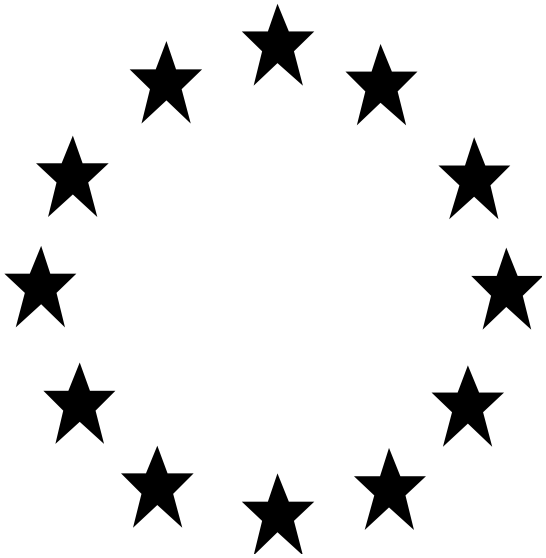

Draft Assessment Report (DAR)

- public version -

Initial risk assessment provided by the rapporteur Member State Sweden for the existing active substance

TOLCLOFOS-METHYL

of the second stage of the review programme referred to in Article 8(2) of Council Directive 91/414/EEC

Volume 3, Annex B, B.7

January 2005

Draft Assessment Report

TOLCLOFOS-METHYL

Rapporteur Member State: Sweden

October 2003

KEMI
NATIONAL CHEMICALS INSPECTORATE

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B.7 Residue data

B.7.1 Metabolism, distribution and expression of residues in plants (Annex IIA 6.1 and Annex IIIA 8.1)

The metabolism and distribution of tolclofos-methyl in plants has been studied in potato and lettuce representing intended use in root vegetables and leafy crops.

B.7.1.1 Root vegetables: Metabolism in potatoes

Reference:	Goodyear, A. (1995) (^{14}C)-Tolclofos methyl: Metabolism of phenyl label in potatoes.	**No of application:**	1
Test substance:	[Phenyl-^{14}C]tolclofos-methyl (Batch No.: C-93-036, Radiochemical purity: >98%, Specific radioactivity: 7.3 MBq/mg)	**Stage of application:**	Surface of seed potatoes.
Dates of experimental work:	June 11,1993 - May 19, 1994	**GLP statement:**	Yes
Test material:	Seed	**Guidelines:**	In house method
Application conc.:	125 mg a.s./kg		

Materials and Methods:

Radiolabelled tolclofos-methyl was applied to the surface of seed potatoes at a rate equivalent to 125 mg a.s./kg. Treated potatoes were planted and maintained in a greenhouse and grown to an immature stage (27 days after planting) and to full maturity (129 days after planting). The harvested plant material was separated into shoots, roots, parent and daughter tubers (where applicable). The plant material was extracted by maceration in the presence of acetone followed by acetone/water (1/1 v/v) and the amount remaining unextracted in the solid residue was determined by combustion analysis. The extracts were analysed by LSC, HPLC, LC/MS-MS, LC/MS and MS-MS.

Findings:

The identity of metabolites present in potatoes is presented in Table B.7.1.1.a. The highest residue was observed in the mature parent tubers (1885.72 mg/kg) and the lowest residue in the mature shoots (0.04 mg/kg). The radioactive residue remaining in the mature daughter tubers was 0.048 mg/kg. The results are presented in Table B.7.1.1.b.

Table B.7.1.1.a: Identity of metabolites

Designation	Chemical name
TM (parent compound)	*O,O*-dimethyl *O*-(2,6-dichloro-4-methylphenyl) phosphorothioate
TMO	*O,O*-dimethyl *O*-(2,6-dichloro-4-methylphenyl) phosphate
DM-TM	*O*-methyl *O*-hydrogen *O*-(2,6-dichloro-4-methylphenyl) phosphorothioate
DM-TMO	*O*-methyl *O*-hydrogen *O*-(2,6-dichloro-4-methylphenyl) phosphate
DM-TM-CH_2OH	*O*-methyl *O*-hydrogen *O*-[2,6-dichloro-4-(hydroxymethyl)phenyl]phosphorothioate
DM-TM-COOH	*O*-methyl *O*-hydrogen *O*-(2,6-dichloro-4-carboxyphenyl)phosphorothioate
ph-COOH	3,5-dichloro-4-hydroxybenzoic acid

Table B.7.1.1.b: Radioactive residues (mg/kg) in immature and mature potato plants following a single application of [phenyl-^{14}C]-tolclofos-methyl to seed potatoes at a rate of 125 mg a.s./kg

Sample	Acetone Extract	Acetone/water Extract	Unextracted residue	Total Residue
Immature shoots	0.21 (84%)	0.029 (12%)	0.016 (6%)	0.25
Immature roots	11.91 (72%)	2.19 (13%)	2.36 (14%)	16.46
Immature parent tuber	53.26 (95%)	2.45 (4%)	0.61 (1%)	56.33
Mature shoots	0.025 (63%)	0.0052 (13%)	0.0092 (23%)	0.040
Mature roots	3.24 (50%)	1.72 (26%)	1.55 (24%)	6.51
Mature parent tuber	1827.82 (97%)	26.31 (1%)	31.59 (2%)	1885.72
Mature daughter tubers	0.029 (60%)	0.0031 (6%)	0.016 (33%)	0.048

Values in parenthesis indicate the percent of the TTR in each extract.

The acetone and acetone/water extracts of immature and mature parent potato tubers contained > 95% TRR present and HPLC analysis showed that the major component present was unchanged tolclofos-methyl in parent tuber. The corresponding extracts from the mature daughter tubers contained 60% and 6% respectively of the TRR present (Table B.7.1.1.b). Tolclofos-methyl was not detected in extracts of daughter tubers. The residue in daughter tubers were DM-TM-CH_2OH (0.013 mg/kg), DM-TM-COOH (0.003 mg/kg) and small amounts (<0.01 mg/kg) of unidentified metabolites (referred to as U2, U3 and U5) (Table B.7.1.1.d).

The immature and mature shoots contained low amounts of residues and the acetone and acetone/water extracts contained 96% and 76% respectively of the TRR present (Table B.7.1.1.b). In immature shoots, TRR comprised small amount of tolclofos-methyl (< 0.01 mg/kg) and the metabolite DM-TM-CH_2OH was the major metabolite at a low level (0.076 mg/kg). Tolclofos-methyl and DM-TM-CH_2OH were not detected in extracts of mature shoots (Table B.7.1.1.c-d).

The acetone and acetone/water extracts of immature and mature roots contained 85% and 76% respectively of the TRR present (Table B.7.1.1.b). The immature roots contained only unchanged tolclofos-methyl (11.955 mg/kg), which decreased to 2.607 mg/kg in the mature roots. In both immature and mature roots (non-edible portions of the crop) there were unidentified metabolites in amounts of 1.147- 1.008 mg/kg and 0.778mg/kg, respectively (Table B.7.1.1.c-d).

Table B.7.1.1.c: Radioactive residue of tolclofos-methyl and its metabolites in immature potato plants

	Radioactive Residue (mg/kg)						
	Shoots			Roots		Parent Tubers	
	Acetone (organic phase)	**Acetone (aqueous phase)**	**Acetone/ Water**	**Acetone**	**Acetone/ Water**	**Acetone**	**Acetone/ Water**
TM (parent)	ND	0.002 (0.9%)	0.001 (0.4%)	11.881 (71.8%)	0.074 (0.4%)	52.424 (93.5%)	2.381 (3.9%)
TMO	ND	ND	ND	ND	ND	ND	ND
DM-TM	0.001 (0.3%)	0.004 (1.5%)	ND	ND	0.049 (0.3%)	ND	ND
DM-TMO	ND	ND	ND	ND	0.060 (0.4%)	ND	ND
Polar metabolites	0.027 (10.0%)	0.162 (65.7%)	0.024 (10.0%)	ND	1.986 (11.8%)	ND	0.049 (0.1%)
DM-TM-CH_2OH	*NA*	*0.076 (30.7%)*	*NA*	*NA*	*0.519 (3.1%)*	*NA*	*NA*
DM-TM-COOH	*NA*	*ND*	*NA*	*NA*	*0.309 (1.8%)*	*NA*	*NA*
ph-COOH	*NA*	*ND*	*NA*	*NA*	*ND*	*NA*	*NA*
U1	*NA*	*0.028 (11.2%)*	*NA*	*NA*	*0.147 (0.9%)*	*NA*	*NA*
U2	*NA*	*0.004 (1.8%)*	*NA*	*NA*	*1.008 (6.0%)*	*NA*	*NA*
U3	*NA*	*0.024 (9.7%)*	*NA*	*NA*	*ND*	*NA*	*NA*
U4	*NA*	*0.018 (7.4%)*	*NA*	*NA*	*ND*	*NA*	*NA*
U5	*NA*	*0.011 (4.4%)*	*NA*	*NA*	*ND*	*NA*	*NA*
Unresolved Background	*NA*	*0.001 (0.5%)*	*NA*	*NA*	*0.003 (<0.1%)*	*NA*	*NA*
Unretained	0.002 (0.6%)	0.009 (3.6%)	0.004 (1.6%)	ND	ND	ND	ND
Unresolved background	<0.001 (0.1%)	0.003 (1.4%)	<0.001 (0.1%)	0.029 (0.2%)	0.021 (0.1%)	0.836 (1.5%)	0.019 (<0.1%)
Total	**0.03 (11%)**	**0.18 (73%)**	**0.029 (12%)**	**11.91 (72%)**	**2.19 (13%)**	**53.26 (95%)**	**2.45 (4%)**

U = unidentified metabolite
NA = not analysed
ND = not detected
Values in parenthesis show the amount of each metabolite present as a percentage of the total residue

Table B.7.1.1.d: Radioactive residue of tolclofos-methyl and its metabolites in mature potato plants

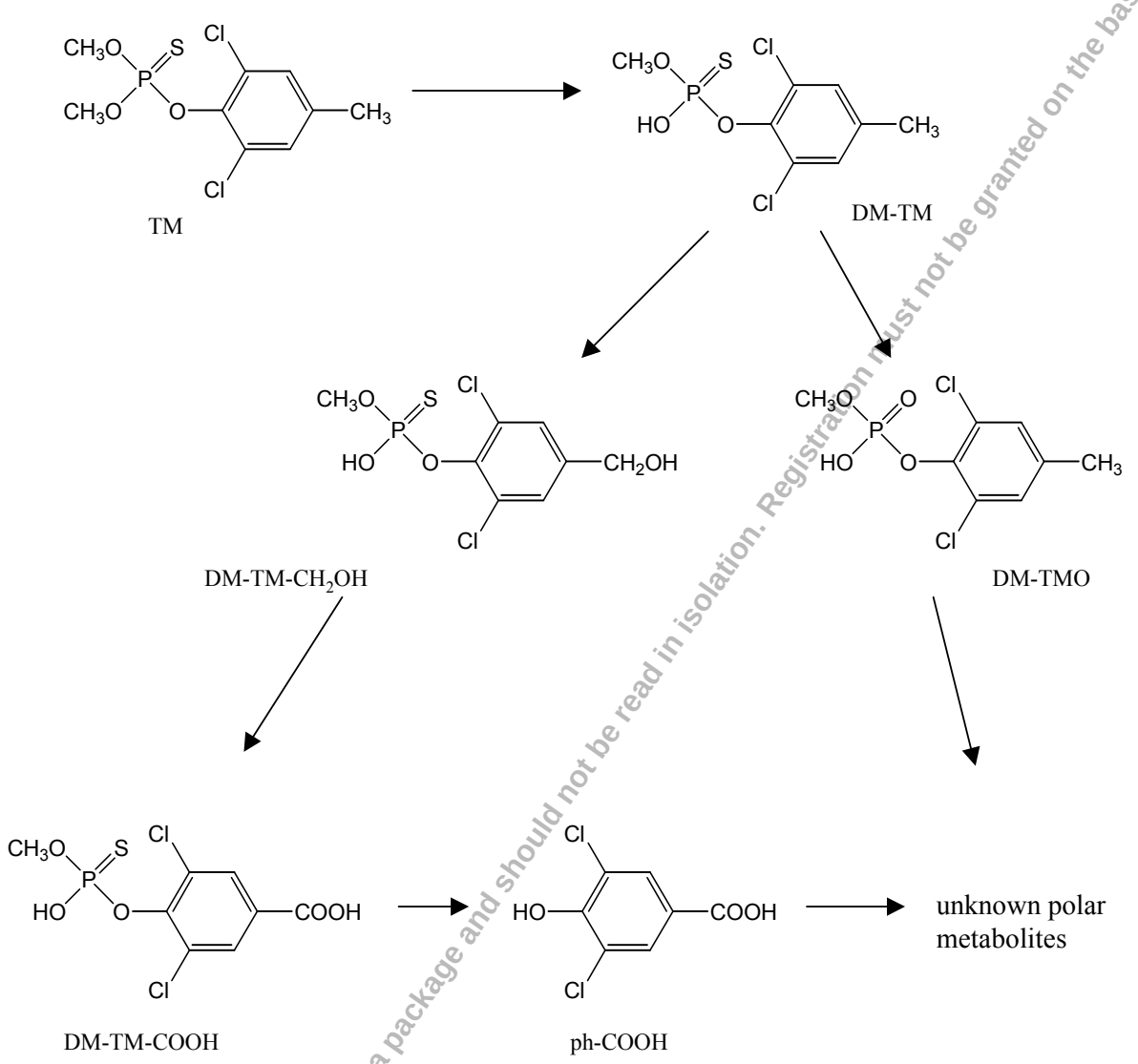
	Radioactive residue (mg/kg)				
	Shoots	**Roots**		**Parent tubers**	**Daughter tubers**
	Acetone	**Acetone**	**Acetone/water**	**Acetone**	**Acetone/water**
TM (parent)	ND	2.607 (40.2%)	ND	1792.178 (95.1%)	ND
TMO	ND	ND	ND	ND	ND
DM-TM	ND	ND	ND	ND	ND
DM-TMO	ND	0.15 (2.3%)	ND	ND	ND
Polar Metabolites	0.023 (57.4%)	0.417 (6.4%)	1.695 (25.6%)	ND	0.027 (56.3%)
DM-TM-CH_2OH	*ND*	*NA*	*0.286 (4.3%)*	*NA*	*0.013 (26.7%)*
DM-TM-COOH	*ND*	*NA*	*0.507 (7.7%)*	*NA*	*0.003 (6.0%)*
ph-COOH	*0.015 (37.2%)*	*NA*	*0.117 (1.8%)*	*NA*	*ND*
U1	*ND*	*NA*	*ND*	*NA*	*ND*
U2	*ND*	*NA*	*0.778 (11.8%)*	*NA*	*0.002 (4.3%)*
U3	*ND*	*NA*	*ND*	*NA*	*0.002 (4.8%)*
U4	*ND*	*NA*	*ND*	*NA*	*ND*
U5	*0.008 (19.4%)*	*NA*	*ND*	*NA*	*0.006 (12.4%)*
Unresolved background	*0.001 (0.8%)*	*NA*	*0.007 (0.1%)*	*NA*	*0.001 (2.1%)*
Unretained	0.001 (2.7%)	0.056 (0.9%)	ND	ND	0.002 (3.4%)
Unresolved background	0.001 (2.9%)	0.011 (0.2%)	0.025 (0.4%)	35.642 (1.9%)	<0.001 (0.3%)
Total	**0.025 (63%)**	**3.24 (50%)**	**1.72 (26%)**	**1827.82 (97%)**	**0.029 (60%)**

U = unidentified metabolite
NA = not analysed
ND = not detected
Values in parenthesis show the amount of each metabolite present as a percentage of the total residue.

