

APPROVED: 4 December 2017

doi: 10.2903/j.efsa.2018.5126

### Peer review of the pesticide risk assessment of the active substance chlorothalonil

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#### Abstract

The conclusions of EFSA following the peer review of the initial risk assessments carried out by the competent authorities of the rapporteur Member State, the Netherlands, and co-rapporteur Member State, Belgium, for the pesticide active substance chlorothalonil are reported. The context of the peer review was that required by Commission Implementing Regulation (EU) No 844/2012. The conclusions were reached on the basis of the evaluation of the representative uses of chlorothalonil as a fungicide on wheat, barley, tomato and potato. The reliable endpoints, appropriate for use in regulatory risk assessment, are presented. Missing information identified as being required by the regulatory framework is listed. Concerns are identified.

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**Keywords:** chlorothalonil, peer review, risk assessment, pesticide, fungicide

**Requestor:** European Commission

**Question number:** EFSA-Q-2014-00646

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**Suggested citation:** EFSA (European Food Safety Authority), Arena M, Auteri D, Barmaz S, Bellisai G, Brancato A, Brocca D, Bura L, Byers H, Chiusolo A, Court Marques D, Crivellente F, De Lentdecker C, Egsmose M, Erdos Z, Fait G, Ferreira L, Goumenou M, Greco L, Ippolito A, Istace F, Jarrah S, Kardassi D, Leuschner R, Lythgo C, Magrans JO, Medina P, Miron I, Molnar T, Nougadere A, Padovani L, Parra Morte JM, Pedersen R, Reich H, Sacchi A, Santos M, Serafimova R, Sharp R, Stanek A, Streissl F, Sturma J, Szentes C, Tarazona J, Terron A, Theobald A, Vagenende B, Verani A and Villamar-Bouza L, 2018. Conclusion on the peer review of the peer review of the pesticide risk assessment of the active substance chlorothalonil. *EFSA Journal* 2018;16(1):5126, 40 pp. <https://doi.org/10.2903/j.efsa.2018.5126>

**ISSN:** 1831-4732

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## Summary

Commission Implementing Regulation (EU) No 844/2012 (hereinafter referred to as 'the Regulation') lays down the procedure for the renewal of the approval of active substances submitted under Article 14 of Regulation (EC) No 1107/2009. The list of those substances is established in Commission Implementing Regulation (EU) No 686/2012. Chlorothalonil is one of the active substances listed in Regulation (EU) No 686/2012.

In accordance with Article 1 of the Regulation, the rapporteur Member State (RMS), the Netherlands, and co-rapporteur Member State (co-RMS), Belgium, received an application from Arysta LifeScience S.A.S., Oxon Italia S.p.A. and Syngenta Crop Protection AG for the renewal of approval of the active substance chlorothalonil. Complying with Article 8 of the Regulation, the RMS checked the completeness of the dossier and informed the applicants, the co-RMS (Belgium), the European Commission and the European Food Safety Authority (EFSA) about the admissibility.

The RMS provided its initial evaluation of the dossier on chlorothalonil in the renewal assessment report (RAR), which was received by EFSA on 2 September 2016. In accordance with Article 12 of the Regulation, EFSA distributed the RAR to the Member States and the applicants, Arysta LifeScience S.A.S., Oxon Italia S.p.A. and Syngenta Crop Protection AG, for comments on 24 October 2016. EFSA also provided comments. In addition, EFSA conducted a public consultation on the RAR. EFSA collated and forwarded all comments received to the European Commission on 4 January 2017.

Following consideration of the comments received on the RAR, it was concluded that additional information should be requested from the applicants, and that EFSA should conduct an expert consultation in the areas of mammalian toxicology, residues, environmental fate and behaviour and ecotoxicology.

In accordance with Article 13(1) of the Regulation, EFSA should adopt a conclusion on whether chlorothalonil can be expected to meet the approval criteria provided for in Article 4 of Regulation (EC) No 1107/2009 of the European Parliament and of the Council.

The conclusions laid down in this report were reached on the basis of the evaluation of the representative uses of chlorothalonil as a fungicide on wheat, barley, tomato and potato, as proposed by the applicants. Full details of the representative uses can be found in Appendix A of this report.

The use of chlorothalonil according to the representative uses proposed at the European Union (EU) level results in a sufficient fungicidal efficacy against a broad spectrum of fungal diseases.

A data gap was identified for a transparent presentation and evaluation of the search of the scientific peer-reviewed open literature on the active substance and its relevant metabolites.

In the area of identity, physical/chemical properties and analytical methods, data gaps were identified for verification of the efficiency of the extraction procedure used in the analytical methods for the determination of residues in dry and high oil content plant commodities and in food of animal origin and for an independent laboratory validation (ILV) of the monitoring method for determination of residues in fat matrix.

In the area of the mammalian toxicology, data gaps were identified for the assessment of the toxicological relevance of some impurities present in the technical specification in comparison with the toxicological profile of the parent, for an *in vitro* interspecies comparative metabolism study, including human tissues, for the residue definition for body fluids (urine and blood/plasma for human biomonitoring purposes), identification and validation of the analytical methods used in the toxicological studies and to address the genotoxic potential of a number of plant and/or groundwater metabolites. According to the proposed classification of chlorothalonil by the peer review as carcinogen category 1B in accordance to the provisions of Regulation (EC) No 1272/2008 (while harmonised classification is category 2), the active substance does not fulfil the approval criteria of Annex II, point 3.6.3 of Regulation (EC) No 1107/2009.

In the area of residues, several data gaps were identified. Only preliminary residue definitions in plant raw agricultural commodities, processed commodities and animal products could be derived. A major plant and animal metabolite, included in the residue definitions, is R182281, for which a genotoxic potential could not be excluded. Residue trial data were insufficient to support the critical Good Agricultural Practice (cGAP) in barley and wheat. Furthermore, for the trials in cereal the integrity of samples has not been fully demonstrated as storage stability tests showed a significant decline (chlorothalonil) or were not available for the entire period the samples were stored (R182281). In general, the available residue trials in wheat, barley, potato and tomato are only compliant with the residue definition for monitoring. Conversion factors for risk assessment could not be derived. Significant degradation into metabolites R613636 and R182281, considered toxicologically relevant

(genotoxic potential not excluded for both compounds), was observed under processing conditions employing higher temperatures, and processing residue trials are not sufficient to exclude formation of significant levels of toxicologically relevant compounds. Reliable livestock dietary burden estimates could not be conducted and therefore the assessment of residues in animal commodities could not be finalised. In the absence of toxicological reference values for R182281, even an indicative consumer risk assessment using the preliminary residue definitions cannot be conducted.

Two of the submitted studies for the renewal of chlorothalonil cover data gaps, which were identified during the Art. 12 MRL review.

For environmental fate and behaviour, a data gap was identified for the adsorption and degradation endpoints to be derived for metabolites SYN548008 (M3) and SYN548581 (M11). Field dissipation studies should be conducted for metabolites SDS-3701 (R182281), R417888, R418503, R419492, R471811, SYN507900, R611966 and R611965 and R613636. A data gap was identified for the identity of metabolites SYN548580 (M2), M10 and M7 which remained unknown. Furthermore, a data gap was set for the identity of metabolite PD4. For groundwater exposure assessment, a critical area of concern was identified for all relevant metabolites. It should be noted that with the available toxicological information, chlorothalonil metabolites would be concluded as relevant groundwater metabolites should they be predicted to occur in groundwater above the parametric drinking water limit of 0.1 µg/L due to the proposed classification of chlorothalonil as carcinogen category 1B. A data gap was identified for information on the effect of water treatment processes on the nature of residues of both the active substance and its identified metabolites potentially present in surface and groundwater, when surface water or groundwater are abstracted for drinking water. This gap leads to the consumer risk assessment from the consumption of drinking water being not finalised for all the representative uses.

In the area of ecotoxicology, data gaps were identified for further information to address the risk to wild mammals for chlorothalonil and metabolite SDS-3701, to aquatic organisms for chlorothalonil and the various surface water metabolites, to honeybees and other non-target arthropods for chlorothalonil only. A high risk to amphibians (acute) and to fish (chronic) for chlorothalonil was identified for all the representative uses (critical area of concern). The chronic risk to amphibians could not be finalised and further information was therefore requested (issue that could not be finalised and critical area of concern).

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## Background

Commission Implementing Regulation (EU) No 844/2012<sup>1</sup> (hereinafter referred to as 'the Regulation') lays down the provisions for the procedure of the renewal of the approval of active substances, submitted under Article 14 of Regulation (EC) No 1107/2009.<sup>2</sup> This regulates for the European Food Safety Authority (EFSA) the procedure for organising the consultation of Member States, the applicant(s) and the public on the initial evaluation provided by the rapporteur Member State (RMS) and/or co-rapporteur Member State (co-RMS) in the renewal assessment report (RAR), and the organisation of an expert consultation where appropriate.

In accordance with Article 13 of the Regulation, unless formally informed by the European Commission that a conclusion is not necessary, EFSA is required to adopt a conclusion on whether the active substance can be expected to meet the approval criteria provided for in Article 4 of Regulation (EC) No 1107/2009 within 5 months from the end of the period provided for the submission of written comments, subject to an extension of an additional 3 months where additional information is required to be submitted by the applicant(s) in accordance with Article 13(3).

In accordance with Article 1 of the Regulation, the RMS the Netherlands and co-RMS Belgium received an application from Arysta LifeScience S.A.S., Oxon Italia S.p.A. and Syngenta Crop Protection AG for the renewal of approval of the active substance chlorothalonil. Complying with Article 8 of the Regulation, the RMS checked the completeness of the dossier and informed the applicants, the co-RMS (Belgium), the European Commission and EFSA about the admissibility.

The RMS provided its initial evaluation of the dossier on chlorothalonil in the RAR, which was received by EFSA on 2 September 2016 (Netherlands, 2016). In accordance with Article 12 of the Regulation, EFSA distributed the RAR to the Member States and the applicants, Arysta LifeScience S.A.S., Oxon Italia S.p.A. and Syngenta Crop Protection AG, for consultation and comments on 24 October 2016. EFSA also provided comments. In addition, EFSA conducted a public consultation on the RAR. EFSA collated and forwarded all comments received to the European Commission on 4 January 2017. At the same time, the collated comments were forwarded to the RMS for compilation and evaluation in the format of a reporting table. The applicants were invited to respond to the comments in column 3 of the reporting table. The comments and the applicants' response were evaluated by the RMS in column 3.

The need for expert consultation and the necessity for additional information to be submitted by the applicants in accordance with Article 13(3) of the Regulation were considered in a telephone conference between EFSA and the RMS on 24 February 2017. On the basis of the comments received, the applicants' response to the comments and the RMS's evaluation thereof, it was concluded that additional information should be requested from the applicants, and that EFSA should conduct an expert consultation in the areas of mammalian toxicology, residues, environmental fate and behaviour and ecotoxicology.

The outcome of the telephone conference, together with EFSA's further consideration of the comments, is reflected in the conclusions set out in column 4 of the reporting table. All points that were identified as unresolved at the end of the comment evaluation phase and which required further consideration, including those issues to be considered in an expert consultation, were compiled by EFSA in the format of an evaluation table.

The conclusions arising from the consideration by EFSA, and as appropriate by the RMS, of the points identified in the evaluation table, together with the outcome of the expert consultation and the written consultation on the assessment of additional information, where these took place, were reported in the final column of the evaluation table.

A final consultation on the conclusions arising from the peer review of the risk assessment took place with Member States via a written procedure in November 2017.

This conclusion report summarises the outcome of the peer review of the risk assessment of the active substance and the representative formulation, evaluated on the basis of the representative uses of chlorothalonil as a fungicide on wheat, barley, tomato and potato, as proposed by the applicants. A list of the relevant endpoints for the active substance and the formulation is provided in Appendix A.

<sup>1</sup> Commission Implementing Regulation (EU) No 844/2012 of 18 September 2012 setting out the provisions necessary for the implementation of the renewal procedure for active substances, as provided for in Regulation (EC) No 1107/2009 of the European Parliament and of the Council concerning the placing of plant protection products on the market. OJ L 252, 19.9.2012, p. 26–32.

<sup>2</sup> Regulation (EC) No 1107/2009 of 21 October 2009 of the European Parliament and of the Council concerning the placing of plant protection products on the market and repealing Council Directives 79/117/EEC and 91/414/EEC. OJ L 309, 24.11.2009, p. 1–50.

In addition, a key supporting document to this conclusion is the peer review report (EFSA, 2017), which is a compilation of the documentation developed to evaluate and address all issues raised in the peer review, from the initial commenting phase to the conclusion. The peer review report comprises the following documents, in which all views expressed during the course of the peer review, including minority views, where applicable, can be found:

- the comments received on the RAR;
- the reporting tables (24 February 2017);
- the evaluation table (29 November 2017);
- the reports of the scientific consultation with Member State experts (where relevant);
- the comments received on the assessment of the additional information (where relevant);
- the comments received on the draft EFSA conclusion.

Given the importance of the RAR, including its revisions (Netherlands, 2017), and the peer review report, both documents are considered as background documents to this conclusion and thus are made publicly available.

It is recommended that this conclusion report and its background documents would not be accepted to support any registration outside the European Union (EU) for which the applicant has not demonstrated that it has regulatory access to the information on which this conclusion report is based.

## The active substance and the formulated product

Chlorothalonil is the ISO common name for tetrachloroisophthalonitrile (IUPAC).

The representative formulated products for the evaluation were 'A14111B' a suspension concentrate (SC) containing 400 g/L chlorothalonil and 80 g/L azoxystrobin; 'ARY-0474-001' and 'Chlorothalonil 500 g/l SC' suspension concentrates (SC) containing 500 g/L chlorothalonil.

The representative uses evaluated were foliar spray applications in wheat, barley, tomato and potato against a wide range of fungal pathogens including *Septoria tritici* in cereals and *Phytophthora infestans* and *Alternaria* spp. in tomatoes and potatoes. Full details of the Good Agricultural Practices (GAPs) can be found in the list of endpoints in Appendix A.

Data were submitted to conclude that the uses of chlorothalonil according to the representative uses proposed at the EU level result in a sufficient fungicidal efficacy against a broad spectrum of fungal diseases, following the guidance document SANCO/2012/11251-rev. 4 (European Commission, 2014).

