodity, mg/kg) was measured in each commodity. Commodities were extracted with acetonitrile: water and the extracts analysed by HPLC and TLC to determine the nature of the residues.

In spinach leaves, the total radioactive residues (TRR) were 0.067, 0.031 and 0.039 mg/kg for the immature (emergence), immature (pre-harvest) and mature crop samples, respectively. The corresponding values for radish leaves were 0.014, 0.019 and 0.026 mg/kg. For radish roots, the TRR values were 0.022, 0.019 and 0.021 mg/kg. In barley forage, the TRR for immature (emergence) and forage (immature plant) samples were 0.018 and 0.019 mg/kg, respectively. The barley harvested at maturity was separated into three parts straw, chaff and grains. The residues in these samples were 0.120, 0.059 and 0.012 mg/kg respectively.

The majority of the radioactive residues were extractable, accounting for 50 to 73% TRR. Due to the very low level of residues in the plant parts remaining after extraction, no additional hydrolysis of the non-extractable residues was performed.

Parent chlorothalonil was detected only in the radish root samples, and at very low levels (0.001 mg/kg).

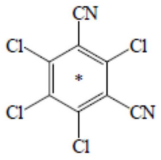
The major identified metabolite was R611965, which represented 13% TRR (0.009 mg/kg), 19% TRR (0.006 mg/kg) and 14% TRR (0.006 mg/kg) in immature (emergence), immature (pre-harvest) and mature spinach respectively. R611965 was detected in all barley samples with the highest level found in mature straw, representing 25% TRR (0.030 mg/kg). In the radish root R61195 accounted for 11.5% TRR (0.003 mg/kg) and 8.3% TRR (0.002 mg/kg) in the immature (emergence) roots and at maturity, respectively. The metabolite R182281 was also identified in all spinach and radish root samples, and the mature barley samples, however at levels less than 0.01 mg/kg.

The remaining radioactive fractions corresponded mainly to conjugates and did not exceed 10% TRR, 0.01 mg/kg for edible plant material (human food) or 0.05 mg/kg for animal feed items.

I. MATERIALS AND METHODS

A. MATERIALS

A1 Test Materials

Structure/Label	[Phenyl-U-^{14}C]-Chlorothalonil
	 (* = ^{14}C position)
CAS Number	1897-45-6
Batch Number	6BLY041 and 8BLY035
Specific Activity	8.49 MBq/mg and 6.96 MBq/mg
Radiochemical Purity	>98 %

A2. Test System

The crops selected to represent the three different groupings (leafy, cereal and root) were spinach (variety Butterblatt), radish (variety Cherry Belle) and barley (variety Mandolin/CEBADA), respectively. These crops and were grown from commercially available seed, outdoors under conditions representative of those used for commercial production.

A3. Test Soil

Soil texture	Silty clay
Soil composition	10% sand, 44.7% silt, 45.3% clay
pH	7.33
Organic carbon	3.15%
Cation exchange capacity	13.3 meq/100 g

B. STUDY DESIGN AND METHODS

B1. Field Phase

Nominal application rate	1kg a.s/ ha
Number of applications	1
Target seasonal application rate	1kg a.s./ ha
Achieved seasonal application rate	99.5%
Formulation type	Suspension concentrate (SC)
Formulation code	209583/A
Spray rate	12 mL/plant pot (equivalent to51 mL/1m^2)
Method of application	manual sprayer
Plant-back intervals	30 days after application

Test Samples

The following crop samples were taken:

Emergence spinach leaves, 20 days after sowing
Pre-harvest spinach leaves, 29 days after sowing
Mature spinach leaves, 40 days after sowing

Emergence radish leaves and roots, 20 days after sowing
Pre-harvest radish leaves and roots, 29 days after sowing
Mature radish leaves and roots, 40 days after sowing

Emergence barley forage, 20 days after sowing
Pre-harvest barley forage, 29 days after sowing
Mature barley, straw, chaff and grain, 111 days after sowing

Sample Preparation

Plant tissue and soil samples were frozen and then milled to form a powder. Total radioactivity was determined by combustion followed by LSC.

B2. Analytical Phase

The following procedure was used for the extraction of all samples except radish leaves which were not extracted. Samples were extracted up to 3 times with acetonitrile: water (1:1, v: v) on a shaker for 30 minutes. The samples were centrifuged to remove the solids after each extraction. Extracts were pooled and concentrated for analysis. The PES were allowed to dry, and then analysed by combustion LSC.

Identification of the radioactive components in the sample extracts was carried out by 2 dimensional TLC with phosphor imaging and HPLC-UV using co-chromatography with reference standards.

II. RESULTS AND DISCUSSION

Total Radioactive Residues and Extractability

Total radioactive residues are summarised in Table 6.6.1-9 and the extractability for all commodities are summarised in Table 6.6.1-10.

Significant TRR were observed in all samples with the lowest TRR in mature grain (0.012 mg/kg) and the highest TRR in mature straw samples (0.120 mg/kg). The majority of the radioactive residues were extractable, accounting for 50 to 73% TRR.

Chlorothalonil was detected only in the radish root samples, and at very low levels (0.001 mg/kg).

The major identified metabolite in all crops was R611965 with residues ranging from 8.3% TRR (0.002 mg/kg, mature radish roots) to 25% TRR (0.030 mg/kg, mature straw samples). R182281 was identified in spinach, radish root and mature barley samples, however at levels less than 0.01 mg/kg.

Table 6.6.1-9: Summary of total radioactive residues by combustion in rotational crop samples grown in soil treated with [phenyl-U-^{14}C]-chlorothalonil and aged for 30 days

Crop	Days after treatment	Crop Commodity	mg/kg Chlorothalonil Equivalents
Spinach	50	Immature leaves (emergence)	0.067
	59	Immature leaves (pre-harvest)	0.031
	70	Mature leaves	0.039
Radish	50	Immature roots (emergence)	0.022
	59	Immature roots (pre-harvest)	0.019
	70	Mature roots	0.021
	50	Immature leaves (emergence)	0.014
	59	Immature leaves (pre-harvest)	0.019
	70	Mature leaves	0.026
Wheat	50	Forage (emergence)	0.018
	59	Immature plant forage (pre-harvest)	0.019
	141	Mature straw	0.120
	141	Mature chaff	0.059
	141	Mature grain	0.012

Table 6.6.1-10: Summary of total radioactive residues and extractability in rotational crop samples grown in soil treated with [phenyl-U-^{14}C]-chlorothalonil and aged for 30 days

Crop	Days after treatment	Crop Commodity	Extractable Radioactivity		Non-extractable Radioactivity		TRR
			%TRR	mg/kg	%TRR	mg/kg	mg/kg
Spinach	50	Immature leaves (emergence)	66.4	0.045	33.6	0.023	0.067
	59	Immature leaves (pre-harvest)	69.4	0.021	30.6	0.009	0.031
	70	Mature leaves	65.2	0.027	34.8	0.014	0.041
Radish	50	Immature roots (emergence)	49.6	0.011	50.4	0.011	0.022
	59	Immature roots (pre-harvest)	63.5	0.012	36.5	0.007	0.019
	70	Mature roots	50.6	0.011	49.4	0.011	0.022
Wheat	50	Forage (emergence)	56.0	0.010	44.0	0.008	0.018
	59	Immature plant forage (pre-harvest)	52.9	0.010	47.1	0.009	0.019
	141	Mature straw	67.4	0.081	32.6	0.039	0.120
	141	Mature chaff	73.4	0.043	26.6	0.016	0.059
	141	Mature grain	50.3	0.006	49.7	0.006	0.012

Characterisation and Identification of Residues

The extracts were analysed as summarised in the previous section. The identified components for each commodity are summarised in Tables 6.6.1-11 to 6.6.1-13.

Table 6.6.1-11: Summary of identification and characterisation of residues in spinach grown in soil treated with [phenyl-U-^{14}C]-chlorothalonil and aged for 30 days

	Immature leaves (emergence)		Immature leaves (pre-harvest)		Mature leaves	
TRR mg/kg	0.067		0.031		0.041	
Component	%TRR	mg/kg	%TRR	mg/kg	%TRR	mg/kg
Chlorothalonil	N/D	N/D	N/D	N/D	N/D	N/D
R611965	13.3	0.009	18.7	0.006	13.5	0.006
R182281	13.9	0.009	12.1	0.004	11.4	0.005
M3	6.2	0.004	2.7	0.001	1.6	0.001
M4	N/D	N/D	N/D	N/D	1.7	0.001
M5	N/D	N/D	N/D	N/D	3.6	0.001
M6	N/D	N/D	N/D	N/D	1.8	0.001
M7	N/D	N/D	N/D	N/D	1.7	0.001
M8	N/D	N/D	N/D	N/D	1.3	0.001
M9	N/D	N/D	N/D	N/D	1.7	0.001
M10	N/D	N/D	N/D	N/D	4.0	0.002
M11	N/D	N/D	N/D	N/D	3.3	0.001
M12	9.3	0.006	10.0	0.003	1.9	0.001
M13	N/D	N/D	9.0	0.003	4.5	0.002
M14	8.0	0.005	6.0	0.002	1.9	0.001
M15	6.4	0.004	3.7	0.001	4.2	0.002
M16	9.3	0.006	7.1	0.002	7.1	0.003
Total identified	66.4	0.044	69.3	0.021	65.2	0.025
Un-extracted	33.6	0.023	30.6	0.009	34.8	0.014

N/D not detected

Table 6.6.1-12: Summary of identification and characterisation of residues in radish roots grown in soil treated with [phenyl-U-^{14}C]-chlorothalonil and aged for 30 days

	Immature roots (emergence)		Immature roots (pre-harvest)		Mature roots	
TRR mg/kg	0.022		0.019		0.021	
Component	%TRR	mg/kg	%TRR	mg/kg	%TRR	mg/kg
Chlorothalonil	4.1	0.001	N/R	N/R	3.4	0.001
R611965	11.5	0.003			8.3	0.002
R182281	22.0	0.005			36.0	0.008
M3	N/D	N/D			N/D	N/D
M10	4.6	0.001			2.0	<0.001
M11	5.0	0.001			0.8	<0.001
M12	2.3	0.001			N/D	N/D
Total identified	49.5	0.011			50.5	0.011
Un-extracted	50.4	0.011			49.4	0.010

N/D not detected

N/R Could not be separated

Table 6.6.1-13: Summary of identification and characterisation of residues in cereals grown in soil treated with [phenyl-U-^{14}C]-chlorothalonil and aged for 30 days

	Forage (emergence)		Immature plant forage (pre-harvest)		Mature straw		Mature chaff		Mature grain	
TRR mg/kg	0.018		0.019		0.120		0.059		0.012	
Component	%TRR	mg/kg	%TRR	mg/kg	%TRR	mg/kg	%TRR	mg/kg	%TRR	mg/kg
Chlorothalonil	N/D	N/D	N/D	N/D	N/D	N/D	N/D	N/D	N/D	N/D
R611965	56.0	0.010	52.9	0.010	24.8	0.03	22.2	0.013	31.8	0.004
R182281	N/D	N/D	N/D	N/D	5.5	0.007	2.3	0.001	18.5	0.002
M3	N/D	N/D	N/D	N/D	N/D	N/D	2.1	0.001	N/D	N/D
M8	N/D	N/D	N/D	N/D	N/D	N/D	1.7	0.001	N/D	N/D
M9	N/D	N/D	N/D	N/D	7.0	0.008	3.2	0.002	N/D	N/D
M10	N/D	N/D	N/D	N/D	7.3	0.009	5.9	0.003	N/D	N/D
M11	N/D	N/D	N/D	N/D	5.5	0.007	8.4	0.005	N/D	N/D
M12	N/D	N/D	N/D	N/D	5.2	0.006	2.1	0.001	N/D	N/D
M13	N/D	N/D	N/D	N/D	N/D	N/D	5.5	0.003	N/D	N/D
M14	N/D	N/D	N/D	N/D	N/D	N/D	1.3	0.001	N/D	N/D
M15	N/D	N/D	N/D	N/D	6.5	0.008	9.4	0.006	N/D	N/D
M16	N/D	N/D	N/D	N/D	5.5	0.007	5.0	0.003	N/D	N/D
M17	N/D	N/D	N/D	N/D	N/D	N/D	4.4	0.003	N/D	N/D
Total identified	56.0	0.01	52.9	0.010	67.3	0.081	73.2	0.043	50.3	0.006
Un-extracted	44.0	0.008	47.1	0.009	32.6	0.039	26.6	0.016	49.7	0.006

N/D not detected

III. CONCLUSIONS

In spinach leaves, the total radioactive residues (TRR) were 0.067, 0.031 and 0.039 mg/kg for the immature (emergence), immature (pre-harvest) and mature crop samples, respectively. The corresponding values for radish leaves were 0.014, 0.019 and 0.026 mg/kg. For radish roots, the TRR values were 0.022, 0.019 and 0.021 mg/kg. In barley forage, the TRR for immature (emergence) and forage (immature plant) samples were 0.018 and 0.019 mg/kg, respectively. The barley harvested at maturity was separated into three parts straw, chaff and grains. The residues in these samples were 0.120, 0.059 and 0.012 mg/kg respectively.

The majority of the radioactive residues were extractable, accounting for 50 to 73% TRR. Due to the very low level of residues in the plant parts remaining after extraction, no additional hydrolysis of the non-extractable residues was performed.

Parent chlorothalonil was detected only in the radish root samples, and at very low levels (0.001 mg/kg).

The major identified metabolite was R611965, which represented 13% TRR (0.009 mg/kg), 19% TRR (0.006 mg/kg) and 14% TRR (0.006 mg/kg) in immature (emergence), immature (pre-harvest) and mature spinach respectively. R611965 was detected in all barley samples with the highest level found in mature straw, representing 25% TRR (0.030 mg/kg). In the radish root R61195 accounted for 11.5% TRR (0.003 mg/kg) and 8.3% TRR (0.002 mg/kg) in the immature (emergence) roots and at maturity, respectively. The metabolite R182281 was also identified in all spinach and radish root samples, and the mature barley samples, however at levels less than 0.01 mg/kg.

The remaining radioactive fractions corresponded mainly to conjugates and did not exceed 10% TRR, 0.01 mg/kg for edible plant material (human food) or 0.05 mg/kg for animal feed items.

(Mamouni A, 2009)

CA 6.6.2 Magnitude of residues in rotational crops

Field studies were conducted in the USA to measure levels of chlorothalonil residues in succeeding or rotated crops following an application to the primary crop. The studies were evaluated under Council

Directive 91/414/EEC and are presented in the chlorothalonil monograph (**Vol.3, Annex B, Section B.7.9.2, January 2000**).

Confined/Outdoor	Author/s	Issue Year	Report Number
Field	Dillon KA and Ballee, DL	1984	535-3CR-81-0199-001-001
Field	Rose CA, Kenyon RG	1991	1401-86-0084-CR-019

Three plots at different sites in the USA were sprayed with 8 applications of chlorothalonil at a rate of 2.5 kg a.s./ha at 7-day intervals. Wheat, carrots, snap beans and spinach were planted 14, 30, 60 and 90 days and about 1 year after the last application. Soil samples were taken after treatment and at each planting and harvest. The crops were harvested at maturity and analysed for chlorothalonil and its metabolites.

Soil residues of chlorothalonil declined over time from 5.18 – 17.46 mg/kg on the day of the last application to <0.01 - 0.10 mg/kg at the final harvest across the three sites. Chlorothalonil degraded in soil to produce the soil metabolites R182281, R613636, R611965, SDS-47523/4 and SDS- 47525. No residues of chlorothalonil were detected in the any of the crop samples. Low levels of R182281 were found in samples across all plant-back intervals (< 0.05 mg/kg), with exception of one spinach sample (0.19 mg/kg for the 90 day plant-back interval) and one wheat straw sample (0.08 mg/kg for the 14 day plant-back interval). R611965 was the major compound identified in rotational crop samples. Significant levels of R611965 were found in crops for plant-back intervals up to 90 days. The highest levels of this metabolite ranged from 1.05 - 2.20 mg/kg in spinach, 0.19 – 1.00 mg/kg in snap beans, 0.10 – 0.59 mg/kg in carrot roots, 0.2 – 0.65 mg/kg in carrot tops, 0.17-0.68 mg/kg in wheat grain and 3.2-10 mg/kg in straw.