Conclusion:

The majority of tolclofos-methyl applied to seed potatoes remained associated with the parent tuber as unchanged parent compound. Limited translocation of radiolabelled residues to roots, shoots and daughter tubers was evident and levels in the daughter tubers low (< 0.05 mg/kg). Analysis of the radioactive residue in the daughter tubers showed that five polar degradation products were present at levels ≤ 0.013 mg/kg. Data obtained from HPLC and LC/MS-MS experiments identified two of these as DM-TM-CH_2OH (0.013 mg/kg) and DM-TM-COOH (0.003 mg/kg).

Figure B.7.1.1.a: Proposed metabolic pathway for tolclofos-methyl in potatoes



Comments:

The application rate was 125 mg a.s./kg, which is less than the proposed practical application rate of 250 mg a.s./kg (critical GAP southern Europe, early potato) and 150 mg as/kg (critical GAP nothern Europe, ware potato). A metabolism study at 250 mg a.s./kg could change proportions of different metabolites as well as reveal other metabolites that at low dosages are below LOQ. Levels of non-extracted residues were 0.016 mg/kg or 33% of TRR in mature daughter tubers. If non-extracted residues exceed 0.05mg/kg or 25% of TRR, further analysis is recommended (guideline doc. 7028/VI/95 rev. 3) to investigate the biological availability. **It is recommended that the metabolism study (Report No. QM-51-0041) in potatoes is supplemented with a metabolism study at 250 mg a.s./kg.**

Metabolism in sugar beet:

Sugar beet is not included in intended use. The submitted study is from 1980 and of low quality, it is not following any guideline and have no GLP statement. The study was therefore not evaluated.

B.7.1.2. Leafy crops: Metabolism in lettuce

Reference:	Croucher, A. (2002) (^{14}C)-Tolclofos-methyl: Metabolism in lettuce.	**No of application:**	1
Test substance:	[Phenyl-UL-^{14}C]-tolclofos-methyl (Batch No.: CP-2427, Radiochemical purity: 98.5%, Specific radioactivity: 8.32 MBq/mg).	**Stage of application:**	3 to 4 leaf stage
Dates of experimental work:	January 8, 2001 – January 7, 2002	**GLP statement:**	Yes
Test material:	lettuce plants	**Guidelines:**	Council Directive 91/414/EC (as amended by Commission Directive 96/68/EC) document 7028/VI/95 Rev. 3, July 1997
Application conc.:	2 kg a.s./ha and 10 kg a.s./ha		

Materials and methods:

Radiolabelled tolclofos-methyl was applied to seedlings grown in soil to the 3 to 4 leaf stages on one occasion at nominal application rates of 2 kg a.s./ha and at an exaggerated application rate of 10 kg a.s./ha, equivalent to 5 times the standard rate. The plants were grown to maturity in the greenhouse and were harvested 34 days after the application. The harvested plant material was extracted by maceration in the presence of acetone/water (1/1 v/v) and analysed by LSC. The amount remaining unextracted in the solid residue was determined by combustion analysis followed by LSC. The solid residue was further extracted sequentially with methanol, 1M hydrochloric acid and finally 5M sodium hydroxide. Extracts were assayed by LSC and, where appropriate, analysed by HPLC, TLC and LC/MS in order to characterise and identify residues. In addition, the total radioactive residue (TRR) in the soil was determined by combustion analysis and further samples were extracted with acetone/glacial acetic acid (98:2 v/v) and analysed.

Findings:

Following application to lettuce seedlings at the standard application rate, mature lettuce plants contained a total residue equivalent to 0.23 mg/kg of which approximately 66% was extracted by acetone/water and 34% remained in the post-extracted solid. The identity of metabolites present in lettuce is presented in Table B.7.1.2.a.

At the exaggerated application rate, mature lettuce plants contained a total residue equivalent to 0.7663 mg/kg, and at the standard application rate mature lettuce plants contained a total residue equivalent to 0.2298 mg/kg. Results are presented in Table B.7.1.2.b.

The mean TRR in soil was 0.7024 mg/kg at the standard rate and 4.2654 mg/kg at the exaggerated (5x) rate. The radioactivity extracted from soil was shown to be tolclofos-methyl only using HPLC and 2D Thin Layer Chromatography (TLC).

Table B.7.1.2.a: Identity of metabolites

Designation	Chemical name
TM (parent compound)	*O,O*-dimethyl *O*-(2,6-dichloro-4-methylphenyl) phosphorothioate
TM-CH_2OH	*O,O*-dimethyl *O*-[2,6-dichloro-4-(hydroxymethyl)phenyl]phosphorothioate
ph-CH_3	2,6-dichloro-4-methylphenol

Table B.7.1.2.b: Radioactive residues (mg/kg) in mature lettuce plants following a single application of [phenyl-^{14}C]-tolclofos-methyl to seedlings at rates of 2 and 10 kg a.s./ha

Sample	Standard rate application		Exaggerated (5x) application rate	
	% of TRR	Residue (mg/kg)	% of TRR	Residue (mg/kg)
Acetone/water extract	65.98	0.1516	65.55	0.5023
Post-extracted solid	34.02	0.0782	34.45	0.2640
Total	100.0	0.2298	100.0	0.7663

At the standard application rate, the concentration of parent compound found in mature lettuce plants was 0.0843 mg/kg (37% of the TRR). In addition, two metabolites, M1 and M2, were found at a concentration of 0.05 mg/kg (23% TRR) and 0.03 mg/kg (14% TRR) respectively. These two main metabolites however, did not co-chromatograph with any of the available reference materials and were characterised by hydrolysis experiments with enzymes or acid and investigations using LC/MS. The major metabolite (M1) was shown to be a sugar conjugate (probably a disaccharide or malonyl glucose) of ph-CH_3 although the exact structure of the conjugate could not be determined. The other main metabolite (M2) was identified as a sugar conjugate of TM-CH_2OH. A similar distribution of residues was observed from lettuce plants applied at the exaggerated rate. Results from the analysis of extracts generated from lettuce plants applied at each application rate are presented in Table B.7.1.2.c.

Based on the identified metabolites, the metabolism of tolclofos-methyl in lettuce is considered to proceed 1) hydrolysis of the P-O-ary linkage (ph-CH_3), 2) hydroxylation of the 4-methyl group (TM-CH_2OH), 3) conjugation of the resultant metabolites with sugars (ph-CH_3-conjugate and TM-CH_2OH-conjugate). The proposed major metabolic pathway is presented in Figure B.7.1.2.a.

Table B.7.1.2.c: Radioactive residues (mg/kg) in lettuce plant extracts following a single application of [phenyl-^{14}C]-tolclofos-methyl to seedlings at rates of 2 and 10 kg a.s./ha

Component	Standard rate application		Exaggerated (5x) application rate	
	% of TRR	Residue (mg/kg)	% of TRR	Residue (mg/kg)
Tolclofos-methyl	36.71	0.0843	39.73	0.3045
ph-CH_3-conjugate	22.50	0.0517	19.88	0.1523
TM-CH_2OH-conjugate	13.73	0.0315	14.72	0.1128
Unknown	4.46	0.0102	8.46	0.0648
1M HCl extract	0.57	0.0013	3.29	0.0252
5M NaOH extraction	12.69	0.0292	10.58	0.0811
Remaining unextracted	1.65	0.0038	0.45	0.0034
Total	100.00	0.2297	99.99	0.7662

Conclusion:

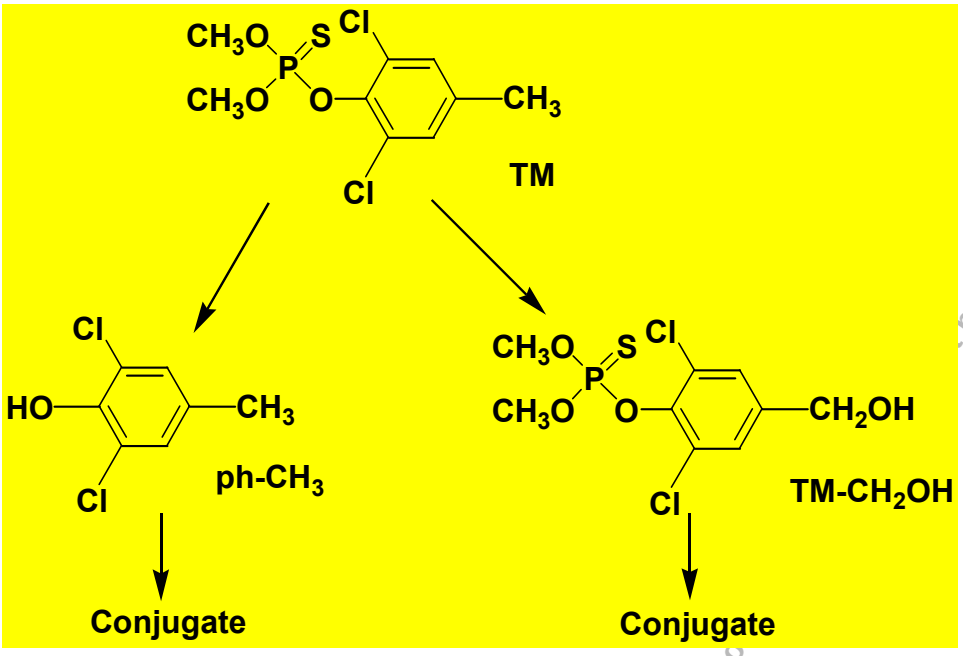
Following application at 2kg a.s./ha, mature lettuce plants contained a total residue equivalent to 0.23 mg/kg of which approximately 0.08 mg/kg was unchanged tolclofos-methyl. Two major components were isolated, referred to as M1 and M2. These comprised 0.05 and 0.03 mg/kg respectively and were more polar than any of the reference compounds available, indicating that they were conjugates. Hydrolysis experiments and LC/MS investigations showed that M1 was a conjugate (probably a disaccharide or malonyl glucose) of pH-CH_3 and M2 was a sugar conjugate of TM-CH_2OH.

The most significant residue in mature lettuce foliage was the parent compound, tolclofos-methyl.

Comments:

The study was well performed and reported.

Figure B.7.1.2.a: Proposed major metabolic pathway for tolclofos-methyl in lettuce



B.7.1.3 Metabolism, distribution and expression of residue in plants - summary and conclusions

The metabolism of tolclofos-methyl in potatoes and lettuce, representing root vegetables and leafy crops, grown in a greenhouse has been studied using tolclofos-methyl uniformly labelled with ^{14}C in the phenyl ring. The application methods were seed treatment for potatoes, and foliar application for lettuce.

After treatment of seed potatoes, the majority of tolclofos-methyl applied to the seed remained unchanged and associated to parent tubers. Limited translocation of ^{14}C-residues to roots, shoots, and daughter tubers was evident, and residue levels in daughter tubers are found to be low (<0.05 mg/kg). Analysis of the residue in the daughter tubers showed that five polar degradation products were present at levels of ≤ 0.013 mg/kg. Data obtained from HPLC and LC/MS-MS identified two of these metabolites as DM-TM-CH_2OH (0.013 mg/kg) and DM-TM-COOH (0.003 mg/kg). However, only one dosage rate 125 mg a.s./kg, that is lower than proposed Good Agricultural Practice (GAP), for southern Europe and early potatoes, was considered for potatoes. Furthermore, 33% of TRR from daughter tubers was unextracted. It is recommended that an additional metabolism study in potato is performed at a dosage rate of critical GAP in southern Europe and early potatoes (250 mg a.s./kg).

Following application to lettuce seedlings in the greenhouse, at the recommended application rate, a total residue (TRR) of 0.23 mg/kg was present in mature plants. The level of tolclofos-methyl was 0.08 mg/kg. Two major metabolites were isolated. These were polar in nature and were shown to be conjugates of ph-CH_3 (0.0517mg/kg) and TM-CH_2OH (0.0315 mg/kg). The rest of TRR were minor metabolites below 0.05 mg/kg.

The metabolism of tolclofos-methyl in lettuce leads to the formation of low levels of a number of free metabolites, some of which occur as conjugates. All these metabolites are known as rat metabolites. When tolclofos-methyl is used according to Good Agricultural Practice, concentrations of all metabolites are expected to be insignificant. For this reason, tolclofos-methyl is considered the only relevant residue for risk assessment and monitoring purposes in lettuce.

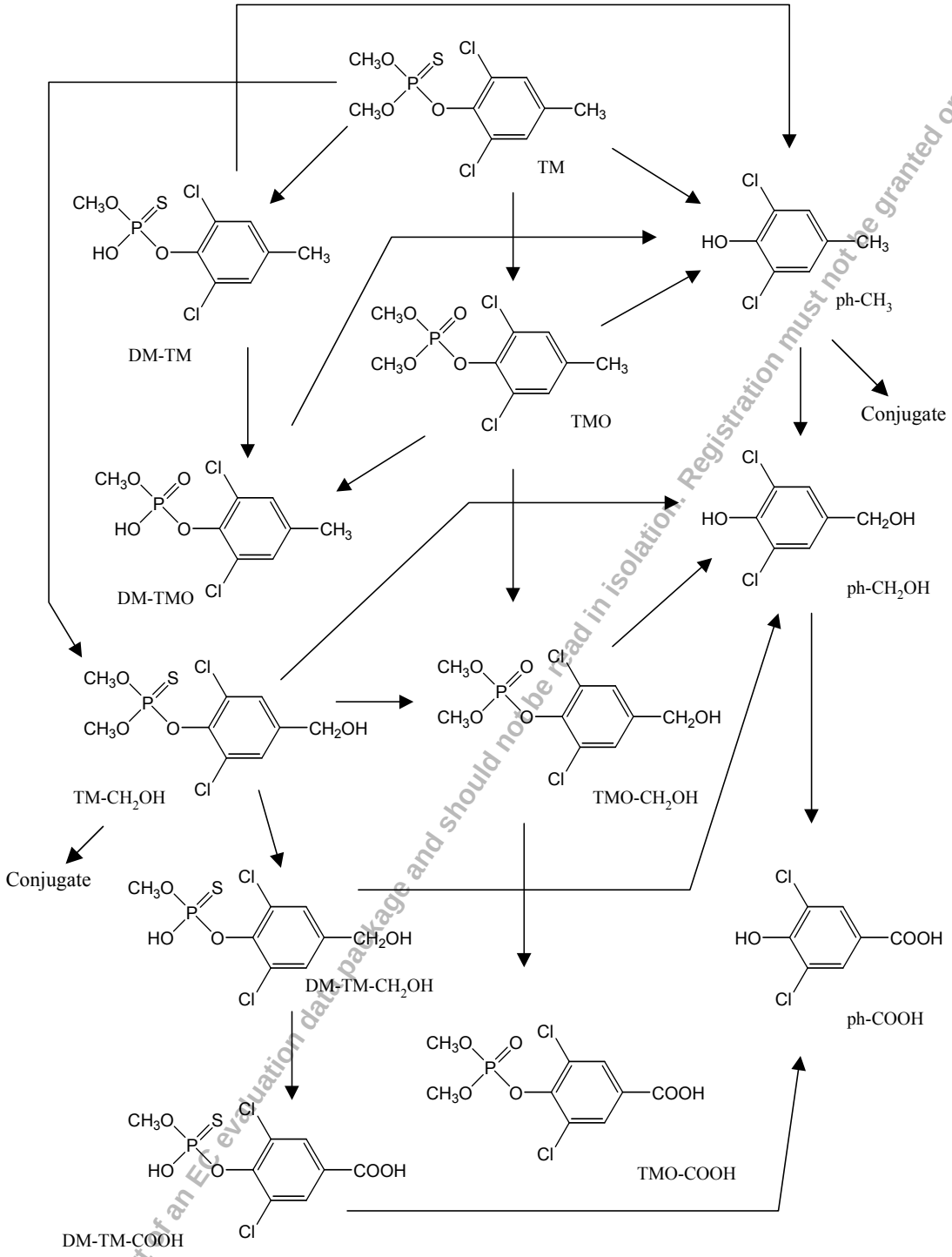
Formulated products: Supplementary studies are not required for Rizolex 50WP (500 g/kg tolclofos-methyl), Rizolex 50 SC or Rizolex DS (10% tolclofos-methyl) since it may be expected that a metabolism different from that of the active substance will not occur. Therefore, it is possible to extrapolate from data obtained on the active substance.