A data gap has been identified for a transparent assessment of the search of the scientific peer-reviewed open literature on the active substance and its relevant metabolites, dealing with side effects on human health and non-target species and published within the 10 years before the date of submission of the dossier, to be conducted and reported in accordance with EFSA guidance on the submission of scientific peer-reviewed open literature for the approval of pesticide active substances under Regulation (EC) No 1107/2009 (EFSA, 2011).

## Conclusions of the evaluation

### 1. Identity, physical/chemical/technical properties and methods of analysis

The following guidance documents were followed in the production of this conclusion: SANCO/3029/99-rev. 4 (European Commission, 2000a), SANCO/3030/99-rev. 4 (European Commission, 2000b) and SANCO/825/00-rev. 8.1 (European Commission, 2010).

The reference specification was supported by batch data from industrial scale productions. The proposed minimum purity of the technical material is 985 g/kg. Hexachlorobenzene (HCB) and decachlorobiphenyl (DCB) are considered relevant impurities with a maximum content of 0.04 g/kg and 0.03 g/kg, respectively. The manufactured technical material meets the requirements of the existing FAO specification (288/TC, October 2015).

The batches used in the (eco)toxicological assessment support the original reference specification (See Sections 2 and 5).

The assessment of the data package revealed no issues that need to be included as critical areas of concern with respect to the identity, physical, chemical and technical properties of chlorothalonil or the representative formulations. The main data regarding the identity of chlorothalonil and its physical and chemical properties are given in Appendix A.

Considering the pre-approval data required for the risk assessment, a data gap was identified for the analytical methods used in the generation of toxicological pre-approval data (see Section 2). Methods of analysis are available for the determination of the active substance and the relevant impurities in the technical material and in the representative formulation.

Chlorothalonil residue (chlorothalonil and SDS-3701) can be monitored in food and feed of plant origin by gas chromatography with mass spectrometry (GC–MS) with limit of quantification (LOQ) of 0.01 mg/kg in all commodity groups. The method requires methylation of the metabolite SDS-3701 (R182281) with trimethylsilyl diazomethane. Liquid chromatography with tandem mass spectrometry (LC–MS/MS) without derivatisation exists for monitoring of this metabolite in all commodity groups with a LOQ of 0.01 mg/kg. However, it should be noted that the efficiency of the extraction procedure used in these methods was not verified for dry and high oil content commodities (data gap). Chlorothalonil residue (SDS-3701 only) in food of animal origin can be determined by individual or multiresidue methods using LC–MS/MS with LOQ of 0.01 mg/kg in all animal matrices. Data gaps were identified for a verification of the extraction procedure used and for an independent laboratory validation (ILV) of the methods for fat matrix.

Chlorothalonil in soil and air can be monitored by GC–MS with LOQs 0.01 mg/kg and 0.21  $\mu\text{g}/\text{m}^3$ , respectively. Appropriate GC–MS method exists for monitoring chlorothalonil in water with a LOQ of 0.05  $\mu\text{g}/\text{L}$ .

Gas chromatography with electron capture detector (GC–ECD) can be used for monitoring chlorothalonil in body fluids and tissues with LOQs of 0.05 mg/L and 0.01 mg/kg, respectively. SDS-3701 in body fluids can be determined by LC–MS/MS with a LOQ 0.01 mg/L. The methods for monitoring of SDS-3701 in food of animal origin can be used for determination of chlorothalonil residue in body tissues.

However, the residue definitions for food and feed of plant origin, animal products, water (drinking/ground and surface water) and body fluids are currently open and additional monitoring methods might be required should new components be included in the residue definitions.

## 2. Mammalian toxicity

The following guidance documents were followed in the production of this conclusion: SANCO/221/2000-rev. 10-final (European Commission, 2003), SANCO/10597/2003-rev. 10.1 (European Commission, 2012), Guidance on dermal absorption (EFSA PPR Panel, 2012) and Guidance on the Application of the CLP Criteria (ECHA, 2015).

Chlorothalonil was discussed during the Pesticides Peer Review Meeting 162.

The batches used in the toxicity studies support the technical specifications from all sources; two relevant impurities are identified, hexachlorobenzene – harmonised classification according to Regulation (EC) No 1272/2008<sup>3</sup> as Carc Cat 1B and STOT RE 1, and decachlorobiphenyl – harmonised classification as STOT RE 2; however, no concerns are raised at the levels specified in the technical specification. The toxicological relevance of impurities present in the technical specification has not been addressed for two impurities in the Syngenta source, and one impurity for each one of the Oxon and Arysta sources, respectively, whose relevance assessments are missing, this was identified as a data gap.

Bioavailability of chlorothalonil was found to be limited after oral administration (20% of the administered low dose of 5 mg/kg body weight (bw) in rats) based on the radioactivity excreted in urine and bile, excluding bile excretion during the first 4 hours that may be considered as not systemically available since the kidneys and not the liver are the target organs of chlorothalonil. This value is supported by the comparison of urine excretion after oral vs. intravenous administrations. The substance is widely distributed, shows affinity to binding to red blood cells, delaying its excretion. The substance undergoes extensive metabolism and is mostly excreted (> 80%) within 168 h via faeces. No potential for accumulation was observed. No *in vitro* interspecies comparative metabolism study has been provided that should include human tissue and it is unknown whether unique human metabolites may be formed (issue not be finalised); the residue definition for body fluids (urine and blood/plasma) relevant for human biomonitoring purposes has not been agreed during the peer review. These two issues were identified as data gaps. In addition, the analytical methods used in the toxicological studies

<sup>3</sup> Regulation (EC) No 1272/2008 of the European Parliament and of the Council of 16 December 2008 on classification, labelling and packaging of substances and mixtures, amending and repealing Directives 67/548/EEC and 1999/45/EC, and amending Regulation (EC) No 1907/2006. OJ L 353, 31.12.2008, p. 1–1355.



has not been reported or validated, which questions the validity of the toxicological studies, in particular the repeated-dose dietary studies (data gap and issue not finalised).

Chlorothalonil presents a low acute toxicity profile when administered via oral or dermal route; however, it was shown to be very toxic if inhaled (harmonised classification: Acute Tox. 2, H330 'Fatal if inhaled') and irritant to the respiratory tract (harmonised classification: STOT SE 3, H335 'may cause respiratory irritation'). It is not a skin irritant but may cause serious eye damage and allergic skin reactions (harmonised classification: Eye Dam. 1, H318 and Skin Sens. 1, H317); the peer review experts considered that a category 1A for skin sensitisation<sup>4</sup> may be appropriate.

The main target organs of chlorothalonil upon short- and long-term exposure in rats and mice are the kidneys (preneoplastic and neoplastic lesions) and forestomach (also preneoplastic and neoplastic lesions, the latter being considered to be rodent-specific and of low relevance to humans). For both tumour types, the mode of action (MoA) has been hypothesised, through biotransformation pathway for the kidneys and through chronic irritation of the forestomach. While it was agreed that the MoA for forestomach tumours is of low relevance to humans, the postulated MoA for kidney tumours is relevant to humans since no specific data has been generated to support a claimed quantitative difference between human and rodent's metabolism. The majority of experts concluded that given the fact that benign and malignant kidney tumours were observed in two species and were observed in two out of three independent studies in rats, and considering that the human relevance could not be excluded, carcinogenicity category 1B (Carc. 1B, H350 'May cause cancer') would be appropriate according to current criteria for classification (ECHA, 2015) – even if no new information appears to be available with regards to the assessment made by the European Chemical Bureau (ECB) responsible for the current harmonised classification. The RMS maintained the opinion that category 2 should be sufficient (in agreement with current harmonised classification). In dogs, the main organs affected by chlorothalonil were the liver, kidneys and adrenals with a no observed adverse effect level (NOAEL) of 5.1 mg/kg bw per day. The relevant short-term NOAEL is 1.5 mg/kg bw per day from the 90-day rat study, and the overall long-term NOAEL of 1.8 mg/kg bw per day from the 26-month study in rats. The relevant NOAEL for carcinogenic effects is 3.8 mg/kg bw per day in rats and 30.4 mg/kg bw per day in mice (excluding the local carcinogenic effects observed in rodents forestomach).

Gene mutation tests gave negative results overall. Positive chromosome aberration results *in vitro* were adequately overruled by *in vivo* micronucleus and chromosome aberration assays; it was concluded that chlorothalonil is unlikely to be genotoxic *in vivo*. No phototoxic potential was observed and therefore it is assumed that there is no photomutagenic concern.

Reproductive effects observed in a multigeneration toxicity study in rats were limited to delay in sexual maturation (i.e. vaginal opening) in females at parental and offspring's toxic dose (kidney and forestomach lesions, reduced pup's body weight, respectively). No delay in sexual maturation was observed in a pubertal development and thyroid function in juvenile/peripubertal rats. Levels 1, 2, 3 and 4 of the OECD conceptual framework (OECD, 2012) to assess the endocrine disrupting properties of chlorothalonil gave all negative results; therefore, no endocrine-mediated MoA with regard to androgen, oestrogen, steroidogenesis and thyroid (EATS) modalities could be linked to the single reproductive effect observed at high dose of 261 mg/kg bw per day in rats. Developmental toxicity was characterised by skeletal variations in rats and rabbits at maternal toxic dose levels (reduced body weight gain), and reduced fetal survival and increased incidence of malformations (polydactyly) in mice also at maternal toxic dose levels (clinical signs and reduced body weight and body weight gain). The opinion of the experts was divided and a small majority of experts, including the RMS, considered that there was insufficient evidence to propose classification with regards to developmental toxicity (possibly applicable to mice malformations). The interim provisions of Annex II, Point 3.6.5 of Regulation (EC) No 1107/2009 concerning human health for the consideration of endocrine-disrupting properties are not met. According to current methodology, chlorothalonil is unlikely to present endocrine-disrupting properties regarding the EATS modalities (OECD, 2012; EFSA Scientific Committee, 2013). Chlorothalonil did not present potential for neurotoxicity or immunotoxicity.

The toxicity profile of three plant, livestock and/or environmental metabolites has been provided; for other metabolites, genotoxicity studies were submitted. Regarding the plant and livestock **metabolite R182281 (SDS-3701)**, a number of toxicity studies are available showing a distinct toxicity profile compared to the parent chlorothalonil. The metabolite was shown to be acutely toxic after oral administration; in the absence of *in vivo* follow-up of positive and equivocal results in *in vitro* gene

<sup>4</sup> It should be noted that harmonised classification and labelling is formally proposed and decided in accordance with Regulation (EC) No 1272/2008.

mutation tests, its genotoxicity potential could not be concluded, therefore, no toxicological reference values could be set. Regarding the plant and groundwater **metabolite R611965 (SDS-46851)**, it was concluded that the compound present low acute toxicity after oral administration, it is unlikely to be genotoxic, carcinogenic or toxic for the reproduction or the development in rats; developmental toxicity in rabbits (reduced live fetuses and fetal weight) was associated with maternal toxicity and specific toxicological reference values could be set; the acceptable daily intake (ADI) of the metabolite is 0.5 mg/kg bw per day based on the NOAEL of 50 mg/kg bw per day from the 90-day toxicity study in dogs applying a standard uncertainty factor (UF) of 100; the acute reference dose (ARfD) is 0.83 mg/kg bw, based on a maternal and developmental lowest observable adverse effect level (LOAEL) of 250 mg/kg bw per day from the developmental toxicity study in rabbits, applying an increased UF of 300 to account for the use of a LOAEL. With regard to the plant and environmental **metabolite R417888**, according to a 90-day toxicity study in rats, it does not share the kidneys as target organs as the parent chlorothalonil; however, a genotoxic potential could not be excluded due to a positive and an equivocal *in vitro* gene mutation assay in mammalian cells which were not followed up *in vivo* and due to a potential for aneugenicity *in vivo*. Groundwater metabolites **R418503** (SYN548708), **R419492** (SYN548765), **R471811** (SYN548766), **SYN548008** (SYN548738), **SYN548580**, **R611968** (SDS-47525), **SYN507900** (SDS-66882) are unlikely to be genotoxic while a genotoxic potential could not be excluded for metabolite **R613636** (SDS-47525) because aneugenicity has not been adequately addressed and no data are available on metabolite **SYN548581** (SYN548764). All metabolites except R611965 (and R417888, if its genotoxic potential would be clarified) are considered toxicologically relevant according to the guidance document on the assessment of metabolites in groundwater if identified above the parametric value of 0.1 µg/L in groundwater according to fate and behaviour in the environment models, since it has not been demonstrated that they do not share the carcinogenic potential of the parent chlorothalonil; read across from a 'source' metabolite was not considered appropriate by the majority of the experts as they considered that the guidance document refers always to the parent as reference compound. A minority of experts including RMS and EFSA considered however, that read across against a 'source' metabolite could be done in some cases and based on this principle, the lack of carcinogenicity as observed in the source metabolite R417888 and R182281, could also be assumed for the downstream metabolites R471811, SYN507900 and R611968, respectively.

The ADI of chlorothalonil is 0.015 mg/kg bw per day based on kidney toxicity with a NOAEL of 1.5 mg/kg bw per day from the 90-day study in rat, supported by the rat, 2-year study, applying an UF of 100. This confirms the ADI previously established during the first review of chlorothalonil (European Commission, 2006).

The ARfD is 0.05 mg/kg bw, based on the NOAEL for acute effects in the rabbit developmental toxicity study of 5 mg/kg bw per day for bw loss observed at the beginning of exposure at 10 mg/kg bw per day; 100 UF applied. The previously established ARfD was 0.6 mg/kg bw based on an ARfD-specific study and applying a standard uncertainty factor of 100 (European Commission, 2006).

The acceptable operator exposure level (AOEL) is 0.003 mg/kg bw per day based on the NOAEL of 1.5 mg/kg bw per day from the 90-day rat study, applying an UF of 100 and a correction factor to account for the limited systemic bioavailability of 20%. The previously established AOEL was 0.009 mg/kg bw per day, based on the long-term rat study corrected by 30% oral absorption (European Commission, 2006).

