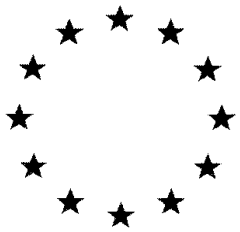
European Commission



VOLUME 1

Chlorothalonil

Rapporteur Member State: The Netherlands

September 2016

Renewal Assessment Report and Proposed decision of the Netherlands prepared in the context of the possible approval of Chlorothalonil under Regulation (EC) 1107/2009

Version history page

Date	Version history
May 2016	Draft Renewal Assessment Report
August 2016	Renewal Assessment Report

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Statement of subject matter and purpose for which this report has been prepared and background information on the application

1 Statement of subject matter and purpose for which this report has been prepared and background information on the application

1.1 Context in which the draft assessment was prepared.

1.1.1 Purpose for which the draft assessment report was prepared

This Renewal Assessment Report (RAR) is prepared for the renewal of the approval of the existing active substance chlorothalonil. Chlorothalonil is part of the AIR3 renewal programme for active substances (Commission Implementing Regulation (EU) No 844/2012).

New MRL-proposals have been included (see 2.7.10). Furthermore, some of the submitted studies for the renewal of chlorothalonil cover 'general' (not crop-specific) data gaps, which were identified during the Art-12 MRL-review (EFSA Journal 2012;10(10):2940).

No changes for Classification & Labelling are proposed.

1.1.2 Arrangements between rapporteur Member State and co-rapporteur Member State

The Netherlands conducted the full evaluation (RMS) and prepared the RAR for the active substance chlorothalonil, and the RAR was peer reviewed by the Co-Rapporteur Member Belgium.

1.1.3 EU Regulatory history for use in Plant Protection Products

Chlorothalonil is re-evaluated as an existing active substance by the Rapporteur Member State The Netherlands. The main data at that time was submitted by Zeneca (nowadays Syngenta Crop protection AG.

Chlorothalonil is approved since 1 March 2006 (Commission Directive 2005/53/EC of 16 September 2005). The original expiry date of 28 February 2016 is extended to 31 October 2017 (Regulation (EU) No 533/2013 of 10 June 2013). The Review Report – chlorothalonil SANCO/4343/2000 final (revised) - is dated 28 september 2006 and provides endpoints as agreed during the first inclusion evaluation (Appendix II of the Review Report).

There is no EFSA conclusion available.

A review of the existing Maximum residue levels (MRLs) for chlorothalonil according to Article 12 of Regulation (EC) No 396/2005 is available in EFSA Journal 2012; 10(10): 2940, as published on 24th October 2012.

Chlorothalonil is currently included in Annex VI of Regulation 1272/2008 with index Number 608-014-00-4 and the following classifcations:

Classification Reg. 1272/2008

Skin Sens. 1 - H317	Eye Dam. 1 - H318
Acute Tox. 2 - H330	STOT SE 3 - H335
Carc. 2 - H351	Aquatic Acute 1 - H400
Aquatic Chronic 1 - H410	

1.1.4 Evaluations carried out under other regulatory contexts

The FAO derived the ADI and the ARfD for chlorothalonil.
The active substance chlorothalonil is not approved as a biocide and no procedure for inclusion is on-going. No other evaluation(s) of chlorothalonil in Europe is going on.
The Joint FAO/WHO Meeting on Pesticides Residues (JMPR) has conducted several residues evaluations on chlorothalonil.

1.2 Applicant(s) information

1.2.1 Name and address of applicant(s) for approval of the active substance

Arysta LifeScience
Route d'Artix
64150 Noguères
France

Oxon Italia SpA
Via Sempione, 195
20016 Pero (MI) Italy

Syngenta Crop Crop protection AG
Schwarzwaldallee 215
CH-4058 Basel
Switzerland

1.2.2 Producers of the active substance

For the locations of the plants, please refer to volume 4 (confidential information).

1.2.3 Information relating to the collective provisions of dossiers:

The Applicant is a co-operative group who are submitting a joint dossier which consists of the following companies who are each producers of chlorothalonil for sale, supply and use in Europe:

Arysta LifeScience Route d'Artix 64150 Noguères France	Oxon Italia SpA Via Sempione, 195 20016 Pero (MI) Italy	Syngenta Crop Crop protection AG Schwarzwaldallee 215 CH-4058 Basel Switzerland

1.3 Identity of the active substance

1.3.1 Common name proposed or ISO-accepted and synonyms

Chlorothalonil (ISO 1750 published)

1.3.2 Chemical name (IUPAC and CA nomenclature)

IUPAC: Tetrachloroisophthalonitrile
CA: 2,4,5,6-Tetrachloro-1,3-benzenedicarbonitrile

1.3.3 Producer's development code numbers

Code No.: R044686

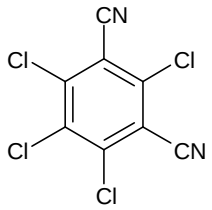
1.3.4 CAS, EC and CIPAC numbers

CAS No.: 1897-45-6
EC No.: 217-588-1
CIPAC No.: 288

1.3.5 Molecular and structural formulae, molecular mass

Molecular formula: $C_8Cl_4N_2$

Structure:



Molecular mass: 265.9 $g.mol^{-1}$

1.3.6 Method of manufacture (synthesis pathway) of the active substance

Confidential information – see Volume 4 for further details

1.3.7 Specification of purity of the active substance in g/kg

Minimum purity: 985 g/kg

1.3.8 Identity and content of additives (such as stabilisers) and impurities

1.3.8.1 Additives

Technical chlorothalonil does not contain additives.

1.3.8.2 Significant impurities

Confidential information – see Volume 4 for further details.

1.3.8.3 Relevant impurities

Two relevant impurities were identified during the evaluation:
Hexachlorobenzene (HCB): upper limit 0.04 g/kg
Decachlorobiphenyl (DCB): upper limit 0.03 g/kg

1.3.9 Analytical profile of batches

Confidential information – see Volume 4 for further details.

1.4 Information on the plant protection product

A Task Force has been formed with the purpose of defending chlorothalonil renewal. Each member has presented their own CP dossier for their representative formulation. Syngenta Crop Protection AG is the contact point for the Chlorothalonil Task Force.

1.4.1 Applicant

SYNGENTA
Syngenta Crop Protection AG
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CH-4002 Basel, Switzerland

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Fax: +41 (61) 323 6155

E-mail: ralph.moray@syngenta.com

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20016 Pero (MI)

Italy

Marina Ciccotelli

Tel: +39 02 35378217

E-mail: MCiccotelli@oxon.it

ARYSTA

Arysta LifeScience S.A.S.

Route d'Artix

BP80

64150 Noguères

France

Dr. Florence Leconte

Tel: +33 (0) 559 609 225

Fax: +33 (0) 559 717 996

E-mail: florence.leconte@arysta.com

1.4.2 Producer of the plant protection product

SYNGENTA

Syngenta Supply AG

CH4002 Basel, Switzerland

Simon Baker

Jealott's Hill, UK

Tel: +44 (0) 1344 414 803

Fax: +44 (0) 1344 416 687

E-mail: simon.baker@syngenta.com

Location of the manufacturing site

Confidential information – see Volume 4 for further details.

OXON

Confidential information – see Volume 4 for further details.

ARYSTA

Confidential information – see Volume 4 for further details.

1.4.3 Trade name or proposed trade name and producer's development code number of the plant protection product

SYNGENTA

Trade name/code number:	Amistar Opti
Alternative trade name:	Olympus, Curator, Ortiva Opti, Vertik Opti, Diskobol, Arenda 20L
Company code number:	A14111B

OXON

Trade name/code number:	Chlorothalonil 500 g/L SC
Alternative trade name:	Visclor, Visclor 500L, Rover 500, Pugil, Pugil 500 SC, Clortosip, Clortosip 500
Company code number:	SIT05210F

ARYSTA

Trade name/code number:	Chlorothalonil 500 g/L
Alternative trade name:	None
Company code number:	ARY-0474-001

1.4.4 Detailed quantitative and qualitative information on the composition of the plant protection product

1.4.4.1 Composition of the plant product

SYNGENTA

Pure active substance Chlorothalonil

content of pure active substance :	400 g/L	(32.8 % w/w)
limits :	380 – 420 g/L	(31.2 – 34.5 % w/w)

Technical active substance

content of technical active substance :	406 g/L	(33.3 % w/w)
limits :	386 – 426 g/L	(31.6 – 35.0 % w/w)

At a minimum purity of the technical active substance of 98.5 % w/w.

Pure active substance: Azoxystrobin

content of pure active substance :	80 g/L	(6.56 % w/w)
limits :	72.0 – 88.0 g/L	(5.91 – 7.22 % w/w)

Technical active substance

content of technical active substance :	86.0 g/L	(7.06 % w/w)
limits :	77.4 – 94.6 g/L	(6.35 – 7.76 % w/w)

At a minimum purity of the technical active substance of 93%.

OXON

Pure active substance

content of pure active substance :	500 g/L	(40.32 % w/w)
limits :	475 – 525 g/L	(38.3 – 42.3 % w/w)

Technical active substance

content of technical active substance :	507.53 g/L	(40.93 % w/w)
limits :	482.15 – 532.91 g/L	(38.88 – 42.98 % w/w)

At a minimum purity of the technical active substance of 98.5%.

ARYSTA

Pure active substance

content of pure active substance :	500 g/L	(40.16 % w/w)
limits :	475 – 525 g/L	(38.15 – 42.17% w/w)

Technical active substance

content of technical active substance :	507.6 g/L	(40.77% w/w)
limits :	482.6 – 532.6 g/L	(38.73 – 42.81 % w/w)

At a minimum purity of the technical active substance of 98.5 % w/w.

1.4.4.2 Information on the active substances

SYNGENTA

Type	Name/Code Number
ISO common name	Chlorothalonil (R044686)
CAS No	1897-45-6
EC No	217-588-1
CIPAC No	288
Salt, ester anion or cation present	None

Type	Name/Code Number
ISO common name	Azoxystrobin
CAS No	131860-33-8
EC No	Not available
CIPAC No	571
Salt, ester anion or cation present	None

OXON

Type	Name/Code Number
ISO common name	Chlorothalonil
CAS No	1897-45-6
EC No	217-588-1
CIPAC No	288
Salt, ester anion or cation present	None

ARYSTA

Type	Name/Code Number
ISO common name	Chlorothalonil
CAS No	1897-45-6
EC No	217-588-1
CIPAC No	288
Salt, ester anion or cation present	None

1.4.4.3 Information on safeners, synergists and co-formulants

None of the representative products contains safeners or synergists. For information on co-formulants, see Volume 4 (confidential information).

1.4.5 Type and code of the plant protection product

SYNGENTA

Suspension Concentrate [Code: SC]

OXON

Suspension Concentrate [Code: SC]

ARYSTA

Suspension Concentrate [Code: SC]

1.4.6 Function

Chlorothalonil based products are used as fungicides.

1.4.7 Field of use envisaged

Chlorothalonil containing products are used against a wide range of highly destructive organisms including *Septoria tritici* in cereals and *Phytophthora infestans* and *Alternaria* spp in tomatoes. Chlorothalonil is also active on *Phytophthora infestans* and *Alternaria* spp. on potatoes and on various diseases in other vegetables.

The representative uses concern field applications in wheat, barley, tomatoes and potato to control various pathogens of these crops. Please refer to the Details of intended use in Table 1.5.1-1, 1.5.1-2 and 1.5.1-3.

1.4.8 Effects on harmful organisms

Chlorothalonil is a non-systemic fungicide, active against a broad spectrum of fungal diseases. It has a fungitoxic action.

Chlorothalonil has a unique mode of action with the primary target being the sulfhydryl group of glutathione. Studies have indicated that chlorothalonil ties up free glutathione and thus prevents the activation (reduction) of glyceraldehyde-3-phosphate dehydrogenase and other similar enzymes. Chlorothalonil's interference with these glutathione-dependent enzymes results in disturbance of cell metabolism, ultimately leading to loss of fungal cell viability. For best disease control, chlorothalonil must be present on the plant prior to the onset of infection. This prevents the fungal cells from obtaining necessary energy to infect the plant. In effect, chlorothalonil stops spore germination and zoospore motility.

1.5 **Detailed uses of the plant protection product** (to be included for each preparation for which documentation was submitted).

1.5.1 Details of representative uses

Details of representative uses for the three preparations are provided in:
Table 1.5.1-1 for A1411B, containing Chlorothalonil 400 g/L and Azoxystrobin 80 g/L SC.
Table 1.5.1-2 for ARY-0474-001, containing 500 g/L chlorothalonil, an SC formulation.
Table 1.5.1-3 for Chlorothalonil 500 g/L SC.

Table 1.5.1-1 Representative uses of A14111B

Tradename: A14111B
Active Substances: Chlorothalonil 400 g/L + Azoxystrobin 80 g/L SC

PPP (product name/code):	A14111B	Formulation type:	SC
Active substance 1:	Chlorothalonil	Conc. of as 1:	400g/L
Active substance 2:	Azoxystrobin	Conc. of as 2:	80 g/L
Active substance….:	-	Conc. of as ….:	-
Safener:	-	Conc. of safener:	-
Synergist:	-	Conc. of synergist:	-
Applicant:	Syngenta	Professional use:	☒
Zone(s):	All zones	Non professional use:	☐
Verified by MS:	yes		
Field of use:	fungicide		

1	2	3	4	5	6	7	8	9	10	11	11	12	13	14
					Application				Application rate					
Use No.	**Member state(s)**	**Crop and/or situation (crop destination/ purpose of crop)**	**F G or I**	**Pests or Group of pests controlled (additionally: developmental stages of the pest or pest group)**	**Method/ Kind**	**Timing/Growth stage of crop & season**	**Max. Number a) per use b) per crop/ season**	**Minimum interval between applications (days)**	**L A14111B / ha a) max. rate per appl. b) max. total rate per crop/season**	**g CTL / ha a) max. rate per appl. b) max. total rate per crop/season**	**g AZT / ha a) max. rate per appl. b) max. total rate per crop/season**	**Water L/ha min/max**	**PHI (days)**	**Remarks: e.g. safener/synergist per ha**
1	EU	Wheat	F	*Pyrenophora teres, Puccinia hordei, Rhynchosporium secalis,Gaeumanomyces graminis var tritici*	Foliar	BBCH 30-69 Winter Wheat: March-June Spring Wheat: May-July	2	14 (2nd application not before BBCH 40)	a) 1.875 b) 3.75	a) 750 b) 1500	a) 150 b) 300	100-400	n.a.	No need to set PHI. See growth stage at last application
2	EU	Barley	F	*Pyrenophora teres, Puccinia hordei, Rhynchosporium secalis,Gaeumanomyces graminis var tritici*	Foliar	BBCH 30-59 Winter barley: March-June Spring barley: May-July	2	14 (2nd application not before BBCH 40)	a) 1.875 b) 3.75	a) 750 b) 1500	a) 150 b) 300	100-400	n.a.	No need to set PHI. See growth stage at last application
3	EU	Tomatoes	F	*Phytophthora infestans, Alternaria sp.*	Foliar	BBCH 51-89 From June up to PHI of 3 days	1	n.a.	a) 2.5	a) 1000	a) 200	500-1500	3	

Table 1.5.1-2 Representative uses of ARY-0474-001

PPP (product name/code):	*ARY-0474-001*	Formulation type:	SC
Active substance 1:	Chlorothalonil	Conc. of as 1:	500 g/L
Active substance 2:	-	Conc. of as 2:	-
Safener:	-	Conc. of safener:	-
Synergist:	-	Conc. of synergist:	-
Applicant:	Arysta	Professional use:	☒
Zone(s):	Central/southern zone	Non professional use:	☐
Verified by MS:	yes		
Field of use:	fungicide		

1	2	3	4	5	6	7	8	9	10	11	12	13	14
					Application				Application rate				
Use No.	**Member state(s)**	**Crop and/or situation (crop destination/ purpose of crop)**	**F G or I**	**Pests or Group of pests controlled (additionally: developmental stages of the pest or pest group)**	**Method/ Kind**	**Timing/Growth stage of crop & season**	**Max. Number a) per use b) per crop/ season**	**Minimum interval between applications (days)**	**ARY-0474-001 / ha a) max. rate per appl. b) max. total rate per crop/season**	**g CTL / ha a) max. rate per appl. b) max. total rate per crop/season**	**Water L/ha min/max**	**PHI (days)**	**Remarks: e.g. safener/synergist per ha**
1	CEU SEU	Wheat	F	*Septoria sp.*	Foliar	BBCH 30-69 Winter wheat: March-June Spring wheat: May-July	2	14 (2nd application not before BBCH 40)	a) 1.5 b) 3.0	a) 750 b) 1500	100-400	n.a.	No need to set PHI. See growth stage at last application
2	CEU SEU	Barley	F	*Pyrenophora teres, Rhynchosporium secalis,*	Foliar	BBCH 30-59 Winter barley: March-June Spring barley: May-July	2	14 (2nd application not before BBCH 40)	a) 1.5 b) 3.0	a) 750 b) 1500	100-400	n.a.	No need to set PHI. See growth stage at last application
3	CEU SEU	Tomatoes	F	*Phytophthora infestans, Alternaria solani, Botrytis cinerea*	Foliar	BBCH 51-89 June up to PHI 3	1	-	2	1 000	500-1500	3	

Table 1.5.1-3 Representative uses of Chlorothalonil 500 g/L SC

PPP (product name/code):	Chlorothalonil 500 g/L SC	Formulation type:	SC
Active substance 1:	Chlorothalonil	Conc. of as 1:	500g/L
Safener:	-	Conc. of safener:	-
Synergist:	-	Conc. of synergist:	-
Applicant:	Oxon	Professional use:	☒
Zone(s):	All zones	Non professional use:	☐
Verified by MS:	yes		
Field of use:	fungicide		

1	2	3	4	5	6	7	8	9	10	11	12	13	14
					Application				**Application rate**				
Use No.	**Member state(s)**	**Crop and/or situation (crop destination/ purpose of crop)**	**F G or I**	**Pests or Group of pests controlled (additionally: developmental stages of the pest or pest group)**	**Method/ Kind**	**Timing/Growth stage of crop & season**	**Max. Number a) per use b) per crop/ season**	**Minimum interval between applications (days)**	**L 14111B / ha a) max. rate per appl. b) max. total rate per crop/season**	**g CTL / ha a) max. rate per appl. b) max. total rate per crop/season**	**Water L/ha min/max**	**PHI (days)**	**Remarks: e.g. safener/synergist per ha**
1	EU	Wheat	F	*Pyrenophora teres, Puccinia hordei, Rhynchosporium secalis,Gaeumanomyces graminis var tritici*	Foliar	BBCH 30-69 Winter wheat: March-June Spring wheat: May-July	2	14 (2nd application not before BBCH 40)	a) 1.5 b) 3.0	a) 750 b) 1500	200-400	n.a.	No need to set PHI. See growth stage at last application
2	EU	Barley	F	*Pyrenophora teres, Puccinia hordei, Rhynchosporium secalis,Gaeumanomyces graminis var tritici*	Foliar	BBCH 30-59 Winterbarley: March-June Spring barley: May-July	2	14 (2nd application not before BBCH 40)	a) 1.5 b) 3.0	a) 750 b) 1500	200-400	n.a.	No need to set PHI. See growth stage at last application

1	2	3	4	5	6	7	8	9	10	11	12	13	14
					Application				**Application rate**				
Use No.	**Member state(s)**	**Crop and/or situation (crop destination/ purpose of crop)**	**F G or I**	**Pests or Group of pests controlled (additionally: developmental stages of the pest or pest group)**	**Method/ Kind**	**Timing/Growth stage of crop & season**	**Max. Number a) per use b) per crop/ season**	**Minimum interval between applications (days)**	**L 14111B / ha a) max. rate per appl. b) max. total rate per crop/season**	**g CTL / ha a) max. rate per appl. b) max. total rate per crop/season**	**Water L/ha min/max**	**PHI (days)**	**Remarks: e.g. safener/synergist per ha**
3	EU	Tomatoes	F	*Phytophthora infestans, Alternaria sp.*	Foliar	BBCH 51-89 From June up to PHI of 3 days	1		a) 2.0	a) 1000	500-1000	3	
4	EU	Potato	F	*Phytophthora infestans Alternaria solani*	Foliar	BBCH 40-85 May-September	1		a)1.5	a)750	200-800	28	

1.5.2 Further information on representative uses

A1411B, containing Chlorothalonil 400 g/L and Azoxystrobin 80 g/L SC (Table 1.5.1-1).
The method of application is by spray application using a hydraulic vehicle-mounted spray equipment or hand-held equipment with a water volume generally of 100-400 L/ha for wheat and barley and 500 - 1500 L/ha for tomatoes.

Maximum number of applications and their timings: two applications for wheat and barley per season; one application for tomatoes per season.

Growth stages of crops or plants to be protected:
Wheat: 2 applications, 14 day interval, BBCH 30-69, second application not before BBCH 40
Barley: 2 applications, 14 day interval, BBCH 30-59, second application not before BBCH 40
Tomato: 1 application, BBCH 51-89

Development stages of the harmful organism concerned: Not applicable. For best disease control, chlorothalonil must be present on the plant prior to the onset of infection.
Duration of protection afforded by each application: Variable due to various factors, but spay interval can be used as orientation. Cereals around +/-14 days, tomatoes around +/-7 days
Duration of protection afforded by the maximum number of applications: See above.

Minimum waiting periods or other precautions between last application and sowing or planting succeeding crops: No restrictions need to be applied
Limitations on choice of succeeding crops: No restrictions need to be applied

Proposed instructions for use as printed on labels are not relevant to this application. However national labels can be provided on request. Detailed consideration of efficacy will occur in the subsequent product authorisation process.

ARY-0474-001, containing 500 g/L chlorothalonil (Table 1.5.1-2).
The method of application is by spray application with a water volume generally of 100-400 L/ha for wheat and barley and 500- 1500 L/ha for tomatoes.
Maximum number of applications and their timings and Growth stages of crops or plants to be protected:
Wheat: 2 applications, 14 day interval, BBCH 30-69, second application not before BBCH 40
Barley: 2 applications, 14 day interval, BBCH 30-59, second application not before BBCH 40
Tomato: 1 application, BBCH 51-89
For best disease control, chlorothalonil must be present on the plant prior to the onset of infection.

Duration of protection afforded by each application: spray interval can be used as orientation. Cereals around +/-14 days, tomatoes around +/-7 days.

Minimum waiting periods or other precautions between last application and sowing or planting succeeding crops: Not necessary.
Limitations on choice of succeeding crops: No restrictions need to be applied

Proposed instructions for use as printed on labels are not relevant to this application. However national labels can be provided on request. Detailed consideration of efficacy will occur in the subsequent product authorisation process.

Chlorothalonil 500 g/L SC (Table 1.5.1-3)

In all crops the product is administered to the crop by spray application. The amount of water used is 100-400 L/ha when applying Chlorothalonil 500 g/L in wheat and barley. In tomato the water volume used is 500-1000 L water per ha and in potato 200-800 L/ha.

The number of applications is restricted to one in tomato and potato. In Wheat and barley 1-2 applications can be made.
Growth stages of crops or plants to be protected:
Wheat: 2 applications, 14 day interval, BBCH 30-69, second application not before BBCH 40
Barley: 2 applications, 14 day interval, BBCH 30-59, second application not before BBCH 40
Tomato: 1 application, BBCH 51-89
Potato: 1 application, BBCH 40-85

For best disease control, chlorothalonil must be present on the plant prior to the onset of infection.
Duration of protection afforded by each application: spray interval can be used as orientation. Cereals around +/-14 days, tomatoes around +/-7 days

Minimum waiting periods or other precautions between last application and sowing or planting succeeding crops: not necessary.
Limitations on choice of succeeding crops: No restrictions need to be applied

Proposed instructions for use as printed on labels are not relevant to this application. However national labels can be provided on request. Detailed consideration of efficacy will occur in the subsequent product authorisation process.

1.5.3 Details of other uses applied for to support the setting of MRLs for uses beyond the representative uses

This information should also be provided in the format of a GAP table; however these uses should not be covered by the GAP table under 1.5.1.

1.5.4 Overview on authorisations in EU Member States

Authorisations of the three representative formulated products are provided in table 1.5.4-1 (A14111B), table 1.5.4-2 (ARY-0474-001) and table 1.5.4-3 (500 g/L Chlorothalonil).

Table 1.5.4-1: **List of currently authorized uses and extent of use** Overview of existing registrations for A14111B (AMISTAR OPTI) in Europe/representative products containing azoxystrobin and chlorothalonil

Country	**Product name**	**Authorisation no.**	**Use(s)**	**Valid since**	**Expiry date**
Austria	AMISTAR OPTI	3066	Asparagus; Barley; Rye; Triticale; Wheat	15-Feb-2011	No date
Belgium	AMISTAR OPTI	9493P/B	Barley; Rye; Spelt; Triticale; Wheat	06-Nov-2006	31-Okt-2018
Bulgaria	AMISTAR OPTI 480 SC	01210-PRZ	Barley; Triticale; Wheat	29-Jan-2014	28-Feb-2017
Bulgaria	OLYMPUS	01210	Barley; Rye; Triticale	16-Jun-2015	28-Feb-2017
Bulgaria	ORTIVA OPTI	01210	Wheat	16-Jun-2015	28-Feb-2017
Bulgaria	PRIORI OPTI	01210	Barley; Wheat	16-Jun-2015	28-Feb-2017
Croatia	AMISTAR OPTI	UP/I-320-20/08-01/349	Barley; Legume animal feeds; Rye; Triticale; Wheat	28-Dez-2010	28-Dez-2020
Cyprus	ORTIVA OPTI 8/40 SC	2824	Beans (dry); Lupin; Pea	09-Jul-2010	31-Dez-2021
Czech republic	AMISTAR OPTI	4589-0	Barley	27-Mai-2011	28-Feb-2016
Czech republic	AMISTAR OPTI	4589-0	Wheat	24-Nov-2008	28-Feb-2016
Estonia	AMISTAR OPTI	0349/19.09.08	Barley	29-Jun-2012	31-Dez-2015
France	AMISTAR OPTI	2100179	Wheat	14-Okt-2010	No date
France	AMISTAR OPTI	2100179	Barley; Triticale; Wheat	06-Mrz-2013	No date
France	VERTIK OPTI	2100179	Rye	06-Mrz-2013	No date
France	VERTIK OPTI	2100179	Asparagus	04-Mai-2011	No date
Germany	AMISTAR OPTI	005748-00/06	Barley; Rye; Spring wheat; Triticale; Winter wheat	17-Nov-2010	31-Dez-2016
Germany	AMISTAR OPTI	005748-00	Barley; Rye; Triticale; Wheat	21-Feb-2006	31-Dez-2016
Germany	AMISTAR OPTI	005748-00/02	Barley; Wheat	07-Apr-2006	31-Dez-2016

Country	Product name	Authorisation no.	Use(s)	Valid since	Expiry date
Germany	AMISTAR OPTI	005748-00/01	Barley; Legume, forage; Rye; Triticale; Wheat	07-Apr-2006	31-Dez-2016
Germany	AMISTAR OPTI	005748-00/03	Barley; Legume animal feeds; Rye; Triticale; Wheat	07-Apr-2008	31-Dez-2016
Germany	AMISTAR OPTI	005748-00/05	Wheat	11-Feb-2009	31-Dez-2016
Germany	AMISTAR OPTI	005748-00/04	Barley; Triticale; Wheat	13-Feb-2007	31-Dez-2016
Greece	ORTIVA OPTI	60265	Barley; Rye; Triticale; Wheat	11-Feb-2010	28-Feb-2016
Hungary	AMISTAR OPTI 480 SC	02.5/10948-1/2010.	Cereals; Fruiting vegetables, cucurbits	25-Aug-2010	28-Feb-2016
Ireland	AMISTAR OPTI	PCS 03408	Carrot; Cauliflower	25-Nov-2011	No date
Ireland	CURATOR	PCS 04504	Garden bean; Onion, bulb; Pea; Tomato	31-Jan-2012	No date
Latvia	AMISTAR OPTI	325	Barley; Rye; Spring wheat; Triticale; Winter wheat	25-Mrz-2009	24-Mrz-2019
Lithuania	AMISTAR OPTI	0347F/08	Barley; Winter wheat	20-Feb-2008	20-Feb-2018
Netherlands	OLYMPUS	12787N	Winter barley; Winter wheat	13-Jan-2012	01-Jan-2022
Netherlands	OLYMPUS	12787N	Barley; Rye; Triticale; Wheat	29-Jun-2012	01-Jan-2022
Poland	AMISTAR OPTI 480 SC	R-130/2012d	Wheat	19-Jun-2012	06-Mrz-2021

Country	Product name	Authorisation no.	Use(s)	Valid since	Expiry date
Poland	AMISTAR OPTI 480 SC	R-20/2011	Barley; Bulb vegetables; Rye; Spelt; Triticale	07-Mrz-2011	06-Mrz-2021
Poland	DISKOBOL 480 SC	R-5/2012	Winter barley; Winter wheat	09-Jan-2012	24-Mai-2021
Poland	OLYMPUS 480 SC	MRiRW nr: R-32/2011	Barley; Rye; Triticale; Wheat	25-Mai-2011	24-Mai-2021
Poland	AMISTAR OPTI	3066	Melon	15-Feb-2011	No date
Portugal	AMISTAR OPTI	407	Melon; Onion; Pumpkins; Watermelon	18-Apr-2013	18-Apr-2023
Portugal	AMISTAR OPTI	407	Cucumber; Tomato	18-Apr-2013	No date
Portugal	ORTIVA OPTI	508	Melon	21-Aug-2013	21-Aug-2023
Romania	ORTIVA OPTI	069PC	Barley; Rye; Triticale; Wheat	21-Jan-2015	21-Jan-2025
Slovakia	AMISTAR OPTI	10-02-1150	Beans (dry); Lupin; Pea	29-Nov-2010	28-Feb-2016
Slovenia	AMISTAR OPTI	3433-604/2008/5	Barley; Legume animal feeds; Rye; Triticale; Wheat	06-Mai-2009	06-Mai-2019
United Kingdom	CURATOR	14955	Asparagus; Barley; Rye ; Triticale; Wheat	25-Feb-2014	31-Okt-2018

Table 1.5.4-2 List of currently authorized uses and extent of use: Overview of existing registrations for ARY-0474-001 containing 500 g/L chlorothalonil

1	*2*	*3*	*4*	*5*	*6*	*7*	*8*	*9*	*10*	*11*	*12*	*13*	*14*
					Application				*Application rate*				
Use No.	*Member state(s)*	*Crop and/or situation (crop destination/ purpose of crop)*	*F G or I*	*Pests or Group of pests controlled (additionally: developmental stages of the pest or pest group)*	*Method/ Kind*	*Timing/Growth stage of crop & season*	*Max. Number a) per use b) per crop/ season*	*Minimum interval between applications (days)*	*ARY-0474-001 / ha a) max. rate per appl. b) max. total rate per crop/season*	*g CTL / ha a) max. rate per appl. b) max. total rate per crop/season*	*Water L/ha min/max*	*PHI (days)*	*Remarks: e.g. safener/synergist per ha*
1	*PL, SK*	*Wheat*	*F*	*Septoria sp.*	*Foliar*	*BBCH 31 - 51*	*2*	*15*	*a) 1 b) 2*	*a) 500 b) 1000*	*200 - 400*	*60*	*actually used*
1	*LU*	*Wheat, Triticale, Spelt*	*F*	*Septoria sp.*	*Foliar*	*In case of attack*	*2*	*-*	*a) 1 b) 2*	*a) 500 b) 1000*	*200 - 400*	*-*	*actually used*
1	*FR*	*Wheat*	*F*	*Septoria sp.*	*Foliar*	*BBCH 31 - 51*	*2*	*-*	*a) 1,5 b) 2*	*a) 750 b) 1250*	*150 - 300*	*42*	*actually used*
1	*SL*	*Wheat*	*F*	*Septoria sp.*	*Foliar*	*BBCH 31 - 55*	*2*	*15*	*a) 1 b) 2*	*a) 500 b) 1000*	*200 - 400*	*60*	*actually used*
1	*CZ*	*Wheat*	*F*	*Septoria sp.*	*Foliar*	*BBCH 31 - 39*	*1*	*n.a*	*a) 1 b) 1*	*a) 500 b) 500*	*200 - 400*	*60*	*actually used*
2	*PL*	*Carrots*	*F*	*Alternaria nauci, Erysiphe heraclei*	*Foliar*	*BBCH 55-75*	*1*	*n.a*	*a) 2 b) 2*	*a) 1000 b) 1000*	*600-800*	*14*	*actually used*
3	*PL*	*Celery*	*F*	*Septoria apiicola*	*Foliar*	*BBCH 55-75*	*1*	*n.a*	*a) 2 b) 2*	*a) 1000 b) 1000*	*600-800*	*14*	*actually used*
4	*PL, SK*	*Tomato*	*F*	*Phytophthora infestans, Alternaria solani*	*Foliar*	*BBCH 20-88*	*1*	*n.a*	*a) 2 b) 2*	*a) 1000 b) 1000*	*PL : 200-400 SK :*	*3*	*actually used*

1	2	3	4	5	6	7	8	9	10	11	12	13	14
					Application				Application rate				
Use No.	Member state(s)	Crop and/or situation (crop destination/ purpose of crop)	F G or I	Pests or Group of pests controlled (additionally: developmental stages of the pest or pest group)	Method/ Kind	Timing/Growth stage of crop & season	Max. Number a) per use b) per crop/ season	Minimum interval between applications (days)	ARY-0474-001 / ha a) max. rate per appl. b) max. total rate per crop/season	g CTL / ha a) max. rate per appl. b) max. total rate per crop/season	Water L/ha min/max	PHI (days)	Remarks: e.g. safener/synergist per ha
											600 - 800		
4	CZ	Tomato	F	Phytophthora infestans, Alternaria solani	Foliar	Preventively, by signaling	1	n.a	a) 2 b) 2	a) 1000 b) 1000	600 - 800	3	actually used
4	SL	Tomato	F	Phytophthora infestans	Foliar	BBCH 20-88	1	n.a	a) 2 b) 2	a) 1000 b) 1000	400 - 1000	3	actually used
4	RO	Tomato	F	Phytophthora infestans	Foliar	-	-	-	a) 4 b) -	a) 2000 b) -	-	-	actually used
5	PL, SK, SL	Potato	F	Phytophthora infestans	Foliar	BBCH 40-89	1	n.a	a) 2 b) 2	a) 1000 b) 1000	PL, SK : 600-800 SL : 200 - 800	8	actually used
5	RO	Potato	F	Phytophthora infestans, Alternaria sp.	Foliar	-	-	-	a) 1.5-2.0 b) -	a) 750 - 1000 b) -	200 – 400	-	actually used
5	CZ	Potato	F	Phytophthora infestans	Foliar	Preventively, by signaling	1	n.a	a) 2 b) 2	a) 1000 b) 1000	200 - 400	8	actually used
6	PL, SK	Cucumber	F	Peronoplasmopara cubensis	Foliar	BBCH 20-88	1	n.a	a) 2 b) 2	a) 1000 b) 1000	600-800	3	actually used

1	2	3	4	5	6	7	8	9	10	11	12	13	14
					Application				Application rate				
Use No.	Member state(s)	Crop and/or situation (crop destination/ purpose of crop)	F G or I	Pests or Group of pests controlled (additionally: developmental stages of the pest or pest group)	Method/ Kind	Timing/Growth stage of crop & season	Max. Number a) per use b) per crop/ season	Minimum interval between applications (days)	ARY-0474-001 / ha a) max. rate per appl. b) max. total rate per crop/season	g CTL / ha a) max. rate per appl. b) max. total rate per crop/season	Water L/ha min/max	PHI (days)	Remarks: e.g. safener/synergist per ha
7	PL	Horse bean	F	Botrytis fabae, Ascochyta fabae	Foliar	BBCH 55-75	1	n.a	a) 2 b) 2	a) 1000 b) 1000	150-300	14	actually used
7	FR	Horse bean	F	Ascochyta so.	Foliar	BBCH 61-69	2	-	a) 2 b) 4	a) 1000 b) 2000	150-300	30	actually used
8	PL	Lupinus	F	Colletotrichum gloeosporioides	Foliar	BBCH 55-75	1	n.a	a) 2 b) 2	a) 1000 b) 1000	150-300	14	actually used
9	PL	Onions	F	Peronospora destructor	Foliar	BBCH 55-75	1	n.a	a) 2 b) 2	a) 1000 b) 1000	600-800	14	actually used
10	PL	Bean	F	Colletotrichum lindemuthianum	Foliar	BBCH 55-75	1	n.a	a) 2 b) 2	a) 1000 b) 1000	600-800	35	actually used
11	PL	Pea	F	Ascochyta sp.	Foliar	BBCH 55-75	1	n.a	a) 2 b) 2	a) 1000 b) 1000	600-800	35	actually used
11	LU	Pea (garden pea, pea for canning, fodder pea, dry pea)	F	Aschochyta sp. Botrytis cinerea	Foliar	n.a	1	n.a	a) 2 b) 2	a) 1000 b) 1000	150-300	n.a	actually used
12	FR	Pea (Pea for canning, Fresh pea,,	F	Sclerotinia sp, Botrytis cinerea, Pseudomonas	Foliar	BBCH 61-69	1	n.a	a) 2 b) 2	a) 1000 b) 1000	150-300	35	actually used

1	2	3	4	5	6	7	8	9	10	11	12	13	14
					Application				Application rate				
Use No.	Member state(s)	Crop and/or situation (crop destination/ purpose of crop)	F G or I	Pests or Group of pests controlled (additionally: developmental stages of the pest or pest group)	Method/ Kind	Timing/Growth stage of crop & season	Max. Number a) per use b) per crop/ season	Minimum interval between applications (days)	ARY-0474-001 / ha a) max. rate per appl. b) max. total rate per crop/season	g CTL / ha a) max. rate per appl. b) max. total rate per crop/season	Water L/ha min/max	PHI (days)	Remarks: e.g. safener/synergist per ha
		dry pea)		syringae									
13	PL	Ornamentales	F	Flowers leaf spot	Foliar	n.a	3	10 – 14	a) 0,2% b) -	a) 0,2% b) -	500-1000	n.a	actually used
14	FR	Seed crop – Leguminous fodder plants	F	Sclerotinia sclerotiorum	Foliar	n.a	1	n.a	a) 2 b) 2	a) 1000 b) 1000	150-300	n.a	actually used
15	FR	Seed crop – beet	F	Sclerotinia sclerotiorum	Foliar	n.a	1	n.a	a) 2 b) 2	a) 1000 b) 1000	150-300	n.a	actually used
16	FR	Seed crops – Vegetable gardens, perfume, aromatic, medicinal and condiment plants, flowers	F	Foliar diseases, Sclerotia diseases, Anthracnose	Foliar	n.a	1	n.a	a) 2 b) 2	a) 1000 b) 1000	150-300	n.a	actually used
17	FR	Seed crop– Umbelliferae	F	Septoria sp.	Foliar	BBCH 31 – 69	2	-	a) 1,5 b) 2	a) 750 b) 1250	150 - 300	n.a	actually used

1	2	3	4	5	6	7	8	9	10	11	12	13	14
					Application				Application rate				
Use No.	Member state(s)	Crop and/or situation (crop destination/ purpose of crop)	F G or I	Pests or Group of pests controlled (additionally: developmental stages of the pest or pest group)	Method/ Kind	Timing/Growth stage of crop & season	Max. Number a) per use b) per crop/ season	Minimum interval between applications (days)	ARY-0474-001 / ha a) max. rate per appl. b) max. total rate per crop/season	g CTL / ha a) max. rate per appl. b) max. total rate per crop/season	Water L/ha min/max	PHI (days)	Remarks: e.g. safener/synergist per ha
18	LU	Barley	F	Puccini asp.	Foliar	BBCH 37-39	2	-	a) 2 b) 4	a) 1000 b) 2000	150 - 300	n.a	actually used
19	LU	Barley, escourgeon	F	Helminthosporium teres, Rhynchosoporium secalis.	Foliar	BBCH 37-39	2	-	a) 1 b) 2	a) 500 b) 1000	150 - 300	42	actually used
20	LU	Triticale	F	Puccinia sp.	Foliar	BBCH 32-59	2	-	a) 2 b) 4	a) 1000 b) 2000	150 - 300	n.a	actually used
21	FR	Mushroom	I	Mycogone sp., Verticilium sp	Soil	After roughing-in	1	n.a	a) 3 ml/m² b) 3 ml/m²	-	-	14	actually used
22	RO	Wheat	F	Erysiphe graminis, Septoria sp., Puccinia sp.	Foliar	-	-	-	a) 1,5 b) -	a) 750 b) -	-	-	actually used
23	RO	Vine	F	Plasmopara viticola Botrytis cinerea (efect secundar)	Foliar	-	-	-	a) 2,0 b) -	a) 1000 b) -	1000	-	actually used
24	RO	Onions	F	Peronospora destructor	Foliar	-	-	-	a) 3,2 b) -	a) 1600 b) -	-	-	actually used
25	RO	Beet	F	Cercospora beticola	Foliar	-	-	-	a) 4,0 b) -	a) 2000 b) -	-	-	actually used

1	*2*	*3*	*4*	*5*	*6*	*7*	*8*	*9*	*10*	*11*	*12*	*13*	*14*
					Application				*Application rate*				
Use No.	*Member state(s)*	*Crop and/or situation (crop destination/ purpose of crop)*	*F G or I*	*Pests or Group of pests controlled (additionally: developmental stages of the pest or pest group)*	*Method/ Kind*	*Timing/Growth stage of crop & season*	*Max. Number a) per use b) per crop/ season*	*Minimum interval between applications (days)*	*ARY-0474-001 / ha a) max. rate per appl. b) max. total rate per crop/season*	*g CTL / ha a) max. rate per appl. b) max. total rate per crop/season*	*Water L/ha min/max*	*PHI (days)*	*Remarks: e.g. safener/synergist per ha*
26	*RO*	*OSR*	*F*	*Phoma lingam, Botrytis cinerea, Erysiphe spp., Alternaria spp. (side effect)*	*Foliar*	*-*	*-*	*-*	*a) 3,0 b) -*	*a) 1500 b) -*	*-*	*-*	*actually used*

Table 1.5.4-3 List of currently authorized uses and extent of use: Chlorothalonil Authorized and Actual Uses-OXON products

Registrations of Oxon Italia S.p.A Chlorothalonil 500 g/L SC in Europe-all uses .

Country	Product name	Authorisation no.	Use(s)	Valid since	Expiry date
Italy	Visclor	15341	Wheat	05/03/2012	31/10/2017
Italy	Clortosip 500 SC	14005	Wheat, Sugar beet	27/11/2009	31/10/2017
Belgium	Pugil	10112P/B	Wheat (Winter & Spring), Barley ornamentals	01/06/2012	31/10/2018
Romania	Rover 500 SC	2196	Wheat, Grape, Cucumber, Potato	27/03/2003	27/03/2013
France	Visclor 500 L	9100482	Wheat, Potato, asparagus, cucumber Pickles, tomato, combining peas, peas	01/10/1991	2017
France	Pugil 500	9500374	Wheat, Potato	01/10/1995	2017
Ireland	Rover 500	04467	Wheat (Winter & Spring), Barley, Rye, triticale	04/01/2012	n.a.
UK	Rover 500	MAPP 15496	Wheat (Winter & Spring), Barley, Field beans	26/09/2011	31/10/2018
Spain	Clortosip 50 SC	17051	Wheat, Triticale, Barley, Potato, Cucumber, Gherkin, Cucurbits non edible peel, Solanacea, Chickpeas, Dry beans and peas, Carrot, Onion, Garlic, Shallot, Spring onions, Apricot, Peach, Nectarine, Pome fruits, Strawberry, Cranberries, Currants, Broccoli, Brussels sprouts, Cauliflower, Head cabbage, Celery, Leek, Chervil, Parsley, Ornamentals (woody & herbaceous)	08/02/1988	30/01/2014
	Pugil LA	23672		31/01/2005	31/01/2015

Volume 1

Level 2

- *Chlorothalonil* –

Summary of active substance hazard and of product risk assessment

2 Summary of active substance hazard of product risk assessment

2.1 Identity

2.1.1 Summary of identity

Chlorothalonil belongs to the aromatic fungicides. Further identity information is given in level 1, paragraph 1.3. Information on the composition of technical chlorothalonil is confidential information, which can be found in volume 4, the confidential annex, of this document.

2.2 Physical and chemical properties

2.2.1 Summary of physical and chemical properties of the active substance

Chlorothalonil melts at 251°C and boils at 347°C. The vapour pressure is 7.62×10^{-5} Pa at 25°C, with a low water solubility of 0.81 mg/L at 25°C, a Henry's law constant of 2.5×10^{-2} $Pa.m^3.mol^{-1}$ was calculated. Its solubility in organic solvents is high, resulting in a log Pow of 2.94. In water, chlorothalonil shows no tendency to dissociate and it is not surface active.

Classification with regard to physical and chemical hazards is not required. Chlorothalonil is not flammable, not explosive, oxidising or self-heating.

2.2.2 Summary of physical and chemical properties of the plant protection product

SYNGENTA

The representative product, A14111B is a greenish beige suspension concentrate with a sweetish odour and a density of 1.219 g/mL at 20°C. It is not classified with regard to its physical and chemical properties, has a pH of 6.7 and a viscosity in the range 65 to 502 mPa.s at 40°C, displaying non-Newtonian flow behaviour. A14111B is surface active, with a surface tension of 29.5 mN/m at 20°C.

Storage data is available showing the product is stable in PET and HDPE for at least 2 years. Under accelerated conditions at 54°C and at low temperature, the product also remains stable. Its technical properties indicate that the product can be safely applied as intended.

OXON

Chlorothalonil 500 g/L SC is a white suspension concentrate, with a density of approximately 1.2 g/mL. It is not classified with regard to its physical and chemical properties, has a pH of 8.9 undiluted. The viscosity of the product shows a non-Newtonian flow behaviour and ranges between 554 and 6152 mPa.s at 20°C. Its surface tension is 36.6 mN/m at 20°C, indicating the product is surface active. A study for the surface tension at the highest in-use concentration is ongoing (expected late 2016).

A final shelf-life study is not yet available (final report expected May 2017), but accelerated storage data indicate the product is stable for at least 2 years when stored in HDPE.

ARYSTA

Arysta's Chlorothalonil 500 g/L SC product is a grey opaque liquid with a light chemical odour. It is not explosive, oxidising or otherwise classified with regard to its physical and chemical properties. It has a relative density of 1.245, pH of 8.3 and a viscosity in the range of 150-756 mPa.s at 20°C, showing non-Newtonian flow behaviour. The surface tension of a 1 g/L dispersion is 43.7 mN/m, but data on the undiluted product and at the highest proposed in-use concentration were not provided. A study is ongoing and is expected to be available in September 2016.

The product is stable for 2 years in HDPE and under accelerated conditions and at low temperatures. The technical properties of the product are acceptable.

2.3 Data on application and efficacy

2.3.1 Summary of effectiveness

According to the latest guidance on the preparation of dossiers for the renewal of active substances, information on efficacy is not required (SANCO/10181/2013 – rev. 2.1, 13 May 2013). More detailed consideration of effectiveness will be fully assessed in the context of subsequent applications for product authorisations.

2.3.2 Summary of information on the development of resistance

Chlorothalonil is a multi-site contact fungicide with little or no risk of causing a sensitivity shift for the active substance of the fungal population. The compound has been intensively used in agriculture for almost 50 years with no resistance issues being reported for the target pathogens on key crops. As such chlorothalonil is a key tool nowadays in a resistance management program either in alternation or in mixture with other active substances and will be in the future. Chlorothalonil slows the development of resistance to single site mode of action fungicides effectively increasing the life span of these active substances.

2.3.3 Summary of adverse effect on treated crops

The representative products have all been authorised at Member State level for > 10 years and have therefore been assessed in line with Uniform Principles. No unacceptable adverse effects are known.

2.3.4 Summary of observations on other undesirable or unintended side-effects

The representative products have all been authorised at Member State level for > 10 years and have therefore been assessed in line with Uniform Principles. No unacceptable adverse effects are known.

2.4 Further information

2.4.1 Summary of methods and precautions concerning handling, storage, transport or fire

Relevant information was provided and available in volume 3CA – B4.

2.4.2 Summary of procedures for destruction or decontamination

Relevant information was provided and available in volume 3CA – B4.

2.4.3 Summary of emergency measures in case of an accident

Relevant information was provided and available in volume 3CA – B4.

2.5 Methods of analysis

2.5.1 Methods used for the generation of pre-authorisation data

Adequate methods were provided by all applicants to determine the purity of chlorothalonil its significant and relevant impurities both in the TC and in the representative products.

Arysta's study Walker, AF, 2008 (KCP 5.1.1//04) the quantitation ions mentioned in the chromatographic conditions do not correspond to the mass fragments of the reference standard. It seems the reported mass fragments are of DCB rather than HCB. This should be clarified.

To support the risk assessment a large number of methods were provided, which were considered adequate to support the risk assessment (see volume 3CA B-5 for details).

2.5.2 Methods for post control and monitoring purposes

Methods for food/feed of plant origin

Residue definition for monitoring: chlorothalonil and SDS-3701 (R182281)

Chlorothalonil

A GC-MSD method (RAM 365/01 and RAM365/02) using matrix matched standards was provided for determination of chlorothalonil in a wide range of crops. A GC-ECD method is available for confirmatory purposes. The LOQ is 0.01 mg/kg in all crop types for both analytes.

SDS-3701 (R182281)

RAM 365/01 and 365/02 were also validated for R182281. The method requires methylation of R182281 with trimethylsilyl diazomethane. Therefore, the RMS considers method GRM005.01A the preferred method for determination of the metabolite R182281.

The LC-MS/MS method GRM005.01A (based on RAM365/01 and /02) was validated for determination of R182281 in crops. Both mass transitions were validated in the ILV study. The LOQ is 0.01 mg/kg in all crop groups.

Extraction efficiency

Efficiency of the acidified solvent extraction is considered addressed based on the data in the plant metabolism studies (95% recovery of labelled material with acidified acetone).

Methods for food/feed of animal origin

Residue definition for monitoring: SDS-3701 (R182281)

LC-MS/MS method GRM005.05A was validated in muscle, fat, liver, kidney, blood and eggs with an LOQ of 0.01 mg/kg for SDS-3701. Two mass transitions were validated and an ILV was provided for egg, liver and milk.

The extraction efficiency was not addressed.

Methods for soil

Residue definition for monitoring: chlorothalonil

GC-MS method GRM005.012A is available for determination of chlorothalonil in soil with an LOQ of 0.01 mg/kg. Validation of an additional mass fragment was provided as confirmatory method.

Acceptable validation is also available for metabolite R182281, but it requires methylation using trimethylsilyl diazomethane.

Methods for water

Residue definition for monitoring: chlorothalonil

GC-MS method GRM005.10A was validated for surface, ground and drinking water. Three mass fragments were validated, which makes the method highly specific. The LOQ in all matrices is 0.05 µg/L.

An ILV was performed for ground and surface water. Considering surface water is considered a worst-case matrix, the validation can be extrapolated to drinking water. The requirement for an ILV as laid down in Reg. 183/2013/EU is considered fulfilled.

Methods for air

Residue definition for monitoring: chlorothalonil

GC-MS method GRM005.014A is available for determination of chlorothalonil in air with an LOQ of 0.21 µg/m^3. The method was adequately validated at two temperature/humidity levels and complies with the requirements of SANCO/825/00 rev 8.1.

Methods for body tissues and fluids

Residue definition for monitoring: SDS-3701

Method GRM005.05A was validated for animal tissues, including blood with an LOQ of 0.01 mg/kg for SDS-3701 (R182281).

For urine, and human plasma, a LC-MS/MS method is validated with an LOQ of 0.01 mg/kg for SDS-3701 (R182281).

2.6 Effects on human and animal health

2.6.1 Summary of absorption, distribution, metabolism and excretion in mammals

Absorption

As deduced from urinary excretion and the radiolabel contents in the body after subtraction of the GIT-contents, at least 10% is absorbed within 168 h upon administration of a single oral dose of chlorothalonil (1.5, 15, and 105 mg/kg bw) to mice.

After repeated oral dosing (14-days) of 1.5 mg/kg bw/day to female rats, at least 7% is absorbed.

After single oral administration of 5 mg/kg bw/day to male and female bile-cannulated Han Wistar rats, 91 and 85% (168 hours) of radio label was recovered in faeces, respectively, urinary elimination accounted for 7.0 and 5.5% (168 hours) of the administered dose and biliary elimination accounted for 11-12% (72 hours) of the administered dose, resulting in an oral absorption of 18% in males and 17.5% in females. After single oral administration of 200 mg/kg bw/day to male and female bile-cannulated Han Wistar rats, 115 and 99% (168 hours) of radio label was recovered in faeces in males and females respectively, urinary elimination accounted for 2.4 and 3.0% (168 hours) of the administered dose and biliary elimination accounted for 4.9 and 7.5% (72 hours) of the administered dose, resulting in an oral absorption of 7.3% in males and 10.5% in females.

After single oral administration of 1.5, 5, 50, and 200 mg/kg bw chlorothalonil to bile duct cannulated male rats, **32%**, 25%, 26%, and 16% of the administered dose was absorbed within 48 h, respectively.

In germ-free rats dosed 50 mg/kg bw chlorothalonil, absorption was at least 3%, based on urinary excretion within 96 h. In rats, a significant difference was observed between males and females that were estimated by the reviewer to absorb at least 5.9 and 9.3%, respectively, of a single oral dose of 1.5 mg/kg bw (upon administration of 50 mg/kg bw, these percentages were a little lower).

Furthermore, absorption appeared to continue for a longer period in female rats as T_{max} was 20 and 40 h in males and females, respectively.

Upon a 50 mg/kg oral dose to bile duct cannulated dogs, approx. 8% of ^{14}C-chlorothalonil was absorbed within 48 h. In male dogs, absorption of 1.5 mg ^{14}C-chlorothalonil was at least 3.4%.

After single oral administration of 50 mg/kg bw to monkeys, at least 2-4% of the administered dose was absorbed.

Based on the available results of the initial and new data, the **oral absorption of chlorothalonil in rats at a dose level of 1.5 mg/kg bw/day is 32% in males and females, based on bile, urine, and carcass**. At a high dose of 200 mg/kg bw/day, the oral absorption of chlorothalonil is 16% in males and females.

Distribution

After single oral administration of chlorothalonil (1.5, 15, and 105 mg/kg bw) to mice, highest tissue levels were found in stomach, lung, kidneys, and liver. Tissues, altogether, contained less than 0.4% of the dose 168 h post administration.

After repeated oral dosing (14-days) of 1.5 mg/kg bw/day to female rats, the tissue distribution did not change upon multiple dosing and a plateau level was achieved after 5 days. In most tissues the residues did not exceed the LOQ; the highest levels were found in liver and kidney. In tissues the depletion half-live was 2-10 days. The blood kinetics showed increasing concentrations with ongoing administrations with a steady state after 12 days. The terminal half-life in blood was calculated to be 89 hours.
After a single dose of 5 mg/kg bw to rats, the Cmax in blood was 0.21 and 0.31 µg equiv/g in males and females, respectively, observed at 8 hours in males and 4 hours in females, with a T1/2 of 58 hours and 60 hours in males and females respectively. After a single dose of 200 mg/kg bw to rats, the Cmax was 3.2 and 6.0 µg equiv/g in males and females, respectively, observed at 12 hours post dose in both males and females.

After a single oral dose of 1.5 mg/kg chlorothalonil to bile duct-cannulated rats a maximum blood level (0.08 µg equivalents/ml) was reached 2 hours after administration. At a dose of 200 mg/kg a maximum blood level of 4.5 µg equivalents/ml was reached after 24 hours.
After a single dose of 5 and 50 mg/kg bw highest tissue levels were found in kidneys and liver. At 120 h after a single dose administration of 1.5 and 50 mg/kg bw, kidney levels were 0.077 mg eq/kg in males and 0.14 mg eq/kg tissue in females and 2.3 mg eq/kg in males and 4.4 mg eq/kg tissue in females, respectively. Upon five daily oral doses of 1.5-160 mg/kg bw to male rats, highest concentration of radiolabel were found in kidneys, 168 hours after the last dose accounting for up to 27 µg/kg tissue. Multiple administration did not result in higher blood concentrations when compared to single administration.

Upon a single oral administration of 50 mg/kg ^{14}C-chlorothalonil to dogs, less than 0.1% of the administered dose was present in liver and kidneys 48 h post administration. Radiolabel in blood, muscle, and fat, together accounted for 0.15-1.95% of the administered dose. Upon administration of a single oral dose of 1.5 mg/kg bw to male dogs, kidneys maintained a concentration of 0.37 mg eq/kg tissue at 6 and 12 h which decreased only slowly to 0.15 mg eq/kg at 48 h post dose administration. Concentrations of radioactivity in plasma declined gradually but were always twice as high as the levels in whole blood.

It may be concluded that for mice, rats, as well as for dogs, the liver and particularly, the kidneys, contained the highest levels of radiolabel upon oral administration of chlorothalonil. Multiple administration to rats did not result in higher radiolabel levels in blood when compared to single administration. Levels were higher in female compared to male rats.
After dermal administration of chlorothalonil to monkeys, highest tissue levels were obtained in the skin and intestines.

Excretion

In mice, chlorothalonil was primarily excreted via the faeces (65, 78 and 90% within 168 hours after a single oral dose of 1.5, 15 and 105 mg/kg bw, respectively). About 10-15% of the radiolabel was excreted via the urine within 168 hours. For the low doses, over 77% of the administered radiolabel was already excreted within 9 hours.