Table: B.7.1.3.a: List of identified compounds in potatoes and lettuce

Designation	**Chemical Name (IUPAC)**	**Presence in mature potatoes mg/kg, (%TRR)**	**Presence in lettuce mg/kg, (%TRR)**
Tolclofos-methyl	*O,O*-dimethyl*O*-(2,6-dichloro-4-methylphenyl) phosphorothioate	Parent tuber: 1792.178 (95.1%) Daughter tuber: ND	0.0843 (36.71%)
TMO	*O,O*-dimethyl *O*-(2,6-dichloro-4-methylphenyl) phosphate	Parent tuber: ND Daughter tuber: ND	ND
DM-TM	*O*-methyl *O*-hydrogen *O*-(2,6-dichloro-4-methylphenyl) phosphorothioate	Parent tuber: ND Daughter tuber: ND	ND
DM-TMO	*O*-methyl *O*-hydrogen *O*-(2,6-dichloro-4-methylphenyl) phosphate	Parent tuber: ND Daughter tuber: ND	ND
DM-TM-CH_2OH	*O*-methyl *O*-hydrogen *O*-[2,6-dichloro-4-(hydroxymethyl)phenyl]phosphorothioate	Parent tuber: NA Daughter tuber: 0.013 (26.7%)	ND
DM-TM-COOH	*O*-methyl *O*-hydrogen *O*-(2,6-dichloro-4-carboxyphenyl)phosphorothioate	Parent tuber: NA Daughter tuber: 0.003 (6.0 %)	ND
ph-COOH	3,5-dichloro-4-hydroxybenzoic acid	Parent tuber: NA Daughter tuber: ND	ND
TM-CH_2OH-conjugate	*O,O*-dimethyl *O*-[2,6-dichloro-4-(hydroxymethyl)phenyl]phosphorothioate		0.0315 (13.73%)
ph-CH_3-conjugate	2,6-dichloro-4-methylphenol		0.0517 (22.5 %)
Unknown U1-U5		Parent tuber: NA Daughter tuber: < 0.01 (21.5%)	
Unknown lettuce			0.0102 (4.46 %)
1M HCl ext.			0.0013 (0.57 %)
5M NaOH ext.			0.0292 (12.69%)
Unextracted		Parent tuber: 31.59 (2%) Daughter tuber: 0.016 (33%)	0.0038 (1.65%)

NA = not analysed; ND = not detected; Values in parenthesis show the amount of each metabolite present as a percentage of the total residue

Figure B.7.1.3 a. Proposed metabolic major pathway for tolclofos-methyl in plants



B.7.2 Metabolism, distribution and expression of residues in livestock (Annex IIA 6.2)

B.7.2.1 Metabolism studies on laying hen

Reference:	Yu, C.C., Guirguis, A.S. (1987). Metabolism of ^{14}C tolclofos-methyl in laying hens	**Guidelines:**	EPA Pesticide Assessment Guideline, Subdivision O, Residue Chemistry, October 1982
Test substance:	[Phenyl-^{14}C]tolclofos-methyl (Batch No.: Not specified, Radiochemical purity: Not specified, Specific radioactivity: 35.5 mCi/mmol)	**GLP:**	Yes (Self certification by the laboratory)
		Treatments:	Control and 10 mg/kg bw/day at 1, 24, 48 and 72 h
Species:	White Leghhorn hens	**Number of animals:**	3/treatment
Duration:	79 hours		

Materials and methods:

Hens were placed in individual metabolism cages for a pre-treatment period of at least 2 days and the treated period with free access to feed and water. [Phenyl-^{14}C]tolclofos-methyl was diluted with tolclofos-methyl analytical reference standard to a specific activity of 0.68 mCi/mmole to achieve a radiochemical limit of detection of about 0.02 ppm. Samples of excreta were taken at 7, 24, 48, 72 hours and at sacrifice. Eggs were collected twice daily. The hens were killed 7 hours after the last dosing: muscle, liver, kidney, fat, heart, lung, spleen, and ovary were excised and frozen prior to analysis. All samples were subjected to combustion analysis using a biological materials oxidiser to determine total radiocarbon content. Tissues with sufficient radiocarbon were extracted with solvent followed by analysis of extracts using TLC, GC and other suitable methods. Radioassay was performed using LSC.

Findings:

Absorption and elimination

Tolclofos-methyl was rapidly eliminated in the excreta. Seven hours after first dose, over 71% of the administered radiocarbon was eliminated (Table B.7.2.1.a). Additional 16% were eliminated between 7-24 hours. Elimination of the administered doses reached equilibrium within 3 days. The amounts of radiocarbon excreted each day during the three-day period were about the same. This indicated that equilibrium was reached between absorption and elimination. No build-up of residue in hen tissues is expected after treatment for a prolonged period of time.

Table B.7.2.1.a: Metabolism of [phenyl-^{14}C]tolclofos-methyl in laying hens: Radiocarbon in excreta

Collection time (hr)	% of ^{14}C dose [1]
0 – 7	71.00 ± 15.60
7 – 24	15.94 ± 8.78
24 – 48	95.15 ± 5.54
48 – 72	75.31 ± 6.79
72 – 79	86.30 ± 14.59

1: Mean ± SD from 3 animals based on single dose.

Residue levels: Residue levels in various tissues and eggs were low. Only about 1.4% of the dose was found in tissues and eggs 7 hours after the last dose. Among tissues, kidney and liver had higher residue level than other tissues (Table B.7.2.1.b). Residue levels in tissues and eggs were expected to decrease rapidly when treatment was stopped because tolclofos-methyl elimination from body was rapid.

Table B.7.2.1.b: Metabolism of [phenyl-^{14}C]tolclofos-methyl in laying hens: Radiocarbon distribution in the body and eggs

Sample[1]			Radiocarbon concentration (ppm equivalent) [2]
Plasma			0.76 ± 0.77
Blood cell			0.24 ± 0.16
Heart			0.18 ± 0.18
Lung			0.44 ± 0.43
Kidney			6.00 ± 2.70
Liver			3.43 ± 0.27
Spleen			0.12 ± 0.08
Muscle			0.11 ± 0.05
Fat			1.02 ± 0.43
Ovary			0.47 ± 0.03
Eggs [3]	7 hr	yolk	0.04
		albumen	0.05
	48 hr	yolk	0.01
		albumen	0.03
	72 hr	yolk	0.37
		albumen	0.07
	79 hr	yolk	0.27
		albumen	0.06

1: Animals killed at 79 hr (7 hr after last dose)
2: Mean ± SD (n = 3 except as noted)
3: From 1 hen

Radiocarbon characteristics and identity: Radiolabelled material in excreta, kidney and liver was characterised and analysed. In excreta unchanged tolclofos-methyl comprised 36% of the excreted radioactivity. Eleven metabolites were identified (Tables B.7.2.1.c and B.7.2.1.d). Tolclofos-methyl was metabolised via oxidative desulfuration, oxidation of 4-methyl group, and cleavage of P-O-aryl and P-O-methyl linkages. Combinations of these processes resulted in a variety of metabolites in free and conjugated forms. The major metabolite was ph-COOH.

Table B.7.2.1.c: Metabolism of [phenyl-^{14}C]tolclofos-methyl in laying hens: Identity of metabolites identified

Designation	Chemical name
TM (parent compound)	*O,O*-dimethyl *O*-(2,6-dichloro-4-methylphenyl) phosphorothioate
DM-TM	*O*-methyl *O*-hydrogen *O*-(2,6-dichloro-4-methylphenyl) phosphorothioate
TM-COOH	*O,O*-dimethyl *O*-(2,6-dichloro-4-carboxyphenyl) phosphorothioate
ph-CH_3	2,6-dichloro-4-methylphenol
TM-CHO	*O,O*-dimethyl *O*-(2,6-dichloro-4-formylphenyl) phosphorothioate
ph-CHO	3,5-dichloro-4-hydroxybenzaldehyde
ph-COOH	3,5-dichloro-4-hydroxybenzoic acid
TMO	*O,O*-dimethyl *O*-(2,6-dichloro-4-methylphenyl) phosphate
ph-CH_2OH	3,5-dichloro-4-hydroxybenzyl alcohol
TMO-COOH	*O,O*-dimethyl *O*-(2,6-dichloro-4-carboxyphenyl) phosphate
DM-TMO	*O*-methyl *O*-hydrogen *O*-(2,6-dichloro-4-methylphenyl) phosphate
DM-TMO-CH_2OH	*O*-methyl *O*-hydrogen *O*-[2,6-dichloro-4-(hydroxymethyl)phenyl] phosphate

Table B.7.2.1.d: Metabolism of [phenyl-^{14}C]tolclofos-methyl in laying hens: Identity of radiocarbon in excreta

Spot No. and Identity	Percentage of excreta ^{14}C	
	Free	Acid-released
1. TM	35.06 ± 10.25	1.21 ± 0.89
2. TM-CHO	8.55 ± 1.53	0.17 ± 0.09
3. ph-CH_3	1.03 ± 0.18	0.05 ± 0.03
4. TM-COOH	3.31 ± 0.58	0.05 ± 0.02
5. ph-COOH	22.13 ± 5.19	0.88 ± 0.44
6. TMO	2.14 ± 0.50	0.11 ± 0.06
7. ph-CHO	0.28 ± 0.08	0.01 ± 0.00
8. ph-CH_2OH	1.41 ± 0.38	0.17 ± 0.07
9. TMO-COOH	6.59 ± 1.78	0.08 ± 0.03
10. DM-TM	0.65 ± 0.09	0.07 ± 0.04
11. Unknown	0.65 ± 0.09	0.02 ± 0.01
12. Unknown	0.18 ± 0.03	0.02 ± 0.01
13. DM-TMO	0.08 ± 0.01	0.00 ± 0.00
14. Unknown	0.33 ± 0.09	0.16 ± 0.06
15. Unknown	1.43 ± 0.42	0.06 ± 0.03
16. Unknown	2.30 ± 0.15	0.03 ± 0.01
17. DM-TMO-CH_2OH	1.92 ± 0.12	0.22 ± 0.10
18. Unknown	0.63 ± 0.04	0.16 ± 0.07

Excreta collected at 7 hr and 79 hr; data expressed as mean ± SD (n = 3)

Conclusion:

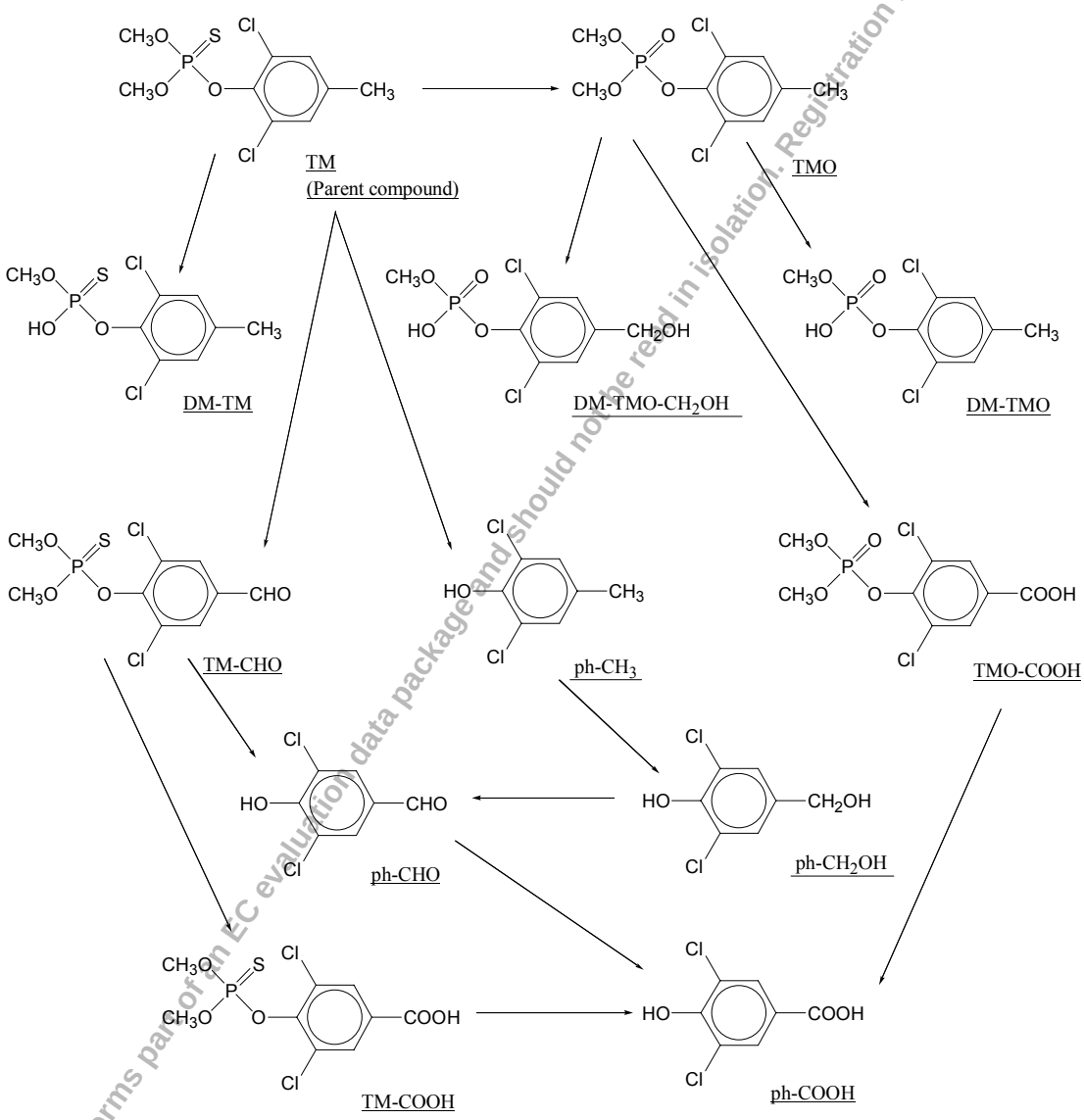
Tolclofos-methyl was extensively metabolised by hens. Unchanged parent compound constituted 36% of excreta radiocarbon. Terminal residues were derived from oxidative desulfuration, oxidation of 4-methyl group, and cleavage of P-O-aryl and P-O-methyl linkages.

A proposed metabolic pathway for tolclofos-methyl in hens is presented in Figure B.7.2.1.a.

Comments:

The study was well performed and reported.