The acute acceptable operator exposure level (AAOEL) is 0.01 mg/kg bw based on the developmental toxicity study in rabbits; 100 UF and 20% oral absorption factor applied.

Non-dietary exposure risk assessment has been provided for three representative formulations. Considering the lower values obtained from the different models presented (German model, UK POEM and/or EFSA calculator), the following outcome has been calculated: personal protective equipment (PPE) has to be worn by operators to ensure that the AOEL is not exceeded for cereals and tomato tractor-mounted applications (A14111B, SC, 400 g/L formulation only). The AOEL is exceeded for operators treating potatoes (tractor-mounted equipment) or tomatoes (tractor-mounted equipment for Oxon Chlorothalonil 500 g/L SC and ARY-0474-001, SC, 500 g/L formulations) and hand-held applications, even when PPE are worn. PPE has to be worn by workers re-entering treated crops (cereals, potatoes and tomatoes, the latter for A14111B, SC, 400 g/L formulation only) to ensure that the AOEL is not exceeded; the AOEL is exceeded for workers re-entering tomato crops (for Oxon Chlorothalonil 500 g/L SC and ARY-0474-001, SC, 500 g/L formulations). Bystander exposure exceeds the AOEL depending on the distance from the application, the crop, the application equipment and the formulation under consideration. Resident's exposure is estimated to remain below the AOEL for all

scenarios (except hand-held applications in tomatoes at 3 m distance (Oxon Chlorothalonil 500 g/L SC only) and tractor-mounted applications at 1 m distance (ARY-0474-001, SC, 500 g/L only).

### 3. Residues

The assessment in the residue section is based on the OECD guidance document on overview of residue chemistry studies (OECD, 2009), the OECD publication on maximum residue level (MRL) calculations (OECD, 2011), the European Commission guideline document on MRL setting (European Commission, 2011) and the Joint Meeting on Pesticide Residues (JMPR) recommendations on livestock burden calculations (JMPR, 2004, 2007).

Chlorothalonil was discussed at the Pesticides Peer Review Meeting 164.

Primary crop metabolism of chlorothalonil was investigated in cereal/grass crops (wheat), root crops (carrot), leafy crops (lettuce and celery), fruit (tomato), and pulses & oilseeds (peas and snap beans) upon foliar application, covering the five main crop categories. In the light of the toxicological concerns identified for chlorothalonil and several of its metabolites (see Section 2) and the specific requirements for identification efforts in metabolism studies in such cases, the detail of reporting of the metabolism information was considered insufficient. Moreover, as a consequence of the limited reporting, the compliance with requirements for metabolism studies could not be properly assessed (data gap). From the available metabolism information, chlorothalonil and R182281 (SDS-3701) seem to be the predominant compounds of the total residues in all investigated crops, but uncertainties remain in view of the significant proportions of unidentified fractions observed in each crop. There is indication from the studies in peas and wheat that also diglutathione conjugates of R182281 and di/triglutathione conjugates of chlorothalonil are formed in plants.

Given that chlorothalonil and R182281 do not share the same toxicological properties (see Section 2), the following preliminary residue definitions are proposed for primary crops: for monitoring, separately chlorothalonil and R182281, and for risk assessment, chlorothalonil (free and conjugated) and R182281 (free and conjugated), separately, pending full elucidation of the metabolic pattern in plants.

Confined rotational crop metabolism studies in leafy crops (lettuce, spinach), root crops (carrots, radish) and cereal crops (wheat) were provided, investigating varying plant back intervals up to one year. Deficiencies were noted in two of the three studies with regard to the study design, and moreover the detail of reporting of information was limited. In the study complying with current recommendations, further clarification is requested regarding actual levels and proportions of identified metabolites (data gaps) as this information is necessary to conduct a sound risk assessment. Moreover, for some of the rotational crop metabolites a toxicological concern could not be ruled out (see Section 2). Based on the available information and pending further clarification regarding the data on identity, levels and toxicity of metabolites in rotational crops, the compounds that should be considered for risk assessment could only be preliminarily identified as: R611965/R417888 (not separated but likely of different toxicity) and the conjugates of R613636, R611968 and R613800 (C15). For effective monitoring of residues in rotational crops, if applicable, metabolite R611965 might be a suitable marker to be included in the plant residue definition once the assessment of rotational crop residues is finalised and monitoring of residues in rotational crops would be considered relevant as outcome of this assessment.

In a hydrolysis study simulating food processing conditions, chlorothalonil was degraded with increasing temperatures into R182281 (up to 59% applied radioactivity (AR)), R613636 (up to 23% AR) and 4-amino-2,5,6-trichloroisophthalonitrile (up to 28% AR), the latter said to be an artefact while this still has to be demonstrated (data gap). For monitoring the same residue definition as for primary crops was proposed for processed commodities: Chlorothalonil and R182281, separately. The residue definition for risk assessment for processed commodities is preliminarily proposed as chlorothalonil, R182281 and R613636, separately, and should also consider conjugated residues where hydrolysis of conjugates present in the raw commodities cannot be assumed during food processing (e.g. cereals milling). R613636 and R182281 are toxicologically relevant metabolites since a genotoxic potential could not be excluded for both compounds (see Section 2). The potential inclusion of 4-amino-2,5,6-trichloroisophthalonitrile is pending information to address the related data gap. Whether the nature of R182281 residues under standard hydrolysis conditions at processing has to be investigated separately, could currently not be concluded.

The reported data on metabolism of chlorothalonil in lactating ruminants appeared to be incomplete and were not conclusively presented as to be readily accessible for review and to

demonstrate the study is reliable and compliant with current requirements (data gap). An acceptable metabolism study with chlorothalonil in poultry is available. In addition, in metabolism studies with R182281 in ruminants and poultry, the absorption and distribution of residues of R182281 in animal matrices was investigated while the studies are providing limited information with regard to the identity of residues in each of the animal commodities. Provided a summary of the ruminant metabolism studies of acceptable quality will not lead to the conclusion that additional compounds of relevance might be expected in ruminant commodities or that significant residues were not identified, the residue definition for both monitoring and risk assessment of animal commodities should be defined as R182281. For fish, no data on metabolism or feeding were available, however based on the log  $P_{OW}$  for compounds included in the plant residue definition, such data appears not to be triggered. Information available on fish in the section on ecotoxicology confirms that bioaccumulation is not expected for chlorothalonil and R182281; however, metabolites di- and triglutathione conjugates of chlorothalonil were found in fish and the relevance of this finding for the assessment of metabolism and residues in fish should be considered (data gap).

A sufficient number of critical GAP (cGAP) conform residues trials with separate analysis of chlorothalonil and R182281 residue levels are available in tomato and potato but not in wheat and barley (data gap). It is noted that the assessed potato GAP does not cover new potatoes.

Potato and tomato samples were stored for duration of time and under conditions for which integrity was demonstrated by acceptable storage stability studies with chlorothalonil and R182281. For the cereal trials, however, residues of chlorothalonil could not be demonstrated as sufficiently stable over the entire period for which the majority of the grain and/or straw samples in the wheat and barley trials were stored (observed decline of greater 30%). Moreover, storage stability of residues of R182281 was not addressed in cereal grain (data gap) and the storage duration of straw samples in some trials exceeded the period covered by storage stability data on R182281 in straw (data gap). Storage duration and conditions of sample extracts for all plant commodities has to be clarified (data gap). None of the trials in tomato, wheat, barley and potato determined levels of conjugates of chlorothalonil and R182281, included in the preliminary plant residue definition for risk assessment. Hence, the available residue trials do only address residues according to the preliminary residue definition for monitoring and MRL setting. Conversion factors for risk assessment purposes could not be derived and further data in line with the residue definition for risk assessment should be generated for all representative uses to facilitate the establishment of appropriate conversion factors for the concerned commodities (data gaps).

The submitted rotational crop residue trials conducted in the USA are considered of limited relevance for assessment of the representative uses in terms of the application rate and the geological, climatic and/or agricultural conditions under which the trials were performed, but may be used as indicative information. The study design in the four trials conducted in EU in spinach, wheat, barley and carrots is sufficiently reflecting representative conditions and showed significant residues for R611965 at the short and medium plant-back interval while residues of chlorothalonil and R182281 were always below LOQ. However, the integrity of samples and reliability of the residue levels was only conclusively demonstrated for R611965 by sufficient storage stability data while stability of chlorothalonil and R182281 during sample storage (up to 30 months) could not be demonstrated (data gap). Other rotational crops metabolites included in the preliminary residue definition for risk assessment, such as R417888 ( $DT_{90}$  205–3,320 days) for which a genotoxic potential could not be excluded, were not investigated in any of the rotational crop residue trials.

In the majority of the available processing trials in potato, tomato and cereal commodities the residue levels of chlorothalonil and R182281 were investigated, not fully addressing the residue definition proposed for risk assessment of processed commodities. Conjugated residues of chlorothalonil and R182281 were determined neither in the raw nor the processed commodity and thus the relevance of conjugated residues in processed products is unclear. Moreover, only two residue trials on cereals and one trial in tomato are investigating in addition to chlorothalonil and R182281 the residues of R613636 in processed commodities. The finding that R613636 is predominantly formed under conditions employing higher temperatures and pressure might be relevant to processes such as high-pressure pasteurisation and sterilisation, and targeted investigations might be necessary when the assessment of the toxicological properties, specifically of the genotoxic potential of R613636 was finalised (data gap).

A data gap was also identified with regard to residue levels in pollen and bee products for human consumption.

A reliable livestock dietary burden calculation can only be conducted following availability of data sufficiently addressing the relevant residues for risk assessment in feed items (primary and rotational crops) and their magnitude. Therefore, the assessment on the carry-over of residues in animal commodities and estimation of their levels could not be finalised, but it is expected that residues in animal commodities might be significant. Whether a feeding study in poultry might be triggered is pending finalisation of this assessment. Feeding studies in ruminants are available; however, an assessment of their acceptability is pending (integrity of fat samples and/or of extracts during storage to be demonstrated (data gaps)).

The consumer risk assessment cannot be finalised in view of the multiple identified data gaps, leading to derivation of preliminary residue definitions in plant, including processed commodities, and in animal commodities. However, as R182281 is a pertinent residue in all these commodities and in the absence of toxicological reference values for R182281, even an indicative consumer risk assessment using the preliminary residue definitions cannot be conducted. It is noted that for R182281 a genotoxic potential could not be excluded. Moreover, under processing conditions employing higher temperatures, degradation of chlorothalonil into R613636 was observed next to formation of R182281. Also for R613636, a genotoxic potential could not be excluded. Further to that, a genotoxic potential could not be excluded for R417888, a medium to very high persistent soil metabolite that together with R611965 formed the major residue in the rotational crop metabolism study but was not investigated in rotational crop residue trials. Altogether, the data situation regarding chlorothalonil residues does not permit the conclusion that, for at least one of the representative uses, any harmful effect on human or animal health can be excluded.

Two of the submitted studies for the renewal of chlorothalonil cover data gaps, which were identified during the Art. 12 MRL review (EFSA, 2012): a storage stability study for chlorothalonil in high acid content commodities and a new poultry metabolism study with chlorothalonil, addressing the request for further characterisation of the total radioactive residue (TRR) in poultry commodities.

#### 4. Environmental fate and behaviour

Chlorothalonil was discussed at the Pesticides Peer Review TC 163.

The rates of dissipation and degradation in the environmental matrices investigated were estimated using FOCUS (2006) kinetics guidance. In soil laboratory incubations under aerobic conditions in the dark, chlorothalonil exhibited very low to moderate persistence, forming the major (> 10% AR) metabolite R419492 (max. 12.4% AR), which exhibited high to very high persistence, metabolites R417888 (max. 15.2% AR) and R471811 (max. 11.9% AR), which exhibited medium to very high persistence, metabolites SDS-3701 (R182281) (max. 32.2% AR), R611965 (max. 13.2% AR), and R611966 (max. 8.1% AR), which exhibited moderate to very high persistence, respectively, metabolite SYN507900 (max. 5.8% AR), which exhibited medium to very high persistence, metabolite R418503 (max. 6.1% AR), which exhibited low to very high persistence, and metabolites R611967 (max. 13.2% AR) and R613636 (max. 10.4% AR) which exhibited low to high persistence, respectively. Mineralisation of the phenyl ring <sup>14</sup>C radiolabel to carbon dioxide accounted for 23.8% AR after 92 days. The formation of unextractable residues (not extracted by acetonitrile/water) for this radiolabel accounted for 43.4% AR after 125 days.

In anaerobic soil incubations, chlorothalonil transformation was similar to that under aerobic conditions, forming the major (> 10% AR) metabolites SDS-3701 (R182281) (max. 28.3% AR), R417888 (max. 15.4% AR), R471811 (max. 5.3% AR), SYN507900 (max. 10.0% AR), R611965 (max. 7.8% AR), R611966 (max. 10.7% AR), R613636 (max. 4.8% AR). Anaerobic conditions were not considered to be of major importance for the representative uses. In a soil photolysis study, no new metabolites were formed at > 10% AR. The contribution of photolytic transformation processes on soil surfaces to the dissipation of chlorothalonil from the soil environment is regarded as negligible.

Chlorothalonil exhibited medium mobility to immobility. Metabolite SDS-3701 (R182281) exhibited medium to low soil mobility, metabolites R417888, R418503, R419492, R471811 and SYN507900 exhibited very high soil mobility. Metabolite R611965 exhibited very high to high mobility, metabolites R611966 and R611967 exhibited medium to low mobility. Metabolite R613636 exhibited high to medium mobility and R611968 exhibited high mobility. It was concluded that the adsorption of chlorothalonil and its metabolites was not pH dependent.

In reliable field soil dissipation studies carried out at two sites in the EU, chlorothalonil exhibited low persistence. The field data endpoints were not combined with laboratory values to derive modelling endpoints as EFSA guidance (EFSA, 2014) was not in place when the dossier was deemed

admissible. Field  $DT_{50}$  estimates are not available for metabolites SDS-3701 (R182281), R417888, R418503, R419492, R471811, SYN507900, R611966, R611965 and R613636 which in some laboratory soil incubations, had single first-order  $DT_{50}$  greater than 60 days. In this situation, field  $DT_{50}$  and  $DT_{90}$  estimates are needed according to the data requirements. Therefore, this has been identified as a data gap (see Section 7).