In a second study, various primary crops grown at test sites across the USA were treated with chlorothalonil at rates ranging from 3 applications at 1.7 kg a.s./ha to 8 applications at 2.6 kg a.s./ha). Following treatment, the primary crops were harvested at normal maturity and following crops representing leafy vegetables, root vegetables, bulb vegetables, oilseeds and legumes were planted. The crops were harvested at maturity and analysed for chlorothalonil and metabolites.

Following crops planted into areas previously treated with chlorothalonil formulations did not contain any residues of chlorothalonil above 0.03 mg/kg, except peanut vines at one site (0.22 mg/kg) , and pea fodder and bean hay at another site (0.06 and 0.09 mg/kg, respectively). R182281was found in one pea fodder sample only, at 0.07 mg/kg. R182281 levels were all at or below 0.04 mg/kg in all other samples. R611965 was the major metabolite detected in the rotational crops. In root and tuber vegetable crops residues of R611965 were < 0.03 – 0.64 mg/kg and <0.03 – 0.59 mg/kg for roots and tops, respectively. For leafy vegetables, residues were <0.03 – 0.80 mg/kg and for fruiting vegetables residues were <0.03 – 1.05 mg/kg. In cereals residues in grain were < 0.03 – 0.4 mg/kg, in forage 0.08 – 0.26 mg/kg and <0.03 – 3.0 in straw. Residues in oilseeds and dried pulses were all < 0.05 mg/kg for all sites and all plant-back intervals.

An additional field crop rotation study has also been conducted. This study was not available during the first EU evaluation of chlorothalonil and a full summary is presented here.

Report:	K-CA 6.6.2/01. Eversfield S, (2014) Chlorothalonil – Residue study on Rotational Crops in Germany and the United Kingdom in 2011 and 2012. Eurofins Agroscience Services Ltd, Report Number S11-00508. (Syngenta File No. A7867A_11262)

Guidelines

FAO Guidelines on Producing Pesticide Residues Data from Supervised Trials (Rome, 1990).

Commission of the European Communities, General Recommendations for the Design, Preparation and Realization of Residue Trials; (**SANCO 7029/V1/95 rev. 5 22/7/1997**)

OECD Test Guideline 504. Residues in Rotational Crops (limited Field Studies).

Commission of the European Communities, Testing of plant protection products in rotational crops: (**SANCO 7524/V1/95 rev. 2 22/7/1997**)

European Commission Guidance Document on Residue Analytical Method, SANCO/825/00 revision 8.1 (16 Nov 2010).

European Commission Guidance for Generating and Reporting Methods of Analysis in Support of Pre-registration Requirements for Annex II (Part A, Section 4) of Directive 91/414, SANCO/3029/99 revision 4 (11 Jul 2000).

GLP

The study was carried out according to the principles of Good Laboratory Practice.

EXECUTIVE SUMMARY

Two field trials were conducted during 2011 and 2012, one in Germany and one in the United Kingdom. Chlorothalonil was applied as A7867A, a suspension concentrate (SC) formulation containing 500 g chlorothalonil per litre to bare soil at a rate of 2000 g a.s./ha. At each rotational interval of 30, 60 and 365 days after application (DAT), a representative cereal (spring wheat or barley), leafy vegetable (spinach) and root vegetable (carrot) were sown into the soil. All crops were grown under field conditions and harvested at immature and mature growth stages. Commodities of representative food and feed items (cereal immature whole plant, mature straw and mature grain; immature and mature spinach; mature carrot foliage and roots) were samples at intervals after sowing and analysed for residues of chlorothalonil, R182281 and R611965. The LOQ was 0.01 mg/kg for all compounds.

At all plant-back intervals no residues of chlorothalonil or R182281 were found at or above the LOQ (0.01 mg/kg) in any of the treated samples.

Residues of R611965 were found in samples taken after the 30 and 60 day plant-back intervals (PBI). For spinach these ranged from 0.02 – 0.06 mg/kg at the 30 day PBI and from 0.01-0.03 mg/kg for the 60 day PBI. In cereals residues of R611965 in immature plant, grain and straw were in the range 0.08 – 0.16 mg/kg, 0.01 – 0.11 mg/kg and 0.09 – 0.29 mg/kg respectively for the 30 day PBI. Residues in cereals for the 60 day PBI were 0.11 mg/kg, 0.02 -0.09 mg/kg and 0.08-10.25 mg/kg in immature plant, grain and straw respectively. For carrots residues in roots were in the range <0.01 -0.01 mg/kg for the 30 day PBI and were < LOQ for the 60 day PBI. Residues in carrot leaves were in the range <0.01 – 0.04 mg/kg and <0.01 – 0.02 mg/kg for the 30 and 60 day PBIs respectively. No residues of R611965 were found at or above the LOQ in the any of the samples from the 365 day plant-back interval.

I. MATERIALS AND METHODS

A. MATERIALS

A1. Test Materials

Test Material	A7867A
Description	Suspension concentrate formulation containing chlorothalonil
Purity	495 g/L

Batch number	SAV0L00018
Stability of test compound	The test substance is assumed to be stable for the period of use in the study

A2. Test System

Trial site	01, Niedersachsen, Germany	02, Oxfordshire, UK
Soil	Loamy sand	Clay loam
Leafy vegetable	Spinach (variety: Tornado)	Spinach (variety: Renegade)
Cereal	Spring wheat (variety: Shasin)	Spring barley (variety: Doyen/Westminster)
Root vegetable	Carrot (variety: Laguna F1)	Carrot (variety: Napoli)

A3. Test Facilities

Field trials	Niedersachsen, Germany	Oxfordshire, UK
Analytical phase	Eurofins Agroscience Services Ltd., Slade Lane, Wilson, Melbourne, Derbyshire DE73 8AG, UK	

B. STUDY DESIGN AND METHODS

B1. Field Phase

Plots were treated with chlorothalonil formulated as a SC at a rate of 2000 g a.s./ha (actual rates were 1956-1988 g a.s./ha) in a spray volume of approximately 300 L/ha to bare soil. The soil was aged for 30, 60 and 365 days (trial 1) and 27, 60 and 365 days (trial 2) after which the plots were lightly cultivated before drilling of representative crops of carrot, spinach and spring wheat or barley. The crops were grown outdoors in accordance with usual agricultural practice.

Test Samples

Samples of spinach (immature plant and mature leaves), carrot (roots and tops with leaves) and spring wheat / spring barley (immature whole plant, grain and straw) were taken by hand (or with a combine harvester for mature grain and straw) and the samples were stored deep frozen at <-18 °C before analysis. Samples were stored for up to 901 days (30 months) before analysis.

B2. Analytical Phase

Samples were analysed for chlorothalonil and R182281 using method GRM005.01A, and for R611965 using method GRM005.06A. The LOQ was 0.01 mg/kg for all analytes in all commodities. Full method descriptions and validation data are presented in document M-CA Section 4, CA 4.1.2.

II. RESULTS AND DISCUSSION

Method Validation

Procedural recoveries were determined for each compound for each commodity. Individual and mean recoveries are summarised in Table 6.6.2-1.

Table 6.6.2-1: Summary of procedural recoveries for chlorothalonil, R182281 and R611965 in following crops

Commodity	Fortification level (mg/kg)	Chlorothalonil		R182281		R611965	
		Recovery (%)	Mean recovery (%)	Recovery (%)	Mean recovery (%)	Recovery (%)	Mean recovery (%)
Spinach leaves	0.01	84, 87, 84	85	103, 99, 93	98	95	-
	0.10	81, 84, 91	85	85, 83, 85	84	96	-
Cereal whole plant	0.01	97, 93	95	115, 102	109	77	-
	0.10	89, 99	94	100, 99	100	77	-
Cereal grain	0.01	91, 85	88	102, 105	104	97	-
	0.10	95, 90	93	84, 96	90	95	-
Cereal straw	0.01	92, 93	93	101, 99	100	70	-
	0.10	98, 97	98	85, 100	93	75	-
Carrot root	0.01	85, 85	85	101, 101	101	100	-
	0.10	92, 86	89	86, 101	94	100	-
Carrot leaves	0.01	88, 85	87	91, 102	97	105	-
	0.10	93, 88	91	92, 96	94	99	-

Residues in following crops

The results of the rotational crop trials for chlorothalonil, R182281 and R611965 are presented in Tables 6.2.2-2 to 6.2.2-4. The results are not corrected for recoveries.

Table 6.2.2-2: Residues in rotational spinach grown in soil treated with chlorothalonil at 2000 g a.s/ha

Spinach commodity	Interval: treatment to sampling (days)	Trial 01, Germany			Interval: treatment to sampling (days)	Trial 02, UK		
		Chloroth alonil	R182281	R611965		Chlorotha lonil	R182281	R611965
Plant-back interval:		**30 days**				**27 days**		
Immature leaves	77	<0.01	<0.01	0.06	77	<0.01	<0.01	0.02
Mature leaves	87	<0.01	<0.01	0.04	88	<0.01	<0.01	0.02
Plant-back interval:		**63 days**				**60 days**		
Immature leaves	98	<0.01	<0.01	0.02	105	<0.01	<0.01	0.01
Mature leaves	104	<0.01	<0.01	0.03	112	<0.01	<0.01	0.01
Plant-back interval:		**365 days**				**365 days**		
Immature leaves	419	<0.01	<0.01	<0.01	440	<0.01	<0.01	<0.01
Mature leaves	437	<0.01	<0.01	<0.01	449	<0.01	<0.01	<0.01

Table 6.2.2-3: Residues in rotational cereals grown in soil treated with chlorothalonil at 2000 g a.s/ha

Wheat (trial 01) / barley (trial 02) commodity	Interval: treatment to sampling (days)	Trial 01, Germany			Interval: treatment to sampling (days)	Trial 02, UK		
		Chloroth alonil	R182281	R611965		Chlorotha lonil	R182281	R611965
Plant-back interval:		**30 days**				**27 days**		
Immature plant	73	<0.01	<0.01	0.16	85	<0.01	<0.01	0.08
Grain	140	<0.01	<0.01	0.11	145	<0.01	<0.01	0.01
Straw	140	<0.01	<0.01	0.29	145	<0.01	<0.01	0.09
Plant-back interval:		**63 days**				**60 days**		
Immature plant	104	<0.01	<0.01	0.11	112	<0.01	<0.01	0.11
Grain	174	<0.01	<0.01	0.09	173	<0.01	<0.01	0.02
Straw	174	<0.01	<0.01	0.25	173	<0.01	<0.01	0.08
Plant-back interval:		**365 days**				**365 days**		
Immature plant	440	<0.01	<0.01	<0.01	449	<0.01	<0.01	<0.01
Grain	500	<0.01	<0.01	-	529	<0.01	<0.01	<0.01
Straw	500	<0.01	<0.01	-	529	<0.01	<0.01	<0.01

- not analysed.

Table 6.2.2-4: Residues in rotational carrot grown in soil treated with chlorothalonil at 2000 g a.s/ha

Carrot commodity	Interval: treatment to sampling (days)	Trial 01, Germany			Interval: treatment to sampling (days)	Trial 02, UK		
		Chloroth alonil	R182281	R611965		Chlorotha lonil	R182281	R611965
Plant-back interval:		**30 days**				**27 days**		
Mature roots	126	<0.01	<0.01	0.01	167	<0.01	<0.01	<0.01
Mature tops	126	<0.01	<0.01	0.04	167	<0.01	<0.01	<0.01
Plant-back interval:		**63 days**				**60 days**		
Mature roots	156	<0.01	<0.01	<0.01	176	<0.01	<0.01	<0.01
Mature tops	156	<0.01	<0.01	0.02	176	<0.01	<0.01	<0.01
Plant-back interval:		**365 days**				**365 days**		
Mature roots	483	<0.01	<0.01	<0.01	543	<0.01	<0.01	<0.01
Mature tops	483	<0.01	<0.01	<0.01	543	<0.01	<0.01	<0.01

No residues of chlorothalonil, R182281 or R611965 were found at or above the LOQ (0.01 mg/kg) in any of the untreated samples.

After all plant-back intervals (PBIs) no residues of chlorothalonil or R182281 were found at or above the LOQ (0.01 mg/kg) in any of the treated samples.

No residues of R611965 were found above the LOQ in the any of the samples from the 365 day plant-back interval. Residues of R611965 were found in samples taken after the 30 and 60 day PBI. For spinach these were 0.02 – 0.06 mg/kg at the 30 day PBI and 0.01-0.03 mg/kg for the 60 day PBI. In cereals residues of R611965 in immature plant, grain and straw were 0.08 – 0.16 mg/kg, 0.01 – 0.11 mg/kg and 0.09 – 0.29 mg/kg respectively, for the 30 day PBI. Residues in cereals for the 60 day PBI

were 0.11 mg/kg, 0.02 -0.09 mg/kg and 0.08-10.25 mg/kg in immature plant, grain and straw, respectively. For carrots residues in roots were <0.01 -0.01 mg/kg for the 30 day PBI and < LOQ for the 60 day PBI. Residues in carrot leaves were <0.01 – 0.04 mg/kg and <0.01 – 0.02 mg/kg for the 30 and 60 day PBIs, respectively.

III. CONCLUSIONS

Residues of chlorothalonil and R182281 were not found above the LOQ in following crops of spinach, cereals and carrot planted at nominal intervals of 30, 60 and 365 days after treatment of bare soil with chlorothalonil at a nominal rate of 2000 g a.s./ha. Residues of R611965 were not found in crops from the 365 day plant-back interval. Residues above the LOQ were found in all crops in the 30 and 60 day plant-back interval.

(Eversfield S, 2014)

Summary of residues in succeeding crops

A confined rotational crop study was evaluated under Council Directive 91/414/EEC and is presented in the chlorothalonil monograph (**Vol.3, Annex B, Section B.7.9.1, January 2000**). At 30 and 80 days after soil treatment with [phenyl-U-^{14}C] - chlorothalonil, the major soil residue was R611965 (almost 25% of the total soil residues), followed by chlorothalonil. R611965 was the major residue identified in rotational crop samples with R182281 present at low levels. Chlorothalonil was not detected in crop samples.

Two additional confined crop rotation studies have been presented in this summary.

In the first study bare soil was treated with [phenyl-U-^{14}C]-chlorothalonil at 7.5 kg a.s./ha, and after ageing for 30, 120 and 365 days, representative cereal, leafy vegetable and root vegetables were sown. Significant total residues (TRR) were found in all crops (max. 0.24 mg/kg for lettuce, 0.43 mg/kg for carrot roots, 25 mg/kg in cereal straw and 2.2 mg/kg in cereal grain). In all crops the majority of the radioactive residue was assigned to the metabolites R611965 and R417888. Up to 30% TRR in was assigned as conjugated material. Other identified metabolites identified, including R611553, R182281 and R612636, represented minor percentages of the TRR. R611968 accounted for up to 10% TRR in grain. No chlorothalonil was detected in any crop.

In the second study [phenyl-U-^{14}C] - chlorothalonil formulated as a SC was applied at 1kg a.s/ha to bare soil. The soil was aged for 30 days and representative crops sown. TRR in mature crops ranged from 0.02 mg/kg in radish roots to 0.120 mg/kg in cereal straw. Parent chlorothalonil was detected only in the radish root samples, and at very low levels (0.001 mg/kg). The major identified metabolite was R611965 which represented 14% TRR (or 0.006 mg/kg) in mature spinach and represented 25% TRR (or 0.030 mg/kg) in barley straw. In the radish root R611965 amounted to 8.3% TRR (0.002 mg/kg). The metabolite R182281 was also identified in spinach, radish root and mature barley samples, however at levels less than 0.01 mg/kg. The remaining radioactive fractions corresponded mainly to conjugates and did not exceed 10% TRR, 0.01 mg/kg for edible plant material (human food) or 0.05 mg/kg for animal feed items.