Figure B.7.2.1.a: Proposed metabolic pathway for tolclofos-methyl in hens



B.7.2.2 Metabolism studies on lactating goat

Reference:	Yu, C.C., Guirguis, A.S. (1987). Metabolism of ^{14}C tolclofos-methyl in a lactating goat	**Guidelines:**	EPA Pesticide Assessment Guideline, Subdivision O, Residue Chemistry, October 1982
Test substance:	[Phenyl-^{14}C]tolclofos-methyl (Batch No.: C-59-2, Radiochemical purity: ≥99 %, Specific radioactivity: 35.5 mCi/mmol)	**GLP :**	Yes (Self certification by the laboratory)
		Treatments:	10 mg/kg bw/day at 1, 24, 48 and 72 h
Species:	Nubian goat	**Number of animals:**	1
Duration:	79 hours		

Materials and methods:

One Nubian lactating goat (weight about 40 kg) received the test substance, premixed with starch or feed, by oral gavage in gelatine capsules. [phenyl-^{14}C]tolclofos-methyl was diluted with tolclofos-methyl analytical reference standard to a specific activity of 0.339 mCi/mmole to achieve a radiochemical limit of detection of about 0.05 ppm. The goat was held in a metabolism stall, with free access to feed and water. Samples were taken separately for urine and feces, at 7 and 24 hours and daily thereafter. Milk was collected twice daily. The goat was killed 7 hours after the last dosing: muscle, liver, kidney and fat were excised and frozen prior to analysis. All samples were subjected to combustion analysis using a biological materials oxidiser to determine total radiocarbon content. Tissues with sufficient radiocarbon were extracted with solvent followed by analysis of extracts using TLC, GC and other suitable methods. Radioassay was performed using LSC.

Findings:

Absorption and elimination: Tolclofos-methyl was mainly eliminated in urine. Seven hours after first dose, about 34% of the administered radiocarbon was excreted in urine (Table B.7.2.2.a). In the first 24-hour period, about 49% of the dose was eliminated in urine and fecal elimination accounted for only about 1% of the daily dose. A steady increase in the concentration of radiocarbon in feces with time indicated that passage of orally administered [^{14}C]tolclofos-methyl through the GI tract of the goat was very slow. At the end of the experimental period (79 hours), considerable amounts of the administered dose still remained in the GI tract (amounts not determined).

Table B.7.2.2.a: Metabolism of [phenyl-^{14}C]tolclofos-methyl in lactating goat: Radiocarbon excretion in urine and feces

Time (hr) after first dosing	% of daily ^{14} C dose	
	In urine	In feces
7	33.70	0.16
24	15.06	0.12
48	42.44	1.44
72	20.04	0.48
79	18.72	0.80

Residue levels: Residue levels in tissues and milk were low. Residue levels in milk reached equilibrium of about 0.8 ppm equivalent within 4 days after dose initiation (Table B.7.2.2.b). Thus parent tolclofos-methyl and its metabolites will not build up in milk after prolonged exposure to tolclofos-methyl.

Table B.7.2.2.b: Metabolism of [phenyl-^{14}C]tolclofos-methyl in lactating goat: Radiocarbon distribution in the body

Sample	Collection time [1] (hr)	Concentration (ppm equivalent)	% of applied dose
Urine	7	180	4.21
	24	430	3.77
	48	514	10.61
	72	401	5.01
	79	485	2.34
Feces	7	4	0.02
	24	24	0.03
	48	44	0.36
	72	81	0.12
	79	143	0.10
Milk	7	0.32	<0.001
	24	0.77	0.001
	31	0.67	0.001
	48	0.41	0.001
	55	0.42	<0.001
	72	0.80	0.001
	79	0.87	<0.001
Kidney	79	4.3	0.035
Fat	79	1.1	0.142
Muscle	79	0.2	0.250
Liver	79	3.0	0.120
Bile	79	9.4	0.010

1: Animals killed at 79 hr (7 hr after last dose).

Radiocarbon characteristics and identity: Radiocarbon in excreta, tissues and milk was characterised and analysed. Nineteen metabolites were identified in these samples (Tables B.7.2.2.c and B.7.2.2.d). Tolclofos-methyl was metabolised via oxidative desulfuration, oxidation of 4-methyl group, and cleavage of P-O-aryl and P-O-methyl linkages. Combinations of these processes resulted in a variety of metabolites. Combinations of these processes resulted in a variety of metabolites in free and conjugated form.

Table B.7.2.2.c: Metabolism of [phenyl-^{14}C]tolclofos-methyl in lactating goat: Identity of metabolites identified

Designation	Chemical name
TM (parent compound)	*O,O*-dimethyl *O*-(2,6-dichloro-4-methylphenyl) phosphorothioate
DM-TM	*O*-methyl *O*-hydrogen *O*-(2,6-dichloro-4-methylphenyl) phosphorothioate
TM–CH_2OH	*O,O*-dimethyl *O*-2,6-dichloro-4-(hydroxymethyl)phenylphosphorothioate

DM-TM–CH_2OH	*O*-methyl *O*-hydrogen *O*-2,6-dichloro-4-(hydroxymethyl)phenylphosphorothioate
TM-COOH	*O,O*-dimethyl *O*-(2,6-dichloro-4-carboxyphenyl) phosphorothioate
DM-TM-COOH	*O*-methyl *O*-hydrogen *O*-(2,6-dichloro-4-carboxyphenyl) phosphorothioate
ph-CH_3	2,6-dichloro-4-methylphenol
TM-CHO	*O,O*-dimethyl *O*-(2,6-dichloro-4-formylphenyl) phosphorothioate
ph-CHO	3,5-dichloro-4-hydroxybenzaldehyde
ph-COOH	3,5-dichloro-4-hydroxybenzoic acid
TMO	*O,O*-dimethyl *O*-(2,6-dichloro-4-methylphenyl) phosphate
TMO-CH_2OH	*O,O*-dimethyl *O*-2,6-dichloro-4-(hydroxymethyl)phenylphosphate
ph-CH_2OH	3,5-dichloro-4-hydroxybenzyl alcohol
TMO-COOH	*O,O*-dimethyl *O*-(2,6-dichloro-4-carboxyphenyl) phosphate
ph-CO-glycine	3,5-dichloro-4-hydroxyhippuric acid
DM-TMO	*O*-methyl *O*-hydrogen *O*-(2,6-dichloro-4-methylphenyl) phosphate
DM-TMO-CH_2OH	*O*-methyl *O*-hydrogen *O*-[2,6-dichloro-4-(hydroxymethyl)phenyl] phosphate
TMO-CHO	*O,O*-dimethyl *O*-(2,6-dichloro-4-formylphenyl) phosphate
DM-TMO-COOH	*O*-methyl *O*-hydrogen *O*-(2,6-dichloro-4-carboxyphenyl) phosphate

Table B.7.2.2.d: Metabolism of [phenyl-^{14}C]tolclofos-methyl in lactating goat: Identity of radiocarbon in urine

Spot No. and identity	% of urinary radiocarbon [1]	
	Free fraction	Methanol fraction
1. ph-CH_3	1.47	0.00
2. TM-COOH	0.21	0.00
3. ph-CHO	2.76	0.00
4. ph-COOH	8.90	0.00
5. TMO	0.70	0.00
6. Unknown	0.26	0.00
7. ph-CH_2OH	14.21	0.00
8. Unknown	0.07	0.00
9. ph-CO-Gly	0.70	1.10
10. TMO-CH_2OH	0.14	0.00
11. Unknown	0.19	0.00
12. DM-TM	0.08	0.00
13. DM-TM-CH_2OH	0.02	2.92
14. DM-SM-TM	0.02	0.00
15. DM-TM-COOH	0.05	1.80
16. Unknown	0.98	0.00
17. DM-TMO	10.38	34.39
18. DM-TMO-COOH	2.16	0.00
19. DM-TMO-CH_2OH	0.58	7.36
20. Unknown	0.00	4.04

1 Average of urine samples taken at 24 hr and 79 hr.

Conclusion:

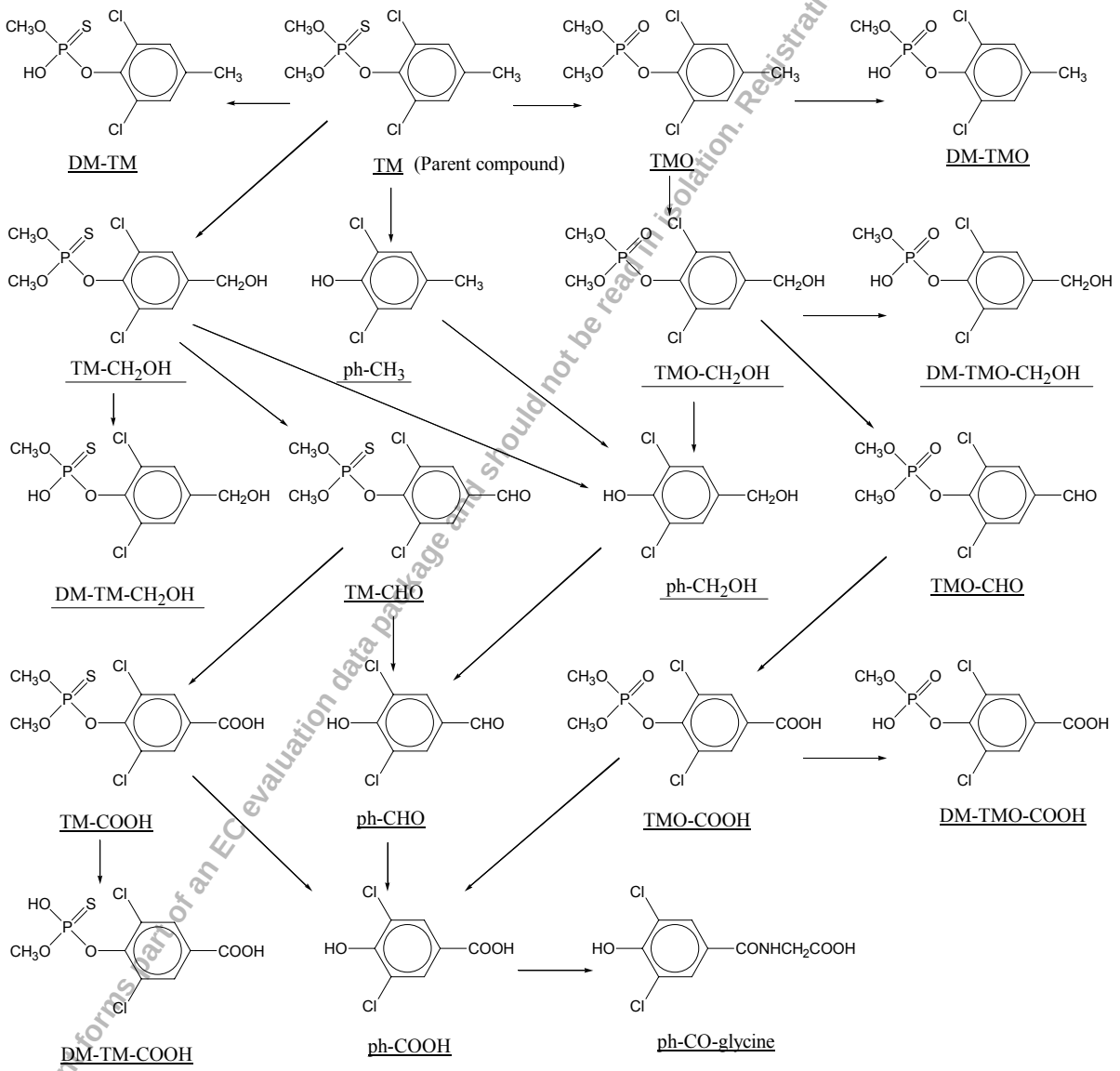
Tolclofos-methyl was rapidly metabolised in the lactating goat. No parent compound was detected in tissues and milk. Terminal residues were derived from oxidative desulfuration, oxidation of 4-methyl group, and cleavage of P-O-aryl and P-O-methyl linkages.

A proposed metabolic pathway for tolclofos-methyl in goat is presented in Figure B.7.2.2.a.

Comments:

The study was well performed and reported.

Figure B.7.2.2.a: Proposed metabolic pathway for tolclofos-methyl in goats



B.7.2.3 Metabolism studies on cow

As a study on lactating ruminants has been conducted on goat, hence it is not needed to conduct a study on cow.

B.7.2.4 Metabolism studies on pig

As metabolic patterns in ruminants do not significantly differ from those in the rat, a study on pig is not required.

B7.2.3 Metabolism, distribution and expression of residue in livestock - summary and conclusions.

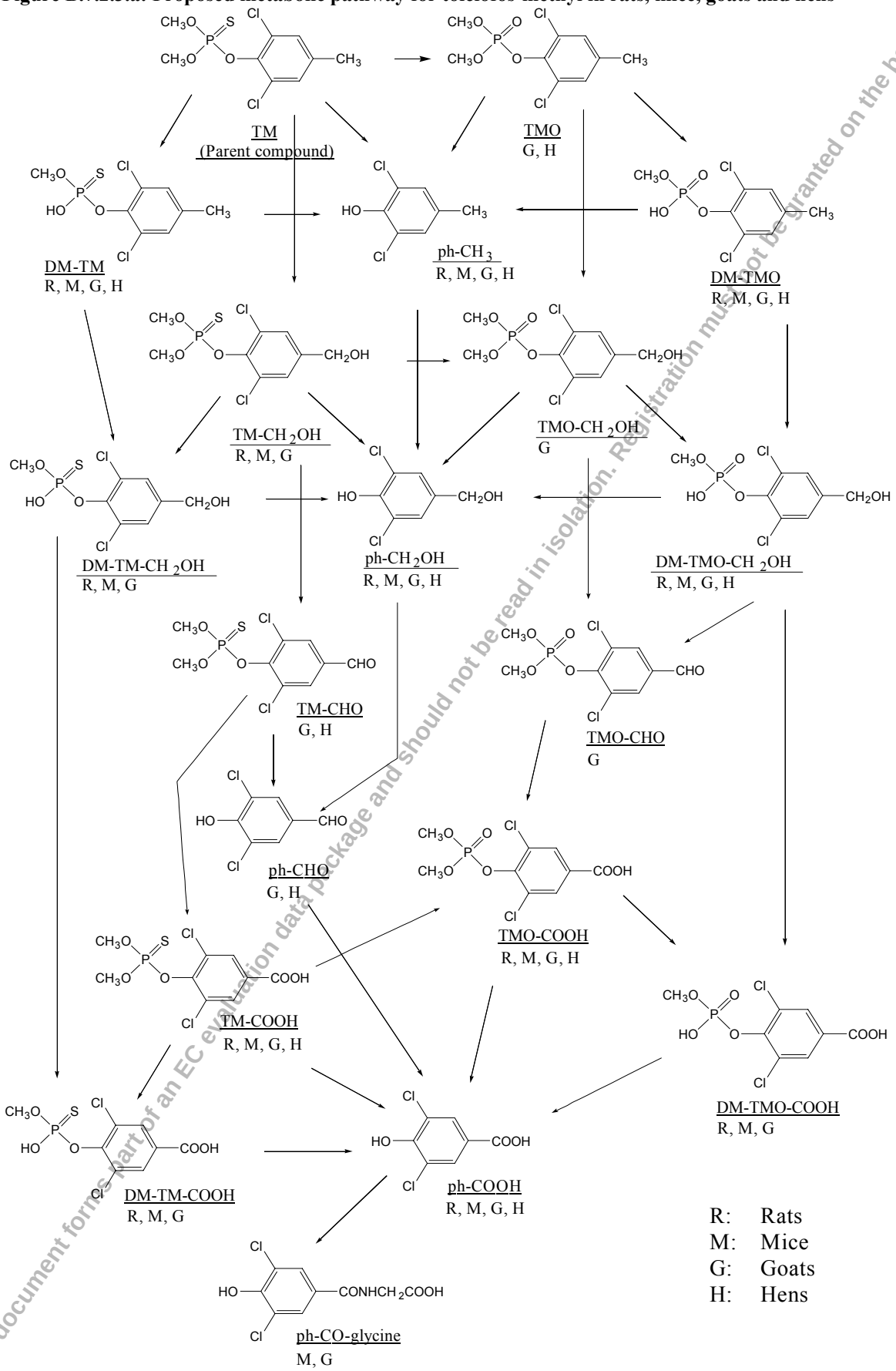
Tolclofos-methyl was rapidly metabolised and excreted in rats, mice, goat and hen, predominantly in the urine. Residues 7 days after dosing are generally very low in all tissues (less than 1% of the initial dose was retained in all tissues). No indication for build-up of residues in tissues is expected after treatment for a prolonged period in all species.