In a new lysimeter study of 2 years duration done using an application rate of 2,500 g/ha to wheat in June, no chlorothalonil was detected in the leachates. However, the following metabolites were detected exceeding 0.1 µg parent equivalents/L as annual mean concentrations: R417888, R418503, R419492, R471811, R611965, R611968, and R613636. Also, metabolites SYN548008 (M3), SYN548581 (M11), SYN548580 (M2), M10 and M7 were detected in the leachates, but not in soil. Metabolites SYN548008 (M3) and SYN548581 (M11) were identified, but a data gap (see Section 7) was set for these metabolites for deriving degradation and adsorption parameters in three representative soils. Metabolites SYN548580 (M2), M10 and M7 remained not identified in spite of the efforts made to elucidate their nature. Therefore, this has been identified as a data gap (see Section 7).

In laboratory incubations in dark aerobic natural sediment water systems, chlorothalonil exhibited very low to low persistence, forming the major metabolites SDS-3701 (R182281) (max. 44.5% AR in water and 9.55% AR in sediment, exhibiting moderate to very high persistence based on the available data), R613841 (max. 34.2% AR in water and 11.6% AR in sediment, exhibiting moderate to medium persistence), R613842 (max. 9.0% AR in sediment, exhibiting moderate persistence), R613801 (max. 7.1% AR in water and 20.0% AR in sediment, exhibiting low to moderate persistence) and SYN546671 (max. 12.2% AR in sediment, exhibiting moderate to very high persistence). The unextractable sediment fraction was the major sink for the phenyl ring  $^{14}C$  radiolabel, accounting for 29.6–68.9% AR at study end (100 days). Mineralisation of this radiolabel accounted for 0.3–9.0% AR at the end of the study.

The rate of decline of chlorothalonil in a laboratory sterile aqueous photolysis experiment was similar to that occurred in the aerobic sediment water incubations. The major (> 10% AR) metabolites formed were SYN546934 (max. 9.4% AR), PD1 (R613911) (max. 53.2% AR), PD2 (R613801) (max. 34.4% AR), and PD3 (max. 14.4% AR). Irradiation of phenyl-labelled chlorothalonil in natural water resulted in formation of the major photodegradation products PD1 (R613911) (max. 12.2% AR), PD2 (R613801) (max. 20.5% AR), PD4 (max. 19.9% AR) and PD5 (SYN549430) (max. 32.7% AR). Metabolite PD4 remained not identified. Therefore, this has been identified as a data gap (see Section 7).

The necessary surface water and sediment exposure assessments (predicted environmental concentrations (PEC) calculations) were carried out for the metabolites SDS-3701 (R182281), R417888, R418503, R419492, R471811, SYN507900, SYN546671, SYN546934, R611965, R611966, R611967, R613636, R613801 (PD2), R613841, R613842, PD1 (R613911), PD4, PD5 (SYN549430), U38, U40 and U44, using the FOCUS (2001) step 1 and step 2 approach (version 2.1 of the Steps 1-2 in FOCUS calculator).

For the active substance chlorothalonil, appropriate step 3 (FOCUS, 2001) and step 4 calculations were available. The step 4 calculations appropriately followed the FOCUS (2007) guidance, with no-spray drift buffer zones of up to 20 m being implemented for the drainage scenarios (representing a 57–91% spray drift reduction), and combined no-spray buffer zones with vegetative buffer strips of up to 20 m (reducing solute flux in run-off by 80% erosion runoff by 95%) being implemented for the run-off scenarios. The SWAN tool (version 1.1.4) was appropriately used to implement these mitigation measures in the simulations. However, risk managers and others may wish to note that while run-off mitigation is included in the step 4 calculations available, the FOCUS (2007) report acknowledges that for substances with  $K_{Foc} < 2000$  mL/g (i.e. chlorothalonil), the general applicability and effectiveness of run-off mitigation measures had been less clearly demonstrated in the available scientific literature, than for more strongly adsorbed compounds.

The necessary groundwater exposure assessments were appropriately carried out using FOCUS (2009) scenarios and the models PEARL 4.4.4 and PELMO 5.5.3 for the active substance chlorothalonil and metabolites SDS-3701 (R182281), R417888, R418503, R419492, R471811, SYN507900, R611965, R611966, R611967, R613636, R611968, SYN548008 (M3), SYN548581 (M11), M2, M7, M10. For the unidentified metabolites from the lysimeter (M2, M7, and M10), a transfer factor based on the ratio of measured versus modelled concentrations of known metabolites was used in order to derive a groundwater exposure assessment.

The potential for groundwater exposure from the representative uses by chlorothalonil above the parametric drinking water limit of 0.1 µg/L was concluded to be low in geoclimatic situations that are

represented by all nine FOCUS groundwater scenarios for chlorothalonil and metabolites SDS-3701 (R182281), R611966, R611967, R613636.

For representative uses on winter and spring cereals, the 80th percentile annual average recharge concentrations leaving the top 1 m soil layer were estimated to be  $> 0.1 \mu\text{g/L}$  at seven out of nine scenarios for metabolite R611968 and  $> 0.75 \mu\text{g/L}$  at nine out of nine scenarios for metabolites R417888, R419492, R471811, SYN507900, R611965, SYN548008 (M3), SYN548581 (M11), M2, M7, and M10 and at two out of nine scenarios for metabolite R418503, considering two applications per year.

For representative uses on tomatoes, the 80th percentile annual average recharge concentrations leaving the top 1 m soil layer were estimated to be  $> 0.1 \mu\text{g/L}$  at five out of five scenarios for metabolites R611968 and R418503 and  $> 0.75 \mu\text{g/L}$  at five out of five scenarios for metabolites R417888, R419492, R471811, SYN507900, R611965, SYN548008 (M3), SYN548581 (M11), M2, M7, and M10, considering annual application.

For representative uses on potatoes were estimated to be  $> 0.1 \mu\text{g/L}$  at seven out of nine scenarios for metabolites R611968 and R418503 and  $> 0.75 \mu\text{g/L}$  at nine out of nine scenarios for metabolites R417888, R419492, R471811, SYN507900, R611965, SYN548008 (M3), SYN548581 (M11), M2, M7, and M10, considering annual application.

It should be noted that with the available toxicological information, chlorothalonil metabolites (except metabolite R611965) would be concluded as relevant groundwater metabolites should they be predicted to occur in groundwater above the parametric drinking water limit of  $0.1 \mu\text{g/L}$  due to the proposed classification of chlorothalonil as carcinogen category 1B (see Section 2). Therefore, for groundwater exposure assessment, a critical area of concern was identified for all relevant metabolites.

The PEC in soil, surface water, sediment and groundwater covering the representative uses assessed can be found in Appendix A of this conclusion.

The applicant did not provide appropriate information to address the effect of water treatments processes on the nature of the residues that might be present in surface water and groundwater, when surface water or groundwater are abstracted for drinking water. This has led to the identification of a data gap (see Section 7) and results in the consumer risk assessment not being finalised (see Section 9).

## 5. Ecotoxicology

The risk assessment was based on the following documents: European Commission (2002a,b), SETAC (2001), EFSA (2009), EFSA PPR Panel (2013) and EFSA (2013). According to Regulation (EU) No. 283/2013 data should be provided regarding the acute and chronic toxicity to honeybees and data to address the development of honeybee brood and larvae. As the European Commission (2002a) does not provide a risk assessment scheme which is able to use the chronic toxicity data for adult honeybees and the honeybee brood, when performing the risk assessment according to European Commission (2002a), the risk to adult honeybees from chronic toxicity and the risk to bee brood, could not be finalised due to the lack of a risk assessment scheme. Therefore, the EFSA (2013) was used for risk assessment in order to reach a conclusion for the representative uses.

Several aspects of the risk assessment to non-target organisms were discussed at the Pesticides Peer Review Meeting 165.

It is noted that formulations different than the representative formulations were tested. The endpoints from these tests were considered appropriate for the risk assessment of the representative formulations.

The risk assessment (acute and long-term) to **birds** via dietary exposure resulted in a low risk at the lower tier levels for the representative use on cereals, tomatoes and potatoes. The assessment was performed in order to cover the combined exposure to chlorothalonil and its plant metabolite SDS-3701 for the acute risk and individual exposure to the parent and the metabolite for the long-term risk assessment. For the long-term risk to birds of chlorothalonil, the endpoint derived by the RMS with a benchmark dose modelling, i.e.  $\text{BMDL}_5$  of  $119 \text{ mg/kg bw per day}$  was used. This was agreed at the experts' meeting as the most appropriate value to use for the reproductive risk assessment for birds.

The dietary exposure assessment at lower tier levels (e.g. screening or tier I) of the metabolite SDS-3701 were discussed and agreed at the experts' meeting. In particular, it was agreed to adjust the tier I shortcut values with the highest residues level of  $1.1 \text{ mg/kg}$  in plant material, of  $0.02 \text{ mg/kg}$  in tomatoes and the soil PEC of  $0.351 \text{ mg/kg soil}$  as surrogate for residue level in insects and seeds. These values were used for the risk assessment to both birds and mammals.

The acute risk to **mammals** was low at lower tier level for all the representative uses for both chlorothalonil and the metabolite SDS-3701, while a long-term high risk was identified for small herbivorous mammals for all the representative uses both for chlorothalonil and the metabolite SDS-3701; a high risk was identified for frugivorous mammals for chlorothalonil. To refine the risk assessment for small herbivorous mammals, higher interception factors based on EFSA (2009) were considered. The refined risk was low for cereals and potatoes but it was still high for chlorothalonil for the use in tomatoes. A focal species study in tomato field in Italy was provided; however, it was considered not sufficient to exclude the risk, therefore a data gap for further refinement was identified. For the risk assessment refinement for frugivorous mammals, default residues in tomatoes according to the EFSA (2009) were considered. However, the toxicity exposure ratio (TER) was still below the trigger (4.6), therefore a data gap was identified for further information to address the risk identified for chlorothalonil.

A risk assessment from secondary poisoning to birds and mammals was not needed. A low risk was identified from consumption of contaminated water.

Valid endpoints addressing the effects on **aquatic organisms** were available for fish (acute and chronic), aquatic invertebrates (acute and chronic), algae, aquatic plants and sediment dwellers. In addition, acute toxicity studies on amphibians were available. By using the available and agreed endpoints in the risk assessment, a high risk to aquatic organisms (with the exception of aquatic plants for all uses) was concluded for all the representative uses and for most of the FOCUS scenarios at Step 3 level. During the Pesticide Peer Review meeting 165, the experts agreed that the acute risk to fish could be refined by calculating a HC5 derived with the species sensitivity distribution (SSD) approach. By using this refinement, together with the available FOCUS step 4 PEC, a low acute risk to fish was concluded for all the representative uses when mitigation measures are considered. It is noted that the experts considered not acceptable to include the available acute data on amphibians in the SSD since amphibians appeared to be more sensitive than fish; therefore, a separate acute risk assessment was performed with this group of organisms. A high acute risk to amphibians (aquatic life stages) was concluded for all the representative uses (data gap). The available refinement to the chronic risk assessment for fish (FSTRA, pulse exposure study) was discussed at the Pesticide Peer Review meeting 165 meeting but was considered not acceptable by the experts (data gap). With respect to the chronic risk to amphibians, considering the effects observed in the available amphibians metamorphosis assay, the Tier 1 chronic endpoint on fish was not considered sufficient to cover chronic effects on amphibians. Therefore, a Larval Amphibian Growth and Development Assay (LAGDA) study was requested (data gap). At the PPR 165 meeting, the experts agreed to use in the refined risk assessment for aquatic invertebrates and algae the ETO-RAC derived from the available mesocosm study (Ashwell et al., 2002 in Netherlands (2017)) with an assessment factor of 3. By using this refinement in the risk assessment, a high risk was still concluded for the uses on cereals and tomatoes for FOCUS scenario R4 (data gap) while a low risk was concluded for the use on potatoes for all scenarios uses when mitigation measures are considered. It is noted that an ERO-RAC from an additional mesocosms (Schaefers et al., 2015 in Netherlands (2017)) was available which was considered relevant to refine the risk for the uses on tomatoes and potatoes. The use of the ERO-RAC for the refined risk assessment on cereals is considered questionable since in the study from Schaefers et al., 2015 only one application was performed. It is noted that a full comparison between the exposure in the mesocosms and the FOCUS profiles for the representative uses in line with EFSA PPR Panel (2013) was not available, therefore, a data gap was identified. It is noted that the above described refinements covered also the risk to sediment dwellers.

Valid endpoints addressing the acute toxicity to fish, aquatic invertebrates and algae were available for the surface water metabolites R182281, R611965, R417888, R613636, R613841 and R613842. It is noted that a literature study was available indicating a higher toxicity of R182281 than the parent; however, this observation came from an *in vitro* bioassay and was not confirmed in the standard toxicity tests. For metabolite R613801, data were available only for aquatic invertebrates and algae, therefore, the risk assessment for fish was conducted by considering this metabolite as 10 times more toxic than the parent. The same approach was used for the remaining pertinent surface water metabolites since toxicity data were not available for all taxa of aquatic organisms. A low risk to aquatic organisms for all the representative uses was concluded for metabolites R182281, R611965, R417888, R613636, and R613842. A high risk to aquatic organism was concluded for metabolite R613841. A high risk to aquatic organisms could not be excluded for all the representative uses for all the remaining metabolites (data gap). It is noted that, in line with EFSA PPR Panel (2013), metabolites SYN548008, SYN548581, M2, M7, M10 and R611968 were not further considered in the aquatic risk



assessment since found exclusively in a lysimeter study. It is noted that a data gap for the identification of metabolites M2, M7 and M10 was set in Section 4, therefore, pending on this data gap further information may be needed to address the risk to aquatic organisms for these metabolites. The RMS disagreed with the data gaps set for the surface water metabolites and considered the risk to aquatic organisms for the pertinent surface water metabolites as low. A low risk to sediment dwellers was concluded for all the pertinent metabolites.