The metabolism of chlorothalonil in rotational crops is similar to that in primary crops, though levels of R611965 were higher in rotational crops metabolism studies.

Rotational crop field studies conducted in the USA were evaluated under Council Directive 91/414/EEC and are presented in the chlorothalonil monograph (**Vol.3, Annex B, Section B.7.9.2, January 2000**).

Three plots at different sites in the USA were sprayed with 8 applications of chlorothalonil at a rate of 2.5 kg a.s/ha at 7-day intervals. Wheat, carrots, snap beans and spinach were planted 14, 30, 60 and 90 days and about 1 year after the last application. No residues of chlorothalonil were detected in the any of the crop samples. Low levels of R182281were found in samples at all plant-back intervals (< 0.05 mg/kg), with exception of one spinach sample (0.19 mg/kg for the 90 day plant-back interval) and one wheat straw sample (0.08 mg/kg for the 14 day plant-back interval). R611965 was the major compound identified in rotational crop samples with significant levels found in crops for plant-back intervals up to 90 days. The highest levels of R611965 were 1.05 - 2.20 mg/kg in spinach, 0.19 – 1.00 mg/kg in snap beans, 0.10 – 0.59 mg/kg in carrot roots, 0.2 – 0.65 mg/kg in carrot tops, 0.17-0.68 mg/kg in wheat grain and 3.2-10 mg/kg in straw.

In a second study, various primary crops grown at sites across the USA were treated with chlorothalonil at rates ranging from 3 applications at 1.7 kg a.s./ha to 8 applications at 2.6 kg a.s./ha. The primary crops were harvested at normal maturity, and following crops were planted. Residues of chlorothalonil were not found at levels greater than 0.03 mg/kg, except peanut vines (0.22 mg/kg), pea fodder and bean hay (0.06 and 0.09 mg/kg, respectively). One residue of R182281was found in pea fodder at 0.07 mg/kg; R182281 levels were all at or below 0.04 mg/kg in all other samples. R611965 was the major metabolite detected in the rotational crops. In root and tuber vegetable crops residues were < 0.03 – 0.64 mg/kg and <0.03 – 0.59 mg/kg for roots and tops, respectively. For leafy vegetables residues were < 0.03 – 0.80 mg/kg and for fruiting vegetables residues were <0.03 – 1.05 mg/kg. In cereals residues in grain were < 0.03 – 0.4 mg/kg, in forage 0.08 – 0.26 mg/kg and <0.03 – 3.0 in straw. Residues in oilseeds and dried pulses were all < 0.05 mg/kg for all sites and all plant-back intervals.

An additional field crop rotation study in the EU has been presented. Chlorothalonil was applied to bare soil at a rate of 2000 g a.s/ha at one trial site in Germany and one trial site in the United Kingdom. At each rotational interval representative cereal, leafy vegetable and root vegetable crops were sown. Samples of representative food and feed items were analysed for residues of chlorothalonil, R182281 and R611965.

For all plant-back intervals (PBIs) no residues of chlorothalonil or R182281 were found at or above the LOQ (0.01 mg/kg) in any of the treated samples. No residues of R611965 were found at or above the LOQ in the any of the samples from the 365 day PBI. Residues of R611965 were found in samples taken after the 30 and 60 day PBIs. For spinach these were 0.02 – 0.06 mg/kg at the 30 day PBI and 0.01-0.03 mg/kg for the 60 day PBI. In cereals residues of R611965 in immature plant, grain and straw were 0.08 – 0.16 mg/kg, 0.01 – 0.11 mg/kg and 0.09 – 0.29 mg/kg, respectively, for the 30 day PBI. Residues in cereals for the 60 day PBI were 0.11 mg/kg, 0.02 -0.09 mg/kg and 0.08-10.25 mg/kg in immature plant, grain and straw, respectively. For carrots residues in roots were <0.01-0.01 mg/kg for the 30 day PBI and < LOQ for the 60 day PBI.

The maximum total application rate proposed for chlorothalonil is 2 kg a.s./ha for tomatoes (field crops), 1.5 kg a.s./ha for cereals and 2.25 kg a.s./ha for potatoes. The proposed uses for tomatoes and potatoes involve spraying when crop foliage is present meaning there will be some crop interception and not all the spray will be in contact with the soil. On this basis and considering the results of the EU crop rotation trials where application at 2 kg a.s./ha was made to *bare soil* it can be concluded that residues of chlorothalonil and R182281 in following crops are not expected to exceed 0.01 mg/kg. Residues of R611965 may be expected at low levels in following crops. The toxicology of R611965 has been extensively investigated, and it has been shown to have a different toxicology profile to chlorothalonil. R611965 does not cause the kidney and fore stomach toxicity to rodents and is not carcinogenic. R611965 has no notable toxicology and is of much lower toxicity than chlorothalonil. The NOAEL for R611965 (50 mg/kg bodyweight/day) is substantially higher than the NOAEL for parent chlorothalonil (2.7 mg/kg bodyweight/day). As this metabolite is of lower toxicity than chlorothalonil it does not need to be included in the residue definition for either monitoring or risk assessment (see section CA 6.7).

It is concluded that sufficient data are available to address residues in following crops. The metabolism of chlorothalonil in following crops is similar to that in primary crops and the proposed definition of the residue in primary and following crops is the same. Residues of chlorothalonil and R182281 are not expected in following crops above the LOQ and it is not necessary to set MRLs for either chlorothalonil or R182281.

CA 6.7 Proposed Residue Definitions and Maximum Residue Levels

CA 6.7.1 Proposed residue definitions

Crops

The residue definition for both enforcement and risk assessment derived in the framework of the Annex I inclusion was parent chlorothalonil (**Vol.3, Annex B, Section B.7.3, January 2000**). This has subsequently been reviewed as discussed below.

Plant uptake, distribution and metabolism of ^{14}C labelled chlorothalonil was investigated in leafy vegetables (lettuce, celery), root vegetables (carrot), fruiting vegetables (tomato), fresh legumes (peas, snap beans) and cereals (wheat).

In all crops, fairly high TRR levels were observed in crop parts that were directly exposed to treatment, varying from 0.9 mg/kg in beans to 4.6 mg/kg in celery stalks. Highest TRR levels were identified in lettuce leaves (118-170 mg/kg) and in celery, beans and carrot foliage (13-263 mg/kg). However, in carrot roots, the TRR was in the range of 0.01-0.07 mg/kg, leading to the conclusion that translocation from foliage to roots is very limited.

Generally, parent chlorothalonil constituted the most important component of the residue in all crops. It accounted for at least 50 % of the TRR (beans) up to 90 % of the TRR (lettuce) in edible parts of the investigated crops. Two metabolites (R182281 and R611965) were also identified. Metabolite R182281 was mostly present at levels below 10 % of the TRR and the level of R611965 always remained below the LOD.

An EFSA reasoned opinion[2] reconsidered the definition of the residue. EFSA noted that in tomato foliage, metabolite R182281 increased with longer PHI, from 4 % TRR (1 DAT) to 14 % TRR (12 DAT). In carrot foliage also, it was apparent that R182281 was the major identified residue at longer pre-harvest intervals (up to 75 % TRR at 21 DAT). Toxicological reference values were derived for R182281 (**SANCO/4343/2000, September 2006**) indicating that metabolite R182281 is of higher acute and chronic toxicity than chlorothalonil. This metabolite, however, follows a different toxicological mechanism to chlorothalonil. The metabolism studies showed that the metabolic pathway is similar in all crops and that chlorothalonil will be metabolised to a greater extent after longer intervals, which is relevant for GAPs with PHI intervals exceeding 21/28 days.

EFSA was of the opinion that R182281 should also be considered for inclusion in in the residue definition for risk assessment purposes. As R182281 follows a different toxicological mechanism to chlorothalonil,

[2]Reasoned opinion on the review of the existing maximum residue levels (MRLs) for chlorothalonil according to Article 12 of Regulation (EC) No 396/2005", EFSA Journal 2012;10(10):2940

it is appropriate to consider parent chlorothalonil and R182281 separately in the risk assessment. This is consistent with conclusions reached by the JMPR (FAO, 2010)[3].

EFSA also proposed that considering that the occurrence of R182281 in processed commodities is highly expected (see section CA 6.5.1) and that the consumer risk assessment for R182281 may result in a more critical outcome than for the parent compound, a residue definition for enforcement of R182281 should also be considered.

In their conclusions, EFSA proposed to establish in all plant commodities a residue definition for enforcement and risk assessment of chlorothalonil alone and a separate residue definition for R182281, also for enforcement and risk assessment purposes. This proposal is supported by the Notifier in this dossier. This means that two residue definitions are each proposed for both enforcement and risk assessment, namely chlorothalonil alone and R182281 alone. Consequently, MRLs for both chlorothalonil and R182281 are proposed and separate risk assessments are presented for both chlorothalonil and R182281.

Animal products

The residue definition for both enforcement and risk assessment previously derived in the framework of the Annex I inclusion was R182281 (**Vol.3, Annex B, Section B.7.3, January 2000**).

On the basis of the additional metabolism data disused in this document it is proposed that this definition does not change. This is consistent with the conclusions of EFSA in their reasoned opinion (EFSA Journal 2012; 10(10): 2940).

Summary of the definition of the residue

Endpoint	Proposed EU endpoints
Definition of the residue in crops for enforcement purposes	Two separate residue definitions: (1) Chlorothalonil and (2) R182281
Definition of the residue in crops for risk assessment purposes	Two separate residue definitions: (1) Chlorothalonil and (2) R182281
Definition of the residue in animal products for enforcement purposes	R182281
Definition of the residue in animal products for risk assessment purposes	R182281

CA 6.7.2 Proposed maximum residue levels (MRLs) and justification of the acceptability of the levels proposed

EU MRLs for chlorothalonil are currently detailed in Annexes of Regulation (EC) No 396/2005. A recent proposal currently being considered (SANCO 12240/2013) has proposed new MRLs for chlorothalonil. There are currently no EU MRLs for R182281. EU MRLs for commodities relevant to this submission are detailed in Table 6.7.2–1 and 6.7.2-2. The residue values used and the calculations for MRLs are presented in Section CA 6.3.

[3] FAO (Food and Agriculture Organisation of the United Nations), 2010. Chlorothalonil. In: Pesticide residues in food – 2010. Report of the Joint Meeting of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Expert Group on Pesticide Residues. FAO Plant Production and Protection Paper 200.

A change to the residue definition for enforcement (see section CA 6.7.1) is proposed as a result of this submission indicating MRLs should be proposed separately for chlorothalonil and R182281. No changes to the most recent EU MRLs for tomato, barley grain, wheat grain or potato are proposed as a result of this submission. The EU does not currently set MRLs in livestock feed commodities, but may do so in future.

Table 6.7.2–1: Established and proposed MRLs for chlorothalonil for commodities in this submission

Code	Commodity	Current EU MRL[1] (mg/kg)	Proposed EU MRL (mg/kg)
231010	Tomato (fruit)	2/6	6
500010	Barley (grain)	0.3/0.4	0.3
500090	Wheat (grain)	0.1	0.1
211000	Potato (tuber)	0.02/0.01*	0.01*

[1] – MRLs as given in EC Reg. 396/2005 and SANCO 12240/2013 respectively

Table 6.7.2–2: Established and proposed MRLs for R182281 for commodities in this submission

Commodity	Current EU MRL[1] (mg/kg)	Proposed EU MRL (mg/kg)
Tomato (fruit)	-	0.015
Barley (grain)	-	0.04
Wheat (grain)	-	0.02*
Potato (tuber)	-	0.02*
Muscle (bovine)	0.02/0.02	0.02
Muscle (sheep, goat, equine)	0.02/0.02	0.04
Muscle (swine)	0.02/0.02	0.01*
Fat tissue (bovine)	0.07/0.07	0.02
Fat tissue (sheep, goat, equine)	0.07/0.07	0.07
Fat tissue (swine)	0.07/0.07	0.01*
Liver (bovine)	0.2/0.2	0.1
Liver (sheep, goat, equine)	0.2/0.2	0.2
Liver (swine)	0.2/0.2	0.01*
Kidney (bovine)	0.3/0.7	0.3
Kidney (sheep, goat, equine)	0.3/0.7	0.3
Kidney (swine)	0.3/0.7	0.03
Other edible offal (bovine)	0.2/0.2	0.2
Other edible offal (sheep, goat, equine)	0.2/0.2	0.2
Other edible offal (swine)	0.2/0.2	0.03

Commodity	Current EU MRL[1] (mg/kg)	Proposed EU MRL (mg/kg)
Poultry muscle	0.01*/0.01*	0.01*
Poultry fat	0.07/0.01*	0.01*
Poultry liver	0.07/0.01*	0.01*
Poultry kidney	0.07/0.07	0.01*
Poultry, edible offals	0.07/0.01*	0.01*
Milk	0.07/0.1	0.05
Eggs	0.01*/0.01*	0.01*

[1] – MRLs as given in EC Reg. 396/2005 and SANCO 12240/2013 respectively for chlorothalonil as R182281

CA 6.7.3 Proposed maximum residue levels (MRLs) and justification of the acceptability of the levels proposed for imported products (import tolerance)

Not applicable.

CA 6.8 Proposed Safety Intervals

Pre-harvest intervals

Proposed pre-harvest intervals for the use of chlorothalonil on the representative use crops (tomato, barley and wheat) are detailed in Table 6.8.1-1.

Table 6.8.1-1: Proposed Pre-harvest Intervals

Crop	Application method	Pre-Harvest Interval (days)
Tomato	Foliar spray (BBCH 51-89)	3
Barley	Foliar spray (BBCH 39-59)	Not relevant[1]
Wheat	Foliar spray (BBCH 39-69)	Not relevant[1]
Potato	Foliar spray (BBCH 40-85)	28

1 - Application is growth stage dependent and crops are harvested at maturity.

Re-entry intervals for livestock to areas to be grazed

A re-entry interval for livestock is not applicable as tomato and cereals are not grazed.

Re-entry period for man into treated areas

The worker re-entry risk assessments for the representative use were conducted assuming the maximum rate with no allowance for any decline in the default dislodgeable foliar residue and passed. Thus, no re-entry period is required.

Withholding periods for animal feeding stuffs

An additional period of withholding after harvest is not required for livestock feed commodities.

Waiting period between last application and sowing or planting the crops to be protected

As chlorothalonil is applied post-emergence to crops no waiting period is required.

Waiting period between last application and handling treated products

The worker re-entry risk assessments for the representative use were conducted assuming the maximum rate with no allowance for any decline in the default dislodgeable foliar residue and passed. Thus, no waiting period is required.

Waiting periods between last application and sowing or planting succeeding crops

The rotational crop studies showed that even at minimum 30 day plant back interval no residues of chlorothalonil above 0.01 mg/kg were observed. Thus, a waiting period is not required.

CA 6.9 Estimation of the Potential and Actual Exposure through Diet and other Sources

Acceptable Daily Intake (ADI) and Dietary Exposure Calculation

No change from the existing EU ADI of 0.015 mg/kg body weight/day for chlorothalonil and 0.01 mg/kg body weight/day for R182281 (see **SANCO/4343/2000 final (revised), 28 September 2006** and **Document M-CA, Section 5** of this submission) is proposed.

Long-term consumer exposure to potential residues of chlorothalonil and R182281 resulting from the proposed representative use of chlorothalonil is estimated according to the EFSA PRIMo model[4] for chronic risk assessment.

The TMDI values are calculated based on proposed MRL values as listed in Table 6.9-1. The residues as entered into the EFSA model are for tomato, barley grain, wheat grain and potato only for chlorothalonil and for tomato, barley grain, wheat grain, potato and animal commodities for R182281 as the residue definition for chlorothalonil for risk assessment in products of plant origin is chlorothalonil alone and R182281 alone (each considered separately) and in products of animal origin is R182281.