In all species, metabolism was mainly by oxidation of the P=S group to P=O, oxidation of 4-methyl group and cleavage of the P-O-aryl and P-O-methyl linkages. The major metabolite in all species was 3,5-dichloro-4-hydroxybenzoic acid. This metabolite was excreted as the glycine conjugate in mice and goat and as the free form in rats and hens.

Formulated products: Supplementary studies are not required for Rizolex 50WP (500 g a.s./kg (w/w)) or Rizolex DS (10%) tolclofos-methyl since it may be expected that a metabolism different from that of the active substance will not occur. Therefore, it is possible to extrapolate from data obtained on the active substance.

The proposed metabolic pathway for tolclofos-methyl in rats, mice, goats and hens is illustrated hereafter (Figure B.7.2.c)

Figure B.7.2.3.a: Proposed metabolic pathway for tolclofos-methyl in rats, mice, goats and hens



B.7.3 Definition of the residue (Annex IIA 6.7; Annex IIIA 8.6)

Proposed residue definition (plants, plant products):
Based on the results of the studies on the metabolism in plants (root vegetables and leafy crops) and in consideration of the presence and toxicological significance of metabolites and the suitability of analytical methods for routine monitoring, residues in plants and plant products should be defined in terms of parent compound, i.e. tolclofos-methyl.

Proposed residue definition (products of animal origin):
Since significant residues of tolclofos-methyl (> 0.1 mg/kg of the total diet) do not occur in crops or crop parts fed to animals, it is not considered necessary to propose a residue definition for products of animal origin.

If the intended use of tolclofos-methyl is extended the definition of residue in plants and animal products may need to be reconsidered.

B.7.4 Use pattern

Potatoes:
The aim of the treatment with tolclofos-methyl is the protection against soil borne fungus diseases of the parent tuber, which serves, as reservoir for the initial growth of the root and the sprout system. Once the green plant parts have formed they take over the further development of the potato plant including the formation of the daughter tubers. At this stage, the parent tuber is exhausted.
In northern European potato production a distinction is made between early potatoes and ware potatoes. In southern Europe all potatoes are considered early potatoes since under favourable climatic conditions in the south the period from sowing to harvest lasts 80 to 100 days after planting.

Specific formulations, i.e. a DS formulation containing 10% of tolclofos-methyl and a FS formulation containing 500 g of tolclofos-methyl/kg, have been developed for the application in seed potatoes. Their trade names are Rizolex (DS) and Rizolex 50 SC.

The fungicide tolclofos-methyl is applied to seed potatoes either shortly before or at sowing. The application shortly before sowing is made by diluting the FS formulation in 2 to 3 L of water/ton of potatoes and by directing the spray through nozzles mounted over a conveyor belt that transports a single layer of seed potatoes. A second method consists of spreading a DS formulation of tolclofos-methyl over the potatoes in the seed hopper while they wait to be sown. A third method is the application of the FS formulation diluted in 2 to 3 l of water/ton of potatoes through spray nozzles directed to the exit of the seed hopper and treating the tubers while they leave the hopper.

Table B.7.4.a: Use pattern of tolclofos-methyl in potatoes

Crop	Country	Formulation type (code) & content of a.s. (g/kg)	Application				PHI days
			Method[1]	Rate kg a.s./ton	Spray conc. kg a.s./hl[1]	Number	
Potato	EU, North	FS 500 DS 100	Tuber treatment	0.15	n.a.	1	80
Potato	EU, South	FS 500 DS 100	Tuber treatment	0.25	n.a	1	80

[1] Tuber treatment by FS: Suspension of the formulated product in about 2 to 3 l of water/ton.
Tuber treatment by DS: Dusting

Lettuce:

The fungicide tolclofos-methyl protects young lettuce plants against soil borne fungus diseases attacking the root system. It is applied to protected lettuce plants until one week after transplanting. A spray volume of 1000 to 2000 L/ha is recommended to ensure the penetration of the fungicide into the root zone. Spray concentrations are given in Table B.7.4.b

Specific formulation is a WP formulation containing 50 tolclofos-methyl. The trade name is Rizolex 50 WP.

In northern Europe, distinction is made between winter lettuce and summer lettuce. Winter lettuce is transplanted into the greenhouse in autumn. Growing during the cold and dark months of winter, supported by little heating it requires a minimum of 56 days from transplanting to harvest. Summer lettuce is transplanted during spring/summer. Profiting from the long day length, intense sunshine and high temperatures it grows to a marketable size within a minimum period of 28 days.
In southern Europe all protected lettuce is considered summer lettuce since under favourable climatic conditions in the south the period from transplanting to harvesting is short with little fluctuation during the year.

Table B.7.4.b: Use pattern of tolclofos-methyl in protected lettuce

Crop	Country	Formulation type & content of a.s. (g/kg)	Application				PHI days
			Method	Rate kg a.s./ha	Spray conc. kg a.s./hL	Number	
Lettuce	EU, North	WP 500	Spray	2	0.08-0.2	1	28/56[1]
Lettuce	EU, South	WP 500	Spray	2	0.08-0.2	1	28

[1] PHI set by Dutch authorities: 56 days in winter lettuce, 28 days in summer lettuce

B.7.5 Identification of critical GAPs

The critical Good Agricultural Practice (GAP) of Tolclofos-methyl 50WP for early potatoes and ware potatoes in northern and southern Europe are identified as follows Table B.7.5.a-b.

In **early potatoes** 20 residue trials were conducted in accordance with critical GAP, in **ware potatoes** 10 residue trials were conducted in accordance with critical GAP.

Table B. 7.5.a: Critical Good Agricultural Practices for early potatoes

Application rate	Northern Europe: 0.15 kg a.s./ton Southern Europe: 0.25 kg a.s./ton
Spray volume	2 - 3 L/ton
Spray concentration	n.a.
Number of applications per season	1
Pre-Harvest Interval	80 days

Table B. 7.5.b: Critical Good Agricultural Practices for ware potatoes

Application rate	Northern Europe: 0.15 kg a.s./ton
Spray volume	2 - 3 L/ton
Spray concentration	n.a.
Number of applications per season	1
Pre-Harvest Interval	120 days

The critical Good Agricultural Practice (GAP) of Tolclofos-methyl 50WP for protected **lettuce** in northern and southern Europe are identified as follows Table B.7.5.c. Eight residue trials were carried out in accordance with critical GAP.

Table B.7.5.c: Critcal Good Agricultural Practices for **lettuce**

Application rate	2 kg a.s./ha
Spray volume	1000 - 2500 L/ha
Spray concentration	0.08 - 0.2 kg a.s./hL
Number of applications per season	1
Pre-Harvest Interval	28 days summer lettuce / Southern Europe
	28 days summer lettuce/Northern Europe
	56 days winter lettuce / Northern Europe

B.7.6 Residues resulting from supervised trials (Annex IIA 6.3; Annex IIIA 8.2)

Potatoes:

The magnitude of tolclofos-methyl residues in potatoes was monitored in early potatoes in a total of 25 trials from 1982-2001 and in ware potatoes in 18 trials from 1980-2001. From these 20 supervised residue trials in early potatoes (4 in southern EU and 16 in northern EU) and 10 supervised residue trials in ware potatoes in northern EU were in accordance with critical GAP ± 25%. Only 4 trials are present in southern EU, in two trials residues (0.01mg/kg) were found. However, the residue level did not differ much from the levels in northern EU. All residue trials are presented in tables B.7.6.a-b.

Table B.7.6.a summarises the residue levels in early potatoes, which are harvested 100 days ± 20% after application/planting. Table B.7.6.b summarises the residue levels in ware potatoes, which are harvested around 120 to 200 days after application/planting.

In trials from 2000, and according to critical GAP and GLP, residues were determined using conditions and procedures described in DFG method S19 which is an officially established multi-residue method and already used for the determination of tolclofos-methyl in commodities with high water content for monitoring purposes. The method is evaluated in chapter B.4.

Table B.7.6.a: Results of residue trials performed with tolclofos-methyl in early potatoes (data used for calculations of proposed MRLs are underlined, i.e. those corresponding to critical GAP and a PHI of 80 days).

State, year	Formulation	Application			PHI days	Residues mg/kg	Reference
	(type & content of a.s.)	No.	Rate kg a.s./ton	Spray conc. kg a.s./ton			
UK 1982	DS 100	1	0.25	n.a. [1]	98	0.03 * < 0.01 [2] * 0.07 [3] *	Longland, R.C. 1983
UK 1982	DS 100	1	0.25	n.a.	89	0.18 * 0.01 [2] * 1.19 [3] *	
UK, 1982	DS 50	1	0.125	n.a.	<u>98</u>	<u>0.02</u>	Longland, R.C. 1983
UK, 1982	DS 50	1	0.125	n.a.	<u>99</u>	<u>0.02</u>	
UK, 1982	DS 50	1	0.125	n.a.	<u>89</u>	<u>0.01</u>	
UK, 1982	DS 50	1	0.125	n.a.	119	0.02*	
UK, 1992	FS 500	1	0.125	n.a.	<u>84</u>	<u>0.04</u>	Brown, D.C. 1992
UK, 1992	FS 500	1	0.125	n.a.	<u>84</u>	<u>0.06</u>	
UK, 1993	DS 100	1	0.125	n.a.	110 124	0.08* <0.05*	Burden, A.N. 1994 QR-41-0101
UK, 1993	DS 100	1	0.125	n.a.	<u>96</u> 115	<u><0.05</u> <0.05	
DK, 1993	DS 100	1	0.15	n.a.	<u>60</u> 109 148	<u>0.07</u> 0.04 0.04	Holmgaard, M. 1994
DK, 1993	FS 500	1	0.15	n.a.	<u>60</u> 109 148	<u>0.05</u> < 0.01 0.02	
UK, 1993	FS 500	1	0.125	n.a.	0 <u>84</u>	46 <u>0.10</u>	Burden, A.N. 1994 QR-41-0103
UK, 1993	FS 500	1	0.125	n.a.	0 <u>84</u>	41 <u>0.07</u>	
UK, 2000	FS 500	1	0.125	n.a.	<u>93</u>	<u><0.01</u>	Grolleau, G. 2001
UK, 2000	FS 500	1	0.125	n.a.	<u>93</u>	<u><0.01</u>	
UK, 2000	FS 500	1	0.125	n.a.	<u>85</u>	<u>0.01</u>	
UK, 2000	FS 500	1	0.125	n.a.	<u>95</u>	<u><0.01</u>	
UK, 2000	FS 500	1	0.125	n.a.	<u>95</u>	<u><0.01</u>	
UK, 2000	FS 500	1	0.125	n.a.	<u>80</u>	<u><0.01</u>	
FR North, 2001	FS 500	1	0.250	n.a.	120	0.01*	Grolleau, G. 2002
GR, 2001	FS 500	1	0.220	n.a.	<u>99</u>	<u>0.01</u>	
GR, 2001	FS 500	1	0.220	n.a.	<u>99</u>	<u><0.01</u>	
IT, 2001	FS 500	1	0.220	n.a.	<u>98</u>	<u><0.01</u>	
IT, 2001	FS 500	1	0.220	n.a.	<u>96</u>	<u>0.01</u>	

[1] n.a. = not applicable
[2] peeled potato
[3] potato peel

Note: Underlined residue values result from treatments within 25% of the GAP (application rate: 0.15 kg a.s./ton in Northern Europe, 0.25 kg a.s./ha in Southern Europe, PHI: 80 days ± 25% in early potatoes)
*Residue values resulting from treatments 'worse' than GAP (outside 25% range)

Table B.7.6.b: Results of residue trials performed with tolclofos-methyl in ware potatoes (data used for calculations of proposed MRLs are underlined, i.e. those corresponding to critical GAP and a PHI of 120 days).

State, year	Formulation	Application			PHI days	Residues mg/kg	Reference
	(type & content of a.s.)	No.	Rate kg a.s./ton	Spray conc. kg a.s./ton			
UK, 1980	WP 500	1	0.125	n.a. [1]	155	< 0.01*	Cron, J.H. 1982
UK, 1980	WP 500	1	0.125	n.a.	162	0.07 *	
UK, 1980	WP 500	1	0.125	n.a.	167	0.01*	
UK, 1980	WP 500	1	0.125	n.a.	196	0.03*	
UK, 1980	WP 500	1	0.125	n.a.	153	< 0.01*	
UK, 1980	WP 500	1	0.125	n.a.	155	< 0.01*	
UK, 1980	WP 500	1	0.125	n.a.	153	< 0.01*	
UK, 1982	DS 50	1	0.125	n.a.	134	0.01	Longland, R.C. 1983
DE, 1986	FS 250	1	0.15	n.a.	125 139	≤ 0.002 ≤ 0.002	Anon, 1987
DE, 1986	FS 250	1	0.15	n.a.	147 165	≤ 0.002 < 0.002	Anon, 1986 QR-61-0038G
DE, 1986	FS 250	1	0.15	n.a.	123 136	≤ 0.002 < 0.002	Anon, 1986 QR-61-0040G
DE, 1986	FS 250	1	0.15	n.a.	136 147	0.007 < 0.002	Anon, 1986 QR-61-0042G
DE, 1986	FS 250	1	0.15	n.a.	150 165	≤ 0.002 < 0.002	Anon, 1986 QR-61-0044G
DK, 1993	DS 100	1	0.15	n.a.	60 109 148	0.07 0.04 0.04	Holmgaard, M. 1994
DK, 1993	FS 500	1	0.15	n.a.	60 109 148	0.05 < 0.01 0.02	
UK, 1993	FS 500	1	0.125	n.a.	0 141 155	123 0.20 0.06	Burden, A.N. 1994 QR-41-0102
DE, 1993	FS 500	1	0.142	n.a.	149	≤ 0.02	Tillkes, M. 1994
FR North, 2001	FS 500	1	0.250	n.a.	125	0.02*	Grolleau, G 2002

[1] n.a. = not applicable

*Residue values resulting from treatments 'worse' than GAP (outside 25% range)

Comments:

Residue trials of the years 1982 to 1993 have not been performed according with GLP as they were completed before the time that GLP became applicable to residue trials. The EU Working Document 7017/VI/95 rev. 4 refers to studies initiated before the time of GLP became applicable to residue trials. The working document states that studies initiated before 1993 and before Directive 91/414/EEC not should be rejected for the reason that GLP was not applied, provided that they are valid scientifically. RMS considers the trials before 1982-1993 as scientifically valid.

The formulations in trials from 1982-1993 differ from formulation in trials from 2000-2001. In Commission Working Document 7525/VI/95 rev.7, a guideline to changes of formulations is given. Where treatments are made to the seed, the formulation is considered to be of no importance and thus no further studies on formulations are required.

In residue trials not performed according to GLP, i.e. in studies of 1982 to 1993, residues ranged from < 0.002 to 0.2 mg/kg. It is assumed that this phenomenon originates in a sampling under more practical conditions by which the originally treated and, at the time of harvest, exhausted parent tuber might have contaminated the daughter tubers. This is also illustrated in a study by Longland (Table B.7.6.1) where the effect of peeling was studied. Residues on the peel were 0.07 and 1.19 mg/kg while those in peeled tubers were below or at the limit of quantification. This allows the conclusion that the residues resulted from an external contamination of the daughter tubers by the parent tuber. To reflect practical conditions these trials are included in the MRL calculation in section B.7.12.