After repeated oral dosing (14-days) of 1.5 mg/kg bw/day to female rats, 7% of the administered dose is excreted in urine. During the dosing period of 14 days, a steady state in terms of excretion was reached just 2 days after the first administration.
After single oral administration of 5 mg/kg bw/day to male and female bile-cannulated Han Wistar rats, 91 and 85% (168 hours) of radio label was recovered in faeces, respectively, urinary elimination accounted for 7.0 and 5.5% (168 hours) and biliary elimination accounted for 11-12% (72 hours) of the administered dose. The majority of the (>91%) of the radio label was excreted by 96 h post dose. Excretion was essentially complete by 168 h post dose.
After single oral administration of 200 mg/kg bw/day to male and female bile-cannulated Han Wistar rats, 115 and 99% (168 hours) of radio label was recovered in faeces in males and females respectively, urinary elimination accounted for 2.4 and 3.0% (168 hours) of the administered dose and biliary elimination accounted for 4.9 and 7.5% (72 hours) of the administered dose. Excretion was complete by 168 h post dose.
Upon single oral administration of chlorothalonil to bile duct cannulated male rats, excretion into bile was 23, 16, 16, and 7.8% at dose levels of 1.5, 5, 50, and 200 mg/kg bw, respectively. Differences in dose levels of chlorothalonil did not significantly affect the percentage of the administered dose excreted in urine within 48 h (7.9-7.3% for a dose range of 1.5 to 50 mg/kg). However, the rate of excretion during the first 6 hours was much lower in the 50 mg/kg bw group. Excretion via faeces was 53, 71, 59, and 33%, for the graded dose levels. Upon single dose administration of 1.5 and 50 mg chlorothalonil/kg bw to cannulated male rats, recovery from bile and urine was 18 and 4.4% for low dose and 8.7 and 5.5% for high dose animals.
After a single dose to non-bile duct cannulated female rats, 12, 9, and 5.4% of the dose was excreted via urine, and 82, 87, and 92% was recovered from faeces at dose levels of 5, 50, and 200 mg/kg bw. Within 9 h, 9.2 and 3.8% of the administered radiolabel was excreted via urine of 5 and 50 mg/kg bw dosed animals. Faecal excretion was minimal within 9 h. Upon single dose administration of 1.5 and 50 mg chlorothalonil/kg bw to intact male and female rats, urinary excretion was 4.7-5.6% in males and 8.3-9% in females, respectively. Faecal excretion represented 82-93% of the dose with the largest portion excreted within 48 h.

Upon 5 daily doses to male rats about 7% was excreted in urine of animals dosed 1.5 and 5.0 mg/kg, and about 4% was excreted at higher dose levels. Faecal excretion was high, 82%-85% for dose ranges of 1.5 to 160 mg/kg bw.

Upon an oral dose of 50 mg ^{14}C-chlorothalonil/kg bw to bile duct cannulated dogs, within 48 h post administration, excretion into bile and urine accounted for approx. 5.1 and 1.4% of the administered dose, respectively. In non-bile duct cannulated dogs, the urinary excretion was comparable (1.2-1.7%). Faeces appeared the major route of excretion in orally dosed dogs (approx. 81% and 89-99% of the administered dose for bile duct and non-bile duct cannulated animals, respectively). In male dogs, urinary and faecal excretion represented an average 3.4% and 87% of an administered single dose of 1.5 mg/kg bw with the largest portion excreted within 24 h.

After oral administration of 50 mg/kg bw to monkeys, after 96 hours 2-4% of the administered dose was found in urine and 53-92% of the administered dose in faeces.

After dermal administration to 5 mg/kg bw chlorothalonil to rats (50 µg/cm^2) during 48 hours and 4.8 mg/kg bw (121 µg/cm^2) to monkeys, urinary excretion was 3% and 1%, respectively.

Metabolism

In rats, extractability of the radioactivity in faeces upon administration of 1.5 and 50 mg/kg bw radiolabelled chlorothalonil was generally lower in females compared to male rats. However, in the new study with rats, the recovery of radio label in faeces was only slightly lower in females (75 and 81% in 0-72 hours in 5 and 200 mg/kg bw) when compared to males (80 and 95% in 0-72 hours in 5 and 200 mg/kg bw).

Following oral administration of 5 or 200 mg/kg bw/day to male and female rats, metabolite profiles were qualitatively and quantitatively similar regardless of sex and dose. Chlorothalonil was metabolised via hydroxylation (R182281), oxidation of the nitrile groups to amides (R911966 and R611965) and glutathione conjugation (R613823, R613825, R417888 and R419492).

In plasma, R182281 was the most abundant metabolite accounting for 28-37% of the total radioactivity AUC, with R611966, R44686 and R417888 each accounting for 5.5-17% of the TRA. R182281 was excreted in faeces and accounted for <3.8% of the administered dose. Three other components were identified in plasma: chlorothalonil, R611966 and R417888. Although chlorothalonil was observed in plasma, the majority of parent compound remained unabsorbed and was the most abundant component excreted in faeces accounting for up to 64% of the administered dose. Of the other circulating components, R611966 was excreted in faeces and accounted for <5.4% of the dose. However, R417888 was only detected in plasma.

R611965, R613823, R613825 and R419492 each accounted for <5.1% of the dose in excreta. No single component accounted for >10% of the dose. Each of these components were also observed in bile, with each accounting for <2% of the administered dose.

In urine and bile a monoglutathione conjugate and metabolites containing one and/or two or more mercapturate moieties were found. In faeces, chlorothalonil was the only identified compound.
Both free thiol and thiomethyl metabolites (di- and tri-thiols) were excreted in urine of rats, upon five daily oral administrations of 5, 50, or 160 mg/kg bw chlorothalonil. An increase in the non-extractable fraction of radiolabel and a decrease in the ratio of the sum of thiol metabolites to the total radiolabel in urine were observed with increase of the dose level and time increase of the dose frequency. Furthermore, for the 160 mg/kg bw/day dose group, the ratio of tri-thiol to di-thiol metabolites in urine increased from 1.1 after the first dose to 52 after the third dose.

Upon oral administration of 50 mg/kg bw chlorothalonil to dogs, no mono- and di-thiol derivatives of chlorothalonil were detected in urine within 48 h post-administration. A tri-thiol derivative was detected in one urine sample from one dog. At least 17 metabolites were found in urine and faeces of male dogs that were given 1.5 mg chlorothalonil/kg bw. The diglutathione conjugate of chlorothalonil was found to be the major metabolite in urine, representing 0.3% of the dose. In faeces, preliminary evidence was found for the formation of 2,4,5-trichloro-6-methylthioisophthalonitrile. In liver and kidneys, the di- and triglutathione conjugates of chlorothalonil were found, in kidneys also the monoglutathione and the dicysteine conjugates. The dicysteine conjugate was also found in plasma. Thiol derivatives of chlorothalonil were also detected in urine samples of several monkeys upon oral administration of 50 mg/kg bw chlorothalonil.

Upon dermal administration of 5 mg/kg bw ^{14}C-chlorothalonil to rats (50 µg/cm^2) during 48 h, mono-, di- and tri-thiol metabolites of chlorothalonil were found in urine, however, a large variation existed among the rats. In some pooled urine samples no mono- or di-thiol derivatives were detected, in others up to 0.1% of the radiolabel recovered in the urine. The urinary excretion of the tri-thiol metabolites varied from 0.0173 to 1.16% of the radiolabel in the urine.
In monkeys, after single dermal exposure to 4.8 mg/kg bw (121 µg/cm^2) for 48 hours, no thiol derivates were detected in urine. However, according to the rapporteur the results obtained with the method of analysis used in the present study do not fully exclude urinary excretion of thiol metabolites.

Without further structural information regarding the positions of the thiol- or thiomethyl groups in the aromatic ring, the following metabolites were identified in urine of rats, dogs and/or monkeys. The actual identification of metabolites in the urine of specific species is presented in the proposed metabolic pathway.

- Mono-, di- and triglutathione conjugates of chlorothalonil.
- A dicysteine conjugate of chlorothalonil.
- Metabolites containing one and/or two or more mercapturate moieties.
- A mono-thiol derivative of chlorothalonil.
- A methylated mono-thiol derivative of chlorothalonil.
- A di-thiol derivative of chlorothalonil.
- A methylated di-thiol derivatives of chlorothalonil.
- A tri-thiol derivative of chlorothalonil.

- A methylated tri-thiol derivatives of chlorothalonil.

In Table 2.6.1-1 the metabolites identified and proposed codes or names are given. In Figure 2.6.1-1 and 2.6.1-2 the proposed metabolic pathway is given.

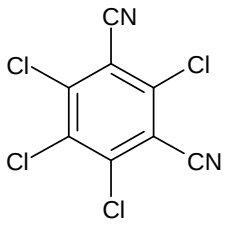
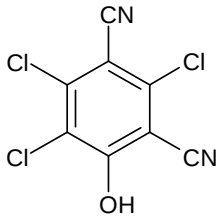
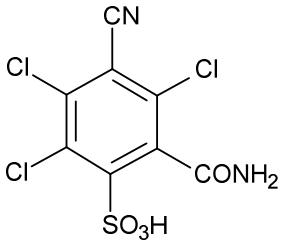
Special studies

A few special studies were submitted. From one of these studies it was concluded that one di- and one tri-thiol derivative of chlorothalonil inhibited the mitochondrial respiration *in vitro*.

In vitro species comparison

As there is no existing validated or harmonized test method available for in vitro comparative metabolism, nor guidance for interpretation of the results, an comparative in vitro metabolism study is not considered required.

Table 2.6.1-1 Metabolites found in rats; structures, codes, synonyms

Code Number (Synonyms)	**Description**	**Compound found in:**	**Structure**
Chlorothalonil R044686 SDS 2787 1897-45-6	IUPAC name: 2,4,5,6-tetrachloro-isophtalonitrile	Soil (aerobic, anaerobic, photolysis) Aquatic (water- sediment) Crop (lettuce, tomato, carrot, celery, snap beans, wheat) Rat	
R182281 SDS 3701 R1 Compound 2 C5 28343-61-5 CSCA105253	IUPAC name: 2,5,6-trichloro-4-hydroxyisophthalonitrile	Soil (aerobic, anaerobic, photolysis) Aquatic (hydrolysis) Crop (lettuce, tomato, carrot, wheat, rotated crops) Livestock (hen, goat) Rat	
R417888 M12 VIS01 R6 Compound 10 U6 CSCC890840	IUPAC name: 2-amido-3,5,6-trichloro-4-cyanobenzenesulfonic acid	Soil (aerobic, anaerobic) Crop (rotated crops) Rat	

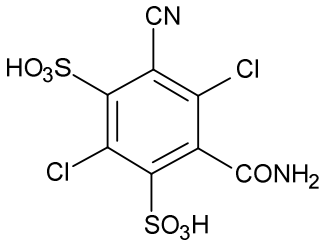
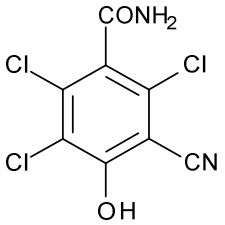
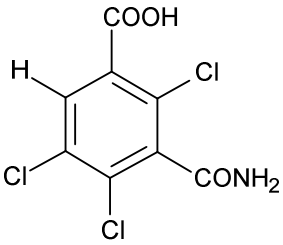
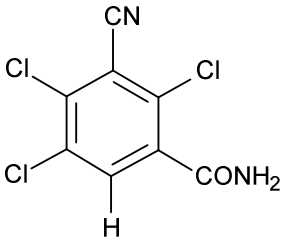
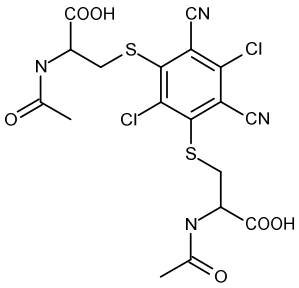
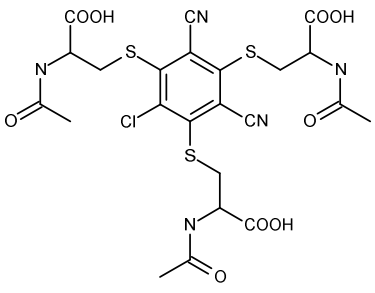
Code Number (Synonyms)	**Description**	**Compound found in:**	**Structure**
R419492 M8 R15 Compound 12 CSCA655149	IUPAC name: 4-amido-2,5-dichloro-6-cyano benzene-1,3-disulfonic acid	Soil (aerobic) Rat	
SYN507900 SDS66882 CSCC210323	IUPAC name: 2,4,5-trichloro-3-cyano-6-hydroxy-benzamide	Soil (aerobic, anaerobic)	
R611965 M5 SDS 46851 R14 Compound 4	IUPAC name: 3-amido-2,4,5-trichlorobenzoic acid	Soil (aerobic, anaerobic) Crop (snap beans, rotated crops) Rat	
R611966 SDS 47523 Compound 5	IUPAC name: 2,4,5-trichloro-3-cyano benzamid	Soil (aerobic, anaerobic) Rat	
R613823	IUPAC name: 2-acetamido-3-[3-(2-acetamido-3-hydroxy-3-oxo-propyl)sulfanyl-2,5-dichloro-4,6-dicyano-phenyl]sulfanyl-propanoic acid	Rat	
R613825	IUPAC name: 2-acetamido-3-[3,5-bis[(2-acetamido-3-hydroxy-3-oxo-propyl) sulfanyl]-4-chloro-2,6-dicyano-phenyl] sulfanyl-propanoic acid	Rat	

Figure 2.6.1-1 Proposed metabolic pathway

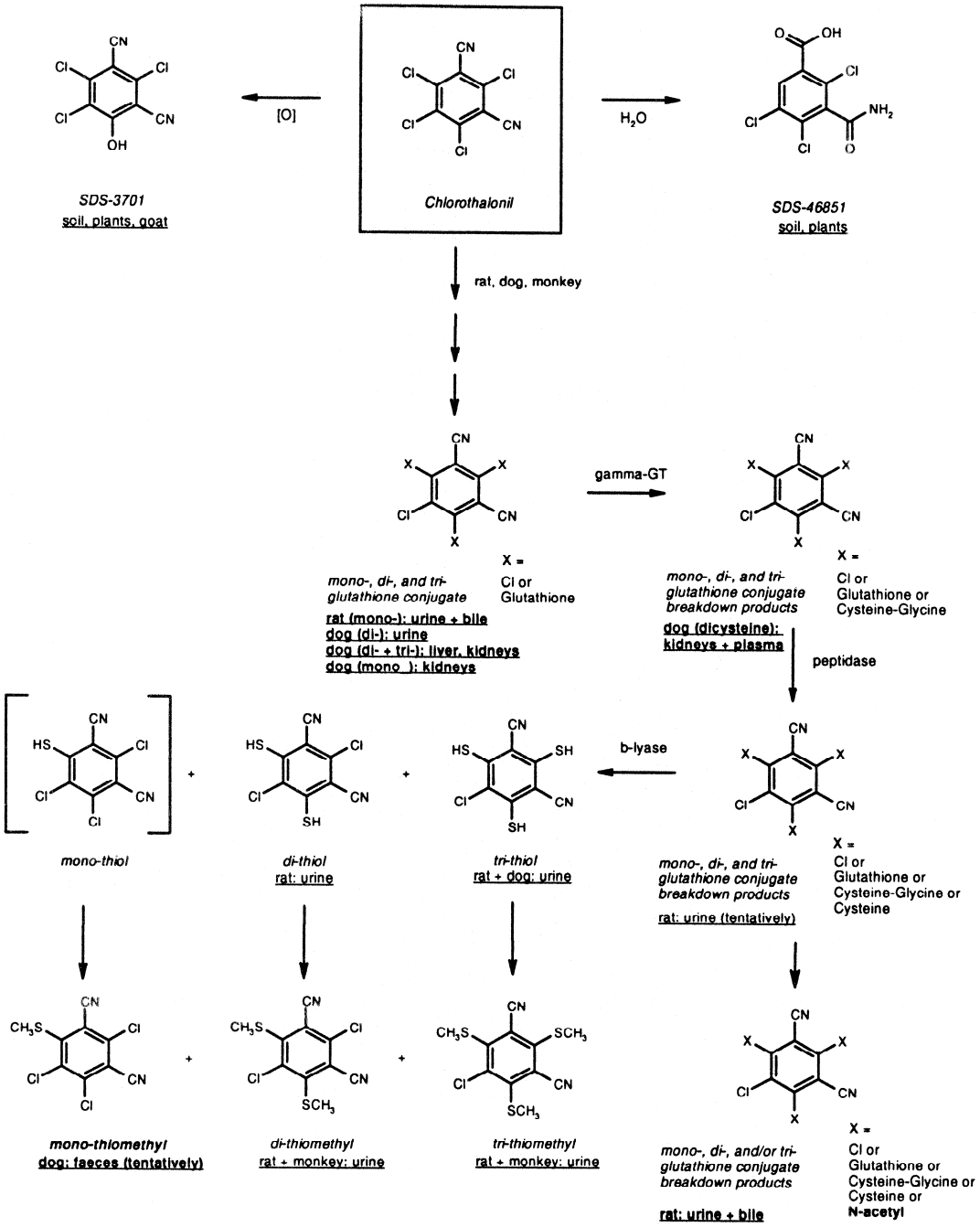
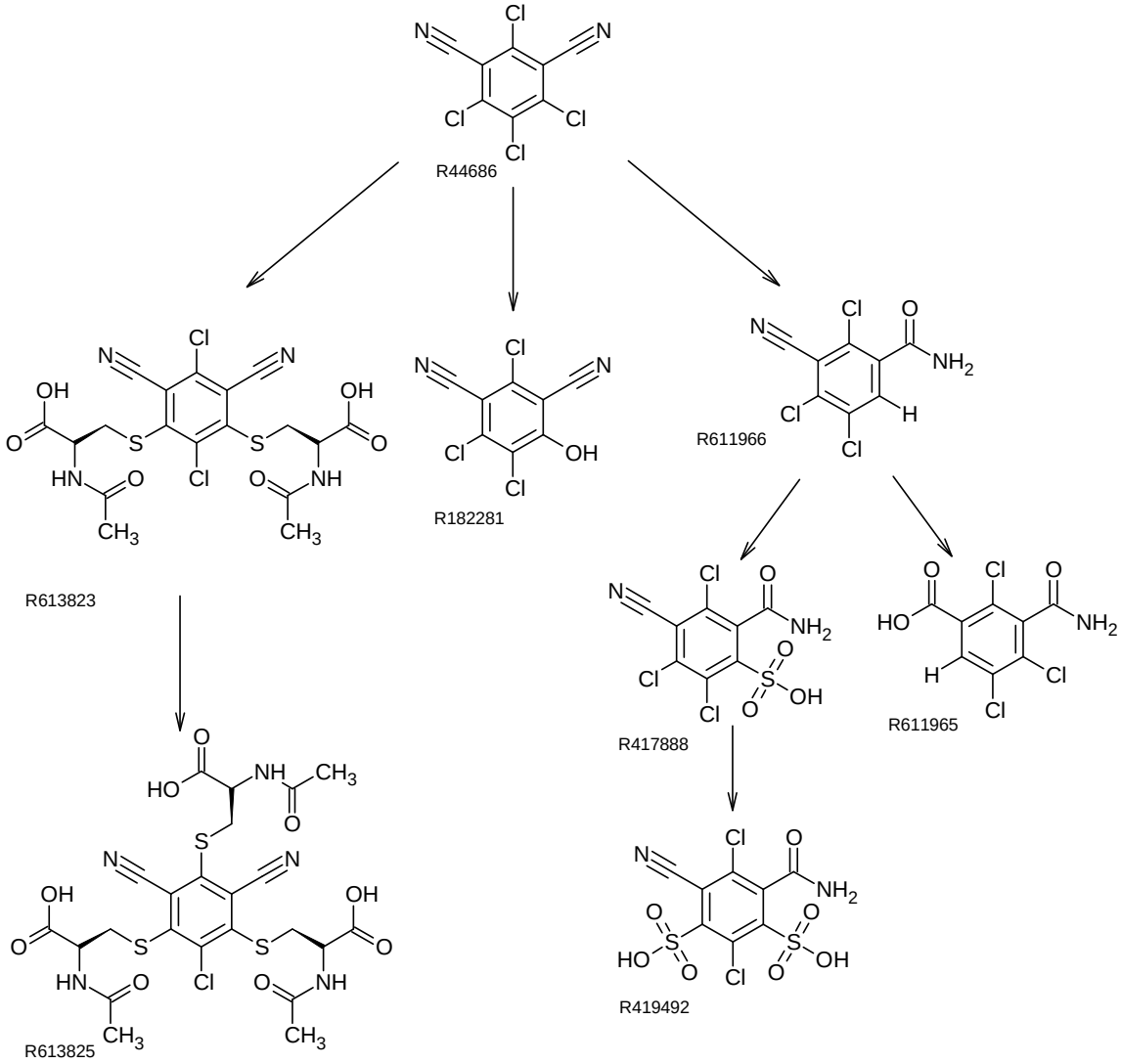


Figure 2.6.1-2 **Biotransformation pathway for chlorothalonil following oral administration to rats**



2.6.2 Summary of acute toxicity

Chlorothalonil does not need classification on the basis of its acute oral and dermal toxicity. Based on the acute inhalation toxicity data, chlorothalonil should be classified with H330 'Fatal if inhaled'. Chlorothalonil is considered to be non-irritating to the skin and is classified with H318 'Causes serious eye damage'.
In view of the positive finding in the sensitization study of Allan (1995) and the differences in dose levels used for the challenge applications, the strong possibility that a too low challenge concentration has been selected in the sensitization study performed by Pore (1993), it is concluded that chlorothalonil is a skin sensitizer and is classified with H317 'May cause skin sensitization'.

Chlorothalonil showed no phototoxic effect in an in vitro 3T3 NRU phototoxicity test.

The results of the acute toxicity, irritation and sensitisation studies are presented in table 2.6.2-1 and 2.6.2-2.

Table 2.6.2-1 Summary of the acute toxicity studies

Test substance	Route	Species	LD_{50}/LC_{50}	Classification	Reference
Chlorothalonil technical, 98.6%	oral	rat	>5000 mg/kg bw	none	Moore, 2000
Chlorothalonil technical, > 98%	oral	rat	>10000 mg/kg bw	none	Shultz, 1981a
Chlorothalonil technical, 98.63%	oral	rat	>5000 mg/kg bw	none	Cummins, 1988a
Chlorothalonil technical, 98.63%	oral	mouse	>5000 mg/kg bw	none	Cummins, 1989
Chlorothalonil technical, 98%	oral	rat	>5000 mg/kg bw	none	Apte, 1992
Chlorothalonil technical, 98%	oral	mouse	>5000 mg/kg bw	none	Apte, 1992
Chlorothalonil technical, 98.6%	dermal	rat	>5000 mg/kg bw	none	Johnson, 2000
Chlorothalonil technical, > 97%	dermal	rat	>10000 mg/kg bw	none	Shultz, 1981b
Chlorothalonil technical, 98.63%	dermal	rabbit	>2000 mg/kg bw	none	Cummins, 1988b
Chlorothalonil technical, 98%	dermal	rabbit	>2000 mg/kg bw	none	Pore, 1992
Chlorothalonil technical, 98.2%	inhalation	rat	0.10 mg/L	H330	Shults, 1993
Chlorothalonil technical, 98.63%	inhalation	rat	0.217 mg/L	H330	Cracknell, 1988

Table 2.6.2-2 Summary of the irritation and sensitisation studies

Test substance	Route	Species	Effect	Classification	Reference
Chlorothalonil technical, 98.6%	skin irritation	rabbit	mild-irritant	none	Johnson, 2000a
Chlorothalonil technical, purity unknown	skin irritation	rabbit	non-irritating	none	Shults, 1981c
Chlorothalonil technical, 98.6%	skin irritation	rabbit	non-irritating	none	Smith, 1988

Test substance	Route	Species	Effect	Classification	Reference
Chlorothalonil technical, 98%	skin irritation	rabbit	non-irritating	none	Pore, 1992
Chlorothalonil technical, 99.6%	eye irritation	rabbit	severe eye damage	H318	Major, 1982
Chlorothalonil technical, purity unknown	eye irritation	rabbit	severe eye damage	H318	Macrae, 1985
Chlorothalonil technical, 98%	eye irritation	rabbit	severe eye damage	H318	Pore, 1993
Chlorothalonil technical, purity unknown	skin sensitization, maximization	guinea-pig	sensitizing	H317 (Category 1A)	Allan, 1995
Chlorothalonil technical, purity unknown	skin sensitization, maximization	guinea-pig	non-sensitizing	none	Pore, 1993
Chlorothalonil technical, 98.6%	Phototoxicity	mouse fibroblast	No phototoxicity	none	Gehrke, 2014

2.6.3 Summary of short-term toxicity

Three oral subacute studies with the parent compound were conducted in rats, mice and dogs. Despite several shortcomings, a NOAEL of <80 mg/kg bw/day was established in the rat study, based on increased relative liver and kidney weights. In another 28-day oral toxicity study in rats, aimed specifically at analysing hyperplastic changes in stomach and kidney of male rats, effects were observed at dose levels of 15 and 175 mg/kg bw/day. No effects were observed at 1.5 mg/kg bw/day. The 28-d dog study was not considered suitable for evaluation, due to several shortcomings (resulting from the experimental design). A 66-day subacute study with the parent compound in the mouse was considered inappropriate for the overall evaluation, due to various shortcomings. A 21 day dermal toxicity study with the parent compound in rabbits was unsuitable for evaluating the systemic effects of the test substance, because the kidneys (target organ) were affected by a parasite. A MOAEL for local effects was established at 0.1 mg/kg bw/day, based on very slight erythema in females up to day 21. In a 21-day dermal toxicity study with male rats, a NOAEL of < 60 mg/kg bw/day was established for both systemic and local effects. No repeated inhalation exposure studies were submitted by the notifiers.

The dossier contains ten semichronic toxicity studies. Four oral 90-day studies were conducted in rats. Two studies were not evaluated (NOAELs < 4.4 and 40 mg/kg bw/day), because more recent 90-day toxicity studies in rats were submitted. In these latter studies a NOAEL of 3.0 mg/kg bw/day, based on an increased incidence of irregular intracytoplasmic inclusion bodies in cells of the proximal tubules in males and forestomach hyperplasia and hyperkeratosis, and a conservative marginal systemic effect level of 4.7 mg/kg bw/day, based on increased kidney weights, were established. Two oral toxicity studies were conducted in mice. In 95-day study, a NOAEL for systemic effects was 47.7 mg/kg bw/day, based on histopathological changes in kidneys, an increased kidney weight and effects on clinical chemistry and body weight. In a 90-day study, a NOAEL for systemic effects was established at 38 mg/kg bw/day, based on increased kidney weights. Four oral toxicity studies were conducted in

dogs. In a 90-day toxicity study a NOAEL of 5.6 mg/kg bw/day was established based on effects on body weight, increased liver, adrenal and kidney weight, vomiting and histopathological changes in the kidneys and adrenals at 56.5 mg/kg bw/day. In a 13-week toxicity study in dogs a NOAEL of 15 mg/kg bw/day was based on decreased body weight, increased plasma cholesterol and decreased plasma albumin. An oral one-year toxicity study in dogs revealed decreased body weight gains, increased relative liver and kidney weights and changes in various clinical chemistry parameters in males and females receiving a dose of 150 mg/kg bw/day. The NOAEL in this study was established at 15 mg/kg bw/day. In another oral one-year study in dogs a NOAEL of 5.1 mg/kg bw/day was established based on effects on body weight and clinical chemistry and histopathological changes in stomach and kidneys at dose levels of 43.3 and 374 mg/kg bw/day.
The JMPR described a study in dogs (no study report was submitted), in which no adverse effects were observed and a NOAEL of 3.0 mg/kg bw was established.

In the semichronic toxicity studies, the most sensitive toxicological endpoint in dogs appears to be body weight and liver and kidney weight. In mice however, local effects on the (fore)stomach were observed at lower dose levels. At higher dose levels effects on body weight and histopathological changes in the kidneys were observed. In rats the NOAELs were based on a combination of the effects described above.
Of the submitted semichronic toxicity studies, the lowest observed adverse effect level of 1.5 mg/kg bw/day (minimal effect level) was established in the 13 week toxicity study in rats. The lowest NOAEL in dogs is a factor 2 higher.

In Table 2.6.3-1 the results of the short-term studies, which are acceptable for evaluation, are summarized.

Table 2.6.3-1 Summary of the short-term toxicity studies

Test substance	Duration, route	Species	NOAEL (mg/kg bw/day	LOAEL (mg/kg bw/day)	Critical effects	Reference
Chlorothalonil technical, DS-2787, purity 98%	28-days, oral	rat	< 80	80	increased relative liver and kidney weights	Wilson et al., 1982bB
Chlorothalonil technical, GC30M2 (I-680), purity 98.98%	28-days, oral	rat	1.5[1]	15	histopathological changes in stomach and kidneys	Hironaka et al., 1996
Chlorothalonil, 98%	13 weeks, oral	rat	< 40	40	increased relative kidney weight, hyperplasia and increased size of the renal tubule and acute gastritis	Wilson et al., 1981, 1985a

Chlorothalonil, 97.7-98.2%	13 weeks, oral	rat	3.0	10	increased incidence of irregular intracytoplasmic inclusion bodies in renal tubules in males, : histopathological changes in forestomach	Wilson et al., 1983a, b, 1984a,b
Chlorothalonil, 98.5%	13 weeks, oral	rat	< 4.4	4.4	Minimal eosinophilia debris in the lumens of the inner cortical tubules of the kidneys in males	Watson et al., 1985
Chlorothalonil, 99.2%	13 weeks, oral	rat	local: <2.3 syst.: 4.7	local: 2.3 syst.: 23.6	Local: histopathological changes in forestomach Syst: kidney weights (<10%)	Spencer-Briggs et al., 1994a
Chlorothalonil, 98.4%	13 weeks, oral	mouse	local: 2.5 syst: 47.7	local: 8.5 syst.: 123.6	Local: histopathological changes in forestomach Syst: kidney (weight and histopathology), increased body weight, clinical chemistry.	Shultz et al., 1983, 1985
Chlorothalonil, 99.2%	13 weeks oral	mouse	local: 9 syst: 38	local: 38 syst: 167	Local: roughened forestomach Syst: kidney (weight and histopathology), thyroid weight	Spencer-Briggs et al., 1992b
Chlorothalonil, 97.9-98.2%	13 weeks oral	dog	15	150	body weight, cholesterol, albumin	Fillmore et al., 1993
Chlorothalonil, 99.2%	13 weeks oral	dog	5.6	56.5	Vomiting, body weight, liver, kidney and adrenal weight, and histopathology in kidneys and adrenals.	Spencer-Briggs et al., 1994b
Chlorothalonil technical, T-117-12, purity 97.9%	52 weeks oral	dog	15	150	liver and kidney weights (10-26%)	Mizens et al., 1994
Chlorothalonil, Lot NF 28/01, purity 99.28%	52 weeks oral	dog	5.1	43.3	body weight, histopathology in kidneys and stomach	Spencer-Briggs et al., 1995
Chlorothalonil technical, SDS-2787, purity 98.4%	21-day, dermal	rabbit	(<0.1)[2]	(0.1)	skin effects:very slight erythema	Shults et al., 1986
Chlorothalonil technical, lot. 313012, purity 98.1%	21-day, dermal	rat	< 60	60	increased kidney weight and skin effects	Mizens et al., 1996

1 The study was aimed specifically at analysing hyperplastic changes in stomach and kidney of male rats. Therefore only a limited number of parameters were investigated.

Because of effects on the kidneys (target organ), caused by an Encephalitozoon parasite, only a local NOAEL could be established. Therefore the value is given between brackets.

2.6.4 Summary of genotoxicity

Chlorothalonil did not induce gene mutations in bacteria or in mammalian cells *in vitro*, neither in the presence nor the absence of metabolic activation. Chlorothalonil was negative in a TK-assay in mouse

lymphoma cells. *In-vitro* testing for chromosomal aberrations in human lymphocytes and CHO cells in the absence of metabolic activation resulted in a statistically significant increased frequency of aberrations, whereas no increase was observed in the presence of metabolic activation.
Chlorothalonil was found negative in *in-vivo* tests for micronuclei and chromosomal aberrations in bone-marrow of rat and mice. A negative result was also obtained in the micronucleus test with Chinese hamsters. Two *in-vivo* tests for chromosomal aberrations with this species suggested in-vivo clastogenicity. Chlorothalonil was found negative in another *in vivo* chromosome aberration assay in bone-marrow of Chinese hamsters.
In general, the available data on the genotoxicity of chlorothalonil shows the compound to be clastogenic *in vitro,* and this effect is suppressed in the presence of metabolic activation. The *in-vivo* results are largely negative, and allow the conclusion that the compound in all likelihood is not clastogenic *in vivo*.

Co-RMS

Co-RMS BE indicates that the results *in-vivo* are unclear. There is a mixed result of positive and negative clastogenicity findings, which, in association with the same profile *in-vitro* shed doubts on the negative outcome of the *in-vivo* studies overall.

Reply RMS

These results were already discussed during the first peer review process. There are 2 *in vivo* studies in Chinese hamsters with equivocal results; in one study increased frequency of chromosomal gaps was only observed at the highest dose, in which also 4/13 animals died, and in the other study the statistical increase after acute exposure was only at the high dose after 48h, not after 24h, and after subacute dosing the increase was only in the low and mid dose, not in the high dose.
On the other hand there are three studies in rats, four in mice, and two in Chinese hamster that showed a negative response. Based on the weight of evidence it can be concluded that chlorothalonil is not clastogenic *in vivo*.

Table 2.6.4-1 *In vitro* genotoxicity studies

Test substance	Type of study		Result		Reference
	Indicator cells	Endpoint	without activation	with activation	
Chlorothalonil, purity 99.1%	B: S. typh. TA 98 TA 100 TA 1535 TA 1537 TA 102	 point mut. point mut. point mut. point mut. point mut.	 - - - - -	 - - - - -	Jones, Killeen and Haworth, 1984
Chlorothalonil, purity 98.74%	B: S. typh. TA 98 TA 100 TA 1538 TA 1535 TA 1537	 point mut. point mut. point mut. point mut. point mut.	 - - - - -	 - - - - -	Forster, 1988
Chlorothalonil,	B: S, typh.				Auletta and

purity unknown	TA1978 TA1538	Diff. killing Diff. killing	+ +	+ +	Kouri, 1977
Chlorothalonil, purity 98.8%	Chinese hamster ovary (CHO) cells	Chromosome aberration	+	-	Mizens, et al, 1986
Chlorothalonil, purity 97.8%	mouse BALB/3T3, Clone A31	Point mutations	-	-	Kouri, 1977
Chlorothalonil, purity 99.1%	L 5178Y mouse lymphoma cells	TK deficiency	-	-	Adams and Kirkpatrick, 1996
Chlorothalonil, purity 96%	Fischer rat embryo cells F1706 P95 H4536 P97	Cell transformation	- -		Price and Ballee, 1979

n.d. = not determined

Table 6.4.3.2 *In vivo* genotoxicity studies

Test substance	Type of study		Result	Reference
	Species	**Endpoint**		
Chlorothalonil, purity 98.2%	Rat Mouse Chinese hamster	Micronuclei in bone-marrow erythrocytes	- - -	Killeen and Siou, 1983
Chlorothalonil, purity 98.18%	Mouse (CD-1)	Micronuclei in bone-marrow erythrocytes	-	Proudlock and Elmore, 1992
Chlorothalonil, purity 98.2%	Rat Mouse Chinese hamster	Chromosome aberrations in bone-marrow cells	- - +/-	Killeen, 1983
Chlorothalonil, purity 98.2%	Chinese hamster (males only)	Chromosome aberrations	+/-	Siou et al, 1985
Chlorothalonil, purity 98.2%	Rat (males only)	Chromosome aberrations	-	Siou and Mizens, 1985a
Chlorothalonil, purity 98.2%	Mouse (males only)	Chromosome aberrations	-	Siou and Mizens,1985 b
Chlorothalonil, purity 98.3%	Chinese hamster (males only)	Chromosome aberrations in bone-marrow cells	-	Mizens and Laveglia, 1995

2.6.5 Summary of long-term toxicity and carcinogenicity

The most sensitive toxicological endpoints in the chronic studies with rats were kidney and forestomach morphology. In mice, the most sensitive endpoint was pathology of the forestomach. In rats, all dose levels exhibited systemic toxicity. In one with rats the LOAEL was 40 mg/kg bw/day, based on non-neoplastic and neoplastic lesions on kidneys and forestomach. In another study in rats, the lowest dose with histopathological effects on the target organs (pre-neoplastic lesions in kidneys and forestomach and benign tumours in the forestomach) was 3.8 mg/kg bw/day.

In a 104-week study in rats, a NOAEL of 0.7 mg/kg bw/day was established for local effects, based on (histo)pathological changes in the stomach. Based on histopathological changes in liver and kidneys, and effects on haematology, a NOAEL for systemic effects was established at 2.7 mg/kg bw/day.

In mice, the lowest dose tested, 119 mg/kg bw/day, still revealed an increased incidence of pre-neoplastic lesions in the forestomach. In a second study in male mice only (as the most sensitive gender) and a limited set of parameters tested, no effects were observed at 1.9 mg/kg bw/day. A positive tumour response was observed in the forestomach at 99.7 mg/kg bw/day. No increased incidences in tumours were observed at 23.2 mg/kg bw/day.
In a 80-week oral carcinogenicity study in mice, an increased incidence of non-neoplastic lesions in the stomach was still observed in the lowest dose level of 1.9 mg/kg bw/day. Based on these findings a NOAEL for local effects was established at < 1.9 mg/kg bw/day. Based on the observed histopathological findings in the kidneys a NOAEL of 1.9 mg/kg bw/day was established for systemic effects. At the highest dose level (130 mg/kg bw/day) a statistically significant increase in squamous cell papilloma in the non-glandular stomach of both sexes was observed.
Based on data from mechanistic studies, carcinogenicity data and genotoxicity data on chlorothalonil, the mechanism of carcinogenicity of chlorothalonil is supposed to be non-genotoxic.

Table 2.6.5-1 Summary of the long-term toxicity studies

Test substance	Duration, route	Species	NOAEL (mg/kg bw/day	LOAEL (mg/kg bw/day)	Critical effects	Reference
Chlorothalonil, purity 98.1%	116 weeks, oral	rat	< 40	40	body weight, liver/kidney (clinical chemistry, urine, organs weights), kidney/forestomach (histopathology, including tumours)	Wilson et al., 1985c
Chlorothalonil, purity 98.1%	26 months, oral	rat	1.8	3.8	Kidney tubular hyperplasia **Kidney tumours at 15 mg/kg bw/d**.	Wilson & Killeen, 1989a
Chlorothalonil, 99.28%	104 weeks, oral	rat	Local: 0.7 Systemic: 2.7	Local: 2.7 Systemic: 10.6	Local: stomach (histopathology) Systemic: liver and kidneys (hematology and histopathology)	Spencer-Briggs et al., 1996
Chlorothalonil, purity 97.7%	104 weeks, oral	mouse	< 119	119	kidney weight, kidney and stomach: histopathology including tumours	Wilson et al., 1983c
Chlorothalonil, purity 98%	24 months, oral	mouse	n.d.	n.d.	Indications for carcinogenicity were weak and in the stomach only, at high dose of 99.7 mg/kg bw/day.	Johnson et al., 1987
Chlorothalonil, 99.28%	80 weeks, oral	mouse	Local: < 1.9 Systemic: 1.9	Local: 1.9 Systemic: 7.8	Local: stomach (histopathology) Syst: kidney (histopathology), stomach tumours at 130 mg/kg bw/d	Spencer-Briggs et al., 1996

n.d. = not determined

2.6.6 Summary of reproductive toxicity

From two multigeneration studies in rats, it was concluded that chlorothalonil did not affect the reproductive performance of rats at doses (261 mg/kg bw/day) lying well above those causing parental effects (NOAEL for parental effects established at < 22.6 mg/kg bw/day). A NOAEL for developmental effects was found to be 22.6 mg/kg bw/day, based on a decreased pup body weight.
Developmental toxicity and teratogenicity studies with chlorothalonil were conducted in rabbits and rats. In rabbits, maternal effects were observed at a dose level of 20 mg/kg bw/day. Developmental effects were also found at 20 mg/kg bw/day. Therefore, the NOAEL for maternal and developmental toxicity is established at 10 mg/kg bw/day. In the rat, a decrease in body weight gain of the dams was found at 25 mg/kg bw/day. Therefore, for rats the NOAEL for maternal toxicity is < 25 mg/kg bw/day. At 80 mg/kg bw/day, the number of rudimentary ribs was increased in rats. It is concluded that the NOAEL for developmental toxicity is < 80 mg/kg bw/day in rats.
In the renewal dossier a new study from the public domain was submitted. In a teratogenicity study in mice, the NOAEL for maternal and developmental toxicity was set at 100 mg/kg bw/day, based on clinical signs and reduced maternal body weight (gain), and reduced foetal survival and growth.
No indication for a teratogenic potential of chlorothalonil was observed in rats, rabbits and mice.

Table 2.6.6-1 Summary of the reproduction and teratogenicity studies

Test substance	Duration, route	Species	NOAEL (mg/kg bw/day	LOAEL (mg/kg bw/day)	Critical effects	Reference
Chlorothalonil, purity 98.1%	Oral, 2-generation study	rat	Par: < 22.6 Dev: 22.6 Repro:>145.1	Par: 22.6 Dev: 68.2 Repro: -	body weight, stomach and kidneys (histopathology) Decreased F1 pup weights No effects	Lucas, et al, 1990
Chlorothalonil, purity 99.2%	Oral, 2-generation study	rat	Par: < 32.7 Dev: <32.7 Repro: > 261	Par: 32.7 Dev: 32.7 Repro: -	stomach and kidneys (histopathology), kidney weight, enlarged lymph nodes. stomach and kidneys (histopathology) No effects	Meyers, et al, 1985
Chlorothalonil, purity 98.1%	Oral developmental toxicity study	rabbit	Mat:10.0 Dev:≥20 Ter:≥20	Mat:20 Dev:- Ter:-	Body weight No effects No effects	Wilson, 1988i
Chlorothalonil, purity 98%	Oral developmental toxicity study	rabbit	Mat:10 Dev: 10 Ter: ≥20	Mat:20 Dev: 20 Ter:-	body weight and food intake, related to anorexia Skeletal variation (rib, sternebrae) No effects	Meyers, 1994c
Chlorothalonil,	Oral	rat	Mat:<25	Mat:25	Body weight and food	Mizens,

purity 99.15%	develop mental toxicity study		Dev:100 Ter: ≥400	Dev:400 Ter:-	intake Live foetuses, early resorptions No effects	1983
Chlorothalonil, purity 99.15%	Oral develop mental toxicity study	rat	Mat:80 Dev:<80 Ter: ≥200	Mat:200 Dev:80 Ter:-	Body weight, food and water intake, wet faeces Rudimentary ribs No effects	Meyers, 1994b
Chlorothalonil, purity 97%	Oral develop mental toxicity study	mouse	Mat:100 Dev: 100 Ter: >600	Mat: 400 Dev: 400 Ter: -	Clinical signs, body weight Resorptions, foetal survival and weight. No effects	Farag et al., 2006

2.6.7 Summary of neurotoxicity

According to Commission regulation (EU) No 283/2013 neurotoxicity studies are required for active substances with structures that are similar or related to those capable of inducing neurotoxicity, and for active substances which induce specific indications of potential neurotoxicity, neurological signs or neuropathological lesions in toxicity studies at dose levels not associated with marked general toxicity. Chlorothalonil does not fulfil these criteria and neurotoxicity studies would not be required. In the available studies there are no indications for neurotoxicity.

2.6.8 Summary of further toxicological studies on the active substance

An acute reference dose study was submitted in which administration of a single oral dose of chlorothalonil at dose levels of up to 250 mg/kg was well tolerated and did not result in treatment-related adverse effects. The no observed adverse effect level (NOAEL) for this acute reference dose study was 250 mg/kg for both male and female Fisher 344 rats. In the preliminary study, single dosing with chlorothalonil at 180 mg/kg and 1000 mg/kg produced minimal evidence of renal toxicity at 96 hours post dosing

Several studies were performed in rats to gain more information on the underlying mechanisms of the observed effects in (semi) chronic toxicity studies in rats.
In a study with serial sacrifices, the hepatic glutathion content (GSH) was lowered and the renal glutathion content was increased after single administration of chlorothalonil to rats when compared to the controls. Hepatic GSH returned to control levels after 48 hours, possibly due to stimulation of the glutathion synthesis after formation of a chlorothalonil-glutathion conjugate. The mechanism underlying the increase in renal glutathion remains unknown.
In another study, administration of chlorothalonil and a monoglutathione conjugate of chlorothalonil to rats for 90 days, produced comparable effects in kidneys. Effects in the (fore) stomach were only observed after administration of chlorothalonil, indicating that addition of one glutathion residue to chlorothalonil suppresses its irritating properties. In another 90-day toxicity study in rats, the di- and tri-thiol metabolites were determined in urine. The trithiol metabolite was identified in urine, however, the dithiol metabolite was not detected. A cyclic pattern of trithiol excretion occurred throughout the study. The presence of the trithiol metabolite is consistent with the involvement of glutathion conjugation in the

metabolism of chlorothalonil. The cyclic pattern suggested that switching between different metabolic pathways may have occurred several times during this study.
When chlorothalonil was administered to rats by gavage or via the diet, histopathological changes in the kidneys were observed in all treated animals, regardless of the method of administration. Moreover, kidneys of rats from a study in which rats were treated during two days were more affected than animals treated for only one day (with an equal total dose).
Rats, administered 175 mg/kg bw/day in the diet for 90 days, showed kidney cell-proliferation, histopathological changes in kidneys like cytoplasmic vacuolation, nuclear pyknosis, karyolysis and cellular swelling, histopathological changes in the stomach and effects on body weight and food consumption.
In a summarizing report the notifier concludes an epigenetic mechanism for the development of kidney tumours observed after oral exposure to chlorothalonil in rats (Zeneca, Mizens, 1997).
Chlorothalonil in orally exposed rats has demonstrated to be toxic to the kidneys based on the 28-day oral toxicity study (Zeneca, Hironaka, 1996) and the 90-day oral toxicity study (Zeneca, Mizens, 1996). The kidney toxicity includes cell proliferation and cell death and can lead to regenerative growth and hyperplasia as demonstrated in the proximal convoluted tubule. In case of chronic exposure to chlorothalonil it is suspected that the epithelial degeneration and compensatory hyperplasia result in kidney tumours (Wilkinson and Killeen, 1996). Taking into account the toxicological information on chlorothalonil, especially the data on genotoxicity and mutagenicity, the mechanism of carcinogenicity of chlorothalonil is supposed to be non-mutagenic and related with tubular hyperplasia. A NOAEL for chlorothalonil toxicity in the kidneys (based on the level of kidney cell proliferation) could be derived from the data of the two before-mentioned studies. By means of immuno-labelling techniques (PCNA- and BrdU-labelling), a NOAEL of 1.5 mg/kg bw/day was derived (based on the 28-day study) for renal cell proliferation.
The rapporteur agrees with the author on the explanation of the non-genotoxic carcinogenic potency of chlorothalonil in rat kidney.

2.6.9 Summary of toxicological data on impurities and metabolites

SDS-3701 (R182281)

2,5,6-trichloro-4-hydroxyisophthalonitrile is soil, aquatic, plant, livestock and rat metabolite with the following code names: R182281, SDS3701, R1, Compound 2, C5, 28343-61-5, CSCA105253.
The oral absorption of SDS3701 is set at 26-30%, based on urinary excretion and tissues residues in rats.
The oral LD_{50} value of SDS 3701 in Wistar rats was established to be within the range 50-300 mg/kg bw. Based on CLP criteria the RMS concludes that SDS-3701 needs classification with H301 “Toxic if swallowed”.
SDS-3701 was not irritating to rabbit skin.
In an oral 60-day study with rats, SDS-3701 caused treatment-related changes at 10 mg/kg bw/day (lowest dose tested), namely increased incidence and increase in severity in inactivity and piloerection in both sexes. No NOAEL could be derived.

Two semi chronic toxicity studies were performed with SDS-3701.
In a 90-day oral toxicity study (diet) with rats, based on the changes in haematological and clinical biochemistry parameters primarily at 250 ppm, and in particular the reduced body weights in females at 250 ppm, the NOAEL for SDS3701 was established at 50 ppm, corresponding to 3 and 4 mg/kg bw/day for males and females respectively. A 120-day dietary toxicity study with rats was unsuitable for evaluation, because of several shortcomings in the study methodology and study report.
In a 90-day dietary toxicity study with dogs a NOAEL of 1.25 mg/kg bw/day was established based on dose related tarry stools. In a 1-year study in dogs, based on effects on the hematopoietic system, liver, kidney and testis at 120 ppm in both sexes, on the decreased body weight gain in females at 60 ppm and the dose-related increase of serum glucose at 60 ppm and above in both sexes, the NOAEL is set at 30 ppm (0.83 mg/kg bw/day for males and 0.95 mg/kg bw/day for females).
Several *in vitro* and *in vivo* genotoxicity studies were performed with SDS-3701. SDS-3701 was not mutagenic when tested on S. *typhimurium* strains TA98, TA100, TA1535 or TA1537 and E.coli strain WP_2uvrA, with or without S9-mix activation.
An *in vitro* chromosome aberration test (CHO-cells) was positive, both with and without metabolic activation. The results of a cell-transformation test in rat embryo cells was equivocal. SDS3701 is mutagenic at the TK-locus of mouse lymphoma L5178Y cells, however mutagenicity was observed only at highly cytotoxic concentrations.
An *in vivo* micronucleus test in mice and a dominant lethal test in rats were not acceptable for evaluation. A second and third dominant lethal test in rats was negative. SDS-3701 was negative in an *in vivo* micronucleus test at doses up to 500 mg/kg bw. SDS-3701 was found negative in an *in vivo* chromosome aberration study in bone-marrow of Chinese hamsters. It is concluded that SDS 3701 is non-genotoxic in vivo.
The most notable effects of the metabolite SDS-3701 in a long-term combined toxicity and carcinogenicity study with rats were decreased body weight and food consumption, bilateral cataract, changes in haematology and clinical chemistry, kidney, heart and spleen weight changes and non-neoplastic changes in bone marrow and liver related to the haematological effects. There were no indications for carcinogenicity. The NOAEL was 0.5 mg/kg bw/day for females and 3.0 mg/kg bw/day for males.
In a one-generation reproductive study with SDS-3701 in rats, an increased relative food consumption was observed in the F0-males at the highest dose-level tested. Therefore, the NOAEL for parental toxicity is 3 mg/kg bw/day. The NOAEL for developmental effects is 1.5 mg/kg bw/day, based on a decreased body weight of the F1-pups. No reproductive effects were observed in rats (NOAEL > 6 mg/kg bw/day)
In a teratogenicity study with rabbits hyperthermia, hypoactivity and an increase in post implantation loss were observed at 5 mg/kg bw/day. Therefore, the NOAEL for maternal and developmental toxicity is established at 2.5 mg/kg bw/day. No teratogenic effects were observed.
In a teratogenicity study in rats, the NOAEL for maternal toxicity was set at 5 mg/kg bw/day based on a decreased body weight gain and food intake, and significant decrease in MCHC. Based on a decreased foetal weight and increased incidence of rudimentary 14^{th} rib, the NOAEL for

developmental toxicity was set at 5 mg/kg bw/day. Teratogenic effects were found at 25 mg/kg bw/day consisting of significant increased early resorptions.

R611965 (SDS-46851)

3-amido-2,4,5-trichlorobenzoic acid is a soil, plant and rat metabolite and has the following Code numbers: R611965, M5, SDS 46851, R14 and Compound 4.

Oral absorption of R611965 is set at 22-26%, based on urinary excretion in rats.

The oral LD50 value of SDS 46851 in Wistar rats was established to exceed 2000 mg/kg bw and SDS-46851 was not irritating to rabbit skin.

In an oral 30-day study with SDS 46851 in the rat (doses based on a 14-day study in the rat) a NOAEL of 500 mg/kg bw/day was established, based on increases in weights and histopathological changes in the liver in both sexes at 2000 mg/kg bw/day. It is noted that local effects were observed at the lowest dose level (500 mg/kg bw/day). In an oral 28-day study with SDS 46851 in mice, a MOAEL of 46 mg/kg bw/day was established. Hyperplasia of the renal tubular epithelium in males was noted at this level. The conducted 37/38-day oral toxicity study with SDS 46851 in the dog was not considered appropriate for evaluation, as only 2 dogs were used per dose group.

In a 90-day rat oral dietary toxicity study with SDS46851 (Otterdijk, 2007), no toxicologically significant changes were noted in any of the parameters investigated in this study (i.e. clinical appearance, functional observations, ophthalmologic examinations, body weight, food consumption, clinical laboratory investigations, macroscopic examination, organ weights, and microscopic examination). The NOAEL for SDS46851 is established at ≥2400 ppm was established, corresponding to ≥197 and ≥223 mg SDS46851/kg bw/day for males and females respectively.

In a 90-day dietary toxicity study with dogs a NOAEL was established at 50 mg/kg bw/day, based on increased liver weight, increased incidence of watery stools and decreased body weight at 500 mg/kg bw/d.

Several *in vitro* and *in vivo* genotoxicity studies were performed with SDS-46851. All studies, including two point mutation assays, a sister chromatid exchange assay (in CHO-cells), a forward mutation assay (TK, mouse lymphoma cells), an unscheduled DNA synthesis assay (rat hepatocytes) and three micronucleus tests *in vivo* (mice) were negative. It is concluded R611965 (SDS 46851) is non-genotoxic.

The most notable effects of the metabolite SDS-46851 in a long-term combined toxicity and carcinogenicity study in rats were retinal atrophy and food consumption changes. The NOAEL was 200 mg/kg bw/day. In a long-term carcinogenicity study in mice, clinical signs and body weight changes were observed. No systemic effects were observed at 548 mg/kg bw/day. No indications for carcinogenicity were observed in rats and mice.

In a 2-generations reproductive study in rats a NOAEL for parental toxicity was established at 269 mg/kg bw/day, based on the effects observed in the kidneys in the F0-females and an increased body weight during gestation and lactation. No treatment-related effects were noted in the pups; the NOAEL for developmental effects is >911 mg/kg bw/day. The NOAEL for reproductive effects is >911 mg/kg bw/day.

No treatment related effects were found in a teratogenicity study with rats. Therefore, the NOAEL for developmental and maternal toxicity is established at > 2000 mg/kg bw/day. In the rabbit the same metabolite proved toxic to the dams at all doses tested (NOAEL < 250 mg/kg bw/day). Developmental effects were seen at 1000 mg/kg bw/day (NOAEL 500 mg/kg bw/day). No teratogenic effects were observed.

R417888 (VIS-01)

Soil and rotational crop metabolite 2-amido-3,5,6-trichloro-4-cyanobenzenesulfonic acid had the following Code numbers: R417888, M12, VIS-01, R6, Compound 10, U6 or CSCC890840.
The oral LD50 value of R417888 in rats was established to exceed 2000 mg/kg bw.
In a 90-day dietary toxicity study in rats, a NOAEL of ≥ 59 mg/kg bw/day was established, in absence of significant treatment-related effects.
In another 90-day dietary toxicity study in rats, no toxicologically significant changes were noted in any of the parameters investigated in this study (i.e. clinical appearance, functional observations, ophthalmologic examinations, body weight, food consumption, clinical laboratory investigations, macroscopic examination, organ weights, and microscopic examination). Therefore, the NOAEL was set at ≥192 and ≥218 mg/kg bw/day for males and females respectively.
R417888 (VIS-01) has been assessed for end points of gene mutation and chromosome damage in vitro (three bacterial reverse mutation assays, three in vitro mammalian gene mutation assays and two in vitro chromosome aberration assay). The bacterial gene mutation assays were all negative. Differential results were obtained in the three in vitro gene mutation assays. In one study a negative result was found. In the second study, it was concluded that R417888 is mutagenic at the TK-locus of mouse lymphoma L5178Y cells in the presence of metabolic activation, while in another study no mutagenicity was found in absence and presence of metabolic activation. In one of the in vitro chromosome aberration assay a positive effect was observed following prolonged exposure in the absence of metabolic activation. Two in vivo mammalian erythrocyte micronucleus assays in mice were negative. An in vivo rat unscheduled DNA synthesis assay was also negative. Hence it is concluded R417888 (VIS-01) is non-genotoxic.

SYN548708 (R418503)

Soil and rotational crop metabolite 2,5 dichloro-4,6 dicyano-benzene-1,3 disulfonic acid has the following Code numbers: R418503, M13, R8, Compound 11, CSCA654600 and SYN548708.
R418503 has been assessed for end points of gene mutation and chromosome damage in vitro (bacterial reverse mutation assay, in vitro mammalian gene mutation assay and in vitro chromosome aberration assay). The bacterial and mammalian gene mutation assays were both negative. In an in vitro chromosome aberration study with human lymphocytes SYN548708induced structural chromosomal aberrations in human lymphocytes *in vitro* at the maximum dose level in the absence and presence of a metabolic activation system. In an *in vivo* micronucleus assay in mice, SYN548708is considered to be neither clastogenic nor aneugenic. Overall it is concluded that SYN548708is non-genotoxic.

SYN548765 (R419492)

Soil and rat metabolite 4-amido-2,5-dichloro-6-cyano benzene-1,3-disulfonic acid has the following code numbers: R419492, SYN548765, M8, R15, Compound 12, CSCA655149.
SYN546785 (R419492) has been assessed for end points of gene mutation and chromosome damage *in vitro* (bacterial reverse mutation assay, *in vitro* mammalian gene mutation assay and *in vitro* chromosome aberration assay). These assays all gave negative results. Overall it is concluded that SYN546785 (R419492) is non-genotoxic.

SYN548766 (R471811)

Soil and crop (rotational crop) metabolite sodium 2,4-bis-amido-3,5,6-trichlorobenzenesulfonate with the following code names: R471811, SYN548766, M4, R7, Compound 13, CSCA202566.
SYN548766 (R471811) has been assessed for end points of gene mutation and chromosome damage *in vitro* (bacterial reverse mutation assay, *in vitro* mammalian gene mutation assay and *in vitro* chromosome aberration assay). These assays all gave negative results. Overall it is concluded that SYN548766 (R471811) is non-genotoxic.

SYN548738 (SYN548008)

Lysimeter metabolite 4,6-dicarbamoyl-2,5-dichloro-benzene-1,3-disulfonic acid with the following code names: SYN548008, SYN 548738, M3, CSCY735822.
SYN548738 (SYN548008) has been assessed for end points of gene mutation and chromosome damage *in vitro* (bacterial reverse mutation assay, *in vitro* mammalian gene mutation assay and *in vitro* chromosome aberration assay). All assays gave negative results. Based on these findings, it is concluded that SYN548738 (SYN548008) is non-genotoxic.

SYN548580

2,4,5-trichloro-6-hydroxy-benzene-1,3-dicarboxamide is a metabolite found in a lysimeter study and has the following Code numbers: SYN548580, M2, R12, CSDB870985.
SYN548580 has been assessed for end points of gene mutation and chromosome damage *in vitro* (bacterial reverse mutation assay, *in vitro* mammalian gene mutation assay and *in vitro* chromosome aberration assay). These assays all gave negative results. Overall, it is concluded that SYN548580 is non-genotoxic.