A risk assessment for **bees** was performed by the RMS according to EFSA (2013). A low risk was identified for all the representative uses for acute oral and contact exposure for honeybees and bumblebees; a low chronic risk was identified for honeybee exposures. It is noted that toxicity studies on honeybee larvae were available for the representative formulation 'A14111B' and with a formulation different than those covered by the representative uses, however, a study performed with the active substance was not available (data gap). Exposure from the metabolite SDS-3701 was considered to be covered by the risk assessment with the parent. No data were available for sublethal effect assessment (i.e. hypopharyngeal glands (HPG)) and a risk assessment from exposure to contaminated water was also not available (data gap). No data were provided for the assessment of accumulative effects and for the full assessment of the risk to wild bees.

Tier 1 and extended laboratory studies were available with the two standard **non-target arthropod** species and additional species. The studies were conducted with the representative formulations and different formulations which, however, can be considered worst-case in terms of content of active substance. Based on the available data, high risk (in-field) was identified for non-target arthropods for all the representative uses except for the representative use on tomatoes (A14111B) (data gap).

Toxicity data with **earthworms** were available with the active substance and the pertinent soil metabolites. Data with the representative formulations and additional formulations were also available.

When using the endpoint with the active substance, low risk to earthworms was concluded for the representative uses of chlorothalonil and for the pertinent metabolites. High risk to earthworms was, however, identified for the representative formulation 'Chlorothalonil 500 SC' when applied to cereals and tomatoes. A field study was available to further address the risk to earthworms when exposed to that specific formulated product. However, considering its robustness, the experts, at the Peer review Experts' meeting 165, agreed that the risk identified for this formulation at the Tier I could not be excluded with this field study. Therefore, the higher toxicity exhibited by the active substance when formulated as 'Chlorothalonil 500 SC' needs to be further considered at Member States level.

Low risk to **soil macroorganisms other than earthworms, soil microorganisms, non-target terrestrial plants and biological methods of sewage treatment** was concluded.

With regard to the endocrine disruption potential, as discussed in Section 2, it is unlikely that chlorothalonil is an endocrine disruptor in mammals. However, from the available ecotoxicological data (amphibians metamorphosis assay), endocrine-disrupting properties via the thyroidal modality cannot be excluded (see specific consideration for the risk assessment above). Regarding fish, as reported above a fish short-term screening assay was available, in this study a decrease in fecundity was observed in all concentrations tested while the other parameters assessed (vitellogenin in male and females, histology and sex secondary characteristics) resulted as not statistically different with respect to the control. Some evidence of oestrogen receptor a (ERa) agonist activity of chlorothalonil and R182281 and thyroid receptor b (TRb) agonistic and antagonistic activities of R182281 was available from a non-standard *in vitro* study on zebra fish embryo, however, no firm conclusions could be drawn from this study. No firm conclusion can be drawn regarding birds.

## 6. Overview of the risk assessment of compounds listed in residue definitions triggering assessment of effects data for the environmental compartments (Tables 1–4)

**Table 1:** Soil

Compound (name and/or code)	Persistence	Ecotoxicology
<b>Chlorothalonil</b>	Very low to moderate persistence single first-order order and biphasic kinetics DT <sub>50</sub> 0.44–31.6 days (DT <sub>90</sub> 1.46–68.2 days, 20°C pF 2 soil moisture) European field dissipation studies single first-order DT <sub>50</sub> 7.4–28.4 days	Low risk
<b>SDS-3701 (R182281)</b>	Moderate to very high persistence single first-order DT <sub>50</sub> 38.0–609 days (DT <sub>90</sub> 126–> 1,000 days, 20°C pF 2 soil moisture)	Low risk
<b>R417888</b>	Medium to very high persistence single first-order DT <sub>50</sub> 61.6–> 1,000 days (DT <sub>90</sub> 205–3,320 days, 20°C pF 2 soil moisture)	Low risk
<b>R418503</b>	Low to very high persistence single first-order DT <sub>50</sub> 2.96–1,000 days (DT <sub>90</sub> 9.85–3,320 days, 20°C pF 2 soil moisture)	Low risk
<b>R419492</b>	High to very high persistence single first-order DT <sub>50</sub> 136–1,000 days (DT <sub>90</sub> 451–3,320 days, 20°C pF 2 soil moisture)	Low risk
<b>R471811</b>	Medium to very high persistence single first-order DT <sub>50</sub> 97.9–> 1,000 days (DT <sub>90</sub> 325–3,320 days, 20°C pF 2 soil moisture)	Low risk
<b>SYN507900</b>	Medium to very high persistence single first-order and biphasic kinetics DT <sub>50</sub> 61.6–666 days (DT <sub>90</sub> 205–> 1,000 days, 20°C pF 2 soil moisture)	Low risk
<b>R611965</b>	Moderate to very high persistence single first-order DT <sub>50</sub> 36.6–1,000 days (DT <sub>90</sub> 122–3,320 days, 20°C pF 2 soil moisture)	Low risk
<b>R611966</b>	Moderate to very high persistence single first-order order and biphasic kinetics DT <sub>50</sub> 18.6–885 days (DT <sub>90</sub> 55.9–> 1,000 days, 20°C pF 2 soil moisture)	Low risk
<b>R611967</b>	Low to high persistence single first-order order and biphasic kinetics DT <sub>50</sub> 8.2–128 days (DT <sub>90</sub> 45.2–237 days, 20°C pF 2 soil moisture)	Low risk
<b>R613636</b>	Low to high persistence single first-order order kinetics DT <sub>50</sub> 11.4–106 days (DT <sub>90</sub> 37.7–354 days, 20°C pF 2 soil moisture)	Low risk

DT<sub>50</sub>: period required for 50% dissipation; DT<sub>90</sub>: period required for 90% dissipation.

**Table 2:** Groundwater

Compound (name and/or code)	Mobility in soil	> 0.1 µg/L at 1 m depth for the representative uses <sup>(a)</sup>	Pesticidal activity	Toxicological relevance
<b>Chlorothalonil</b>	Medium mobility to immobile K <sub>Foc</sub> 330–7,000 mL/g	No	Yes	Yes
<b>SDS-3701 (R182281)</b>	Medium to low mobility K <sub>Foc</sub> 250–718 mL/g	No	No data	Yes Acutely toxic when ingested; Genotoxicity potential cannot be excluded in the absence of <i>in vivo</i> follow up to the positive and equivocal results <i>in vitro</i> gene mutation tests
<b>R417888</b>	Very high mobility K <sub>Foc</sub> 4.6–17.2 mL/g	Yes Wheat-barley: 9/9 FOCUS scenario (4.0–23.4 µg/L, bi-annual application) Tomatoes: 5/5 FOCUS scenario (3.6–17.3 µg/L, annual application) Potatoes: 9/9 FOCUS scenario (1.8–9.4 µg/L, annual application)	No	Yes Genotoxic potential cannot be excluded regarding gene mutation and aneugenicity
<b>R418503</b>	Too low to measure – very high mobility K <sub>Foc</sub> 2.0–4.0 mL/g	Yes Wheat-barley: 8/9 FOCUS scenario (0.12–2.2 µg/L, bi-annual application) Tomatoes: 5/5 FOCUS scenario (0.12–0.58 µg/L, annual application) Potatoes: 6/9 FOCUS scenario (0.11–1.14 µg/L, annual application)	No	Yes Based on the harmonised classification of the parent as Carc 2 and proposed classification of the peer review as Carc 1B; Unlikely to be genotoxic
<b>R419492</b>	Too low to measure – Very high mobility	Yes Wheat-barley: 9/9 FOCUS scenario (7.7–45.0 µg/L, bi-annual application) Tomatoes: 5/5 FOCUS scenario (6.1–24.8 µg/L, annual application) Potatoes: 9/9 FOCUS scenario (0.5–13.9 µg/L, annual application)	No	Yes Based on the harmonised classification of the parent as Carc 2 and proposed classification of the peer review as Carc 1B; Unlikely to be genotoxic

Compound (name and/or code)	Mobility in soil	> 0.1 µg/L at 1 m depth for the representative uses <sup>(a)</sup>	Pesticidal activity	Toxicological relevance
<b>R471811</b>	Too low to measure – Very high mobility	Yes Wheat-barley: 9/9 FOCUS scenario (2.2–33.5 µg/L, bi-annual application) Tomatoes: 5/5 FOCUS scenario (1.8–17.2 µg/L, annual application) Potatoes: 9/9 FOCUS scenario (0.9–8.5 µg/L, annual application)	No	Yes Based on the harmonised classification of the parent as Carc 2 and proposed classification of the peer review as Carc 1B; Unlikely to be genotoxic
<b>SYN507900</b>	Very high mobility K <sub>Foc</sub> 11.0–22.0 mL/g	Yes Wheat-barley: 9/9 FOCUS scenario (4.4–26.1 µg/L, bi-annual application) Tomatoes: 5/5 FOCUS scenario (4.6–15.0 µg/L, annual application) Potatoes: 9/9 FOCUS scenario (2.3–8.4 µg/L, annual application)	No	Yes Based on the harmonised classification of the parent as Carc 2 and proposed classification of the peer review as Carc 1B; Unlikely to be genotoxic
<b>R611965</b>	Very high to high mobility K <sub>Foc</sub> 3.2–77.0 mL/g	Yes Wheat-barley: 9/9 FOCUS scenario (3.4–22.1 µg/L, bi-annual application) Tomatoes: 5/5 FOCUS scenario (3.0–14.8 µg/L, annual application) Potatoes: 9/9 FOCUS scenario (1.3–7.7 µg/L, annual application)	No	No (up to step 3 of stage 3) Unlikely to be genotoxic; of lower toxicity than chlorothalonil; does not share the same target organ as the parent (kidneys) responsible to the carcinogenic potential; ADI: 0.5 mg/kg bw per day ARfD: 0.83 mg/kg bw
<b>R611966</b>	Medium to low mobility K <sub>Foc</sub> 389–911 mL/g	No	No data	Yes Based on the harmonised classification of the parent as Carc 2 and proposed classification of the peer review as Carc 1B; No data on genotoxicity
<b>R611967</b>	Medium to low mobility K <sub>Foc</sub> 212–1121 mL/g	No	No data	Yes Based on the harmonised classification of the parent as Carc 2 and proposed classification of the peer review as Carc 1B; No data on genotoxicity

Compound (name and/or code)	Mobility in soil	> 0.1 µg/L at 1 m depth for the representative uses <sup>(a)</sup>	Pesticidal activity	Toxicological relevance
<b>R613636</b>	High to medium mobility K <sub>Foc</sub> 130–325 mL/g	No	No	Yes Based on the harmonised classification of the parent as Carc 2 and proposed classification of the peer review as Carc 1B; Genotoxic potential could not be excluded: aneugenicity has not been addressed
<b>R611968</b>	High mobility K <sub>Foc</sub> 51.0–128.0 mL/g	Yes Wheat-barley: 7/9 FOCUS scenario (0.14–0.66 µg/L, bi-annual application) Tomatoes: 4/5 FOCUS scenario (0.14–0.27 µg/L, annual application) Potatoes: 6/9 FOCUS scenario (0.1–0.27 µg/L, annual application)	No	Yes Based on the harmonised classification of the parent as Carc 2 and proposed classification of the peer review as Carc 1B; Unlikely to be genotoxic
<b>SYN548008 (M3)</b>	Data gap	Yes Wheat-barley: 9/9 FOCUS scenario (1.2–79.2 µg/L, bi-annual application) Tomatoes: 5/5 FOCUS scenario (1.4–22.4 µg/L, annual application) Potatoes: 9/9 FOCUS scenario (0.12–12.0 µg/L, annual application)	No	Yes Based on the harmonised classification of the parent as Carc 2 and proposed classification of the peer review as Carc 1B; Unlikely to be genotoxic
<b>SYN548581 (M11)</b>	Data gap	Yes Wheat-barley: 9/9 FOCUS scenario (3.6–21.0 µg/L, bi-annual application) Tomatoes: 5/5 FOCUS scenario (3.1–14.2 µg/L, annual application) Potatoes: 9/9 FOCUS scenario (1.5–7.5 µg/L, annual application)	No	Yes Based on the harmonised classification of the parent as Carc 2 and proposed classification of the peer review as Carc 1B; No data on genotoxicity
<b>M2</b>	Open	Yes Wheat-barley: 9/9 FOCUS scenario (2.4–8.5 µg/L, bi-annual application) Tomatoes: 5/5 FOCUS scenario (1.9–5.7 µg/L, annual application) Potatoes: 9/9 FOCUS scenario (0.9–3.0 µg/L, annual application)	No	Yes Based on the harmonised classification of the parent as Carc 2 and proposed classification of the peer review as Carc 1B;

Compound (name and/or code)	Mobility in soil	> 0.1 µg/L at 1 m depth for the representative uses <sup>(a)</sup>	Pesticidal activity	Toxicological relevance
<b>M7</b>	Open	Yes Wheat-barley: 9/9 FOCUS scenario (5.6–20.4 µg/L, bi-annual application) Tomatoes: 5/5 FOCUS scenario (4.4–13.7 µg/L, annual application) Potatoes: 9/9 FOCUS scenario (2.0–7.2 µg/L, annual application)	No	Yes Based on the harmonised classification of the parent as Carc 2 and proposed classification of the peer review as Carc 1B; No data on genotoxicity
<b>M10</b>	Open	Yes Wheat-barley: 9/9 FOCUS scenario (2.4–8.5 µg/L, bi-annual application) Tomatoes: 5/5 FOCUS scenario (1.9–5.7 µg/L, annual application) Potatoes: 9/9 FOCUS scenario (0.9–3.0 µg/L, annual application)	No	Yes Based on the harmonised classification of the parent as Carc 2 and proposed classification of the peer review as Carc 1B; No data on genotoxicity

KFoc: Freundlich organic carbon adsorption coefficient; FOCUS: Forum for the Co-ordination of Pesticide Fate Models and their Use; ADI: acceptable daily intake; ARfD: acute reference dose; bw: body weight.

(a): FOCUS scenarios or a relevant lysimeter.