Lettuce:

In 2000, 8 supervised residue trials were performed, in accordance with critical GAP ± 25%, on lettuce grown in glasshouse. 4 of the trials were carried out in winter lettuce with a PHI of 56 days and the other 4 in summer lettuce with a PHI of 28 days. In winter lettuce, residue levels at harvest were between 0.06 and 0.41 mg/kg, in summer lettuce they ranged from 0.23 to 0.39 mg/kg. It is concluded that residue levels in protected lettuce are independent of the growing period.

Table: B.7.6.c: Results of residue trials performed on tolclofos-methyl in protected lettuce (data used for calculations of proposed MRLs are underlined, i.e. those corresponding to critical GAP and a PHI of 28/56 days).

State, year	Formulation	Application			PHI days	Residues mg/kg	Reference
	(type & content of a.s.)	No.	Rate kg a.s./ha	Spray conc. kg a.s./hl			
BE, 2000	SC 500	1	2	0.2	53	<u>0.10</u>	Pigeon,O. 1994
BE, 2000	SC 500	1	2	0.2	0 42 56 70	200.56 1.33 <u>0.41</u> 0.17	
BE, 2000	SC 500	1	2	0.2	56	<u>0.09</u>	
BE, 2000	SC 500	1	2	0.2	0 42 56	149.48 0.14 <u>0.06</u>	
BE, 2000	SC 500	1	2	0.2	27	<u>0.39</u>	
BE, 2000	SC 500	1	2	0.2	0 14 27	182.17 1.32 <u>0.25</u>	
BE, 2000	SC 500	1	2	0.2	28	<u>0.24</u>	
BE, 2000	SC 500	1	2	0.2	0 14 28	213.43 0.98 <u>0.23</u>	

Note: The underlined residue values result from treatments within 25% of the GAP (application rate: 2 kg a.s./ha, PHI: 56 days in winter lettuce, 28 days in summer lettuce)
*Residue values resulting from treatments 'worse' than GAP (outside 25% range)

Comments:

The guideline 7029/VI/95 rev.6 (5.2) states that a minimum of 8 residue trials are required. For crops growing throughout the years, trials should cover different climatic conditions during the year. Due to the inherently higher level of homogeneity in residues arising from protected crops, trials from one growing season will be

acceptable. Furthermore, intended glasshouse uses within the EU should be based on residue data generated within EU assuming that this is one single zone. For these reasons 8 trials in glasshouse are considered sufficient to illustrate residues in protected lettuce. The range of residues is similar in winter and summer lettuce.

B.7.6.1 Storage stability of residues prior to analysis

Crop:	Lettuce	**No of application:**	1
Reference:	Anspach, Th. & Pelz, S. (2002) Freezer storage stability study of Tolclofos-methyl in/on lettuce	**Application conc.:**	0.1 mg/kg
Test substance:	**Test material 1:** Tolclofos-methyl, analytical standard (Batch No.: 70312, Purity: 99.1%, Specification No.: none). Test material used for fortification and determination up to 01.04.2001.	**Dates of experimental work:**	May 2000 to February 2002
		GLP statement:	Yes
	Test material 2: Tolclofos-methyl, analytical standard (Batch No.: 00103, Purity: 99.0%, Specification No.: none). Test material used for fortification and determination after 01.04.2001.	**Guidelines:**	EU Commission Working Document 1607/VI/97, Appendix H: Storage stability 7032/VI/95 rev.5 US EPA Residue chemistry test guidelines, OPPTS 860.1380 storage stability data

Material and methods:

Specimens of lettuce were fortified with tolclofos-methyl in acetone (5.02 µg/ml). This corresponded to a fortification level of 0.1 mg/kg. Over a freezer storage period of 18 months, homogenised specimens of lettuce were analysed for tolclofos-methyl using DFG Method S 19 (extended revision). The weight of each specimen was 50 g. Control and freshly fortified specimens were analysed in single determination. Aged fortified specimens were analysed in duplicate in single extraction with single injection. Specimen material was extracted with acetone. Water was added beforehand in an amount that takes account of the natural water content of the specimens so that during extraction the acetone: water ratio remained constant at 2:1 (v:v). For liquid-liquid partition ethyl acetate/cyclohexane (1+1) and sodium chloride were added and after repeated mixing excess water was separated. The evaporated residue of an aliquot of the organic phase was cleaned up by gel permeation chromatography on Bio Beads S-X3 polystyrene gel using a mixture of ethyl acetate/cyclohexane (1+1) as eluent. The residue-containing fraction was concentrated and analysed for residues of tolclofos-methyl by gas chromatography using a flame photometric detector (FPD, phosphorous mode).

Findings:

The mean recoveries of the frozen samples stored for extended period up to 18 month were 83 - 102%, which showed acceptable stability. Findings are summarised in table B.7.6.4.a.

Table B. 7.6.1.a: Analytical results for lettuce treated with tolclofos-methyl and stored in the freezer at -18 °C for up to 18 months

Time (months)	Frozen samples [1]			Procedural recoveries[2] (%)
	Found (mg/kg)	Recovery (%)	Mean recovery (%)	
0	0.0895, 0.0897	90, 90	90	95
3	0.0919, 0.0946	92, 95	93	99
6	0.0868, 0.0860	87, 86	86	83
12	0.0786, 0.0871	79, 87	83	94
18	0.1028, 0.1012	103, 101	102	91

[1] The untreated control samples showed no interference with other substances at the retention time of tolclofos-methyl.
[2] Recoveries from samples fortified just before analysis. The procedural recoveries were within the range of 70 to 110%, which assures the validity of analytical procedures during the study.

Conclusion:

Residues of tolclofos-methyl in lettuce were stable for up to 18 months following storage at -18°C.

Comments:

The study was well performed and reported.

Crop:	Potatoes	**No of application:**	1
Reference:	Burden, A (1996) Tolcofos-methyl – Evaluation of residue stability in potatoes under deep freeze storage conditions.	**Dates of experimental work**	October 1995
Test substance	Tolcofos-methyl (Batch No.: R00615, Purity: 100% - analytical standard)	**GLP statement**	Yes
Application conc.:	0.50 mg/kg	**Guidelines:**	EPA Pesticide Assessment Guidelines, Subdivision O, Series 171-4 (b)

Materials and methods:

Approximately 25 g of ground untreated potatoes was fortified with the acetone solution of tolclofos-methyl at a concentration of 0.50 mg/kg. The potato samples were thoroughly mixed and left for 30 minutes to allow evaporation of the solvent and then frozen at approximately -18°C in the dark. Samples were analysed at 0, 3, 6, 12 and 22 moths after freezing.

At each time point, analysis was done on one untreated sample, two untreated samples fortified at 0.50 mg/kg just before analysis (procedural recoveries) and three samples stored at -18°C.

The samples were extracted with acetone by Soxhlet, and the extract volumes reduced by evaporation. Water and hexane were added for partition. Clean-up was carried out using pre-packed silica cartridge. Tolclofos-methyl was determined by gas chromatography equipped with a nitrogen phosphorus detector (NPD).

The limit of determination found in the validation study was 0.05 mg/kg. Specificity and linearity were adequately shown in the report. Repeatability was good as the mean recoveries were in the range of 86 to 97 % and relative standard deviations were in the range 6.5 to 14.7 %.

The mean recoveries of the frozen samples stored for extended period up to 22 month were 93 - 105 %, which showed acceptable stability (Table B. 7.6.1.b.).

Table B. 7.6.1.b: Analytical results for potato samples treated with tolclofos-methyl and stored in the freezer (- 18 °C) for up to 22 months

Time (months)	Frozen samples [1]			Procedural recoveries[2] (%)
	Found (mg/kg)	Recovery (%)	Mean recovery (%)	
0	0.49, 0.51, 0.52	98, 102, 104	101	102, 103
3	0.50, 0.54, 0.53	100, 108, 106	105	97, 104
6	0.43, 0.51, 0.46	86, 102, 92	93	88, 92
12	0.48, 0.51, 0.48	96, 102, 96	98	92, 99
22	0.54, 0.45, 0.51	108, 90, 102	100	95, 98

[1] The untreated control samples showed no interference with other substances at the retention time of tolclofos-methyl.
[2] Recoveries from samples fortified just before analysis. The procedural recoveries were within the range of 70 to 110%, which assures the validity of analytical procedures during the study.

Conclusion:

Residues of tolclofos-methyl in potatoes were stable for up to 22 months following storage at -18°C.

Comments:

The study was well performed and reported.

B.7.7 Effects of industrial processing and/or household preparation (Annex IIA 6.5; Annex IIIA 8.4)

In potatoes, major processed fractions are boiled potatoes with or without peel, fried potatoes without peel and potato crisps. The results of the residue trials presented under section B.7.6 and B.7.12 indicate that, after elimination of one outlier according to the Q-test of DIXON, residues of tolclofos-methyl do not exceed 0.1 mg/kg when tolclofos-methyl formulations are used according to Good Agricultural Practice.

Lettuce is a food commodity, which is generally consumed raw. Industrial processing is not applicable to lettuce. Household preparation is limited to removing leaves and washing. Hence, no processing studies are required in lettuce.

Directive 96/68/EC states that processing studies are not normally required if no significant residues, i.e. residues < 0.1 mg/kg, occur in the plant product which would be processed or if the total Theoretical Maximum Daily Intake (TMDI) is less than 10% of the ADI. Since both conditions are met for tolclofos-methyl, processing studies are not required.

Effects on the nature of the residue

Effects of industrial processing and/or household preparation (representative processing situations) on the nature of the residue

Cooking vegetables in water

Processing studies in potatoes and lettuce are not required. Therefore it is not necessary to determine the effects of cooking of vegetables on the nature of the residue.

Effects on the residue levels

Balance studies on a core set of representative processes

Lettuce is not a commodity that is peeled during processing. Balance studies for the determination of the distribution of the residues in potato peel and pulp are not required. However, studies on the effects of peeling of potatoes on residues in peel and peeled potatoes indicate that residues present in non-peeled potatoes are reduced, by peeling, to or below the Limit of Quantification, i.e. 0.01 mg/kg. The transfer factors from whole potato to flesh and peel were less than 0.4 and 6.6, respectively.

Follow-up studies to determine concentration or dilution factors

Distribution of the residue in peel/pulp

Lettuce is not a commodity that is peeled during processing. Follow-up studies for the determination of the distribution of the residue in peel and pulp are not required (see Section B.7.7). Studies on the effects of peeling of potatoes on residues in peel and peeled potatoes indicate that residues present in non-peeled potatoes are reduced, by peeling, to the Limit of Quantification, i.e. 0.01 mg/kg. The transfer factors from whole potatoes to flesh and peel were less than 0.4 and 6.6, respectively.

Conclusions and comments:

In potatoes, residues of tolclofos-methyl did not exceed 0.1 mg/kg. Directive 96/68/EC states that processing studies are not normally required if no significant residues, i.e. residues > 0.1 mg/kg, occur in the plant product which would be processed or if the total Theoretical Maximum Daily Intake (TMDI) is less than 10% of the ADI. Since both conditions are met for this active substance, processing studies are not required. If the intended use is extended this conclusion may need to be reconsidered.

B.7.8 Livestock feeding studies (Annex IIA 6.4; Annex IIIA 8.3)

Of the intended uses of tolclofos-methyl, ware potatoes are the only commodities fed to animals. Significant residues of tolclofos-methyl (> 0.1mg/kg of the total diet) do not occur in ware potatoes.
Metabolism studies do not indicate that significant residues (0.01 mg/kg) may occur in any edible animal tissue.

Therefore, livestock feeding studies are not required. If the intended use is extended this conclusion may need to be reconsidered.

B.7.9 Residues in succeeding or rotational crops (Annex IIA 6.6, Annex III 8.5)

Studies on residues in succeeding crops are not required because tolclofos-methyl is easily degraded in soil and no significant residues remain in soil until sowing or planting time of possible succeeding crops.

Residues of tolclofos-methyl in soil decline rapidly. The DT_{90} values in aerobic soil degradation studies conducted at 20°C are 6.9-20 days (see the section about Fate and behaviour in soil Annex B8: Table 8.1.4.a), which indicates the residues of tolclofos-methyl are less than 10% of the initial after 30 days. In addition, there are no significant metabolites observed in these degradation studies.

Theoretical consideration of the nature and level of the residue:

Theoretical consideration of the nature and level of the residues is not required because no significant residues remain in soil until sowing or planting time of possible succeeding crops.

Metabolism and distribution studies on representative crops:

Root vegetables:

Metabolism and distribution studies on representative crops of root vegetables are not required because no significant residues remain in soil until sowing or planting time of possible succeeding crops.

Brassica vegetables:

Metabolism and distribution studies on representative crops of brassica vegetables are not required because no significant residues remain in soil until sowing or planting time of possible succeeding crops.

Leafy vegetables:

Metabolism and distribution studies on representative crops of leafy vegetables are not required because no significant residues remain in soil until sowing or planting time of possible succeeding crops.

Cereals:

Metabolism and distribution studies on representative crops of cereals are not required because no significant residues remain in soil until sowing or planting time of possible succeeding crops.

Field trials on representative crops:

Root vegetables:

Field trials on representative crops of root vegetables are not required because no significant residues remain in soil until sowing or planting time of possible succeeding crops.

Leafy vegetables:

Field trials on representative crops of leafy vegetables are not required because no significant residues remain in soil until sowing or planting time of possible succeeding crops.

Cereals:

Field trials on representative crops of cereals are not required because no significant residues remain in soil until sowing or planting time of possible succeeding crops.

Residues in succeeding crops - summary and conclusions:

Studies on residues in succeeding crops are not required because tolclofos-methyl is easily degraded in soil and no significant residues remain in soil until sowing or planting time of possible succeeding crops.

Residues of tolclofos-methyl in soil decline rapidly. The DT_{90} values in aerobic soil degradation studies conducted at 20°C are between 6.9 and 20 days which indicates the residues of tolclofos-methyl are less than 10% of the initial after 30 days. In addition, there are no significant metabolites observed in these degradation studies.

The active substance is non-systemic. Even if, due to failure of a crop, plant materials are incorporated into soil, there is no risk of residues in succeeding crops.

Therefore, no residue data for succeeding crops is required for tolclofos-methyl.

B.7.10 Proposed pre-harvest intervals for envisaged uses, or withholding periods, in the case of post-harvest uses (Annex IIA 6.8; Annex IIIA 8.7)

Potatoes:

In potatoes, the proposed pre-harvest interval by the notifier is 80 days. This corresponds to the shortest interval from planting to harvesting observed in the production of early potatoes in northern Europe and of potatoes in southern Europe. In all presented residue trials in early potatoes the PHI was in the range of 80-100 days. Under climatic conditions typical for southern Europe potatoes are harvested within a period of 80-100 days and no distinction is made between early potatoes and ware potatoes. A PHI of 80 days for potato "all" in southern Europe is therefore recommended. In northern Europe however, the PHI in ware potatoes in presented residue trials was on average 153 days. **It is therefore recommended that PHI in ware potatoes should be changed from 80 to 120 days.**

Table B.7.10.a: RMS proposes the following PHI:s

Region	Type	PHI (days)
South	Potatoes, all	80
North	Potatoes, early	80
	Potatoes, ware	120

Lettuce:

In protected lettuce, the proposed pre-harvest interval by the notifier is 28 days in both southern and northern Europe. In northern Europe, distinction is made between winter lettuce and summer lettuce. In southern Europe all protected lettuce is considered summer lettuce since under favourable climatic conditions in the south the

period from transplanting to harvesting is short with little fluctuation during the year. The range of residues is similar in winter and summer lettuce but PHI are different. The MRL calculations are based on residue data from PHI of 28 for summer lettuce and 56 days for winter lettuce. **It is therefore recommended that PHI should be 56 days for winter lettuce and 28 days for summer lettuce**.