SYN548764 (SYN548581)

2,3,6-trichloro-5-cyano-4-sulfanyl-benzamide is a metabolite found in a lysimeter study and has the following code numbers: SYN548581, M11, CSDB870988.
SYN548764 (SYN548581) has been assessed for end points of gene mutation and chromosome damage *in vitro* (bacterial reverse mutation assay, *in vitro* mammalian gene mutation assay and *in vitro* chromosome aberration assay). The *in vitro* gene mutation assays both gave negative results. SYN548764 induced structural chromosomal aberrations in human lymphocytes *in vitro* in the absence of a metabolic activation system at one high cytotoxic concentration. Considering the equivocal results of the in vitro chromosome aberration study, an *in vivo* micronucleus test was

performed. There was no evidence of clastogenicity or aneugenicity in male mice following oral administration of SYN548764 up to the limit dose of 2000 mg/kg/day. SYN548764 is considered to be neither clastogenic nor aneugenic in the mouse bone marrow micronucleus assay. Therefore, it is concluded that SYN548764 (SYN548581) is non-genotoxic.

R611968 (SDS-47525)

2,4,5-trichloro-3-cyano-6-hydroxybenzamide is a metabolite found in a lysimeter study and has the following code numbers: R611968, M9, SDS-47525, R5..

R611968 has been assessed for end points of gene mutation and chromosome damage in an bacterial reverse mutation assay, an *in vitro* mammalian gene mutation assay and an *in vitro* chromosome aberration assay. The *in vitro* gene mutation assays were both negative. In the in vitro chromosome aberration assay equivocal results were seen: a putative positive result was seen in the absence of metabolic activation at concentrations showing higher levels of cytotoxicity. In addition in the presence of metabolic activation, whilst a putative response was observed in the second experiment, this was not seen under the same conditions in the first experiment and hence the lack of reproducibility again questions the relevance of these findings. Considering the equivocal results of the in vitro chromosome aberration study, an *in vivo* micronucleus test was performed. There was no evidence of clastogenicity or aneugenicity following oral administration of R611968 up to 500 mg/kg/day in male mice. R611968 is considered to be neither clastogenic nor aneugenic in the mouse bone marrow micronucleus assay. Overall it is concluded that R611968 is non-genotoxic.

R613636 (SDS-47525)

2,4,5,6-tetrachloro-3-cyanobenzamide is a metabolite in soil, water and crops (rotated crops) with the following code numbers: R613636, M14, SDS-47525, R2, Compound 3, CSCC548417.

R613636 has been assessed for end points of gene mutation and chromosome damage in vitro (bacterial reverse mutation assay, in vitro gene mutation assay (two assay systems) and in vitro chromosome aberration assay) and chromosome damage and aneugencity in vivo (mammalian erythrocyte micronucleus test). The reverse bacterial mutation assay was negative. In the chromosome aberration test the test substance R613636 induced structural chromosomal aberrations in human lymphocytes *in vitro* in the absence and presence of a metabolic activation system.

In a TK assay in mouse lymphoma cells a substantial but not reproducible dose dependent increase of the mutation frequency was observed with and without metabolic activation at (near) toxic doses; these are considered not biologically relevant. Moreover, R613636 did not induce mutations in the HPRT locus in the Chinese hamster cell line V79 in absence or presence of metabolic activation. This supports the lack of biologically relevant response observed in the first mammalian gene mutation assay. Considering the results of the in vitro chromosome aberration study, an i*n* vivo mammalian erythrocyte micronucleus assay was performed. The *in vivo* mammalian erythrocyte micronucleus assay did not show any evidence of clastogenic or aneugenic effects. Hence it is concluded R613636 is not clastogenic or aneugenic *in vivo*.

SYN507900 (SDS66882)

2,4,5-trichloro-3-cyano-6-hydroxy-benzamide is a soil (aerobic, anaerobic) metabolite with the following code numbers: SYN507900, SDS66882, CSCC210323.
SYN507900 has been assessed for end points of gene mutation and chromosome damage in an in vitro bacterial reverse mutation assay, an *in vitro* mammalian gene mutation assay and an *in vitro* chromosome aberration assay. The *in vitro* gene mutation assays were both negative. In the *in vitro* chromosome aberration assay statistically significant increases in aberration frequency we observed in the absence (22 h exposure) and presence (4 h exposure) of metabolic activation.
Considering the results of the in vitro chromosome aberration study, an i*n* vivo mammalian erythrocyte micronucleus assay was performed. The *in vivo* mammalian erythrocyte micronucleus assay did not show any evidence of clastogenic or aneugenic effects. Hence it is concluded SYN507900 is not clastogenic or aneugenic *in vivo*.

DEREK analysis

A DEREK analysis was performed for all soil metabolites indicated above. (Q)SAR analysis revealed a number of alerts common to many of the metabolites and parent chlorothalonil. However, evaluation of the results, e.g. comparison with the available sub chronic, chronic and carcinogenicity data of chlorothalonil, did not result in any relevant toxicological alert.

Table 2.6.9-1 Summary of the toxicity data on ground water metabolites R182281, R417888, SYN548708 (R418503), SYN548765 (R419492), SYN548766 (R471811), SYN548738 (SYN548008), SYN548580, SYN548764 (SYN548581), SYN548580, R611965, R611968 and R613636.

Study type	Author	Result
SDS 3701 (R182281)		
Acute Oral toxicity Rat	Beerens-Heijnen (2005a)	LD_{50} 50-300 mg/kg bw
Acute Oral toxicity Rat	Wazeter (1971a)	LD_{50} 332 mg/kg bw
Acute Oral toxicity Rat	Hastings (1973)	LD_{50} 242-422 mg/kg bw
Skin Irritation Rabbit	Beerens-Heijnen (2005b)	Non-Irritant
60 Day Rat study	Ford (1982a)	NOAEL < 10 mg/kg bw/day
90 Day Rat study	Van-Otterdijk (2007)	NOAEL = 3 mg/kg bw/day
90 Day Dog study	Bundy et al. (1975)	NOAEL = 1.25 mg/kg bw/day
1 Year Dog study	Schetter et al (2000)	NOAEL = 0.83 mg/kg bw/day
Bacterial reverse mutation assay (Ames)	Verspeek-Rip (2004a)	Negative
Cell mutation assay in mouse lymphoma L5178Y cells	Verspeek-Rip (2005)	Positive+/-S9 (at cytotoxic concentrations)
Chromosome aberration study in CHO cells	Mizens et al (1994)	Positive +/-S9
In vivo mouse micronucleus study	Buskens (2004a)	Negative
In vivo chromosome aberration test	Mizens & Laveglia (1995)	Negative
Dominant lethal test, rats	Hastings & Jessup (1975)	Negative
In vivo rat liver UDS study	Honarvar (2006)	Negative
2 Year Rat study	Ford et al (1983)	NOAEL = 3 mg/kg bw/day
Reproductive toxicity study Rat	Ford et al (1982c)	NOAEL par = 3 mg/kg bw/day NOAEL dev = 1.5 mg/kg bw/day NOAEL repro >6 mg/kg bw/day
Teratogenicity Study Rabbit	Wazeter (1976b)	NOAEL mat/dev = 2.5 mg/kg bw/day
Teratogenicity Study Rat	Schroeder (1998)	NOAELmat/dev = 5 mg/kg bw/day
R611965 (SDS 46851)		
Acute Oral toxicity Rat	Beerens-Heijnen (2005c)	LD_{50} >2000 mg/kg
Acute Oral toxicity Rat	Long, 1985	LD_{50} > 5000 mg/kg
Skin Irritation Rabbit	Beerens-Heijnen (2005d)	Non-Irritant
30 Day Oral Rat study	Wilson (1986d)	NOAEL= 500 mg/kg bw/day
28 Day Oral Mouse study	Mizens (1990)	NOAEL = 2028 mg/kg bw/day
90 Day Oral Rat study	van Otterdijk (2007)	NOAEL= 197 mg/kg bw/day
90 Day Oral Dog study	Auletta (1990)	NOAEL= 50 mg/kg bw/day
Bacterial reverse mutation assay (Ames)	Godek et al (1985)	Negative
Bacterial reverse mutation assay (Ames)	Haworth et al (1985)	Negative
Bacterial reverse mutation assay (Ames)	Verspeek-Rip (2004b)	Negative

Study type	**Author**	**Result**
In vitro SCE assay	Jones et al (1985)	Negative
Cell mutation assay in mouse lymphoma L5178Y cells	Jones & Sernau (1985)	Negative
Cell mutation assay in mouse lymphoma L5178Y cells	Verspeek-Rip (2005)	Negative
UDS test with rat hepatocytes	Jones et al (1985)	Negative
In vivo mouse micronucleus study	Siou et al (1985)	Equivocal, repeated negative
In vivo mouse micronucleus study	Fox (2002)	Negative
In vivo mouse micronucleus study	Buskens (2004b)	Negative
2 Year Rat study	Serrone et al (1993)	NOAEL = 200 mg/kg bw/day
Reproductive toxicity study Rat	Lucas et al (1993)	NOAEL par = 269 mg/kg bw/day NOAEL dev > 911 mg/kg bw/day NOAEL repro > 911 mg/kg bw/day
Teratogenicity Study Rabbit	Henwood (1989)	NOAEL mat <250 mg/kg bw/day NOAEL dev 500 mg/kg bw/day
Teratogenicity Study Rat	Schroeder (1989)	NOAELmat/dev >2000 mg/kg bw/day
R417888		
Acute Oral toxicity Rat	Hygevoort (2005)	LD_{50} > 2000mg/kg
Acute Oral toxicity Rat	Johnson, 1999	LD_{50} > 2000mg/kg
90 Day Rat study	Noakes, 2001	NOAEL > 59 mg/kg bw/day
90 Day Rat study	van Otterdijk, 2007	NOAEL > 192 mg/kg bw/day
Bacterial reverse mutation assay (Ames)	Callander (2000)	Negative
Bacterial reverse mutation assay (Ames)	Verspeek-Rip (2005a)	Negative
Bacterial reverse mutation assay (Ames)	Sokolowski (2007)	Negative
In vitro chromosome aberration test in human lymphocytes	Fox (2000b)	Negative
In vitro chromosome aberration test in human lymphocytes	Fox (2000a)	Positive (–S9) Negative (+S9)
In vitro chromosome aberration test in human lymphocytes	Kunz (2007)	Positive (–S9) Negative (+S9)
Cell mutation assay in mouse lymphoma L5178Y cells	Clay (2000)	Negative
Cell mutation assay in mouse lymphoma L5178Y cells	Verspeek-Rip (2006)	Positive (+S9) Negative (-S9)
Cell mutation assay in mouse lymphoma L5178Y cells	Wollny (2007)	Negative
In vivo mouse micronucleus study	Meerts (2005)	Negative
In vivo rat liver UDS study	Honarvar (2006)	Negative
SYN548708 (R418503)		

Study type	**Author**	**Result**
Bacterial reverse mutation assay (Ames)	Sokolowski (2015)	Negative
In vitro chromosome aberration test in human lymphocytes	Sokolowski (2015a)	Positive
Cell mutation assay in mouse lymphoma L5178Y cells	Wollny (2015)	Negative
In vivo mouse micronucleus study	Dunton (2015)	Negative
SYN548765 (R419492)		
Study type	**Author**	**Result**
Bacterial reverse mutation assay (Ames)	Sokolowski (2015b)	Negative
In vitro chromosome aberration test in human lymphocytes	Sokolowski (2015c)	Negative
Cell mutation assay in mouse lymphoma L5178Y cells	Wollny (2015a)	Negative
SYN548766 (R471811)		
Bacterial reverse mutation assay (Ames)	Sokolowski (2015d)	Negative
In vitro chromosome aberration test in human lymphocytes	Sokolowski (2015e)	Negative
Cell mutation assay in mouse lymphoma L5178Y cells	Wollny (2015b)	Negative
SYN548738 (SYN548008)		
Bacterial reverse mutation assay (Ames)	Sokolowski (2015f)	Negative
In vitro chromosome aberration test in human lymphocytes	Sokolowski (2015g)	Negative
Cell mutation assay in mouse lymphoma L5178Y cells	Sokolowski (2015h)	Negative
SYN548580		
Bacterial reverse mutation assay (Ames)	Sokolowski (2015i)	Negative
In vitro chromosome aberration test in human lymphocytes	Sokolowski (2015j)	Negative
Cell mutation assay in mouse lymphoma L5178Y cells	Wollny (2015c)	Negative
SYN548764 (SYN548581)		
Bacterial reverse mutation assay (Ames)	Sokolowski (2015k)	Negative
In vitro chromosome aberration test in human lymphocytes	Sokolowski (2015l)	Equivocal
Cell mutation assay in mouse lymphoma L5178Y cells	Wollny (2015d)	Negative
In vivo mouse micronucleus study	Dunton (2015a)	Negative
R611968 (SDS-47525)		
Bacterial reverse mutation assay (Ames)	Sokolowski (2015m)	Negative
In vitro chromosome aberration test in human lymphocytes	Sokolowski (2015n)	Equivocal

Study type	Author	Result
Cell mutation assay in mouse lymphoma L5178Y cells	Wollny (2015e)	Negative
In vivo mouse micronucleus study	Dunton (2015b)	Negative
R613636 (SDS-47525)		
Bacterial reverse mutation assay (Ames)	Sokolowski (2015o)	Negative
In vitro chromosome aberration test in human lymphocytes	Sokolowski (2015p)	Positive
Cell Mutation assay in mouse lymphoma L5178Y cells	Wollny (2015f)	Negative
In vitro Gene Mutation Assay in Chinese Hamster V79 Cells	Wollny (2015g)	Negative
In vivo mouse micronucleus study	Dunton (2015c)	Negative
SYN507900 (SDS66882)		
Bacterial reverse mutation assay (Ames)	Sokolowski (2015q)	Negative
In vitro chromosome aberration test in human lymphocytes	Sokolowski (2015r)	Positive
Cell mutation assay in mouse lymphoma L5178Y cells	Wollny (2015h)	Negative
In vivo mouse micronucleus study	Dunton (2016)	Negative

2.6.10 Summary of medical data and information

In case of occupational exposure, skin and eye irritation might occur. The reported prevalence of dermatitis and respiratory symptoms is low. There are no indications for severe ocular effects or for respiratory sensitization.

2.6.11 Toxicological end point for assessment of risk following long-term dietary exposure – ADI

Chlorothalonil

No human epidemiological data, volunteer studies or case studies are available which allow the establishment of an acceptable daily intake (ADI) for chlorothalonil. The ADI has, therefore, to be derived from the results of toxicity studies with experimental animals. The calculation of the ADI is based on the highest dose at which no adverse effect is observed in the most appropriate study in the most sensitive species. Chlorothalonil was tested in several semichronic and chronic studies in dogs, rats and mice.

Table 2.6.11 Summary of oral short-term, long-term and reproduction studies with chlorothalonil

Duration, route	Species	NOAEL (mg/kg bw/day	LOAEL (mg/kg bw/day)	Critical effects	Reference
28-days,	rat	< 80	80	increased relative liver and kidney weights	Wilson et al.,

oral					1982b
28-days, oral	rat	1.5	15	histopathological changes in stomach and kidneys	Hironaka et al., 1996
13 weeks, oral	rat	< 40	40	increased relative kidney weight, hyperplasia and increased size of the renal tubule and acute gastritis	Wilson et al., 1981, 1985a
13 weeks, oral	rat	**3.0**	10	increased incidence of irregular intracytoplasmic inclusion bodies in renal tubules in males, histopathological changes in forestomach	Wilson et al., 1983a, b, 1984a,b
13 weeks, oral	rat	**< 4.4**	**4.4**	Minimal eosinophilia debris in lumens of inner cortical tubules of kidneys in males	Watson et al., 1985
13 weeks, oral	rat	local: <2.3 syst.: 4.7	local:2.3[3] syst.: 23.6	Local: histopathological changes in forestomach Syst: kidney weights (≤10%),	Spencer-Briggs et al., 1994a
13 weeks, oral	mouse	local: 2.5 syst: 47.7	local: 8.5 syst.: 123.6	Local: histopathological changes in forestomach Syst: kidney (weight and histopathology) increased body weight, clinical chemistry.	Shultz et al., 1983, 1985
13 weeks oral	mouse	local: 9 syst: 38	local: 38 syst: 167	Local: roughened forestomach Syst: kidney (weight and histopathology), thyroid weight	Spencer-Briggs et al., 1992b
13 weeks oral	dog	15	150	body weight , cholesterol, albumin	Fillmore et al., 1993
13 weeks oral	dog	5.6	56.5	Vomiting, body weight, liver, kidney and adrenal weight, and histopathology in kidneys and adrenals.	Spencer-Briggs et al., 1994b
52 weeks oral	dog	15	150	liver and kidney weights	Mizens et al., 1994
52 weeks oral	dog	5.1	43.3	body weight, histopathology in kidneys and stomach	Spencer-Briggs et al., 1995
116 weeks, oral	rat	< 40	40	body weight, liver/kidney (clinical chemistry, urine, organs weights), kidney/forestomach (histopathology, including tumours)	Wilson et al., 1985c
26 months, oral	rat	1.8	3.8	Kidney tubular hyperplasia **Kidney tumours at 15 mg/kg bw/d**.	Wilson & Killeen, 1989a
104 weeks, oral	rat	Local: 0.7 Syst: 2.7	Local: 2.7 Syst: 10.6	Local: stomach (histopathology) Systemic: liver and kidneys (hematology and histopathology)	Spencer-Briggs et al., 1996
104 weeks, oral	mouse	< 119	119	kidney weight, kidney and stomach: histopathology including tumours	Wilson et al., 1983c
24 months, oral	mouse	n.d.	n.d.	Indications for carcinogenicity were weak and in the stomach only, at high dose of 99.7 mg/kg bw/day.	Johnson et al., 1987
80 weeks, oral	mouse	Local: < 1.9 Syst: 1.9	Local: 1.9 Syst: 7.8	Local: stomach (histopathology) Systemic: kidney (histopathology)stomach tumours at 130 mg/kg bw/d	Spencer-Briggs et al., 1996
Oral, 2-generation study	rat	Par: < 22.6 Dev: 22.6 Repro:>145.1	Par: 22.6 Dev: 68.2 Repro: -	Body weight, stomach and kidneys (histopathology) Decreased F1 pup weights No effects	Lucas, et al, 1990
Oral, 2-	rat	Par: < 32.7	Par: 32.7	Stomach and kidneys (histopathology),	Meyers, et

generation study		Dev: <32.7 Repro: > 261	Dev: 32.7 Repro: -	kidney weight, enlarged lymph nodes. Stomach and kidneys (histopathology) No effects	al, 1985
Oral developmental study	rabbit	Mat:10.0 Dev:≥20 Ter:≥20	Mat:20 Dev:- Ter:-	Body weight No effects No effects	Wilson, 1988i
Oral developmental study	rabbit	Mat:10 Dev: 10 Ter: ≥20	Mat:20 Dev: 20 Ter:-	Body weight and food intake, related to anorexia Skeletal variation (rib, sternebrae) No effects	Meyers, 1994c
Oral developmental study	rat	Mat:<25 Dev:100 Ter: ≥400	Mat:25 Dev:400 Ter:-	Body weight and food intake Live foetuses, early resorptions No effects	Mizens, 1983
Oral developmental study	rat	Mat:80 Dev:<80 Ter: ≥200	Mat:200 Dev:80 Ter:-	Body weight, food and water intake, wet faeces Rudimentary ribs No effects	Meyers, 1994b
Oral developmental study	mouse	Mat:100 Dev: 100 Ter: >600	Mat: 400 Dev: 400 Ter: -	Clinical signs, body weight Resorptions, foetal survival and weight. No effects	Farag et al., 2006

In the original DAR the ADI for chlorothalonil was established at 0.015 mg/kg bw/day on the basis of a NOAEL of 1.5 mg/kg bw/day based on minimal histopathological changes in the kidneys in the 90-day oral rat study. After re-evaluation, the RMS now proposes to increase the NOAEL of this study to 3.0 mg/kg bw/day. The most relevant study for setting the ADI is then the 26-month carcinogenicity study in rats, with a NOAEL of 1.8 mg/kg bw/d, based on tubular hyperplasia in the kidney observed at 3.8 mg/g bw/d. Even though this study was not a full toxicity study according to OECD 451, this NOAEL for non-neoplastic lesions is in accordance with findings and NOAELs in the short-term and long-term studies on dogs, rats and mice.

To account for a sufficient margin of 1000 to the LOAEL for kidney tumours in the long term rat study at 15 mg/kg bw/day, a slightly increased safety factor of 120 should be applied.

The ADI is therefore 0.015 mg/kg bw/d on the basis of a NOAEL of 1.8 mg/kg bw/day in a 26-month oral rat study, and a safety factor of 120.

In the JMPR (2009) an ADI of 0.02 mg/kg bw/d was set for chlorothalonil, based on the NOAEL of 1.8 mg/kg bw/d for kidney toxicity in the long-term study in rats.

Co-RMS

Co-RMS BE agrees with the ADI proposal of **0.015 mg/kg bw/d** on the basis of a NOAEL of 1.8 mg/kg bw/day in a 26-month oral rat study, and a safety factor of 120. This value is not different from that proposed at the first inclusion, but it is derived differently.

SDS-3701 (R182281)

In the DAR, a ADI of 0.01 mg/kg bw/day was set. Based on all data, the overall NOAEL was set at 1.25 mg/kg bw/day (taking into consideration the NOAELs of 1.25 and 0.83 mg/kg bw/day, from the 90-day study and 1-year study in dogs, respectively). Considering an overall NOAEL of 1.25 mg/kg bw/day, application of a safety factor 100 results in an ADI of 0.01 mg/kg bw/day.
In the JMPR (2009) for R182281 (SDS-3701) an ADI is derived based on a NOAEL of 0.83 mg/kg bw/day (LOAEL 1.8 mg/kg bw/day), on the basis of a reduction in body weight gain in females, a reduction in erythrocytes in males and increased serum concentrations of glucose in males and females in a 1-year study in dogs, and using a safety factor of 100. The ADI was set at 0.008 mg/kg bw/day.

SDS-46851 (R611965)
From the previous assessment (European Commission, Review Report, 2006), no new data relevant for the setting of the ADI of SDS-46851 have been made available. New data did not lead to a change in the overall NOAEL of 50 mg/kg bw/day from a 90-day oral toxicity study in dogs. Based on a NOAEL of 50 mg/kg bw/day, and application of a safety factor 100, an ADI of 0.5 mg/kg bw/day is derived.

R417888
From the previous assessment (European Commission, Review Report, 2006), no new data relevant for the setting of the ADI of R417888 have been made available. New data did not lead to a change in the overall NOAEL of 6 mg/kg bw/day from a 90-day oral toxicity study in rats. Based on a NOAEL of 60 mg/kg bw/day and application of a safety factor 1000, an ADI of 0.06 mg/kg bw/day is derived.

2.6.12 Toxicological end point for assessment of risk following acute dietary exposure – ARfD (acute reference dose)

Chlorothalonil
The key endpoint for setting an acute reference dose for chlorothalonil is the mild kidney toxicity, which can be seen after single oral dose in the rat. Following prolonged dosing this toxicity becomes more severe, and eventually leads to tumour development in chronic studies.

In the original monograph, no ARfD was derived. In ECCO 109, it was decided to establish an ARfD of 0.015 mg/kg bw/day, based on the NOAEL of 1.5 mg/kg bw/day from a 28-day oral toxicity study. However, this ARfD is not based on effects observed after a single dose. There were some data from mechanistic studies, in which histopathological effects on the kidney were observed after a single dose at 175 mg/kg bw. However, lower dose levels were not tested in these studies, hence a proper NOAEL for acute kidney effects was not available at that time.

In the submitted ARfD studies in the rat, described in addendum April 2006 post approval, the acute effects on the kidneys were adequately tested (including urinalysis, clinical chemistry, histopathology). In

the dose-range-finding study, slight kidney effects were observed at 180 and 1000 mg/kg bw. In the full ARfD study, a single administration of chlorothalonil to Fisher 344 rats did not induce any adverse effects nor cell proliferation at any dose level (20, 60, and 250 mg/kg bw).
Therefore it can be concluded that a single dose of 60 mg/kg bw is a clear no-effect level for both changes in kidney histopathology, and in renal cell proliferation (as measured by BrdU incorporation). Effects on renal cell proliferation were observed at 175 mg/kg bw in mechanistic studies.
Hence, the most appropriate NOAEL for the setting of an ARfD is 60 mg/kg bw. Application of a safety factor 100, results in an ARfD of 0.6 mg/kg bw. This ARfD was agreed in the SCoFCAH meeting September 2006. From this previous assessment (European Commission, SCoFCAH meeting September 2006), no new data relevant for the setting of the ADI of chlorothalonil have been made available. Therefore, the ARfD remains 0.6 mg/kg bw.

In 2009 the JMPR set for chlorothalonil.an ARfD of 0.6 mg/kg bw, based on the overall NOAEL of 60 mg/kg bw for kidney toxicity in the acute toxicity studies in rats.

Co-RMS

Co-RMS BE indicates that the ARfD proposal of 0.6 mg/kg bw should be discussed. A value of 0.1 mg/kg bw/d is also defendable, based on the severe body weight decreases at the lowest dose of 25 mg/kg bw/d in the rat developmental study (Mizens,1983) and the early clinical signs at the LOAEL of 20 mg/kg bw/d (NOAEL 10 mg/kg bw/d) in the rabbit developmental study (Meyers, 1994).

Reply RMS

The RMS is of the opinion that the clear critical effect of chlorothalonil is a kidney effect, which was the basis for setting the ARfD during the former peer review process.
Body weight effects are observed in (pregnant) rats and rabbits. In rabbits, an early onset of a decrease in body weight gain was seen at 20 mg/kg bw/d in one study, but could not be repeated in the other study, in which anorexia was observed at a later stage of the study (not an acute effect). In pregnant rats, the decrease in body weight gain in the first days of dosing is in absolute numbers not that different from control; only at 400 mg/kg bw/d the effect is statistically different. Moreover, in the other rat developmental study, the maternal NOAEL was 80 mg/kg bw/d.
The RMS is of the opinion that these non-reproducible acute effects on body weight gain and feed consumption, in a gavage study, is not appropriate for setting the ARfD.

SDS-3701 / R182281

Based on the LD_{50} of R182281 of 242-422 mg/kg bw, there is a need for setting an ARfD, taking into consideration the guidance on setting a ARfD. In the initial DAR it was concluded that no suitable study for the derivation of an ARfD for R182281 was available. Therefore, the ARfD was set at the same level as the ADI. Based on the toxicological database of R182281 it was concluded that there is no difference in NOAELs from short-term and chronic exposure duration. The ADI of R182281 is based on the NOAEL of 1.25 mg/kg bw/day from a 90-day oral toxicity study in dogs. The most suitable study for deriving the ARfD for R182281 in the available data set is the teratogenicity study,

although it should be noted that only limited parameters were considered for maternal toxicity. However, since it was concluded that there is no significant effect of exposure duration, and the NOAELs of the 60- and 90-day are above the NOAEL of the teratogenicity study, the latter study can be used for the derivation of the ARfD. In the initial DAR, for the teratogenicity study in rats (Wazeter and Goldenthal, 1976) the NOAEL for material toxicity was set at 2.5 mg/kg bw/day. Therefore, the RMS agrees with the ARfD of 0.03 mg/kg bw/day, as proposed by the applicant. This ARfD is in accordance with the ARfD set for R182281 by the JMPR (2009).

In the JMPR (2009) the ARfD was set at 0.03 mg/kg bw/day, based on a NOAEL of 2.5 mg/kg bw/day, on the basis of early implantation loss. The Meeting considered that the abortions and deaths observed in this study in rabbits at 2.5 and 5 mg/kg bw/day were considered to be unlikely to be induced by a single dose of R182281 (SDS-3701).

SDS-46851

In the original assessment (European Commission, Review Report, 2006), an ARfD of 0.5 mg/kg bw/day was set for SDS-46851, based on the overall NOAEL of 50 mg/kg bw/day from a 90-day oral toxicity study in dogs, and application of a safety factor 100 In addendum 15 (April 2004) the rationale for setting an ARfD was presented: *No studies with low dose levels and short-term exposure are available. Therefore, no final conclusion could be drawn whether an ARfD should or should not be derived. Therefore, the ARfD was established at the same level as the ADI, 0.5 mg/kg bw/day.*
However, upon closer re-evaluation of the available data for SDS-46851, the RMS is of the opinion that there are no indications for acute toxicity properties for this metabolite. The oral LD50 is >2000 mg/kg bw, there are short-term studies available (2- to 4-week studies in rat, mouse and dog, developmental studies in rat and rabbit) which did not indicate a concern for acute toxicity. In the 30-d study in mice, the finding of hyperplasia of the renal tubular epithelium at the lowest dose of 46 mg/kg bw was equivocal, since there was no dose response and the effect was only minimal and in 1 or 2 animals; in this RAR the NOAEL is therefore set at 2028 mg/kg bw/d. In the 90-d dog study, a slight body weight effect (mean body weight loss of 3%) was observed in 50 mg/kg bw/d dogs, but not in the 500 mg/kg bw/d dogs. Moreover, in the 30-d dog study, although considered unacceptable for setting a NOAEL since only 2 animals/sex were used, no effect on body weigh was observed in the first week of dosing, up to doses of 1000 mg/kg bw/d. Overall, in the rather extensive database for SDS-46851, there are no indications for acute toxicity, and therefore the RMS is now proposing that an ARfD for SDS-46851 is not necessary.

R417888

From the previous assessment (European Commission, Review Report, 2006), no new data relevant for the setting of the ARfD of R417888 have been made available. Setting of an ARfD is not considered required.

2.6.13 Toxicological end point for assessment of occupational, bystander and residents risks – AOEL

In the original DAR the AOEL for chlorothalonil was established at 0.0086 mg/kg bw/day on the basis of an overall NOAEL of 2.7 mg/kg bw/day for systemic effects after short-term and long-term repeated exposure to chlorothalonil in rats, and applying an oral absorption of 32%. This was rounded to 0.009 mg/kg bw/d, the AOEL as set during the peer-review.

Re-evaluation of the short-term toxicity data reveals that the overall NOAEL for short-term toxicity could be raised to 3.0 mg/kg bw/d. However, at 4.4 mg/kg bw/d minimal but treatment related effects were observed in one 90-day rat study. The observed effect (eosinophilia debris in lumen of inner cortical tubules) was not accompanied by any other kidney effect; hence it should be considered test substance related, but the adversity of the effect is minimal. Moreover, the effect was not recorded in any other study.
As a conservative approach, the RMS proposes the reconfirm the AOEL of 0.009 mg/kg bw/d, based on the overall NOAEL of 2.7 mg/kg bw/day for systemic effects after short-term and long-term repeated exposure to chlorothalonil in rats, and applying an oral absorption of 32%.

Co-RMS
The Co-RMS BE proposes an AOEL based upon the lowest NOAEL = 1.5 mg/kg b.w./d, representative for both the 90d Wilson (1983) and Watson (1985) studies. It also covers the local effects in the stomach, observed in all studies at about 2 mg/kg bw/d. This would result in an AOEL of 0.015 mg/kg bw/d.

Reply RMS
In the proposal by the co-RMS, the oral absorption of 32% is not yet taken into account. This would result in an AOEL of 0.0048 mg/kg bw/d.
The RMS does not agree with this approach, as the dose spacing in the 28-day rat study with the NOAEL of 1.5 mg/kg bw/d is rather large (LOAEL 15 mg/kg bw/d). The NOAELs in the rat 90d studies are higher, indicating that the true NOAEL in the 28-day rat study is also higher than 1.5 mg/kg bw/d.
The RMS proposes the reconfirm the AOEL of 0.009 mg/kg bw/d as indicated above.

2.6.14 Summary of product and risk assessment

2.6.14.1 *SYNGENTA: A11141B*

Table 2.6.14.1-1 Operator exposure and risk assessment

Application method	Model	Without PPE (mg/kg bw/day)	% of AOEL	With PPE (mg/kg bw/day)	% of AOEL
Tractor-mounted sprayer, field crop **cereals**	German model	0.0137	152	0.0015[a]	17
	UK POEM	0.0601	668	0.0156[b]	173

Tractor-mounted sprayer, field crop **tomato**	German model	0.0416	462	0.0037[a]	41
	UK POEM	0.0444	493	0.0085[b]	94
Hand-held application, field crops **tomato**	German model	0.0469	521	0.0088[c]	98
	UK POEM	0.1069	1188	0.0228[d]	253

[a] Protective gloves and protective garment and sturdy footwear during application

[b] Protective gloves during mixing, loading and application

[c] Protective gloves during mixing, loading and application, and protective garment, sturdy footwear and broad-brimmed headgear during application

[d] Protective gloves during mixing and loading, and gloves and impermeable coverall during application

Table 2. 6.14.1-2 Bystander and resident exposure and risk assessment

Exposure (mg/kg bw/d)	**Bystander**		**Resident**	
	Adult	**Child**	**Adult**	**Child**
Cereals				
Total systemic exposure	0.00011	0.00009	0.00029	0.00055
% of AOEL	1	1	3	6
Tomato, tractor				
Total systemic exposure	0.00034	0.00027	0.00030	0.00056
% of AOEL	4	3	3	6
Tomato, handheld				
Total systemic exposure	0.00007	0.00015	0.00028	0.00051
% of AOEL	1	2	3	6

Table 2. 6.14.1-3 Worker exposure and risk assessment

Application method	**Without PPE (mg/kg bw/day)**	**% of AOEL**	**With PPE (mg/kg bw/day)**	**% of AOEL**
Crop inspection **cereal Refined using DFR study**	0.0018	20	<0.0001	1
Crop inspection **tomato**	0.0014	16	<0.0001	1
Manual harvesting **tomato**	0.0233	259	0.0012	13

Conclusions on risk assessments for operators, bystanders and workers: Syngenta

Operator

- Using the German model, a safe use was identified for operators, with PPE, for:
  - Mechanical downward spraying on cereals and tomato.
  - Manual spraying on tomato.
- Using UK-POEM, a safe use was identified for operators, with PPE, for:
  - Mechanical downward spraying on tomato.

- Using UK-POEM, no safe use was identified for operators, with PPE, for:
  - Mechanical downward spraying on cereals , or
  - Manual spraying on tomato.

Bystander and residents

It is concluded that there is no undue risk to any bystander or residents after accidental short-term exposure to A14111B during or after downward spraying in cereals or tomatoes, using the German model.

Worker

Using the German re-entry model it is concluded that there is no unacceptable risk anticipated for the worker wearing adequate work clothing (but no PPE), when performing crop-inspection activities in cereals or tomato treated with A14111B. For hand-harvesting tomato treated with A14111B it is concluded that there is no unacceptable risk anticipated for the worker wearing adequate PPE..

2.6.14.2 *Oxon: Chlorothalonil 500 g/L SC*

Table 2.6.14.2-1 Operator exposure and risk assessment

Application method	Model	Without PPE (mg/kg bw/day)	% of AOEL	With PPE (mg/kg bw/day)	% of AOEL
Tractor-mounted sprayer, field crop **cereals**	German model	0.0675	750	0.0045[a]	50
	UK POEM	0.2105	2339	0.0332[b]	369
Tractor-mounted sprayer, field crop **potato**	German model	0.1243	1381	0.0085[a]	94
	UK POEM	0.2105	2339	0.0332[b]	369
Tractor-mounted sprayer, field crop **tomato**	German model	0.1599	1777	0.0087[c]	97
	UK POEM	0.2015	2239	0.0295[b]	328
Hand-held application, field crops **tomato**	German model	0.2079	2310	0.0124[d]	138
	UK POEM	0.4570	5078	0.0813[b]	903

[a] Protective gloves during mixing, loading and application, and protective garment and sturdy footwear during application

[b] Protective gloves during mixing, loading and application

[c] Protective gloves during mixing, loading and application, and protective garment, sturdy footwear and broad-brimmed headgear during application

[d] Protective gloves and particle filtering half mask during mixing and loading, and gloves, protective garment, sturdy footwear broad-brimmed headgear, and half mask with combined filter during application

Table 2. 6.14.2-2 Bystander and resident exposure and risk assessment

Exposure (mg/kg bw/d)	Bystander		Resident	
	Adult	Child	Adult	Child

Cereals				
Total systemic exposure	0.00047	0.00038	0.00033	0.00061
% of AOEL	5	4	4	7
Potato				
Total systemic exposure	0.00095	0.00074	0.00035	0.00062
% of AOEL	11	8	4	7
Tomato, tractor				
Total systemic exposure	0.00121	0.00095	0.00036	0.00065
% of AOEL	13	11	4	7
Tomato, handheld				
Total systemic exposure	0.00007	0.00015	0.00028	0.00051
% of AOEL	1	2	3	6

Table 2. 6.14.2-3 Worker exposure and risk assessment

Application method	Without PPE (mg/kg bw/day)	% of AOEL	With PPE (mg/kg bw/day)	% of AOEL
Crop inspection **cereal Refined using DFR study**	0.0077	85	0.0004	4
Crop inspection **potato**	0.0091	101	0.0005	5
Crop inspection **tomato**	0.0117	130	0.0006	7
Manual harvesting **tomato**	0.0833	926	0.0042	46

Conclusions on risk assessments for operators, bystanders and workers: Oxon

Operator

- Using the German model, a safe use was identified for operators, with PPE, for:
  - Mechanical downward spraying on cereals, potato and tomato.
- Using the German model, no safe use was identified for operators, with PPE, for:
  - Manual spraying on tomato.
- Using UK-POEM, no safe use was identified for operators, with PPE, for:
  - Mechanical downward spraying on cereals, potato and tomato, or
  - Manual spraying on tomato.

Bystander and residents

It is concluded that there is no undue risk to any bystander or residents after exposure to Chlorothalonil 500 g/L SC during or after downward spraying in cereals, potatoes or tomatoes, using the German model.

Worker

Using the German re-entry model it is concluded that there is no unacceptable risk anticipated for the worker wearing adequate work clothing (but no PPE), when re-entering cereals treated with Chlorothalonil 500 g/L SC. For tomato and potato it is concluded that there is no unacceptable risk anticipated for the worker wearing adequate PPE, when re-entering potato or tomato crops treated with Chlorothalonil 500 g/L SC.

2.6.14.3 *Arysta: Chlorothalonol 500 g/L SC (ARY-0474-001)*

Table 2.6.14.3-1 Operator exposure and risk assessment

Application method	Model	Without PPE (mg/kg bw/day)	% of AOEL	With PPE (mg/kg bw/day)	% of AOEL
Tractor-mounted sprayer, field crop **wheat, barley**	German model	0.0675	750	0.0045[a]	50
	UK POEM	0.1883	2092	0.0329[b]	366
	AOEM model	0.0304	338	0.0042[f]	26
Tractor-mounted sprayer, field crop **tomato**	German model	0.2240	2489	0.0094[c]	104
	UK POEM	0.2015	2239	0.0295[b]	328
	AOEM model	0.0498	553	0.0029[f]	32
Hand-held application, field crops **tomato**	German model	0.2713	3014	0.0131[c]	146
	UK POEM	0.4570	5078	0.0813[d]	903
Hand-held application, field crops **tomato**	AOEM model	0.0618	687	0.0479[e]	531

[a] Protective gloves during mixing, loading and application, and protective garment and sturdy footwear during application

[b] Protective gloves during mixing, loading and application

[c] Protective gloves and half mask with combined filter during mixing and loading, and gloves, protective garment, sturdy footwear, and hood and visor during application

[d] Protective gloves during mixing and loading, and protective gloves and impermeable coverall during application

[e] Protective gloves and mask with FP2/P2 or similar filter during mixing and loading and application

[f] Protective gloves during mixing and loading

Table 2. 6.14.3-2 Bystander and resident exposure and risk assessment

Exposure (mg/kg bw/d)	Bystander		Resident	
	Adult	Child	Adult	Child
Cereals				
Total systemic exposure	0.00047	0.00038	0.00033	0.00061
% of AOEL	5	4	4	7
Tomato, tractor				
Total systemic exposure	0.00174	0.00137	0.00040	0.00070

% of AOEL	19	15	4	8
Tomato, handheld				
Total systemic exposure	0.00007	0.00015	0.00028	0.00051
% of AOEL	1	2	3	6

Table 2. 6.14.3-3 Worker exposure and risk assessment

Application method	Without PPE (mg/kg bw/day)	% of AOEL	With PPE (mg/kg bw/day)	% of AOEL
Crop inspection **cereal**	0.0091	101	0.0005	5
Crop inspection **tomato**	0.0168	187	0.0008	9
Manual harvesting **tomato**	0.1200	1333	0.0060	67

Conclusions on risk assessments for operators, bystanders and workers: Arysta

Operator

- Using the German model, a safe use was identified for operators, with PPE, for:
  - Mechanical downward spraying on cereals.
- Using the German model, no safe use was identified for operators, with PPE, for:
  - Mechanical downward and manual spraying on tomato.
- Using UK-POEM, no safe use was identified for operators, with PPE, for:
  - Mechanical downward spraying on cereals and tomato, or
  - Manual spraying on tomato.
- Using the AOEM model, a safe use was identified for operators, with PPE, for:
  - Mechanical downward spraying on cereals and tomato.
- Using the AOEM model, no safe use was identified for operators, with PPE, for:
  - Manual spraying on tomato.

Bystander and residents

It is concluded that there is no undue risk to any bystander or residents after exposure to Chlorothalonil 500 g/L SC during or after downward spraying in cereals or tomatoes, using the German model.

Worker

It is concluded that there is no unacceptable risk anticipated for the worker wearing adequate PPE, when performing crop inspection in cereals and tomato or hand harvesting tomatoes treated with Chlorothalonil 500 g/L SC, using the German re-entry model.

2.7 Residues

2.7.1 Summary of storage stability of residues

Storage stability of chlorothalonil, SDS-3701 and SDS-46851 has already been investigated for the original evaluation. For the sake of the renewal of chlorothalonil, several additional storage stability studies have been submitted. A summary of the storage stability results for chlorothalonil and SDS-3701 in plant and animal commodities is presented in table 2.7.1-1. A summary of storage stability results for SDS-46851 in plant commodities is presented in Table 2.7.1-2 and a summary of storage stability results for SDS-19221 in processed commodities is presented in Table 2.7.1-3.

During the initial peer review process, there were discussions about the storage stability of chlorothalonil residues. In addition, it was questioned whether or not acid should be present when samples were homogenised to prevent possible losses of chlorothalonil. It is noted that careful treatment may be required during sample preparation. For field-incurred residues, storage stability of chlorothalonil is not dependent on the presence of acid during homogenisation, probably because chlorothalonil is not readily available for enzymes from the homogenised matrix and residues are directly quenched by the addition of extraction solvent. On the other hand, for the preparation of fortified samples, acid might be required during homogenisation before fortification to prevent the loss of chlorothalonil residues by enzymatic degradation.

In line with OECD guideline 506, chlorothalonil is stable for 48 months in crops representing the high water, for 24 months in high oil (demonstrated in 2 diverse commodities, while stability for 48 months has only been demonstrated in 1 commodity), for 48 months in the high starch group, and stable for 24 months in crops belonging to the high acid crop group. SDS-3701 is stable for 24 months in crops from the high acid and the high water group (except for onions), and stable for 24-27 months in high-oil crops and high-starch crops. SDS-46851 is stable for 30 months in crops representing the high water, high acid, high starch, high protein and high oil crop groups, although only 1 commodity has been investigated in every commodity category. SDS-19221 is stable in a range of commodities processed from barley, wheat, peanut, beans with pods and tomato for 24 months
Residues of SDS-3701 were stable in products of animal origin for 3-24 months.
Of the commodities tested in the freezer stability studies, the results in tomato, cereals, potato and animal commodities are directly relevant to the representative crops in this submission.

Table 2.7.1-1: Stability of chlorothalonil and SDS-3701 in plant and animal commodities following freezer storage

Commodity categories	Commodity	Period of stability (months)		Dossier Reference
		Chlorothalonil	SDS-3701	
High water content	Celery (incurred residues)	48	-	Original DAR[1]
	Cherries (incurred residues)	48	-	Original DAR[1]
	Cucumbers (incurred residues)	48	-	Original DAR[1]
	Cucumbers (incurred residues)	24	-[2]	K-CA 6.1/01
	Cucumbers (fortified, prepared in acid)	24	24	K-CA 6.1/02
	Melons (incurred residues)	24	-[2]	K-CA 6.1/01

Commodity categories	Commodity	Period of stability (months)		Dossier Reference
		Chlorothalonil	SDS-3701	
	Melons (fortified, prepared in acid)	24	24	K-CA 6.1/02
	Onions (fortified, prepared in acid)	24	<3	K-CA 6.1/02
	Tomatoes (incurred residues)	48	-	Original DAR[1]
	Tomatoes (incurred residues)	24	-[2]	K-CA 6.1/01
	Tomatoes (fortified, prepared in acid)	24	24	K-CA 6.1/02
	Apples (fortified, prepared in acid)	24	24	K-CA 6.1/02
	Broccoli (fortified, prepared in acid)	24	24	K-CA 6.1/02
	Brussels sprouts (fortified, prepared in acid)	24	24	K-CA 6.1/02
	Head cabbage (fortified, prepared in acid)	24	24	K-CA 6.1/02
	Cauliflower (fortified, prepared in acid)	24	24	K-CA 6.1/02
	French bean (fortified, prepared in acid)	24	24	K-CA 6.1/02
	Leek (fortified, prepared in acid)	24	24	K-CA 6.1/02
	Peas (fortified, prepared in acid)	24	24	K-CA 6.1/02
	Plum (fortified, excluding stone) (prepared in acid)	24	24	K-CA 6.1/02
	Banana (fortified, prepared in acid)	24	24	K-CA 6.1/02
High oil content	Almond nutmeat and hulls (incurred residues)	24	-	Original DAR[1]
	Peanuts (incurred residues)	18	-	Original DAR[1]
	Soya beans (incurred residues)	48	-	Original DAR[1]
	Soya beans (incurred residues)	27	27	K-CA 6.1/01
	Olive (excluding stone) (fortified, prepared in acid)	24	24	K-CA 6.1/02
High starch content	Carrots (incurred residues)	48	-	Original DAR[1]
	Carrot roots and tops (incurred residues)	24	24[3]	K-CA 6.1/01
	Carrots (fortified, prepared in acid)	24	24	K-CA 6.1/02
	Potatoes (incurred residues)	12	-	Original DAR[1]
	Potatoes (fortified, prepared in acid)	24	24	K-CA 6.1/02
	Sugar beet (fortified, prepared in acid)	24	24	K-CA 6.1/02
	Barley grain (incurred residues)	24	24[3]	K-CA 6.1/01
	Barley straw (incurred residues)	12	27[3]	K-CA 6.1/01
	Wheat grain (incurred residues)	48	-	Original DAR[1]
	Wheat grain (fortified, prepared in toluene)	3	-	K-CA 6.1/05
	Wheat straw (fortified, prepared in toluene)	3	-	K-CA 6.1/05
	Cereal straw (fortified, prepared in acid)	9	12	K-CA 6.1/03
High acid content	Oranges (incurred residues)	24	24	K-CA 6.1/01
	Strawberries (fortified, prepared in acid)	24	24	K-CA 6.1/02
	Grapes (fortified, prepared in acid)	24	3	K-CA 6.1/02
Products of	Bovine milk, liver, muscle, fat	-	12	Addendum 14 to

Commodity categories	Commodity	Period of stability (months)		Dossier Reference
		Chlorothalonil	SDS-3701	
animal origin				original DAR[1]
	Bovine muscle, fat, liver, kidney	-	3	K-CA 6.1/07
	Cow's milk	-	3	K-CA 6.1/07
	Bovine muscle	-	18	K-CA 6.1/08
	Bovine liver	-	24	K-CA 6.1/08
	Bovine milk	-	18	K-CA 6.1/08
	Poultry eggs	-	18	K-CA 6.1/08

[1] Report submitted for the original Annex I listing
[2] Field incurred levels of SDS-3701 are below the LOQ, therefore, no reliable storage stability can be quantified.
[3] Field incurred levels of SDS-3701 increased over time, probably by conversion from chlorothalonil into SDS-3701.

Table 2.7.1-2: Stability of SDS-46851 in plant commodities following freezer storage

Commodity Categories	Commodity	Period of Stability (months)	Dossier Reference
High water content	Tomato	30	K-CA 6.1/04
High oil content	Soya beans	30	
High starch content	Wheat grain	30	
High acid content	Orange	30	
High protein content	Lentil	30	

Table 2.7.1-3: Stability of SDS-19221 in processed commodities following freezer storage

Commodity	Period of Stability (months)	Dossier Reference
Pearl barley	24	K-CA 6.1/06
Beer	24	
Wheat bran	24	
Wheat flour	24	
Peanut meal	24	
Peanut oil	24	
Cooked beans with pods	24	
Tomato juice	24	
Tomato paste	24	
Tomato puree	24	

2.7.2 Summary of metabolism, distribution and expression of residues in plants, poultry, lactating ruminants, pigs and fish

During the initial peer review, the metabolism of chlorothalonil has been studied in lettuce, tomato, carrot, celery, snap beans (French beans), wheat and peas using ^{14}C-chlorothalonil labelled in the phenyl position. No additional studies have been submitted for the renewal of chlorothalonil.

Fairly high TRR levels were observed in edible crop parts that are directly exposed to treatments: up to 4.6 mg/kg in celery stalks and 28 mg/kg in pods (of peas). However, highest TRR levels were identified in lettuce (up to 170 mg/kg), and in crop parts generally not used for human consumption (foliage of celery, beans and carrot, wheat straw) levels up to 263 mg/kg were determined. In carrot roots, the TRR was within the range of 0.01-0.07 mg/kg, leading to the conclusion that translocation from foliage to roots is very limited. Residues in wheat grain were <0.01 mg/kg, therefore, no data are available on the nature of the residue. Data for foliar application on pea plants indicate that systemic transport to the pods is very limited (<10% of the levels observed upon whole plant application) whereas transport to peas is significant (comparable levels to whole plant application).
Generally, parent chlorothalonil constituted the most important component of the residue in all crops. It accounted for at least 3.3% of the TRR (beans) up to 90 % of the TRR (lettuce) in edible parts of the investigated crops. In cereal straw chlorothalonil was only a minor component (0.2% TRR). Except chlorothalonil, metabolite SDS-3701 was identified, mostly at levels below 10% of the TRR. Furthermore, metabolite SDS-46851 was identified below the LOD in beans. It can be noticed that metabolite SDS-3701 increases with longer PHI in lettuce, tomato fruit, carrot foliage, but more pronounced in tomato foliage from 4.2% TRR (PHI 1 day) to 14% (PHI 14 days). In wheat straw, SDS-3701 was minor (0.5% TRR), while glutathione conjugates of chlorothalonil (9.3% TRR) and other components were present (each ≤8.1% TRR).

Parent chlorothalonil is the most important compound in all crops. The metabolism of chlorothalonil in plants is not highly extensive. It involves the substitution of chlorine by a hydroxyl group, leading to metabolite SDS-3701. There were some indications for the existence of other metabolites but all were considered to be toxicologically not relevant as they were water-soluble and assumed to be glutathione conjugates. Furthermore, it can be concluded that the metabolism of chlorothalonil is qualitatively similar in the different crops, and that chlorothalonil will be metabolised to a greater extent after longer intervals, which is relevant for GAPs with PHI intervals exceeding 21/28 days.

Since both parent chlorothalonil and metabolite SDS-3701 may occur in feed crops, the nature of both substances in commodities of animal origin has been investigated during the initial peer review. The metabolism studies include two studies in lactating goats and two studies in laying hens using ^{14}C-U-phenyl labelled chlorothalonil and ^{14}C-U-phenyl labelled SDS-3701. In addition, a new metabolism study has been conducted with hens using labelled chlorothalonil for the sake of the renewal of chlorothalonil.
The original hen study with chlorothalonil (dosing with chlorothalonil at 0.22, 0.65 and 2.18 mg/kg bw/day) demonstrates that transfer of residues to eggs and tissues is limited. Only in the highest dose level (2.18 mg/kg bw/d), the TRR in egg yolk accounted for 0.05 mg/kg. Furthermore, in hens dosed with 0.65 and 2.18 mg/kg bw/d, total residues in liver accounted for 0.1 mg/kg. Further attempts for characterization or identification have not been made. Therefore, a new metabolism study has been carried out.
In the new hen study with chlorothalonil a dose rate of 1.59 mg/kg bw/day was achieved (based on the body weight of the hens at the first dose administration). The majority of the radioactivity was excreted

(91%). Liver (0.139 mg/kg TRR), egg yolk (0.091 mg/kg TRR) and skin samples (0.100 mg/kg TRR), which contained radioactive residues greater than 0.01 mg/kg, were subjected to further analysis to determine the metabolic profile. Chlorothalonil was not detected in any of the samples. The metabolite SDS-3701 was the only identified residue and was found at levels of up to 35.9% TRR and 0.050 mg/kg in liver. Radioactive residues reached a plateau concentration in eggs after 10 days. This new hen study confirms the old study that limited transfer of residues is observed, and that residues can be expected in egg yolk and liver.

From the hen study with SDS-3701 it can be observed that at the dose level of 0.011 mg/kg bw/d residues transfer to eggs and tissues is limited (egg yolk: 0.03-0.040 mg/kg TRR; liver: 0.056 mg/kg TRR). At the intermediate level of 0.033 mg/kg bw/d, residues were found in egg yolk (0.05-0.12 mg/kg TRR), cardiac muscle (0.055 mg/kg TRR) and liver (0.05-0.27 mg/kg TRR), while at the highest dose level of 0.10 mg/kg bw/d significant residues were found in egg yolk (0.06-0.42 mg/kg TRR), cardiac muscle (0.15 mg/kg TRR), liver (0.12-0.78 mg/kg TRR) and skin (0.37 mg/kg TRR). No information with respect to the nature or identity of the residue components is available, and also no new metabolism study with this metabolite has been conducted. However, since the metabolism study with chlorothalonil parent already covers the fate of the metabolite SDS-3701 and includes identification, no additional metabolism study is required.

For the original DAR, the metabolism of chlorothalonil and SDS-3701 has been investigated in 2 studies in lactating ruminants using either ^{14}C-chlorothalonil or ^{14}C-SDS-3701 labelled uniformly in the phenyl ring. No additional study has been submitted for the sake of the renewal of chlorothalonil. Lactating goats were dosed with [phenyl-U-^{14}C]-chlorothalonil at a rate of 6 or 60 mg/day (equivalent to 0.115 and 1.15 mg/kg bw/day). The majority of the radioactivity was excreted. Parent chlorothalonil was not detected in milk and any edible tissue samples. SDS-3701 was the only identified metabolite in milk (25% of the TRR; <0.01-0.05 mg/kg in the high dose group) and tissue samples (high dose group: 10% of the TRR / 0.03-0.04 mg/kg in liver and 3% of the TRR / 0.05-0.07 mg/kg in kidney). No other compounds were identified. Unidentified label presumably was partly attributable to glutathione conjugates and protein bound residue. Total radiolabel levels in milk, liver, and kidneys mounted up to 0.015, 0.08, and 0.22 mg/kg, respectively, for the low dose group, and 0.19, 0.7, and 2.2 mg/kg, respectively, for the high dose group.

In the second study, lactating goats were administered ^{14}C-SDS-3701 at rates of 0.4 and 4 mg daily for 9 consecutive days via capsule (equivalent to 0.0068 and 0.075 mg/kg bw/day). Residue levels in milk reached a plateau after 5 to 7 days and accounted for up to 0.15 and 1.0 mg/kg for the low and high dose group respectively. The highest total residues were detected in kidney (0.17-0.26 and 0.82-1.33 mg/kg for the low and high dose group, respectively), followed by liver (0.07 and 0.57-0.77 mg/kg, respectively), muscle and fat (0.01-0.02 and 0.07-0.14 mg/kg in the low and high does groups, respectively). Over 90% of the total residue in milk and tissues samples was characterised as organosoluble and over 90% of this fraction was attributable to unchanged SDS-3701. No other identifiable metabolites were detected in the milk or tissue samples.

The metabolic pathway in ruminants was characterised as oxidation of chlorothalonil to yield SDS-3701 and, presumably, glutathione conjugation. Results indicated that metabolite SDS-3701 was the major component of the TRR and no significant residues of parent chlorothalonil in ruminants are

expected even at higher dose levels. Also livestock exposure to SDS-3701 via feed results in residues of SDS-3701.

Regarding the metabolism in poultry, the pathway can be characterised as oxidation of chlorothalonil to SDS-3701 as well. Parent chlorothalonil was not detected in any of the samples. The metabolite SDS-3701 was the only identified residue.

The metabolism of chlorothalonil in ruminants was similar to that seen in the rat and therefore a metabolism study in pigs is not required. Previously, there were discussions regarding the requirement of metabolism studies in pigs, since the formation of SDS-3701 was not observed in rat, while it was a major metabolite in ruminants. However, a repeat rat biotransformation study has now demonstrated that SDS-3701 is the most abundant component circulating in rat plasma, accounting for up to 38% of the total circulating radioactivity exposure. Therefore, the metabolic patterns of chlorothalonil are considered not different between the monogastric rat and ruminants.

For the time being there are no agreed test guidelines for the estimation of the dietary burden of pesticide residues for fish or for the design and conduct of fish metabolism studies. Therefore, no fish metabolism studies have been conducted (see also SANCO/10181/2013 rev 2.1). Furthermore, regarding the representative uses, potato, wheat and barley grain are considered potential ingredients for fish feed. Since the low residue levels in these commodities, a significant exposure to fish is unlikely.

2.7.3 Definition of the residue

Plant

The residue definition for plants derived during the initial peer review only included parent chlorothalonil.

Since the levels of metabolite SDS-3701 increase with longer PHI, which is relevant for the GAPs of the defended uses for the renewal of chlorothalonil, this metabolite could be considered for inclusion in the residue definition. Furthermore, the contribution of SDS-3701 to the total residue may increase in plant commodities after processing (see 2.7.6). Toxicological reference values were derived for SDS-3701 (see 2.6.11 and 2.6.12) indicating that metabolite SDS-3701 is of higher acute and chronic toxicity than the parent compound. Furthermore, this metabolite follows a different toxicological mechanism than the parent compound (see 2.6.9). Since metabolite SDS-3701 is more toxic than parent and it can have relevant levels in plants, the consumer risk assessment for SDS-3701 may result in a more critical outcome than for the parent. Therefore, it should be included in the residue definition. Furthermore, because of the different toxicological mechanism compared to parent, SDS-3701 and parent chlorothalonil should be considered in two separate residue definitions, both for monitoring as well as for risk assessment. Consequently, MRLs for both chlorothalonil and SDS-3701 are proposed and separate risk assessments are presented for both chlorothalonil and SDS-3701.