Table 6.9-1: Input values for TMDI calculations

Commodity Code	Commodity	Chlorothalonil		R188281	
		Input value (mg/kg)	Comment	Input value (mg/kg)	Comment
231010	Tomato	6	Proposed MRL value	0.01	Proposed MRL value
500010	Barley	0.3	Proposed MRL value	0.04	Proposed MRL value
500090	Wheat	0.1	Proposed MRL value	0.02	Proposed MRL value
211000	Potato	0.01	Proposed MRL value	0.02	Proposed MRL value
1012010, 1013010, 1014010, 1015010	Muscle (bovine, sheep, goat, equine)	-	Residue definition for risk assessment is R188281	0.04	Proposed MRL value

[4] Revision 2.0 of the EFSA model. Reasoned Opinion on the Potential Chronic and Acute Risk to Consumers' Health Arising from Proposed Temporary EU MRLs According to Regulation (EC) No 396/2005 on Maximum Residue Levels of Pesticides in Food and Feed of Plant and Animal Origin, European Food Safety Authority, 15 March 2007

Commodity Code	Commodity	Chlorothalonil		R188281	
		Input value (mg/kg)	Comment	Input value (mg/kg)	Comment
1011010	Muscle (swine)	-	Residue definition for risk assessment is R188281	0.01	Proposed MRL value
1012020, 1013020, 1014020, 1015020	Fat tissue (bovine, sheep, goat, equine)	-	Residue definition for risk assessment is R188281	0.07	Current MRL value (no change proposed)
1011020	Fat tissue (swine)	-	Residue definition for risk assessment is R188281	0.01	Proposed MRL value
1012030, 1013030, 1014030, 1015030	Liver (swine, bovine, sheep, goat, equine)	-	Residue definition for risk assessment is R188281	0.2	Current MRL value (no change proposed)
1011030	Liver (swine)	-	Residue definition for risk assessment is R188281	0.01	Proposed MRL value
1012040, 1013040, 1014040, 1015040	Kidney (bovine, sheep, goat, equine)	-	Residue definition for risk assessment is R188281	0.7	Current MRL value (no change proposed)
1011040	Kidney (swine)	-	Residue definition for risk assessment is R188281	0.03	Proposed MRL value
1012050, 1013050, 1014050, 1015050	Other edible offal (bovine, sheep, goat, equine)	-	Residue definition for risk assessment is R188281	0.2	Current MRL value (no change proposed)
1011050	Other edible offal (swine)	-	Residue definition for risk assessment is R188281	0.03	Proposed MRL value
1020000	Milk	-	Residue definition for risk assessment is R188281	0.05	Proposed MRL value

The TMDI calculations give unrealistic worst-case estimates of intake because they assume that all commodities with established and proposed uses will contain residues at the MRL. No account is taken of the potential reduction in residues during transport and storage or during commercial and domestic processing. In practice, the actual intake is likely to be much lower than the calculated values.

The TMDI calculations for chlorothalonil and R182281 using the EFSA PRIMo model are presented in Tables 6.9-1 and 6.9-2, respectively. The highest TMDI for chlorothalonil is for WHO Cluster diet B and represents 130% of the ADI. A refined NEDI calculation has therefore been conducted (see below).

The highest TMDI for R182281 is for the French toddler and represents 22% of the ADI. The results indicate that there is no unacceptable chronic risk to human health from the consumption of commodities containing residues of R182281 arising from tomato, barley, wheat and potato treated with chlorothalonil according to the proposed uses.

Table 6.9-1: TMDI for chlorothalonil using the EFSA Model Rev 2.0

The output is taken directly from the EFSA spreadsheet. The proposed EU MRL values have been used.

Chlorothalonil			
Status of the active substance:		Code no.	
LOQ (mg/kg bw):	0.01	proposed LOQ:	
Toxicological end points			
ADI (mg/kg bw/day):	0.015	ARfD (mg/kg bw):	0.6
Source of ADI:	EU	Source of ARfD:	EU
Year of evaluation:	2006	Year of evaluation:	2006

Prepare workbook for refined calculations

Undo refined calculations

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

TMDI (range) in % of ADI minimum - maximum	
7	130
No of diets exceeding ADI:	1

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)
129.8	WHO Cluster diet B	123.3	Tomatoes	5.7	Wheat	0.6	Barley	0.2
61.5	IT kids/toddler	57.0	Tomatoes	4.4	Wheat	0.1	Potatoes	0.1
49.4	IT adult	46.5	Tomatoes	2.8	Wheat	0.0	Potatoes	0.0
46.9	WHO regional European diet	44.0	Tomatoes	2.0	Wheat	0.7	Barley	0.3
45.5	WHO cluster diet D	40.5	Tomatoes	4.3	Wheat	0.4	Barley	0.3
42.4	ES child	39.3	Tomatoes	3.0	Wheat	0.1	Potatoes	0.1
41.6	DE child	38.6	Tomatoes	2.7	Wheat	0.2	Potatoes	0.2
38.8	PT General population	35.8	Tomatoes	2.6	Wheat	0.4	Potatoes	0.4
35.5	PL general population	35.3	Tomatoes	0.2	Potatoes		FRUIT (FRESH OR FROZEN)	0.2
34.0	ES adult	31.4	Tomatoes	1.6	Wheat	1.0	Barley	0.1
33.0	FR toddler	30.9	Tomatoes	1.7	Wheat	0.3	Potatoes	0.3
33.0	SE general population 90th percentile	30.6	Tomatoes	2.1	Wheat	0.3	Potatoes	0.3
31.1	WHO Cluster diet F	27.3	Tomatoes	2.4	Wheat	1.2	Barley	0.2
28.6	NL child	25.0	Tomatoes	3.2	Wheat	0.4	Potatoes	0.4
26.4	UK Toddler	23.6	Tomatoes	2.6	Wheat	0.2	Potatoes	0.2
26.4	UK vegetarian	24.9	Tomatoes	1.4	Wheat	0.1	Potatoes	0.1
25.8	LT adult	24.8	Tomatoes	0.7	Wheat	0.2	Potatoes	0.2
25.6	WHO cluster diet E	21.1	Tomatoes	2.6	Wheat	1.6	Barley	0.3
25.1	DK child	21.3	Tomatoes	3.7	Wheat	0.2	Potatoes	0.2
20.2	IE adult	16.1	Tomatoes	2.5	Barley	1.5	Wheat	0.2
19.6	FR all population	17.3	Tomatoes	2.2	Wheat	0.1	Potatoes	0.1
19.4	NL general	17.1	Tomatoes	1.4	Wheat	0.7	Barley	0.2
18.7	UK Adult	17.4	Tomatoes	1.1	Wheat	0.1	Potatoes	0.1
18.0	DK adult	16.5	Tomatoes	1.3	Wheat	0.1	Potatoes	0.1
17.9	FI adult	17.1	Tomatoes	0.7	Wheat	0.1	Potatoes	0.1
16.7	UK Infant	14.7	Tomatoes	1.7	Wheat	0.2	Potatoes	0.2
6.7	FR infant	5.9	Tomatoes	0.6	Wheat	0.3	Potatoes	0.3

Conclusion:

The estimated Theoretical Maximum Daily Intakes based on MS and WHO diets and pTMRLs were in the range of 6.7 % to 130 % of the ADI.

For 1 diets the ADI is exceeded. Further refinements of the dietary intake estimates have not been performed. A public health risk can not be excluded at the moment.

Table 6.9-2: TMDI for R182281 using the EFSA Model Rev 2.0

The output is taken directly from the EFSA spreadsheet. The proposed EU MRL values have been used.

R182281			
Status of the active substance:		Code no.	
LOQ (mg/kg bw):	0.01	proposed LOQ:	
Toxicological end points			
ADI (mg/kg bw/day):	**0.01**	ARfD (mg/kg bw):	**0.01**
Source of ADI:	**EU**	Source of ARfD:	**EU**
Year of evaluation:	**2006**	Year of evaluation:	**2006**

Prepare workbook for refined calculations

Undo refined calculations

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

TMDI (range) in % of ADI minimum - maximum: 1 - 22

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)
22.3	FR toddler	19.8	Milk and cream,	1.0	Potatoes	0.5	Bovine: Meat	0.0
20.9	UK Infant	19.4	Milk and cream,	0.7	Potatoes	0.5	Wheat	
17.8	NL child	14.7	Milk and cream,	1.2	Potatoes	0.9	Wheat	0.2
14.2	FR infant	12.9	Milk and cream,	0.8	Potatoes	0.2	Bovine: Meat	0.0
12.0	UK Toddler	10.3	Milk and cream,	0.8	Wheat	0.7	Potatoes	
8.8	DE child	7.1	Milk and cream,	0.8	Wheat	0.5	Potatoes	0.0
8.5	ES child	6.3	Milk and cream,	0.9	Wheat	0.6	Bovine: Meat	0.1
8.2	DK child	6.3	Milk and cream,	1.1	Wheat	0.5	Potatoes	
7.8	SE general population 90th percentile	6.2	Milk and cream,	0.8	Potatoes	0.6	Wheat	
6.1	WHO Cluster diet B	1.7	Wheat	1.6	Milk and cream,	0.5	Potatoes	0.1
5.6	WHO cluster diet D	2.5	Milk and cream,	1.3	Wheat	0.8	Potatoes	0.0
5.1	WHO regional European diet	2.4	Milk and cream,	0.8	Potatoes	0.6	Wheat	0.1
4.9	NL general	3.3	Milk and cream,	0.5	Potatoes	0.4	Wheat	0.1
4.5	WHO Cluster diet F	2.0	Milk and cream,	0.7	Wheat	0.7	Potatoes	0.1
4.1	WHO cluster diet E	1.5	Milk and cream,	0.8	Wheat	0.8	Potatoes	0.1
4.1	IE adult	1.4	Milk and cream,	0.5	Barley	0.5	Wheat	0.1
4.0	ES adult	2.5	Milk and cream,	0.5	Wheat	0.3	Bovine: Meat	0.1
3.8	DK adult	2.7	Milk and cream,	0.4	Wheat	0.3	Potatoes	
3.4	FI adult	2.8	Milk and cream,	0.2	Potatoes	0.2	Wheat	
3.2	LT adult	2.0	Milk and cream,	0.6	Potatoes	0.2	Wheat	0.1
2.6	FR all population	1.3	Milk and cream,	0.7	Wheat	0.2	Potatoes	0.0
2.4	UK vegetarian	1.6	Milk and cream,	0.4	Wheat	0.3	Potatoes	
2.2	UK Adult	1.5	Milk and cream,	0.3	Wheat	0.3	Potatoes	0.0
2.0	PT General population	1.1	Potatoes	0.8	Wheat	0.1	Tomatoes	
1.7	IT kids/toddler	1.3	Wheat	0.2	Tomatoes	0.2	Potatoes	
1.1	IT adult	0.8	Wheat	0.2	Tomatoes	0.1	Potatoes	
0.8	PL general population	0.7	Potatoes	0.1	Tomatoes		FRUIT (FRESH OR FROZEN)	

Conclusion:

The estimated Theoretical Maximum Daily Intakes (TMDI), based on pTMRLs were below the ADI.
A long-term intake of residues of R182281 is unlikely to present a public health concern.

Calculation of National Estimated Daily Intake (NEDI)

Long-term consumer exposure to potential residues resulting from the proposed representative uses of chlorothalonil is estimated according to the EFSA PRIMo model for chronic risk assessment.

The NEDI values are calculated based on proposed STMR values derived from supervised residue trials, as listed in Table 6.9-3. The residues as entered into the EFSA model for tomato, barley grain, wheat grain and potato are presented in Table 6.9-3.

Table 6.9-3: Input values for NEDI calculations

Commodity Code	Commodity	Chlorothalonil	
		Input value (mg/kg)	Comment
231010	Tomato	0.41	STMR from residue trials
500010	Barley	0.01	STMR from residue trials
500090	Wheat	0.01	STMR from residue trials
211000	Potato	0.01	STMR from residue trials

A summary of the NEDI calculations for chlorothalonil using the EFSA PRIMo model is presented in Table 6.9-4. The highest NEDI is for the WHO Cluster diet B and represents 18.0% of the ADI.

The results indicate that there is no unacceptable chronic risk to human health from the consumption of tomato, barley, wheat and potato commodities treated with chlorothalonil according to the uses considered.

For R182281, the TMDI value is significantly less than the ADI for R182281 so it is not necessary to calculate NEDI values to give more realistic estimates of intake.

Table 6.9-4: NEDI for chlorothalonil using the EFSA Model Rev 2.0

The output is taken directly from the EFSA spreadsheet. STMR values have been used.

Chlorothalonil			
Status of the active substance:		Code no.	
LOQ (mg/kg bw):	0.01	proposed LOQ:	
Toxicological end points			
ADI (mg/kg bw/day):	0.015	ARfD (mg/kg bw):	0.6
Source of ADI:	EU	Source of ARfD:	EU
Year of evaluation:	2006	Year of evaluation:	2006

Prepare workbook for refined calculations

Undo refined calculations

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

	TMDI (range) in % of ADI minimum - maximum
	1 18
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)
18.0	WHO Cluster diet B	17.3	Tomatoes	0.6	Wheat	0.2	Potatoes	0.8
8.5	IT kids/toddler	8.0	Tomatoes	0.4	Wheat	0.1	Potatoes	0.5
6.8	IT adult	6.5	Tomatoes	0.3	Wheat	0.0	Potatoes	0.3
6.6	WHO regional European diet	6.2	Tomatoes	0.3	Potatoes	0.2	Wheat	0.5
6.4	WHO cluster diet D	5.7	Tomatoes	0.4	Wheat	0.3	Potatoes	0.7
5.9	ES child	5.5	Tomatoes	0.3	Wheat	0.1	Potatoes	0.4
5.9	DE child	5.4	Tomatoes	0.3	Wheat	0.2	Potatoes	0.4
5.6	PT General population	5.0	Tomatoes	0.4	Potatoes	0.3	Wheat	0.6
5.2	PL general population	4.9	Tomatoes	0.2	Potatoes		FRUIT (FRESH OR FROZEN)	0.2
4.8	FR toddler	4.3	Tomatoes	0.3	Potatoes	0.2	Wheat	0.5
4.8	SE general population 90th percentile	4.3	Tomatoes	0.3	Potatoes	0.2	Wheat	0.5
4.6	ES adult	4.4	Tomatoes	0.2	Wheat	0.1	Potatoes	0.3
4.3	WHO Cluster diet F	3.8	Tomatoes	0.2	Wheat	0.2	Potatoes	0.5
4.2	NL child	3.5	Tomatoes	0.4	Potatoes	0.3	Wheat	0.7
3.8	UK Toddler	3.3	Tomatoes	0.3	Wheat	0.2	Potatoes	0.5
3.8	LT adult	3.5	Tomatoes	0.2	Potatoes	0.1	Wheat	0.3
3.7	UK vegetarian	3.5	Tomatoes	0.1	Wheat	0.1	Potatoes	0.2
3.5	WHO cluster diet E	2.9	Tomatoes	0.3	Wheat	0.3	Potatoes	0.6
3.5	DK child	3.0	Tomatoes	0.4	Wheat	0.2	Potatoes	0.5
2.7	NL general	2.4	Tomatoes	0.2	Potatoes	0.1	Wheat	0.3
2.7	FR all population	2.4	Tomatoes	0.2	Wheat	0.1	Potatoes	0.3
2.6	UK Adult	2.4	Tomatoes	0.1	Wheat	0.1	Potatoes	0.2
2.6	IE adult	2.2	Tomatoes	0.2	Wheat	0.2	Potatoes	0.4
2.5	DK adult	2.3	Tomatoes	0.1	Wheat	0.1	Potatoes	0.2
2.5	FI adult	2.4	Tomatoes	0.1	Potatoes	0.1	Wheat	0.1
2.5	UK Infant	2.1	Tomatoes	0.2	Potatoes	0.2	Wheat	0.4
1.2	FR infant	0.8	Tomatoes	0.3	Potatoes	0.1	Wheat	0.3

Conclusion:
The estimated Theoretical Maximum Daily Intakes (TMDI), based on pTMRLs were below the ADI.
A long-term intake of residues of Chlorothalonil is unlikely to present a public health concern.