Table B.7.10.b: RMS proposes the following PHI:s

Region	Type	PHI (days)
South	Summer Lettuce, protected,	28
North	Summer Lettuce, protected	28
	Winter Lettuce, protected	56

Re-entry period (in days) for livestock, to areas to be grazed:

Tolclofos-methyl is intended for pre-sowing application in potatoes and for nursery bed or field application in protected lettuce. These crops are grown on bare soil and are not intended for grazing by livestock. Hence, the establishment of a re-entry period for livestock is not required.

However, if the intended use will be extended this conclusion has to be re-evaluated.

Re-entry period (in hours or days) for man to crops, buildings or spaces treated:

Tolclofos-methyl is intended for pre-sowing application in potatoes and for nursery bed or field application in protected lettuce. Seed potatoes treated with tolclofos-methyl are in the ground. A *re-entry period for man to potato crops* is not required.

Just after transplanting, protected lettuce is at a very early growth stage of development. Under practical conditions, there is no specific re-entry period to be recommended, as there is no reason for workers to enter a greenhouse shortly after treatment. In theory, *re-entry for man to protected lettuce crops* should only be authorised after the spray has reached the soil and has dried. In greenhouses treated by automatic gantry sprayers, this may take 2 to 3 hours.

Withholding period (in days) for animal feeding stuffs:

Tolclofos-methyl is intended for pre-sowing application in potatoes and for nursery bed or field application in protected lettuce. Freshly sown/planted crops do not normally serve as animal feeding stuffs. Protected lettuce is not normally fed to livestock. Hence, the withholding period for animal feeding stuffs corresponds to the shortest cropping season of potatoes, i.e. 80 for southern Europe (early potatoes) and 120 for northern Europe (ware potatoes).

Waiting period (in days) between last application and sowing or planting the crop to be protected:

Tolclofos-methyl is intended for pre-sowing application in potatoes and for nursery bed or field application in lettuce. As tolclofos-methyl and its formulations are not phytotoxic no waiting period is required between the application and sowing or planting of the crop to be protected.

Waiting period (in days) between application and handling treated products:

Tolclofos-methyl is intended for pre-sowing application in potatoes and for nursery bed or field application in protected lettuce. Handling other than harvesting is not required with these crops. Therefore, the waiting period between application and handling, i.e. harvesting, of treated product corresponds to the cropping period. In addition, estimated exposures (using Uniform Principles for safeguarding workers prepared by Germany) for workers not wearing protective clothing are below the AOEL (chapter B.4).

Waiting period (in days) between last application and sowing or planting succeeding crop:

Tolclofos-methyl is intended for pre-sowing application in potatoes and for nursery bed or field application in protected lettuce. As tolclofos-methyl and its formulations are not phytotoxic no waiting period is required between the application and sowing or planting of the crop to be protected. Should the treated crop fail to grow a succeeding crop may be planted immediately as metabolism studies have shown that there was very little uptake of tolclofos-methyl and its metabolites from soil into plants.

B.7.11 Community MRLs and MRLs in EU Member States (Annex IIIA 12.2)

Table B.7.11.a : MRLs in EU Member States

Country/Organisation	Commodity	MRL (mg/kg)	Residue definition
EU	---	---	---
Austria	Potato Lettuce	0.1 1	tolclofos-methyl
Belgium	Potato Lettuce	0.01 0.5	tolclofos-methyl
Denmark	Potato	0.05	tolclofos-methyl
Finland	Lettuce	0.5	tolclofos-methyl
France	---	---	---
Germany	Potato Lettuce	0.05 1	tolclofos-methyl
Greece	---	---	---
Ireland	---	---	---
Italy	Potato Lettuce	0.1 1	tolclofos-methyl
Luxembourg	Potato Lettuce	0.01 0.5	tolclofos-methyl
The Netherlands	Potato Lettuce	0.05 1	tolclofos-methyl
Portugal	---	---	---
Spain	Potato Lettuce	0.01 0.05	tolclofos-methyl
Sweden	---	---	---
United Kingdom	---	---	---
CCPR (CXL)	Potato Lettuce, head/leaf	0.2 2	tolclofos-methyl
Codex Proposal	Potato Lettuce, head/leaf	0.2 2	tolclofos-methyl

B.7.12 Proposed EU MRLs and justification for the acceptability of those MRLs (Annex IIA 6.7; Annex IIIA 8.6)

Potatoes:

20 supervised residue trials (4 in southern EU and 16 in northern EU,) according to proposed GAP ± 25% over a period of more than 2 years (Table B.76.a), are included in the MRL calculation for early potatoes. Only 4 trials are present in southern EU, in two trials residues (0.01mg/kg) were found. However, the residue level did not differ much from the levels in northern EU. Results are presented in Table B.7.12.a.

Table B.7.12.a: MRL calculation for early potatoes

Crop	Method	Rmax mg/kg	Rber mg/kg	STMR
Early potatoes	I, all values	0,096		0,01
	II		0,095	

The MRL for early potato is calculated to be 0.1 mg/kg in both Method 1 and 11

10 residue trials in northern EU (Table B.7.6.b) according to proposed GAP ± 25% over a period of more than 2 years are included in the MRL calculation for ware potatoes.
Results are presented in Table B.7.12.b.

Table B.7.12.b: MRL calculation for ware potatoes

Crop	Method	Rmax mg/kg	Rber mg/kg	STMR
Ware potatoes	I, all values	0,21		0,01
	I, outliers eliminated	0,05		
	II		0,05	

After elimination of one outlier according with the Q-test of DIXON the MRL for ware potatoes is calculated to be 0.05 mg/kg in both Method 1 and 11

However, as tolclofos-methyl is evaluated to be of low toxicological concern chapter B.4, and the potential dietary exposure of tolclofos-methyl only reach less than 10 % of ADI**, RMS propose that MRL should be the same for ware potatoes and early potatoes.**

It is proposed to set the maximum residue level **(MRL)** for early and ware potatoes at
0.1 mg/kg.

It is proposed to set standard medium residue level **(STMR)** for early and ware potatoes at
0.01 mg/kg.

The MRL proposed by the notifier is confirmed.

Lettuce:
8 supervised residue glasshouse trials from 2002 (Table 3.7.6.c) are included in the MRL calculation for protected lettuce. Results are presented in Table B.7.12.c.

Table B.7.12.c

Crop	Method	Rmax mg/kg	Rber mg/kg	STMR
Lettuce	I	0.64		0.24
	II		0.71	

Method II provides practicable results where there are few data (8-12) residue trials. From maximum residue level classes of 0.5 and 1.0 the last class 1.0 is chosen.

As residues were similar in winter and summer lettuce, even though they were harvested at different PHI:s, it was concluded to calculate a general MRL for protected lettuce.

It is proposed to set the maximum residue level **(MRL)** for protected lettuce at **1.0 mg/kg**.
It is proposed to set standard medium residue level **(STMR)** for protected lettuce at **0.24 mg/kg**

The MRL proposed by the notifier is confirmed.

B.7.13 Proposed EU Import tolerances and justification for the acceptability of those residues

Not applicable, since no non-EU applications are proposed in the current dossier.

B.7.14 Basis for differences, if any, in conclusions reached having regard to established or proposed Codex MRLs

Potatoes:
Codex has proposed a MRL of 0.2 mg/kg for potatoes. The use patterns in the JMPR evaluations are both seed and soil treatment. The residue trials (a total of 23) that JMPRs proposal is based on are performed with dust, SC and WP formulations in seed potatoes. In the 10 residue trials (a total of 23) that were done in EU, only 3 were performed at dosage rate within 25% range of critical GAP (250 mg/kg).

Lettuce:
Codex has proposed a MRL of 2.0 mg/kg for lettuce. The use pattern in the JMPR evaluations is EC, WP and dust formulations. In the current dossier only a WP formulation is included.
The UK trials are performed with dosage rates of 5-20 kg a.s. /ha and PHI 38-138 days in 1984. Thus the trials are without 25% range of critical GAP (2 kg a.s./ha).

B.7.15 Estimates of potential and actual dietary exposure through diet and other means (Annex IIA 6.9; Annex IIIA 8.8)

Theoretical Maximum Daily Intake (TMDI) calculations:

WHO European model :
The TMDI based upon the WHO European regional diet was calculated applying proposed MRLs. The results are shown in Table B.7.15.a. The total TMDI is 0.000775 mg/kg b.w./day (adult, 60 kg b.w.). The result indicates that 1.21 % of the ADI is accounted for.

Table B.7.15.a: Theoretical Maximum Daily Intake (TMDI) according to WHO European model

Commodity	European intake (kg/person/day)	MRL (mg/kg)	Body weight (kg)	Exposure TMDI (mg/kg bw/day)
Potato	0.2408	0.1	60	0.00040
Lettuce	0.0225	1.0	60	0.000375

Total exposure (mg/kg bw/day)	0.000775
Proposed ADI (mg/kg bw/day)	0.064
Total dietary exposure (% of ADI)	**1.21**

BBA Guideline:

The TMDIs for a 4 to 6 year old female child (13.5 kg b.w.) were calculated according to BBA Guideline Part IV, 3-7 (1993), applying proposed MRLs. The results are shown in B.7.15.b. The TMDI for a female child is 0.000638 mg/kg b.w./day. The results indicate that 0.99% of the ADI is accounted for.

Table B.7.15.b: Theoretical Maximum Daily Intake (TMDI) according to BBA Guideline Part IV, 3-7 (1993) - 4-6 year old child

Commodity	European intake (kg/person/day)	Proposed MRL (mg/kg)	Body weight (kg)	Exposure TMDI (mg/kg bw/day)
Potato	0.0711	0.1	13.5	0.000527
Lettuce	0.0015	1	13.5	0.000111

Total exposure (mg/kg bw/day)	0.000638
Proposed ADI (mg/kg bw/day)	0.064
Total dietary exposure (% of ADI)	**0.99**

UK Consumer Exposure Model:

The TMDIs for 16-64+ year adults (70.1 kg b.w.), for 10/11and 14/15 year schoolchildren (43.6 kg b.w.), for 1.5-4.5 year toddlers (14.5 kg b.w.) and for 6-12 month infants (8.7 kg b.w.) were calculated according to the PSD Guidance on the Estimation of Dietary Intakes of Pesticides Residues, Part Three/A3/Appendix 1c (1999). Results of the calculations are shown in Tables B.7.15.c-g.

Table B.7.15.c: Theoretical Maximum Daily Intake (TMDI) according to UK Consumer Exposure Model (1999) - 16-64+ year adults

Commodity	European intake (kg/person/day)	MRL (mg/kg)	Body weight (kg)	Exposure TMDI (mg/kg bw/day)
Potato	0.3159	0.1	70.1	0.00045
Lettuce	0.0391	1.0	70.1	0.00058

Total exposure (mg/kg bw/day)	0.00103
Proposed ADI (mg/kg bw/day)	0.064
Total dietary exposure (% of ADI)	**1.60**

Table B.7.15.d: Theoretical Maximum Daily Intake (TMDI) according to UK Consumer Exposure Model (1999) - 10/11 and 14/15 year schoolchildren

Commodity	European intake (kg/person/day)	MRL (mg/kg)	Body weight (kg)	Exposure TMDI (mg/kg bw/day)
Potato	0.3000	0.1	43.6	0.000688
Lettuce	0.0111	1.0	43.6	0.000255

Total exposure (mg/kg bw/day)	0.000943
Proposed ADI (mg/kg bw/day)	0.064
Total dietary exposure (% of ADI)	**1.47**

Table B.7.15.e: Theoretical Maximum Daily Intake (TMDI) according to UK Consumer Exposure Model (1999) - 1.5-4.5 year toddlers

Commodity	European intake (kg/person/day)	MRL (mg/kg)	Body weight (kg)	Exposure TMDI (mg/kg bw/day)
Potato	0.1442	0.1	14.5	0.000994
Lettuce	0.0125	1.0	14.5	0.000862

Total exposure (mg/kg bw/day)	0.001856
Proposed ADI (mg/kg bw/day)	0.064
Total dietary exposure (% of ADI)	**2.9**

Table B.7.15.f: Theoretical Maximum Daily Intake (TMDI) according to UK Consumer Exposure Model (1999) - 6-12 month infants

Commodity	European intake (kg/person/day)	MRL (mg/kg)	Body weight (kg)	Exposure TMDI (mg/kg bw/day)
Potato	0.1003	0.1	8.7	0.00115
Lettuce	L/C	1.0	8.7	0.000000

Total exposure (mg/kg bw/day)	0.00115
Proposed ADI (mg/kg bw/day)	0.064
Total dietary exposure (% of ADI)	**1.79**

Table B.7.15.g: Estimation of the potential through diet and other means - summary and conclusions

Model	Consumer Group	Total TMDI (mg/kg bw/d)	ADI (mg/kg bw/d)	Total TMDI in % of ADI
WHO (1997)	Adult (60 kg bw)	0.000775	0.064	1.21
German BBA (1993)	Girl (13.5 kg bw)	0.000638	0.064	0.99
UK PSD (1999)	Adult (70.1 kg bw)	0.00130	0.064	1.60
	Child (43.6 kg bw)	0.000943	0.064	1.47
	Toddler (14.5 kg bw)	0.001856	0.064	2.90
	Infant (8.7 kg bw)	0.00115	0.064	1.79

Comments:

The WHO European model, the German BBA and the UK PSD consumer exposure models lead to low TMDI values and the contribution to the proposed ADI of 0.064 mg/kg bw is of maximum 1.6 % for adults, 1.47 % for schoolchildren, 2.9 % for toddlers and 1.79 % of the ADI for infants. Considering only the crops in intended use (potato and lettuce) estimates of potential dietary exposure through diet is very low and can be regarded as negligible. If however the intended use of tolclofos-methyl will be extended the conclusion may need to be re-evaluated.

National Estimated Maximum Daily Intake (NEDI) calculations:

National Estimated Maximum Daily Intake (NEDI) calculations are not needed as the Theoretical Maximum Daily Intake (TMDI) calculations demonstrate that the ADI will not be exceeded.

Since the total TMDI, which provides the worst case assessment, does not exceed 10% of the ADI it is not necessary to calculate an EMDI or a NEDI which are more realistic assessments.

Acute dietary exposure (% ARfD) calculations at the international and national level:

It is not considered necessary to set an acute reference dose (ARfD) for tolclofos-methyl because there were no acute or development effects on which it was appropriate to set an acute reference dose (chapter B.4). Therefore

acute dietary exposure (% ARfD) calculations at the international level are not required. It is not considered Therefore NESTI calculations at national and international levels are not required

B.7.16 Summary and evaluation of residue behaviour (Annex IIA 6.10; Annex IIIA 8.9)

Plant metabolism:

The metabolism of tolclofos-methyl in potatoes and lettuce grown in a greenhouse has been studied using tolclofos-methyl uniformly labelled with ^{14}C in the phenyl ring. The application methods were seed treatment for potato and foliar application for lettuce.