Metabolite SDS-46851 is a significant metabolite in rotational crops. SDS-46851 has lower toxicity than parent chlorothalonil, since the ADI is much higher and no ARfD is required (see 2.6.11 and 2.6.12). Therefore, it is not necessary to include metabolite SDS-46851 in the residue definition.

Besides SDS-3701, metabolite SDS-19221 is also found after processing in relatively large amounts (brewing/boiling/baking: 3.4% AR; sterilisation: 15% AR) in nature of the residue studies. In some studies investigating the magnitude of the residue after processing, this metabolite was determined, and it was demonstrated that the SDS-19221 levels were always below LOQ in all products. Although there were only few processing studies in which SDS-19221 was measured, the studies in which this metabolite was determined, the crops of the representative use were considered. Therefore, for the renewal of chlorothalonil, it can be concluded that metabolite SDS-19221 is not relevant to be included in the residue definition.

Animal

Based on the results of the metabolism studies with poultry and ruminants, in which no parent chlorothalonil was detected and the metabolite SDS-3701 was the only identified and major component, it is proposed that the residue definition for animal commodities as it was derived during the initial peer review remains unchanged: SDS-3701, for both risk assessment and monitoring.

2.7.4 Summary of residue trials in plants and identification of critical GAP

Tomato

Chlorothalonil is proposed for use on tomato in NEU and SEU according to the following GAP:
1x 1000 g/ha, PHI 3 days. In total, 8 trials in NEU and 8 trials in SEU have been submitted. All trials have been conducted according to the cGAP. Sufficient acceptable supervised residue trials are available.

Barley

Chlorothalonil is proposed for use on barley in NEU and SEU according to the following GAP:
2x 750 g/ha, interval 14 days, BBCH 30-59 (no PHI). All trial are considered acceptable. In most trials, the second application took place at the exact growth stage of the cGAP (BBCH 59). In some trials, the second application took place at a somewhat later growth stage than the growth stage of the cGAP applied for. Therefore, these trials could be considered more critical. However, the formation of the edible part for cereals starts from stage BBCH 51 onwards. Furthermore, a maximum of 25% deviation of the growth stage is allowed, but this rule is difficult to apply on growth stages. Since the PHIs of the trials in which the second application was later than BBCH 59 are in the same range as the PHIs of the trials in which were the second application was exactly at BBCH 59, these trials are considered acceptable. In addition, the interval between the applications differs often significantly from the interval of the cGAP. However, probably the interval has only minimal influence on the residue values, since the pre-harvest interval is large in comparison to the interval between applications. Therefore, sufficient acceptable supervised residue trials are available to support the requested use on barley in both NEU and SEU.

Wheat

Chlorothalonil is proposed for use on wheat in NEU and SEU according to the following GAP:

2x 750 g/ha, interval 14 days, BBCH 30-69 (no PHI). All trials are acceptable regarding application rate and timing, except for trial F/CH14/WW07 in which the second application was at BBCH 62, which is not according to the cGAP. This trial could be considered less critical. However, the formation of the edible part for cereals starts from stage BBCH 51 onwards. Furthermore, a maximum of 25% deviation of the growth stage is allowed, but this rule is difficult to apply on growth stages. Since the PHI of this trial is in the same range as the PHI of the trials in which were the second application was exactly at BBCH 69, this trial is considered acceptable. Much longer intervals between applications have been used than the interval of the cGAP. However, it is expected that the interval has only minimal influence on the residue values as the pre-harvest interval is large in comparison to the interval between applications. Therefore, trials with an interval that deviates are considered acceptable. Furthermore, results from straw samples for trials from report S12-01272 and S12-01273 are not acceptable, since the period of storage is not covered by demonstrated storage stability. In total, for NEU 16 acceptable residue levels are available for grain and 6 residue levels for straw, while in SEU 16 acceptable residue levels are available for grain and 8 residue levels for straw. Sufficient supervised residue trials are available for the requested use on wheat.

Potato

Chlorothalonil is proposed for use on wheat in NEU and SEU according to the following GAP:

1x 750 g/ha, PHI 28 days. The proposed GAP is for one application; however, all the trials were conducted with three applications. Residues of both chlorothalonil and SDS-3701 were below the LOQ in tubers in all the trials, indicating that the number of applications did not impact on the residue levels at harvest. Since the overdosed trials still do not result in detectable residues, these trials are considered acceptable.

Therefore, in total 4 acceptable supervised residue trials are available in NEU and also 4 acceptable trial in SEU. Although generally a minimum of 8 trials are required in each region, the residues of both chlorothalonil and SDS-3701 were below the LOQ in all trials, therefore, a reduced data set of 4 trials for each region is acceptable.

2.7.5 Summary of feeding studies in poultry, ruminants, pigs and fish

Products from barley, wheat and potato may form part of the global livestock diet in the EU. Therefore, the median and maximum dietary burdens were calculated for the different groups of livestock. Since both chlorothalonil residues as well as SDS-3701 residues could be present in the feed at the same time, the combined residue has been calculated as input for the calculation. The results of the dietary burden calculation (see table 2.7.5-1) show that the trigger value of 0.004 mg/kg bw/d is exceeded for all groups of livestock, except for pigs.

Table 2.7.5-1: Calculation of livestock exposure for combined residues of chlorothalonil and SDS-3701, expressed as chlorothalonil

		Maximum dietary burden (mg/kg bw/d)	Median dietary burden (mg/kg bw/d)	Highest contributing commodity	Max dietary burden (mg/kg DM)	Intake >0.004 mg/kg bw/d

		Maximum dietary burden (mg/kg bw/d)	Median dietary burden (mg/kg bw/d)	Highest contributing commodity	Max dietary burden (mg/kg DM)	Intake >0.004 mg/kg bw/d
Ruminant	Beef cattle	0.059	0.017	Barley straw	2.46	Yes
	Dairy cattle	0.094	0.026	Barley straw	2.44	Yes
	Ram/Ewe	0.158	0.040	Barley straw	4.74	Yes
	Lamb	0.201	0.050	Barley straw	4.72	Yes
Pig/Swine	Breeding	0.003	0.003	Potato, process waste	0.14	No
	Finishing	0.003	0.003	Potato, culls	0.10	No
Poultry	Broiler	0.004	0.004	Potato, culls	0.05	No
	Layer	0.030	0.012	Barley straw	0.44	Yes
	Turkey	0.004	0.004	Potato, culls	0.06	Yes

Feeding studies with poultry would be required based on these calculations, however, no studies were submitted. Since the exposure according to the maximum dietary burden (highest exposure: 0.030 mg/kg bw/d) is 53 times lower than the dose level in the new metabolism study with chlorothalonil, residue levels in poultry commodities are expected to remain below the enforcement LOQ in eggs and tissues. Therefore, no hen feeding study is required. On the other hand, the hen metabolism study with SDS-3701 does show residues in liver (0.056 mg/kg TRR) already at the lowest dose rate of 0.011 mg/kg bw/d. However, in this metabolism study, only SDS-3701 has been dosed. SDS-3701 is besides chlorothalonil part of the exposure of 0.030 mg/kg bw/d (see also the estimated ratio's between chlorothalonil and SDS-3701 in the exposure to livestock, Volume 3, B.7, table B.7.4-7), and the residues of 0.056 mg/kg in liver are total residues (TRR). Therefore, SDS-3701 residues are expected to be below LOQ in poultry, and no hen feeding study is required.

A feeding study with ruminants is available from the original peer review. Four groups of lactating cows were dosed for 28 consecutive days with a 15:1 ratio of chlorothalonil: SDS-3701 at levels of 0.065, 0.13, 0.39, and 1.3 mg/kg bw/d for chlorothalonil, and 0.004, 0.009, 0.026, and 0.087 mg/kg bw/d for SDS-3701. In the dose groups of 0.065 and 0.13 mg/kg bw/d chlorothalonil respectively, the highest SDS-3701 residues were found in kidney (0.14 and 0.28 mg/kg); residue levels were much lower in fat (0.03 and 0.07 mg/kg), liver (0.03 and 0.04 mg/kg) and muscle (not detectable and 0.02 mg/kg). In these two dose groups, the SDS-3701 residue levels in milk were 0.03 and 0.08 mg/kg. Processing of the milk samples did not result in concentration of SDS-3701 in either of the fractions, skimmed milk and cream. The residue levels found in milk, tissues and organs of groups dosed at higher levels were approximately proportional to the administered dose.

Two additional feeding studies with ruminants have been conducted for the renewal of chlorothalonil. In the first study, beef cattle were dosed for 28 consecutive days with chlorothalonil in the feed at a concentration of 0.1, 1.5 or 12.7 mg chlorothalonil/kg bw/day. Residues of SDS-3701 were found in all tissues for all dose levels with the exception of muscle and fat samples from the lowest dose level. Highest residues of SDS-3701 were found in liver and kidney; ranging from 0.008 to 1.04 mg/kg and

0.024 to 1.51 mg/kg, respectively, depending on the dose level. Residues of SDS-3701 showed a broadly linear relationship to dosing level in animal tissues. Residues of SDS-3701 decreased after a 14 day depuration period, although they were still significant.

In the second study, dairy cattle were dosed for 28 consecutive days with chlorothalonil in the feed at a concentration of 0.1, 1.5 or 12.7 mg chlorothalonil/kg bw/day. Maximum residues of SDS-3701 found in milk for the low, medium and high dose levels were 1.2, 150 and 231 µg/L, respectively. Maximum residues of SDS-3701 found in cream for the low, medium and high dose levels were 17.5, 247 and 336 µg/L, respectively. For the highest dose level, residues of SDS-3701 in whole milk decreased after a 14 day depuration period, although they were still significant. Residues in cream increased during the depuration period.

Based on the separate dietary burden calculations (e.g. only chlorothalonil and only SDS-3701), ratio's between chlorothalonil and SDS-3701 could be calculated (see Volume 3, B.7, table B.7.4-7). For ruminants, a range of ratio's from 4.3:1 to 8.8:1 (=chlorothalonil: SDS-3701) can be observed. Another ratio can be determined based on the median of the ratio's of the selected residue values for both grain and straw in the supervised residue trials (see Volume 3, B.7.4). The median ratio from these trials is 5.3:1 (barley trials) and 6.3:1 (wheat trials). Importantly, when residues were <LOQ for both chlorothalonil and SDS-3701, then no ratio has been calculated. Therefore, feeding study from the original peer review with the ratio of 15:1 is not fully reflecting the estimated ratio's.

The two additional feeding studies, conducted for the renewal, can be taken together to have one feeding study, since they are complementary to each other and the same dose is being used in these two studies. However, only chlorothalonil has been administered in these studies and no administration of SDS-3701.

Both feeding studies (i.e. the study from the original peer review and the combined new studies from the renewal) have been considered in the 'OECD animal intake & feeding calculations'-excel sheet (the combined residues exposure of chlorothalonil and SDS-3701 has been used as input). The dosing in the old study from the original peer review has been calculated as the sum of chlorothalonil and SDS-3701, expressed as chlorothalonil, since only one value is possible as input in the excel sheet. The dosing of the 'new study' is the closest to the maximum dietary burden for dairy cattle, i.e. the lowest feeding level is at 1.7 N for beef cattle and 1.1 N for dairy cattle, while the dosing of the 'old feeding study' is the closest to the maximum dietary burden for beef cattle, since the lowest feeding level is at 1.2 N for beef cattle and 0.7 N for dairy cattle.

Subsequently, the results of both sheets are compared. Based on the feeding study from the original peer review, higher MRLs would be calculated. This could be due to the fact that a mixture of chlorothalonil and SDS-3701 has been fed to the animals instead of dosing with only parent in the new feeding study. As a worst-case, the results of the old feeding study could be used for MRL setting. Furthermore, both studies show the highest residues in kidney.

2.7.6 Summary of effects on processing

For the renewal of chlorothalonil, a study investigating the nature of chlorothalonil under conditions simulating representative hydrolytic conditions for pasteurization (20 minutes at 90°C, pH 4), boiling/brewing/baking (60 minutes at 100°C, pH 5) and sterilization (20 minutes at 120°C, pH 6).

Chlorothalonil was stable under conditions simulating pasteurisation, but showed increased degradation under conditions simulating baking/brewing/boiling and sterilisation. Degradation products under conditions simulating brewing/boiling/baking and sterilisation, respectively, were SDS-3701 (19% and 59% AR) and SDS-19221 (3.4% and 15% AR). These studies demonstrate that the contribution of SDS-3701 to the total residue may increase in plant commodities after processing and confirm that the residue definitions derived for primary crops should be applied to the processed commodities as well.

Studies investigating the magnitude of residues in processed commodities of many crops were reported in the framework of the original peer review. However, reliability of these studies is questionable. Furthermore, additional processing studies were submitted for the sake of the renewal of chlorothalonil. An overview of all available processing studies is presented in table 2.7.6-1.

There were only a few processing studies in which SDS-19221 was determined. Furthermore, in all studies (B.7.5.3.18, B.7.5.3.19, B.7.5.3.21 and B.7.5.3.25), SDS-19221 levels were always below LOQ in all products.

Table 2.7.6-1: Overview of the available processing studies

Processed commodity	**Chlorothalonil**		**SDS-3701**		**Reference**
	Individual PF	**Median PF**	**Individual PF**	**Median PF**	
Beans, blanched	<0.012; <0.013	<0.013#	-	-	B.7.5.3.3#
Beans, canned	<0.012	<0.012#	-	-	B.7.5.3.3#
Cherries, canned	0.01	0.01#	-	-	B.7.5.3.4#
Peach, puree, canned	<0.0008	<0.0008#	-	-	B.7.5.3.5#
Grapes, dried (raisins)	0.45	0.45#	0.67	0.67#	B.7.5.3.6#
Grapes, wet pomace	1.62	1.62#	1.0	1.0#	B.7.5.3.6#
Grapes, dry pomace	1.31	1.31#	4.0	4.0#	B.7.5.3.6#
Grapes, fresh juice	0.23	0.23#	<0.33	<0.33#	B.7.5.3.6#
Apple, sauce	0.004	0.004#	-	-	B.7.5.3.7#
Apple, wet pomace	2.9; >4.0	3.5#	-	-	B.7.5.3.7#
Apple, dry pomace	10.1; >19.0	14.6#	-	-	B.7.5.3.7#
Apple, juice (canned)	0.02	0.02#	-	-	B.7.5.3.7#
Apple, hammer milled	0.94; >3.0	2.0#	-	-	B.7.5.3.7#
Apple, cider	0.66	0.66#	-	-	B.7.5.3.7#
Tomato, pomace	0.81; 0.89	0.85#	-	-	B.7.5.3.9#
Tomato, juice	0.008; 0.09; 0.10; 0.11; 0.13; 0.17	0.11	3x 1.0; 1.5	1.0	B.7.5.3.9#; B.7.5.3.18
Tomato, condensate	<0.00006; <0.0001	<0.00008#	-	-	B.7.5.3.9#
Tomato, paste	<0.004; 0.004	0.004#	-	-	B.7.5.3.9#
Tomato, puree	4x <0.001	<0.001	5.5; 6.0; 6.5; 7.5	6.3	B.7.5.3.18
Tomato, canned	4x <0.001	<0.001	4x 1.0; 3x 2.0; 2.5	1.5	B.7.5.3.18
Cucumber, brined sliced pickle	0.29	0.29#	-	-	B.7.5.3.10#
Cucumber, cold canned pickles	0.08	0.08#	-	-	B.7.5.3.10#
Cucumber, cold canned juice	0.005	0.005#	-	-	B.7.5.3.10#
Cucumber, hot canned pickles	0.015	0.015#	-	-	B.7.5.3.10#
Cucumber, hot canned juice	<0.0004	<0.0004#	-	-	B.7.5.3.10#
Orange, chopped peel	<0.33	<0.33#	-	-	B.7.5.3.12#
Orange, peel frits	0.33	0.33#	-	-	B.7.5.3.12#

Processed commodity	Chlorothalonil		SDS-3701		Reference
	Individual PF	Median PF	Individual PF	Median PF	
Orange, finisher pulp	0.003; <0.33	0.17#	-	-	B.7.5.3.12#
Orange, juice	<0.003; <0.33	<0.17#	-	-	B.7.5.3.12#
Orange, peel liquor	<0.33	<0.33#	-	-	B.7.5.3.12#
Orange, molasses	<0.33	<0.33#	-	-	B.7.5.3.12#
Limes, chopped peel	0.08	0.08#	-	-	B.7.5.3.12#
Limes, peel frits	0.22	0.22#	-	-	B.7.5.3.12#
Limes, peel liquor	0.005	0.005#	-	-	B.7.5.3.12#
Limes, molasses	0.01	0.01#	-	-	B.7.5.3.12#
Limes, cold pressed oil	30.9	30.9#	-	-	B.7.5.3.12#
Grapefruit and lemon, cold pressed oil	>4.0	>4.0#	-	-	B.7.5.3.12#
Lemon, dried pulp and peel	>1.0	>1.0#	-	-	B.7.5.3.12#
Peanut, presscake (expeller)	0.5	0.5#	-	-	B.7.5.3.13#
Peanut, presscake (solv. ext.)	<0.5	<0.5#	-	-	B.7.5.3.13#
Peanut, crude oil (expeller)	<0.5	<0.5#	-	-	B.7.5.3.13#
Peanut, crude oil (solv. ext.)	0.5; >2.0	1.25#	-	-	B.7.5.3.13#
Peanut, refined oil	<0.5	<0.5#	-	-	B.7.5.3.13#
Peanut, soapstock	<0.5	<0.5#	-	-	B.7.5.3.13#
Plum, dry prunes	<0.2; <0.33; <1.0	0.51#	-	-	B.7.5.3.14#
Squash, peeled	<0.003	<0.003#	-	-	B.7.5.3.15#
Squash, finisher (partly cooked)	<0.003	<0.003#	-	-	B.7.5.3.15#
Soybean, kernels	<0.5	<0.5#	-	-	B.7.5.3.16#
Soybean, hulls	>3.0; 3.5	3.3#	-	-	B.7.5.3.16#
Soybean meal	<0.5	<0.5#	-	-	B.7.5.3.16#
Soybean, crude oil	1.5	1.5#	-	-	B.7.5.3.16#
Soybean, refined oil	<0.5	<0.5#	-	-	B.7.5.3.16#
Soybean, soapstock	<0.5	<0.5#	-	-	B.7.5.3.16#
Barley, beer	<0.03; 4x <0.01; 2x <0.04; 2x <0.05; <0.09	<0.03	4x <0.05; 0.08; 2x <0.09; <0.13; <0.4; <0.5	0.09	B.7.5.3.19; B.7.5.3.20; B.7.5.3.21
Barley, pot	<0.03; 0.12; 0.13; 0.18; 0.21; 0.24; 0.25; 2x 0.32; 0.36	0.23	0.06; 2x 0.10; 0.11; 0.25; 0.27; <0.4; 0.42; 0.45; <0.5	0.26	B.7.5.3.19; B.7.5.3.20; B.7.5.3.21
Barley, pearl	0.05; 0.11; 0.12; 0.17	0.12	<0.09; 0.13; 0.17; 0.18	0.15	B.7.5.3.20
Barley, flour	0.06; 2x 0.07; 0.08	0.07	0.27; 0.50; 0.58; 0.64	0.54	B.7.5.3.20
Barley, brewing malt	3x 0.02; 0.03; 0.06; <0.09	0.03	0.36; <0.4; 0.45; <0.5; 0.50; 0.75	0.48	B.7.5.3.20; B.7.5.3.21
Barley, brewer's yeast	4x <0.01	<0.01	<0.08; 2x <0.09; <0.13	<0.09	B.7.5.3.20
Wheat, flour	<0.08; 0.08; 0.25; 0.43; 3x <0.5; 2x 0.5; 0.71; 0.75; 4x <1.0; 1.25	0.5	2x <1.0; 1.5; 2x 2.0; 3.0	1.75	B.7.5.3.23; B.7.5.3.24; B.7.5.3.25
Wheat, bran	0.08; <0.25; 0.43; 0.50; 0.58; <1.0; 1.25; 2.0; 2.57; 3; 4; 4.25	1.13	<1.0; 2x 1.0; 3.0; 4.5; 6	2.0	B.7.5.3.23; B.7.5.3.24; B.7.5.3.25

Processed commodity	Chlorothalonil		SDS-3701		Reference
	Individual PF	Median PF	Individual PF	Median PF	
Wheat, wholemeal bread	<0.08; <0.14; 2x <0.25; 2x <0.5; <1.0; 2.0	<0.38	<1.0; 2x 1.0	1.0	B.7.5.3.23; B.7.5.3.24; B.7.5.3.25
Wheat, germs	0.08; <0.25; 0.57; 2x <1.0; 1.25	0.79	<1.0; 1.0; 3.0	1.0	B.7.5.3.24; B.7.5.3.25
Wheat, dried starch	<0.08; <0.14; 2x <0.25	<0.20	<0.5; 2x <1.0	<1.0	B.7.5.3.24
Wheat, dried gluten	<0.08; <0.14; 2x <0.25	<0.20	<0.5; 2x <1.0	<1.0	B.7.5.3.24
Wheat, gluten feed meal	<0.08; <0.14; 2x <0.25	<0.20	<0.5; 2x <1.0	<1.0	B.7.5.3.24

[#]Studies from the original DAR, in which storage stability in the (processed) samples was not assessed. Furthermore, SDS-3701 has often been measured in these studies, but no transfer factors have been calculated. In addition, SDS-46851 has sometimes been measured, but no transfer factors were calculated. The reliability of these studies is therefore questionable.

2.7.7 Summary of residues in rotational crops

During the initial peer review, a confined rotational crop study was conducted using [phenyl-U-^{14}C]-chlorothalonil to address the potential uptake and metabolism of chlorothalonil residues into succeeding crops. Two additional confined crop rotation studies have been submitted for the renewal of chlorothalonil.

In the confined study from the initial peer review, the major identified metabolite was SDS-46851 (partly present in a conjugated form, almost 25 % of the total soil residues) which accounted for up to 2 mg/kg in lettuce at 30 DAT and 0.4 mg/kg at 88 DAT, up to 0.63 and 1.1 mg/kg in carrot roots and tops respectively, as well as 16.5 mg/kg and 33.1 mg/kg in wheat grain and straw, respectively. The parent compound accounted for 11 % and 5 % of the TRR in the soil at the relevant treatment days (30 and 88 DAT). Other soil metabolites (including SDS-3701) were also identified, but accounted for less than 10 % of the total soil residue. Amounts of SDS-3701 were identified at <0.1 mg/kg lettuce, <0.05 mg/kg carrot root, 6.3 mg/kg wheat straw and <0.5 mg/kg wheat grain. SDS-3701 was mainly present in conjugated form. The parent compound chlorothalonil was not detected in any plant part.

In the first confined rotational crop study for the renewal, [phenyl-U-^{14}C]-chlorothalonil was applied at 7.5 kg a.s/ha to bare soil prior to sowing of a representative cereal (spring wheat), leafy vegetable (lettuce) and root vegetable (carrot), at each rotational interval of 30, 120 and 365 days after application (DAT). The highest TRR was observed in 30 and 120 DAT mature lettuces (at both DATs 0.24 mg/kg), 120 DAT carrot leaves (1.52 mg/kg), carrot roots (0.43 mg/kg) and wheat straw (25 mg/kg), and 365 DAT wheat forage (1.4 mg/kg) and wheat grain (2.2 mg/kg). In general, the TRR tended to remain at similar levels across all plant-back intervals. The majority of the radioactive residues were extractable, accounting for 65 to 95% TRR. In all crops the majority of the radioactive residue was assigned to the metabolites SDS-46851 and R417888. These metabolites co-eluted on the TLC systems, however, further analysis indicated that the majority of the residues was due to metabolite SDS-46851. Up to 40% TRR was assigned as conjugated material. Enzyme hydrolysis of the extracts released radioactivity indicating that the conjugated material was made up of glucosyl conjugates of SDS-47525, SDS-19221 and “compound C15”. Other metabolites identified, included R611553, SDS-3701 and R613636, and represented minor percentages of the TRR. SDS-47525 accounted for up to 10% TRR in grain.

In the second confined rotational crop study, [phenyl-U-^{14}C]-chlorothalonil was applied as a single spray application at 1 kg as/ha to the bare soil. The soil was aged for 30 days and representative crops of cereals (barley), leafy vegetable (spinach) and root vegetable (radish) were sown. In spinach leaves, the TRR was 0.067, 0.031 and 0.039 mg/kg for the immature (emergence), immature (pre-harvest) and mature crop samples, respectively. The corresponding values for radish leaves were 0.014, 0.019 and 0.026 mg/kg. For radish roots, the TRR values were 0.022, 0.019 and 0.021 mg/kg. In barley forage, the TRR for immature (emergence) and forage (immature plant) samples were 0.018 and 0.019 mg/kg, respectively. The barley harvested at maturity was separated into straw, chaff and grains. The residues in these samples were 0.120, 0.059 and 0.012 mg/kg respectively. Parent chlorothalonil was detected only in the radish root samples, and at very low levels (0.001 mg/kg). The major identified metabolite was SDS-46851, which represented 13% TRR (0.009 mg/kg), 19% TRR (0.006 mg/kg) and 14% TRR (0.006 mg/kg) in immature (emergence), immature (pre-harvest) and mature spinach respectively. SDS-46851 was detected in all barley samples with the highest level found in mature straw, representing 25% TRR (0.030 mg/kg). In the radish root SDS-46851 accounted for 11.5% TRR (0.003 mg/kg) and 8.3% TRR (0.002 mg/kg) in the immature (emergence) roots and at maturity, respectively. The metabolite SDS-3701 was also identified in all spinach and radish root samples, and the mature barley samples, however at levels less than 0.01 mg/kg.

In general, the TRR remained at similar levels across all plant-back intervals. Parent chlorothalonil is a minor residue (not detected) in rotational crops. Chlorothalonil is metabolised in soil initially to SDS-19221 and SDS-3701 and then to other multiple components which are available for uptake by crops. SDS-46851 and R417888 were significant metabolites in all crops. These metabolites are known soil metabolites with long DT50 values. SDS-3701 was present at low levels. The metabolism of chlorothalonil in rotational crops is similar to that in primary crops, although levels of SDS-46851 were higher in rotational crops metabolism studies.

During the initial peer review, also field studies were conducted in the USA to measure levels of chlorothalonil residues in succeeding or rotated crops following an application to the primary crop. An additional field crop rotation study has been conducted for the renewal of chlorothalonil.
For the peer review, in three studies, the active substance was applied 8 times at an application rate of 2.5 kg a.s./ha on a bare soil (7 day interval between applications). The plant back intervals (PBI) investigated for wheat, carrots, snap beans and spinach were 14, 30, 60, 90 and 372 days after the last application. Mature crops were analysed for the TRR. In the first study, no residues of parent were identified in the rotational crops. The major residue in rotational crops was metabolite SDS-46851 which in all crops at all rotation intervals accounted for >0.1 mg/kg (except at lower levels in samples at 1 year rotation interval). The highest SDS-46851 residues were detected in wheat straw (10.35 mg/kg at 60 d PBI). Metabolite SDS-3701 was the main soil metabolite and was also identified in rotational crop samples. In spinach SDS-3701 residues ranged from 0.02 mg/kg (14 d PBI) to 0.19 mg/kg (90 d PBI). No SDS-3701 residues above the LOQ of 0.01 mg/kg were identified in snap beans and wheat grain at all rotation intervals. In carrot roots and tops and in wheat straw the residues of SDS-3701 did not account for more than 0.04 mg/kg. In the second study, no parent compound was

identified in the rotational crops. Metabolite SDS-3701 was the major residue identified in spinach and wheat straw samples, accounting for a maximum of 0.04 mg/kg (60 d PBI) and 0.02 mg/kg (372 d PBI), respectively. SDS-46851 was the major residue compound in snap beans (max 0.74 mg/kg at 60 d PBI), carrot roots (max 0.02 mg/kg for all PBI) and carrot tops (max 0.04 mg/kg at 30 d PBI). No residues were detected in wheat grain in the only analysed sample (372 d PBI). In the third study, the parent compound was not detected in the crop samples. SDS-46851 was the major residue identified in wheat grain (max 0.06 mg/kg at 372 d PBI) and straw (0.37 mg/kg at 372 d PBI) and in snap beans (max 0.03 mg/kg). SDS-3701 was the major residue in spinach (max 0.05 mg/kg at 60 d PBI).

Another field study is available from the peer review, and was performed by applying the active substance on a wide range of primary crops (potatoes, peanuts, cucumbers, tomatoes, potatoes, broccoli, soybeans) at application rates ranging from 1.3 to 2.6 kg a.s./ha with a number of applications ranging from 3 to 11. After the harvest of primary crops, rotational crops were planted at various plant back intervals. With soybean being the primary crop (treated with chlorothalonil 3 x 1.7 kg a.s./ha), results indicated that in rice the residues of parent and its metabolites SDS-3701 and SDS-46851 were below the LOQ. With peanuts being the primary crop (treated with chlorothalonil 6 x 1.3 kg a.s./ha), results indicated that parent chlorothalonil accounted for a maximum of 0.03 mg/kg in sorghum (392 d PBI) and 0.01 mg/kg in collards (286 d PBI). Residues of metabolites SDS-3701 and SDS-46851 were below the LOQ of 0.01 mg/kg and 0.03 mg/kg respectively, in cotton seed, corn, sorghum, wheat grain and collards. Generally, data after treatment of the remaining primary crops indicated that the major residue in rotational crops was metabolite SDS-46851. Metabolite SDS-3701 was the highest in pea fodder (0.07 mg/kg at 351 d PBI), but in other crops it was at or below 0.04 mg/kg. Rotational crops did not contain residues of parent chlorothalonil at levels exceeding 0.03 mg/kg, except in peanut vines (0.22 mg/kg at 376 d PBI), pea fodder (0.06 mg/kg at 351 d PBI) and bean hay (0.09 mg/kg at 374 d PBI).

The additional field rotational crop study has been conducted in Germany and the UK. Chlorothalonil was applied at a rate of 2 kg as/ha to bare soil. At each rotational interval of 30, 60 and 365 days after application (DAT), a representative cereal (spring wheat or barley), leafy vegetable (spinach) and root vegetable (carrot) were sown into the soil. At all plant-back intervals no residues of chlorothalonil or SDS-3701 were found at or above the LOQ (0.01 mg/kg) in any of the treated samples. It should be noted that storage stability was not fully covered for chlorothalonil and SDS-3701 in this study. Residues of SDS-46851 were found in samples taken after the 30 and 60 day plant-back intervals (PBI). For spinach these ranged from 0.02 – 0.06 mg/kg at the 30 day PBI and from 0.01-0.03 mg/kg for the 60 day PBI. In cereals residues of SDS-46851 in immature plant, grain and straw were in the range 0.08 – 0.16 mg/kg, 0.01 – 0.11 mg/kg and 0.09 – 0.29 mg/kg respectively for the 30 day PBI. Residues in cereals for the 60 day PBI were 0.11 mg/kg, 0.02 – 0.09 mg/kg and 0.08 – 0.25 mg/kg in immature plant, grain and straw respectively. For carrots residues in roots were in the range of <0.01 – 0.01 mg/kg for the 30 day PBI and were <LOQ for the 60 day PBI. Residues in carrot leaves were in the range of <0.01 – 0.04 mg/kg and <0.01 – 0.02 mg/kg for the 30 and 60 day PBIs respectively. No residues of SDS-46851 were found at or above the LOQ in any of the samples from the 365 day plant-back interval.

The results of the field studies confirm the results of the confined study where the major residue in rotational crops being metabolite SDS-46851 and only small amounts of SDS-3701 detected. In most cases, parent chlorothalonil residues were below the LOQ. Metabolite SDS-46851 was shown to be toxicology less relevant compared to parent chlorothalonil. A specific residue definition for rotational crops is therefore not deemed necessary (see 2.7.3).

2.7.8 Summary of other studies

Not required.

2.7.9 Estimation of the potential and actual exposure through diet and other sources

Chlorothalonil

The dietary exposure for consumers was estimated using the toxicological endpoints from 2.6.11 and 2.6.12, the proposed MRLs for the representative uses (see table 2.7.10-1) and EFSA PRIMo rev 2.

The TMDI is maximally 32.7% for WHO Cluster diet B. It is concluded that no chronic risk has to be expected for any of the European consumer groups (see table 2.7.9-1).

Also a calculation of the International Estimated Short Term Intake (IESTI) has been performed. Only the crops of the representative use of the current RAR are being considered. The IESTI for tomatoes is maximally 14.5% of the ARfD (Belgium, children), and for the other representative crops the IESTI is lower (see table 2.7.9-2).

SDS-3701

The dietary exposure for consumers was estimated using the toxicological endpoints from 2.6.11 and 2.6.12, the proposed MRLs for the representative uses (see table 2.7.10-2), the proposed MRL for fat from sheep, the existing MRLs for the other animal commodities, and EFSA PRIMo rev 2.

The TMDI is maximally 44.4% for French toddlers. It is concluded that no chronic risk has to be expected for any of the European consumer groups (see table 2.7.9-3).

The IESTI has been calculated as well, only for the crops of the representative use of the renewal of chlorothalonil. The IESTI is maximally 10.3% of the ARfD for potatoes. The highest IESTI is for milk and milk products for UK infants (41.4% of the ARfD) (see table 2.7.9-4).

It is concluded that no chronic or acute risk has to be expected for European consumers upon consumption of the crops treated with chlorothalonil according to the representative uses supported for the renewal.

Table 2.7.9-1 Report of chronic dietary consumer intake assessment to chlorothalonil for the uses supported for renewal of the approval

Chlorothalonil			
Status of the active substance:		Code no.	
LOQ (mg/kg bw):		proposed LOQ:	
Toxicological end points			
ADI (mg/kg bw/day):	**0.015**	ARfD (mg/kg bw):	**0.6**
Source of ADI:		Source of ARfD:	
Year of evaluation:		Year of evaluation:	

Prepare workbook for refined calculations

Undo refined calculations

The risk assessment has been performed on the basis of the MRLs collected from Member States in April 2006. For each pesticide/commodity the highest national MRL was identified (proposed temporary MRL = pTMRL).
The pTMRLs have been submitted to EFSA in September 2006.

Chronic risk assessment

	TMDI (range) in % of ADI minimum - maximum
	2 33
No of diets exceeding ADI:	---

Highest calculated TMDI values in % of ADI	MS Diet	Highest contributor to MS diet (in % of ADI)	Commodity / group of commodities	2nd contributor to MS diet (in % of ADI)	Commodity / group of commodities	3rd contributor to MS diet (in % of ADI)	Commodity / group of commodities	pTMRLs at LOQ (in % of ADI)
32.7	WHO Cluster diet B	30.8	Tomatoes	1.1	Wheat	0.6	Barley	
15.2	IT kids/toddler	14.3	Tomatoes	0.9	Wheat	0.1	Potatoes	
12.3	WHO regional European diet	11.0	Tomatoes	0.7	Barley	0.4	Wheat	
12.2	IT adult	11.6	Tomatoes	0.6	Wheat	0.0	Potatoes	
11.7	WHO cluster diet D	10.1	Tomatoes	0.9	Wheat	0.4	Barley	
10.5	ES child	9.8	Tomatoes	0.6	Wheat	0.1	Potatoes	
10.4	DE child	9.7	Tomatoes	0.5	Wheat	0.2	Potatoes	
9.9	PT General population	9.0	Tomatoes	0.5	Wheat	0.4	Potatoes	
9.2	ES adult	7.8	Tomatoes	1.0	Barley	0.3	Wheat	
9.1	PL general population	8.8	Tomatoes	0.2	Potatoes		FRUIT (FRESH OR FROZEN)	
8.7	WHO Cluster diet F	6.8	Tomatoes	1.2	Barley	0.5	Wheat	
8.4	FR toddler	7.7	Tomatoes	0.3	Wheat	0.3	Potatoes	
8.4	SE general population 90th percentile	7.7	Tomatoes	0.4	Wheat	0.3	Potatoes	
7.7	WHO cluster diet E	5.3	Tomatoes	1.6	Barley	0.5	Wheat	
7.3	NL child	6.2	Tomatoes	0.6	Wheat	0.4	Potatoes	
7.0	IE adult	4.0	Tomatoes	2.5	Barley	0.3	Wheat	
6.7	UK Toddler	5.9	Tomatoes	0.5	Wheat	0.2	Potatoes	
6.7	LT adult	6.2	Tomatoes	0.2	Potatoes	0.1	Wheat	
6.6	UK vegetarian	6.2	Tomatoes	0.3	Wheat	0.1	Potatoes	
6.2	DK child	5.3	Tomatoes	0.7	Wheat	0.2	Potatoes	
5.5	NL general	4.3	Tomatoes	0.7	Barley	0.3	Wheat	
4.9	FR all population	4.3	Tomatoes	0.4	Wheat	0.1	Potatoes	
4.7	UK Adult	4.4	Tomatoes	0.2	Wheat	0.1	Potatoes	
4.5	FI adult	4.3	Tomatoes	0.1	Wheat	0.1	Potatoes	
4.5	DK adult	4.1	Tomatoes	0.3	Wheat	0.1	Potatoes	
4.2	UK Infant	3.7	Tomatoes	0.3	Wheat	0.2	Potatoes	
1.9	FR infant	1.5	Tomatoes	0.3	Potatoes	0.1	Wheat	

Conclusion:
The estimated Theoretical Maximum Daily Intakes (TMDI), based on pTMRLs were below the ADI.
A long-term intake of residues of Chlorothalonil is unlikely to present a public health concern.

Table 2.7.9-2 Report of acute dietary consumer intake assessment to chlorothalonil for the uses supported for renewal of the approval

	Acute risk assessment /children						Acute risk assessment / adults / general population					
	The acute risk assessment is based on the ARfD.											
	For each commodity the calculation is based on the highest reported MS consumption per kg bw and the corresponding unit weight from the MS with the critical consumption. If no data on the unit weight was available from that MS an average European unit weight was used for the IESTI calculation.											
	In the **IESTI 1** calculation, the variability factors were 10, 7 or 5 (according to JMPR manual 2002), for lettuce a variability factor of 5 was used. In the **IESTI 2** calculations, the variability factors of 10 and 7 were replaced by 5. For lettuce the calculation was performed with a variabilty factor of 3.											
	Threshold MRL is the calculated residue level which would leads to an exposure equivalent to 100 % of the ARfD.											
Unprocessed commodities	**No of commodities for which ARfD/ADI is exceeded (IESTI 1):**		---	**No of commodities for which ARfD/ADI is exceeded (IESTI 2):**		---	**No of commodities for which ARfD/ADI is exceeded (IESTI 1):**		---	**No of commodities for which ARfD/ADI is exceeded (IESTI 2):**		---
	IESTI 1	***)**	****)**	**IESTI 2**	***)**	****)**	**IESTI 1**	***)**	****)**	**IESTI 2**	***)**	**)
	Highest % of ARfD/ADI	Commodities	pTMRL/ threshold MRL (mg/kg)	Highest % of ARfD/ADI	Commodities	pTMRL/ threshold MRL (mg/kg)	Highest % of ARfD/ADI	Commodities	pTMRL/ threshold MRL (mg/kg)	Highest % of ARfD/ADI	Commodities	pTMRL/ threshold MRL (mg/kg)
	14.5	Tomatoes	1.5 / -	10.5	Tomatoes	1.5 / -	3.8	Tomatoes	1.5 / -	3.1	Tomatoes	1.5 / -
	0.3	Potatoes	0.01 / -	0.2	Potatoes	0.01 / -	0.4	Barley	0.3 / -	0.4	Barley	0.3 / -
	0.1	Barley	0.3 / -	0.1	Barley	0.3 / -	0.0	Potatoes	0.01 / -	0.0	Potatoes	0.01 / -
	0.0	Wheat	0.02 / -	0.0	Wheat	0.02 / -	0.0	Wheat	0.02 / -	0.0	Wheat	0.02 / -
	No of critical MRLs (IESTI 1)			---			**No of critical MRLs (IESTI 2)**			---		

Table 2.7.9-3 Report of chronic dietary consumer intake assessment to SDS-3701 for the uses supported for renewal of the approval

SDS-3701			
Status of the active substance:		Code no.	
LOQ (mg/kg bw):		proposed LOQ:	
Toxicological end points			
ADI (mg/kg bw/day):	**0.01**	ARfD (mg/kg bw):	**0.03**
Source of ADI:		Source of ARfD:	
Year of evaluation:		Year of evaluation:	

Prepare workbook for refined calculations

Undo refined calculations

The risk assessment has been performed on the basis of the MRLs collected from Member States in April 2006. For each pesticide/commodity the highest national MRL was identified (proposed temporary MRL = pTMRL).
The pTMRLs have been submitted to EFSA in September 2006.

Chronic risk assessment

TMDI (range) in % of ADI minimum - maximum	
1	44
No of diets exceeding ADI:	---

Highest calculated TMDI values in % of ADI	MS Diet	Highest contributor to MS diet (in % of ADI)	Commodity / group of commodities	2nd contributor to MS diet (in % of ADI)	Commodity / group of commodities	3rd contributor to MS diet (in % of ADI)	Commodity / group of commodities	pTMRLs at LOQ (in % of ADI)
44.4	FR toddler	39.6	Milk and cream,	2.0	Bovine: Meat	1.0	Potatoes	
40.3	UK Infant	38.7	Milk and cream,	0.7	Potatoes	0.5	Wheat	
34.3	NL child	29.3	Milk and cream,	1.8	Bovine: Meat	1.2	Potatoes	
28.0	FR infant	25.7	Milk and cream,	0.9	Bovine: Meat	0.8	Potatoes	
22.3	UK Toddler	20.7	Milk and cream,	0.8	Wheat	0.7	Potatoes	
17.2	ES child	12.5	Milk and cream,	2.1	Bovine: Meat	0.9	Wheat	
16.5	DE child	14.3	Milk and cream,	0.8	Wheat	0.5	Potatoes	
14.5	DK child	12.6	Milk and cream,	1.1	Wheat	0.5	Potatoes	
14.0	SE general population 90th percentile	12.4	Milk and cream,	0.8	Potatoes	0.6	Wheat	
10.1	WHO Cluster diet B	3.2	Milk and cream,	1.7	Wheat	1.2	Bovine: Meat	
10.0	WHO regional European diet	4.8	Milk and cream,	1.6	Bovine: Meat	0.8	Potatoes	
9.9	WHO cluster diet D	5.0	Milk and cream,	1.3	Wheat	0.9	Bovine: Meat	
9.2	NL general	6.6	Milk and cream,	1.1	Bovine: Meat	0.5	Potatoes	
8.3	WHO Cluster diet F	4.0	Milk and cream,	1.3	Bovine: Meat	0.7	Wheat	
7.8	ES adult	5.0	Milk and cream,	1.1	Bovine: Meat	0.5	Wheat	
7.6	WHO cluster diet E	3.0	Milk and cream,	1.1	Bovine: Meat	0.8	Wheat	
7.2	IE adult	2.8	Milk and cream,	0.7	Sheep: Edible offal	0.6	Bovine: Meat	
7.0	DK adult	5.4	Milk and cream,	0.8	Bovine: Meat	0.4	Wheat	
6.2	FI adult	5.7	Milk and cream,	0.2	Potatoes	0.2	Wheat	
5.7	LT adult	4.0	Milk and cream,	0.6	Potatoes	0.4	Bovine: Meat	
4.9	FR all population	2.7	Milk and cream,	0.8	Bovine: Meat	0.7	Wheat	
4.0	UK vegetarian	3.3	Milk and cream,	0.4	Wheat	0.3	Potatoes	
3.7	UK Adult	3.0	Milk and cream,	0.3	Wheat	0.3	Potatoes	
2.0	PT General population	1.1	Potatoes	0.8	Wheat	0.1	Tomatoes	
1.7	IT kids/toddler	1.3	Wheat	0.2	Potatoes	0.1	Tomatoes	
1.1	IT adult	0.8	Wheat	0.1	Potatoes	0.1	Tomatoes	
0.8	PL general population	0.7	Potatoes	0.1	Tomatoes		FRUIT (FRESH OR FROZEN)	

Conclusion:
The estimated Theoretical Maximum Daily Intakes (TMDI), based on pTMRLs were below the ADI.
A long-term intake of residues of SDS-3701 is unlikely to present a public health concern.

Table 2.7.9-4 Report of acute dietary consumer intake assessment to SDS-3701 for the uses supported for renewal of the approval

	Acute risk assessment /children						Acute risk assessment / adults / general population					
	The acute risk assessment is based on the ARfD.											
	For each commodity the calculation is based on the highest reported MS consumption per kg bw and the corresponding unit weight from the MS with the critical consumption. If no data on the unit weight was available from that MS an average European unit weight was used for the IESTI calculation.											
	In the **IESTI 1** calculation, the variability factors were 10, 7 or 5 (according to JMPR manual 2002), for lettuce a variability factor of 5 was used. In the **IESTI 2** calculations, the variability factors of 10 and 7 were replaced by 5. For lettuce the calculation was performed with a variabilty factor of 3.											
	Threshold MRL is the calculated residue level which would leads to an exposure equivalent to 100 % of the ARfD.											
Unprocessed commodities	**No of commodities for which ARfD/ADI is exceeded (IESTI 1):**		---	**No of commodities for which ARfD/ADI is exceeded (IESTI 2):**		---	**No of commodities for which ARfD/ADI is exceeded (IESTI 1):**		---	**No of commodities for which ARfD/ADI is exceeded (IESTI 2):**		---
	IESTI 1	***)**	****)**	**IESTI 2**	***)**	****)**	**IESTI 1**	***)**	****)**	**IESTI 2**	***)**	**)
	Highest % of ARfD/ADI	Commodities	pTMRL/ threshold MRL (mg/kg)	Highest % of ARfD/ADI	Commodities	pTMRL/ threshold MRL (mg/kg)	Highest % of ARfD/ADI	Commodities	pTMRL/ threshold MRL (mg/kg)	Highest % of ARfD/ADI	Commodities	pTMRL/ threshold MRL (mg/kg)
	41.4	Milk and milk	0.1 / -	41.4	Milk and milk	0.1 / -	6.9	Bovine: Edible offal	0.7 / -	6.9	Bovine: Edible offal	0.7 / -
	17.0	Bovine: Edible offal	0.7 / -	17.0	Bovine: Edible	0.7 / -	5.7	Milk and milk	0.1 / -	5.7	Milk and milk products: Cattle	0.1 / -
	10.3	Potatoes	0.02 / -	8.8	Bovine: Kidney	0.7 / -	4.0	Bovine: Kidney	0.7 / -	4.0	Bovine: Kidney	0.7 / -
	8.8	Bovine: Kidney	0.7 / -	8.1	Milk and milk	0.1 / -	3.0	Bovine: Meat	0.15 / -	3.0	Bovine: Meat	0.15 / -
	8.1	Milk and milk	0.1 / -	7.3	Potatoes	0.02 / -	2.4	Sheep: Meat	0.15 / -	2.4	Sheep: Meat	0.15 / -
	No of critical MRLs (IESTI 1)			---			**No of critical MRLs (IESTI 2)**			---		

2.7.10 Proposed MRLs and compliance with existing MRLs

Table 2.7.10-1: Overview of the proposed MRLs and compliance with existing MRLs for chlorothalonil

Commodity	Results from supervised residue trials (mg/kg)	STMR	HR	Pro-posed MRL	Existing MRL[1]	Remarks
Tomatoes	*NEU* 0.13; 0.15; 0.25; 0.26; 0.36; 0.44; 0.63; 0.83	0.31	0.83	1.5	6.0	Sufficient trial data are available. The proposed MRL is lower than the existing MRL.
	SEU 0.06; 0.12; 0.17; 0.36; 0.46; 2x 0.58; 0.59	0.41	0.59	1.5		
Barley, grain	*NEU* 6x <0.01; 2x 0.01; 2x 0.02; 2x 0.03; 4x 0.04	0.02	0.04	0.08	0.4	Sufficient trial data are available. The proposed MRL is lower than the existing MRL.
	SEU 13x <0.01; 0.02; 0.18; 0.19	<0.01	0.19	0.3		
Barley, straw	*NEU* 0.44; 0.45; 0.68; 0.72; 0.74; 1.0; 1.2; 1.3; 1.7; 2.0; 2.2; 2x 2.3; 2.8; 4.9; 5.7	1.5	5.7	n.a.	n.a.	
	SEU 2x 0.06; 2x 0.15; 0.20; 0.25; 0.30; 0.34; 0.43; 0.45; 0.48; 0.64; 0.66; 0.67; 1.8; 3.1	0.39	3.1	n.a.	n.a.	
Wheat, grain	*NEU* 15x <0.01; 0.01	<0.01	0.01	0.02	0.1	Sufficient trial data are available. NEU and SEU data sets are not significantly different according to the U-test. Therefore, the data sets are combined. The proposed MRL is lower than the existing MRL.
	SEU 14x <0.01; 0.01; 0.02	<0.01	0.02			
Wheat, straw	*NEU* 0.44; 0.77; 0.85; 2x 1.1; 1.9	0.98	1.9	n.a.	n.a.	
	SEU 0.07; 3x 0.08; 0.22; 0.33; 0.69; 2.1	0.15	2.1	n.a.	n.a.	
Potatoes	*NEU* 4x <0.01	<0.01	<0.01	0.01*	0.01*	Sufficient trial data are available. NEU and SEU data sets are not significantly different according to the U-test. Therefore, the data sets are combined. The calculated MRL is in line with the existing MRL.
	SEU 4x <0.01	<0.01	<0.01			

[1] Reg. (EU) 2016/67

Table 2.7.10-2: Overview of the proposed MRLs and compliance with existing MRLs for SDS-3701

Commodity	Results from supervised residue trials (mg/kg)	STMR	HR	Pro-posed MRL	Existing MRL[1]	Remarks
Tomatoes	*NEU* 8x <0.01	<0.01	<0.01	0.01*	-	Sufficient trial data are available. NEU and SEU data sets are not significantly different according to the U-test. Therefore, the data sets are combined.
	SEU 8x <0.01	<0.01	<0.01			
Barley, grain	*NEU* 8x <0.01; 8x <0.02	<0.02	<0.02	0.04	-	Sufficient trial data are available. NEU and SEU data sets are not significantly different according to the U-test. Therefore, the data sets are combined.
	SEU 7x <0.01; 0.01; 8x <0.02	0.02	<0.02			
Barley, straw	*NEU* <0.02; 0.02; 2x 0.03; 0.06; 0.07; 2x 0.09; 0.10; 0.11; 0.19; 0.23; 0.30; 0.38; 0.61; 1.1	0.10	1.1	n.a.	n.a.	
	SEU <0.01; 0.02; 2x 0.03; 2x 0.05; 2x 0.06; 0.07; 0.10; 0.11; 0.12; 2x 0.13; 0.19; 0.27	0.07	0.27	n.a.	n.a.	
Wheat, grain	*NEU* 8x <0.01; 8x <0.02	<0.01	<0.02	0.02	-	Sufficient trial data are available. NEU and SEU data sets are not significantly different according to the U-test. Therefore, the data sets are combined. An MRL of 0.02 mg/kg is proposed for wheat grain, and not 0.02* mg/kg, since the analytical method for enforcement is more sensitive (LOQ is 0.01 mg/kg) compared to the analytical method used in some of the residue trials.
	SEU 8x <0.01; 8x <0.02	<0.01	<0.02			
Wheat, straw	*NEU* 0.04; 0.06; 3x 0.07; 0.10	0.07	0.10	n.a.	n.a.	
	SEU 3x <0.02; 2x 0.03; 0.04; 0.08; 0.12	0.03	0.12	n.a.	n.a.	
Potatoes	*NEU* 4x <0.02	<0.02	<0.02	0.02*	-	Sufficient trial data are available. NEU and SEU data sets are not significantly different according to the U-test. Therefore, the data sets are combined.
	SEU 4x <0.02	<0.02	<0.02			

[1] Reg. (EU) 2016/67

All existing MRLs for animal commodities are sufficient for the representative uses of the renewal of chlorothalonil, except for the MRL for fat from sheep. The MRL of 0.1 mg/kg should be increased to 0.15 mg/kg.

2.7.11 Proposed import tolerance and compliance with existing import tolerances

Import tolerances are not proposed in the framework of the renewal of chlorothalonil.

2.8 Fate and behaviour in the environment

Assessment of criteria to be considered a POP (Persistent Organic Pollutant), PBT (Persistent, Bioaccumulative and Toxic) or vPvB (very persistent and very bioaccumulative) substance

Annex II, section 7 of Regulation 1107/2009 states that substances deemed to meet the POP, PBT or vPvB criteria cannot be approved. Also, if an active substance meets two out of three PBT criteria, it will be a 'Candidate for Substitution'. The potential for chlorothalonil to meet the criteria to be considered as a POP, PBT or vPvB substance is shown below.

POP (Persistent Organic Pollutant)

A POP is defined as a chemical which is extremely stable or persistent in the environment; will bioaccumulate in organisms or the food chain; is toxic to humans or animals and has potential to be transported in the environment over long distances far from the place of release. A substance that fulfils all three of the criteria below is a POP.

Criteria for Classification of a Compound as a POP

Criterion	Definition	Chlorothalonil Data	Criteria Met?
Persistence	$DT_{50\ water}$ > 2 months $DT_{50\ soil}$ > 6 months $DT_{50\ sediment}$ > 6 months	DT_{50} (water) – 10 days (longest aerobic dissipation DT_{50} from water-sediment study) DT_{50} (soil) – 19 days (longest non-normalised laboratory DT_{50}, SFO best fit) DT_{50} (sediment) – 9 days (longest aerobic whole system dissipation DT_{50} from water sediment study)	No
Bioaccumulation	BCF or BAF > 5000 or in absence log K_{ow} > 5 or evidence that the substance presents other reasons for concern, such as high bioaccumulation in other non-target species, high toxicity or ecotoxicity.	BCF < 100 Log P <3.0	No
Potential for Long-Range Transport (LRT)	Monitoring data showing that long range transport (LRT) may have occurred via air, water or migrating species or fate properties or modelling demonstration LRT or DT_{50} (air) > 2 days for a chemical migrating through the air.	DT_{50} (air) – 4.7 years	Yes

Chlorothalonil does not fulfil all of the criteria for classification as a POP.

PBT (Persistent, Bioaccumulative, Toxic)

A PBT is defined as a chemical which is extremely stable or persistent in the environment; will bioaccumulate in organisms or the food chain and is toxic to humans or animals. A substance that fulfils all three of the criteria below is a PBT.

Criteria for Classification of a Compound as a PBT

Criterion	Definition	Chlorothalonil Data	Criteria Met?
Persistence	The half-life in marine water is higher than 60days The half-life in fresh or estuarine water is higher than 40 days The half-life in marine sediment is higher than 180 days The half-life in fresh or estuarine water sediment is higher than 120 days, or The half-life in soil is higher than 120 days Assessment of persistency in the environment shall be based on available half-life data collected under appropriate conditions, which shall be described by the applicant.	No half-life in marine water or sediment available Longest DT_{50} in fresh water without suspended sediment – 6 days (aerobic mineralization study) Longest aerobic dissipation DT_{50} (water) - 10 days and (whole system) – 9 days (water sediment study) DT_{50} (soil) – 19 days (longest non-normalised laboratory DT_{50}, SFO best fit)	No
Bioaccumulation	BCF or BAF > 5000 or in absence log K_{ow} > 5 or evidence that the substance presents other reasons for concern, such as high bioaccumulation in other non-target species, high toxicity or ecotoxicity.	BCF < 100 Log P <3.0	No
Toxicity	The long-term no-observed effect concentration for marine or freshwater organisms is < 0.01 mg/L The substance is classificed as carcinogenic (category 1A or 1B), mutagenic (category 1A or 1B), or toxic for reproduction (category 1A, 1B or 2) pursuant to Regulation (EC) No 1272/2008. There is other evidence of chronic toxicity, as identified by the classifications STOT RE 1 or STOT RE 2 pursuant to Regulation (EC) No 1272/2008.	Mysid NOEC 0.00083 mg/L, Daphnia NOEC 0.0085 mg/L, fathead minnow NOEC 0.003 mg/L Chlorothalonil is classified as carcinogenic category 2 under CLP Regulation (EC) No 1272/2008, OJ L 353[1]. It is not classified as mutagenic or toxic for reproduction. No adverse effect has been observed in chronic toxicity tests.	Yes

[1] http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2008:353:0001:1355:EN:PDF

Chlorothalonil does not fulfil all of the criteria for classification as a PBT. It is not a candidate for substitution as it does not meet two of the PBT criteria.

vPvB (very Persistent, very Bioaccumulative)

A vPvB is defined as a chemical which is extremely stable or persistent in the environment and will bioaccumulate in organisms or the food chain. A substance that fulfils both of the criteria below is a vPvB.

Criteria for Classification of a Compound as a vPvB

Criterion	Definition	Chlorothalonil Data	Criteria Met?
Persistence	The half-life in marine, fresh or estuarine water is higher than 60days The half-life in marine, fresh or estuarine sediment is higher than 180 days, or The half-life in soil is higher than 180 days	No half-life in marine water or sediment available Longest DT_{50} in fresh water without suspended sediment – 6 days (aerobic mineralization study) Longest aerobic dissipation DT_{50} (water) - 10 days and (whole system) – 9 days (water sediment study) DT_{50} (soil) – 19 days (longest non-normalised laboratory DT_{50}, SFO best fit)	No
Bioaccumulation	BCF > 5000	BCF < 100 Log P <3.0	No

Chlorothalonil does not fulfil any of the criteria for classification as a vPvB substance.

2.8.1 Summary of fate and behaviour in soil

Route and rate of degradation

Aerobic

Laboratory

The route of chlorothalonil degradation in soil was evaluated during the original Annex I review SANCO/4343/2000 final (revised) 28 September 2006. Additional studies provided for the renewal are Duane (1995), McFadden (1999), Gibbings and Bramley (2000). This last study was conducted to examine the impact of chlorothalonil soil concentrations on route and rate of degradation and is important in understanding the fate of chlorothalonil in the environment. Finally the study of Green *et al* (2015) was submitted, which was conducted to address the identity of metabolites in the range of 5 -10% of applied radioactivity that had not been included in previous studies due to changes in data requirements.

A number of new metabolites have been identified in these studies or have been confirmed to occur at significant levels. However, the three previously identified degradation pathways for chlorothalonil of oxidative dechlorination, reductive dechlorination, and reaction with glutathione to form sulfonic acid

derivitives are still confirmed. No metabolites resulting from any other pathway have been observed in soil.

All reliable studies were subsequently subjected to kinetic evaluation according to FOCUS Degradation Kinetics (study Ford, 2015a).

The following aerobic degradation endpoints result from the (kinetic) evaluation of existing and new studies. The route of degradation is depicted in Figure 2.8.1-01.