Acute Reference Dose (ARfD) and Dietary Exposure Calculation

No change from the existing EU ARfD of 0.6 mg/kg body weight/day for chlorothalonil is proposed (see **SANCO/4343/2000 final (revised), 28 September 2006**). For R182281, an ARfD of 0.01 mg/kg body weight/day was proposed in the original EU review, however the JMPR proposed an ARfD of 0.03 mg/kg bw/day. The JMPR established an ARfD of 0.03 mg/kg bw based on a developmental toxicity study with R182281 on rabbits. EFSA have also concluded that the effects observed in the developmental toxicity study in rabbits would be relevant for setting an ARfD and that the JMPR approach can be supported ("Scientific support for preparing an EU position in the 43rd Session of the Codex Committee on Pesticide Residues (CCPR)" , September 2011, **EFSA Journal 2011; 9(9):2360**). Therefore, for R18331 an ARfD of 0.03 mg/kg bw/day is proposed.

Acute dietary risk assessments are presented for potential residues of chlorothalonil and R182281 arising from the proposed representative use of chlorothalonil. Short-term consumer exposure to potential chlorothalonil and R182281residues is estimated according to the EFSA PRIMO model for acute risk assessment.

IESTI (International Estimate of Short-Term Intake) values are generally calculated assuming that residues are present at the HR, except for commodities bulked or blended during processing, where the STMR is used. The IESTI values are calculated based on proposed HR values for tomato and animal commodities (other than milk), and the proposed STMR values for wheat and barley grain, and milk. The IESTI values are calculated based on the values as listed in Table 6.9-5.

Table 6.9-5: Input values for IESTI calculations

Commodity Code	Commodity	Chlorothalonil		R182281	
		Input value (mg/kg)	Comment	Input value (mg/kg)	Comment
231010	Tomato	0.83	HR from residue trials	0.01	HR from residue trials
500010	Barley	0.01	STMR from residue trials	0.015	STMR from residue trials
500090	Wheat	0.01	STMR from residue trials	0.015	STMR from residue trials
211000	Potato	0.01	HR from residue trials	0.02	HR from residue trials
1012010, 1013010, 1014010, 1015010	Muscle (swine, bovine, sheep, goat, equine)	-	Residue definition for risk assessment is R188281	0.04	HR for sheep, goat and equine muscle calculated from feeding studies (Table 6.4.4-4)
1011010	Muscle (swine)	-	Residue definition for risk assessment is R188281	0.01	HR calculated from feeding studies (Table 6.4.4-4)
1012020, 1013020, 1014020, 1015020	Fat tissue (bovine, sheep, goat, equine)	-	Residue definition for risk assessment is R188281	0.07	HR for sheep, goat and equine fat calculated from feeding studies (Table 6.4.4-4)
1011020	Fat tissue (swine)	-	Residue definition for risk assessment is R188281	0.01	HR calculated from feeding studies (Table 6.4.4-4)
1012030, 1013030, 1014030, 1015030	Liver (swine, bovine, sheep, goat, equine)	-	Residue definition for risk assessment is R188281	0.08	HR for sheep, goat and equine liver calculated from feeding studies (Table 6.4.4-4)
1011030	Liver (swine)	-	Residue definition for risk assessment is R188281	0.01	HR calculated from feeding studies (Table 6.4.4-4)
1012040, 1013040, 1014040, 1015040	Kidney (bovine, sheep, goat, equine)	-	Residue definition for risk assessment is R188281	0.31	HR for sheep, goat and equine kidney calculated from feeding studies (Table 6.4.4-4)
1011040	Kidney (swine)	-	Residue definition for risk assessment is R188281	0.03	HR calculated from feeding studies (Table 6.4.4-4)
1012050, 1013050, 1014050, 1015050	Other edible offal (bovine, sheep, goat, equine)	-	Residue definition for risk assessment is R188281	0.08	HR calculated from feeding studies (Table 6.4.4-4)
1011050	Other edible offal (swine)	-	Residue definition for risk assessment is R188281	0.03	HR calculated from feeding studies (Table 6.4.4-4)
1020000	Milk	-	Residue definition for risk assessment is R188281	0.05	mean residue calculated from maximum dietary intakes and feeding studies (Table 6.4.4-4)

The IESTI results for chlorothalonil and R182281 obtained using the EFSA PRIMo model (Rev. 2.0) are presented in Table 6.9-6 and 6.9-7, respectively. The highest estimated short-term intake for chlorothalonil is for the consumption of tomatoes by children (based on consumption data from Belgium) and represents 40% of the ARfD.

The highest estimated short-term intake for R188281 is for the consumption of milk by UK Infants and represents 21% of the ARfD.

The results indicate that there is no unacceptable acute risk to human health from the consumption of commodities containing residues of chlorothalonil or R182281 arising from tomato, barley, wheat and potato treated with chlorothalonil according to the proposed uses.

Table 6.9-6: IESTI for chlorothalonil using the EFSA Model Rev 2.0

The output is taken directly from the EFSA spreadsheet. The proposed EU HR and STMR values have been used.

	Acute risk assessment /children						Acute risk assessment / adults / general population					
	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)
	39.7	Tomatoes	4.1 / -	28.8	Tomatoes	4.1 / -	10.4	Tomatoes	4.1 / -	8.4	Tomatoes	4.1 / -
	0.3	Potatoes	0.01 / -	0.2	Potatoes	0.01 / -	0.0	Potatoes	0.01 / -	0.0	Potatoes	0.01 / -
	0.0	Wheat	0.01 / -	0.0	Wheat	0.01 / -	0.0	Wheat	0.01 / -	0.0	Wheat	0.01 / -
	0.0	Barley	0.01 / -	0.0	Barley	0.01 / -	0.0	Barley	0.01 / -	0.0	Barley	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)			
	11.9	Tomato juice	4.1 / -				1.3	Tomato (preserved-	4.1 / -			
	0.0	Potato puree (flakes)	0.01 / -				0.0	Bread/pizza	0.01 / -			
	0.0	Wheat flour	0.01 / -				0.0	Potato uree (flakes)	0.01 / -			
	0.0	Fried potatoes	0.01 / -				0.0	Fried potatoes	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 Chlorothalonil 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.											

Table 6.9-7: IESTI for R182281 using the EFSA Model Rev 2.0

The output is taken directly from the EFSA spreadsheet. The proposed EU HR and STMR values have been used.

	Acute risk assessment /children					Acute risk assessment / adults / general population				
	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)
	20.7	Milk and milk products:	0.05 / -	20.7	Milk and milk	0.05 / -	2.9	Milk and milk	0.05 / -	2.9	Milk and milk products: Cattle	0.05 / -
	10.3	Potatoes	0.02 / -	7.3	Potatoes	0.02 / -	2.0	Potatoes	0.02 / -	1.8	Bovine: Kidney	0.31 / -
	4.0	Milk and milk products: Goat	0.05 / -	4.0	Milk and milk	0.05 / -	1.8	Bovine: Kidney	0.31 / -	1.6	Potatoes	0.02 / -
	3.9	Bovine: Kidney	0.31 / -	3.9	Bovine: Kidney	0.31 / -	1.1	Milk and milk	0.05 / -	1.1	Milk and milk products: Goat	0.05 / -
	3.9	Tomatoes	0.02 / -	2.8	Tomatoes	0.02 / -	1.0	Tomatoes	0.02 / -	0.8	Tomatoes	0.02 / -
	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)			
	1.2	Tomato juice	0.02 / -				0.2	Bread/pizza	0.015 / -			
	0.9	Potato puree (flakes)	0.02 / -				0.1	Tomato (preserved-fresh)	0.02 / -			
	0.6	Wheat flour	0.015 / -				0.1	Potato uree (flakes)	0.02 / -			
	0.1	Fried potatoes	0.02 / -				0.1	Fried potatoes	0.02 / -			
	*) 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 R182281 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.											

CA 6.10 Other Studies

CA 6.10.1 Effect on the residue level in pollen and bee products

The data requirement objective of these studies is to determine the residue in pollen and bee products for human consumption resulting from residues taken up by honeybees from crops at blossom.

Chlorothalonil is a fungicide, of low toxicity to bees and therefore data from field studies on bees are not available. Tomatoes, cereals and potatoes are not attractive crops to honey-bees and so for the supported representative uses on tomato applied at BBCH 51 to 89, and barley and wheat applied at BBCH 39 to 69, there is a low likelihood of residues of chlorothalonil and R182281 in pure blossom honey or other bee products from these uses.

Summary of residue behaviour

The stability of residues of chlorothalonil during storage was investigated in various commodities.

Chlorothalonil was stable in crops representing the high water, high oil, high starch and high acid crop groups for 24 months when samples were homogenised in the presence of acid before storage. Chlorothalonil was stable in crops representing the high water, high oil, high starch and high acid crop groups for 48 months when samples were homogenised without acid before storage.

R182281 was stable in crops representing the high water, high oil, high starch and high acid crop groups for 24 months when samples were homogenised in the presence of acid before storage. Residues of R182281 in onions and grapes were found to be stable for 3 months. R182281 was stable in crops representing the high oil, high starch and high acid crop groups for 24 months when samples were homogenised without acid. Residues of R182281 were stable in products of animal origin for 18 months.

R611965 was stable in crops representing the high water, high acid, high starch, high protein and high oil crop groups for 12 months. Residues of chlorothalonil in extracts of representative crop matrices were stable for 35 days at < 7°C and at least 7 days when stored at < -18°C. Residues of R182281 in samples extracts were stable for 7 days.

The metabolism of chlorothalonil has been studied in lettuce, tomato, carrot, celery, snap beans (French beans), wheat and peas using ^{14}C-chlorothalonil labelled in the phenyl position.

In all crops, fairly high TRR levels were observed in crop parts that were directly exposed to treatment, varying from 0.9 mg/kg in beans to 4.6 mg/kg in celery stalks. Highest TRR levels were identified in lettuce leaves (118-170 mg/kg) and in celery, beans and carrot foliage (13-263 mg/kg). However, in carrot roots, the TRR was in the range of 0.01-0.07 mg/kg, leading to the conclusion that translocation from foliage to roots is very limited.

Two metabolites (R182281 and R611965) were identified. The major identified metabolite in primary crops, R182281, never reached a level higher than 10% of the level of the parent compound in edible parts. Only in carrot foliage at longer post-harvest intervals did R182281 represent the major identified residue component. The relative R182281 levels in carrot foliage increased from 14% of the identified residue at a PHI of 7 days to 75% at a PHI of 21 days. The level of R611965 always remained below the LOQ. There were some indications for the existence of other metabolites but all were considered to be toxicologically not relevant as they were water-soluble and assumed to be glutathione conjugates.

A comparison of the data in the different crops indicates that the biotransformation of chlorothalonil is qualitatively similar and chlorothalonil represents the major residue component. In general, this compound accounted for at least 50% of the total residue and over 90% of the identified residue

components in edible parts. Other identified residue components generally accounted for less than 5% of the total residue in edible portions and frequently remained below the LOQ.

The metabolism of chlorothalonil in plants was not highly extensive. It involves the substitution of chlorine by a hydroxyl group, leading to metabolite R182281.

The residue definition for both enforcement and risk assessment derived in the framework of the Annex I inclusion was parent chlorothalonil.

In an EFSA reasoned opinion[5] it was proposed that R182281 should also be considered for inclusion in in the residue definition for risk assessment purposes. EFSA also proposed that as the occurrence of R182281 in processed commodities is expected, and that the consumer risk assessment for R182281 may result in a more critical outcome than for the parent compound, a residue definition for enforcement of R182281 should also be considered. As R182281 follows a different toxicological mechanism to chlorothalonil, it is appropriate to consider parent chlorothalonil and R182281 separately in the risk assessment.

In their conclusions, EFSA proposed therefore to establish in all plant commodities a residue definition for enforcement and risk assessment of chlorothalonil alone and a separate residue definition for R182281, also for enforcement and risk assessment purposes. This proposal is supported in this dossier.

The metabolism of chlorothalonil in laying hens was investigated. Laying hens were treated with [phenyl-U-^{14}C]-labelled chlorothalonil at dose rates of 0.22, 0.65 and 2.18 mg/kg bw/day for 21 consecutive days. The transfer of residues to eggs and tissues was limited. Total radioactive residues were below the LOD in egg white for all dose levels and in egg yolk at all dose levels except the highest. At the highest dose level the total radioactivity in egg yolk accounted for 0.05 mg/kg. Total residue levels in tissue were all below the LOD except in liver for the middle and highest dose levels.

Laying hens were dosed daily with ^{14}C- R182281 labelled uniformly in the phenyl ring at 0.01, 0.03 and 0.1 mg/kg bw/day for 21 consecutive days. At the lowest dose residue levels were close to or below the LOD in all samples. For the middle dose of 0.03 mg/kg bw/day, significant residues were only found in egg yolk and liver. At the highest dose, significant residues were found in egg yolk (0.06-0.42 mg/kg), cardiac muscle (0.15 mg/kg), liver (0.12-0.78 mg kg) and skin (0.37 mg/kg).

In a third study laying hens were dosed orally with [phenyl-U-^{14}C]-chlorothalonil for 14 days at a nominal rate of 15 mg/kg. In excreta, 91% of the administered dose was recovered. The major component in urine was chlorothalonil (43.2% TRR) with R182281 (2.3% TRR) the only other identified metabolite. Chlorothalonil was not detected in any of the tissue and egg samples. The metabolite R182281 was the only identified residue and was found in significant levels in liver (35.9% TRR, 0.05 mg/kg) and egg yolk (12.5% TRR, 0.011 mg/kg).

The metabolism of chlorothalonil and R182281 has been studied in lactating ruminants.

Lactating goats were dosed with [phenyl-U-^{14}C]-chlorothalonil at a rate of 6 or 60 mg/day (equivalent to 0.115 and 1.15 mg/kg bw/day). The majority of the radioactivity was excreted. Parent chlorothalonil was not detected in milk and edible tissue samples. R182281was the only identified metabolite in milk and tissue samples. In liver and kidney, between 17 and 37% of the residue was characterised as organosoluble and 20-30% of this fraction consisted of multiple non-polar residues. The remaining water soluble residues consisted of protein bound and smaller conjugated residue compounds.

[5]Reasoned opinion on the review of the existing maximum residue levels (MRLs) for chlorothalonil according to Article 12 of Regulation (EC) No 396/2005", EFSA Journal 2012;10(10):2940

In a second study, lactating goats were administered ^{14}C- R182281, labelled uniformly in the phenyl ring at rates of 0.4 and 4 mg daily for 9 consecutive days. Radioactivity excreted via urine and faeces accounted for 6-19 % of the total radioactive residue. The highest total residues were detected in kidney, followed by liver, muscle and fat. Over 90 % of the total residue in milk and tissues samples was characterised as organosoluble and over 90 % of this fraction was attributable to unchanged R182281. No other identifiable metabolites were detected in the milk or tissue samples. In urine, the metabolite 2,4,5-trichloro-6-hydroxy-3-cyanobenzamide (R611968) accounted for 3.6% TRR.

The residue definition for both enforcement and risk assessment previously derived in the framework of the Annex I inclusion was R182281. On the basis of the additional metabolism data discussed in this document it is proposed that this definition does not change. This is consistent with the conclusions of EFSA in their reasoned opinion (EFSA Journal 2012; 10(10): 2940).

Residue trials in tomato, barley, wheat and potato conducted in the EU to support the proposed EU GAP were provided.