After treatment of seed potatoes, the majority of tolclofos-methyl applied to the seed remained unchanged and associated parent tubers. Limited translocation of ^{14}C-residues to roots, shoots, and daughter tubers was evident, and residue levels in daughter tubers are found to be low (< 0.05 mg/kg). Analysis of the residue in the daughter tubers showed that five polar degradation products were present at levels of ≤ 0.013 mg/kg. Data obtained from HPLC and LC/MS-MS identified two of these metabolites as DM-TM-CH_2OH (0.013 mg/kg) and DM-TM-COOH (0.003 mg/kg).

However, only one dosage rate 125 mg a.s./kg, which is lower than proposed Good Agricultural Practice, for southern Europe and early potatoes, was studied for potatoes. It is recommended that an additional metabolism study in potato is performed at a dosage rate of critical GAP for southern Europe and early potatoes (250 mg a.s./kg).

Following application to lettuce seedlings in the greenhouse, at the recommended application rate, a total residue of 0.23 mg/kg was present in mature plants. The level of tolclofos-methyl was low (0.08 mg/kg) Two major metabolites were isolated. These were polar in nature and were shown to be conjugates of ph-CH_3 and TM-CH_2OH.

The metabolism of tolclofos-methyl in potato and lettuce leads to the formation of low levels of a number of free metabolites some of which occur as conjugates. All these metabolites are known as rat metabolites. When tolclofos-methyl is used according to Good Agricultural Practice, concentrations of all metabolites are expected to be insignificant. For this reason, tolclofos-methyl is considered the only relevant residue for risk assessment and monitoring purposes in potato and lettuce representing root vegetables and leafy crops.

Livestock metabolism:

Tolclofos-methyl was rapidly metabolised and excreted in rats, mice, goat and hen, predominantly in the urine. Residues 7 days after dosing are generally very low in all tissues (less than 1% of the initial dose was retained in all tissues). No indication of the build-up of residues in tissues is expected after treatment for a prolonged period in all species. In all species, metabolism was mainly by oxidation of the P=S bound to P=O, oxidation of 4-methyl group and cleavage of the P-O-aryl and P-O-methyl linkages. The major metabolite in all species was 3,5-dichloro-4-hydroxybenzoic acid. This metabolite was excreted as the glycine conjugate in mice and goat and

as the free form in rats and hens. For this reason, tolclofos-methyl is considered the only relevant residue for risk assessment and monitoring purposes in livestock.

Definition of the residue:

Proposed residue definition (plants, plant products):

Based on the results of the studies on the metabolism in plants (See B.7.1) and in consideration of the presence and toxicological significance of metabolites and the suitability of analytical methods for routine monitoring, residues in plants and plant products (root vegetables and leafy crops) should be defined in terms of parent compound, i.e. tolclofos-methyl.

Proposed residue definition (products of animal origin):

Since significant residues of tolclofos-methyl (> 0.1 mg/kg of the total diet) do not occur in crops or crop parts (root vegetables and leafy crops) fed to animals, it is not considered necessary to propose a residue definition for products of animal origin.

If the intended use of tolclofos-methyl is extended the definition of residue in plants and animal products may need to be reconsidered.

Residues resulting from supervised residue trials:

The magnitude of tolclofos-methyl residues in potatoes was monitored in a total of 25 trials in early potatoes from 1982-2001 and in 18 trials ware potatoes from 1980-2001. Residues ranged from 0.01-0.07 mg/kg in early potato and from 0.002-0.04 mg/kg in ware potato after elimination of one outlier. In glasshouse lettuce 8 residue trials were performed year 2000. Residues ranged from 0.06-0.41 mg/kg in winter lettuce and from 0.23-0.39 mg/kg in summer lettuce.

Effects of industrial processing and/or household preparation on the nature and magnitude of residues:

Directive 96/68/EC states that processing studies are not normally required if no significant residues, i.e. residues > 0.1 mg/kg, occur in the plant product which would be processed or if the total Theoretical Maximum Daily Intake (TMDI) is less than 10% of the ADI. Since both conditions are met for tolclofos-methyl, processing studies are not required for potatoes. Lettuce is consumed as raw and no processing studies are required.

Residues in succeeding or rotational crops:

Studies on residues in succeeding crops are not required because tolclofos-methyl is easily degraded in soil and no significant residues remain in soil until sowing or planting time of possible succeeding crops. Residues of tolclofos-methyl and its metabolites in soil were hardly taken up by plants. The active substance is non-systemic. Even if, due to failure of a crop, plant materials are incorporated into soil, there is no risk of residues in succeeding crops.

Livestock feeding studies:

Of the intended uses of formulations of tolclofos-methyl, ware potatoes are commodities fed to animals. Significant residues of tolclofos-methyl (> 0.1mg/kg of the total diet) do not occur in ware potatoes. Metabolism studies do not indicate that significant residues (0.01 mg/kg) may occur in any edible animal tissue.

Therefore, livestock feeding studies are not required. This conclusion may be changed if intended uses are extended.

Pre-harvest intervals:

In all presented residue trials in early potatoes the PHI was in the range of 80-100 days. In northern Europe however, the PHI ware potatoes was on average 153 in presented supervised residue trials. It is therefore recommended that PHI in for ware potatoes should be changed from 80 to 120 days

In northern Europe, distinction is made between winter lettuce and summer lettuce. The MRL calculations are based on residue data with PHI of 28 days for summer lettuce and 56 days for winter lettuce. It is therefore recommended that PHI should be 56 days for winter lettuce and 28 days for summer lettuce.

Table B.7.16.a: Proposed PHIs of tolclofos-methyl

Commodity	Region	Proposed PHI (days)
Potatoes all	South	80
Potato early	North	80
Potato ware	South	120
Summer Lettuce, protected,	South	28
Summer Lettuce, protected,	North	28
Winter Lettuce, protected	North	56

Withholding periods:

Tolclofos-methyl is intended for pre-sowing application in potatoes and for nursery bed or field application in protected lettuce. Freshly sown/planted crops do not normally serve as animal feeding stuffs. Protected lettuce is not normally fed to livestock. Hence, the withholding period for animal feeding stuffs corresponds to the shortest cropping season of potatoes, i.e. 80 for southern Europe (early potatoes) and 120 for northern Europe (ware potatoes).

Proposed EU MRLs:

The magnitude of tolclofos-methyl residues in early potatoes was monitored in a total of 20 trials (4 from southern EU and 16 from northern EU) from 1982-2001, according with critical GAP. The magnitude of tolclofos-methyl residues in ware potatoes was monitored in a total of 18 trials (from northern EU) from 1980-

2001, according with critical GAP. The magnitude of tolclofos-methyl residues in lettuce was monitored in 8 trials in northern EU year 2002, according with critical GAP.

Table B.7.16.b Proposed MRLs of tolclofos-methyl

Commodity	Proposed MRL (mg/kg)	Residue definition
Potato	0.1	tolclofos-methyl
Lettuce	1.0	tolclofos-methyl

Consumers risk assessment:

The WHO European model, the German BBA and the UK PSD consumer exposure models lead to low TMDI values and the contribution to the proposed ADI of 0.064 mg/kg bw is of maximum 1.6 % for adults, 1.47 % for schoolchildren, 2.9 % for toddlers and 1.79 % of the ADI for infants. Considering only the crops in intended use (potato and lettuce) estimates of potential dietary exposure through diet is very low and can be regarded as negligible. If however the intended use of tolclofos-methyl will be extended the conclusion needs to be re-evaluated..

National Estimated Maximum Daily Intake (NEDI) calculations:

National Estimated Maximum Daily Intake (NEDI) calculations are not needed as the Theoretical Maximum Daily Intake (TMDI) calculations demonstrate that the ADI will not be exceeded.

Acute dietary exposure (% ARfD) calculations at the international and national level:

It is not considered necessary to set an acute reference dose (ARfD) for tolclofos-methyl because there were no acute or development effects on which it was appropriate to set an acute reference dose (chapter B.4) Therefore acute dietary exposure (% ARfD) calculations at the international level are not required.

B.7.17 References

Annex point / reference number	Author (s)	Year	Titel Company, Report No GLP or GEP Status (where relevant) Published or not	Eu Data Protection Claimed Y/N	Owner **
IIA, 6.0/01	Anspach, T. Pelz, S.	2002	Freezer storage stability study of tolclofos-methyl in lettuce Sumitomo Chemical Co., Ltd. Report No. QR-0127 GLP: Yes Published: No	Y*	SUM
IIA, 6.0/02	Burden, A.N	1996	Tolclofos-methyl - Evaluation of residue stability in potato under deep freeze storage conditions AgrEvo UK Limited Report No. 194/100-1012 Sumitomo Chemical Co., Ltd. Report No. QR-0122 GLP:Yes Published: No	Y*	AVS
IIA, 6.1/01	Goodyear, A.	1995	(^{14}C)-Tolclofos methyl: Glasshouse study. Metabolism of phenyl label in potatoes AgrEvo UK Limited Report No. 194/85-1015 Sumitomo Chemical Co., Ltd. Report No. QM-51-0041 GLP: Yes Published: No	N	AVS
IIA, 6.1/02	Mikami, N., Yoshimura, J., Yamada, H., Miyamoto, J.	1980	Metabolic fate of tolclofos-methyl (Rizolex®) in sugar beets Sumitomo Chemical Co., Ltd. Report No. QM-00-0003 GLP: No Published: No	N	SUM
IIA, 6.1/03	Croucher, A.	2002	(^{14}C)-Toclofos-methyl: Metabolism in lettuce Sumitomo Chemical Co., Ltd. Report No. QM-0053 GLP: Yes Published: No	Y*	SUM
IIA, 6.2/01	Yu, C.C., Guirguis, A.S.	1987	Metabolism of ^{14}C tolclofos-methyl in laying hens [redacted] Report No. 8 Sumitomo Chemical Co., Ltd. Report No. QM-71-0028 GLP: Yes Published: No	N	SUM

Annex point / reference number	Author (s)	Year	Titel Company, Report No GLP or GEP Status (where relevant) Published or not	Eu Data Protection Claimed Y/N	Owner **
IIA, 6.2/02	Yu, C.C.	1987	Metabolism of ^{14}C tolclofos-methyl in a lactating goat [redacted] Report No. 9 Sumitomo Chemical Co., Ltd. Report No. QM-71-0027 GLP: Yes Published: N	N	SUM
IIA, 6.3/01	Longland, R. C., Churchill, J.H.M.	1983	Residues of tolclofos-methyl (S-3349) in potatoes following seed treatment in the UK, 1982 [redacted] Report No. RESID/83/27 Sumitomo Chemical Co., Ltd. Report No. QR-21-0069 GLP: No Published: No	N	SUM
IIA, 6.3/02	Brown, D.C.	1992	The determination of concentrations of tolclofos-methyl (Rizolex Flowable) in potatoes – Jersey 1992 AgrEvo UK Limited Report No. PP3/92, PP4/92 Sumitomo Chemical Co., Ltd. Report No. QR-0119 GLP: Yes Published: No	N	AVS
IIA, 6.3/03	Burden, A.N.	1994	Tolclofos-methyl: 10% Dust (CR 17495; Rizolex); Seed treatment; Potatoes; AI Residues; UK; 1993 AgrEvo UK Limited Report No. 194/101-102 Sumitomo Chemical Co., Ltd. Report No. QR-41-0101 GLP: Yes Published: No	Y*	AVS
IIA, 6.3/04	Holmgaard, M.	1994	Residue study of tolclofos-methyl in potatoes [redacted] Report No. Not allocated Sumitomo Chemical Co., Ltd. Report No. QR-31-0104 GLP: Yes Publihsed: No	N	SUM
IIA, 6.3/05	Burden, A.N.	1994	Tolclofos-methyl: 50SC (CR-20677 Rizolex Flowable); Seed treatment; Potatoes; AI Residues; Jersey; 1993 AgrEvo UK Limited Report No. 194/103-1012 Sumitomo Chemical Co., Ltd. Report No. QR-41-0103 GLP: Yes Published: No	Y*	AVS

Annex point / reference number	Author (s)	Year	Titel Company, Report No GLP or GEP Status (where relevant) Published or not	Eu Data Protection Claimed Y/N	Owner **
IIA, 6.3/06	Grolleau, G.	2001	Magnitude of the residue of tolclofos-methyl in potato raw agricultural commodity Sumitomo Chemical Co., Ltd. Report No. QR-0125 GLP: Yes Published: No	Y*	SUM
IIA, 6.3/07	Grolleau, G.	2002	Magnitude of the residue of tolclofos-methyl in potato raw agricultural commodity Northern France, Italy & Greece - 2001 Sumitomo Chemical Co., Ltd. Report No. QR-0123 GLP: Yes Published: No	Y*	SUM
IIA, 6.3/08	Cron, J.H.	1982	Residues of Tolclofos-methyl (S-2349) in potatoes following seed treatment and in-furrow application in the UK, 1980 and 1981 [redacted] Report No. RESID/82/59 Sumitomo Chemical Co., Ltd. Report No. QR-01-0068 GLP: No Published: No	N	SUM
IIA, 6.3/09	Anon.	1987	Residue trials with Rizolex Flowable formulation on potatoes in Germany [redacted] Report No. SPI 01683 Sumitomo Chemical Co., Ltd. Report No. QR-61-0036G GLP: No Published: No	N	SUM
IIA, 6.3/10	Anon.	1986	Residue trials with Rizolex flowable formulation on potatoes in Germany [redacted] Report No. SPI 01423 Sumitomo Chemical Co., Ltd. Report No. QR-61-0038G GLP: No Published: No	N	SUM
IIA, 6.3/11	Anon.	1986	Residue trials with Rizolex flowable formulation on potatoes in Germany [redacted] Report No. SPI 02458 Sumitomo Chemical Co., Ltd. Report No. QR-61-0040G GLP: No Published: No	N	SUM

Annex point / reference number	Author (s)	Year	Titel Company, Report No GLP or GEP Status (where relevant) Published or not	Eu Data Protection Claimed Y/N	Owner **
IIA, 6.3/12	Anon.	1986	Residue trials with Rizolex Flowable formulation on potatoes in Germany [redacted] Report No. SPI 02457 Sumitomo Chemical Co., Ltd. Report No. QR-61-0042G GLP: No Published: No	Y	SUM
IIA, 6.3/13	Anon.	1986	Residue trials with Rizolex Flowable formulation on potatoes in Germany [redacted]. Report No. SPI 01470 Sumitomo Chemical Co., Ltd. Report No. QR-61-0044G GLP: No Published: No	N	SUM
IIA, 6.3/14	Burden, A.N.	1994	Tolclofos-methyl: 50 SC (CR 20677; Rizolex Flowable); Seed treatment; Potatoes; Al Residues; UK; 1993 AgrEvo UK Limited Report No. 194/102-1012 Sumitomo Chemical Co., Ltd. Report No. QR-41-0102 GLP: Yes Published: No	Y*	AVS
IIA, 6.3/15	Tillkes, M.	1994	Determination of the residue of methyl tolclofos in potatoes [redacted]. Report No. SPI-9401; Az. 19339/94 Sumitomo Chemical Co., Ltd. Report No. QR-41-0107 GLP: Yes Published: No	Y*	SUM
IIA, 6.3/16	Pigeon, O.	2001	Determination of residues of tolclofos-methyl in lettuce growing in greenhouse after treatment with Rizolex vloeibaar Sumitomo Chemical Co., Ltd. Report No. QR-0126 GLP: Yes Published: No	Y*	SUM

*: Protection for 5 years claimed from date of decision concerning listing in Annex I - the study report has not been submitted any of the Member States in support of an application for authorization, or (though the study report has been submitted) has not been used any of the Member States as the basis for decision on the initial authorization, or to maintain a given authorization, of a plant protection product before the date of submission of the dossier to Rapporteur Member State.

**: Owners code identifications and names (Code identification: SUM, Name: Sumitomo Chemical)