Table 2.8.1-01: Summary of maximum soil DT50 values (not normalised) to be used for PECsoil calculation

Substance	**Maximum DT_{50} [d] (SFO kinetics unless specified otherwise)**	**Max. observed %**
Chlorothalonil	19 (lab)/ 28.4 (field)	-
R182281	609 (lab)	32.0
R417888	1000	15.2
R418503	1000	6.1
R419492	1000	12.4
R471811	1000	11.9
SYN507900	355 (DFOP)	5.8
R611965	1000	13.2
R611966	156	8.1
R611967	16.4	13.24
R611968	*416 (Not triggered)*	*6.5 (1x>5%, assessment not triggered)*
R613636	106	10.4

Table 2.8.1-02: Summary of modelling degradation in soil endpoints for chlorothalonil and its metabolites

Substance	**Geometric mean $DegT_{50}$ [d]**	**Arithmetic mean formation fraction (from)**		
Chlorothalonil	4.29[a]/2.90[b]	--		
R182281	143.9	0.186 (chlorothalonil)		
R417888	332	0.106 (chlorothalonil)		
R418503	30.8	0.042 (chlorothalonil)		
R419492	377	0.049 (chlorothalonil)	1.0 (R418503)	0.451 (R417888)
R471811	582	0.022 (chlorothalonil)	0.755 (R417888)	
SYN507900	180	- (1 by default)		
R611965	381	0.062 (chlorothalonil)	0.946 (R611966)	
R611966	75.2	0.079 (chlorothalonil)		
R611967	26.5	0.150 (chlorothalonil)		
R611968	55.1	0.067 (chlorothalonil) (1x>5%, assessment not triggered but modelled for completeness)		
R613636	33.0	0.091 (chlorothalonil)		
SYN548008 (M3) (lysimeter)	Tier 1: 1000 Tier 2: 377*	0.0292 [c]		
SYN548580 (M2) (lysimeter)	Tier 1: 1000 Tier 2: 180**	0.0292 [c]		
SYN548581 (M11) (lysimeter)	Tier 1: 1000 Tier 2: 33.0***	0.0292 [c]		
M7 (lysimeter)	Tier 1: 1000 Tier 2: 381****	0.0292 [c]		
M10 (lysimeter)	Tier 1: 1000 Tier 2: 55.1*****	0.0292 [c]		

a DT50 for calculation of parent PEC

b DT50 for calculation of metabolite PEC (all SFO fit)

c default values for DT50 and formation fraction based on the remainder of (1-all other metabolite fractions): 1-0.854 = 0.146, divided over 5 constituents yields 0.0292 for each metabolite

* no data; extrapolated from R419492

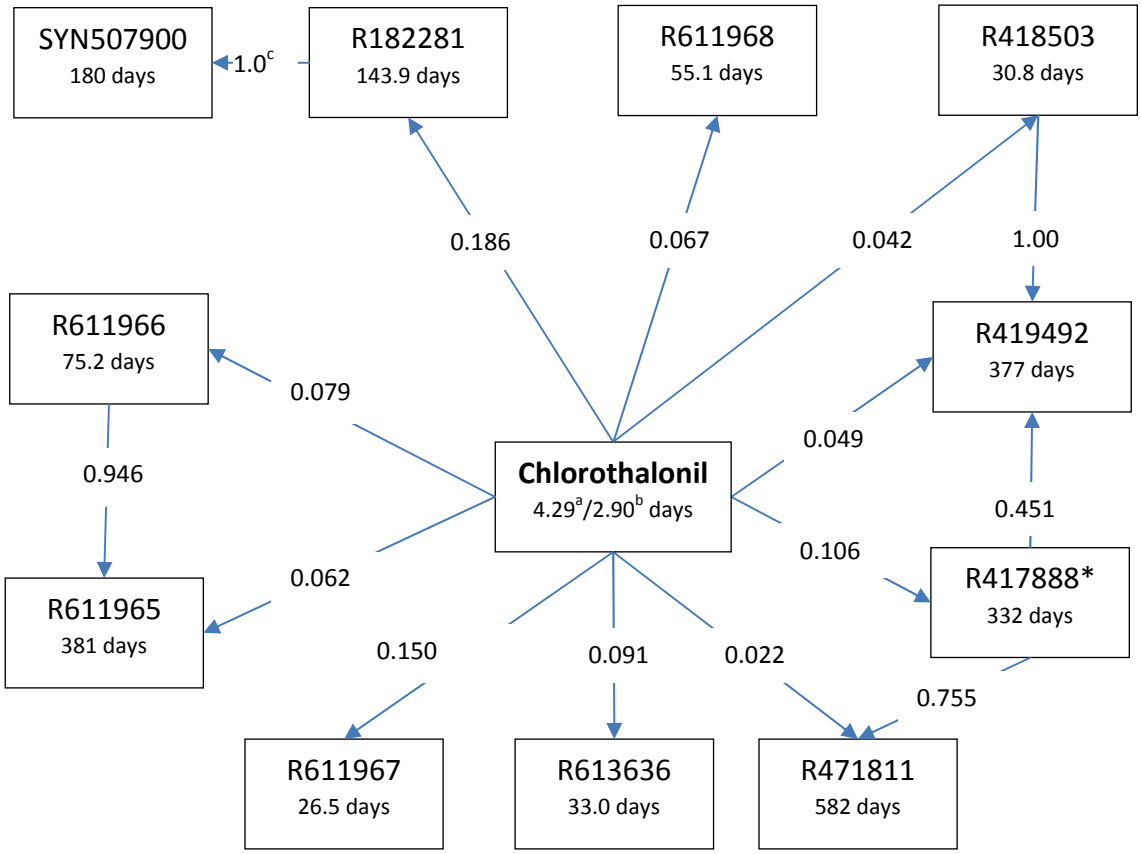
** no data; extrapolated from SYN507900

*** no data; extrapolated from R613636

**** no data; extrapolated from R611965

***** no data; extrapolated from R611968

Figure 2.8.1-01: Schematic representation of the chlorothalonil degradation pathway in soil as implemented for environmental models (not containing the lysimeter metabolites)



[a] DT_{50} for calculation of parent PEC
[b] DT_{50} for calculation of metabolite PEC
[c] No reliable modelled value available, conservatively set to 1.0.
* the pathways from R417888 yield a total formation fraction of more than 1. This is caused by conservative choices in the fitting of R419492 (see Ford 2015a, Volume 3 CA section B.8.1.1.2)

Field studies

The existing field studies were not taken forward for the renewal because they were dosed above the expected concentrations for the proposed uses. A new field study was submitted and kinetically evaluated. Only dissipation DT_{50} values (7.44 and 28.4 days) could be established and the maximum is used for PECsoil calculations.

Soil accumulation studies

Six new studies were submitted No accumulation of parent occurred. R182281 accumulated in several trials and did not always reach a plateau. R417888 did not accumulate.

Anaerobic

A new anaerobic soil metabolism study is presented in this dossier. Melville and Jewkes (2015) investigated the anaerobic route and rate of degradation of chlorothalonil at one rate (approximately

1 kg/ha) in four soils (silty clay, sandy clay loam, loam and loam/silt loam) under anaerobic conditions following an initial aerobic incubation for 2-4 days.

Acceptable data on the route and rate of degradation of [^{14}C]-chlorothalonil under anaerobic flooded conditions were obtained in 3 of the 4 soils giving persistence DT50 values of 3.7, 2.6 and 4.2 days (persistence DT90 values of 109, >1000 and 73.5 days), whilst DT50 values for modelling were 5.0, 8.9 and 22.1 days. A total of 7 degradates were detected at >5% AR in this study: R182281 (maximum 28.3% AR); R417888 (maximum 15.4% AR); R611966 (maximum 10.7% AR); SYN507900 (maximum 10.0% AR); R611965 (2 x >5% AR, maximum 7.8% AR); R471811 (single detection at >5% AR, maximum 5.3% AR); unknown metabolite tentatively identified as a monochlorinated sulfonic acid (Rf 0.54), maximum 7.4% AR (increasing at study end).

Photolysis

The submitted guideline compliant study shows that degradation of chlorothalonil occurred in both moist and dry irradiated and dark control soil layers. Degradation was fastest under moist irradiated conditions and the net photolysis degradation rates ($DegT_{50}$) were 124.8 and 40.3 days summer sunlight equivalent for dry and moist soil conditions, respectively.

The main degradation product observed was R182281 (SDS-3701) which reached a maximum of 4.5 and 3.8% of applied radioactivity after 15 days incubation in the dry irradiated and dry dark soil samples, respectively. R182281 reached a maximum of 7.0% AR after 5 days incubation in the moist irradiated samples and a maximum of 13.0% AR after 10 days in the moist dark samples. Other minor (<5% AR) radiolabelled components were present, but not identified.

Sorption

Batch sorption

Table 2.8.1-03 provides an overview of relevant endpoints for use in further assessment. For several metabolites sorption was very low and the dataset contains soils where sorption was negligible and could not be assessed quantitatively.For these soils, sorption has been set to 0 in combination with a 1/n value of 0.9.

Table 2.8.1-03: Summary of sorption endpoints for chlorothalonil and its metabolites

Substance	**Geometric mean $K_{(F)oc}$**	**Arithmetic mean 1/n**
Chlorothalonil	1288.4	0.90

R182281	395.3 (385.9 all data)	0.89 (0.94 all data)
R417888	8.34*	1.01
R418503	2.0*	0.87
R419492	0*	0.9
R471811	0*	0.9
SYN507900	15.74*	1.16
R611965	15.62*	0.87
R611966	234.7**	0.87**
R611967	234.7**	0.87**
R611968	15.74***	1.16***
R613636	234.7	0.87
SYN548008 (M3) (lysimeter)	Tier 1&2: 0	Tier 1: 1.0 Tier 2: 0.9
SYN548580 (M2) (lysimeter)	Tier 1: 0 Tier 2: 15.74***	Tier 1: 1.0 Tier 2: 1.16***
SYN548581 (M11) (lysimeter)	Tier 1: 0 Tier 2: 234.7**	Tier 1: 1.0 Tier 2: 0.87**
M7 (lysimeter)	Tier 1: 0 Tier 2: 7.1****	Tier 1: 1.0 Tier 2: 0.87****
M10 (lysimeter)	Tier 1: 0 Tier 2: 15.74***	Tier 1: 1.0 Tier 2: 1.16***

* since the data set contains K(F)oc values of 0 L/kg, no geometric mean could be calculated. Instead the arithmetic mean is used for further assessment
** no data; extrapolated from R613636
*** no data; extrapolated from SYN507900
**** no data; extrapolated from R611965/R613636

Column leaching

When considered relevant column leaching endpoints have been used in the overall derivation of sorption endpoints. For parent chlorothalonil the available column leaching studies were not used in the overall endpoint derivation since sufficient Freundlich values were available.

Field leaching

One new field leaching study has been conducted to investigate the subsurface drainage losses of chlorothalonil and two chlorothalonil metabolites, R417888 and R511965 at one location in Italy.

No residues of chlorothalonil were determined in the tile drainage samples analysed. The annual average concentration of the metabolite R417888 in drain water ranged from 1.8-3.1 µg/L and for R611965 from 0.02-0.10 µg/L.

Lysimeters

An existing radiolabelled lysimeter study (location Munster, Germany, 2 lysimeters, duration 3 years, start 1995) showed total amounts of radioactivity equivalents (annual average) of 31.76 and 25.56 µg/l for both lysimeters respectively in the first year and 4.94 and 4.86 µg/l in the second year. Maximum individual concentrations of a.i. equivalents were 78.96 and 59.09 µg/l for the two lysimeters respectively in the first year. No parent compound and none of the main metabolites available as reference substance

(SDS-3701; SDS-19221; SDS-47523; SDS-47524; SDS-47525; SDS-66882 and SDS-67042) were detected by radio HPLC, except for SDS-46851, detected in a selected sample (19-11-96) at 0.2 µg/l.
R417888 is the main metabolite leaching from a lysimeter in a maximum of 24% of radioactivity present in the leachate during the first year. Mean annual measured concentrations are 9.3 µg/l and 7.4 µg/l a.i. equivalent for the two lysimeters respectively. Based on the relative molar mass of 1.23, the averaged annual concentration amounts to 10.3 µg/l. Compound 12 (R419492; 4-amido-2,5-dichloro-6-cyanobenzene-1,3-disulfonic acid) was detected in the leachate as well in a concentration of 11% of the applied r.a.. Based on the relative molar mass of 1.4, the averaged annual concentration amounts to 4.4 µg/l. At least five other unknown (polar) metabolites are found in amounts >0.1 µg/l as chlorothalonil equivalents.

One new lysimeter study is presented (Borstel, Germany, duration 2 years, start 2005), investigating the degradation and leaching potential of chlorothalonil and its metabolites in two lysimeters. Average yearly concentrations of 36.6 and 33.7 µg parent equivalents/L were found in the leachates of lysimeter I and II, respectively, during the first year. The corresponding value for the second experimental year was 11 µg parent equivalents/L for both lysimeters.
No parent chlorothalonil was detected in the leachates. Thirteen metabolites were detected exceeding 0.1 µg parent equivalents/L as annual mean concentrations. Full characterisation was possible for 11 of the 13 metabolites, all of which belonged to three families of compounds, namely benzamide sulfonic acids, benzamide carboxylic acids and benzamides. Extensive analytical efforts were made to elucidate the nature of the remaining metabolites, M10 and M7. However the LC/MS analysis for metabolites M10 and M7 were inconclusive. No molecular ion or characteristic chlorine isotope pattern could be identified, and therefore no molecular weight or structural assignment for the radioactive fraction M10 and M7 was possible.
The 11 metabolites identified included R417888 (M12), R418503 (M13), R419492 (M8), R471811 (M4), SYN548008 (M3), SYN548580 (M2), SYN548581 (M11), R611965 (M5), R611968 (M9) and R613636 (M14). Mean annual concentrations of both replicates of each metabolite detected in the leachates did not exceed 10 µg/L during the first year and remained below 1.0 µg/L during the second year.

2.8.2 Summary of fate and behaviour in water and sediment

Hydrolysis
Two new studies investigating the hydrolytic degradation of chlorothalonil have been performed (Adam 2006, Wicksted *et al* 2014) because the existing studies pre-date the current guideline and showed some shortcomings (although quantitative endpoints were derived during the original review).

At pH 9 and at two temperatures 25 ^{o}C and 50 ^{o}C half-lives are 9.5 and 0.61 days, respectively. One hydrolytic metabolite R613636 was formed (maximum of 40% and 76%, respectively) and was stable to further hydrolysis.

Hydrolytic degradation under dark sterile conditions at pH 4, pH 7 and pH 9 at 50°C for 5 days showed that chlorothalonil is hydrolytically stable under acidic conditions, but is prone to hydrolysis under neutral or basic conditions, especially at higher temperatures. Further investigations were carried out at pH 7 at 50, 60, and 70°C and at pH 9 at 15, 25 and 35°C for 30 days. The principal route of degradation was by hydrolysis of a cyano group to yield the amide (R613636) with subsequent oxidation/hydrolysis to form the diamide (VIS-02/SYN546872). Substitution of chlorine for oxygen occurred to form R182281 along with 2 of its positional isomers.

At pH 7 the rate of chlorothalonil degradation decreased with increasing temperature, with DT_{50} values of 29.7, 6.9 and 2.1 days at 50, 60 and 70 ^{o}C, respectively. At pH 9, the rate of chlorothalonil degradation also decreased with increasing temperature, with DT_{50} values of 83.5, 11.5 and 3.9 days at 15, 25, and 35 ^{o}C, respectively. Using the Arrhenius equation, at 25°C the half-life for chlorothalonil was calculated to be 1386 days at pH 7 and 15 days at pH 9.

In conclusion, under normal environmental conditions hydrolytic degradation will not play a significant part in the dissipation of chlorothalonil in the aquatic environment.

Aqueous photolysis (direct and indirect)

Two new studies have been performed investigating the direct aqueous photochemical degradation of chlorothalonil in sterile buffer solution (in the second study also natural water), conducted to address shortcomings identified in existing studies (unvalidated methods or concentrations above the water solubility).

In the first study chlorothalonil underwent very rapid photolysis in the aquatic environment with a SFO half-life of 6.3 h under test conditions. The quantum yield was calculated to be 1.24×10^{-3}. Using the quantum yield, the half-life of Chlorothalonil in aqueous systems at latitudes between 30°N and 50°N was calculated and ranged from 0.63 to 5.74 days depending on the season and water depth.

Up to four metabolites were detected (but not all quantified) due to subsequent oxidative and reductive dechlorination of the test item, namely 4-hydroxy-2,5,6-trichloroisophthalonitrile (SDS-3701), trichloro-1,3-dicyano-benzene, dichloro-1,3-dicyanobenzene and chloro-1,3-dicyanobenzene. Trichloro-1,3-dicyano-benzene and dichloro-1,3-dicyanobenzene were transient metabolites. The corresponding half-lives were calculated to be 0.36 and 1.16 days, respectively.

In the second study experimental half-lives ($DegT_{50}$) of 14.0 hours and 2.7 hours were determined in buffer (pH 5) and natural water, respectively, equivalent to 23.0 and 5.1 hours summer sunlight at 30-50°N. No degradation in the dark control samples was observed. An additional study concerned indirect photochemical degradation. Three major (>10%) degradation products were observed in buffer (PD1, PD2, PD3) and four in natural water (PD1, PD2, PD4, PD5).

An additional study concerning indirect photochemical degradation was conducted and provides DT_{50} and DT_{90} values for the photodegradation of chlorothalonil in sterile natural water of 35 days and 1.16 days of Tokyo spring sunlight, respectively. Six unknown metabolites reached the following maximum levels: Unknown B, tentatively considered to be an N-oxide of chlorothalonil (16.1% AR, 2.5 hours), unknown G

(5.7% AR, 2.5 hours), unknown I (12.9% AR, 24 hours), unknown J (12.4% AR, 8 hours), unknown K (29.0% AR, 24 hours) and unknown L (35.8%, 24 hours).

Ready biodegradability

Chlorothalonil is not ready biodegradable.

Aerobic mineralisation

One new study investigating the aerobic mineralisation of chlorothalonil is presented to fullfill the new data requirement since the original Annex I submission. The rate and route of degradation of [^{14}C]-chlorothalonil was investigated in surface water at nominal rates of 10 and 50 µg/L under aerobic conditions and maintained in dark conditions at *ca* 20°C for up to 60 days.

The degradation ($DegT_{50}$) of chlorothalonil in surface water was 0.4 and 6 days for the low and high rate incubations, respectively.

R182281 and R613636 were the major degradation products detected in the low rate samples, reaching mean maximums of 86.3% AR (5 DAT) and 6.3% AR (60 DAT), respectively. R182281, R613636 and R613841 were the major degradation products detected in the high rate samples, reaching mean maximums of 12.2% AR (5 DAT), 13.9% AR (60 DAT) and 32.1% AR (60 DAT), respectively. For the sterilised samples, chlorothalonil degraded slower than in non-sterile samples with 3.3% and 22.4% AR remaining at 65 and 59 DAT for low and high rates, respectively.

Water-sediment studies

Only one existing reliable water-sediment study was available (the other studies merely were shaken flask experiments or were performed at too high dose rates). Two new studies investigating the rate and route of degradation of chlorothalonil in water sediment systems were submitted to address shortcomings identified during the original review. All reliable studies were subsequently subjected to kinetic evaluation according to FOCUS Degradation Kinetics (study Ford, 2015b).

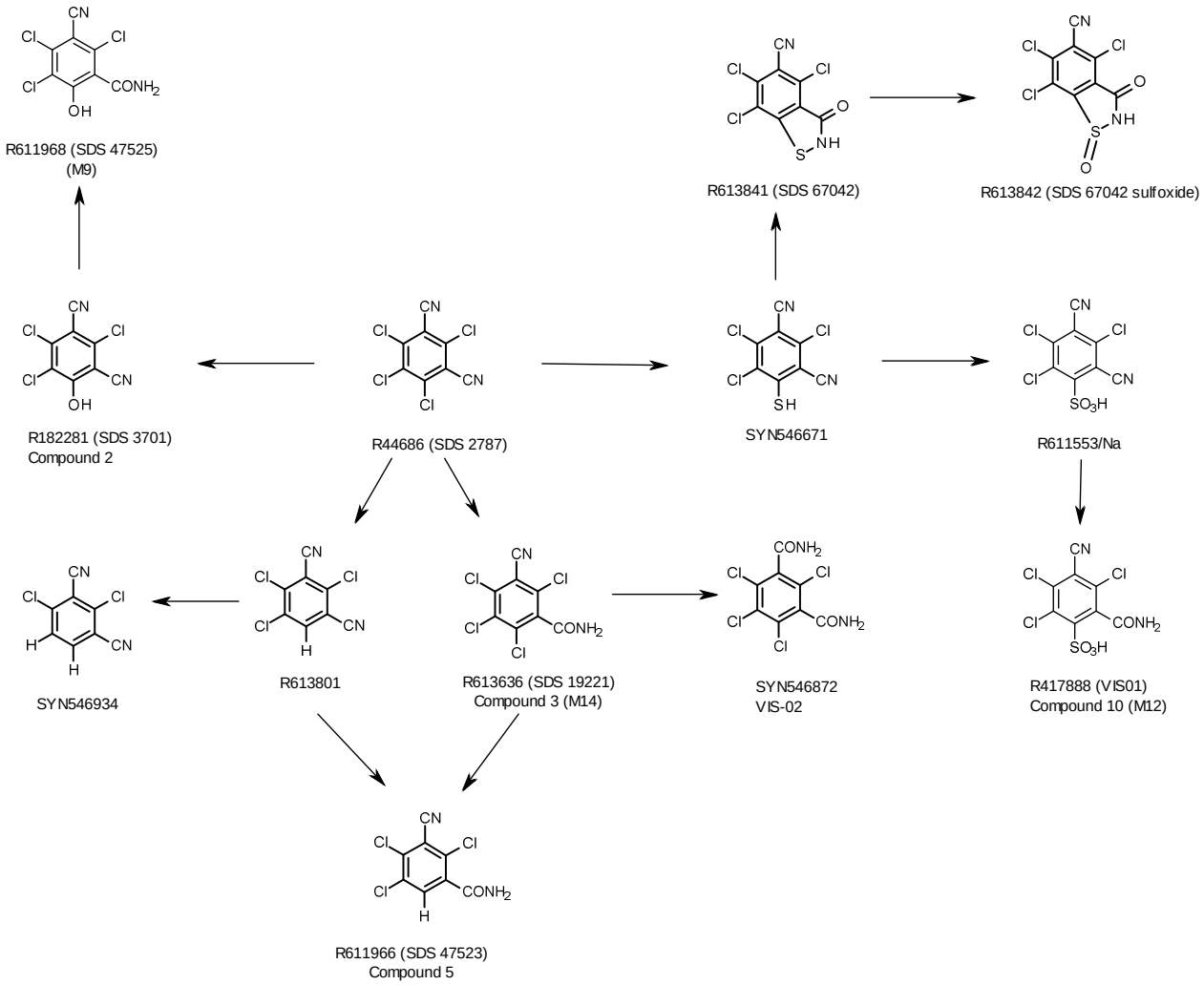
The following whole system endpoints result from the (kinetic) evaluation of existing and new studies. The route of aerobic aquatic degradation is depicted in Figure 2.8.2-01.

Table 2.8.2-1 Overview of whole system level PI and MI persistence and modelling endpoints for chlorothalonil and water-sediment metabolites

substance	Maximum DT50 (persistence) * (SFO unless indicated otherwise) [days]	Geomean DT50 (modelling) [days]	Arithmetic mean formation fraction
Chlorothalonil (n=6)	8.9 (DT90 29.7)	1.87	N/A
R182281 (n=4)	1000	265	N/A
R613841 (n=3)	90.8	47.0	0.245 (from a.s.)
R613842 (n=1)	34.7	34.7	N/A
R613801 (n=3)	22.8	15.5	0.223
SYN546671 (n=2)	1000	160	N/A
R611966	No data, 1000 used for assessment	No data, 1000 used for assessment	

* only for parent separate persistence endpoints were determined, for metabolites the persistence endpoints are derived from the kinetic fits for modelling endpoints. As these are always derived on the basis of SFO kinetics this does not influence the outcome.

Figure 2.8.2-01: Proposed degradation pathway for chlorothalonil in aerobic aquatic systems



No irradiated water-sediment studies were conducted as this is not a guideline requirement. As supplementary information, an external literature paper and two non-regulatory microcosm dissipation studies (existing studies, Addendum 2 to the DAR) are presented. These studies provide additional information on the very rapid dissipation and degradation of chlorothalonil (hours) in the water phase.

2.8.3 Summary of fate and behaviour in air

Chlorothalonil is of moderate volatility, the vapour pressure and Henry's law constant are 7.62 x 10^{-5} Pa at 25 °C and 2.5 x 10^{-2} Pa m^3 mol^{-1} at 25 °C respectively. Volatilisation from soil and from plant surfaces is not significant.
The rate of photochemical oxidation in air is 4.7 years calculated by the Atkinson method.

2.8.4 Summary of monitoring data concerning fate and behaviour of the active substance, metabolites, degradation and reaction products

Soil
No data available.

groundwater
Groundwater monitoring studies investigating concentrations of chlorothalonil and metabolites R417888, R419492, R471811 and R611965 in groundwater, in regions of high cereal production and high chlorothalonil use have been conducted in two EU countries: Germany and France. These studies were performed to investigate the potential for chlorothalonil metabolites to leach to groundwater based on lysimeter results and groundwater modelling results presented during the original EU review. Only metabolites indicated in the original review (R417888 and R611965) and two disulphonic acids thought to be highly mobile (R419492 and R471811) were included in this monitoring program.

19 out of 21 German wells and springs are considered suitable for monitoring (2 wells in the Thuringian basin had too long filter screens). For the 19 suitable locations, connection between filter screen and infiltration area was demonstrated, although for one location possibly only partial (which leaves 18 fully reliable locations). Based on general hydrological information, it is plausible that sampled water infiltrated from treated fields. This is supported by simulations, although a number of flaws were identified in the so-called time of flight calculations.
From the frequency of sampling and the length of the filter screens, it can be concluded that individual samples cannot be considered independent. Less frequent sampling could have been considered. Moving yearly averaged concentrations could have been calculated. For all acceptable locations, the moving yearly averages will be below the stated maximum for individual wells and not exceed the value of 10 µg/L.

Chlorothalonil and its metabolite R611965 were determined to be below 0.05 µg/L (LOQ) at all sampling intervals. Metabolite R417888 was determined to be below 0.05 µg/L (LOQ) in 14 out of 21 wells at all sampling intervals. In the remaining seven wells R417888 was detected at levels between 0.05 to 8.93 µg/L.
Metabolite R419492 was found at all monitoring sites with a maximum concentration of 10.77 µg/L (above 10 µg/L on two occasions). The metabolite R471811 was found at all monitoring sites with a maximum concentration of 11.73 µg/L (above 10 µg/L, one occasion).
Although some individual samples had concentrations above the guidance limit of 10 µg/L, the moving annual averages were below this value.

The French monitoring sites are situated in hydrologically highly complex situations. Monitoring wells in general are large and have long filter screens. It is possible that wells are used for other purposes than monitoring as well. Information on use of chlorothalonil is only known for a short period. The set-up of the monitoring is considered not to deliver sufficient answers to the questions about leaching of chlorothalonil metabolites to groundwater. Therefore the French monitoring studies are not used further.

The studies putting the monitoring results into context (Sweeney et al, 2015, 2015a) need justification of some of the substance parameters; the general approach is considered adequate and corroborate that the monitoring programme in itself was adequate. The simulated concentrations cannot be used as such without further justification.

Surface water
No data available.

Air
No data available.

2.8.5 Definition of the residue in the environment requiring further assessment

Soil: Chlorothalonil, R182281, R417888, R418503, R419492, R471811, SYN507900, R611965, R611966, R611967, and R613636

Groundwater: Chlorothalonil, R182281, R417888, R418503, R419492, R471811, SYN507900, R611965, R611966, R611967, and R613636; lysimeter metabolites SYN548008 (M3), SYN548580 (M2), SYN548581 (M11), M7 and M10

Surface water (and sediment): Chlorothalonil, R182281(via soil and water/sediment), R417888 (via soil), R418503 (via soil), R419492 (via soil), R471811 (via soil), SYN507900 (via soil), R611965 (via soil), R611966 (via soil an water/sediment), R611967 (via soil), and R613636 (via soil); R613841(water/sediment), R613842 (water/sediment), R613801 (water/sediment),

SYN546671(water/sediment); Aqueous photolysis: PD1, PD2, PD4, PD5; lysimeter metabolites SYN548008 (M3), SYN548580 (M2), SYN548581 (M11), M7 and M10
Air: chlorothalonil

2.8.6 Summary of exposure calculations and product assessment

PEC soil

Syngenta (A14111B)

Table 2.8.6-01 PECsoil for representative uses of A14111B, chlorothalonil and metabolites. Values in bold are relevant for ecotoxicological risk assessment

Formulation/ compound	$PEC_{S, initial}$ [mg a.s./kg]	$PEC_{S, plateau}$ [mg/kg]	$PEC_{S, peak\ accum}$ [mg/kg]
cereals, 1x 750 g a.s./ha, interception 80%			
A14111B	**0.610**	-	-
chlorothalonil	**0.200**	-	-
R182281	0.060	0.116	**0.175**
R417888	0.038	0.131	**0.169**
R418503	**0.016**	-	-
R419492	0.035	0.122	**0.157**
R471811	0.033	0.115	**0.148**
SYN507900	0.012	0.018	**0.03**
R611965	0.027	0.093	**0.119**
R611966	**0.015**	-	-
R611967	**0.025**	-	-
R613636	**0.022**	-	-
cereals, 2x 750 g a.s./ha, interval 14 days, interception 80%			
chlorothalonil	**0.342**	-	-
R182281	0.118	0.233	**0.351**
R417888	0.075	0.263	**0.338**
R418503	**0.033**	-	-
R419492	0.066	0.244	**0.314**
R471811	0.020	0.231	**0.297**
SYN507900	0.053	0.036	**0.089**
R611965	0.066	0.186	**0.239**
R611966	**0.029**	-	-
R611967	**0.039**	-	-
R613636	**0.042**	-	-
Tomatoes, 1x 1000 g a.s./ha, interception 80%			
A14111B	**0.813**	-	-
chlorothalonil	**0.267**	-	-
R182281	0.079	0.154	**0.234**

R417888	0.050	0.174	**0.225**
R418503	**0.022**	-	-
R419492	0.047	0.162	**0.209**
R471811	0.044	0.153	**0.197**
SYN507900	0.015	0.024	**0.039**
R611965	0.036	0.123	**0.159**
R611966	**0.020**	-	-
R611967	**0.033**	-	-
R613636	**0.030**	-	-

Table 2.8.6-02 PECsoil for representative uses of A14111B, azoxystrobin and metabolites. Values in bold are relevant for ecotoxicological risk assessment

Formulation/ compound	**$PEC_{S,\ initial}$ [mg a.s./kg]**	**$PEC_{S,\ plateau}$ [mg/kg]**	**$PEC_{S,\ peak\ accum}$ [mg/kg]**
cereals, 1x 150 g a.s./ha, interception 80%			
Azoxystrobin	0.040	0.025	**0.065**
R234886	**0.017**		
R401553	**0.005**		
R402173	**0.009**		
cereals, 2x 150 g a.s./ha, interval 14 days, interception 80%			
Azoxystrobin	0.079	0.050	**0.129**
R234886	**0.032**		
R401553	**0.005**		
R402173	**0.012**		
Tomatoes, 1x 200 g a.s./ha, interception 80%			
Azoxystrobin	0.053	0.033	**0.086**
R234886	**0.022**		
R401553	**0.007**		
R402173	**0.011**		

Oxon (Chlorothalonil 500 g/L SC)

Table 2.8.6-03 PECsoil for representative uses of Chlorothalonil 500 g/L SC, chlorothalonil and metabolites. Values in bold are relevant for ecotoxicological risk assessment

Formulation/ compound	**$PEC_{S,\ initial}$ [mg a.s./kg]**	**$PEC_{S,\ plateau}$ [mg/kg]**	**$PEC_{S,\ peak\ accum}$ [mg/kg]**
cereals, 1x 750 g a.s./ha, interception 80%			
chlorothalonil	**0.200**	-	-
R182281	0.060	0.116	**0.175**
R417888	0.038	0.131	**0.169**
R418503	**0.016**	-	-
R419492	0.035	0.122	**0.157**

R471811	0.033	0.115	**0.148**
SYN507900	0.012	0.018	**0.03**
R611965	0.027	0.093	**0.119**
R611966	**0.015**	-	-
R611967	**0.025**	-	-
R613636	**0.022**	-	-
cereals, 2x 750 g a.s./ha, interval 14 days, interception 80%			
chlorothalonil	**0.342**	-	-
R182281	0.118	0.233	**0.351**
R417888	0.075	0.263	**0.338**
R418503	**0.033**	-	-
R419492	0.066	0.244	**0.314**
R471811	0.020	0.231	**0.297**
SYN507900	0.053	0.036	**0.089**
R611965	0.066	0.186	**0.239**
R611966	**0.029**	-	-
R611967	**0.039**	-	-
R613636	**0.042**	-	-
Tomatoes, 1x 1000 g a.s./ha, interception 80%			
chlorothalonil	**0.267**	-	-
R182281	0.079	0.154	**0.234**
R417888	0.050	0.174	**0.225**
R418503	**0.022**	-	-
R419492	0.047	0.162	**0.209**
R471811	0.044	0.153	**0.197**
SYN507900	0.015	0.024	**0.039**
R611965	0.036	0.123	**0.159**
R611966	**0.020**	-	-
R611967	**0.033**	-	-
R613636	**0.030**	-	-
Potatoes, 1x 750 g a.s./ha, interception 85%			
chlorothalonil	**0.150**	-	-
R182281	0.045	0.087	**0.131**
R417888	0.028	0.098	**0.126**
R418503	**0.012**	-	-
R419492	0.026	0.091	**0.117**
R471811	0.025	0.086	**0.111**
SYN507900	0.009	0.014	**0.023**
R611965	0.020	0.069	**0.089**
R611966	**0.011**	-	-
R611967	**0.019**	-	-
R613636	**0.017**	-	-

Table 2.8.6-04 PECsoil for representative uses of ARY-474-001, chlorothalonil and metabolites. Values in bold are relevant for ecotoxicological risk assessment

Formulation/ compound	$PEC_{S, initial}$ [mg a.s./kg]	$PEC_{S, plateau}$ [mg/kg]	$PEC_{S, peak\ accum}$ [mg/kg]
cereals, 1x 750 g a.s./ha, interception 80%			
ARY-474-001	**0.813**	-	-
chlorothalonil	**0.200**	-	-
R182281	0.060	0.116	**0.175**
R417888	0.038	0.131	**0.169**
R418503	**0.016**	-	-
R419492	0.035	0.122	**0.157**
R471811	0.033	0.115	**0.148**
SYN507900	0.012	0.018	**0.03**
R611965	0.027	0.093	**0.119**
R611966	**0.015**	-	-
R611967	**0.025**	-	-
R613636	**0.022**	-	-
cereals, 2x 750 g a.s./ha, interval 14 days, interception 80%			
chlorothalonil	**0.342**	-	-
R182281	0.118	0.233	**0.351**
R417888	0.075	0.263	**0.338**
R418503	**0.033**	-	-
R419492	0.066	0.244	**0.314**
R471811	0.020	0.231	**0.297**
SYN507900	0.053	0.036	**0.089**
R611965	0.066	0.186	**0.239**
R611966	**0.029**	-	-
R611967	**0.039**	-	-
R613636	**0.042**	-	-
Tomatoes, 1x 1000 g a.s./ha, interception 80%			
ARY-474-001	**0.501**	-	-
chlorothalonil	**0.267**	-	-
R182281	0.079	0.154	**0.234**
R417888	0.050	0.174	**0.225**
R418503	**0.022**	-	-
R419492	0.047	0.162	**0.209**
R471811	0.044	0.153	**0.197**
SYN507900	0.015	0.024	**0.039**
R611965	0.036	0.123	**0.159**
R611966	**0.020**	-	-
R611967	**0.033**	-	-
R613636	**0.030**	-	-

PEC groundwater

Winter cereal results (2 applications, interval 14 days) calculated by RMS using FOCUS-PEARL 4.4.4 on the basis of above endpoints for degradation and sorption, covering for the other proposed uses are presented below. Only the highest values across scenarios has been presented. Tier 2 results for lysimeter metabolites are based on input parameters derived via structural resemblance with known metabolites, as no degradation and sorption studies are available (tier 1 assumes no degradation and no sorption). For details see the respective Volumes 3 CP section B.8.3.

Syngenta (A14111B)

Table 2.8.6-4 PECgw values for chlorothalonil, and soil metabolites R182281, R417888, R418503, R419492, R471811, SYN507900, R611965, R611966, R611967, R611968 and R613636, and tier 1 and tier 2 lysimeter metabolites SYN548008, SYN548580, SYN548581, M7 and M10, for winter cereals (FOCUS-PEARL 4.4.4).

Chlorothalonil	**R182281**	**R417888**	**R418503**	**R419492**	**R471811**
<0.001	0.012523	**23.48509**	1.19604	**44.27109**	**33.40975**

Table 2.8.6-4 continued (soil metabolites)

SYN507900	**R611965**	**R611966**	**R611967**	**R611968***	**R613636**
26.10001	**22.37471**	0.000138	<0.001	4.18107	<0.001

*Please note that for this metabolite an assessment was not triggered (only once above 5%)

Table 2.8.6-4 continued (lysimeter metabolites)

SYN548008	**SYN548580**	**SYN548581**	**M7**	**M10**
16.04670 (tier 1) **10.23563** (tier 2)	**11.56979** (tier1) **10.44852** (tier 2)	**13.44707** (tier1) <0.001 (tier 2)	**11.61060** (tier1) 4.62838 (tier 2)	**10.83520** (tier1) 1.89756 (tier 2)

Oxon (Chlorothalonil 500 g/L SC)

See Table 2.8.6-4 above, as the same results are valid for all products based on the same GAP.

Arysta (ARY-474-001)

See Table 2.8.6-4 above, as the same results are valid for all products based on the same GAP.

The (non-)relevance of metabolites exceeding 0.1 µg/L is further addressed in section 2.11.

PEC surface water and sediment

Calculations presented below are based on applicant (taskforce) input values, which for parent chlorothalonil were more worst-case than the values derived by RMS. For metabolites, some of the RMS derived input values were slightly more conservative, but given the margin of safety in the ecotoxicological assessment (minimum MOS is a factor 4) and the expected small impact on the outcome of the PEC calculations RMS did not recalculate the metabolite STEP 1 and 2 PECsw/sed values.
For confirmation, the impact of the change in endpoints on the predicted concentrations for R182281 was assessed and the results did not differ significantly (see Volume 3 CP B.8.5 for details).

Lysimeter metabolites are addressed on the basis of a leachate toxicity testing (see Volume 3 CA Section B.9.2) and no PEC calculations are deemed necessary.

Syngenta (A14111B)

Parent

chlorothalonil

An overview of maximum PECsw and PECsed at STEP 1-4 is given in Table 2.8.6-5.

Table 2.8.6-5: Summary of overall maximum initial PEC_{SW} and PEC_{SED} of chlorothalonil (Steps 1 – 4) following spray treatment application to winter and spring cereals at an application rate of 1x and 2 x 750g/ha, and tomatoes at an application rate of 1x 1000 g/ha.

Use pattern	Step	Max. PEC_{SW} [a] [µg/L]	Max. PEC_{SED} [a] [µg/kg]	Mitigation Applied SD = spray drift buffer RO = runoff buffer
Winter Cereals				
Winter Cereals 1 x 750 g a.s./ha BBCH 30	Step 1	103	1160	--
	Step 2	12.0	144	--
	Step 3	4.79	4.37	--
	Step 4	2.99	1.45	10m SD
	Step 4	1.35	0.79	10m SD; 10m RO
	Step 4	0.707	0.42	20m SD; 20m RO
Winter Cereals 2 x 750 g a.s./ha BBCH 30	Step 1	103	1160	--
	Step 2	13.2	160	--
	Step 3	4.26	6.84	--
	Step 4	3.53	5.16	10m SD
	Step 4	1.61	1.51	10m SD; 10m RO
	Step 4	0.846	0.714	20m SD; 20m RO
Spring Cereals				
Spring Cereals 1 x 750 g a.s./ha BBCH 30	Step 1	103	1160	--
	Step 2	12.0	144	--
	Step 3	4.80	4.95	--
	Step 4	0.86	0.88	10m SD
	Step 4	0.86	0.88	10m SD; 10m RO

Use pattern	Step	Max. PEC_{SW} [a] [µg/L]	Max. PEC_{SED} [a] [µg/kg]	Mitigation Applied SD = spray drift buffer RO = runoff buffer
	Step 4	0.45	0.48	20m SD; 20m RO
Spring Cereals 2 x 750 g a.s./ha BBCH 30	Step 1	103	1160	--
	Step 2	13.2	160	--
	Step 3	5.43	6.62	--
	Step 4	5.43	3.66	10m SD
	Step 4	2.44	1.55	10m SD; 10m RO
	Step 4	1.27	0.80	20m SD; 20m RO
Tomatoes				
Tomatoes 1 x 1000 g a.s./ha BBCH 51	Step 1	137	1540	--
	Step 2	9.20	99.3	--
	Step 3	6.32	4.35	--
	Step 4	5.58	4.15	10m SD
	Step 4	2.54	1.56	10m SD; 10m RO
	Step 4	1.33	0.792	20m SD; 20m RO

[a] maximum PEC across all scenarios; i.e. the reported PEC_{SW} and PEC_{SED} do not necessarily result from the same scenario

azoxystrobin

An overview of maximum PECsw and PECsw at STEP 1-4 is given in Table 2.8.6-6.

Table 2.8.6-6: Summary of overall maximum initial PEC_{SW} and PEC_{SED} of azoxystrobin (FOCUS steps 1-4) following applications to winter and spring cereals and tomatoes

Use pattern	Step	Max. PEC_{SW} [a] [µg/L]	Max. PEC_{SED} [a] [µg/kg]	Main route of entry to water body for max. PEC_{SW} (Steps 3 and 4)
Winter Cereals				
Winter Cereals 1 x 150 g a.s./ha BBCH 30	Step 1	66.7	277	--
	Step 2	133	55.3	--
	Step 3	2.11	16.4	Drainage
	Step 4	np	np	na
Winter Cereals 2 x 150 g a.s./ha BBCH 30	Step 1	66.7	277	--
	Step 2	133	55.3	--
	Step 3	2.11	16.4	Drainage
	Step 4	np	np	na
Spring Cereals				
Spring Cereals 1 x 150 g a.s./ha BBCH 30	Step 1	66.7	277	--
	Step 2	133	55.3	--
	Step 3	2.11	16.4	Drainage
	Step 4	np	np	na
Spring Cereals 2 x 150 g a.s./ha	Step 1	66.7	277	--
	Step 2	133	55.3	--

Use pattern	Step	Max. PEC_{SW} [a] [µg/L]	Max. PEC_{SED} [a] [µg/kg]	Main route of entry to water body for max. PEC_{SW} (Steps 3 and 4)
BBCH 30	Step 3	2.11	16.4	Drainage
	Step 4	np	np	na
Tomatoes				
Tomatoes 1 x 200 g a.s./ha BBCH 39	Step 1	44.5	185	--
	Step 2	9.56	39.7	--
	Step 3	2.11	16.4	Drainage
	Step 4	np	np	na

np = not performed
na = not applicable
nr = not reported

metabolites

chlorothalonil

An overview of STEP 1-2 for chlorothalonil metabolites is given in Table 2.8.6-7.

Table 2.8.6-7: Summary of overall maximum PEC_{SW} and PEC_{SED} of chlorothalonil metabolites R182281, R417888, R418503, R419492, following applications to cereals and tomatoes (Steps 1 & 2)

Use pattern [a]	Step	Region	R182281		R417888		R418503		R419492	
			Max. PEC_{SW} [µg/L][a]	Max. PEC_{SED} [µg/kg][a]	Max. PEC_{SW} [µg/L][a]	Max. PEC_{SED} [µg/kg][a]	Max. PEC_{SW} [µg/L][a]	Max. PEC_{SED} [µg/kg][a]	Max. PEC_{SW} [µg/L][a]	Max. PEC_{SED} [µg/kg][a]
Winter cereals 1 x 750 BBCH 30	1	-	51.8	200	64.5	4.49	20.5	0.021	43.7	0
	2	North Europe	6.97	26.5	6.40	0.446	1.87	0.002	4.34	0
		South Europe	11.8	45.4	12.8	0.893	3.74	0004	8.68	0
Winter cereals 2 x 750 BBCH 30	1	-	104	399	129	8.99	40.9	0.041	87.5	0
	2	North Europe	13.1	49.9	12.7	0.882	3.23	0.003	8.57	0
		South Europe	22.4	86.5	25.3	1.76	6.45	0.007	17.1	0
Spring cereals 1 x 750 BBCH 30	1	-	51.8	200	64.5	4.49	20.5	0.021	43.7	0
	2	North Europe	6.97	26.5	6.40	0.446	1.87	0.002	4.34	0
		South Europe	11.8	45.4	12.8	0.893	3.74	0.004	8.68	0
Spring cereals 2 x 750 BBCH 30	1	-	104	399	129	8.99	40.9	0.041	87.5	0
	2	North Europe	13.1	49.9	12.7	0882	3.23	0.003	8.57	0
		South Europe	22.4	86.5	25.3	1.76	6.45	0.007	17.1	0
Tomatoes 1 x 1000	1	-	69.0	266	85.9	5.99	27.3	0.027	58.3	0
	2	North Europe	6.74	25.3	5.12	0.357	1.50	0.002	3.47	0

Use pattern [a]	Step	Region	R182281		R417888		R418503		R419492	
			Max. PEC_{SW} [µg/L][a]	Max. PEC_{SED} [µg/kg][a]	Max. PEC_{SW} [µg/L][a]	Max. PEC_{SED} [µg/kg][a]	Max. PEC_{SW} [µg/L][a]	Max. PEC_{SED} [µg/kg][a]	Max. PEC_{SW} [µg/L][a]	Max. PEC_{SED} [µg/kg][a]
BBCH 51		South Europe	8.66	32.9	7.68	0.536	2.24	0.002	5.21	0

[a.] Applications to winter cereals are assumed to occur during the March to May period and spring cereals during the June to September period in NEU and the March to May period in the SEU.

Continued……Table 2.8.6-7: Summary of overall maximum PEC_{SW} and PEC_{SED} of chlorothalonil metabolites R471811, SYN507900, SYN546671 and SYN546872 following applications to cereals and tomatoes (Steps 1 & 2)

Use pattern [a]	Step	Region	R471811		SYN507900		SYN546671		SYN546872	
			Max. PEC_{SW} [µg/L][a]	Max. PEC_{SED} [µg/kg][a]	Max. PEC_{SW} [µg/L][a]	Max. PEC_{SED} [µg/kg][a]	Max. PEC_{SW} [µg/L][a]	Max. PEC_{SED} [µg/kg][a]	Max. PEC_{SW} [µg/L][a]	Max. PEC_{SED} [µg/kg][a]
Winter cereals 1 x 750 BBCH 30	1	-	41.3	0	14.2	2.23	0.896	0	106	0
	2	North Europe	4.12	0	1.40	0.220	0.895	0	10.6	0
		South Europe	8.23	0	2.80	0.440	0.895	0	21.1	0
Winter cereals 2 x 750 BBCH 30	1	-	82.7	0	28.4	4.45	1.79	0	212	0
	2	North Europe	8.17	0	2.75	0.432	1.22	0	21.1	0
		South Europe	16.3	0	5.50	0.864	1.22	0	42.1	0
Spring cereals 1 x 750 BBCH 30	1	-	41.3	0	14.2	2.23	0.896	0	106	0
	2	North Europe	4.12	0	1.40	0.220	0.895	0	10.6	0
		South Europe	8.23	0	2.80	0.440	0.895	0	21.2	0
Spring cereals 2 x 750 BBCH 30	1	-	82.7	0	28.4	4.45	1.79	0	212	0
	2	North Europe	8.17	0	2.75	0.432	1.22	0	21.1	0
		South Europe	16.3	0	5.50	0.864	1.22	0	42.1	0
Tomatoes 1 x 1000 BBCH 51	1	-	55.1	0	18.9	2.97	1.19	0	142	0
	2	North Europe	3.29	0	1.12	0.176	1.19	0	8.47	0
		South Europe	4.94	0	1.68	0.264	1.19	0	12.7	0

[a.] Applications to winter cereals are assumed to occur during the March to May period and spring cereals during the June to September period in NEU and the March to May period in the SEU.

Continued……Table 2.8.6-7: Summary of overall maximum PEC_{SW} and PEC_{SED} of chlorothalonil metabolites SYN546934, R611965, R611966 and R611967 following applications to cereals and tomatoes (Steps 1 & 2)

Use pattern [a]	Step	Region	SYN546934		R611965		R611966		R611967	
			Max. PEC_{SW} [µg/L][a]	Max. PEC_{SED} [µg/kg][a]	Max. PEC_{SW} [µg/L][a]	Max. PEC_{SED} [µg/kg][a]	Max. PEC_{SW} [µg/L][a]	Max. PEC_{SED} [µg/kg][a]	Max. PEC_{SW} [µg/L][a]	Max. PEC_{SED} [µg/kg][a]
Winter cereals 1 x 750 BBCH 30	1	-	0.481	0	33.0	2.34	14.8	34.6	23.6	55.4
	2	North Europe	0.480	0	3.27	0.232	1.69	3.92	2.06	4.85
		South Europe	0.480	0	6.54	0.464	3.09	7.21	4.13	9.70
Winter cereals 2 x 750 BBCH 30	1	-	0.961	0	66.0	4.69	29.6	69.2	47.2	111
	2	North Europe	0.845	0	6.42	0.456	3.16	7.34	3.36	7.89
		South Europe	0.845	0	12.8	0.912	5.82	13.6	6.72	15.8
Spring cereals 1 x 750 BBCH 30	1	-	0.481	0	33.0	2.34	14.8	34.6	23.6	55.4
	2	North Europe	0.480	0	3.27	0.232	1.69	3.92	2.06	4.85
		South Europe	0.480	0	6.54	0.464	3.09	7.21	4.13	9.70
Spring cereals 2 x 750 BBCH 30	1	-	0.961	0	66.0	4.69	29.6	69.2	47.2	111
	2	North Europe	0.845	0	6.42	0.456	3.16	7.34	3.36	7.89
		South Europe	0.845	0	12.8	0.912	5.82	13.6	6.72	15.8
Tomatoes 1 x 1000 BBCH 51	1	-	0.641	0	44.0	3.13	19.8	46.1	31.4	73.9
	2	North Europe	0.641	0	2.61	0.186	1.51	3.46	1.65	3.88
		South Europe	0.641	0	3.92	0.278	2.07	4.78	2.48	5.82

[a.] Applications to winter cereals are assumed to occur during the March to May period and spring cereals during the June to September period in NEU and the March to May period in the SEU.

Continued…….Table 2.8.6-7: Summary of overall maximum PEC_{SW} and PEC_{SED} of chlorothalonil metabolites R611968, R613636, R613801 and R613841 following applications to cereals and tomatoes (Steps 1 & 2)

Use pattern [a]	Step	Region	R611968		R613636		R613801		R613841	
			Max. PEC_{SW} [µg/L][a]	Max. PEC_{SED} [µg/kg][a]	Max. PEC_{SW} [µg/L][a]	Max. PEC_{SED} [µg/kg][a]	Max. PEC_{SW} [µg/L][a]	Max. PEC_{SED} [µg/kg][a]	Max. PEC_{SW} [µg/L][a]	Max. PEC_{SED} [µg/kg][a]
Winter cereals 1 x 750 BBCH 30	1	-	15.9	2.50	24.6	55.9	0.835	0	2.63	0
	2	North Europe	1.51	0.236	4.84	10.8	0.835	0	2.63	0
		South Europe	3.01	0.473	6.78	15.4	0.835	0	2.63	0
Winter cereals 2 x 750	1	-	31.8	4.99	49.3	112	1.67	0	5.26	0
	2	North Europe	2.75	0432	8.48	19.0	0.982	0	4.23	0

Use pattern [a]	Step	Region	R611968		R613636		R613801		R613841	
			Max. PEC_{SW} [µg/L][a]	Max. PEC_{SED} [µg/kg][a]	Max. PEC_{SW} [µg/L][a]	Max. PEC_{SED} [µg/kg][a]	Max. PEC_{SW} [µg/L][a]	Max. PEC_{SED} [µg/kg][a]	Max. PEC_{SW} [µg/L][a]	Max. PEC_{SED} [µg/kg][a]
BBCH 30		South Europe	5.50	0.864	11.9	26.9	0.982	0	4.23	0
Spring cereals 1 x 750 BBCH 30	1	-	15.9	2.05	24.6	55.9	0.835	0	2.63	0
	2	North Europe	1.51	0.236	4.84	10.8	0.835	0	2.63	0
		South Europe	3.01	0.473	6.78	15.4	0.835	0	2.63	0
Spring cereals 2 x 750 BBCH 30	1	-	31.8	4.99	49.3	112	1.67	0	5.26	0
	2	North Europe	2.75	0.432	8.48	19.0	0.982	0	4.23	0
		South Europe	5.50	0.864	11.9	26.9	0.982	0	4.23	0
Tomatoes 1 x 1000 BBCH 51	1	-	21.2	3.33	32.9	74.6	1.11	0	3.51	0
	2	North Europe	1.20	0.189	5.42	12.0	1.11	0	3.51	0
		South Europe	1.81	0.284	6.19	13.8	1.11	0	3.51	0

[a.] Applications to winter cereals are assumed to occur during the March to May period and spring cereals during the June to September period in NEU and the March to May period in the SEU.

Continued……..Table 2.8.6-7: Summary of overall maximum PEC_{SW} and PEC_{SED} of chlorothalonil metabolites R613842, postulated isomer 2 (R182281 isomer), PD1 and PD2 following applications to cereals and tomatoes (Steps 1 & 2)

Use pattern [a]	Step	Region	R613842		Postulated isomer 2/R950107 (R182281 isomer)		PD1		PD2	
			Max. PEC_{SW} [µg/L][a]	Max. PEC_{SED} [µg/kg][a]	Max. PEC_{SW} [µg/L][a]	Max. PEC_{SED} [µg/kg][a]	Max. PEC_{SW} [µg/L][a]	Max. PEC_{SED} [µg/kg][a]	Max. PEC_{SW} [µg/L][a]	Max. PEC_{SED} [µg/kg][a]
Winter cereals 1 x 750 BBCH 30	1	-	0.897	0	0.655	0	0.565	0	1.13	0
	2	North Europe	0.897	0	0.655	0	0.565	0	1.13	0
		South Europe	0.897	0	0.655	0	0.565	0	1.13	0
Winter cereals 2 x 750 BBCH 30	1	-	1.79	0	1.31	0	1.13	0	2.27	0
	2	North Europe	1.39	0	1.15	0	0.994	0	1.99	0
		South Europe	1.39	0	1.15	0	0.994	0	1.99	0
Spring cereals 1 x 750 BBCH 30	1	-	0.897	0	0.655	0	0.565	0	1.13	0
	2	North Europe	0.897	0	0.655	0	0.565	0	1.13	0
		South Europe	0.897	0	0.655	0	0.565	0	1.13	0
Spring cereals 2 x 750	1	-	1.79	0	1.31	0	1.13	0	2.27	0
	2	North Europe	1.39	0	1.15	0	0.994	0	1.99	0

Use pattern [a]	Step	Region	R613842		Postulated isomer 2/R950107 (R182281 isomer)		PD1		PD2	
			Max. PEC_{SW} [µg/L][a]	Max. PEC_{SED} [µg/kg][a]	Max. PEC_{SW} [µg/L][a]	Max. PEC_{SED} [µg/kg][a]	Max. PEC_{SW} [µg/L][a]	Max. PEC_{SED} [µg/kg][a]	Max. PEC_{SW} [µg/L][a]	Max. PEC_{SED} [µg/kg][a]
BBCH 30		South Europe	1.39	0	1.15	0	0.994	0	1.99	0
Tomatoes 1 x 1000 BBCH 51	1	-	1.20	0	0.874	0	0.754	0	1.51	0
	2	North Europe	1.20	0	0.873	0	0.754	0	1.51	0
		South Europe	1.20	0	0.873	0	0.754	0	1.51	0

[a.] Applications to winter cereals are assumed to occur during the March to May period and spring cereals during the June to September period in NEU and the March to May period in the SEU.

Continued……Table 2.8.6-7: Summary of overall maximum PEC_{SW} and PEC_{SED} of chlorothalonil metabolites PD3, PD4 and PD5 following applications to cereals and tomatoes (Steps 1 & 2)

Use pattern [a]	Step	Region	PD3		PD4		PD5	
			Max. PEC_{SW} [µg/L][a]	Max. PEC_{SED} [µg/kg][a]	Max. PEC_{SW} [µg/L][a]	Max. PEC_{SED} [µg/kg][a]	Max. PEC_{SW} [µg/L][a]	Max. PEC_{SED} [µg/kg][a]
Winter cereals 1 x 750 BBCH 30	1	-	0.787	0	1.18	0	2.24	0
	2	North Europe	0.787	0	1.18	0	2.24	0
		South Europe	0.787	0	1.18	0	2.24	0
Winter cereals 2 x 750 BBCH 30	1	-	1.57	0	2.36	0	4.47	0
	2	North Europe	1.38	0	2.08	0	3.93	0
		South Europe	1.38	0	2.08	0	3.93	0
Spring cereals 1 x 750 BBCH 30	1	-	0.787	0	1.18	0	2.24	0
	2	North Europe	0.787	0	1.18	0	2.24	0
		South Europe	0.787	0	1.18	0	2.24	0
Spring cereals 2 x 750 BBCH 30	1	-	1.57	0	2.36	0	4.47	0
	2	North Europe	1.38	0	2.08	0	3.93	0
		South Europe	1.38	0	2.08	0	3.93	0
Tomatoes 1 x 1000 BBCH 51	1	-	1.05	0	1.58	0	2.98	0
	2	North Europe	1.05	0	1.58	0	2.98	0
		South Europe	1.05	0	1.58	0	2.98	0

[a.] Applications to winter cereals are assumed to occur during the March to May period and spring cereals during the June to September period in NEU and the March to May period in the SEU.

azoxystrobin

An overview of STEP 1-2 for azoxystrobin metabolites is given in Table 2.8.6-8.