~~Sixteen supervised residue trials were conducted on tomatoes in northern and southern Europe. Treatments with chlorothalonil were conducted as post emergence (BBCH 69-89) spray applications at a nominal application rate of 1000 g a.s./ha with an interval of 7 days between applications. Samples were analysed for residues of parent chlorothalonil and the metabolite R182281 with an LOQ of 0.01 mg/kg for both compounds.~~

~~The available trials are sufficient to support the EU critical GAP for tomato. Residues found in the trials from northern and southern Europe are comparable, leading to the same STMR value and similar HR values.~~

~~The data from trials supporting the proposed EU critical GAP indicate that residues will be within the recently proposed EU MRL of 6 mg/kg; however the MRL calculated for northern Europe data according to the OECD method gives a value of 7 mg/kg. Taking into account the data from both northern and southern Europe gives sufficient confidence that the MRL of 6 mg/kg for chlorothalonil will not be exceeded.~~

~~There are currently no EU MRLs for R182281. The data from trials supporting the proposed EU critical GAP indicate that an MRL of 0.015 mg/kg is appropriate.~~

Sixteen supervised residue trials were conducted on tomatoes in northern and southern Europe. Treatments with chlorothalonil were conducted as post emergence (BBCH 61-89) spray applications at a nominal application rate of 1 x 1000 g a.s./ha. Samples were analysed for residues of parent chlorothalonil and the metabolite R182281 with an LOQ of 0.01 mg/kg for both compounds.

The available trials are sufficient to support the EU critical GAP for tomato. Residues found in the trials from northern and southern Europe are comparable, leading to the same STMR value and similar HR values.

The data from trials supporting the proposed EU critical GAP indicate that residues will be within the recently proposed EU MRL of 6 mg/kg. Taking into account the data from both northern and southern Europe provides sufficient confidence that the MRL of 6 mg/kg for chlorothalonil will not be exceeded.

There are currently no EU MRLs for R182281. The data from trials supporting the proposed EU critical GAP indicate that an MRL of 0.01 mg/kg is appropriate.

Thirty-two supervised residue trials were conducted on barley in 2011, 2012, 2013 and 2014 in northern or southern Europe. Treatments with chlorothalonil were conducted as post emergence (BBCH 30-32 and BBCH 59) spray applications at a nominal application rate of 750 g a.s./ha. Samples were analysed for

residues of chlorothalonil and R182281 with an LOQ of 0.01 mg/kg for chlorothalonil and an LOQ of 0.01 mg/kg or 0.02 mg/kg for R182281. The available trials are sufficient to support the EU critical GAP for barley.

The data from trials supporting the proposed EU critical GAP suggest that a MRL value of 0.3 mg/kg for chlorothalonil is appropriate. There are currently no EU MRLs for R182281. The data from trials supporting the proposed EU critical GAP indicate that a MRL of 0.04 mg/kg is appropriate.

Thirty-two supervised residue trials were conducted on wheat in 2012, 2013 and 2014 in northern or southern Europe. Treatments with chlorothalonil were conducted as post emergence (BBCH 30-32 and BBCH 69) spray applications at a nominal application rate of 750 g a.s./ha. Samples were analysed for residues of chlorothalonil and R182281 with an LOQ of 0.01 mg/kg for chlorothalonil and an LOQ of 0.01 mg/kg or 0.02 mg/kg for R182281. The available trials are sufficient to support the EU critical GAP for wheat.

The data from trials supporting the proposed EU critical GAP indicate that residues of chlorothalonil will be within the existing EU MRL of 0.1 mg/kg. There are currently no EU MRLs for R182281. The data from trials supporting the proposed EU critical GAP indicate that an MRL of 0.02 mg/kg (LOQ) is appropriate.

Eight supervised residue trials were conducted on field grown potato in 2013 and 2014, in northern or southern Europe. Three treatments with chlorothalonil were conducted as post emergence (BBCH 39-47 based on growth stages of the tuber) spray applications at a nominal application rate of 750 g a.s./ha with an interval of 7 days between applications and PHI of 28 days. Samples were analysed for residues of chlorothalonil and R182281 with an LOQ of 0.01 mg/kg for chlorothalonil and an LOQ of 0.02 mg/kg for R182281.

The available trials are sufficient to support the EU critical GAP for potato. 4 acceptable trials are available for northern Europe and 4 acceptable trials are available for southern Europe. Although generally a minimum of 8 trials are required in each region the residue of both chlorothalonil and R182281 were below the LOQ in all trials, therefore a reduced data set of 4 trials for each region is acceptable. The data from trials supporting the proposed EU critical GAP indicate that residues of chlorothalonil will be within the existing EU MRL of 0.01 mg/kg (LOQ). There are currently no EU MRLs for R182281. The data from trials supporting the proposed EU critical GAP indicate that an MRL of 0.02 mg/kg (LOQ) is appropriate.

The potential dietary exposure of poultry, dairy cattle, beef cattle and pigs to chlorothalonil and R182281 residues in the supported representative crops of tomato, barley, wheat and potato or their processed products has been calculated.

The maximum dietary burden of combined residues of chlorothalonil and R182281 in poultry is 0.0089 mg/kg bw/day. The highest median dietary burden of combined residues of chlorothalonil and R182281 in poultry is 0.014 mg/kg bw/day.

In metabolism studies, laying hens were treated with ^{14}C-chlorothalonil at dose rates equivalent to 2.5, 7.3 and 24 times the estimated maximum intake of chlorothalonil and R182281 combined. Total radioactive residues were below the LOD in egg white, egg yolk and all tissues at the lowest dose level. In a recent study (2014), hens were dosed at a rate equivalent to 11 times the estimated maximum intake. Residues of R182281 were 0.01 mg/kg in egg yolk, 0.003 mg/kg in whole egg, 0.05 mg/kg in liver and 0.004 mg/kg in skin with fat. Residues in muscle were < 0.001 mg/kg. Residues in eggs and tissues at the maximum and median estimated intakes of chlorothalonil (0.078 mg/kg) are therefore expected to be < 0.01 mg/kg.

It can be concluded that residues of R182281 will not occur in poultry products at levels above 0.01 mg/kg on the basis of livestock intakes of chlorothalonil and R182281. MRLs for poultry products are not required.

The maximum dietary burden of combined residues of chlorothalonil and R182281 in ruminants is 0.216 mg/kg bw/day for lambs. . The highest estimated livestock intake of combined chlorothalonil and R182281 residues for dairy cattle is 0.111 mg/kg bw/day and for beef cattle is 0.071 mg/kg bw/day. The median estimated livestock intake of combined chlorothalonil and R182281 residues is 0.060 mg/kg bw/day for lambs. The median estimated livestock intake of combined chlorothalonil and R182281 residues for dairy cattle is 0.040 mg/kg bw/day and for beef cattle is 0.027 mg/kg bw/day.

Feeding studies conducted at dose rates relevant to the estimated dietary burden and where a combined dose of chlorothalonil and R182281 was used were chosen as being most relevant to derive residue levels in products of animal origin. Groups of cattle were dosed with a mixture of chlorothalonil and R182281 (ratio of 15:1) at 1.5, 3, 9 and 30 mg/kg chlorothalonil in the diet for 27/28 days. The combined dose rates of both chlorothalonil were calculated to be 1.59, 3.19, 9.56 and 31.86 mg/kg in the diet.

MRL, STMR and HR values for ruminant products of animal origin have been proposed by interpolation between the maximum or mean residues measured at the relevant dose levels for the estimated combined maximum or median chlorothalonil and R182281 intake values.

Calculated only for the supported crop use in this submission, the maximum dietary burden of combined residues of chlorothalonil and R182281in pigs is 0.013 mg/kg bw/day for breeding swine. Metabolism and feeding studies in pigs are not required, as data for ruminants can be used to address the potential for residues in pigs. MRL, STMR and HR values for products of swine origin have been proposed by extrapolation from the lowest dose level of 0.061 mg/kg bw/day combined residue.

The hydrolytic stability of [phenyl-U-^{14}C]-labelled chlorothalonil was investigated in aqueous buffer solutions at three pH values and temperatures to simulate pasteurisation, baking/brewing/boiling, and sterilisation. Chlorothalonil undergoes hydrolysis at two positions in the molecule; nucleophilic substitution of a chloride ion by a hydroxyl group to give R182281 and hydrolysis of the cyano functionality to give the amide R613636. Both temperature and pH are determining factors in the hydrolysis of chlorothalonil.

The magnitude of chlorothalonil residues in processed tomatoes, wheat and barley was investigated. Residues of chlorothalonil are not expected to concentrate in tomato or wheat and barley processed products with the exception of wheat bran and a slight increase in tomato pomace. Residues of R182281 are not expected to concentrate in wheat and barley processed products with the exception of wheat bran. Residues of R182281 are not expected to concentrate in tomato juice but were shown to concentrate in wet and dry tomato pomace, tomato puree and canned tomato. Suitable transfer factors have been derived. Processing data for potatoes are not required as residues in whole tubers were < LOQ for both chlorothalonil and R182281.

A confined rotational crop study was evaluated. At 30 and 80 days after soil treatment with [phenyl-U-^{14}C] - chlorothalonil, the major soil residue compound was R611965 (almost 25% of the total soil residues), followed by chlorothalonil. R611965 was the major residue compound identified in rotational crop samples with R182281 present at low levels. Chlorothalonil was not detected in crop samples.

In additional confined crop rotation studies treated with [phenyl-U-^{14}C]-chlorothalonil at 7.5 kg a.s./ha, in all crops the majority of the radioactive residue was assigned to the metabolites R611965 and R417888. Up to 30% TRR in was assigned as conjugated material. Other identified metabolites identified, including R611553, R182281 and R612636, represented minor percentages of the TRR. R611968 accounted for up to 10% TRR in grain. No chlorothalonil was detected in any crop.

In representative crops, grown in soil treated with phenyl-U-^{14}C]-chlorothalonil and aged for 30 days, chlorothalonil was detected only in radish root samples, and only at very low levels. The major identified metabolite was R611965 which represented 14% TRR (or 0.006 mg/kg) in mature spinach and represented 25% TRR (or 0.030 mg/kg) in barley straw. In the radish root R611965 amounted to 8.3% TRR (0.002 mg/kg). The metabolite R182281 was also identified in spinach, radish root and mature barley samples, however at levels less than 0.01 mg/kg. The remaining radioactive fractions corresponded mainly to conjugates and did not exceed 10% TRR, 0.01 mg/kg for edible plant material (human food) or 0.05 mg/kg for animal feed items.

The metabolism of chlorothalonil in rotational crops is similar to that in primary crops, though levels of R611965 were higher in rotational crops metabolism studies. The proposed definition of the residue in primary and following crops is the same.

In rotational crop field studies, sites in the USA were sprayed with 8 applications of chlorothalonil at a rate of 2.5 kg a.s/ha. Representative crops were planted at intervals up to 1 year after application. No residues of chlorothalonil were detected in the any of the crop samples. Low levels of R182281were found in samples at all plant-back intervals (< 0.05 mg/kg). R611965 was the major compound identified in rotational crop samples for plant-back intervals up to 90 days. In a second study, various primary crops grown across the USA were treated with chlorothalonil at rates ranging from 3 applications at 1.7 kg a.s./ha to 8 applications at 2.6 kg a.s./ha. The primary crops were harvested at normal maturity, and following crops were planted. R611965 was the major metabolite detected in the rotational crops. In root and tuber vegetable crops residues were < 0.03 – 0.64 mg/kg and <0.03 – 0.59 mg/kg for roots. For leafy vegetables residues were < 0.03 – 0.80 mg/kg and for fruiting vegetables residues were <0.03 – 1.05 mg/kg. In cereals residues in grain were < 0.03 – 0.4 mg/kg, and <0.03 – 3.0 mg/kg in straw. Residues in oilseeds and dried pulses were all < 0.05 mg/kg. Residues of chlorothalonil were not found at levels greater than 0.03 mg/kg, except peanut vines (0.22 mg/kg), pea fodder and bean hay (0.06 and 0.09 mg/kg, respectively). One residue of R182281was found in pea fodder at 0.07 mg/kg; R182281 levels were all at or below 0.04 mg/kg in all other samples.

Chlorothalonil was applied to bare soil at a rate of 2000 g a.s/ha at one trial site in Germany and one trial site in the United Kingdom. At each rotational interval representative cereal, leafy vegetable and root vegetable crops were sown. Samples of representative food and feed items were analysed for residues of chlorothalonil, R182281 and R611965. For all plant-back intervals (PBIs) no residues of chlorothalonil or R182281 were found at or above the LOQ (0.01 mg/kg) in any of the treated samples. No residues of R611965 were found at or above the LOQ in the any of the samples from the 365 day PBI. Residues of R611965 were found in samples taken after the 30 and 60 day PBIs only.

The maximum total application rate proposed for chlorothalonil is 2 kg a.s./ha for tomatoes (field crops), 1.5 kg a.s./ha for cereals and 2.25 kg a.s./ha for potatoes. The proposed uses for tomatoes and potatoes involve spraying when crop foliage is present meaning there will be some crop interception and not all the spray will be in contact with the soil. On this basis and considering the results of the EU crop rotation trials where application at 2 kg a.s./ha was made to *bare soil* it can be concluded that residues of chlorothalonil and R182281 in following crops are not expected to exceed 0.01 mg/kg. Residues of R611965 may be expected at low levels in following crops. However this metabolite is of lower toxicity than parent chlorothalonil and is not included in the residue definition for either monitoring or risk assessment.

Residues of chlorothalonil and R182281 are not expected in following crops above the LOQ and it is not necessary to propose MRLs in following crops for either chlorothalonil or R182281.

Long-term consumer exposure to potential residues of chlorothalonil and R182281 resulting from the proposed representative use of chlorothalonil have been estimated according to the EFSA PRIMo model

for chronic risk assessment. No change from the existing EU ADI of 0.015 mg/kg body weight/day for chlorothalonil and 0.01 mg/kg body weight/day for R182281 is proposed.

The highest TMDI for chlorothalonil is for WHO Cluster diet B and represents 130% of the ADI. A refined NEDI calculation has therefore been conducted based on proposed STMR values derived from supervised residue trials. The highest NEDI is for the WHO Cluster diet B and represents 18% of the ADI. The highest TMDI for R182281 is for the French toddler and represents 22% of the ADI. As the TMDI value is significantly less than the ADI for R182281 it is not necessary to calculate NEDI values. There is no unacceptable chronic risk to human health from the consumption of commodities containing residues of chlorothalonil or R182281 arising from tomato, barley, wheat and potato treated with chlorothalonil according to the proposed uses.

Short-term consumer exposure to potential chlorothalonil and R182281residues is estimated according to the EFSA PRIMO model for acute risk assessment. No change from the existing EU ARfD of 0.6 mg/kg body weight/day for chlorothalonil is proposed. A change to the existing EU ARfD for R182281 to 0.03 mg/kg body weight/day is proposed.

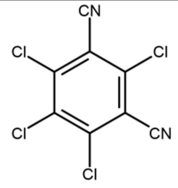
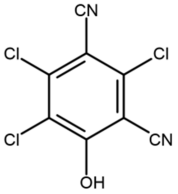
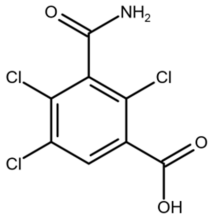
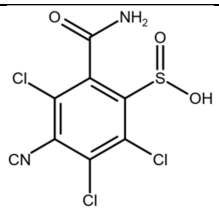
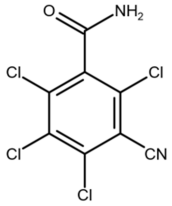
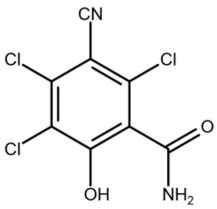
The highest estimated short-term intake for chlorothalonil is for the consumption of tomatoes by children (based on consumption data from Belgium) and represents 40% of the ARfD. The highest estimated short-term intake for R188281 is for the consumption of milk by UK Infants and represents 21% of the ARfD. There is no unacceptable acute risk to human health from the consumption of commodities containing residues of chlorothalonil or R182281 arising from tomato, barley, wheat and potato treated with chlorothalonil according to the proposed uses.