**Table 3:** Surface water and sediment

Compound (name and/or code)	Ecotoxicology
<b>Chlorothalonil</b>	High risk
<b>SDS-3701 (R182281)</b>	Low risk
<b>R417888</b>	Low risk
<b>R418503</b>	Data gap
<b>R419492</b>	Data gap
<b>R471811</b>	Data gap
<b>SYN507900</b>	Data gap
<b>R611965</b>	Low risk
<b>R611966</b>	Data gap
<b>R611967</b>	Data gap
<b>R613636</b>	Low risk

Compound (name and/or code)	Ecotoxicology
<b>SYN546671</b>	Data gap
<b>R613841</b>	High risk
<b>R613842</b>	Low risk
<b>U38</b>	Data gap
<b>U40</b>	Data gap
<b>U44</b>	Data gap
<b>PD2 (R613801)</b>	Data gap
<b>PD1 (R613911)</b>	Data gap
<b>SYN546934</b>	Data gap
<b>PD4</b>	Data gap
<b>PD5 (SYN549430)</b>	Data gap

**Table 4:** Air

Compound (name and/or code)	Toxicology
<b>Chlorothalonil</b>	Rat LC <sub>50</sub> inhalation 0.1 mg/L air per 4 h (nose only); Acute Tox 2, H330 'Fatal if inhaled'; STOT SE; H335 'May cause respiratory irritation'

LC<sub>50</sub>: lethal concentration, median.

## 7. Data gaps

This is a list of data gaps identified during the peer review process, including those areas in which a study may have been made available during the peer review process but not considered for procedural reasons (without prejudice to the provisions of Article 56 of Regulation (EC) No 1107/2009 concerning information on potentially harmful effects).

- A transparent presentation and assessment of the search of the scientific peer-reviewed open literature on the active substance and its relevant metabolites, dealing with side effects on human health and non-target species and published within the 10 years before the date of submission of the dossier, to be conducted and reported in accordance with EFSA guidance on the submission of scientific peer-reviewed open literature for the approval of pesticide active substances under Regulation (EC) No 1107/2009 (EFSA, 2011; relevant for all representative uses evaluated; submission date proposed by the applicant: unknown).
- Efficiency of the extraction procedure used in the analytical methods for the determination of residues in dry and high oil content plant commodities (relevant for all representative uses evaluated; submission date proposed by the applicant: unknown; see Section 1).
- Efficiency of the extraction procedure used in the analytical methods for the determination of residues in food from animal origin (relevant for all representative uses evaluated; submission date proposed by the applicant: unknown; see Section 1).
- ILV of the monitoring methods for determination of residues in fat matrix (relevant for; submission date proposed by the applicant: unknown; see Section 1).
- The toxicological relevance of impurities present in the technical specification in comparison with the toxicological profile of the parent for two impurities in the Syngenta source, and one impurity in the Oxon and Arysta sources, respectively (relevant for all representative uses evaluated; submission date proposed by the applicant: unknown; see Section 2).
- *In vitro* interspecies comparative metabolism study, including human tissues (relevant for all representative uses evaluated; submission date proposed by the applicant: unknown; see Section 2).
- Residue definition for body fluids (urine and blood/plasma for human biomonitoring purposes) (relevant for all representative uses evaluated; submission date proposed by the applicant: unknown; see Section 2).
- Identification and validation of the analytical methods used in each toxicological study, in particular repeated-dose dietary studies critical in setting the toxicological reference values (relevant for all representative uses evaluated; submission date proposed by the applicant: unknown; see Section 2).
- The genotoxic potential of the plant and/or groundwater metabolites R182281 (SDS-3701) (genotoxic potential inconclusive in the absence of *in vivo* follow-up of positive and equivocal results in *in vitro* gene mutation tests), R417888 (genotoxic potential could not be excluded regarding gene mutation and aneugenicity), R613636 (SDS-47525) (genotoxic potential could not be excluded: aneugenicity has not been addressed), and SYN548581 (SYN548764), R611966, R611967, M7, M10 (no data), and possibly M2 (if different structure from metabolite SYN548580) has not been addressed (relevant for all representative uses evaluated; submission date proposed by the applicant: unknown; see Sections 2–4).
- Demonstration of the integrity of samples and reliability of results for chlorothalonil residues in cereal grain and straw in primary and rotational crops field trials with cereals or new trials where analysis was conducted after an adequate period of sample storage (relevant for all representative uses; submission date proposed by the applicant: unknown; see Section 3).
- Storage stability data for R182281 in cereal grain, and as appropriate, data with extended duration in cereal straw to cover the maximum storage interval in the primary and rotational crop residue trials with cereal crops (relevant for all representative uses evaluated; submission date proposed by the applicant: unknown; see Section 3).
- Clarification regarding the storage duration and conditions of sample extracts in magnitude of residues (MOR) plant and livestock studies and, if applicable, a presentation of the information regarding storage stability of chlorothalonil and R182281 in sample extracts of plant and animal commodities in line with OECD recommendations, i.e. reporting of individual uncorrected results (relevant for all representative uses evaluated; submission date proposed by the applicant: unknown; see Section 3).



- A completed summary of storage stability study King C, Prince P (1995) with animal matrices to validate the residue levels of R182281 in fat in the ruminant feeding studies (relevant for the representative uses in wheat, barley and potato; submission date proposed by the applicant: unknown; see Section 3).
- Completion and correction, as appropriate, of the figures in the metabolism studies in primary crops, and demonstration that these studies are compliant with the OECD recommendations, considering also the identified toxicological concerns for a number of chlorothalonil metabolites (relevant for all representative uses evaluated; submission date proposed by the applicant: unknown; see Section 3).
- Clarification regarding the individual contribution of the co-eluted compounds R611965 and R417888 in the major fraction in the rotational crop metabolism study Rizzo (2005) (relevant for all representative uses evaluated; submission date proposed by the applicant: unknown; see Section 3).
- Clarification regarding the distribution of the different metabolites in the fraction of glucosyl conjugates of R613636, R611968 and R613800 (C15), which was identified in all rotational crops in the metabolism study Rizzo (2005) (relevant for all representative uses evaluated; submission date proposed by the applicant: unknown; see Section 3).
- Completion of the figures and a conclusive presentation of the data in the metabolism studies in ruminants, and demonstration that these studies are compliant with the OECD recommendations (relevant for the representative uses in wheat, barley and potato; submission date proposed by the applicant: unknown; see Section 3).
- A reliable livestock dietary burden calculation following availability of data sufficiently addressing the relevant residues for risk assessment in feed items and their magnitude (relevant for the representative uses in wheat, barley and potato; submission date proposed by the applicant: unknown; see Section 3).
- The relevance of the findings in the fish bioconcentration study McEwen (1997) to address metabolism and residues in fish with regard to the dietary exposure potential (nature and magnitude) resulting from residues in feed items should be addressed (relevant for the representative uses in wheat, barley and potato; submission date proposed by the applicant: unknown; see Section 3).
- A sufficient residue trial data set on barley (NEU/SEU) compliant with the cGAP and the residue definition for monitoring and risk assessment in plants, once confirmed, and taking into account the limited storage stability of residues in cereal commodities (relevant for the representative use in barley; submission date proposed by the applicant: unknown; see Section 3).
- A sufficient residue trial data set on wheat (NEU/SEU) compliant with the cGAP and the residue definition for monitoring and risk assessment in plants, once confirmed, and taking into account the limited storage stability of residues in cereal commodities (relevant for the representative use in wheat; submission date proposed by the applicant: unknown; see Section 3).
- A sufficient residue trial data set on tomato (NEU/SEU) compliant with the residue definition for risk assessment in plants, once confirmed, in order to establish appropriate conversion factors (relevant for the representative use in tomato; submission date proposed by the applicant: unknown; see Section 3).
- A sufficient residue trial data set on potato (NEU/SEU) compliant with the residue definition for risk assessment in plants, once confirmed, in order to establish appropriate conversion factors (relevant for the representative use in potato; submission date proposed by the applicant: unknown; see Section 3).
- Further evidence that the compound 4-amino-2,5,6-trichloroisophthalonitrile, said to be an artefact in the hydrolysis study simulating food processing conditions, will not result from the degradation of chlorothalonil under actual processing conditions (relevant for the representative use in barley; submission date proposed by the applicant: unknown; see Section 3).
- Investigations of the relevance of conjugated residues in processed products and pending finalisation of the assessment of the toxicological properties of R613636, investigation of residue levels of this compound in processed commodities prepared under conditions employing higher temperatures and/or pressure (relevant for the representative use in barley; submission date proposed by the applicant: unknown; see Section 3).

- Information against the data requirement on residue levels in pollen and in bee products for human consumption resulting from residues taken up by honeybees from crops at blossom (relevant for all representative uses evaluated; submission date proposed by the applicant: unknown; see Section 3).
- Adsorption and degradation endpoints to be derived for metabolites SYN548008 (M3) and SYN548581 (M11) (relevant for all representative uses evaluated, submission date proposed by the applicant: unknown; see Section 4).
- Field dissipation studies to be conducted for metabolites SDS-3701 (R182281), R417888, R418503, R419492, R471811, SYN507900, R611966, R611965 and R613636 (relevant for all representative uses evaluated; submission date proposed by the applicant: unknown; see Section 4).
- The identity of metabolites PD4, SYN548580 (M2), M10 and M7 is unknown (relevant for all representative uses evaluated; submission date proposed by the applicant: unknown; see Section 4).
- Information on the effect of water treatment processes on the nature of residues of both the active substance and its identified metabolites potentially present in surface and groundwater, when surface water or groundwater are abstracted for drinking water, were not sufficient in order to assess the consumer risk from the consumption of drinking water (relevant for all representative uses evaluated, submission date proposed by the applicant: unknown; see Section 4).
- The long-term risk to herbivorous mammals and to frugivorous mammals for chlorothalonil should be further addressed (relevant for use in tomatoes; submission date proposed by the applicant: unknown; see Section 5).
- Further data to address the risk to aquatic organisms for chlorothalonil including: data to address the chronic risk to fish (relevant for all representative uses), data to address the acute risk to amphibians (relevant for all representative uses) and data to address the risk identified for aquatic invertebrates and algae (relevant for the uses on cereals) (submission date proposed by the applicant: unknown; see Section 5).
- A LAGDA with chlorothalonil (relevant for all representative uses evaluated; submission date proposed by the applicant: unknown; see Section 5).
- A full comparison of the exposure in the mesocosm studies with the FOCUS profiles for the representative uses in line with EFSA PPR Panel (2013) (relevant for all representative uses evaluated; submission date proposed by the applicant: unknown; see Section 5).
- Further data to address the risk to aquatic organisms for metabolites R613841, R418503, R419492, R471811, SYN507900, R611966, R611967, SYN546671, R613841, U38, U40, U44, PD2 (R613801), PD1 (R613911), SYN546934, PD4, PD5 (SYN549430) (relevant for all representative uses evaluated; submission date proposed by the applicant: unknown; see Section 5).
- Assessment of sublethal effect (i.e. HPG) and the risk to honeybees from consumption of contaminated water should be performed (relevant for all representative uses evaluated; submission date proposed by the applicant: unknown; see Section 5).
- A toxicity study on honeybee larvae (preferably with a repeated exposure regime) performed with the active substance (relevant for all representative uses evaluated; submission date proposed by the applicant: unknown; see Section 5).
- Further data to address the risk to non-target arthropods (relevant for all representative uses evaluated except for the representative use on tomatoes (A14111B); submission date proposed by the applicant: unknown; see Section 5).

## **8. Particular conditions proposed to be taken into account to manage the risk(s) identified**

- PPE has to be worn by operators to ensure that the AOEL is not exceeded for cereals and tomato tractor-mounted applications (A14111B, SC, 400 g/L formulation only) (see Section 2).
- PPE has to be worn by workers re-entering treated crops (cereals, potatoes and tomatoes – A14111B, SC, 400 g/L formulation only) to ensure that the AOEL is not exceeded (see Section 2).

## 9. Concerns

### 9.1. Issues that could not be finalised

An issue is listed as 'could not be finalised' if 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 in accordance with Article 29(6) of Regulation (EC) No 1107/2009 and as set out in Commission Regulation (EU) No 546/2011<sup>5</sup> and if 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).

An issue is also listed as 'could not be finalised' if the available information is considered insufficient to conclude on whether the active substance can be expected to meet the approval criteria provided for in Article 4 of Regulation (EC) No 1107/2009.

- 1) The analytical methods used in the toxicological studies were not identified and therefore not validated, these questions the validity of the studies, in particular repeated-dose dietary studies (see Section 2).
- 2) The need for further tests and risk assessment to unique human metabolites could not be finalised while an *in vitro* comparative metabolism study was not submitted (see Section 2).
- 3) The chronic risk to amphibians could not be finalised (see Section 5).
- 4) The consumer risk assessment from the consumption of water could not be finalised, whilst satisfactory information was not available to address the effect of water treatment processes on the nature of the residues that might be present in surface water, when surface water is abstracted for drinking water (see Section 4).
- 5) The consumer risk assessment is not finalised. The residue definitions for risk assessment in plant and animal commodities are preliminary. In the absence of toxicological reference values for R182281, even an indicative consumer risk assessment using the preliminary residue definitions cannot be conducted (see Section 3).

### 9.2. Critical areas of concern

An issue is listed as a critical area of concern if there is enough information available to perform an assessment for the representative uses in line with the uniform principles in accordance with Article 29 (6) of Regulation (EC) No 1107/2009 and as set out in Commission Regulation (EU) No 546/2011, and if this assessment does not permit the conclusion 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 if the assessment at the higher tier level could not be finalised due to lack of information, and if the assessment performed at the lower tier level does not permit the conclusion 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 if, in the light of current scientific and technical knowledge using guidance documents available at the time of application, the active substance is not expected to meet the approval criteria provided for in Article 4 of Regulation (EC) No 1107/2009.

- 6) The proposed classification of chlorothalonil by the peer review as carcinogen category 1B in accordance to the provisions of Regulation (EC) No 1272/2008 (while harmonised classification is category 2) does not fulfil the approval criteria of Annex II, point 3.6.3 of Regulation (EC) No 1107/2009 (see Section 2).
- 7) High risk to amphibians (acute and chronic) and to fish (chronic) for chlorothalonil was identified for all the representative uses (see Section 5).

<sup>5</sup> Commission Regulation (EU) No 546/2011 of 10 June 2011 implementing Regulation (EC) No 1107/2009 of the European Parliament and of the Council as regards uniform principles for evaluation and authorisation of plant protection products. OJ L 155, 11.6.2011, p. 127–175.