Table 2.8.6-8: Summary of overall maximum PEC_{SW} and PEC_{SED} of R234886, R401553 and R402173 following application of azoxystrobin to various crops calculated according to FOCUS STEPS 1-2

Use pattern	Step	Region	R234886		R234886		R401553		R402173	
			Acidic soil		Alkaline soil		--		--	
			Max. PEC_{SW} [a] [µg/L]	Max. PEC_{SED} [b] [µg/kg]	Max. PEC_{SW} [a] [µg/L]	Max. PEC_{SED} [b] [µg/kg]	Max. PEC_{SW} [µg/L]	Max. PEC_{SED} [µg/kg]	Max. PEC_{SW} [µg/L]	Max. PEC_{SED} [µg/kg]
Winter Cereals 1 x 150 g a.s./ha, BBCH 30	1	-	10.9	24.7	13.5	4.94	3.66	6.85	6.82	11.1
	2	North Europe	1.24	2.79	1.46	0.535	0.084	0.152	0.404	0.657
		South Europe	2.27	5.15	2.69	0.986	0.113	0.206	0.780	1.27
Winter Cereals 2 x 150 g a.s./ha, BBCH 30	1	-	21.8	49.5	27.0	9.89	7.31	13.7	13.6	22.2
	2	North Europe	2.33	5.25	2.59	0.95	0.126	0.225	0.472	0.768
		South Europe	4.30	9.80	4.76	1.75	0.155	0.280	0.896	1.46
Spring Cereals 1 x 150 g a.s./ha, BBCH 30	1	-	10.9	24.7	13.5	4.94	3.66	6.85	6.82	11.1
	2	North Europe	1.24	2.79	1.46	0.535	0.084	0.152	0.404	0.657
		South Europe	2.27	5.15	2.69	0.986	0.113	0.206	0.780	1.27
Spring Cereals 2 x 150 g a.s./ha, BBCH 30	1	-	21.8	49.5	27.0	9.89	7.31	13.7	13.6	22.2
	2	North Europe	2.33	5.25	2.59	0.95	0.126	0.225	0.472	0.768
		South Europe	4.30	9.80	4.76	1.75	0.155	0.280	0.896	1.46
Tomatoes 1 x 200 g a.s./ha, BBCH 39	1	-	2.27	5.15	2.69	0.986	4.88	9.13	9.10	14.8
	2	North Europe	1.65	3.71	1.95	0.714	0.112	0.202	0.538	0.877
		South Europe	2.34	5.29	2.77	1.01	0.132	0.238	0.789	1.29

[a] alkaline soils
[b] acidic soils

Oxon (Chlorothalonil 500 g/L SC)

Parent

An overview of maximum PECsw and PECsed at STEP 1-4 is given in Table 2.8.6-9.

Table 2.8.6-9: Summary of overall maximum initial PEC_{SW} and PEC_{SED} of chlorothalonil (Steps 1 – 4) following spray treatment application to winter and spring cereals at an application rate of 1x and 2 x 750g/ha, tomatoes at an application rate of 1x 1000 g/ha, and potatoes at an application rate of 1 x 750 g/ha.

Use pattern	Step	Max. PEC_{SW} [a] [µg/L]	Max. PEC_{SED} [a] [µg/kg]	Mitigation Applied SD = spray drift buffer RO = runoff buffer
Winter Cereals				
Winter Cereals 1 x 750 g a.s./ha BBCH 30	Step 1	103	1160	--
	Step 2	12.0	144	--
	Step 3	4.79	4.37	--
	Step 4	2.99	1.45	10m SD
	Step 4	1.35	0.79	10m SD; 10m RO
	Step 4	0.707	0.42	20m SD; 20m RO
Winter Cereals 2 x 750 g a.s./ha BBCH 30	Step 1	103	1160	--
	Step 2	13.2	160	--
	Step 3	4.26	6.84	--
	Step 4	3.53	5.16	10m SD
	Step 4	1.61	1.51	10m SD; 10m RO
	Step 4	0.846	0.714	20m SD; 20m RO
Spring Cereals				
Spring Cereals 1 x 750 g a.s./ha BBCH 30	Step 1	103	1160	--
	Step 2	12.0	144	--
	Step 3	4.80	4.95	--
	Step 4	0.86	0.88	10m SD
	Step 4	0.86	0.88	10m SD; 10m RO
	Step 4	0.45	0.48	20m SD; 20m RO
Spring Cereals 2 x 750 g a.s./ha BBCH 30	Step 1	103	1160	--
	Step 2	13.2	160	--
	Step 3	5.43	6.62	--
	Step 4	5.43	3.66	10m SD
	Step 4	2.44	1.55	10m SD; 10m RO
	Step 4	1.27	0.80	20m SD; 20m RO
Tomatoes				
Tomatoes 1 x 1000 g a.s./ha BBCH 51	Step 1	137	1540	--
	Step 2	9.20	99.3	--
	Step 3	6.32	4.35	--
	Step 4	5.58	4.15	10m SD
	Step 4	2.54	1.56	10m SD; 10m RO
	Step 4	1.33	0.792	20m SD; 20m RO
Potatoes				
Potatoes 1 x 750 g a.s./ha BBCH 40	Step 1	103	1160	--
	Step 2	8.60	93.5	--
	Step 3	3.95	8.38	--
	Step 4	n.c.	n.c	10m SD

Use pattern	Step	Max. PEC_{SW} [a] [µg/L]	Max. PEC_{SED} [a] [µg/kg]	Mitigation Applied SD = spray drift buffer RO = runoff buffer
	Step 4	1.503	1.795	10m SD; 10m RO
	Step 4	0.787	0.759	20m SD; 20m RO

[a] maximum PEC across all scenarios; i.e. the reported PEC_{SW} and PEC_{SED} do not necessarily result from the same scenario

n.c. not calculated

Metabolites

An overview of maximum PECsw and PECsed at STEP 1-2 is given in Table 2.8.6-10.

Table 2.8.6-10: Summary of overall maximum PEC_{SW} and PEC_{SED} of chlorothalonil metabolites R182281, R417888, R418503, R419492, following applications to cereals, tomatoes and potatoes (Steps 1 & 2)

Use pattern [a]	Step	Region	R182281		R417888		R418503		R419492	
			Max. PEC_{SW} [µg/L][a]	Max. PEC_{SED} [µg/kg][a]	Max. PEC_{SW} [µg/L][a]	Max. PEC_{SED} [µg/kg][a]	Max. PEC_{SW} [µg/L][a]	Max. PEC_{SED} [µg/kg][a]	Max. PEC_{SW} [µg/L][a]	Max. PEC_{SED} [µg/kg][a]
Winter cereals 1 x 750 BBCH 30	1	-	51.8	200	64.5	4.49	20.5	0.021	43.7	0
	2	North Europe	6.97	26.5	6.40	0.446	1.87	0.002	4.34	0
		South Europe	11.8	45.4	12.8	0.893	3.74	0004	8.68	0
Winter cereals 2 x 750 BBCH 30	1	-	104	399	129	8.99	40.9	0.041	87.5	0
	2	North Europe	13.1	49.9	12.7	0.882	3.23	0.003	8.57	0
		South Europe	22.4	86.5	25.3	1.76	6.45	0.007	17.1	0
Spring cereals 1 x 750 BBCH 30	1	-	51.8	200	64.5	4.49	20.5	0.021	43.7	0
	2	North Europe	6.97	26.5	6.40	0.446	1.87	0.002	4.34	0
		South Europe	11.8	45.4	12.8	0.893	3.74	0.004	8.68	0
Spring cereals 2 x 750 BBCH 30	1	-	104	399	129	8.99	40.9	0.041	87.5	0
	2	North Europe	13.1	49.9	12.7	0882	3.23	0.003	8.57	0
		South Europe	22.4	86.5	25.3	1.76	6.45	0.007	17.1	0
Tomatoes 1 x 1000 BBCH 51	1	-	69.0	266	85.9	5.99	27.3	0.027	58.3	0
	2	North Europe	6.74	25.3	5.12	0.357	1.50	0.002	3.47	0
		South Europe	8.66	32.9	7.68	0.536	2.24	0.002	5.21	0
Potatoes 1 x 750	1	-	51.76	192.66	64.46	4.49	20.47	0.02	43.74	0.00
	2	North Europe	5.06	18.98	3.84	0.27	1.12	0.00	2.61	0.00

Use pattern [a]	Step	Region	R182281		R417888		R418503		R419492	
			Max. PEC_{SW} [µg/L][a]	Max. PEC_{SED} [µg/kg][a]	Max. PEC_{SW} [µg/L][a]	Max. PEC_{SED} [µg/kg][a]	Max. PEC_{SW} [µg/L][a]	Max. PEC_{SED} [µg/kg][a]	Max. PEC_{SW} [µg/L][a]	Max. PEC_{SED} [µg/kg][a]
BBCH 40		South Europe	7.93	30.32	7.68	0.54	2.24	0.00	5.21	0.00

[a.] Applications to winter cereals are assumed to occur during the March to May period and spring cereals during the June to September period in NEU and the March to May period in the SEU.

Continued……Table 2.8.6-10: Summary of overall maximum PEC_{SW} and PEC_{SED} of chlorothalonil metabolites R471811, SYN507900, SYN546671 and SYN546872 following applications to cereals, tomatoes and potatoes (Steps 1 & 2)

Use pattern [a]	Step	Region	R471811		SYN507900		SYN546671		SYN546872	
			Max. PEC_{SW} [µg/L][a]	Max. PEC_{SED} [µg/kg][a]	Max. PEC_{SW} [µg/L][a]	Max. PEC_{SED} [µg/kg][a]	Max. PEC_{SW} [µg/L][a]	Max. PEC_{SED} [µg/kg][a]	Max. PEC_{SW} [µg/L][a]	Max. PEC_{SED} [µg/kg][a]
Winter cereals 1 x 750 BBCH 30	1	-	41.3	0	14.2	2.23	0.896	0	106	0
	2	North Europe	4.12	0	1.40	0.220	0.895	0	10.6	0
		South Europe	8.23	0	2.80	0.440	0.895	0	21.1	0
Winter cereals 2 x 750 BBCH 30	1	-	82.7	0	28.4	4.45	1.79	0	212	0
	2	North Europe	8.17	0	2.75	0.432	1.22	0	21.1	0
		South Europe	16.3	0	5.50	0.864	1.22	0	42.1	0
Spring cereals 1 x 750 BBCH 30	1	-	41.3	0	14.2	2.23	0.896	0	106	0
	2	North Europe	4.12	0	1.40	0.220	0.895	0	10.6	0
		South Europe	8.23	0	2.80	0.440	0.895	0	21.2	0
Spring cereals 2 x 750 BBCH 30	1	-	82.7	0	28.4	4.45	1.79	0	212	0
	2	North Europe	8.17	0	2.75	0.432	1.22	0	21.1	0
		South Europe	16.3	0	5.50	0.864	1.22	0	42.1	0
Tomatoes 1 x 1000 BBCH 51	1	-	55.1	0	18.9	2.97	1.19	0	142	0
	2	North Europe	3.29	0	1.12	0.176	1.19	0	8.47	0
		South Europe	4.94	0	1.68	0.264	1.19	0	12.7	0
Potatoes 1 x 750 BBCH 40	1	-	41.34	0.00	19.74	3.10	29.13	0.00	37.18	0.00
	2	North Europe	2.46	0.00	1.17	0.18	1.74	0.00	2.22	0.00
		South Europe	4.92	0.00	2.34	0.37	3.49	0.00	4.45	0.00

[a.] Applications to winter cereals are assumed to occur during the March to May period and spring cereals during the June to September period in NEU and the March to May period in the SEU.

Continued……Table 2.8.6-10: Summary of overall maximum PEC_{SW} and PEC_{SED} of chlorothalonil metabolites SYN546934, R611965, R611966 and R611967 following applications to cereals, tomatoes and potatoes (Steps 1 & 2)

Use pattern [a]	Step	Region	SYN546934		R611965		R611966		R611967	
			Max. PEC_{SW} [µg/L][a]	Max. PEC_{SED} [µg/kg][a]	Max. PEC_{SW} [µg/L][a]	Max. PEC_{SED} [µg/kg][a]	Max. PEC_{SW} [µg/L][a]	Max. PEC_{SED} [µg/kg][a]	Max. PEC_{SW} [µg/L][a]	Max. PEC_{SED} [µg/kg][a]
Winter cereals 1 x 750 BBCH 30	1	-	0.481	0	33.0	2.34	14.8	34.6	23.6	55.4
	2	North Europe	0.480	0	3.27	0.232	1.69	3.92	2.06	4.85
		South Europe	0.480	0	6.54	0.464	3.09	7.21	4.13	9.70
Winter cereals 2 x 750 BBCH 30	1	-	0.961	0	66.0	4.69	29.6	69.2	47.2	111
	2	North Europe	0.845	0	6.42	0.456	3.16	7.34	3.36	7.89
		South Europe	0.845	0	12.8	0.912	5.82	13.6	6.72	15.8
Spring cereals 1 x 750 BBCH 30	1	-	0.481	0	33.0	2.34	14.8	34.6	23.6	55.4
	2	North Europe	0.480	0	3.27	0.232	1.69	3.92	2.06	4.85
		South Europe	0.480	0	6.54	0.464	3.09	7.21	4.13	9.70
Spring cereals 2 x 750 BBCH 30	1	-	0.961	0	66.0	4.69	29.6	69.2	47.2	111
	2	North Europe	0.845	0	6.42	0.456	3.16	7.34	3.36	7.89
		South Europe	0.845	0	12.8	0.912	5.82	13.6	6.72	15.8
Tomatoes 1 x 1000 BBCH 51	1	-	0.641	0	44.0	3.13	19.8	46.1	31.4	73.9
	2	North Europe	0.641	0	2.61	0.186	1.51	3.46	1.65	3.88
		South Europe	0.641	0	3.92	0.278	2.07	4.78	2.48	5.82
Potatoes 1 x 750 BBCH 40	1	-	17.41	0.00	33.01	2.34	14.82	34.00	23.58	55.41
	2	North Europe	1.04	0.00	1.96	0.14	1.13	2.60	1.24	2.91
		South Europe	2.08	0.00	3.92	0.28	1.97	4.57	2.48	5.82

[a.] Applications to winter cereals are assumed to occur during the March to May period and spring cereals during the June to September period in NEU and the March to May period in the SEU.

Continued…….Table 2.8.6-10: Summary of overall maximum PEC_{SW} and PEC_{SED} of chlorothalonil metabolites R611968, R613636, R613801 and R613841 following applications to cereals, tomatoes and potatoes (Steps 1 & 2)

Use pattern [a]	Step	Region	R611968		R613636		R613801		R613841	
			Max. PEC_{SW} [µg/L][a]	Max. PEC_{SED} [µg/kg][a]	Max. PEC_{SW} [µg/L][a]	Max. PEC_{SED} [µg/kg][a]	Max. PEC_{SW} [µg/L][a]	Max. PEC_{SED} [µg/kg][a]	Max. PEC_{SW} [µg/L][a]	Max. PEC_{SED} [µg/kg][a]
Winter cereals 1 x 750	1	-	15.9	2.50	24.6	55.9	0.835	0	2.63	0
	2	North Europe	1.51	0.236	4.84	10.8	0.835	0	2.63	0

Use pattern [a]	Step	Region	R611968		R613636		R613801		R613841	
			Max. PEC_{SW} [µg/L][a]	Max. PEC_{SED} [µg/kg][a]	Max. PEC_{SW} [µg/L][a]	Max. PEC_{SED} [µg/kg][a]	Max. PEC_{SW} [µg/L][a]	Max. PEC_{SED} [µg/kg][a]	Max. PEC_{SW} [µg/L][a]	Max. PEC_{SED} [µg/kg][a]
BBCH 30		South Europe	3.01	0.473	6.78	15.4	0.835	0	2.63	0
Winter cereals 2 x 750 BBCH 30	1	-	31.8	4.99	49.3	112	1.67	0	5.26	0
	2	North Europe	2.75	0432	8.48	19.0	0.982	0	4.23	0
		South Europe	5.50	0.864	11.9	26.9	0.982	0	4.23	0
Spring cereals 1 x 750 BBCH 30	1	-	15.9	2.05	24.6	55.9	0.835	0	2.63	0
	2	North Europe	1.51	0.236	4.84	10.8	0.835	0	2.63	0
		South Europe	3.01	0.473	6.78	15.4	0.835	0	2.63	0
Spring cereals 2 x 750 BBCH 30	1	-	31.8	4.99	49.3	112	1.67	0	5.26	0
	2	North Europe	2.75	0.432	8.48	19.0	0.982	0	4.23	0
		South Europe	5.50	0.864	11.9	26.9	0.982	0	4.23	0
Tomatoes 1 x 1000 BBCH 51	1	-	21.2	3.33	32.9	74.6	1.11	0	3.51	0
	2	North Europe	1.20	0.189	5.42	12.0	1.11	0	3.51	0
		South Europe	1.81	0.284	6.19	13.8	1.11	0	3.51	0
Potatoes 1 x 750 BBCH 40	1	-	15.89	2.50	24.65	49.67	0.83	0.00	2.18	0.00
	2	North Europe	0.90	0.14	4.06	9.00	0.83	0.00	2.18	0.00
		South Europe	1.81	0.28	5.23	11.73	0.83	0.00	2.18	0.00

[a.] Applications to winter cereals are assumed to occur during the March to May period and spring cereals during the June to September period in NEU and the March to May period in the SEU.

Continued……..Table 2.8.6-10: Summary of overall maximum PEC_{SW} and PEC_{SED} of chlorothalonil metabolites R613842, postulated isomer 2 (R182281 isomer), PD1 and PD2 following applications to cereals, tomatoes and potatoes (Steps 1 & 2)

Use pattern [a]	Step	Region	R613842		Postulated isomer 2/R950107 (R182281 isomer)		PD1		PD2	
			Max. PEC_{SW} [µg/L][a]	Max. PEC_{SED} [µg/kg][a]	Max. PEC_{SW} [µg/L][a]	Max. PEC_{SED} [µg/kg][a]	Max. PEC_{SW} [µg/L][a]	Max. PEC_{SED} [µg/kg][a]	Max. PEC_{SW} [µg/L][a]	Max. PEC_{SED} [µg/kg][a]
Winter cereals 1 x 750 BBCH 30	1	-	0.897	0	0.655	0	0.565	0	1.13	0
	2	North Europe	0.897	0	0.655	0	0.565	0	1.13	0
		South Europe	0.897	0	0.655	0	0.565	0	1.13	0
Winter cereals 2 x 750	1	-	1.79	0	1.31	0	1.13	0	2.27	0
	2	North Europe	1.39	0	1.15	0	0.994	0	1.99	0

Use pattern [a]	Step	Region	R613842		Postulated isomer 2/R950107 (R182281 isomer)		PD1		PD2	
			Max. PEC_{SW} [µg/L][a]	Max. PEC_{SED} [µg/kg][a]	Max. PEC_{SW} [µg/L][a]	Max. PEC_{SED} [µg/kg][a]	Max. PEC_{SW} [µg/L][a]	Max. PEC_{SED} [µg/kg][a]	Max. PEC_{SW} [µg/L][a]	Max. PEC_{SED} [µg/kg][a]
BBCH 30		South Europe	1.39	0	1.15	0	0.994	0	1.99	0
Spring cereals 1 x 750 BBCH 30	1	-	0.897	0	0.655	0	0.565	0	1.13	0
	2	North Europe	0.897	0	0.655	0	0.565	0	1.13	0
		South Europe	0.897	0	0.655	0	0.565	0	1.13	0
Spring cereals 2 x 750 BBCH 30	1	-	1.79	0	1.31	0	1.13	0	2.27	0
	2	North Europe	1.39	0	1.15	0	0.994	0	1.99	0
		South Europe	1.39	0	1.15	0	0.994	0	1.99	0
Tomatoes 1 x 1000 BBCH 51	1	-	1.20	0	0.874	0	0.754	0	1.51	0
	2	North Europe	1.20	0	0.873	0	0.754	0	1.51	0
		South Europe	1.20	0	0.873	0	0.754	0	1.51	0
Potatoes 1 x 750 BBCH 40	1	-	0.90	0.00	0.66	0.00	0.70	0.00	1.13	0.00
	2	North Europe	0.90	0.00	0.65	1.69	0.70	0.00	1.13	0.00
		South Europe	0.90	0.00	0.65	1.69	0.70	0.00	1.13	0.00

[a] Applications to winter cereals are assumed to occur during the March to May period and spring cereals during the June to September period in NEU and the March to May period in the SEU.

Continued……Table 2.8.6-10: Summary of overall maximum PEC_{SW} and PEC_{SED} of chlorothalonil metabolites PD3, PD4 and PD5 following applications to cereals, tomatoes and potatoes (Steps 1 & 2)

Use pattern [a]	Step	Region	PD3		PD4		PD5	
			Max. PEC_{SW} [µg/L][a]	Max. PEC_{SED} [µg/kg][a]	Max. PEC_{SW} [µg/L][a]	Max. PEC_{SED} [µg/kg][a]	Max. PEC_{SW} [µg/L][a]	Max. PEC_{SED} [µg/kg][a]
Winter cereals 1 x 750 BBCH 30	1	-	0.787	0	1.18	0	2.24	0
	2	North Europe	0.787	0	1.18	0	2.24	0
		South Europe	0.787	0	1.18	0	2.24	0
Winter cereals 2 x 750 BBCH 30	1	-	1.57	0	2.36	0	4.47	0
	2	North Europe	1.38	0	2.08	0	3.93	0
		South Europe	1.38	0	2.08	0	3.93	0
Spring cereals 1 x 750	1	-	0.787	0	1.18	0	2.24	0
	2	North Europe	0.787	0	1.18	0	2.24	0

Use pattern [a]	Step	Region	PD3		PD4		PD5	
			Max. PEC_{SW} [µg/L][a]	Max. PEC_{SED} [µg/kg][a]	Max. PEC_{SW} [µg/L][a]	Max. PEC_{SED} [µg/kg][a]	Max. PEC_{SW} [µg/L][a]	Max. PEC_{SED} [µg/kg][a]
BBCH 30		South Europe	0.787	0	1.18	0	2.24	0
Spring cereals 2 x 750 BBCH 30	1	-	1.57	0	2.36	0	4.47	0
	2	North Europe	1.38	0	2.08	0	3.93	0
		South Europe	1.38	0	2.08	0	3.93	0
Tomatoes 1 x 1000 BBCH 51	1	-	1.05	0	1.58	0	2.98	0
	2	North Europe	1.05	0	1.58	0	2.98	0
		South Europe	1.05	0	1.58	0	2.98	0
Potatoes 1 x 750 BBCH 40	1	-	0.79	0.00	1.18	0.00	2.24	0.00
	2	North Europe	0.79	0.00	1.18	0.00	2.24	0.00
		South Europe	0.79	0.00	1.18	0.00	2.24	0.00

[a.] Applications to winter cereals are assumed to occur during the March to May period and spring cereals during the June to September period in NEU and the March to May period in the SEU.

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Parent

An overview of maximum PECsw and PECsed at STEP 1-4 is given in Table 2.8.6-11.

Table 2.8.6-11: Summary of overall maximum initial PEC_{SW} and PEC_{SED} of chlorothalonil (Steps 1 – 4) following spray treatment application to winter and spring cereals at an application rate of 1x and 2 x 750g/ha, and tomatoes at an application rate of 1x 1000 g/ha.

Use pattern	Step	Max. PEC_{SW} [a] [µg/L]	Max. PEC_{SED} [a] [µg/kg]	Mitigation Applied SD = spray drift buffer RO = runoff buffer
Winter Cereals				
Winter Cereals 1 x 750 g a.s./ha BBCH 30	Step 1	103	1160	--
	Step 2	12.0	144	--
	Step 3	4.79	4.37	--
	Step 4	2.99	1.45	10m SD
	Step 4	1.35	0.79	10m SD; 10m RO
	Step 4	0.707	0.42	20m SD; 20m RO
Winter Cereals 2 x 750 g a.s./ha BBCH 30	Step 1	103	1160	--
	Step 2	13.2	160	--
	Step 3	4.26	6.84	--
	Step 4	3.53	5.16	10m SD
	Step 4	1.61	1.51	10m SD; 10m RO

Use pattern	Step	Max. PEC_{SW} [a] [µg/L]	Max. PEC_{SED} [a] [µg/kg]	Mitigation Applied SD = spray drift buffer RO = runoff buffer
	Step 4	0.846	0.714	20m SD; 20m RO
Spring Cereals				
Spring Cereals 1 x 750 g a.s./ha BBCH 30	Step 1	103	1160	--
	Step 2	12.0	144	--
	Step 3	4.80	4.95	--
	Step 4	0.86	0.88	10m SD
	Step 4	0.86	0.88	10m SD; 10m RO
	Step 4	0.45	0.48	20m SD; 20m RO
Spring Cereals 2 x 750 g a.s./ha BBCH 30	Step 1	103	1160	--
	Step 2	13.2	160	--
	Step 3	5.43	6.62	--
	Step 4	5.43	3.66	10m SD
	Step 4	2.44	1.55	10m SD; 10m RO
	Step 4	1.27	0.80	20m SD; 20m RO
Tomatoes				
Tomatoes 1 x 1000 g a.s./ha BBCH 51	Step 1	137	1540	--
	Step 2	9.20	99.3	--
	Step 3	6.32	4.35	--
	Step 4	5.58	4.15	10m SD
	Step 4	2.54	1.56	10m SD; 10m RO
	Step 4	1.33	0.792	20m SD; 20m RO

[a] maximum PEC across all scenarios; i.e. the reported PEC_{SW} and PEC_{SED} do not necessarily result from the same scenario

Metabolites

An overview of maximum PECsw and PECsed at STEP 1-2 is given in Table 2.8.6-12.

Table 2.8.6-12: Summary of overall maximum PEC_{SW} and PEC_{SED} of chlorothalonil metabolites R182281, R417888, R418503, R419492, following applications to cereals and tomatoes (Steps 1 & 2)

Use pattern [a]	Step	Region	R182281		R417888		R418503		R419492	
			Max. PEC_{SW} [µg/L][a]	Max. PEC_{SED} [µg/kg][a]	Max. PEC_{SW} [µg/L][a]	Max. PEC_{SED} [µg/kg][a]	Max. PEC_{SW} [µg/L][a]	Max. PEC_{SED} [µg/kg][a]	Max. PEC_{SW} [µg/L][a]	Max. PEC_{SED} [µg/kg][a]
Winter cereals 1 x 750 BBCH 30	1	-	51.8	200	64.5	4.49	20.5	0.021	43.7	0
	2	North Europe	6.97	26.5	6.40	0.446	1.87	0.002	4.34	0
		South Europe	11.8	45.4	12.8	0.893	3.74	0.004	8.68	0
Winter cereals 2 x 750	1	-	104	399	129	8.99	40.9	0.041	87.5	0
	2	North Europe	13.1	49.9	12.7	0.882	3.23	0.003	8.57	0

Use pattern [a]	Step	Region	R182281		R417888		R418503		R419492	
			Max. PEC_{SW} [µg/L][a]	Max. PEC_{SED} [µg/kg][a]	Max. PEC_{SW} [µg/L][a]	Max. PEC_{SED} [µg/kg][a]	Max. PEC_{SW} [µg/L][a]	Max. PEC_{SED} [µg/kg][a]	Max. PEC_{SW} [µg/L][a]	Max. PEC_{SED} [µg/kg][a]
BBCH 30		South Europe	22.4	86.5	25.3	1.76	6.45	0.007	17.1	0
Spring cereals 1 x 750 BBCH 30	1	-	51.8	200	64.5	4.49	20.5	0.021	43.7	0
	2	North Europe	6.97	26.5	6.40	0.446	1.87	0.002	4.34	0
		South Europe	11.8	45.4	12.8	0.893	3.74	0.004	8.68	0
Spring cereals 2 x 750 BBCH 30	1	-	104	399	129	8.99	40.9	0.041	87.5	0
	2	North Europe	13.1	49.9	12.7	0882	3.23	0.003	8.57	0
		South Europe	22.4	86.5	25.3	1.76	6.45	0.007	17.1	0
Tomatoes 1 x 1000 BBCH 51	1	-	69.0	266	85.9	5.99	27.3	0.027	58.3	0
	2	North Europe	6.74	25.3	5.12	0.357	1.50	0.002	3.47	0
		South Europe	8.66	32.9	7.68	0.536	2.24	0.002	5.21	0

[a.] Applications to winter cereals are assumed to occur during the March to May period and spring cereals during the June to September period in NEU and the March to May period in the SEU.

Continued……Table 2.8.6-12: Summary of overall maximum PEC_{SW} and PEC_{SED} of chlorothalonil metabolites R471811, SYN507900, SYN546671 and SYN546872 following applications to cereals and tomatoes (Steps 1 & 2)

Use pattern [a]	Step	Region	R471811		SYN507900		SYN546671		SYN546872	
			Max. PEC_{SW} [µg/L][a]	Max. PEC_{SED} [µg/kg][a]	Max. PEC_{SW} [µg/L][a]	Max. PEC_{SED} [µg/kg][a]	Max. PEC_{SW} [µg/L][a]	Max. PEC_{SED} [µg/kg][a]	Max. PEC_{SW} [µg/L][a]	Max. PEC_{SED} [µg/kg][a]
Winter cereals 1 x 750 BBCH 30	1	-	41.3	0	14.2	2.23	0.896	0	106	0
	2	North Europe	4.12	0	1.40	0.220	0.895	0	10.6	0
		South Europe	8.23	0	2.80	0.440	0.895	0	21.1	0
Winter cereals 2 x 750 BBCH 30	1	-	82.7	0	28.4	4.45	1.79	0	212	0
	2	North Europe	8.17	0	2.75	0.432	1.22	0	21.1	0
		South Europe	16.3	0	5.50	0.864	1.22	0	42.1	0
Spring cereals 1 x 750 BBCH 30	1	-	41.3	0	14.2	2.23	0.896	0	106	0
	2	North Europe	4.12	0	1.40	0.220	0.895	0	10.6	0
		South Europe	8.23	0	2.80	0.440	0.895	0	21.2	0
Spring cereals 2 x 750 BBCH 30	1	-	82.7	0	28.4	4.45	1.79	0	212	0
	2	North Europe	8.17	0	2.75	0.432	1.22	0	21.1	0
		South Europe	16.3	0	5.50	0.864	1.22	0	42.1	0

Use pattern [a]	Step	Region	R471811		SYN507900		SYN546671		SYN546872	
			Max. PEC_{SW} [µg/L][a]	Max. PEC_{SED} [µg/kg][a]	Max. PEC_{SW} [µg/L][a]	Max. PEC_{SED} [µg/kg][a]	Max. PEC_{SW} [µg/L][a]	Max. PEC_{SED} [µg/kg][a]	Max. PEC_{SW} [µg/L][a]	Max. PEC_{SED} [µg/kg][a]
Tomatoes 1 x 1000 BBCH 51	1	-	55.1	0	18.9	2.97	1.19	0	142	0
	2	North Europe	3.29	0	1.12	0.176	1.19	0	8.47	0
		South Europe	4.94	0	1.68	0.264	1.19	0	12.7	0

[a.] Applications to winter cereals are assumed to occur during the March to May period and spring cereals during the June to September period in NEU and the March to May period in the SEU.

Continued……Table 2.8.6-12: Summary of overall maximum PEC_{SW} and PEC_{SED} of chlorothalonil metabolites SYN546934, R611965, R611966 and R611967 following applications to cereals and tomatoes (Steps 1 & 2)

Use pattern [a]	Step	Region	SYN546934		R611965		R611966		R611967	
			Max. PEC_{SW} [µg/L][a]	Max. PEC_{SED} [µg/kg][a]	Max. PEC_{SW} [µg/L][a]	Max. PEC_{SED} [µg/kg][a]	Max. PEC_{SW} [µg/L][a]	Max. PEC_{SED} [µg/kg][a]	Max. PEC_{SW} [µg/L][a]	Max. PEC_{SED} [µg/kg][a]
Winter cereals 1 x 750 BBCH 30	1	-	0.481	0	33.0	2.34	14.8	34.6	23.6	55.4
	2	North Europe	0.480	0	3.27	0.232	1.69	3.92	2.06	4.85
		South Europe	0.480	0	6.54	0.464	3.09	7.21	4.13	9.70
Winter cereals 2 x 750 BBCH 30	1	-	0.961	0	66.0	4.69	29.6	69.2	47.2	111
	2	North Europe	0.845	0	6.42	0.456	3.16	7.34	3.36	7.89
		South Europe	0.845	0	12.8	0.912	5.82	13.6	6.72	15.8
Spring cereals 1 x 750 BBCH 30	1	-	0.481	0	33.0	2.34	14.8	34.6	23.6	55.4
	2	North Europe	0.480	0	3.27	0.232	1.69	3.92	2.06	4.85
		South Europe	0.480	0	6.54	0.464	3.09	7.21	4.13	9.70
Spring cereals 2 x 750 BBCH 30	1	-	0.961	0	66.0	4.69	29.6	69.2	47.2	111
	2	North Europe	0.845	0	6.42	0.456	3.16	7.34	3.36	7.89
		South Europe	0.845	0	12.8	0.912	5.82	13.6	6.72	15.8
Tomatoes 1 x 1000 BBCH 51	1	-	0.641	0	44.0	3.13	19.8	46.1	31.4	73.9
	2	North Europe	0.641	0	2.61	0.186	1.51	3.46	1.65	3.88
		South Europe	0.641	0	3.92	0.278	2.07	4.78	2.48	5.82

[a.] Applications to winter cereals are assumed to occur during the March to May period and spring cereals during the June to September period in NEU and the March to May period in the SEU.

Continued…….Table 2.8.6-12: Summary of overall maximum PEC_{SW} and PEC_{SED} of chlorothalonil metabolites R611968, R613636, R613801 and R613841 following applications to cereals and tomatoes (Steps 1 & 2)

Use pattern [a]	Step	Region	R611968		R613636		R613801		R613841	
			Max. PEC_{SW} [µg/L][a]	Max. PEC_{SED} [µg/kg][a]	Max. PEC_{SW} [µg/L][a]	Max. PEC_{SED} [µg/kg][a]	Max. PEC_{SW} [µg/L][a]	Max. PEC_{SED} [µg/kg][a]	Max. PEC_{SW} [µg/L][a]	Max. PEC_{SED} [µg/kg][a]
Winter cereals 1 x 750 BBCH 30	1	-	15.9	2.50	24.6	55.9	0.835	0	2.63	0
	2	North Europe	1.51	0.236	4.84	10.8	0.835	0	2.63	0
		South Europe	3.01	0.473	6.78	15.4	0.835	0	2.63	0
Winter cereals 2 x 750 BBCH 30	1	-	31.8	4.99	49.3	112	1.67	0	5.26	0
	2	North Europe	2.75	0432	8.48	19.0	0.982	0	4.23	0
		South Europe	5.50	0.864	11.9	26.9	0.982	0	4.23	0
Spring cereals 1 x 750 BBCH 30	1	-	15.9	2.05	24.6	55.9	0.835	0	2.63	0
	2	North Europe	1.51	0.236	4.84	10.8	0.835	0	2.63	0
		South Europe	3.01	0.473	6.78	15.4	0.835	0	2.63	0
Spring cereals 2 x 750 BBCH 30	1	-	31.8	4.99	49.3	112	1.67	0	5.26	0
	2	North Europe	2.75	0.432	8.48	19.0	0.982	0	4.23	0
		South Europe	5.50	0.864	11.9	26.9	0.982	0	4.23	0
Tomatoes 1 x 1000 BBCH 51	1	-	21.2	3.33	32.9	74.6	1.11	0	3.51	0
	2	North Europe	1.20	0.189	5.42	12.0	1.11	0	3.51	0
		South Europe	1.81	0.284	6.19	13.8	1.11	0	3.51	0

[a.] Applications to winter cereals are assumed to occur during the March to May period and spring cereals during the June to September period in NEU and the March to May period in the SEU.

Continued……..Table 2.8.6-12: Summary of overall maximum PEC_{SW} and PEC_{SED} of chlorothalonil metabolites R613842, postulated isomer 2 (R182281 isomer), PD1 and PD2 following applications to cereals and tomatoes (Steps 1 & 2)

Use pattern [a]	Step	Region	R613842		Postulated isomer 2/R950107 (R182281 isomer)		PD1		PD2	
			Max. PEC_{SW} [µg/L][a]	Max. PEC_{SED} [µg/kg][a]	Max. PEC_{SW} [µg/L][a]	Max. PEC_{SED} [µg/kg][a]	Max. PEC_{SW} [µg/L][a]	Max. PEC_{SED} [µg/kg][a]	Max. PEC_{SW} [µg/L][a]	Max. PEC_{SED} [µg/kg][a]
Winter cereals 1 x 750 BBCH 30	1	-	0.897	0	0.655	0	0.565	0	1.13	0
	2	North Europe	0.897	0	0.655	0	0.565	0	1.13	0
		South Europe	0.897	0	0.655	0	0.565	0	1.13	0

Use pattern [a]	Step	Region	R613842		Postulated isomer 2/R950107 (R182281 isomer)		PD1		PD2	
			Max. PEC_{SW} [µg/L][a]	Max. PEC_{SED} [µg/kg][a]	Max. PEC_{SW} [µg/L][a]	Max. PEC_{SED} [µg/kg][a]	Max. PEC_{SW} [µg/L][a]	Max. PEC_{SED} [µg/kg][a]	Max. PEC_{SW} [µg/L][a]	Max. PEC_{SED} [µg/kg][a]
Winter cereals 2 x 750 BBCH 30	1	-	1.79	0	1.31	0	1.13	0	2.27	0
	2	North Europe	1.39	0	1.15	0	0.994	0	1.99	0
		South Europe	1.39	0	1.15	0	0.994	0	1.99	0
Spring cereals 1 x 750 BBCH 30	1	-	0.897	0	0.655	0	0.565	0	1.13	0
	2	North Europe	0.897	0	0.655	0	0.565	0	1.13	0
		South Europe	0.897	0	0.655	0	0.565	0	1.13	0
Spring cereals 2 x 750 BBCH 30	1	-	1.79	0	1.31	0	1.13	0	2.27	0
	2	North Europe	1.39	0	1.15	0	0.994	0	1.99	0
		South Europe	1.39	0	1.15	0	0.994	0	1.99	0
Tomatoes 1 x 1000 BBCH 51	1	-	1.20	0	0.874	0	0.754	0	1.51	0
	2	North Europe	1.20	0	0.873	0	0.754	0	1.51	0
		South Europe	1.20	0	0.873	0	0.754	0	1.51	0

[a.] Applications to winter cereals are assumed to occur during the March to May period and spring cereals during the June to September period in NEU and the March to May period in the SEU.

Continued……Table 2.8.6-12: Summary of overall maximum PEC_{SW} and PEC_{SED} of chlorothalonil metabolites PD3, PD4 and PD5 following applications to cereals and tomatoes (Steps 1 & 2)

Use pattern [a]	Step	Region	PD3		PD4		PD5	
			Max. PEC_{SW} [µg/L][a]	Max. PEC_{SED} [µg/kg][a]	Max. PEC_{SW} [µg/L][a]	Max. PEC_{SED} [µg/kg][a]	Max. PEC_{SW} [µg/L][a]	Max. PEC_{SED} [µg/kg][a]
Winter cereals 1 x 750 BBCH 30	1	-	0.787	0	1.18	0	2.24	0
	2	North Europe	0.787	0	1.18	0	2.24	0
		South Europe	0.787	0	1.18	0	2.24	0
Winter cereals 2 x 750 BBCH 30	1	-	1.57	0	2.36	0	4.47	0
	2	North Europe	1.38	0	2.08	0	3.93	0
		South Europe	1.38	0	2.08	0	3.93	0
Spring cereals 1 x 750 BBCH 30	1	-	0.787	0	1.18	0	2.24	0
	2	North Europe	0.787	0	1.18	0	2.24	0
		South Europe	0.787	0	1.18	0	2.24	0
Spring cereals 2 x 750	1	-	1.57	0	2.36	0	4.47	0
	2	North Europe	1.38	0	2.08	0	3.93	0

Use pattern [a]	Step	Region	PD3		PD4		PD5	
			Max. PEC_{SW} [µg/L][a]	Max. PEC_{SED} [µg/kg][a]	Max. PEC_{SW} [µg/L][a]	Max. PEC_{SED} [µg/kg][a]	Max. PEC_{SW} [µg/L][a]	Max. PEC_{SED} [µg/kg][a]
BBCH 30		South Europe	1.38	0	2.08	0	3.93	0
Tomatoes 1 x 1000 BBCH 51	1	-	1.05	0	1.58	0	2.98	0
	2	North Europe	1.05	0	1.58	0	2.98	0
		South Europe	1.05	0	1.58	0	2.98	0

[a.] Applications to winter cereals are assumed to occur during the March to May period and spring cereals during the June to September period in NEU and the March to May period in the SEU.

PEC air

Due to the low volatility in the atmosphere, the PEC_A is estimated to be negligible and therefore long-range transport is not considered to be of relevance for all products and uses considered.

Other routes of exposure

For the proposed uses in cereals and tomatoes (and potatoes, only for applicant Oxon) other routes of exposure can be excluded (no seed treatment, no indoor use).

2.9 Effects on non-target species

2.9.1 Summary of effects on birds and other terrestrial vertebrates

Species	Endpoint	Value [mg a.s./kg bw (/d)]	Old/new dossier	Reference
Birds				
Chlorothalonil				
Acute oral (gavage)				
Anas platyrhynchos (mallard duck)	14d LD_{50}	**> 2000**	Old: DAR 2000 & Review report Chlorothalonil,	Hakin (1992) CA 8.1.1.1/01
Anas platyrhynchos (mallard duck)	8d LD_{50}	> 4640	Old: DAR 2000 & Review report Chlorothalonil,	Beavers and Fink (1977) CA 8.1.1.1/02
Coturnix japonica (japanese quail)	14d LD_{50}	> 200	Old: DAR 2000 & Review report Chlorothalonil,	Shults et al. (1987) CA 8.1.1.1/03
Short-term oral (dietary)				
Colinus virginianus (bobwhite quail)	5d LC_{50}	> 5200 mg/kg diet	Old: DAR 2000	Hakin et al. (1992) CA 8.1.1.2/01-02

Species	Endpoint	Value [mg a.s./kg bw (/d)]	Old/new dossier	Reference
Anas platyrhynchos (mallard duck)	5d LC_{50}	> 5200 mg/kg diet	Old: DAR 2000	Hakin et al. (1992) CA 8.1.1.2/01-02
Colinus virginianus (bobwhite quail)	5d LC_{50}	> 10000 mg/kg diet	Old: DAR 2000	Shults et al. (1979) CA 8.1.1.2/03-04
Anas platyrhynchos (mallard duck)	5d LC_{50}	> 10000 mg/kg diet	Old: DAR 2000	Shults et al. (1979) CA 8.1.1.2/03-04
Reproduction				
Colinus virginianus (bobwhite quail)	NOAEL EC_{10} EC_{20}	160 mg/kg feed **14 mg/kg bw/d**	Old: DAR 2000	Redgrave et al. (1993) CA 8.1.1.3/03
Anas platyrhynchos (mallard duck)	NOAEL EC_{10} EC_{20}	5000 mg/kg feed 500 mg/kg bw/d[b]	Old: DAR 2000	Shults et al. (1988) CA 8.1.1.3/01
Colinus virginianus (bobwhite quail)	NOAEL EC_{10} EC_{20}	1000 mg/kg feed 100 mg/kg bw/d[b]	Old: DAR 2000	Shults et al. (1988) CA 8.1.1.3/02
metabolite R182281 (SDS-3701)				
Acute oral (gavage)				
Anas platyrhynchos (mallard duck)	8d LD_{50}	**158** [b]	Old: DAR 2004	Killeen et al. (1978) CA 8.1.1.1/04
Short-term oral (dietary)				
Anas platyrhynchos (mallard duck)	5d LC_{50}	2000	Old: final DAR 2004	Beavers & Fink (1981) CA 8.1.1.2/05-06
Colinus virginianus (bobwhite quail)	5d LC_{50}	1780	Old: final DAR 2004	Beavers & Fink (1981) CA 8.1.1.2/05-06
Reproduction				
Anas platyrhynchos (mallard duck)	NOEC EC_{10} EC_{20}	50 mg/kg feed **7 mg/kg bw/d**	Old: DAR 2000	Shults et. al. (1988) CA 8.1.1.3/04
Colinus virginianus (bobwhite quail)	NOEC EC_{10} EC_{20}	250 mg/kg feed 25 mg/kg bw/d[b] (highest tested dose)	Old: DAR 2000	Shuts et. al. (1988) CA 8.1.1.3/05
Formulation (Rover)				
Acute oral (gavage)				
Anas platyrhynchos (mallard duck)	14d LD_{50}	> 2000	New Study	Fairley, C. (1985); CP 10.1.1.1/01
Mammals				
Chlorothalonil				

Species	Endpoint	Value [mg a.s./kg bw (/d)]	Old/new dossier	Reference
Acute Oral				
Rat	LD_{50}♂ LD_{50}♀	**> 5000**	Old: DAR 2000	Moore, 2000; CA 6.2.1/01
Rat	LD_{50}♂ LD_{50}♀	> 10000	Old: DAR 2000	Shults, 1981a; CA 6.2.1/02
Rat	LD_{50}♂ LD_{50}♀	> 5000	Old: DAR 2000	Cummins, 1988a; CA 6.2.1/03
Mouse	LD_{50}♂ LD_{50}♀	> 5000	Old: DAR 2000	Cummins 1989; CA 6.2.1/04
Rat	LD_{50}♂ LD_{50}♀	> 5000	Old: DAR 2000	Apte, 1992; CA 6.2.1/05
Mouse	LD_{50}♂ LD_{50}♀	> 5000	Old: DAR 2000	Apte, 1992; CA 6.2.1/06
Reproduction				
Rat	$NOAEL_{parental}$ $NOAEL_{developmental}$ $NOAEL_{reproductive}$	< 22.6 **22.6** 145.1[a]	Old: DAR 2000	Lucas et. al., 1990; CA 6.6.1.1/01
Rat	$NOAEL_{parental}$ $NOAEL_{developmental}$ $NOAEL_{reproductive}$	< 32.7 <32.7 261[a]	Old: DAR 2000	Myers et. al., 1995; CA 6.6.1.1/02
Developmental				
Rabbit	$NOAEL_{parental}$ $NOAEL_{developmental}$	10 20	Old: DAR 2000	Wilson, 1988i; CA 6.6.2.4/01
Rabbit	$NOAEL_{parental}$ $NOAEL_{developmental}$	10 20	Old: DAR 2000	Meyers, 1994c; CA 6.6.2.4/02
Rat	$NOAEL_{parental}$ $NOAEL_{developmental}$	<25 100	Old: DAR 2000	Mizens, 1983; CA 6.6.2.4/03
Rat	$NOAEL_{parental}$ $NOAEL_{developmental}$	80 <80	Old: DAR 2000	Meyers, 1994b; CA 6.6.2.4/04
Mouse	$NOAEL_{parental}$ $NOAEL_{developmental}$	100 100	New Study	Farag et al., 2006; CA 6.6.2.6
metabolite R182281 (SDS-3701)				
Acute Oral				
Rat	LD_{50}	332	Old: DAR 2000	Wazeter, 1971a CA 6.8.1-6.2.1
Rat	LD_{50}♂ LD_{50}♀	422 **242**	Old: DAR 2000	Hastings, 1973 CA 6.8.1-6.2.3

Species	Endpoint	Value [mg a.s./kg bw (/d)]	Old/new dossier	Reference
Rat	LD_{50}	50-300	New study	Beerens-Heijnen, 2005 CA 6.8.1-6.2.4
Reproduction				
Rat (1-generation)[c]	$NOAEL_{parental}$ $NOAEL_{developmental}$ $NOAEL_{reproductive}$	3 **1.5** 6	Old: DAR 2000	Ford et. al., 1982c; CA 6.8.1-6.6.1.1
Developmental				
Rabbit	$NOAEL_{parental}$ $NOAEL_{developmental}$	2.5 2.5	Old: DAR 2000	Wazeter, 1976b; CA 6.8.1-6.6.1.2.1
Rat	$NOAEL_{parental}$ $NOAEL_{developmental}$	5 5	Old: DAR 2000	Killeen, 1998; CA 6.8.1-6.6.1.2.2
Rat	$NOAEL_{parental}$ $NOAEL_{developmental}$	5 5	Old: Addendum 14 to the DAR (2004)	Schroeder, 1998; CA 6.8.1-6.6.1.2.3
A14111B				
Rat	Oral LD_{50}	Not certain (> 2000 likely)	New Study	Kuhn, 2004; CP 6.1.1
Chlorothalonil 500 g/L				
Rat	Oral LD_{50}	> 4000	Old: DAR 2000	Nunziata, 1982a; CP 6.1.1
Chlorothalonil 500 g/L SC (ARY-0474-001)				
Rat	Oral LD_{50}	> 2000	New Study	Clouzeau, 1988; CP 6.1.1.

ahighest tested dose

b based on default value of 10 from mg/kg diet to mg/kg bw/d

cstudy performed as a follow up to a 3-generation study where the NOAEL for parental/development was < 10 mg/kg food based on lower mean body weight of pups in all generations. The follow-up study was conducted to better define the NOAEL.

Discussion of endpoints to be used in the risk assessment

The endpoints for birds used in risk assessment are as shown in **bold** in the table above, and are the same as those in the original DAR for chlorothalonil. The applicant used values of 16 mg/kg bw/d and 5 mg/kg bw/d, based on the default conversion factor from the EFSA (2009) Guidance, however, the RMS uses the values from the original DAR, which were based upon actual food consumption in the studies.

In the original DAR (2000), the wild mammalian endpoint for chronic/reproductive toxicity was based on the value of 10 mg/kg bw/d from Meyers, 1994c; CA 6.6.2.4/02, a developmental toxicity study in rabbits. The notifier argues that:

…the LOAEL was defined as 20 mg/kg bwt/day for dams based on a significant reduction in food consumption and bodyweight gain and as 20 mg/kg bwt/day for developmental effects based on an increased incidence of rudimentary ribs, reduced sternebrae and other indications of delayed ossification of the skeleton. A slightly higher incidence of post-implantation loss at 20 mg/kg/day in the Myers study was considered to be within the incidence normally seen in rabbits.
A choice of 10 mg/kg bwt/day as the NOEC for ecological risk assessment is considered inappropriate. The developmental finding of reduce sternebrae and rudimentary ribs seen in the Myers study are considered likely attributable to delays in the normal ossification pattern of the skeleton. An effect on ossification was seen at the same dose level in the Wilson study. Such delays are often seen in highly labile areas of the skeleton in association with maternal toxicity. They are considered transitory[2] and do not impact survival of the young. Hence such finding would have no consequence on population dynamics and does not provide a basis for an ecologically relevant endpoint.
The choice of a developmental study to derive an ecologically relevant endpoint for long term risk assessment is further considered inappropriate because the study uses gavage dosing. Animals receive a bolus dose directly into the stomach once per day. This method of exposure can result in different levels of toxicity to those seen after dietary dosing which is clearly more representative of repeated wild mammal exposure.

The RMS agrees that the endpoint of 10 mg/kg bw/d from the developmental toxicity studies with rabbit is no longer valid. We agree with the notifer that this NOAEL should be 20 mg/kg bw/d (no effect at the highest tested dose) for developmental endpoints, in both developmental toxicity studies in rabbits. This has been shown in the mammalian toxicology section (CA 6). We do not agree with the notifier that it is not possible to set an endpoint for use in wild mammal risk assessment based upon a study performed via gavage dosing, though we agree that this can result in more conservative endpoints. Nonetheless, the developmental toxicity studies look at different endpoints than are investigated in the multi-generation studies, and may therefore provide better information on potentially relevant effects of the tested substance. The conservativeness of the endpoint and the relevance of the effect should be weighed.
In this case, since there were no effects on development at the highest tested dose in the developemental toxicology studies (effects on dams were seen at 10 mg/kg bw/d, relating to anorexia), we agree that the endpoint from the multigeneration study is more relevant.

Regarding the endpoint from the multigeneration study, the notifier states the following:
A relevant endpoint can be derived from the two generation study in the rat (Lucas and Killeen 1990). This study used dietary dose levels of 0, 500, 1500 and 3000 mg/kg diet (equivalent to 0, 22.6, 68 and 145 mg/kg bwt/day). There was no effect of chlorothalonil on fertility, litter size, pup survival or development. A consistently lower bodyweight was noted in pups at 3000 ppm in each of 2 litters in both generations at 21 days post partum. Although the maximum reduction compared to concurrent control values was 14% in the F1b litter and despite the fact that these animals went on to produce normal litters

[2] Palmer AK (1968) Spontanous malformations in the New Zealand White rabbit: The background to safety evaluation tests Lab. Anim. 2, 195-206

of their own, the consistency of this effect leads to the conclusion that this is potentially an ecologically significant effect. At 1500 mg/kg diet a statistically significant reduction of 8% compared to concurrent control weight was seen only in the F1b litter. The F1a litter and both F2 litters showed no significant difference from control values. There is, therefore, no consistent effect on litter weight up to day 21 post partum at 1500 mg/kg diet and this is considered to be the ecologically relevant NOEC.

The appropriate NOEC for wild mammal risk assessment of chlorothalonil is therefore 1500 mg/kg diet (68 mg/kg/bw/day).

The robustness of this endpoint is reinforced with a literature study on maternal and developmental toxicity in mice reviewed in MCA Section 5 supplement (Farag 2006), where maternal toxicity was observed at 400 and 600 mg/kg bw/day including weakness and depressed maternal activity, and reduced body weight and body weight gain. At 400 and 600 mg/kg bw/day, the number of live foetuses, early resorptions and mean foetal weight was significantly reduced. The NOAEL for maternal and developmental toxicity in this study was 100 mg/kg bw/day.

The RMS not agree with the proposal of the notifier, as although the F1a pup weight decrease had not reached siginificance, there was a clear trend, and the F1b pup weight was already statistically significantly decreased. Further, in a 2nd multigeneration study, the developmental NOAEL was set at < 32.7 mg/kg bw/d, based on gastric changes in pups in all generations at the lowest tested dose (of 32.7 mg/kg bw/d). Although these gastric changes are not considered relevant for ectoxicological risk assessment, they do show effects which may, after prolonged exposure, result in weight effects occurring at doses greater than 22.6 mg/kg bw/d. Pup weight effects were seen in the 2nd study at the next highest dose of 100 and at the highest tested dose of 261 mg/kg bw/d. Taken together, the RMS concludes that the endpoint from the 1st multigeneration study in rats, of **22.6 mg/kg bw/d** should be used in risk assessment.