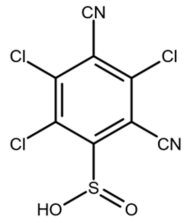
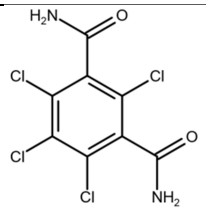
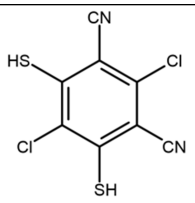
Appendix 1: Summary of the intended use pattern

Crop and/ or situation (a)	Member State or Country	Code name	F G or I (b)	Pests or Group of pests controlled (c)	Formulation		Application				Application rate per treatment			PHI (days) (l)	Remarks: (m)
					Type (d-f)	Conc. of as (i)	method kind (f-h)	growth stage & season (j)	number min max (k)	interval between applications (min)	g as/hL min max	water L/ha min max	g as/ha max		
Wheat	EU	A14111B Chlorothalonil 500 g/L SC; ARY-0474-001	F	*Pyrenophora teres, Puccinia hordei, Rhynchosporium secalis,Gaeumanomyces graminis var tritici Septoria sp*	SC	a) Chlorothalonil: 400 g/l b) Azoxystrobin: 80g/l	Foliar	BBCH 30-69	2	14 (not before GS 40)	-	100-400	a) 750 b) 150	n.a.	No need to set PHI. See growth stage at last application
Barley	EU	A14111B Chlorothalonil 500 g/L SC; ARY-0474-001	F	*Pyrenophora teres, Puccinia hordei, Rhynchosporium secalis,Gaeumanomyces graminis var tritici*	SC	a) Chlorothalonil: 400 g/l b) Azoxystrobin: 80g/l	Foliar	BBCH 30-59	2	14 (not before GS 40)	-	100-400	a) 750 b) 150	n.a.	No need to set PHI. See growth stage at last application
Tomatoes	EU	A14111B Chlorothalonil 500 g/L SC; ARY-0474-001	F	*Phytophthora infestans, Alternaria sp. Botritis cinereza*	SC	a) Chlorothalonil: 400 g/l b) Azoxystrobin: 80g/l	Foliar	BBCH 51-89	1	-	-	500-1500	a) 1000 b) 200	3	
Potatoes	EU	Chlorothalonil 500 g/L SC	F	*Phytophthora infestans Alternaria solani*	SC	Chlorothalonil: 500 g/l	Foliar	BBCH 40-85	1	-	-	200-800	750	28	Growth stages are expressed for foliage. The equivalent growth stages for tubers are BBCH 39-47

Remarks:
(a) For crops, the EU and Codex classifications (both) should be used; where relevant, the use situation should be described (*eg.* fumigation of a structure)
(b) Outdoor or field use (F), glasshouse application (G) or indoor application (I)
(c) eg. biting and suckling insects, soil born insects, foliar fungi, weeds
(d) eg. wettable powder (WP), watersoluble granule (WG)
(e) GCPF Codes - GIFAP Technical Monograph No 2, 1989
(f) All abbreviations used must be explained
(g) Method, eg. high volume spraying, low volume spraying, spreading, dusting, drench
(h) Kind, eg. overall, broadcast, aerial spraying, row, individual plant, between the plants - type of equipment used must be indicated
(i) g/kg or g/l
(j) Growth stage at last treatment (BBCH Monograph, Growth Stages of Plants, 1997, Blackwell, ISBN 3-8263-3152-4), including where relevant, information on season at time of application
(k) The minimum and maximum number of application possible under practical conditions of use must be provided
(l) PHI - minimum pre-harvest interval
(m) Remarks may include: Extent of use/economic importance/restrictions

Appendix 2: List of metabolites and related structural formulae

Common name/code	Structural formula
Chlorothalonil	
R182281 (SDS-3701)	
R611965 (SDS-46851)	
R417888 (VIS-01)	
R613636 (SDS-19221)	
R611968 (SDS-47525)	

Common name/code	Structural formula
R611553	
VIS 02	
Compound C15	

Appendix 3: Additional studies

The following studies are not relied upon and the reports are not included in the dossier. However summaries are provided for information.

Report:	App3/01. Lister N. (2001), Chlorothalonil: storage stability in various prepared crops stored deep frozen for up to one year. Syngenta, Jealott's Hill International Research Centre, Bracknell, UK. Syngenta Report Number RJ2967B. Syngenta File No R44686/2176

Guidelines

Not stated but meets the requirements of Guideline: Commission of the European Communities: Storage Stability of Residue Samples (**SANCO 7032/V1/95 rev. 5 22/7/1997**).

GLP

The study was carried out according to the principles of Good Laboratory Practice.

EXECUTIVE SUMMARY

Samples of peach, strawberry, orange, potato, carrot, bulb onion, head cabbage, leek, pea, lentil, tomato, melon, sugar beet, barley straw and barley forage were fortified with chlorothalonil at 1.0 mg/kg, stored under frozen conditions (≤-18° C) and analysed at intervals up to 12 months (three or four time points). The LOQ was 0.01 mg/kg. All samples other than lentils and barley straw were prepared in the presence of acid.

There was no significant decrease in the levels of chlorothalonil in peach, strawberry, orange, potato, carrot, bulb onion, head cabbage, leek, lentil, tomato, melon, sugar beet and barley forage tested over 12 months. Residues of chlorothalonil were therefore stable for at least 12 months in these commodities when stored in the freezer at ≤-18°C.

Residue of chlorothalonil decreased by more than 30% in pea stored for 6 months or longer. Residues of chlorothalonil were therefore stable for 3 months in pea when stored in the freezer at ≤-18°C. Residue of chlorothalonil also decreased in barley straw but the recoveries in barley straw at zero time were low and therefore the results in barley are inconclusive.

I. MATERIALS AND METHODS

A. MATERIALS

A1. Test Materials

The purity of the analytical standard used in this study is listed in Table APP3-1.

Table APP3-1: Purity of analytical standards

Analyte	Standard reference no.	Purity (wt. %)
Chlorothalonil	ASJ10125-03S ASW01791-01A	99.6 99.5

A2. Test Commodity

Sugar beet, barley straw and barley forage were obtained from Syngenta field trials. The peach, strawberry, orange, potato, carrot, bulb onion, head cabbage, leek, pea, lentil, tomato and melon commodities were purchased.

A3. Test Facilities

Sample preparation and analysis was performed at Syngenta, Jealott's Hill International Research Centre, Bracknell, Berkshire, RG42 6EY, UK.

B. STUDY DESIGN AND METHODS

B1. Fortification and Storage of Samples

The peaches, strawberries, oranges, potatoes, carrots, bulb onions, head cabbages, leeks, peas, tomatoes, melons, sugar beet and barley forage were homogenised with sulphuric acid. The barley straw was milled. The lentils received no preparation. All samples were frozen at ≤-18°C.

The bulk samples were allowed to thaw and sub-samples (11 g for samples prepared with acid or 10 g for samples prepared without acid) were fortified with chlorothalonil in toluene at 1.0 mg/kg. Triplicate samples were stored under frozen conditions (≤-18°C) and analysed at intervals up to 12 months (four time points). Control samples were analysed at the zero time and at each time point.

B2. Analytical Method

Analysis of the samples was performed according to analytical method RAM 320/01 or RAM 320/02 at intervals of 0, 3, 6, 9 and 12 months. At the 3 month and subsequent time points, the lentil grains were ground in extraction solvent using an Ultra-Turrax homogeniser. At zero time the lentil grains were shaken in extraction solvent.

The method involved extraction of the samples into acidified acetone and clean-up by adsorption chromatography on a C18 cartridge. Final determination was gas chromatography using a mass selective detector operating in selective ion monitoring mode (GC-MSD). The LOQ was 0.01 mg/kg.

The method validation is reported in report number RJ2872B. Full method descriptions and validation data are presented in document M-CA Section 4, CA 4.1.2.

Commodity	Author/s	Issue Year	Report Number
High water, high acid, high protein, high starch, dry crops	Lister, N	2000	RJ2872B

II. RESULTS AND DISCUSSION

Method Validation

Procedural recoveries were determined using freshly fortified samples. Samples were fortified with chlorothalonil at 1.0 mg/kg. Individual recoveries, mean recoveries and %RSD are summarised in Table APP3-2.

Table APP3-2: Summary of procedural recoveries for chlorothalonil

Crop	Fortification level (mg/kg)	Recovery (%)	Mean recovery (%)	RSD (%)
Peach	1.0	97, 97, 80, 83, 86, 92, 96, 93	91	7
Strawberry	1.0	90, 87, 86, 83, 88, 93, 86, 100	89	6
Orange	1.0	93, 90, 92, 83, 97, 99, 100, 99	94	6
Potato	1.0	95, 92, 87, 91, 100, 97, 98, 96, 98, 101	96	5
Carrot	1.0	97, 94, 79, 87, 91, 92, 89, 97	91	7
Bulb onion	1.0	98, 96, 90, 89, 98, 96, 101, 97	96	4
Head cabbage	1.0	95, 96, 83, 78, 94, 94, 109, 105	94	11
Leek	1.0	87, 94, 76, 78, 85, 99, 102, 104, 86, 103, 87, 98, 97, 96	92	10
Pea	1.0	84, 88, 80, 81, 87, 84, 97, 93, 96, 94, 94, 97	90	7
Lentil	1.0	78, 90, 77, 94, 92, 83, 78, 81	84	8
Tomato	1.0	81, 89, 80, 89, 88, 94, 90, 87	87	5
Melon	1.0	84, 93, 95, 97, 91, 92, 90, 91	92	4
Sugar beet	1.0	85, 84, 76, 80, 100, 103, 100, 102	91	12
Barley straw	1.0	73, 69, 91, 89, 90, 96, 84, 95, 90, 88, 86, 88	87	9
Barley forage	1.0	85, 92, 77, 86, 89, 93, 90, 88	88	6

Storage Stability of Residues

The recoveries of chlorothalonil in commodities stored at ≤-18°C are summarised in Table APP3-3.

Table APP3-3: Freezer storage stability for chlorothalonil

Sampling interval (nominal months)	Sampling interval (actual days)	Recovery (%), uncorrected	Mean uncorrected recovery (%)	Mean procedural recovery (%)	Mean recovered uncorrected recovery (% of time 0)
Peach					
0	1	91, 89, 96	92	91	100
3	80	83, 89, 82	85		92
6	187	80, 84, 88	84		91
12	729	102, 98, 97	99		108
Strawberry					
0	1	96, 94, 95	95	89	100
3	80	91, 90, 83	88		93
6	187	84, 89, 84	86		91
12	729	99, 96, 88	94		99
Orange					
0	2	93, 95, 91	93	94	100
3	81	83, 87, 81	84		90
6	184	89, 95, 82	89		96
12	730	91, 92, 81	88		95
Potato					
0	2	100, 94, 96	97	96	100
3	81	88, 82, 78	83		86
6	184, 192	77, 78, 79, 94, 97, 96	87		90
12	730	91, 84, 82	86		89
Carrot					
0	0	94, 94, 91	93	91	100
3	79	86, 79, 70	78		84
6	185	87, 92, 98	92		99
12	731	95, 92, 95	94		101
Bulb onion					
0	0	99, 92, 98	96	96	100
3	79	69, 89, 81	80		83
6	185	78, 100, 91	86		90
12	731	95, 90, 89	91		95
Head cabbage					
0	3	97, 97, 101	98	94	100
3	90	86, 82, 86	85		87
6	181	91, 94, 86	90		92
12	366	87, 92, 96	92		94
Leek					
0	0	93, 92, 92	92	92	100
3	90	66, 82, 85	78		85
6	181	85, 88, 82	85		92

Sampling interval (nominal months)	Sampling interval (actual days)	Recovery (%), uncorrected	Mean uncorrected recovery (%)	Mean procedural recovery (%)	Mean recovered uncorrected recovery (% of time 0)
12	363, 369, 378	82, 66, 65, 86, 82, 71, 81, 84, 78, 80, 76, 81	78		85
Pea					
0	1	93, 91, 99	91	90	100
3	89	75, 75, 76	75		82
6	180, 181	63, 65, 64, 61, 63, 62	63		69
9	271	51, 53, 63	56		62
12	363	60, 56, 51	56		62
Lentil					
0	24	88, 92, 89	90	84	100
3	109	86, 83, 85	85		94
6	193	76, 80, 82	79		88
12	382	79, 78, 76	78		87
Tomato					
0	0	88, 96, 92	92	87	100
3	92	88, 85, 84	86		95
6	181	90, 83, 96	90		98
12	370	89, 95, 84	89		97
Melon					
0	0	94, 94, 94	94	92	100
3	91	90, 88, 92	90		96
6	180	87, 99, 91	92		98
12	369	84, 89, 92	88		94
Sugar beet					
0	6	85, 87, 83	85	91	100
3	91	86, 79, 82	82		96
6	183	94, 85, 97	92		108
12	370	89, 84, 95	89		105
Barley straw					
0	0	72, 76, 72	73	87	100
3	92	76, 73, 86	78		107
6	183	70, 69, 66, 69, 70, 71	69		95
9	273	59, 59, 61	60		82
12	367	53, 51, 55	53		73
Barley forage					
0	0	92, 95, 87	91	88	100
3	92	77, 81, 83	80		88
6	182	79, 82, 81	81		89
12	370	80, 84, 82	82		90

Mean recovered uncorrected recovery = mean uncorrected recovery / recovery at time 0 x 100.

III. CONCLUSIONS

Residues of chlorothalonil were stable in peach, strawberry, orange, potato, carrot, bulb onion, head cabbage, leek, lentil, tomato, melon, sugar beet and barley forage for at least 12 months when stored in the freezer at ≤-18°C. Residues of chlorothalonil were stable in peas for 3 months when stored in the freezer at ≤-18°C. All commodities except lentils were prepared in the presence of acid.

The report concludes that residues of chlorothalonil were stable in barley straw for 6 months when stored in the freezer at ≤-18°C. However, the recoveries in barley straw at zero time were low and therefore the results in barley are inconclusive. The barley straw was not prepared in the presence of acid.

(Lister N, 2001)

Report:	App3/02. Krainz A. (2006), Chlorothalonil: Frozen storage stability in tomato. RCC Ltd, Switzerland. Report Number A71267. (Syngenta File No: R044686_11198).

Guidelines

Commission of the European Communities: Storage Stability of Residue Samples (**SANCO 7032/V1/95 rev. 5 22/7/1997**).

GLP

The study was carried out according to the principles of Good Laboratory Practice.

EXECUTIVE SUMMARY

Samples of homogenised tomato were fortified at 0.2 mg/kg with chlorothalonil. Triplicate samples were stored under frozen conditions (-20°C) and analysed at intervals up to 3 months (three sampling points). The LOQ for chlorothalonil was 0.01 mg/kg.

Residues of chlorothalonil were stable in tomato for at least 3 months when stored in the freezer at -20°C.

I. MATERIALS AND METHODS

A. MATERIALS

A1. Test Materials

The purity of the analytical standard used in this study is listed in Table APP3-4.

Table APP3-4: Purity of analytical standards

Analyte	Standard reference no.	Purity (wt. %)
Chlorothalonil	337-98B	98

A2. Test Commodity

The test commodities were untreated homogenised tomatoes.

A3. Test Facilities

This study was performed at RCC Ltd, Analytics, Zelgliweg 1, CH-4452 Itingen, Switzerland.

B. STUDY DESIGN AND METHODS

B1. Fortification and Storage of Samples

Homogenised samples were fortified at 0.2 mg/kg with chlorothalonil in toluene. Triplicate samples were stored under frozen conditions (-20°C) and analysed at intervals up to 3 months (three sampling points). Control samples were analysed for all time points to ensure that no residues of chlorothalonil were present at levels above 30% of the LOQ.

B2. Analytical Method

Analysis of the samples was performed according to analytical method A75813 at intervals of 0, 1, and 3 months. The method validation is reported in report number A75813 and A71188. A full method description and validation data are presented in document M-CA Section 4, CA 4.1.2.