- 8) Chlorothalonil metabolites (except metabolite R611965) are relevant groundwater metabolites should they be predicted to occur in groundwater above the parametric drinking water limit of 0.1 µg/L due to the proposed classification of chlorothalonil as carcinogen category 1B (see Section 4).
- 9) A genotoxicity concern cannot be excluded for residues to which consumers will be exposed (see Section 3).

### **9.3. Overview 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 Section 8, has been evaluated as being effective, then 'risk identified' is not indicated in Table 5.)

**Table 5:** Overview of concerns

Representative use		Wheat			Barley	Tomatoes tractor mounted			Tomatoes hand-held			Potatoes
Formulation		A14111B	ARY-0474-001	Oxon Chlorothalonil 500	All	A14111B	ARY-0474-001	Oxon Chlorothalonil 500	A14111B	ARY-0474-001	Oxon Chlorothalonil 500	Oxon Chlorothalonil 500
<b>Operator risk</b>	Risk identified						X	X	X	X	X	X
	Assessment not finalised											
<b>Worker risk</b>	Risk identified						X	X		X	X	
	Assessment not finalised											
<b>Bystander risk</b>	Risk identified	X (< 5 m distance)	X (< 5 m distance)	X (< 5 m distance)	X (< 5 m distance)	X (< 5 m distance)	X (< 10 m distance)	X (< 5 m distance)	X (< 15 m distance)	X	X (< 15 m distance)	X (< 5 m distance)
	Assessment not finalised											
<b>Resident</b>	Risk identified						X (1 m distance)				X (3 m distance)	
	Assessment not finalised											
<b>Consumer risk</b>	Risk identified	X <sup>9</sup>	X <sup>9</sup>	X <sup>9</sup>	X <sup>9</sup>	X <sup>9</sup>	X <sup>9</sup>	X <sup>9</sup>	X <sup>9</sup>	X <sup>9</sup>	X <sup>9</sup>	X <sup>9</sup>
	Assessment not finalised	X <sup>4,5</sup>	X <sup>4,5</sup>	X <sup>4,5</sup>	X <sup>4,5</sup>	X <sup>4,5</sup>	X <sup>4,5</sup>	X <sup>4,5</sup>	X <sup>4,5</sup>	X <sup>4,5</sup>	X <sup>4,5</sup>	X <sup>4,5</sup>
<b>Risk to wild non-target terrestrial vertebrates</b>	Risk identified					X	X	X	X	X	X	
	Assessment not finalised											
<b>Risk to wild non-target terrestrial organisms other than vertebrates</b>	Risk identified	X	X	X	X	X	X	X	X	X	X	X
	Assessment not finalised											
<b>Risk to aquatic organisms</b>	Risk identified	X <sup>7</sup>	X <sup>7</sup>	X <sup>7</sup>	X <sup>7</sup>	X <sup>7</sup>	X <sup>7</sup>	X <sup>7</sup>	X <sup>7</sup>	X <sup>7</sup>	X <sup>7</sup>	X <sup>7</sup>
	Assessment not finalised	X <sup>3</sup>	X <sup>3</sup>	X <sup>3</sup>	X <sup>3</sup>	X <sup>3</sup>	X <sup>3</sup>	X <sup>3</sup>	X <sup>3</sup>	X <sup>3</sup>	X <sup>3</sup>	X <sup>3</sup>
<b>Groundwater exposure to active substance</b>	Legal parametric value breached											
	Assessment not finalised											

Representative use		Wheat			Barley	Tomatoes tractor mounted				Tomatoes hand-held			Potatoes
Groundwater exposure to metabolites	Legal parametric value breached <sup>(a)</sup>	X <sup>8</sup>	X <sup>8</sup>	X <sup>8</sup>	X <sup>8</sup>	X <sup>8</sup>	X <sup>8</sup>	X <sup>8</sup>	X <sup>8</sup>	X <sup>8</sup>	X <sup>8</sup>	X <sup>8</sup>	X <sup>8</sup>
	Parametric value of 10 µg/L <sup>(a)</sup> breached												
	Assessment not finalised												

Columns are grey if no safe use can be identified. The superscript numbers relate to the numbered points indicated in Sections 9.1 and 9.2. Where there is no superscript number, see Sections 2–6 for further information.

(a): Value for non-relevant metabolites prescribed in SANCO/221/2000-rev. 10 final, European Commission, 2003.

## References

- ECHA (European Chemicals Agency), 2015. Guidance on the Application of the CLP Criteria; Guidance to Regulation (EC) No 1272/2008 on classification, labelling and packaging (CLP) of substances and mixtures. Version 4.1, June 2015. Reference: ECHA-15-G-05-EN; ISBN: 978-92-9247-413-3; Available online: [http://echa.europa.eu/documents/10162/13562/clp\\_en.pdf](http://echa.europa.eu/documents/10162/13562/clp_en.pdf)
- EFSA (European Food Safety Authority), 2009. Guidance on Risk Assessment for Birds and Mammals on request from EFSA. EFSA Journal 2009;7(12):1438, 358 pp. <https://doi.org/10.2903/j.efsa.2009.1438>
- EFSA (European Food Safety Authority), 2011. Submission of scientific peer-reviewed open literature for the approval of pesticide active substances under Regulation (EC) No 1107/2009. EFSA Journal 2011;9(2):2092, 49 pp. <https://doi.org/10.2903/j.efsa.2011.2092>
- EFSA (European Food Safety Authority), 2012. Reasoned opinion on the review of the existing MRLs for chlorothalonil. EFSA Journal 2012;10(10):2940, 87 pp. <https://doi.org/10.2903/j.efsa.2012.2940>
- EFSA (European Food Safety Authority), 2013. EFSA Guidance Document on the risk assessment of plant protection products on bees (*Apis mellifera*, *Bombus* spp. and solitary bees). EFSA Journal 2013;11(7):3295, 268 pp. <https://doi.org/10.2903/j.efsa.2013.3295>
- EFSA (European Food Safety Authority), 2014. EFSA Guidance Document for evaluating laboratory and field dissipation studies to obtain DegT50 values of active substances of plant protection products and transformation products of these active substances in soil. EFSA Journal 2014;12(5):3662, 37 pp. <https://doi.org/10.2903/j.efsa.2014.3662>
- EFSA (European Food Safety Authority), 2017. Peer review report to the conclusion regarding the peer review of the pesticide risk assessment of the active substance chlorothalonil. Available online: [www.efsa.europa.eu](http://www.efsa.europa.eu)
- EFSA PPR Panel (EFSA Panel on Plant Protection Products and their Residues), 2012. Guidance on dermal absorption. EFSA Journal 2012;10(4):2665, 30 pp. <https://doi.org/10.2903/j.efsa.2012.2665>
- EFSA PPR Panel (EFSA Panel on Plant Protection Products and their Residues), 2013. Guidance on tiered risk assessment for plant protection products for aquatic organisms in edge-of-field surface waters. EFSA Journal 2013;11(7):3290, 186 pp. <https://doi.org/10.2903/j.efsa.2013.3290>
- EFSA Scientific Committee, 2013. Scientific Opinion on the hazard assessment of endocrine disruptors: scientific criteria for identification of endocrine disruptors and appropriateness of existing test methods for assessing effects mediated by these substances on human health and the environment. EFSA Journal 2013;11(3):3132, 84 pp. <https://doi.org/10.2903/j.efsa.2013.3132>
- European Commission, 2000a. Residues: guidance for generating and reporting methods of analysis in support of pre-registration data requirements for Annex II (Part A, Section 4) and Annex III (Part A, Section 5) of Directive 91/414. SANCO/3029/99-rev. 4, 11 July 2000.
- European Commission, 2000b. Technical material and preparations: guidance for generating and reporting methods of analysis in support of pre- and post-registration data requirements for Annex II (Part A, Section 4) and Annex III (Part A, Section 5) of Directive 91/414. SANCO/3030/99-rev. 4, 11 July 2000.
- European Commission, 2002a. Guidance Document on Terrestrial Ecotoxicology Under Council Directive 91/414/EEC. SANCO/10329/2002-rev. 2 final, 17 October 2002.
- European Commission, 2002b. Guidance Document on Aquatic Ecotoxicology Under Council Directive 91/414/EEC. SANCO/3268/2001-rev. 4 final, 17 October 2002.
- European Commission, 2003. Guidance Document on Assessment of the Relevance of Metabolites in Groundwater of Substances Regulated under Council Directive 91/414/EEC. SANCO/221/2000-rev. 10 final, 25 February 2003.
- European Commission, 2006. Review report for the active substance chlorothalonil finalised in the Standing Committee on the Food Chain and Animal Health at its meeting on 15 February 2005 in view of the inclusion of chlorothalonil in Annex I of Directive 91/414/EEC. SANCO/4343/2000 final (revised). 28 September 2006.
- European Commission, 2010. Guidance Document on residue analytical methods. SANCO/825/00-rev. 8.1, 16 November 2010.
- European Commission, 2011. Guidelines on comparability, extrapolation, group tolerances and data requirements for setting MRLs. SANCO 7525/VI/95-rev. 9. March 2011, p. 1–46.
- European Commission, 2012. Guidance document on the assessment of the equivalence of technical materials of substances regulated under Regulation (EC) No 1107/2009. SANCO/10597/2003-rev. 10.1, 13 July 2012.
- European Commission, 2014. Guidance document on the renewal of approval of active substances to be assessed in compliance with Regulation (EU) No 844/2012. SANCO/2012/11251-rev. 4, 12 December 2014.
- FOCUS (Forum for the Co-ordination of Pesticide Fate Models and their Use), 2001. FOCUS surface water scenarios in the EU evaluation process under 91/414/EEC. Report of the FOCUS Working Group on Surface Water Scenarios. EC Document Reference SANCO/4802/2001-rev. 2, 245 pp., as updated by Generic guidance for FOCUS surface water scenarios, v. 1.1, March 2012.
- FOCUS (Forum for the Co-ordination of Pesticide Fate Models and their Use), 2006. Guidance document on estimating persistence and degradation kinetics from environmental fate studies on pesticides in EU Registration Report of the FOCUS Work Group on Degradation Kinetics. EC Document Reference SANCO/10058/2005-v. 2.0, 434 pp.

- FOCUS (Forum for the Co-ordination of Pesticide Fate Models and their Use), 2007. Landscape and mitigation factors in aquatic risk assessment. Volume 1. Extended summary and recommendations. Report of the FOCUS Working Group on Landscape and Mitigation Factors in Ecological Risk Assessment. EC Document Reference SANCO/10422/2005 v. 2.0, 169 pp.
- FOCUS (Forum for the Co-ordination of Pesticide Fate Models and their Use), 2009. Assessing potential for movement of active substances and their metabolites to ground water in the EU. Report of the FOCUS Workgroup. EC Document Reference SANCO/13144/2010-v. 1, 604 pp., as outlined in Generic guidance for tier 1 FOCUS groundwater assessment, v. 2.0, January 2011.
- JMPR (Joint Meeting on Pesticide Residues), 2004. Report of the Joint Meeting of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Core Assessment Group on Pesticide Residues, Rome, Italy, 20–29 September 2004, 383 pp.
- JMPR (Joint Meeting on Pesticide Residues), 2007. Report of the Joint Meeting of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Core Assessment Group on Pesticide Residues, Geneva, Switzerland, 18–27 September 2007, 164 pp.
- Netherlands, 2016. Renewal Assessment Report (RAR) on the active substance chlorothalonil prepared by the rapporteur Member State the Netherlands, in the framework of Commission Implementing Regulation (EU) No 844/2012, September 2016. Available online: [www.efsa.europa.eu](http://www.efsa.europa.eu)
- Netherlands, 2017. Revised Renewal Assessment Report (RAR) on chlorothalonil prepared by the rapporteur Member State the Netherlands in the framework of Commission Implementing Regulation (EU) No 844/2012, October 2017. Available online: [www.efsa.europa.eu](http://www.efsa.europa.eu)
- OECD (Organisation for Economic Co-operation and Development), 2009. Guidance document on overview of residue chemistry studies. ENV/JM/MONO(2009)31, 28 July 2009.
- OECD (Organisation for Economic Co-operation and Development), 2011. OECD MRL calculator: spreadsheet for single data set and spreadsheet for multiple data set, 2 March 2011. In: Pesticide Publications/Publications on Pesticide Residues. Available online: [www.oecd.org](http://www.oecd.org)
- OECD (Organisation for Economic Co-operation and Development), 2012. Series on Testing and Assessment: No 150: Guidance document on Standardised Test Guidelines for Evaluating Chemicals for Endocrine Disruption. ENV/JM/MONO(2012)22, 524 pp.
- SETAC (Society of Environmental Toxicology and Chemistry), 2001. Guidance document on regulatory testing and risk assessment procedures for plant protection products with non-target arthropods. ESCORT 2.