2.9.2 Summary of effects on aquatic organisms

Summary of the toxicity values of the active substance chlorothalonil and the formulated products for aquatic organisms

Organism	Endpoint	Value [mg a.s./L]	Old/new dossier	Reference
chlorothalonil				
Fish				
Acute (water only tests:				
Oncorhynchus mykiss	96-h LC50	0.017	Old: DAR	CA 8.2.1/01 Douglas et al., 1992
Oncorhynchus mykiss	96-h LC50	0.039	New	CA 8.2.1/01 Peither, 2003
Salmo gairdneri	96-h LC50	0.0171	Old: DAR	CA 8.2.2.2.3/02 Davies, 1985

Organism	Endpoint	Value [mg a.s./L]	Old/new dossier	Reference
Cyprinus carpio	96-h LC50	0.060	new	CA 8.2.1/02 Douglas et al., 1992
Cyprinodon variegatus	96-h LC50	0.028	New	CA 8.2.1/02 Fournier, 2013
Galaxias maculatus	96-h LC50	0.0163	Old: DAR	CA 8.2.2.2.3/02 Davies, 1985
Galaxias truttaceus	96-h LC50	0.0189	Old: DAR	CA 8.2.2.2.3/02 Davies, 1985
Galaxias auratus	96-h LC50	0.0292	Old: DAR	CA 8.2.2.2.3/02 Davies, 1985
Gasterosteus aculeatus	96-h LC50	0.027	Old: DAR	CA 8.2.2.2.3/02 Davies, 1985
Pimephales promelas	96-h LC50	0.0226	New	Sherrard et al., 2003
Pagrus major	96-h LC50	0.035	New	Onduka et al., 2012
Fundulus heteroclitus	96-h LC50	0.061	New	Onduka et al., 2012
Acute (water/sediment tests				
Oncorhynchus mykiss	96-h LC50	0.0044	Old: DAR	CA 8.2.1/11 Forster, 1998
Chronic (water only tests):				
Oncorhynchus mykiss	21-d NOEC (juvenile growth)	0.0069	Old: DAR	CA 8.2.2/01 Douglas, 1992
Pimephales promelas	45 weeks NOEC 45 weeks EC10 (2-generation test)	0.0014 0.00142	Old: DAR	CA 8.2.2/01 Shults et al., 1980
Pimephales promelas	21-d NOEC (Fish short term reproduction assay)	<0.000078	New	CA 8.2.3/01 York, 2012
Fundulus heteroclitus	8 weeks NOEC (ELS test)	0.011	New	Onduka et al, 2012
Amphibians				
Acute				
Xenopis laevis (larvae)	96-h LC50	0.0082 and 0.0144 (2 experiments)	New	Yu et al., 2013

Organism	Endpoint	Value [mg a.s./L]	Old/new dossier	Reference
Spea multiplicata	96-h LC50	0.0107	New	Yu et al., 2013
Chronic				
Xenopis laevis	21-d NOEC	0.00061	New	CA 8.2.3/02 Lee, 2012
Invertebrates				
Acute (water-only tests)				
Daphnia magna	48-h EC50	0.054	Old: DAR	Douglas et al., 1992
Crassostrea virginica	96-h EC50	0.005	Old: DAR	Shults, 1983
Amphiascus tenuiremis	96-h LC50	0.027	New	Bejarano et al., 2005
Lampsilis siliquiidea	48-h EC50	0.040	New	Bringolf et al., 2007
Tigriopus japonicas	24-h EC50	0.016	New	Onduka et al., 2012
Ceriodaphnia dubia	96-h LC50	0.156	New	Sherrard et al., 2003
Chronic (water-only)				
Daphnia magna	21-d NOEC	0.0006	Old: DAR	Douglas et al., 1992
Mysidopsis bahia	28-d NOEC	0.0004	New	Schwader, 2014
Chronic (water/sediment (water-spiked)				
Chironomus riparius	28-d NOEC	0.040	Old: DAR	Forster, 1998
Chronic (water/sediment (sediment-spiked)				
Chironomus dilutus	10-d LC10	9.4 mg as/kg sed	New	Bradley, 2014a
Hyalella azteca	10-d NOEC	7.5 mg as/kg sed	New	Bradley, 2014b
Leptocheirus plumulosus	10-d LC10	>100 mg as/kg sed	New	Bradley, 2014c
Algae				
(water-only tests)				
Scenedesmus subspicatus	96-h EbC50 24-h ErC50	0.45 0.61	Old: DAR	Douglas, 1992
Navicula pelliculosa	72-h EbC50 ErC50	0.0051 0.013	Old: DAR	Smith, 2000

Organism	Endpoint	Value [mg a.s./L]	Old/new dossier	Reference
Navicula pelliculosa	72-h EbC50 EyC50 ErC50	0.0069 0.0074 0.025	New	Seyfried, 2007b
Anabaena flos-aquae	120-h EbC50 ErC50	0.074 0.210	Old: DAR	Smith, 1998
Anabaena flos-aquae	72-h EbC50 EyC50 ErC50	0.0527 0.0439 0.142	New	Seyfried, 2007c
Skeletonema costatum	72-h ErC50	0.95	New	Onduka et al., 2012
(water/sediment tests)				
Navicula pelliculosa	120-h EbC50 ErC50	0.069 >0.096	Old: DAR	Smith, 2000
Aquatic plants				
Lemna gibba	14-d EC50 (fronds) 14-d EC50 (dry mass)	0.720 0.510	Old: DAR	Smith, 1998
Lemna gibba	7-d EyC50 (fronds) 7-d ErC50 (fronds) 7-d EyC50 (dry mass) 7-d ErC50 (dry mass)	0.187 0.797 0.134 0.421	New	Batscher, 2007
Formulated product: A14111B (azoxystrobin/chlorothalonil SC (80/400))				

Organism	Endpoint	Value [mg a.s./L]	Old/new dossier	Reference
Oncorhynchus mykiss	96-h LC50	0.061 mg form/L (= 0.021 mg chlorothalonil/L	New	Volz, 2004
Daphnia magna	48-h EC50	0.35 mg form/L (= 0.12 mg chlorothalonil/L)	New	Volz, 2004
Pseudokirchneriella subcapitata	72-h EbC50	0.11 mg form/L (= 0.037 mg chlorothalonil/L)	New	Volz, 2004
	72-h EyC50	0.095 mg form/L (= 0.033 chlorothalonil/L)		
	72-h ErC50	0.58 mg form/L (= 0.20 mg chlorothalonil/L)		
Formulated product: BRAVO 720				
Lepomis macrochirus	96-h LC50	0.064 mg form/L (= 0.046 mg a.s./L	Old:DAR (2000)	Gelin et al., 1992
Oncorhynchus mykiss	96-h LC50	0.061 mg form/L (= 0.044 mg a.s./L	Old:DAR (2000)	Shults et al., 1994
Daphnia magna	48-h EC50	0.097 mg form/L (= 0.070 mg a.s./L)	Old:DAR (2000)	Gelin et al., 1992
Formulated product: 750 g/L WG form				

Organism	Endpoint	Value [mg a.s./L]	Old/new dossier	Reference
Oncorhynchus mykiss	96-h LC50	0.033 mg form/L (= 0.025 mg a.s./L)	Old:DAR (2001, Addendum 09)	Magor et al., 1999
Daphnia magna	48-h EC50	0.112 mg form/L (= 0.084 mg a.s./L)	Old:DAR (2001, Addendum 09)	Magor et al., 1999
Selenastrum capricornutum	72-h EbC50 72-h ErC50	0.11 mg form/L (= 0.083 mg a.s./L) 0.33 mg form/L (= 0.25 mg a.s./L)	Old:DAR (2001, Addendum 09)	Smyth et al., 1999
Formulated product: Daconil 2787 Extra				
Oncorhynchus mykiss	21-d NOEC	0.00087 mg form/L (= 0.00035 mg a.s./L)	Old: DAR (2000)	Voigt, 1989
Daphnia magna	22-d NOEC	<0.0023 (mg form/L (= <0.0009 mg a.s./L)	Old: DAR (2000)	Coenen, 1989
Formulated product: Chlorothalonil 75 WG				
Oncorhynchus mykiss	96-h LC50	0.04 mg form/L (= 0.03 mg a.s./L)	Old:DAR (2000)	Bell et al., 1995
Daphnia magna	48-h EC50	0.05 mg form/L (= 0.038 mg a.s./L)	Old:DAR (2000)	Bell et al., 1995
Selenastrum capricornutum	72-h EbC50 72-h ErC50	0.21 mg form/L (= 0.16 mg a.s./L) 0.43 mg form/L (= 0.33 mg a.s./L)	Old:DAR (2000)	Bell et al., 1995
Oncorhynchus mykiss	21-d NOEC	0.015 mg form/L (= 0.011 mg a.s./L)	Old: DAR (2000)	Bell et al., 1995

Organism	Endpoint	Value [mg a.s./L]	Old/new dossier	Reference
Daphnia magna	21-d NOEC	0.0007 mg form/L (= 0.00053 mg a.s./L)	Old: DAR (2000)	Bell et al., 1996
Formulated product: Rover 500 (= Chlorothalonil 500 g/L SC)				
Salmo gairdneri	96-h LC50	0.40 mg form/L (= 0.20 mg a.s./L)	New	Douglas, 1985
Cyprinus carpio	96-h LC50	0.21 mg form/L (= 0.11 mg a.s./L)	New	Douglas, 1986
Pseudokirchneriella subcapitata	72-h EbC50 72-h EyC50 72-h ErC50	0.042 0.035 0.43	New	Büche, 2007
Higher tier study Chlorothalonil 720 g/L SC				
Effect assessment on macroinvertebrates, zooplankton, phytoplankton, periphyton and macrophytes in outdoor mesocosm	NOEC NOEAEC	0.003 0.010	New	Tattersfield et al., 2002
Effect assessment on macrozoobenthoses, zooplankton, phytoplankton, periphyton and macrophytes in outdoor mesocosm	NOEC NOEAEC	<0.004 0.0125	New	Schäfers et al., 2005

Summary of the toxicity values of the metabolites of chrlorthalonil for aquatic organisms (endpoints in mg metabolite/L)

Organism	Endpoint	Value [mg met/L]	Old/new dossier	Reference
Metabolite SDS-3701 (R182281)				

Oncorhynchus mykiss	96-h LC50	9.1	Old: DAR	CA 8.2.1/03 Bell, 1997
Mysidopsis bahia	96-h LC50	19	New	CA 8.2.4.2/09 Putt, 1998c
Chironomus riparius	48-h EC50	76.0	Old: Addendum 1 Vol. 3 (Oct 2002)	CA 8.2.4.2/04 Putt, 2001
Metabolite SDS-46851				
Oncorhynchus mykiss	96-h LC50	>120	Old: DAR	Magor & Shillabeer, 1999
Daphnia magna	48-h EC50	>123.6	Old: DAR	Magor & Shillabeer, 2000
Daphnia magna	48-h EC50	>100	New	Volz, 2007
Selenastrum capricornutum	72-h EbC50 72-h ErC50	45 55	Old: DAR	Magor, 2000
Pseudokirchneriella subcapitata	72-h EbC50 72-h EyC50 72-h ErC50	>45 >45 >45	New	Seyfried, 2007
Metabolite R417888				
Oncorhynchus mykiss	96-h LC50	>100	Old: DAR	Magor & Shillabeer, 1999
Daphnia magna	48-h EC50	>110	Old: DAR	Magor & Shillabeer, 1999
Selenastrum capricornutum	72-h EbC50 72-h ErC50	>100 >100	Old: DAR	Magor & Shillabeer, 1999
Pseudokirchneriella subcapitata	72-h EbC50 72-h EyC50 72-h ErC50	>100 >100 >100	New	Seyfried, 2007a
Metabolite SDS-19221 (R613636)				
Oncorhynchus mykiss	96-h LC50	18	Old: DAR	Magor & Shillabeer, 1999
Daphnia magna	48-h EC50	12.4	Old: DAR	Magor & Shillabeer, 1999
Selenastrum capricornutum	72-h EbC50 72-h ErC50	5 12	Old: DAR	Magor & Shillabeer, 1999
Metabolite SDS-67042 (R613841)				
Oncorhynchus mykiss	96-h LC50	>0.83	New	O'Meara et al.,, 1996
Daphnia magna	48-h EC50	>0.94	New	O'Meara et al.,, 1996
Selenastrum capricornutum	72-h EbC50 72-h EyC50 72-h ErC50	0.00086 0.00092 >0.041	New	O'Meara et al., 1996

Pseudokirchneriella subcapitata	72-h EbC50 72-h EyC50 72-h ErC50	0.12 0.14 1.3	New	Vryenhoef, 2007a
Navicula pelliculosa	72-h EbC50 72-h EyC50 72-h ErC50	0.060 0.065 0.117	New	Vryenhoef, 2007a
Metabolite SDS-67042 Sulfoxide				
Oncorhynchus mykiss	96-h LC50	>0.99	New	O'Meara et a., 1997
Daphnia magna	48-h EC50	>0.89	New	O'Meara et al., 1997
Selenastrum capricornutum	72-h EbC50 72-h ErC50	>0.88 >0.88	New	O'Meara et al., 1997
Metabolite R613801				
Daphnia magna	48-h EC50	0.56	New	Hengsberger & Hartel, 2015
Pseudokirchneriella subcapitata	72-h EbC50 72-h EyC50 72-h ErC50	0.17 0.11 0.38	New	Hengsberger & Hartel, 2015

Selection of endpoints

The lowest acute and chronic endpoints for each taxonomic group have been chosen for risk assessment in first instance. The available data show that the formulations are not more toxic than the a.s. chlorothalonil and therefore the data on the active substance have been used for risk assessment. For the acute risk to aquatic vertebrates (fish and amphibians) a higher tier endpoint has been determined, i.e. an HC5 value, based on the available acute LC50 data for fish and amphibians.

For aquatic invertebrates and primary producers endpoint from two mesocosm studies are available and used in the risk assessment.

2.9.3 Summary of effects on arthropods

2.9.3.1 Bees

The table below presents an overview of the available toxicity data for bees.

Table 2.9.3.1-01: Overview of available toxicity data for bees

Species	Test item	Test type	Endpoint		Comments	Reference
Apis mellifera	Chlorothalonil	Acute oral	EU	48 h LD_{50} >40 µg a.s./bee	Ri = 2	***Cole (1992)*** [a]
		Acute contact		48 h LD_{50} >40 µg a.s./bee		
Apis mellifera		Acute oral		48 h LD_{50} >63 µg a.s./bee	-	***Thompson (2000)*** [b]
		Acute contact		48 h LD_{50} >101 µg a.s./bee	-	
Bombus terrestris		Acute oral	New study	96 h LD_{50} >94 µg a.s./bee	-	***Fauser-Misslin (2015)***
		Acute contact		96 h LD_{50} >100 µg a.s./bee	-	
Apis cerena indica		Acute contact	EU	24 h LD_{50} 2.6 µg a.s./bee	Ri = 2	***Dighe (1992a)*** [c]
		Adult chronic contact	EU	Moderately toxic	-	***Dighe (1992b)*** [c]
Apis mellifera	Chlorothalonil [d]	Adult chronic	New study	LC_{50} = 1779 mg a.s./kg food LD_{50} = 53.9 µg a.s./bee/day NOEC = 188 mg a.s./kg food NOED = 6.5 µg a.s./bee/day	-	***Kleebaum (2014)***
		7-day larval development	New study	7 day NOEC = 91 mg a.s./kg diet (14.5 µg total a.s./larva = 3.6 µg a.s./larva/day	-	***Kleebaum (2014)***
Apis mellifera	Chlorothalonil	6-day larval limit test	Public literature	6 day LD_{50} < 34 mg a.s/L	Ri = 2	***Zhu, et. al. (2014)***
Apis mellifera	A14111B	Acute oral	New study	LD_{50} = >917 µg/bee (> 317 µg chlorothalonil/bee)	-	***Bocksch (2004); CP B.9.5.1.1***
		Acute contact		LD_{50} >1531 µg/bee (> 523 µg chlorothalonil/bee)		
		Chronic adult	New study	NOEC = 606 mg/kg food; NOED = 29.1 µg/bee/day LD_{50} = 171 µg/bee/day	-	***Ruhland (2014); CP B.9.5.1.2***
		Larval development	New study	8 d NOEC = 198 mg/kg diet NOED =31.3 µg total prod/larva = 7.8 µg prod/larva/day	-	***Kleebaum (2015) CP B.9.5.1.3***

[a] Previous submitter = Vischim S.R.L.
[b] Previous submitter = Zeneca Agrochemicals
[c] Previous submitter = Gharda Chemicals Ltd.
[d]Tested as A7867A (formulation containing 498 g/L chlorothalonil)

2.9.3.2 **Non-target arthropods**

The table below gives an overview of the available toxicity data for non-target arthropods.

Overview of toxicity data for non-target arthropods: Tier 1 laboratory tests

Species	Exposed life stage	Study type	Application rate [kg a.s./ha]	Corrected mortality [%]	Sublethal effects [%]	Reference
BRAVO 720 g/L SC						
Typhlodromus pyri Predatory mite	protonymphs	Tier 1 laboratory test	7.7 6 1.5	5 0 0	94 94 78	Vinall, 2000 [b]
Aphidius rhopalosiphi Parasitoid	adult	Tier 1 laboratory test	0.044 0.173 1.1 4.3 7.7	5 55 41 62 55	5 - - - -	Baxter, 2000 [b]
Chrysoperla carnea	larvae	Tier 1 laboratory test	0.31 6 7.67	8 8 5	2.7 5.4 -2	Sankanu, 2000 [b]
Poecilus cupreus	adult	Tier 1 laboratory test	10.5	0	0	Baxter, 2000 [b]
Chlorothalonil 500 g/L SC						
Typhlodromus pyri Predatory mite	protonymphs	Tier 1 laboratory test	1.5	23	11	Wiles, 1997 [a]
Aphidius rhopalosiphi Parasitoid	adult	Tier 1 laboratory test	1.5	0	9	Wiles, 1997 [a]
Aleochara bilineata	adult	Tier 1 laboratory test	1.5	0	0	Wiles, 1997 [a]
Poecilus cupreus	adult	Tier 1 laboratory test	1.5	0	0	Wiles, 1997 [a]
Chlorothalonil 75 WG						

Overview of toxicity data for non-target arthropods: Tier 1 laboratory tests

Species	Exposed life stage	Study type	Application rate [kg a.s./ha]	Corrected mortality [%]	Sublethal effects [%]	Reference
Typhlodromus pyri Predatory mite	protonymphs	Tier 1 laboratory test	1.5	5	9	Kühner, 1996 [a]
Aphidius rhopalosiphi Parasitoid	adult	Tier 1 laboratory test	1.5	6.7	31	Kühner, 1996 [a]
Aleochara bilineata	adult	Tier 1 laboratory test	1.5	11	9	Kühner, 1996 [a]
Poecilus cupreus	adult	Tier 1 laboratory test	1.5	0	0	Kühner, 1996 [a]
A14111B						
Typhlodromus pyri Predatory mite	protonymphs	Tier 1 laboratory test	0.131 0.262 0.524 1.048 2.095	10 33 33 21 36	 79 77 91	Waterman, 2004 [c]
			LR50 > 2.095 kg chlorothalonil/ha	ER50 < 0.524 kg chlorothalonil/ha		
Aphidius rhopalosiphi Parasitoid	adult	Tier 1 laboratory test	0.131 0.262 0.524 1.048 2.095	19 17 58 42 50	-6 19 17 	Fussel, 2004 [c]
			LR50 > 0.262 kg chlorothalonil/ha	ER50 > 1.048 kg chlorothalonil/ha		
Metabolite SDS-3701						
Poecilus cupreus	adult	Tier 1 laboratory test	10 mg/kg soil 100 mg/kg soil	0 0	0 0	Travis, 1999 [b]
Metabolite R417888						
Poecilus cupreus	adult	Tier 1 laboratory test	100 mg/kg soil 1000 mg/kg soil	0 3	0 0	Travis, 1999 [b]

[a] DAR chloorthalonil, 2000
[b] Addendum 9 to the DAR (2001)
[c] Newly submitted

Overview of toxicity data for non-target arthropods: Extended laboratory studies

Species	Exposed life stage	Study type old/new	Application rate [kg a.s./ha]	Corrected mortality [%]	Sublethal effects [%]	Reference
BRAVO 720 g/L SC						
Typhlodromus pyri Predatory mite	protonymphs	Extended lab study on leaf discs (2-D)	1.50 1.88 5.63 12.00 18.75	0 0 9 17 13	42 47 56 49 64	Vinall, 2000 [a]
Aphidius rhopalosiphi Parasitoid (adult)	adult	Extended lab study on barley seedlings (3-D)	4.33 7.70 18.75	20 20 44	no significant effects at do-sages up to 7.70 kg as/ha (at 18.75 kg as/ha the effects of fecundity are not assessed)	Baxter, 2000 [a]
Chlorothalonil 75 WG						
Aphidius rhopalosiphi Parasitoid (adult)	adult	Extended lab study on barley seedlings (3-D)	0.47 1.5 5.4	16.7 43.3 63.3	40 50 64	Wainwright, 2003 [a]
Chlorothalonil 500 SC						
Typhlodromus pyri Predatory mite	protonymphs	Extended lab study on leaf discs (2-D)	0.047 1.5 5.4	0 12.25 9.18	20 70 75	Wainwright, 2003 [a]
Typhlodromus pyri Predatory mite	protonymphs	Extended lab study on bean leaf discs (2-D)	1.5 3.0 6.0 12.0 24.0	-3.6 -9.1 5.5 5.5 10.9 LR50 > 24 kg a.s./ha	65.1 68.7 79.9 81.2 82.0 ER50 < 1.5 kg a.s./ha	Schmidt, 2007 [b]
Aphidius	adult	Extended	1.5	-3.4	11.6	Schmidt,

rhopalosiphi Parasitoid (adult)		lab study on barley seedlings (3-D)	3.0 6.0 12.0 24.0	0 0 6.9 6.9 LR50 > 24 kg a.s./ha	13.4 21.5 82.6 43.6 ER50 > 24 kg a.s./ha	2007 [b]
A14111B						
Typhlodromus pyri Predatory mite	protonymphs	Extended lab study on leaf discs (2-D)	0.017 0.084 0.419 2.095	0 0 0 12 LR50 > 2.095 kg chlorothalonil/ha	-1 9 36 58 ER50 = 1.187 kg chlorothalonil/ha	Waterman, 2004 [b]
Aphidius rhopalosiphi Parasitoid (adult)	adult	Extended lab study on barley seedlings (3-D)	0.524 1.048 2.095	0 0 0 LR50 > 2.095 kg chlorothalonil/ha	17 27 9 ER50 > 2.095 kg chlorothalonil/ha	Fussel, 2004 [b]
Chrysoperla carnea	larvae	Extended lab study on bean leaves (2-D)	0.017 0.084 0.419 1.048 2.095	16 10 19 15 7 LR50 > 2.095 kg chlorothalonil/ha	0 0 0 ER50 > 2.095 kg chlorothalonil/ha	Douglas, 2004 [b]

[a] Addendum 14 of the DAR (2004)
[b] Newly submitted

2.9.4 Summary of effects on non-target soil meso- and macrofauna

Table 2.9.4-1: Summary of earthworm toxicity endpoints for the active substance chlorothalonil, the formulations and metabolites

Test material	Study type	Endpoint [c]	Result (mg a.s./kg soil dw)	Reference
Earthworms				
Chlorothalonil	Chronic, 8 weeks	NOEC	50 (10% o.m.)	CP 9.7.1.2 Moser, 2001 [b]
Chlorothalonil	Chronic, 8 weeks	NOEC	100 (5% o.m.)	Schmidt, 2007 [c]
BRAVO 500	Chronic, 8 weeks	NOEC	5 (5.74% o.m.)	Leitão et al., 2014 [c]
A14111B	Chronic, 8 weeks	NOEC	>27.5 (10% o.m.)	Staebler, 2004 [c]
Chlorothalonil 500 g/L SC	Chronic, 8 weeks	NOEC	1.5 (10% o.m.)	Rodgers, 2003 [c]
Chlorothalonil 500 g/L SC	Field study	Effects	Chlorothalonil did not affect total abundance and biomass of the earthworm population.	Schmidt, 2009 [c]
SDS-3701	Chronic, 8 weeks	NOEC	25 (10% o.m.)	Moser & Rombke, 2000 [b]
SDS-3701	Chronic, 8 weeks	EC10	11 (5% o.m.)	Schmidt, 2007 [c]
SDS-3701	Chronic, 8 weeks	NOEC	25 (10% o.m.)	Rodgers, 2003 [c]
R417888	Acute, 14 days	LC_{50}	> 1000 (10% o.m.)	CA 9.4.1.1/03 Travis, 1999 [a]
R417888	Chronic, 8 weeks	NOEC	100 (10% o.m.)	Moser, 2001 [b]
R417888	Chronic, 8 weeks	EC10 (body weight)	2.2 (10% o.m.)	Taylor, 2015 [c]
R417888	Chronic, 8 weeks	NOEC	12.5 (5% o.m.)	Schmidt, 2007 [c]
SDS-46851	Acute, 14 days	LC_{50}	> 1000 (10% o.m.)	CA 9.4.1.1/04 Moser & Rombke, 2000 [b]

[a] DAR chloorthalonil, 2000
[b] Addendum 14 of the DAR (2004)
[c] Newly submitted

Table 2.9.4-2: Summary of toxicity endpoints for other soil meso- and macrofauna for the active substance chlorothalonil, the formulations and metabolitesTest material	**Study type**	**Endpoint**	**Result (mg as/kg)**	**Reference**
Hypoaspis aculeifer				
Chlorothalonil 500 SC	Chronic, 14 days	NOEC	399 (5% o.m.)	CA 9.4.1.1/01 Vinall, 2014 [a]
Folsomia candida				
BRAVO 500	Chronic, 28 days	EC20	18.2 (5.74% o.m.)	Leitão et al., 2014 [a]
A14111B	Chronic, 28 days	EC10	12 (5% o.m.)	Fauser-Misslin, 2015 [a]
SDS-3701	Chronic, 28 days	NOEC	59.6 (10% o.m.)	Kölzer, 2005 [a]
VIS-01	Chronic, 28 days	EC10	3.1 (10% o.m.)	Kölzer, 2005 [a]
Litter bags				
SDS-3701	268 days	Dose rate: 3400 g SDS-3701/ha	No significant effects	Schmidt, 2009 [a]
SDS-3701	60 days	Dose rate: 2.0 mg SDS-3701/kg soil	No significant effects	Galicia, 2002 [b]

[a] Newly submitted
[b] Addendum 14 of the DAR (2004)

2.9.5 Summary of effects on soil nitrogen transformation

The table below gives an overview of the available data on soil microbial processes:

Test substance	**Endpoint**	**Effects ≤ 25% at test concentration (expressed in mg a.s./kg dry soil):**	**Reference***
Chlorothalonil	Effects on nitrogen transformation	4.4	Carter & Jackson, 1995 (Dar (2000))
Chlorothalonil		10.0	Seyfried, 2003 (New)
BRAVO 720 g/L SC		3.2 and 4.8	McMurray, 2001 (addendum 14 (DAR 2004)
A14111B		2.57	Schulz, 2010 (New)

Chlorothalonil 75 WG		3.3	Carter et al., 1995 (DAR, 2000)
SDS-3701		1.3	Carter, 1997 (DAR (2000))
SDS-3701		2.9 and 5.8	Seyfried, 2003 (New)
SDS-46851		1.25 and 2.5	Völkel, 2008 (New)
VIS-01		2.48 and 4.96	Kölzer, 2005 (New)
R417888		1.5 and 3.0	Völkel, 2008 (New)
Chlorothalonil	Effects on carbon transformation	4.4	Carter & Jackson, 1995 (Dar (2000))
Chlorothalonil		10.0	Seyfried, 2003 (New)
BRAVO 720		3.2 and 4.8	McMurray, 2001 (addendum 14 (DAR 2004)
A14111B		2.57 and 12.8	Schulz, 2010 (New)
SDS-3701		1.3	Carter, 1997 (DAR (2000))
SDS-3701		2.9 and 5.8	Seyfried, 2003 (New)
VIS-01		2.48 and 4.96	Kölzer, 2005 (New)
SDS-46851		1.25 and 2.5	Völkel, 2008 (New)
R417888		1.5 and 3.0	Völkel, 2008 (New)
SDS-3701		2.0 and 4.0	Völkel, 2006 (New)

2.9.6 Summary of effects on terrestrial non-target higher plants

Screening data

Test with chlorothalonil and the following species: *Fagopyrum esculentum; Zea mays; Cucumis sativus, Brassica kaber; Avena sativa; Allium cepa; Raphanus sativus; Sorghum bicolor; Glycine max; Lycopersicon esculentem*: NOEL (germination, emergence, vigor) is 18 kg a.s./ha. (Backus, 1992)

Laboratory dose response tests

Species	Test substance	ER_{50} vegetative vigour	ER_{50} emergence	
Avena fatua, Allium cepa, Cucumus sativus, Beta vulgaris, Brassica napus and Glycine max	A14111B[2]	>2500 mL product/ha	>2500 mL product/ha	Walder, 2004*
Avena sativa, Zea mays, Allium cepa, Glycine max, Daucus carota and Brassica oleracea	Chlorothalonil 75 WG	>4.2 kg product/ha	-	Fiebig, 2000
maize, onion, sorghum, oat, radish, white mustard , cucumber, tomato, buckwheat and soybean	Chlorothalonil 500 SC	>8000 mL product/ha	>8000 mL product/ha	Büche, 2007
Allium cepa	SDS-3701	-	143 g SDS-3701/ha (= 0.19 mg SDS-3701/kg soil	Balluf, 2005

*indicative data

2.9.7 Summary of effects on other terrestrial organisms (flora and fauna)

There are no other terrestrial organism data available at this time.

2.9.8 Summary of effects on biological methods for sewage treatment

2.9.9 Summary of product exposure and risk assessment

2.9.9.1 Birds and other terrestrial vertebrates

A risk assessment for birds from chlorothalonil and the metabolite SDS-3701 resulted in a safe use in cereals only, assuming that only 1 application is possible before BBCH 40 (according to the GAPs). The acute risk from the formulations, the active substance chlorothalonil, and the metabolite SDS-3701 was acceptable in the Tier 1 assessment. However, in the long term risk assessment, only use in cereals showed an acceptable risk to birds. The notifiers proposed several refinements, only one of which was accepted by the RMS.

The risk assessment for mammals also did not result in a safe use. The acute risk from the formulations, the active substance chlorothalonil, and the metabolite SDS-3701 was acceptable in the Tier 1 assessment. However, in the long term risk assessment, no safe use was found. The notifiers proposed several refinements, only one of which was accepted by the RMS.

The acute and long term risk to birds and mammals from drinking water and secondary poisoning were acceptable.

2.9.9.2 Aquatic organisms

Aquatic vertebrates

The acute risk to aquatic vertebrates is acceptable, based on a HC5 approach, provided that risk mitigation measures (spray drift buffer and run-off mitigation) are applied. The only scenario which does not achieve acceptable mitigation is R4 stream in spring cereals and tomatoes. For this scenario further risk reduction measures are necessary.

The chronic risk to fish is based on a NOEC of 1.4 µg a.s./L from the FFLC test with fish.
All the FOCUS Step 3 and 4 PECsw values for all uses are higher than the RAC based on the chronic NOEC and hence, there is a high chronic risk to fish. A further refinement of the chronic risk to fish is necessary.

In addition, effects on amphibians seen in the AMA indicated that the NOEC of 1.4 µg a.s./L may not be sufficiently protective of amphibians. The risk assessment could not be finalized and a LAGDA has been requested to establish an appropriate reproductive endpoint for amphibians for use in risk assessment.

Aquatic invertebrates and primary producers

The risk assessment based on first tier endpoints and FOCUS Step 3 values showed that there is a risk in case of all scenarios for all uses. Two mesocosm studies are available. Based on the ETO-RAC the risk to aquatic vertebrates is acceptable, provided that risk mitigation measures (spray drift buffer and run-off mitigation) are applied. The only scenario which does not achieve acceptable mitigation is R4 stream in spring cereals and tomatoes. For this scenario further risk reduction measures are necessary. Based on the ERO-RAC all scenarios of all uses have an acceptable risk with consideration given to appropriate mitigation requirements.

2.9.9.3 Non-target arthropods

2.9.9.3.1 Bees

All proposed uses resulted in acceptable risks for bees for acute oral and contact exposure, as well as from chronic adult exposures. The risk to larvae from the formulation A14111B was acceptable, but the risk to larvae from the other two formulations could not be finalized. Further, the risk to bees from the relevant plant metabolite, SDS-3701 could not be finalized.

2.9.9.3.2 Other non-target arthropods

All proposed uses of the product A14111B resulted in acceptable in-field and off-field risks for non-target arthropods.
With respect to the proposed uses of the product Chlorothalonil 500 g/L SC it was not possible to conclude on the in-field risk, due to reproduction effects > 50% for *T. pyri* at the lowest tested dose of 1.5 kg as/ha., indicating the need for further refinement of the risk. The off-field risk was considered to be acceptable.

2.9.9.4 Soil meso and macro organisms

Earthworms

All proposed uses of the product A14111B have an acceptable acute and chronic risk to earthworms for chlorothalonil, the formulation and the metabolites R182281 and R417888.

All proposed uses of the product Chlorothalonil 500 g/L SC have an an acceptable acute and chronic risk to earthworms for chlorothalonil and the metabolites R182281 and R417888, assuming acceptable methods validation is submitted for the earthworm field study.

Furthermore, the acute risk from the metabolite R611965 is also acceptable (no chronic data for this metabolite). However, ten relevant soil metabolites are identified and it is concluded that more data or argumentation is necessary with respect to the non-tested soil metabolites.

Non-target soil meso- and macrofauna (other than earthworms)

All proposed uses of the product A14111B have an acceptable chronic risk to *Folsomia candida* for the formulation and the metabolites R182281 and R417888.

All proposed uses of the product Chlorothalonil 500 g/L SC have an an acceptable chronic risk to *Folsomia candida* and *Hypoaspis aculeifer* for the formulation and the metabolites R182281 and R417888.

However, ten relevant soil metabolites are identified and it is concluded that more data or argumentation is necessary with respect to the non-tested soil metabolites. The notifiers have indicated this data will be available in December 2016.

2.9.9.5 Soil nitrogen transformation

The risk from chlorothalonil, the product A14111B and the metabolites R182281, R417888 and R611965 for soil nitrogen transformation is acceptable for all uses. Further argumentation or data on soil metabolites not tested yet, regarding the risk to soil nitrogen transformation, is considered necessary. The notifier(s) have indicated that this data will be available in December 2016.

2.9.9.6 Terrestrial non-target plants

The risk from the products A14111B and Chlorothalonil 500 g/L SC and the metabolite SDS-3701 for terrestrial non-target plants is acceptable for all uses.

2.10 Classification and labelling

The following structured tables - in line with the ECHA-report- should be included here.

Proposed classification according to Regulation (EC) No 1272/2008 on the classification, labelling and packaging of substances and mixtures

CLP Annex I ref	Hazard class	Proposed classification	Proposed SCLs and/or M-factors	Current classification [1)]	Reason for no classification [2)]
2.1.	Explosives				
2.2.	Flammable gases				
2.3.	Flammable aerosols				

2.4.	Oxidising gases				
2.5.	Gases under pressure				
2.6.	Flammable liquids				
2.7.	Flammable solids				
2.8.	Self-reactive substances and mixtures				
2.9.	Pyrophoric liquids				
2.10.	Pyrophoric solids				
2.11.	Self-heating substances and mixtures				
2.12.	Substances and mixtures which in contact with water emit flammable gases				
2.13.	Oxidising liquids				
2.14.	Oxidising solids				
2.15.	Organic peroxides				
2.16.	Substance and mixtures corrosive to metals				
3.1.	Acute toxicity - oral				
	Acute toxicity - dermal				
	Acute toxicity - inhalation	H330		H330	
3.2.	Skin corrosion / irritation				
3.3.	Serious eye damage / eye irritation	H318		H318	
3.4.	Respiratory sensitisation				
3.4.	Skin sensitisation	H317		H317	
3.5.	Germ cell mutagenicity				
3.6.	Carcinogenicity	Cat 2 H351		Cat 2 H351	
3.7.	Reproductive toxicity				
3.8.	Specific target organ toxicity –single exposure	STOT SE 3 H335		STOT SE 3 H335	
3.9.	Specific target organ toxicity – repeated exposure				
3.10.	Aspiration hazard				
4.1.	Hazardous to the aquatic environment			Acute: H400 Chronic: H410 M=10	
5.1.	Hazardous to the ozone layer				

[1)] Including specific concentration limits (SCLs) and M-factors
[2)] Data lacking, inconclusive, or conclusive but not sufficient for classification

Labelling: Signal word:

Hazard statements:

Precautionary statements:

Proposed notes assigned to an entry:

Notes in accordance with CLP Regulation, Annex VI, Section 1.1.3

2.11 Relevance of metabolites in groundwater

2.11.1 STEP 1: Exclusion of degradation products of no concern

2.11.2 STEP 2: Quantification of potential groundwater contamination

Step 2 of the guidance document (SANCO/221/2000) requires consideration of FOCUS groundwater models and scenarios and results of lysimeter studies:
SANCO/221/2000: - All metabolites not excluded in Step 1 that are found in soil degradation and/or available lysimeter or field leaching studies should in principle be characterised and identified by the notifiers to the extent that is technically feasible. For these metabolites the predicted environmental concentration in groundwater needs to be estimated.

Lysimeter Study

Two lysimeter studies have been conducted following application of chlorothalonil. The results of the lysimeter show that parent chlorothalonil was not detected in the leachate. A total of twelve metabolites were identified as exceeding 0.1 µg/l on an annual average basis, all of which had also been detected in soil metabolism studies with the exception of five metabolites which were unique to the lysimeter leachate: SYN548008, SYN548580 and SYN548581, M7 and M10. No metabolites reached an annual average leachate concentration of >10 µg/L. Seven of the metabolites reached an annual average concentration above 0.75 µg/L during the first year after application.

Modelling

FOCUS modelling results (PEARL, 2x 750 g a.s./ha to winter cereals, covering the other uses) are presented below for chlorothalonil metabolites. Details on input parameters, scenario's etc. can be found in section 2.8.6 or in Volume 3 CP Section B.8.
For metabolites, based on the results of the lysimeter study (as trigger for potential further assessment) and the FOCUS groundwater modelling, it is concluded that a maximum annual average concentration of ≥ 0.1 µg/L in groundwater cannot be ruled out for selected chlorothalonil metabolites listed in Table 2.11.2-1, shown below, and should be considered further in the non-relevance assessment.

Table 2.11.2-1: Metabolites included for Higher Tier Risk Assessment (groundwater monitoring analysis) according to results of the soil metabolism studies, lysimeter studies and FOCUS modelling results.

Metabolite Reference	Max in Soil (% AR)	Lysimeter Leachate [max mean annual conc µg/L]	Max* FOCUS PEC_{GW} [µg/L]	To be Considered Further in the Non-Relevance Assessment	
			Winter Cereals (2 x 750)	Yes/No	Comments
Chlorothalonil	--	nd	<0.001	No	Parent compound
R182281	32	nd	0.0125	No	not detected in lysimeter leachate (higher-tier study)
R417888	20.7	7.5	23.49	**Yes**	Detected in lysimeter study
R418503	6.1	1.5	1.20	**Yes**	Detected in lysimeter study
R419492	12.4	3.3	44.27	**Yes**	Detected in lysimeter study
R471811	11.9	1.9	33.41	**Yes**	Detected in lysimeter study
SYN507900	5.8[b]	--	26.10	**Yes**	FOCUS modelling >0.1 ug/L
SYN548008 (M3) (Tier II)	--	3.7	10.24	**Yes**	Detected in lysimeter study
SYN548580 (M2) (Tier II)	--	0.5	10.45	**Yes**	Detected in lysimeter study
SYN548581 (M11) (Tier II)	--	0.3	<0.001	No	Detected in lysimeter study
R611965	13.2	1.3	22.37	**Yes**	Detected in lysimeter study
R611966	8.1[b]	--	<0.001	No	not detected in lysimeter leachate (higher-tier study)
R611967	13.2	--	<0.001	No	not detected in lysimeter leachate (higher-tier study)
R611968	6.5[a]	0.7	4.18	**Yes**	Detected in lysimeter study
R613636	10.4	0.2	<0.001	No	Detected in lysimeter study
M7 (Tier II)	--	1.2	4.63	Not possible	Structure of metabolite not identified
M10 (Tier II)	--	0.5	1.90	Not possible	Structure of metabolite not identified

*Value taken from RMS recalculation of the twofold application in winter cereals, FOCUS-PEARL 4.4.4 modelling.
[a] Metabolite occurs at >5% on only one occasion
[b] Metabolite occurs at >5% on two occasions
-- not observed

Maximum levels found in monitoring studies.

For detailed decription of the monitoring program and results see section 2.8.7 or Volume 3 CA, B.8.5. A summary of the maximum values found at the 18 acceptable German sites is given in Table 2.11.2-2 below.

Table 2.11.2-2: Maximum individual values and maximum annual means for chlorothalonil and metabolites R417888, R611965, R419492 and R471811 monitored at individual groundwater monitoring wells in the region Schleswig-Holstein, Mecklenburg-West Pomerania, Thuringian Basin and Rottal, Germany (maximum individual and annual mean detections highlighted in bold)

	Substance Detected (max. conc. µg/L/annual mean µg/L)				
Location	**Chlorothalonil**	**R417888**	**R611965**	**R419492**	**R471811**
Soenderby (SH)	<0.05/<0.05	8.28/2.52	<0.05/<0.05	10.71/**9.29**	7.97/4.75
Rohlstorf (SH)	<0.05/<0.05	1.53/0.73	<0.05/<0.05	6.03/3.13	2.68/1.81
Wahlstedt (SH)	<0.05/<0.05	**8.93**/6.24	<0.05/<0.05	5.47/2.15	4.88/1.47
Schlamersdorf (SH)	<0.05/<0.05	0.4/0.33	<0.05/<0.05	2.29/2.02	1.28/1.11
Ekelsdorf (SH)	<0.05/<0.05	7.86/**6.69**	<0.05/<0.05	**10.77**/7.26	**11.73/5.55**
Kittlitz (SH)	<0.05/<0.05	0.06/0.03	<0.05/<0.05	0.22/0.11	0.07/0.05
Torgelow (MWP)	<0.05/<0.05	<0.05/<0.05	<0.05/<0.05	<0.05/<0.05	<0.05/<0.05
Reez (MWP)	<0.05/<0.05	<0.05/<0.05	<0.05/<0.05	<0.05/<0.05	<0.05/<0.05
Warnow (MWP)	<0.05/<0.05	<0.05/<0.05	<0.05/<0.05	<0.05/<0.05	<0.05/<0.05
Pinnow (MWP)	<0.05/<0.05	<0.05/<0.05	<0.05/<0.05	<0.05/<0.05	<0.05/<0.05
Luettow (MWP)	<0.05/<0.05	<0.05/<0.05	<0.05/<0.05	<0.05/<0.05	<0.05/<0.05
Gispersleben (TB)	<0.05/<0.05	<0.05/<0.05	<0.05/<0.05	0.27/<0.05	<0.05/<0.05
Schillingstedt (TB)	<0.05/<0.05	<0.05/<0.05	<0.05/<0.05	<0.05/<0.05	<0.05/<0.05
Spring Backleben (TB)	<0.05/<0.05	<0.05/<0.05	<0.05/<0.05	<0.05/<0.05	0.11/<0.05
Tabeckendorf (R)	<0.05/<0.05	<0.05/<0.05	<0.05/<0.05	0.09/0.056	0.14/0.10
Postmuenster (R)	<0.05/<0.05	<0.05/<0.05	<0.05/<0.05	0.09/0.056	0.06/0.02
Kirchham-Pfaffenhof (R)	<0.05/<0.05	<0.05/<0.05	<0.05/<0.05	0.2/0.09	0.13/0.12
Spring Simback-Stolln (R)	<0.05/<0.05	0.71/0.4	<0.05/<0.05	0.78/0.06	1.84/1.15

Limit of quantitation (LOQ): 0.05 ug/L for all substances
SH = Schleswig-Holstein; MWP = Mecklenburg-West Pomerania, TB = Thuringian Basin, R = Rottal

Based on the monitoring data, it can be concluded that residues of parent chlorothalonil and metabolite R611965 are not present in groundwater in concentrations above the limit of 0.1 µg/L. It is also unlikely

that the remaining monitored metabolites of chlorothalonil (R417888, R419492 and R471811) are present in groundwater above an annual average value of 10 µg/L in the monitored agricultural regions with a long-term history of chlorothalonil use and in comparable extreme worst-case scenarios. The data presented above shows that under extremes of groundwater vulnerability, the metabolites R419492 and R471811 were found to only just exceed 10 µg/L for a very brief period over the 7-year groundwater sampling period under conditions of a higher annual use patterns of 2 x 1000g/ha around each well than the currently supported use pattern of 2 x 750 g/ha. Under the higher use pattern rates, metabolite R417888 remained below 10 µg/L at all sampling times.

For all acceptable locations, the moving yearly averages will be below the stated maximum for individual wells and not exceed the value of 10 µg/L. The setting into context of the monitoring data was not completely acceptable. Although parameter setting in the monitoring study is not that different from the endpoints reached after evaluation, RMS is of the opinion that it cannot be established on beforehand what the influence of the differences in the parameters (especially the Freundlich exponent) will be on the frequency distribution of the relative vulnerability and the ranking of the monitoring sites.

As the lysimeter studies and monitoring data are not (adequately) put into context, the results cannot be used to refine the FOCUS modelling outcome, according to the tiered approach as described in the working document on potential for movement to groundwater (*European Commission (2014) "Assessing Potential for Movement of Active Substances and their Metabolites to Ground Water in the EU" Report of the FOCUS Ground Water Work Group, EC Document Reference Sanco/13144/2010 version 3, 613 pp*).

For the non-relevance assessment, therefore RMS proposes to use the FOCUS modelling results (cf. Tier 1 of the working document).

2.11.3 STEP 3: Hazard assessment – identification of relevant metabolites

2.11.3.1 STEP 3, Stage 1: screening for biological activity

Guidance on the testing for biological activity of metabolites is given below :

EC (2003). SANCO/221/2000: - metabolites with a comparable or higher biological activity than the parent are considered as relevant and must, therefore, not exceed a level of 0.1 µg/L in groundwater …. In screening assays …it should be sufficient to demonstrate that the biological activity of a metabolite is clearly less that 50% of the activity of the parent molecule. Otherwise the biological activity should be considered as "comparable".

Michalski et al (2004) - A metabolite is defined as having a pesticidal activity if in a screening test it exhibits > 30% effects compared to an untreated control and the parent substance used as a positive control simultaneously exhibits > 70% effects.[3]

[3] Michalski B, Stein B, Niemann L, Pfeil R and Fischer R (2004). Beurteilung der Relevanz von Metaboliten im Grundwasser im Rahmen des nationalen Zulassungsverfahrens fur Pflanzenschutzmittel (Assessment of the relevance of metabolies in groundwater in the context of national approval procedure of plant protection products), *Nachrichtenbl. Deut. Pflanzenschutzd*. 56: 53-59

Glutathione reactivity is considered the biological basis for the fungicidal activity of chlorothalonil, therefore testing for biological activity of metabolites includes a glutathione reactivity assay, in addition to activity against fungal targets of chlorothalonil.

See Table 2.11.3-1 for the results of the assays. Detailed information on the studies is given below the table.

Table 2.11.3-1: Overview of Biological Activity Data for Chlorothalonil Metabolites

Metabolite	Glutathione Reactivity[A]	Fungicidal Activity - level of control (%)			
		Zymoseptoria tritici	***Phytophora infestans***	***Alternaria solani***	***Puccinia recondita***
R417888	29,000	0	0	0	0
R418503	Analytical method not suitable	0	0	6	planned
R419492	1.4×10^6	0	0	0	0
R471811	3.3×10^6	0	0	0	0
SYN507900	-	0	0	3-9	0
SYN548008	10,200	0	4	1	planned
SYN548580	10,000	0	11	0	planned
SYN548581	9,000	0	7	0	planned
R611965	1.5×10^7	0	0	0	0
R611968	8,900	0	0	0-15	0
R613636	4,800	0	0	0	0

[A] Reduction in GSH reactivity relative to parent chlorothalonil

Glutathione Reactivity

Chlorothalonil exerts its fungicidal activity through reaction with cellular nucleophiles, including glutathione. The glutathione reactivity of metabolites was compared to parent chlorothalonil, deriving the second-order rate constants for the loss of glutathione (GSH) with and without catalysis by glutathione transferases (GST) in an HPLC based assay (Clarke et al 1998). Glutathione reactivity is increased with pH, temperature and GSH and GST level. These parameters were adjusted to give a measurable loss of each compound over 16 hours incubation. Rate constants for the reactions were then derived for comparison, taking into account temperature, pH and GSH level.

In these *in vitro* glutathione reactivity studies, R417888, R419492, R471811, SYN548008, SYN548580, SYN548581, R611965, R611968 and R613636 were ≥ 4,800 times less reactive to GSH than parent chlorothalonil, respectively (Seville 1999a, b, Pierce 2001, Pierce 2015).

Conclusion: It is predicted that R417888, R611965, R419492, R471811, SYN548008, SYN548580, SYN548581, R611965, R611968 and R613636 will not show efficacy against fungi or display the characteristic toxicity of chlorothalonil to mammals or other non-target organisms.

Fungicidal Activity

In greenhouse studies, the fungicidal activity of the metabolites R419492, R417888, R471811, R613636, R611965, R611968 and SYN507900 was compared to parent chlorothalonil against four pathogens - *Zymoseptoria tritici, Phytophora infestans, Alternaria solani* and *Puccinia recondita* (Schneiter 2014a, b, c

& d) and metabolites R418503, SYN548008, SYN548580 and SYN548581 were compared to *Zymoseptoria tritici, Phytophora infestans* and *Alternaria solani*. Rates tested were from the range 6, 20, 60, 200, 600 and 2000 mg/L. The efficacy of the metabolites were compared to rates at which chlorothalonil gave good activity (efficacy >70%).

No disease control of *Zymoseptoria tritici,* and *Puccinia recondita* was observed at any metabolite concentrations. With *Alternaria solani* between 3 and 9% control was observed for SYN507900, but there was no dose response relationship. With R611968, 15% control of *A. solani* was observed at the highest rate of 600 mg/L, but no control at 200 mg/L where chlorothalonil was giving 88% control. For R418503 and SYN548008, 6 and 1% control was observed, respectively, at 600 mg/L where the chlorothalonil was giving 93% control. With *Phytphthora infestans*, SYN548008, SYN548580 and SYN548581 4, 11 aand 7% control was recorded at 600 mg/L compared to 94% for chlorothalonil. The very low activity observed is related to the variability of disease development within these test systems in glasshouse. The level of disease damage observed is in the range of the untreated infected checks (40 – 70 % disease damage) and up to 30% activity in such a test is generally considered as indicating no effect. Furthermore it is well below the 50 (EC 2003) or 30% (Michalski et al 2004), level considered to show activity.

Conclusion: The data generated in the glasshouse assays demonstrate that when metabolites R419492, R417888, R471811, R613636, R611965, R611968, SYN507900, R418503, SYN548008, SYN548580 and SYN548581 are screened at concentrations related to the field equivalent rate of chlorothalonil in a glasshouse they show significantly less than 30% effect compared to untreated controls. They are therefore considered to have no pesticidal activity.

2.11.3.2 STEP 3, Stage 2: screening for genotoxicity

SANCO/221/2000: - All metabolites should be screened for their genotoxic activity by at least the following package of in vitro genotoxicity studies: Ames test, gene mutation test with mammalian cells and chromosome aberration test. Equivocal results in in vitro studies should be substantiated by in vivo experiments.

The Task Force has undertaken *in vitro* genotoxicity testing for those metabolites exceeding 0.1 µg/L in groundwater in order to provide confirmatory evidence supporting the absence of genotoxic potential for these metabolites. A summary is given in Table 2.11.3.2-1.

Table 2.11.3.2-1: A summary of the genotoxicity testing of the metabolites

Study type	Author	Result	Overall conclusion
SDS 3701 (R182281)			SDS-37091 (R182281) is considered to be non genotoxic in vivo.
Bacterial reverse mutation assay (Ames)	Verspeek-Rip (2004a)	Negative	
Cell mutation assay in mouse lymphoma L5178Y cells	Verspeek-Rip (2005)	Positive+/-S9 (at cytotoxic concentrations)	
Chromosome aberration study in CHO cells	Mizens et al (1994)	Positive +/-S9	
In vivo mouse micronucleus study	Buskens (2004a)	Negative	
In vivo chromosome aberration test	Mizens & Laveglia (1995)	Negative	
Dominant lethal test, rats	Hastings & Jessup (1975)	Negative	
In vivo rat liver UDS study	Honarvar (2006)	Negative	
R611965 (SDS 46851)			No evidence for genotoxicity for R611965 (SDS 46851)
Bacterial reverse mutation assay (Ames)	Godek et al (1985)	Negative	
Bacterial reverse mutation assay (Ames)	Haworth et al (1985)	Negative	
Bacterial reverse mutation assay (Ames)	Verspeek-Rip (2004b)	Negative	
In vitro SCE assay	Jones et al (1985)	Negative	
Cell mutation assay in mouse lymphoma L5178Y cells	Jones & Sernau (1985)	Negative	
Cell mutation assay in mouse lymphoma L5178Y cells	Verspeek-Rip (2005)	Negative	
UDS test with rat hepatocytes	Jones et al (1985)	Negative	
In vivo mouse micronucleus study	Siou et al (1985)	Equivocal, repeated negative	
In vivo mouse micronucleus study	Fox (2002)	Negative	
In vivo mouse micronucleus study	Buskens (2004b)	Negative	
R417888			R417888 is considered to be non genotoxic in vivo.
Bacterial reverse mutation assay (Ames)	Callander (2000)	Negative	
Bacterial reverse mutation assay (Ames)	Verspeek-Rip (2005a)	Negative	
Bacterial reverse mutation assay (Ames)	Sokolowski (2007)	Negative	
In vitro chromosome aberration test in human lymphocytes	Fox (2000b)	Negative	
In vitro chromosome aberration test in human lymphocytes	Fox (2000a)	Positive (–S9) Negative (+S9)	
In vitro chromosome aberration test in human lymphocytes	Kunz (2007)	Positive (–S9) Negative (+S9)	
Cell mutation assay in mouse lymphoma L5178Y cells	Clay (2000)	Negative	
Cell mutation assay in mouse lymphoma L5178Y cells	Verspeek-Rip (2006)	Positive (+S9) Negative (-S9)	
Cell mutation assay in mouse lymphoma L5178Y cells	Wollny (2007)	Negative	
In vivo mouse micronucleus study	Meerts (2005)	Negative	
In vivo rat liver UDS study	Honarvar (2006)	Negative	
SYN548708 (R418503)			SYN548708 is considered to be non-
Bacterial reverse mutation assay (Ames)	Sokolowski (2015)	Negative	

Study type	**Author**	**Result**	**Overall conclusion**
In vitro chromosome aberration test in human lymphocytes	Sokolowski (2015a)	Positive	genotoxic in vivo
Cell mutation assay in mouse lymphoma L5178Y cells	Wollny (2015)	Negative	
In vivo mouse micronucleus study	Dunton (2015)	Negative	
SYN548765 (R419492)			SYN548765 is considered to be non-genotoxic in vitro
Study type	**Author**	**Result**	
Bacterial reverse mutation assay (Ames)	Sokolowski (2015b)	Negative	
In vitro chromosome aberration test in human lymphocytes	Sokolowski (2015c)	Negative	
Cell mutation assay in mouse lymphoma L5178Y cells	Wollny (2015a)	Negative	
SYN548766 (R471811)			SYN548766 is considered to be non-genotoxic in vitro
Bacterial reverse mutation assay (Ames)	Sokolowski (2015d)	Negative	
In vitro chromosome aberration test in human lymphocytes	Sokolowski (2015e)	Negative	
Cell mutation assay in mouse lymphoma L5178Y cells	Wollny (2015 b)	Negative	
SYN548738 (SYN548008)			SYN548738 is considered to be non-genotoxic in vitro
Bacterial reverse mutation assay (Ames)	Sokolowski (2015f)	Negative	
In vitro chromosome aberration test in human lymphocytes	Sokolowski (2015g)	Negative	
Cell mutation assay in mouse lymphoma L5178Y cells	Sokolowski (2015h)	Negative	
SYN548580			SYN548580 is considered to be non-genotoxic in vitro
Bacterial reverse mutation assay (Ames)	Sokolowski (2015i)	Negative	
In vitro chromosome aberration test in human lymphocytes	Sokolowski (2015j)	Negative	
Cell mutation assay in mouse lymphoma L5178Y cells	Wollny (2015c)	Negative	
R611968 (SDS-47525)			R611968 is considered to be non-genotoxic
Bacterial reverse mutation assay (Ames)	Sokolowski (2015m)	Negative	
In vitro chromosome aberration test in human lymphocytes	Sokolowski (2015n)	Equivocal	
Cell mutation assay in mouse lymphoma L5178Y cells	Wollny (2015e)	Negative	
In vivo mouse micronucleus study	Dunton (2015b)	Negative	
SYN507900 (SDS66882)			SYN507900 (SDS66882)is considered to be non-genotoxic
Bacterial reverse mutation assay (Ames)	Sokolowski (2015q)	Negative	
In vitro chromosome aberration test in human lymphocytes	Sokolowski (2015r)	Positive	
Cell mutation assay in mouse lymphoma L5178Y cells	Wollny (2015h)	Negative	
In vivo mouse micronucleus study	Dunton (2016)	Negative	

It can be concluded that none of the metabolites exceeding 0.1 µg/L in groundwater had any genotoxic potential.

2.11.3.3 STEP 3, Stage 3: screening for toxicity

SANCO/221/2000: - A metabolite is considered "relevant" if its toxicological properties lead to a classification as toxic or very toxic (T or T+) according to Directive 67/548/EEC. ……the toxicity classification of the parent active substance as determined according to Directive 67/548/EEC is used for pragmatic reasons as a starting point to focus the screening activity…… All metabolites passing stage 3 of step 3 and are not considered as "relevant" are subject to an exposure and/or risk assessment….

In the absence of toxicity data for several of the metabolites and in order to avoid unnecessary animal studies, careful evaluation of the available data for the soil metabolites exceeding 0.1 µg/L has been undertaken and used in a weight of the evidence analysis based on the following considerations;

a. The presence and significance of any toxicological alerts from parent chlorothalonil
b. Review of existing toxicity data on R417888 , R611965 and R182281 (metabolites considered representative of the three major soil degradation pathways; sulphonic acid, carboxylic acid and substituted hydroxyl respectively) compared with data on parent chlorothalonil, as potential surrogate data for other metabolites from these pathways
c. The presence and significance of Qualitative Structure Activity Relationship ((Q)SAR) data
d. "Matched pairs" analysis to identify structurally similar metabolites undergoing common metabolic processing compared to the three reference metabolites and potential to bridge to existing toxicity data.
e. Review of existing/ongoing chemical (LUMO/Glutathione) and biological (Fungicidal activity) data as a measure of potential reactivity compared to parent chlorothalonil

Details of each element for this weight of the evidence analysis including a detailed toxicological assessment for each metabolite are presented in the section below.

a. Toxicological Alerts from Parent Chlorothalonil

The following two toxicological endpoints have been considered;

- The parent substance meets the criteria for classification as "Fatal if inhalation"
- The parent substance meets the criteria for classification as "carcinogenic"

Acute Inhalation Toxicity

Whilst chlorothalonil is classified as fatal if inhalation, this is not considered a relevant endpoint for further evaluation. In the absence of any exposure potential coming from groundwater metabolites, the inhalation toxicity of groundwater metabolites is of no relevance.

Chronic toxicity (carcinogenicity)

The key toxicological finding in studies conducted on parent chlorothalonil are histopathological and organ weight changes in the rodent kidney from sub-chronic studies and pre-neoplastic/neoplastic change in the rodent kidney from chronic/carcinogenicity studies.

Chronic administration of chlorothalonil to rodents causes treatment related increases in the incidence of adenomas and carcinomas of the kidney. The available data indicates that renal toxicity and subsequent sustained cell proliferation precede tumour formation. Thresholds have been established for the

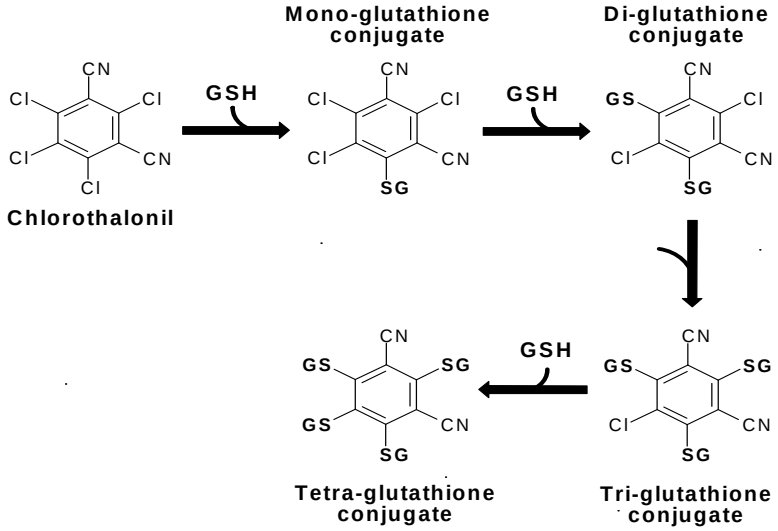
occurrence of pre-neoplastic and neoplastic changes and chlorothalonil has been shown not be genotoxic in rats and mice in vivo.

The time-course of histopathological changes that occur in the kidney has been established by regulatory and investigative toxicity studies. These studies provide unequivocal evidence that increased cell proliferation, sustained renal cytotoxicity and hyperplasia precede subsequent tumour development. Sustained renal hyperplasia is a necessary pre-requisite for tumour formation, such that doses of chlorothalonil that do not cause hyperplasia, will not cause cancer.

The metabolism of chlorothalonil plays a central role in the kidney toxicity seen in rodents. It has been demonstrated that administration of the monoglutathione conjugate of chlorothalonil for up to 90 days produced morphologically similar changes in the rat kidney when compared to the effects seen with equimolar doses of chlorothalonil is the same study (Ford et al, 1987a, see Vol 3 B6.8.4 study 2). This study provides strong evidence that glutathione conjugation is involved in the metabolic pathway leading to kidney toxicity.