Commodity	Author/s	Issue Year	Report Number
Tomato	Krainz, A.	2006	A75813
Wheat	Krainz, A.	2006	A71188

The method involved extraction of the samples with acetone/5M sulphuric acid followed by centrifugation. An aliquot of the extract was taken, diluted and subjected to SPE (C18) clean up, before analysis by gas chromatography with electron capture detection (GC-ECD) using two columns of different polarity for quantification and confirmation. The LOQ was 0.01 mg/kg.

II. RESULTS AND DISCUSSION

Method Validation

Procedural recoveries were determined using freshly fortified samples at each interval. Samples were fortified with chlorothalonil at 0.2 mg/kg. Individual recoveries, mean recoveries and %RSD are summarised in Table APP 3-5.

Table APP 3-5: Summary of procedural recoveries for chlorothalonil in tomato

Recovery at zero time (%)	Recovery at 1 month (%)	Recovery at 2 months (%)	Recovery at 3 months (%)	Mean recovery (%)	RSD (%)
100, 107, 103, 100	103	104	103	103	2.3

Storage Stability of Residues

The recoveries of chlorothalonil in tomatoes stored at -20°C are summarised in Table APP 3-6 below. The results are not corrected for freshly fortified recoveries.

Table APP 3-6: Freezer storage stability for chlorothalonil at 0.2 mg/kg in tomato

Sampling interval (nominal months)	Sampling interval (actual days)	Uncorrected residue (mg/kg)	Mean uncorrected residue (mg/kg)	Procedural recovery (%)	Mean recovered uncorrected residue (%)
0	0	0.20, 0.21, 0.21, 0.20	0.21	103	-
1	30	0.17, 0.20, 0.19	0.19	103	95
2	61	0.19, 0.19, 0.18	0.18	104	90
3	92	0.17, 0.18, 0.18	0.18	103	90

Percentage recovered residue = residue concentration / initial residue concentration x 100.
Calculations performed on unrounded values.
No residues were present above the LOQ in control samples.

III. CONCLUSIONS

There was no significant decrease in the observed residue levels of chlorothalonil in tomato after deep frozen storage for 3 months.

(Krainz A, 2006)

Report:	App3/03. Sala A. (2014), Determination of chlorothalonil and its metabolite SDS3701 residues in raw agricultural commodity tomato following two applications of chlorothalonil 500 SC, 2 trials, northern Europe, year 2013. Syngenta File No: R044686_11183. Report Number RAU-024-13.

Report:	App3/04 Sala A. (2014a), Determination of chlorothalonil and its metabolite SDS3701 residues in raw agricultural commodity tomato following two applications of chlorothalonil 500 SC, 2 trials, southern Europe, year 2013. Syngenta File No: R044686_11184. Report Number RAU-023-13

Guidelines

The studies meet the requirements of the Commission of the European Communities: General Recommendations for the Design, Preparation and Realization of Residue Trials (**7029/V1/95 rev. 5, 22/7/1997**), and are designed to comply with **Regulation (EC) 1107/2009**.

GLP

All trials (field and analytical phases) were carried out in compliance with the principles of Good Laboratory Practice.

Materials and Methods

Four supervised residue trials were conducted on field grown tomato in 2013 in northern or southern Europe. A summary of the trials conducted is presented in Table APP 3-7.

Table APP 3-7: Summary of chlorothalonil residue trials on tomato

Country	2013
Northern Europe	
France (north)	2 Harvest
Southern Europe	
France (south)	1 Harvest
Italy	1 Harvest

Decline trials are those with three or more sampling times.

Treatments with chlorothalonil were conducted as post emergence (BBCH 69-89) spray applications utilising the formulation as detailed in Table APP 3-8 at a nominal application rate of 1000 g a.s./ha (actual rates 989 - 1075 g a.s./ha) with an interval of 7 days between applications.

Table APP 3-8: Summary of chlorothalonil formulations used in the presented trials

Product code	Formulation type	Composition
Chlorothalonil 500 SC	SC	502 g/L chlorothalonil (batch O232)

Samples of whole fruits were taken and analysed for residues of parent chlorothalonil and the metabolite R182281 using analytical methods described in report BIU-016-14, with an LOQ of 0.01 mg/kg for chlorothalonil and 0.02 mg/kg for R182281. Full method descriptions and validation data are presented in document M-CA Section 4, CA 4.1.2. Procedural recovery data are presented with the results of the residues trials in Table APP 3-9.

Samples were stored up to a maximum of 8 months from sampling to extraction. Residues of chlorothalonil and R18221 are stable in acidified homogenised tomatoes for at least 24 months (see section CA 6.1) and therefore no degradation will have occurred between sampling and analysis.

The results of the residue trials for chlorothalonil and R182281 are presented in Table APP 3-9.

Table APP 3-9: Summary of residue data supporting the EU critical GAP for chlorothalonil on tomato

GLP and Trial Details	Crop (Variety)	Country (Region)	Application Rate Product Code	Growth Stage at application	PHI (days)	Crop Part (Growth stage at sampling)	Residue Found (Uncorrected)		Recovery Data
							chlorothalonil mg/kg	R182281 (mg/kg)	
Northern Europe									
Report: RAU-024-13 Study: RAU-024-13 Trial: F/CH13/TO03 - Study to GLP - Study carried out in 2013	Tomato (Pyros)	FRANCE (Europe North)	1014 g a.s./ha 989 g a.s./ha 500 g/L SC	BBCH 81 BBCH 85	7	Fruit (BBCH 89)	0.10	<0.02	Chlorothalonil Fruit: mean = 88% RSD = 3.9% (n = 4 in 0.01 -1.0 mg/kg spiking range) R182281 Fruit: mean = 99% RSD = NA (n = 2 in 0.02- 0.20 mg/kg spiking range)
Report: RAU-024-13 Study: RAU-024-13 Trial: F/CH13/TO04 - Study to GLP - Study carried out in 2013	Tomato (Pyros)	FRANCE (Europe North)	1019 g a.s./ha 1031 g a.s./ha 500 g/L SC	BBCH 83 BBCH 83	7	Fruit (BBCH 87)	0.06	<0.02	
Southern Europe									
Report: RAU-023-13 Study: RAU-023-13 Trial: I/CH13/TO01 - Study to GLP - Study carried out in 2013	Tomato (Heinz 3402)	ITALY (Europe South)	1004 g a.s./ha 991 g a.s./ha 500 g/L SC	BBCH 53-54 BBCH 59-61	71	Fruit (BBCH 89)	<0.01	<0.02	Chlorothalonil Fruit: mean = 93% RSD = NA (n = 2 in 0.01 -1.0 mg/kg spiking range) R182281 Fruit: mean = 101% RSD = 6.6% (n = 3 in 0.02- 0.20 mg/kg spiking range)
Report: RAU-023-13 Study: RAU-023-13 Trial: F/CH13/TO02 - Study to GLP - Study carried out in 2013	Tomato (Ondina)	FRANCE (Europe South)	1049 g a.s./ha 1075 g a.s./ha 500 g/L SC	BBCH 55-71 BBCH 57-72	54	Fruit (BBCH 89)	<0.01	<0.02	
Unless otherwise stated residues of chlorothalonil and R182281 in untreated samples were less than the LOQ. NA = not applicable									

(Sala A, 2014 and 2014a)

Report:	App3/06. Balluff M, 2006. Rotational crop study after application of chlorothalonil 500 SC in 2005 on 1 site in northern and southern Europe respectively, 2005-2006, report No. 20054054/E1-FRC, (Syngenta File No: R044686_11219).

Guidelines

FAO Guidelines on Producing Pesticide Residues Data from Supervised Trials (Rome, 1990).

Commission of the European Communities, General Recommendations for the Design, Preparation and Realization of Residue Trials; (**SANCO 7029/V1/95 rev. 5 22/7/1997**)

SETAC (1995): Procedures for assessing the environmental fate and ecotoxicity of pesticides,

European Commission Guidance for Generating and Reporting Methods of Analysis in Support of Pre-registration Requirements for Annex II (Part A, Section 4) of Directive 91/414, SANCO/3029/99 revision 4 (11 Jul 2000).

GLP

The study was carried out according to the principles of Good Laboratory Practice.

EXECUTIVE SUMMARY

Two field trials were conducted during 2005, one in Germany and one in Italy. Chlorothalonil was applied as a suspension concentrate (SC) formulation containing 500 g chlorothalonil per litre to bare soil four times at a rate of 900 g a.s/ha (total application rate 3600 g a.s./ha). Representative cereal (winter wheat), leafy vegetable (lettuce) and root vegetable (carrots and sugar beet) crops were sown into the soil. All crops were grown under field conditions and harvested at immature and mature growth stages. Commodities of representative food and feed items were sampled and analysed for residues of chlorothalonil, R182281, R611965 and R417888. The LOQ was 0.01 mg/kg for chlorothalonil and 0.02 mg/kg for the metabolite in all commodities.

No residues of chlorothalonil, R182281, R611965 or R417888 were found at or above the LOQ (0.01 mg/kg for chlorothalonil and 0.02 mg/kg for the metabolites) in any of the untreated samples.

Chlorothalonil was detected only in two occasions in winter wheat; considering the time of field application and the fast chlorothalonil soil dissipation, as well as the fact that no residues of chlorothalonil were found in any other rotational crops, these residues data are considered outliers.

After all plant-back intervals (PBIs) no residues of R182281 or R417888 were found at or above the LOQ (0.02 mg/kg) in any of the treated samples. A residue of R611965 was found in one sample of immature carrot whole plant taken after the 30 day PBI. Residues of R611965 were below the LOQ for all other samples and all other PBIs.

I. MATERIALS AND METHODS

A. MATERIALS

A1. Test Materials

Test Material	Chlorothalonil 500 SC
Description	Suspension concentrate formulation containing chlorothalonil
Purity	500 g/L
Batch number	BPL 191
Stability of test compound	The test substance is assumed to be stable for the period of use in the study

A2. Test System

Trial site	01, Germany	02, Italy
Soil	Silty sand	Silty sand
Root vegetable	Carrot (variety: Mokum F1)	Carrot (variety: Bolero)
Leafy vegetable	Lettuce (variety: Ponchieto)	Lettuce (variety: Justina)
Cereal	Winter wheat (variety: Astron)	Winter wheat (variety: Mieti)
Root vegetable	Sugar beet (variety: Felicita)	Sugar beet (variety: Licia)

A3. Test Facilities

Field trials	Lower Saxony, Germany	Lodi, Italy
Analytical phase	Sipcam Spa Residue Analysis Unit, Research Centre “Emilio Gagliardini”, Via Vittorio Veneto 81, I-2687 Salerano sul Lambro (Lodi), Italy	

B. STUDY DESIGN AND METHODS

B1. Field Phase

Plots were treated with chlorothalonil formulated as a SC four times at weekly intervals at a rate of 900g a.s./ha (total application rate of 3600 g a.s./ha) in a spray volume of approximately 300 L/ha to bare soil. The soil was aged for 29, 114 and 310 days (trial 1) and 32, 122 and 242 days (trial 2) after which the plots were lightly cultivated before drilling of representative crops of carrot, lettuce, winter wheat and sugar beet. Carrot and lettuce were sown at the 30 day interval, winter wheat at the 120 day interval and sugar beet at the 300 day interval. The crops were grown outdoors in accordance with usual agricultural practice.

Test Samples

Samples of carrot (immature whole plants, mature roots), lettuce (immature plant and mature leaves), carrot (immature whole plants, mature roots), wheat (immature whole plant, mature grain and straw) and sugar beet (immature tops) were taken and the samples were stored deep frozen at <-18 °C before analysis. Samples were stored for up to 12 months before analysis.

Soil samples were taken within 3 hours of the last application, on the days of sowing or transplanting and at the harvest dates of the following crops. Assessments of phytotoxicity were also made shortly after emergence, at immature crop sampling and at harvest.

B2. Analytical Phase

Samples were analysed for chlorothalonil using the following method:

Residues of chlorothalonil were extracted with acidified ethyl acetate and analysed by gas chromatography with an electron capture detector. For method validation, samples fortified at 0.01 mg/kg (11 replicates), 0.05 mg/kg (3 replicates) and 0.1 mg/kg (13 replicates) were analysed, yielding an overall mean accuracy of 93% (%RSD = 7.4, n=27). The mean recovery at the LOQ was 92% (%RSD = 9.9, n=11). An assessment of linearity gave $r^2 > 0.99$.

Samples were analysed for R182281, R611965 and R417888 using the following method:

Residues of the metabolites were extracted with methanol and analysed by liquid chromatography with a mass selective detector in single reaction monitoring acquisition mode. An assessment of linearity gave $r^2 > 0.99$ for all three compounds. Accuracy and precision were determined using fortifications made at 0.02 mg/kg (LOQ, 12 replicates and 0.2 mg/kg (12 replicates). For R182281 the overall mean accuracy was 97% (%RSD = 10, n=24). The mean recovery at the LOQ was 100% (%RSD = 11, n=12). For R611965 the overall mean accuracy was 86% (%RSD = 19, n=24). The mean recovery at the LOQ was 85% (%RSD = 19, n=12). For R417888 the overall mean accuracy was 94% (%RSD = 8.3, n=24). The mean recovery at the LOQ was 97% (%RSD = 7.9, n=12).

II. RESULTS AND DISCUSSION

No phytotoxicity was observed except for slight symptoms in lettuce plants sampled at BBCH 19. Results for residue levels in soil are not presented.

Residues in following crops

The results of the rotational crop trials for chlorothalonil, R182281, R611965 and R417888 are presented in Table APP3-12. The results are not corrected for recoveries.

Table APP3-12: Residues in rotational crops grown in soil treated with chlorothalonil at 3600 g a.s/ha

Commodity	Trial 01, Germany				Trial 02, Italy			
	Chlorothalonil	R182281	R611965	R417888	Chlorothalonil	R182281	R611965	R417888
Plant-back interval: 30 days								
Carrot Immature whole plant	<0.01	<0.02	<0.02	<0.02	<0.01	<0.02	0.032	<0.02
Carrot Mature root	<0.01	<0.02	<0.02	<0.02	<0.01	<0.02	<0.02	<0.02
Lettuce Immature leaves	<0.01	<0.02	<0.02	<0.02	<0.01	<0.02	<0.02	<0.02
Lettuce Mature leaves	<0.01	<0.02	<0.02	<0.02	<0.01	<0.02	<0.02	<0.02
Plant-back interval: 120 days								
Wheat Immature whole plant	<0.01	<0.02	<0.02	<0.02	0.07	<0.02	<0.02	<0.02
Wheat mature grain	-	-	-	-	<0.01	<0.02	<0.02	<0.02
Wheat mature straw	-	-	-	-	0.03	<0.02	-	<0.02
Plant-back interval: 300 days								
Sugar beet tops	<0.01	<0.02	<0.02	<0.02	<0.02	<0.02	<0.02	<0.02

- not analysed.

No residues of chlorothalonil, R182281, R611965 or R417888 were found at or above the LOQ (0.01 mg/kg for chlorothalonil and 0.02 mg/kg for the metabolites) in any of the untreated samples.

Chlorothalonil was detected only in two occasions in winter wheat; considering the time of field application and the fast chlorothalonil soil dissipation, as well as the fact that no residues of chlorothalonil was found in any other rotational crops, these residues data are considered outliers.

After all plant-back intervals (PBIs) no residues of R182281 or R417888 were found at or above the LOQ (0.02 mg/kg) in any of the treated samples. A residue of R611965 was found in one sample of immature carrot whole plant taken after the 30 day PBI. Residues of R611965 were below the LOQ for all other samples and all other PBIs.

III. CONCLUSIONS

No residues of R182281, R611965 or R417888 were found at or above the LOQ (0.02 mg/kg) in any mature crops planted 30, 120 or 300 days after treatment of bare soil with chlorothalonil at a nominal rate of 3600 g a.s./ha. Low residues of chlorothalonil (0.03 mg/kg) were found in straw from following wheat planted 120 days after treatment.

(Balluff M, 2006)