Chlorothalonil can readily undergo nucleophilic substitutions with glutathione to form mono-, di-, tri- and tetra-glutathione conjugates (Figure 2.11.3.3-1). The preferential positions for glutathione substitution are at the 4- and 6-positions about the benzene ring which are favoured over the 2- and the 5-position. The electron withdrawing cyano groups enhance the reactivity of this aryl halide to nucleophilic attack and direct the nucleophiles to their ortho and para positions (4- and 6- positions). Conjugation of chlorothalonil to glutathione occurs spontaneously in aqueous solution, although the rate of the reaction is accelerated markedly in the presence of glutathione-S-transferases (Rosner et al, 1996).

Figure 2.11.3.3-1: Preferred positions of substitution for conjugation of chlorothalonil with glutathione

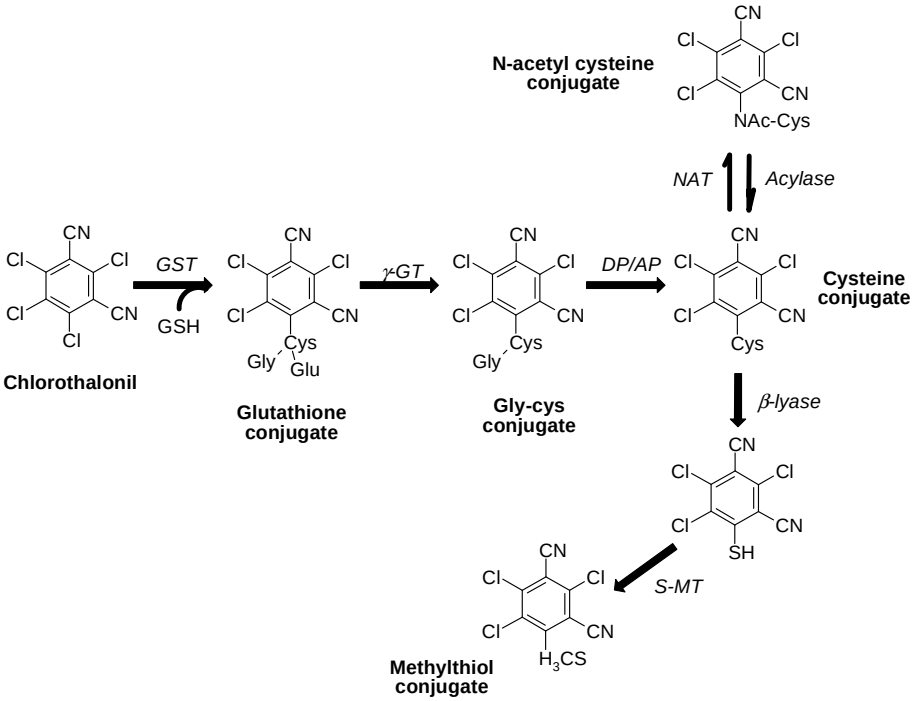


Previous studies have further elucidated the metabolic pathway in the rat. These studies indicate that the principal urinary metabolites in the rat are formed by replacement of either two or three of the chlorine atoms of chlorothalonil with glycinyl-cysteine (gly-cys), N-acetylcysteine (N-Ac-cys), S-methyl (H3CS) or hydrogen (H). All of these substituents, with the exception of hydrogen, can be attributed to initial

glutathione conjugation, then enzymic processing of the glutathione moieties via the mercapturic acid and cysteine conjugate β-lyase pathways (Anders & Dekant, 1998).

These reactions are illustrated in Figure 2.11.3.3-2 for the mono-glutathione conjugate of chlorothalonil.

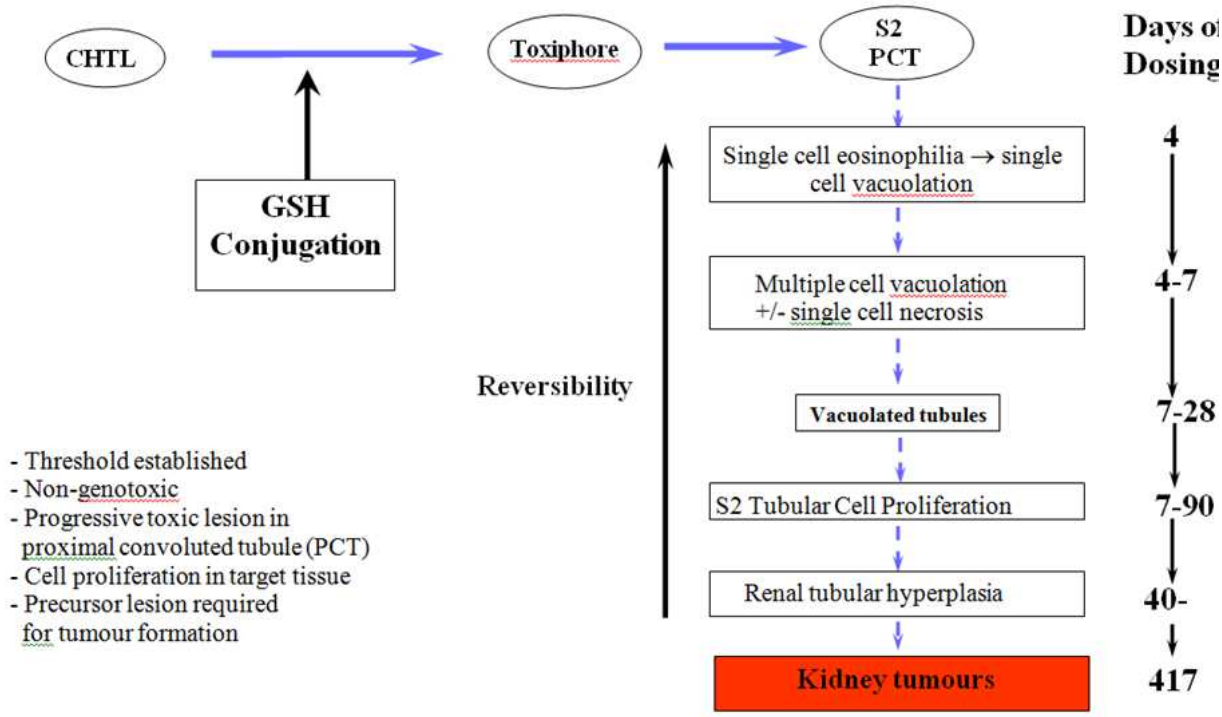
Figure 2.11.3.3-2: Enzymic processing of glutathione conjugates of chlorothalonil via the mercapturic acid and cysteine conjugate β-lyase pathways



Abbreviations are: GSH, reduced glutathione; GST, glutathione-S-transferase; γ-GT: □-glutamyl transpeptidase; DP, dipeptidase; AP, aminopeptidase; NAT, N-acetyltransferase; βlyase, cysteine conjugate β-lyase; S-MT, thiol-*S*-methyltransferase.

Taking account of the central role of glutathione metabolism in the toxicity of chlorothalonil and the biochemical and histopathological observations from regulatory and investigative toxicity studies, a mode of action for rodent kidney tumour formation has been proposed and is outlined in Figure 2.11.3.3-3.

Figure 2.11.3.3-3: Schematic outlining the mode of action for rodent kidney tumour formation

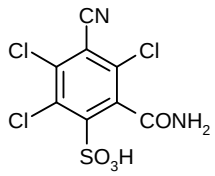
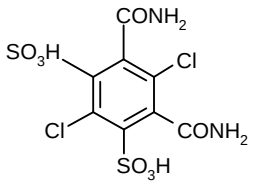
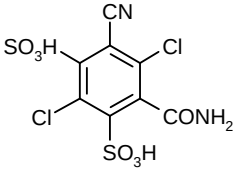
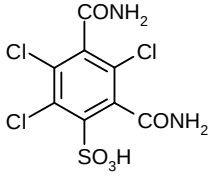


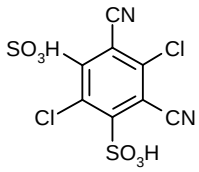
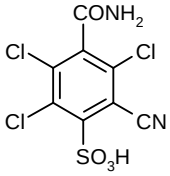
b. Review of Existing Toxicity Data on R417888, R611965 and R182281

As described in the original EU review, the degradation of chlorothalonil in soil proceeds principally by three distinct pathways, namely;

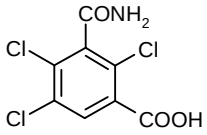
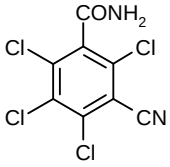
- glutathione conjugation, leading to sulphonic acid derivatives, characterised by the major metabolite **R471888**, 2-amido-3,5,6-trichloro-4-cyano-benzenesulphonic acid;
- reductive dechlorination, leading to carboxylic acid derivatives, characterised by the major metabolite **R611965 (SDS-46851)**, 3-amido-2,4,5-trichlorobenzoic acid;
- oxidative dechlorination, leading to dechlorinated hydroxy substituted metabolites, characterised by the major metabolite **R182281 (SDS-3701)**, 2,5,6-trichloro-4-hydroxyisophthalonitrile;

R47188, representative for sulphonic acid derivatives after glutathione conjugation

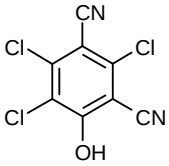
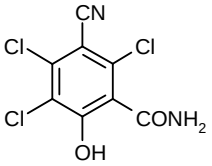
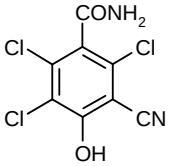
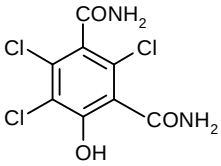
Metabolite Code	Structure	Metabolite Code	Structure
R417888 VIS01 Compound 10 M12		SYN548008 M3	
R419492 Compound 12 M8		R471811 Compound 13 M4	

Metabolite Code	Structure	Metabolite Code	Structure
R418503 M13		SYN548581 M11	

R611965 (SDS-46851), representative for carboxylic acid derivatives after reductive dechlorination

Metabolite Code	Structure	Metabolite Code	Structure
R611965 Compound 4 M5		R613636 Compound 3 M14	

R182281 (SDS-3701), representative for dechlorinated hydroxy substituted metabolites after oxidative dechlorination

Metabolite Code	Structure	Metabolite Code	Structure
R182281 SDS 3701 Compound 2		R611968 M9	
SYN507900		SYN548580	

Toxicity data are available for R417888, R611965 and R182281 which were concluded to be representative of the three major soil degradation pathways (sulphonic acid, carboxylic acid and substituted hydroxyl respectively) in the previous EU review.

R417888

R417888 is not acutely toxic. Repeated exposure to R417888 in two separate rat studies for up to 90 days at maximum dose levels in excess of 59 and 192 mg/kg bw/day respectively failed to produce any evidence of toxicity and in particular no evidence of pre-neoplastic key events in the kidney known to be a pre-requisite for kidney tumour development for chlorothalonil.

R417888 is not considered to be genotoxic *in vivo* and contains no structural alerts for genotoxic activity. The ADI for R417888 established at EU review was 0.06 mg/kg bw/day based on the first 90 day rat study and applying a safety factor of 1000 and is proposed as a common reference dose for all sulphonic acid metabolites exceeding 0.1µg/L in groundwater. This can be considered as a highly conservative figure given the more recent 90 day study of van Otterdijk, 2007 (Vol 3 B6.8.1-6.3.13) which concluded a NOAEL of 192 mg/kg bw/day (corresponding to an ADI of 0.2 mg/kg bw/day again using a safety factor of 1000).

R611965 (SDS-46851)

R611965 is not acutely toxic and in the 28 and 90-day studies, there was no target organ toxicity common to the 3 species tested; the lowest 90-day NOAEL was 50 mg/kg bw/day in the dog. R611965 is not genotoxic in *in vitro* and *in vivo* mutagenicity studies.
R611965 did not show any evidence of kidney tumours or any other tumours in carcinogenicity studies and the NOAEL for chronic toxicity was 200 mg/kg bw/day, based on ocular lesions in the rat (the only treatment-related finding in the chronic studies).
R611965 showed no effects on reproduction or development.
The ADI for R611965 established at EU review was 0.5 mg/kg bw/day based on the 90 day dog and applying a safety factor of 100.

R182281 (SDS-3701)
R182281 is of moderate acute oral toxicity. Short-term feeding studies showed effects on the hemopoietic system of the rat and degenerative effects in the livers and kidneys of rats and dogs, with an overall NOAEL of 1.25 mg/kg bw/day in the dog 90d and 1 year studies. R182281 is not considered to be genotoxic *in vivo* and contains no structural alerts for genotoxic activity.
In long-term feeding studies, R182281 which only differs from chlorothalonil by dechlorination followed by hydroxy substitution at position C4, did not show any evidence of kidney tumours and the NOAEL for chronic toxicity was 0.5 mg/kg bw/day in the rat study.
R182281 showed no effects on reproductive performance in multi-generation toxicity studies. In the absence of maternal toxicity, there were no adverse effects on development in rats and rabbits. The overall reproductive NOAEL was 1.5 mg/kg bw/day, based on lower pup weight gain during lactation at higher doses in the rat reproductive toxicity study.
The ADI established at EU review was 0.01 mg/kg bw/day based on the 90 day/1 year dog and applying a safety factor of 100.

The chronic/carcinogenicity studies for R417888, R611965 and R182281 showed no evidence of kidney tumours or key pre-neoplastic key events in the kidney known to be a pre-requisite for kidney tumour development. These findings suggest that dechlorination at position C4 leads to the formation of metabolites with reduced chemical reactivity such that significant kidney toxicity seen with parent chlorothalonil is no longer evident.

c. Qualitative Structure Activity Relationship ((Q)SAR) analysis

All soil metabolites (including those not exceeding 0.1 µg/L) and parent chlorothalonil were included in a Qualitative Structure Activity Relationship ((Q)SAR) analysis using the predictive toxicology program DEREK (**D**eductive **E**stimation of **R**isk from **E**xisting **K**nowledge), which is an expert system that searches a knowledgebase against a number of predictive endpoints.

This QSAR analysis was evaluated in Vol 3 B.6.8.1-6.8. It was concluded that (Q)SAR analysis of the soil metabolites of chlorothalonil when considered alongside the available sub-chronic/chronic/carcinogenicity data of chlorothalonil did not provide any relevant toxicological alerts based on the known kidney mode of action for parent chlorothalonil.

d. Matched pairs analysis

The applicant provided the following information.

The chlorothalonil soil degradation pathway shows several instances where common metabolic processing of metabolites takes place. The ability to identify such "matched pairs" undergoing common positional metabolic substitutions has been used as an additional tool to justify bridging to related key metabolites undergoing the same positional modification and for which there are sufficient toxicity data available to evaluate toxicological significance.

Conversion of the nitrile to an amide at position C3

This a common processing step observed across the soil degradation pathway (Figure 3.3.3-4)

Toxicity data are available for R417888 and R611965 which are both downstream metabolites undergoing the same type of biotransformation and can therefore be used to address the significance of this positional change for common metabolites.

Conversion of the chlorine to the sulphonic acid at position C6

This is a common processing step observed across several of the sulphonic acid metabolites R417888 to R419492, R471811 to SYN548008, R611553 to R418503) which according to the lysimeter data are the most abundant soil metabolites exceeding 0.1 µg/L accounting more than 82% of the total concentration of chlorothalonil metabolites exceeding 0.1 µg/L (Figure 3.3.3-5).

Toxicity data are available for R417888. Both R417888 and R419492 are present in the Plasma or urine/bile from the chlorothalonil biotransformation study indicating animals exposed to R417888 would have been co-exposed to R419492. This provides further evidence to support the use of existing data on R417888 to address the toxicological significance of this positional change for common metabolites.

e. Review of chemical (LUMO/Glutathione) and biological (Fungicidal activity) data

The applicant provided the following information.

LUMO analysis

Analysis of the theoretical **L**owest **U**noccupied **M**olecular **O**rbital analysis (**LUMO**) was undertaken as a tool to assess relative chemical reactivities for chlorothalonil metabolites. It is well-established that calculations of the Lowest Unoccupied Molecular Orbital (LUMO) of molecules can be used to predict reactivities towards soft nucleophiles like glutathione. A soft nucleophile has a loosely-bound pair of electrons and as it reacts with its target molecule, this pair of electrons transfers to the lowest unoccupied molecular orbital of the target; the lower in energy in this orbital, the more energetically favourable the reaction will be (i.e. negative electron volt values indicate higher chemical reactivity as compared with higher positive electron volt values). This approach has been used to investigate the reactivity of chlorothalonil and its metabolites.

LUMO analysis for the metabolites undergoing conversion of the nitrile to an amide at position C3 indicates these to be less reactive than chlorothalonil. This observation is consistent with the toxicity

findings for R417888 and R611965 which were both qualitatively and quantitatively distinct from parent chlorothalonil and considered to be of low toxicological concern (Figure 3.3.3-4).

LUMO analysis for the metabolites undergoing conversion of the chlorine to the sulphonic acid at position C6 indicates these polar sulphonic acid metabolites possess the lowest reactivity potential of all of the soil metabolites and most likely subject to rapid elimination. This observation is consistent with the toxicity findings for R417888 which is both qualitatively and quantitatively distinct from parent chlorothalonil and considered to be of low toxicological concern (Figure 3.3.3-5)

Figure 3.3.3-4
Chlorothalonil GW Metabolites
Matched Pairs analysis + Chemical Reactivity (LUMO e-volt energies)

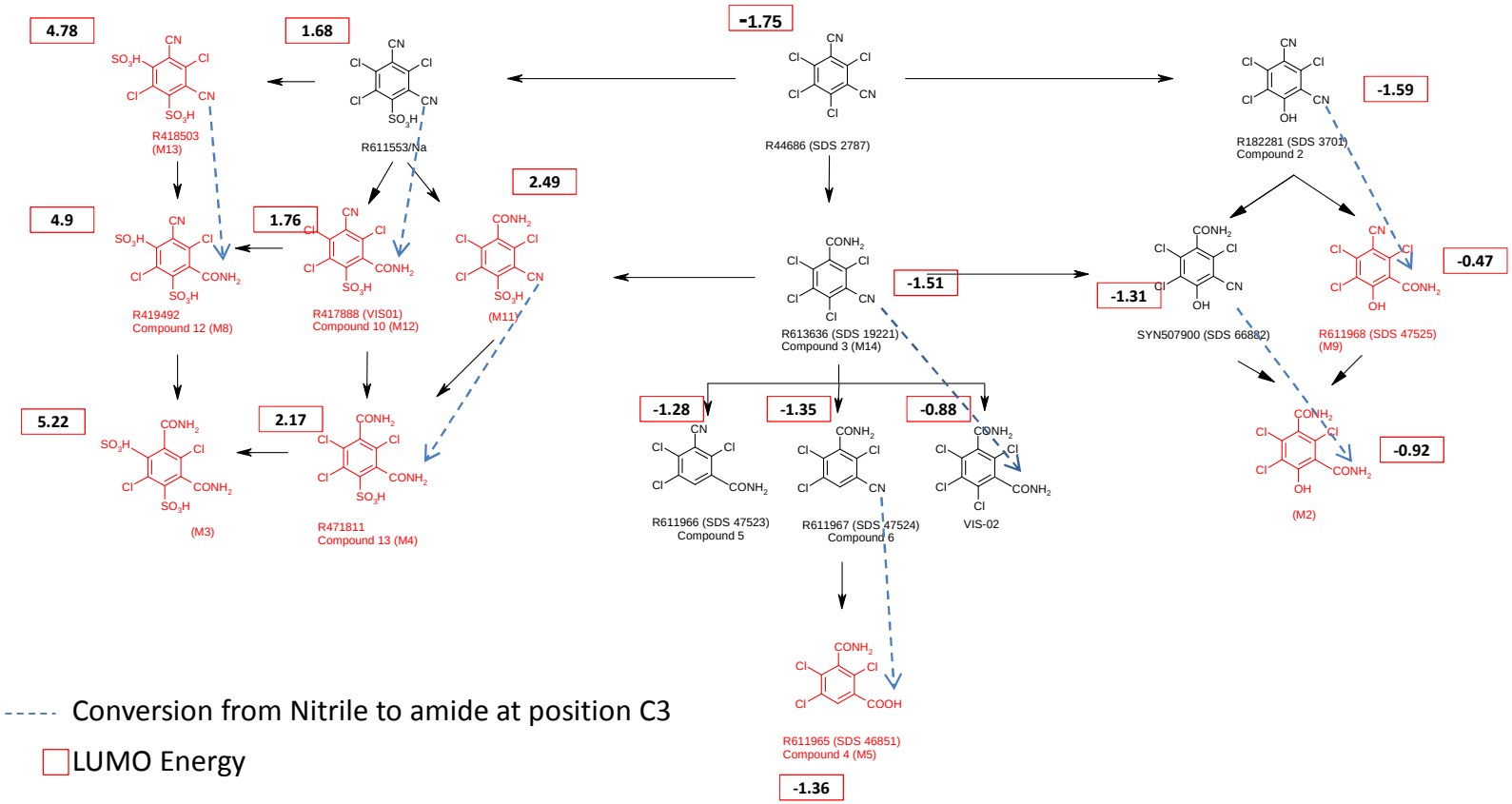
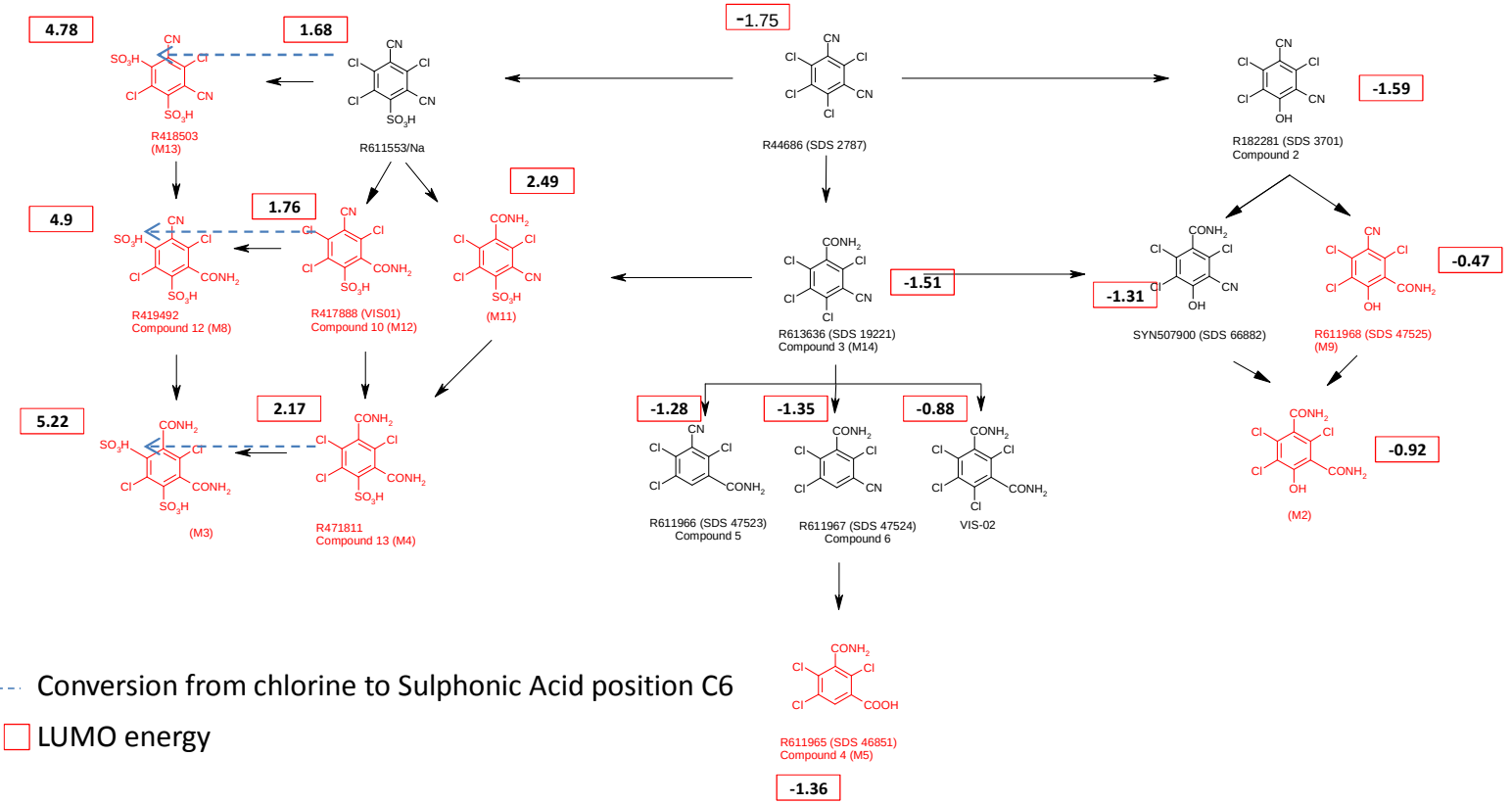


Figure 3.3.3-5
Chlorothalonil GW Metabolites
Chemical Reactivity : LUMO (e-volt energies)



Glutathione Reactivity and Fungicidal Activity

Glutathione reactivity and fungicidal activity are included as part of a weight of evidence analysis in the overall toxicological assessment for each metabolite described below.

Overall Toxicological Assessment

The overall conclusion regarding the toxicological assessment of metabolite found in groundwater at levels exceeding 0.1 µg/L is presented in Table 2.11.3.3-1.

None of the metabolites are considered toxicologically relevant, according to the criteria for step 3 stage 3.

Based on this weight of the evidence analysis, the existing data are considered adequate to address the absence of key toxicities associated with parent chlorothalonil and support the use of existing toxicity data covering the three major routes of degradation required to address step 5 of the GW metabolite guidance for metabolites exceeding 0.75 µg/L.

Table 2.11.3.3-1: A summary of Step 3: Hazard Assessment: Identification of relevant metabolites.

Metabolite	**Step 3 - Stage 3 Screening for toxicity**	**ADI (mg/kg bw/day)**
R417888	Already concluded non-relevant at the previous EU review.	0.06
R418503	Considered non-relevant Structurally similar to R417888 Polar – rapidly eliminated No SAR alerts Predicted to be functionally distinct from chlorothalonil (LUMO/ glutathione reactivity/fungicidal activity)	See R417888
R419492	Considered non-relevant Structurally similar to R417888 Polar – rapidly eliminated No SAR alerts Functionally distinct from chlorothalonil (LUMO/glutathione reactivity/fungicidal activity)	See R417888
R471811	Considered non-relevant Structurally similar to R417888 Polar – rapidly eliminated No SAR alerts Functionally distinct from chlorothalonil (LUMO/glutathione reactivity/fungicidal activity)	See R417888
R182281	Already concluded non-relevant at the previous EU review.	0.01
SYN507900	Considered non-relevant Structurally similar to R182281 No SAR alerts Functionally distinct from chlorothalonil (LUMO/glutathione reactivity/fungicidal activity)	See R182281
SYN548008	Considered non-relevant Structurally similar to R417888 Polar – rapidly eliminated No SAR alerts Functionally distinct from chlorothalonil (LUMO/glutathione reactivity/fungicidal activity)	See R417888

SYN548580	Considered non-relevant Structurally similar to R182281 No SAR alerts Predicted to be functionally distinct from chlorothalonil (LUMO/ glutathione reactivity/fungicidal activity)	See R182281
SYN548581	Considered non-relevant Structurally similar to R417888 Polar – rapidly eliminated No SAR alerts Predicted to be functionally distinct from chlorothalonil (LUMO/ glutathione reactivity/fungicidal activity)	See R417888
R611965	Already concluded non relevant in previous EU review.	0.5
R611968	Considered non-relevant Structurally similar to R182281 No SAR alerts Functionally distinct from chlorothalonil (LUMO/ glutathione reactivity/fungicidal activity)	See R182281

2.11.4 STEP 4: Exposure assessment – threshold of concern approach

SANCO/221/2000: - Metabolites which have not been identified as being relevant according to the screening outlined in step 3, should be further tested in an exposure assessment to make sure that any contamination of groundwater will not lead to unacceptable exposure of consumers via their drinking water.

As underlined by the guidance document, metabolites that pass through the biological activity, genotoxicity and toxicity assessments of Step 3 must be considered in the context of an exposure assessment.

None of the metabolites from step 3 were predicted to be below the threshold of 0.75 µg/Lin the (worst case) FOCUS predictions. Therefore, further refinement of risk assessment is required for the metabolites: R417888, R418503, R419492, R471811, SYN507900, SYN548008, SYN548580, R611965, R611968 and the metabolites originally designated M7 and M10.

2.11.5 STEP 5: Refined risk assessment

SANCO/221/2000: - Metabolites which have passed steps 1 to 3 and for which levels of estimated concentrations of metabolites in groundwater (as defined in Step 2) lie between 0.75 µg/L (from Step 4) and 10 µg/L will require a refined assessment of their potential toxicological significance for consumers.

R417888, R418503, R419492, R471811, SYN507900, SYN548008, SYN548580, R611965, R611968 and the unidentified metabolites M7 and M10, are predicted to exceed the threshold of 0.75 µg/L, therefore, a refined risk assessment for consumers is required.

The toxicological properties of these metabolites have been evaluated in Volume 3 B.6.8.1 and summarised in 2.6.9 of this document. Based on a weight of the evidence approach it is proposed to use existing data on R417888, R611965 and R182281 as surrogate data for use in deriving the

respective reference dose for the sulphonic acid, carboxylic acid and dechlorinated hydroxyl metabolites.

On the basis of the available studies, an Acceptable Daily Intake has been agreed for all three of these representative metabolites as shown in Table 2.11.5-1.

Table 2.11.5-1: Acceptable Daily Intake for R417888, R611965 and R182281

	Lowest NO(A)EL (mg/kg bw/day)	Safety Factor	Justification for Safety Factor	ADI (mg/kg bw/day)
R417888 (Sulphonic acids)	59	1000	Conservative value based on studies up to 90 day duration only	0.06
R611965 (Carboxylic acids)	50	100	Based on 90day study	0.50
R182281 (Dechlorinated hydroxy)	1	100	Based on 90 day/1yr study	0.01

For the refined risk assessment, the ADI values are compared with the theoretical maximum daily intake (TMDI) of the metabolites from the groundwater modelling data, as a conservative approach. For this refined risk assessment adults, children, and toddlers are considered. The WHO only considers a 60 kg adult, however, children are more at risk due to their lower body weight. Therefoer a 18 kg child and a 10 kg toddler, consuming 1 and 0.75 L water per day, respectively, are also taken into account. Comparing their exposure with a life-long reference dose (ADI) is considered a worst case approach.

For the unidentified metabolites M7 and M10 and calculated from groundwater modelling data at 4.63 and 1.9 µg/L, respectively, it is not possible to evaluate the toxicological significance in the absence of a structure. However, on the basis that the three major soil degradation pathways representing the relevant detoxification, decomposition and transformation processes of the parent molecule chlorothalonil are known, then it is assumed that the unidentified metabolites M7 and M10 are associated with one of these established groups and can be assessed against the worst case ADI for R182281.

Table 2.11.5-2: Refined risk assessment – Comparison between theoretical maximum daily intake (TMDI) of groundwater metabolites with ADI

Metabolite in groundwater	Maximum residues from groundwater modelling data (µg/L)	Exposure (L/day)	Individual Bodyweight (kg)	TMDI (mg/kg bw /day)	ADI	% of ADI
Adults						
R417888	23.49	2	60	0.00078	0.06	1.3%
R418503	1.2	2	60	0.00004	0.06	0.1%
R419492	44.27	2	60	0.00148	0.06	2.5%

Metabolite in groundwater	Maximum residues from groundwater modelling data (µg/L)	Exposure (L/day)	Individual Bodyweight (kg)	TMDI (mg/kg bw /day)	ADI	% of ADI
R471811	33.41	2	60	0.00111	0.06	1.9%
SYN507900	26.1	2	60	0.00087	0.01	8.7%
SYN548008	10.24	2	60	0.00034	0.06	0.6%
SYN548580	10.45	2	60	0.00035	0.01	3.5%
R611965	22.37	2	60	0.00075	0.50	0.1%
R611968	4.18	2	60	0.00014	0.01	1.4%
M7	4.63	2	60	0.00015	0.01	1.5%
M10	1.9	2	60	0.00006	0.01	0.6%
Children						
R417888	23.49	1	18	0.00131	0.06	2.2%
R418503	1.2	1	18	0.00007	0.06	0.1%
R419492	44.27	1	18	0.00246	0.06	4.1%
R471811	33.41	1	18	0.00186	0.06	3.1%
SYN507900	26.1	1	18	0.00145	0.01	14.5%
SYN548008	10.24	1	18	0.00057	0.06	0.9%
SYN548580	10.45	1	18	0.00058	0.01	5.8%
R611965	22.37	1	18	0.00124	0.50	0.2%
R611968	4.18	1	18	0.00023	0.01	2.3%
M7	4.63	1	18	0.00026	0.01	2.6%
M10	1.9	1	18	0.00011	0.01	1.1%
Toddlers						
R417888	23.49	0.75	10	0.00176	0.06	2.9%
R418503	1.2	0.75	10	0.00009	0.06	0.2%
R419492	44.27	0.75	10	0.00332	0.06	5.5%
R471811	33.41	0.75	10	0.00251	0.06	4.2%
SYN507900	26.1	0.75	10	0.00196	0.01	19.6%
SYN548008	10.24	0.75	10	0.00077	0.06	1.3%
SYN548580	10.45	0.75	10	0.00078	0.01	7.8%
R611965	22.37	0.75	10	0.00168	0.50	0.3%
R611968	4.18	0.75	10	0.00031	0.01	3.1%
M7	4.63	0.75	10	0.00035	0.01	3.5%
M10	1.9	0.75	10	0.00014	0.01	1.4%

According to the WHO drinking water guidance, the intake should be maximally 20% of the ADI.

In conclusion, drinking water containing the maximum predicted residues of R417888, R418503, R419492, R471811, SYN507900, SYN548008, SYN548580, R611965, R611968 and the metabolites originally designated M7 and M10 in ground water do not present any risk to the consumer.

2.11.6 Overall conclusion

All the metabolites discussed can be considered to be non-relevant in the context of the criteria outlined in the "Guidance Document on the Assessment of the Relevance of Metabolites in Groundwater of Substances Regulated Under Council Directive 91/414/EEC. (SANCO/221/2000-rev.10; 25 February 2003).

2.12 Consideration of isomeric composition in the risk assessment

Chlorothalonil is an aromatic compound with no chiral atoms. Therefore, the substance is not optically active.

Structural isomers are not considered likely as the two nitrile moieties have have a preferred *meta* configuration. Substitution or resonance on *para* or *ortho* positions are not expected.

2.13 Residue definitions

2.13.1 Definition of residues for exposure/risk assessment

To be specified for the following matrices:

Food of plant origin: 1. Chlorothalonil; 2. SDS-3701

Food of animal origin: SDS-3701

Soil: Chlorothalonil, R182281, R417888, R418503, R419492, R471811, SYN507900, R611965, R611966, R611967, and R613636

Groundwater: Chlorothalonil, R182281, R417888, R418503, R419492, R471811, SYN507900, R611965, R611966, R611967, and R613636; lysimeter metabolites SYN548008 (M3), SYN548580 (M2), SYN548581 (M11), M7 and M10

Surface water: Chlorothalonil, R182281(via soil and water/sediment), R417888 (via soil), R418503 (via soil), R419492 (via soil), R471811 (via soil), SYN507900 (via soil), R611965 (via soil), R611966 (via soil and water/sediment), R611967 (via soil), and R613636 (via soil); R613841(water/sediment), R613842 (water/sediment), R613801 (water/sediment), SYN546671(water/sediment); Aqueous photolysis: PD1, PD2, PD4, PD5; lysimeter metabolites SYN548008 (M3), SYN548580 (M2), SYN548581 (M11), M7 and M10

Sediment: Chlorothalonil, R182281(via soil and water/sediment), R417888 (via soil), R418503 (via soil), R419492 (via soil), R471811 (via soil), SYN507900 (via soil), R611965 (via soil), R611966 (via soil and water/sediment), R611967 (via soil), and R613636 (via soil); R613841(water/sediment), R613842 (water/sediment), R613801 (water/sediment), SYN546671(water/sediment); Aqueous

photolysis: PD1, PD2, PD4, PD5; lysimeter metabolites SYN548008 (M3), SYN548580 (M2), SYN548581 (M11), M7 and M10

Air: chlorothalonil

2.13.2 Definition of residues for monitoring

To be specified for the following matrices:

Food of plant origin: 1. Chlorothalonil; 2. SDS-3701

Food of animal origin: SDS-3701

Soil: Chlorothalonil

Groundwater: Chlorothalonil

Surface water: Chlorothalonil

Sediment: Chlorothalonil

Air: Chlorothalonil

Volume 1

Level 3

- Chlorothalonil-

Summary and consideration with respect to the approval criteria of Regulation (EC) No 1107/2009

Identification of data gaps, proposed conditions, risk management measures, issues that could not be finalized and critical areas of concern

Proposed decisions

3 Proposed decision with respect to the application

3.1 Background to the proposed decision

3.1.1 Proposal on acceptability against the decision making criteria – Article 4 and Annex II of Regulation (EC) No 1107/2009

3.1.1.1 Article 4				
		Yes	No	
i)	It is considered that Article 4 of Regulation (EC) No 1107/2009 is complied with. Specifically the RMS considers that authorisation in at least one Member State is expected to be possible for at least one plant protection product containing the active substance for at least one of the representative uses.			Inconclusive. Additional information (which can be submitted during the peer review) is needed to finalise the evaluation. Please refer to tables 3.1.4, 3.1.5 and 3.1.7.
3.1.1.2 Submission of further information				
		Yes	No	
i)	It is considered that a complete dossier has been submitted	X		
ii)	It is considered that in the absence of a full dossier the active substance may be approved even though certain information is still to be submitted because: (a) the data requirements have been amended or refined after the submission of the dossier; or (b) the information is considered to be confirmatory in nature, as required to increase confidence in the decision.			*Not applicable*
3.1.1.3 Restrictions on approval				
		Yes	No	
	It is considered that in line with Article 6 of Regulation (EC) No 1107/2009 approval should be subject to conditions and restrictions.		x	
3.1.1.4 Criteria for the approval of an active substance				
Dossier				
		Yes	No	
	It is considered the dossier contains the information needed to	x		

	establish, where relevant, Acceptable Daily Intake (ADI), Acceptable Operator Exposure Level (AOEL) and Acute Reference Dose (ARfD).			
	It is considered that the dossier contains the information necessary to carry out a risk assessment and for enforcement purposes (relevant for substances for which one or more representative uses includes use on feed or food crops or leads indirectly to residues in food or feed). In particular it is considered that the dossier: (a) permits any residue of concern to be defined; (b) reliably predicts the residues in food and feed, including succeeding crops (c) reliably predicts, where relevant, the corresponding residue level reflecting the effects of processing and/or mixing; (d) permits a maximum residue level to be defined and to be determined by appropriate methods in general use for the commodity and, where appropriate, for products of animal origin where the commodity or parts of it is fed to animals; (e) permits, where relevant, concentration or dilution factors due to processing and/or mixing to be defined.			The metabolism of chlorothalonil has been studied in several crops, already for the initial peer review. Parent is the major residue in all crops. Furthermore, it can be concluded that the metabolism of chlorothalonil is qualitatively similar in the different crops, and that chlorothalonil will be metabolised to a greater extent after longer intervals, which is relevant for GAPs with PHI intervals exceeding 21/28 days. One of the important metabolites is SDS-3701. Metabolite SDS-3701 is more toxic than parent; it can have relevant levels in plants; and it follows a different toxicological mechanism than the parent. Therefore, two separate residue definitions are proposed for plants, both for monitoring as well as risk assessment: chlorothalonil and SDS-3701. For all representative uses, sufficient supervised residue trials are available. Studies show that metabolite SDS-3701 is formed during processing, confirming the relevance of including this metabolite in the plant residue definition. Several processing studies are available, investigating the magnitude of residues in processed commodities. The metabolism of chlorothalonil in rotational crops is similar to that in primary crops, although levels of SDS-46851 were higher in rotational crops metabolism studies. This has been confirmed in field rotation crop studies. Since metabolite SDS-46851 is toxicologically less relevant compared to parent, a specific residue definition for rotation crops is considered not necessary. Since both parent chlorothalonil and metabolite SDS-3701 may occur in feed crops, the nature of both substances in commodities of animal origin has been investigated. The results indicate that metabolite SDS-3701 is the major component of the TRR. Therefore, the residue definition for animal commodities is defined as SDS-3701. The dietary burden calculation shows that the trigger value of 0.004 mg/kg bw/d is exceeded for all groups of livestock, except pigs. No poultry feeding study is required, since residue levels are expected to remain below LOQ, based on the metabolism study. Two different ruminant feeding

				studies are available. As a worst-case, the 'old' feeding study from the original peer review could be used for MRL setting. New SDS-3701-MRLs are proposed for tomatoes, barley wheat, potatoes and sheep fat.
	It is considered that the dossier submitted is sufficient to permit, where relevant, an estimate of the fate and distribution of the active substance in the environment, and its impact on non-target species.	X		
Efficacy				
		Yes	No	
	It is considered that it has been established for one or more representative uses that the plant protection product, consequent on application consistent with good plant protection practice and having regard to realistic conditions of use is sufficiently effective.	X		According to the latest guidance on the preparation of dossiers for the renewal of active substances, information on efficacy is not required (SANCO/10181/2013 – rev. 2.1, 13 May 2013). The representative products have all been authorised at Member State level for > 10 years and have therefore been assessed in line with Uniform Principles.
Relevance of metabolites				
		Yes	No	
	It is considered that the documentation submitted is sufficient to permit the establishment of the toxicological, ecotoxicological or environmental relevance of metabolites.	x		
Composition				
		Yes	No	
	It is considered that the specification defines the minimum degree of purity, the identity and maximum content of impurities and, where relevant, of isomers/diastereo-isomers and additives, and the content of impurities of toxicological, ecotoxicological or environmental concern within acceptable limits.	X		
	It is considered that the specification is in compliance with the relevant Food and Agriculture Organisation specification, where such specification exists.	x		
	It is considered for reasons of protection of human or animal		X	

	health or the environment, stricter specifications than that provided for by the FAO specification should be adopted			
Methods of analysis				
		Yes	No	
	It is considered that the methods of analysis of the active substance, safener or synergist as manufactured and of determination of impurities of toxicological, ecotoxicological or environmental concern or which are present in quantities greater than 1 g/kg in the active substance, safener or synergist as manufactured, have been validated and shown to be sufficiently specific, correctly calibrated, accurate and precise.	X		
	It is considered that the methods of residue analysis for the active substance and relevant metabolites in plant, animal and environmental matrices and drinking water, as appropriate, shall have been validated and shown to be sufficiently sensitive with respect to the levels of concern.	X		
	It is confirmed that the evaluation has been carried out in accordance with the uniform principles for evaluation and authorisation of plant protection products referred to in Article 29(6) of Regulation 1107/2009.	X		
Impact on human health				
Impact on human health - ADI, AOEL, ARfD				
		Yes	No	
	It is confirmed that (where relevant) an ADI, AOEL and ARfD can be established with an appropriate safety margin of at least 100 taking into account the type and severity of effects and the vulnerability of specific groups of the population.	X		
Impact on human health – proposed genotoxicity classification				
		Yes	No	
	It is considered that, on the basis of assessment of higher tier genotoxicity testing carried out in accordance with the data requirements and other available data and information, including a review of the scientific literature, reviewed by the Authority, **the substance SHOULD BE classified or proposed for classification**, in accordance with the provisions of Regulation (EC) No 1272/2008, **as mutagen category 1A or 1B.**		x	
Impact on human health – proposed carcinogenicity classification				

		Yes	No	
i)	It is considered that, on the basis of assessment of the carcinogenicity testing carried out in accordance with the data requirements for the active substances, safener or synergist and other available data and information, including a review of the scientific literature, reviewed by the Authority, **the substance SHOULD BE classified or proposed for classification**, in accordance with the provisions of Regulation (EC) No 1272/2008, **as carcinogen category 1A or 1B.**		x	The current classification Carc Cat2 is proposed to be maintained based on kidney tumors in rats.
ii)	Linked to above classification proposal. It is considered that exposure of humans to the active substance, safener or synergist in a plant protection product, under realistic proposed conditions of use, is negligible, that is, the product is used in closed systems or in other conditions excluding contact with humans and where residues of the active substance, safener or synergist concerned on food and feed do not exceed the default value set in accordance with Article 18(1)(b) of Regulation (EC) No 396/2005.			
Impact on human health – proposed reproductive toxicity classification				
		Yes	No	
i)	It is considered that, on the basis of assessment of the reproductive toxicity testing carried out in accordance with the data requirements for the active substances, safeners or synergists and other available data and information, including a review of the scientific literature, reviewed by the Authority, **the substance SHOULD BE classified or proposed for classification**, in accordance with the provisions of Regulation (EC) No 1272/2008, **as toxic for reproduction category 1A or 1B.**		x	
ii)	Linked to above classification proposal. It is considered that exposure of humans to the active substance, safener or synergist in a plant protection product, under realistic proposed conditions of use, is negligible, that is, the product is used in closed systems or in other conditions			

	excluding contact with humans and where residues of the active substance, safener or synergist concerned on food and feed do not exceed the default value set in accordance with Article 18(1)(b) of Regulation (EC) No 396/2005.			
Impact on human health – proposed endocrine disrupting properties classification				
		Yes	No	
i)	It is considered that **the substance SHOULD BE classified or proposed for classification** in accordance with the provisions of Regulation (EC) No 1272/2008, as **carcinogenic category 2 and toxic for reproduction category 2 and on that basis shall be considered to have endocrine disrupting properties**	x		The current classification Carc Cat2 is proposed to be maintained based on kidney tumors in rats.
ii)	It is considered that **the substance SHOULD BE classified or proposed for classification** in accordance with the provisions of Regulation (EC) No 1272/2008, as **toxic for reproduction category 2 and** in addition the RMS considers the substance **has toxic effects on the endocrine organs and on that basis shall be considered to have endocrine disrupting properties**		X	
iii)	Linked to either i) or ii) immediately above. It is considered that exposure of humans to the active substance, safener or synergist in a plant protection product, under realistic proposed conditions of use, is negligible, that is, the product is used in closed systems or in other conditions excluding contact with humans and where residues of the active substance, safener or synergist concerned on food and feed do not exceed the default value set in accordance with Article 18(1)(b) of Regulation (EC) No 396/2005.		X	The products are applied by spray equipment.
Fate and behaviour in the environment				
Persistent organic pollutant (POP)				
		Yes	No	
	It is considered that the active substance **FULFILS** the criteria of a persistent organic pollutant (POP) as laid out in Regulation 1107/2009 Annex II Section 3.7.1.		x	See level 2 secion 2.8 for a detailed description. Chlorothalonil is not persistent in soil and water/sediment studies. Chlorothalonil meets the criteria for potential for long range transport. Hence, chlorothalonil does not fulfil all of the criteria for classification as a POP.

Persistent, bioaccumulative and toxic substance (PBT)				
		Yes	No	
	It is considered that the active substance **FULFILS** the criteria of a persistent, bioaccumulative and toxic (PBT) substance as laid out in Regulation 1107/2009 Annex II Section 3.7.2.		X	See level 2 section 2.8 for a detailed description for persistence. Chlorothalonil is not persistent in soil and freshwater water/sediment studies according to the PBT criteria.. See level 2 section 2.6: chlorothalonil is not (proposed to be) classified as toxic for human health according to the PBT criteria. See level 2 section 2.9: chlorothalonil is not (proposed to be) bio-accumulative according to the PBT criteria.
Very persistent and very bioaccumulative substance (vPvB).				
		Yes	No	
	It is considered that the active substance **FULFILS** the criteria of a a very persistent and very bioaccumulative substance (vPvB) as laid out in Regulation 1107/2009 Annex II Section 3.7.3.		x	See level 2 section 2.8 for a detailed description for persistence. Chlorothalonil is not persistent in soil and freshwater water/sediment studies. See level 2 section 2.9: chlorothalonil is not (proposed to be) bio-accumulative according to the PBT criteria.
Ecotoxicology				
		Yes	No	
	It is considered that the risk assessment demonstrates risks to be acceptable in accordance with the criteria laid down in the uniform principles for evaluation and authorisation of plant protection products referred to in Article 29(6) under realistic proposed conditions of use of a plant protection product containing the active substance, safener or synergist. The RMS is content that the assessment takes into account the severity of effects, the uncertainty of the data, and the number of organism groups which the active substance, safener or synergist is expected to affect adversely by the intended use.		X	Please refer to the tables 3.1.4, 3.1.5. and 3.1.7.
	It is considered that, on the basis of the assessment of Community or internationally agreed test guidelines, the substance **HAS** endocrine disrupting properties that may cause adverse effects on non-target organisms.	X		Chlorothalonil showed thyroid disruption in an Amphibian metamorphosis assay but not in mammalian tests. The RMS has requested a LAGDA in order to establish a regulatory endpoint for the amphibian risk assessment.

	Linked to the consideration of the endocrine properties immediately above. It is considered that the exposure of non-target organisms to the active substance in a plant protection product under realistic proposed conditions of use is negligible.			
	It is considered that it is established following an appropriate risk assessment on the basis of Community or internationally agreed test guidelines, that the use under the proposed conditions of use of plant protection products containing this active substance, safener or synergist: — will result in a negligible exposure of honeybees, or — has no unacceptable acute or chronic effects on colony survival and development, taking into account effects on honeybee larvae and honeybee behaviour.		x	The risk assessment for the Arysta and Oxon formulations could not yet be finalized without bridging information for the formulation used in the larval (and chronic adult) toxicity studies.
Residue definition				
		Yes	No	
	It is considered that, where relevant, a residue definition can be established for the purposes of risk assessment and for enforcement purposes.	X		
Fate and behaviour concerning groundwater				
		Yes	No	
	It is considered that it has been established for one or more representative uses, that consequently after application of the plant protection product consistent with realistic conditions on use, the predicted concentration of the active substance or of metabolites, degradation or reaction products in groundwater complies with the respective criteria of the uniform principles for evaluation and authorisation of plant protection products referred to in Article 29(6) of Regulation 1107/2009.	X		*Chlorothalonil poses no risk for leaching to groundwater. Many of the metabolites exceed the 0.1 µg/L trigger and some even the 10 µg/L. However based on the toxicological non relevance assessment it has been established that all metabolites can be declared non-relevant.* *It was also established that none of the concerned metabolites show biological activity.* *Whether the exceedance of 10 µg/L is acceptable is a risk management decision.*

3.1.2 Proposal – Candidate for substitution

Candidate for substitution				
		Yes	No	
	It is considered that the active substance shall be approved as a candidate for substitution		X	

3.1.3 Proposal – low risk active substance

Low-risk active substances				
		Yes	No	
	It is considered that the active substance **shall be considered of low risk.** In particular it is considered that the substance **should NOT be classified or proposed for classification** in accordance with Regulation (EC) No 1272/2008 as at least one of the following: — carcinogenic, — mutagenic, — toxic to reproduction, — sensitising chemicals, — very toxic or toxic, — explosive, — corrosive. In addition it is considered that **the substance is NOT**: — persistent (half-life in soil more than 60 days), — has a bioconcentration factor higher than 100, — is deemed to be an endocrine disrupter, or — has neurotoxic or immunotoxic effects.		x	Chlorothalonil should remain the current classification for carcinogenicity (Cat 2), and skin sensitisation.

3.1.4 List of studies to be generated, still ongoing or available but not peer reviewed

Data gap	Relevance in relation to representative use(s)	Study status		
		No confirmation that study available or on-going.	**Study on-going and anticipated date of completion**	**Study available but not peer-reviewed**
3.1.4.1 Identity of the active substance or formulation				
Arysta: 1. The producer of the plant protection product and the active substances (CP 1.2) 2. A description of the formulation process (CP 1.4.3) 3. The composition of the antifoam (CP 1.4.3) 4. The level of ethoxylation of the wetting agent 5. A summary of the toxicological data with regard to the co-formulants (CP 7.4) Syngenta: 1. The level of alkoxylation should be given for the surfactants		X		
Arysta: 1. The pathway for formation of impurity 1 of manufacturing site 2 should be provided.				

2. It should be clarified whether the batches from site 2 can be considered representative as they were all produced on the same day according to information in the batch analysis report. Syngenta: 1. The reason that the content of the compounds in the tox/ecotox batches are expressed as a range should be given and justified (volume 4, table C.1.4-1).				
3.1.4.2 Physical and chemical properties of the active substance and physical, chemical and technical properties of the formulation				
Arysta: surface tension of the product at the highest in-use concentration			September 2016	
Oxon: surface tension of the product at the highest in-use concentration			Q4 2016	
Oxon: shelf-life study of the representative product			May 2017	
Arysta: effectiveness of cleaning procedures			September 2016	
3.1.4.3 Data on uses and efficacy				
3.1.4.4 Data on handling, storage, transport, packaging and labelling				

3.1.4.5 Methods of analysis				
Arysta: The chromatographic conditions in study Walker, AF, 2008 (KCP 5.1.1/04) should be clarified with regard to the mass fragments used for quantification of the relevant impurity DCB.		X		
Task force: The extraction efficiency of the method for food/feed of animal origin should be addressed.				
3.1.4.6 Toxicology and metabolism				
3.1.4.7 Residue data				
3.1.4.8 Environmental fate and behaviour				
Sorption properties for metabolites R611966, R611967 and R611968 Degradation and sorption properties for lysimeter metabolites SYN548008, SYN548580 and SYN548581			Studies ongoing. Studies ongoing…	
3.1.4.9 Ecotoxicology				
Soil organism (macro and micro) studies with the relevant soil metabolites of chlorothalonil	Relevant for all uses		December 2016	

LAGDA study	Relevant for all uses		Study ongoing or completed…	

3.1.5 Issue that could not be finalized

An issue is listed as an issue that could not be finalised where there is not enough information available to perform an assessment, even at the lowest tier level, for the representative uses in line with the Uniform Principles, as laid out in Commission Regulation (EU) No 546/2011, and where the issue is of such importance that it could, when finalised, become a concern (which would also be listed as a critical area of concern if it is of relevance to all representative uses).

Area of the risk assessment that could not be finalised on the basis of the available data	**Relevance in relation to representative use(s)**
Long term risk to birds	Tomato and potato only.
Long term risk to mammals	All uses.
Risk to bee larvae	All uses, Arysta and Oxon formulations only.
Risk to bees from metabolites	All uses.
Reproductive risk to aquatic stage amphibians	All uses.
Risk to soil macro and micro organisms from chlorothalonil metabolites	All uses.

3.1.6 Critical areas of concern

An issue is listed as a critical area of concern:
(a) where the substance does not satisfy the criteria set out in points 3.6.3, 3.6.4, 3.6.5 or 3.8.2 of Annex II of Regulation (EC) No 1107/2009 and the applicant has not provided detailed evidence that the active substance is necessary to control a serious danger to plant health which cannot be contained by other available means including non-chemical methods, taking into account risk mitigation measures to ensure that exposure of humans and the environment is minimised, or
(b) where there is enough information available to perform an assessment for the representative uses in line with the Uniform Principles, as laid out in Commission Regulation (EU) 546/2011, and where this assessment does not permit to conclude that for at least one of the representative uses it may be expected that a plant protection product containing the active substance will not have any harmful effect on human or animal health or on groundwater or any unacceptable influence on the environment.

An issue is also listed as a critical area of concern where the assessment at a higher tier level could not be finalised due to a lack of information, and where the assessment performed at the lower tier level does not permit to conclude that for at least one of the representative uses it may be expected that a plant protection product containing the active substance will not have any harmful effect on human or animal health or on groundwater or any unacceptable influence on the environment.

Critical area of concern identified	**Relevance in relation to representative use(s)**

3.1.7 Overview table of the concerns identified for each representative use considered

(If a particular condition proposed to be taken into account to manage an identified risk, as listed in 3.3.1, has been evaluated as being effective, then 'risk identified' is not indicated in this table.)
If the columns are grey the material tested in the toxicological studies has not been demonstrated to be representative of the technical specification.

Representative use		Use "tomato" (X^1)	Use "barley" (X^1)	Use "wheat" (X^1)	Use "potato" (X^1)
Operator risk	Risk identified				
	Assessment not finalised				
Worker risk	Risk identified				
	Assessment not finalised				
Bystander risk	Risk identified				
	Assessment not finalised				
Consumer risk	Risk identified				
	Assessment not finalised				
Risk to wild non target terrestrial vertebrates	Risk identified				
	Assessment not finalised	x	x	x	x
Risk to wild non target terrestrial organisms other than vertebrates	Risk identified				
	Assessment not finalised	x	x	x	x
Risk to aquatic organisms	Risk identified				
	Assessment not finalised	x	x	x	x
Groundwater exposure active substance	Legal parametric value breached				
	Assessment not finalised				

Groundwater exposure metabolites	Legal parametric value breached	x	x	x	x
	Parametric value of 10µg/L[(a)] breached	x	x	x	x
	Assessment not finalised				
Comments/Remarks					

The superscript numbers in this table relate to the numbered points indicated within chapter 3.1.5 and 3.1.6. Where there is no superscript number, see level 2 for more explanation.
(a): Value for non relevant metabolites prescribed in SANCO/221/2000-rev 10-final, European Commission, 2003

3.1.8 Area(s) where expert consultation is considered necessary

It is recommended to organise a consultation of experts on the following parts of the assessment report:

Area(s) where expert consultation is considered necessary	**Justification**
Fate and behaviour (B.8) Use of groundwater monitoring data to refine the risk for leaching (in relation to non-relevance assessment of metabolites)	*Currently there is no clear guidance on how to use specific regional monitoring data for EU wide decision on safe use, and how to address the setting into context (e.g., choice of 1/n).*

3.1.9 Critical issues on which the co-RMS did not agree with the assessment by the RMS

Points on which the co-rapporteur Member State did not agree with the assessment by the rapporteur member state. Only the points relevant for the decision making process should be listed.

Issue on which Co-RMS disagrees with RMS	**Opinion of Co-RMS**	**Opinion of RMS**

3.2 Proposed decision

It is still inconclusive whether chlorothalonil can be approved under Regulation (EC) No 1107/2009. Additional information (which can be submitted during the peer review) is needed to finalize the risk assessment.

3.3 Rational for the conditions and restrictions to be associated with the approval or authorisation(s), as appropriate

3.3.1 Particular conditions proposed to be take into account to manage the risks identified

Proposed condition/risk mitigation measure	Relevance in relation to representative use(s)

Appendices

Appendix 1 Guidance documents used in this assessment

Guidances applicable at the time of submission of the additional dossier were used in this assessment.

Appendix 2 Reference list

Not applicable.