## Abbreviations

a.s.	active substance
AAOEL	acute acceptable operator exposure level
ADI	acceptable daily intake
AOEL	acceptable operator exposure level
AR	applied radioactivity
ARfD	acute reference dose
bw	body weight
CLP	classification, labelling and packaging
DAR	draft assessment report
DAT	days after treatment
DCB	decachlorobiphenyl
DT <sub>50</sub>	period required for 50% dissipation (define method of estimation)
DT <sub>90</sub>	period required for 90% dissipation (define method of estimation)
EATS	oestrogen, androgen, thyroid and steroidogenesis modalities
ECB	European Chemical Bureau
ECHA	European Chemicals Agency
EEC	European Economic Community
ERa	oestrogen receptor a ( )
FAO	Food and Agriculture Organization of the United Nations
FOCUS	Forum for the Co-ordination of Pesticide Fate Models and their Use
GAP	Good Agricultural Practice
GC	gas chromatography
HCB	hexachlorobenzene
HPG	hypopharyngeal glands
ILV	independent laboratory validation
ISO	International Organization for Standardization
IUPAC	International Union of Pure and Applied Chemistry

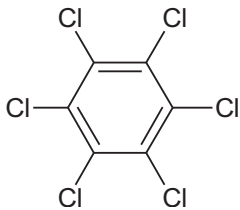
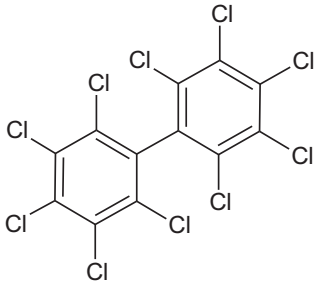
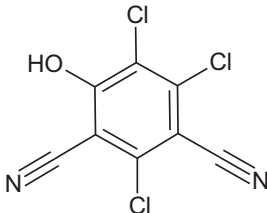
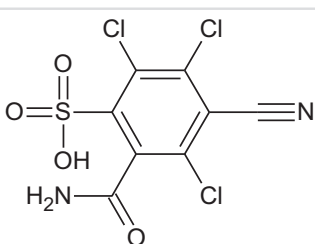
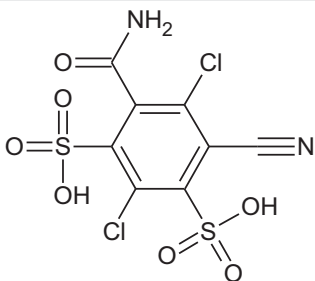
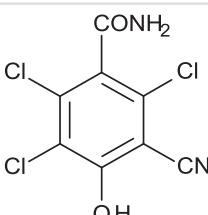


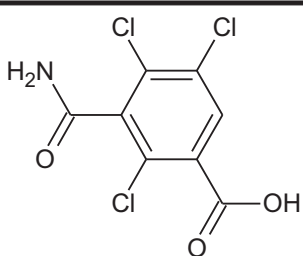
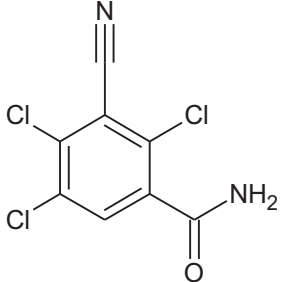
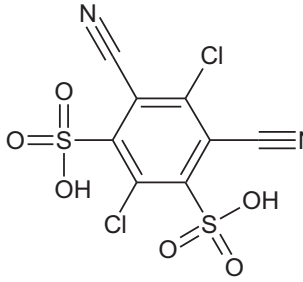
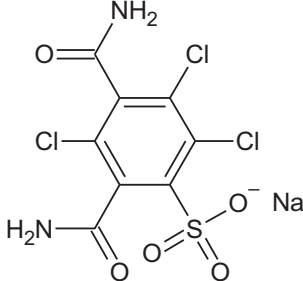
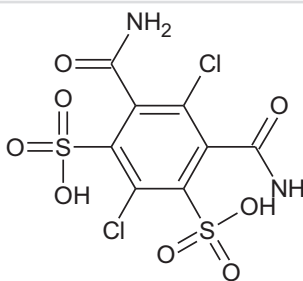
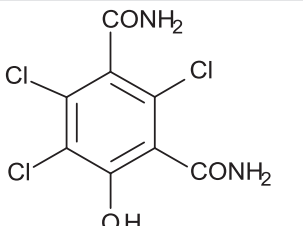
JMPR	Joint Meeting of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Expert Group on Pesticide Residues (Joint Meeting on Pesticide Residues)
$K_{Foc}$	Freundlich organic carbon adsorption coefficient
LAGDA	Larval Amphibian Growth and Development Assay
$LC_{50}$	lethal concentration, median
LC-MS/MS	liquid chromatography with tandem mass spectrometry
LOAEL	lowest observable adverse effect level
LOQ	limit of quantification
MoA	mode of action
MRL	maximum residue level
MS	mass spectrometry
NOAEL	no observed adverse effect level
OECD	Organisation for Economic Co-operation and Development
$P_{ow}$	partition coefficient between <i>n</i> -octanol and water
PEC	predicted environmental concentration
$PEC_{air}$	predicted environmental concentration in air
$PEC_{gw}$	predicted environmental concentration in groundwater
$PEC_{sed}$	predicted environmental concentration in sediment
$PEC_{soil}$	predicted environmental concentration in soil
$PEC_{sw}$	predicted environmental concentration in surface water
PPE	personal protective equipment
RAR	renewal assessment report
RMS	rapporteur Member State
SANCO	Directorate-General for Health and Consumers
SC	suspension concentrate
SFO	single first-order
SMILES	simplified molecular-input line-entry system
SSD	species sensitivity distribution
STOT-RE	specific target organ toxicity – repeated exposure
STOT-SE	specific target organ toxicity – single exposure
TER	toxicity exposure ratio
TRb	thyroid receptor b
TRR	total radioactive residue
UF	uncertainty factor
WHO	World Health Organization

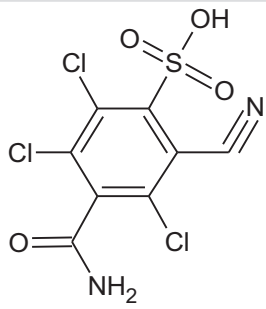
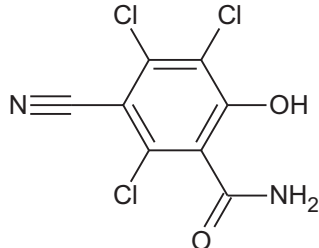
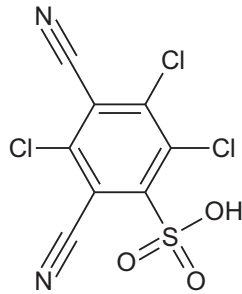
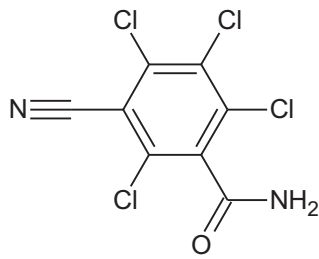
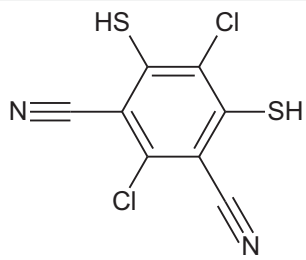
## **Appendix A – List of endpoints for the active substance and the representative formulation**

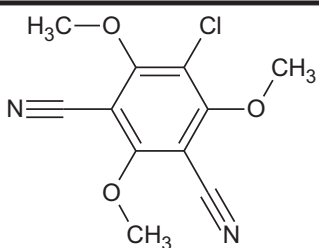
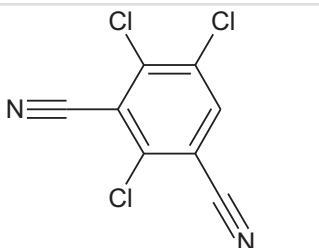
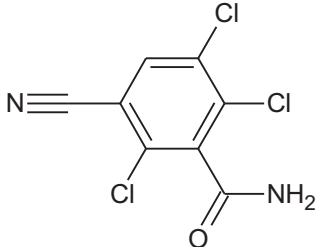
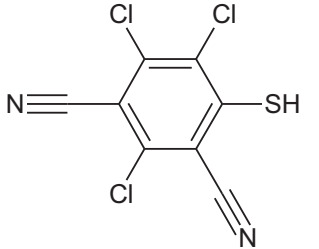
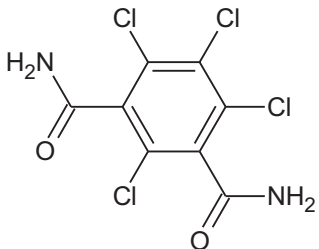
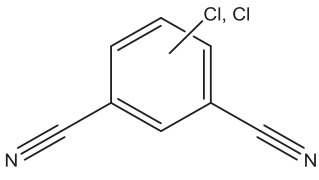
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<https://doi.org/10.2903/j.efsa.2018.5126>

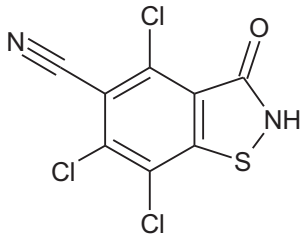
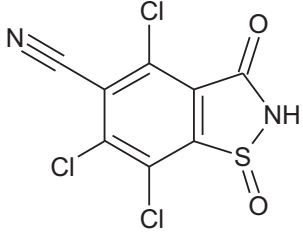
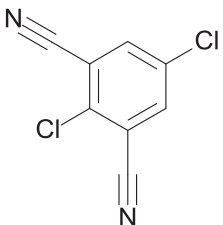
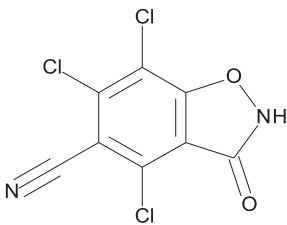
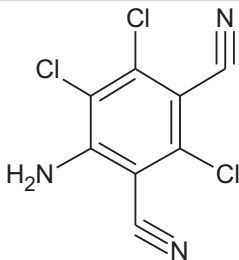
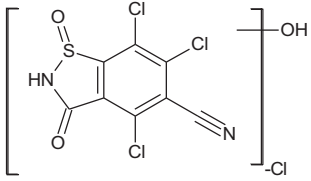
## Appendix B – Used compound codes

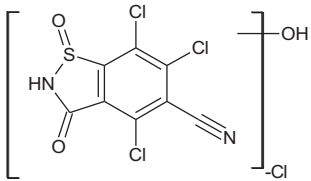
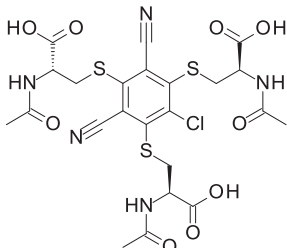
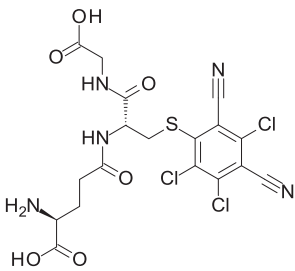
Code/trivial name	Chemical name/SMILES notation	Structural formula
<b>Hexachlorobenzene (HCB)</b>	Hexachlorobenzene <chem>ClC1 = C(Cl)C(Cl)=C(Cl)C(Cl)=C1Cl</chem>	
<b>Decachlorobiphenyl (DCB)</b>	2,2',3,3',4,4',5,5',6,6'-decachloro-1,1'-biphenyl <chem>ClC1 = C(Cl)C(Cl)=C(Cl)C(Cl)=C1C2 = C(Cl)C(Cl)=C(Cl)C(Cl)=C2Cl</chem>	
<b>SDS-3701, R182281, C5 4-Hydroxy-2,5,6-Trichloro-1,3-Dicyanobenzene</b>	2,4,5-trichloro-6-hydroxybenzene-1,3-dicarbonitrile <chem>N#CC1 = C(Cl)C(Cl)=C(O)C(C#N)=C1Cl</chem>	
<b>R417888 M12 VIS01 R6 Compound 10 U6 CSCC890840</b>	2-carbamoyl-3,5,6-trichloro-4-cyanobenzene-1-sulfonic acid <chem>ClC1 = C(C#N)C(Cl)=C(Cl)C(S(=O)(O)=O)=C1C(N)=O</chem>	
<b>R419492 SYN548765 M8 R15 Compound 12 CSCA655149</b>	4-carbamoyl-2,5-dichloro-6-cyanobenzene-1,3-disulfonic acid <chem>O=S(C1 = C(C#N)C(Cl)=C(C(N)=O)C(S(=O)(O)=O)=O)=C1Cl)(O)=O</chem>	
<b>SYN507900 SDS-66882 CSCC210323</b>	2,3,6-trichloro-5-cyano-4-hydroxybenzamide <chem>O=C(C1 = C(C(Cl)=C(C(C#N)=C1Cl)O)Cl)N</chem>	

Code/trivial name	Chemical name/SMILES notation	Structural formula
<b>R611965</b> <b>M5</b> <b>SDS-46851</b> <b>R14</b> <b>Compound 4</b>	3-carbamoyl-2,4,5-trichlorobenzoic acid <chem>O=C(O)C1=CC(Cl)=C(Cl)C(C(N)=O)=C1Cl</chem>	
<b>R611966</b> <b>SDS 47523</b> <b>Compound 5</b>	2,4,5-trichloro-3-cyanobenzamide <chem>Clc1c(C#N)c(Cl)c(cc1Cl)C(N)=O</chem>	
<b>R418503</b> <b>M13</b> <b>R8</b> <b>Compound 11</b> <b>CSCA654600</b> <b>SYN548708 (Na salt)</b>	2,5-dichloro-4,6-dicyanobenzene-1,3-disulfonic acid <chem>O=S(C1=C(C#N)C(Cl)=C(C#N)C(S(=O)(O)=O)=C1Cl)(O)=O</chem>	
<b>R471811</b> <b>M4</b> <b>R7</b> <b>Compound 13</b> <b>CSCA202566</b> <b>SYN548766</b>	Sodium 2,4-dicarbamoyl-3,5,6-trichlorobenzene-1-sulfonate <chem>O=S(C1=C(C(N)=O)C(Cl)=C(C(N)=O)C(Cl)=C1C(N)=O)[O-])=O.[Na+]</chem>	
<b>SYN548008</b> <b>SYN548738</b> <b>M3</b> <b>CSCY735822</b>	4,6-dicarbamoyl-2,5-dichlorobenzene-1,3-disulfonic acid <chem>O=S(C1=C(C(N)=O)C(Cl)=C(C(N)=O)C(S(=O)(O)=O)=C1Cl)(O)=O</chem>	
<b>SYN548580</b> <b>R12</b> <b>CSDB870985</b>	2,4,5-trichloro-6-hydroxy-benzene-1,3-dicarboxamide <chem>NC(=O)c1c(O)c(Cl)c(Cl)c(C(=O)N)c1Cl</chem>	

Code/trivial name	Chemical name/SMILES notation	Structural formula
<b>M2</b>	Unknown	
<b>SYN548581</b> <b>SYN548764</b> <b>M11</b> <b>CSDB870988</b>	4-carbamoyl-2,3,5-trichloro-6-cyanobenzene-1-sulfonic acid <chem>Clc1c(C(N)=O)c(Cl)c(C#N)c(c1Cl)S(=O)(=O)O</chem>	
<b>R611968</b> <b>M9</b> <b>SDS-47525</b> <b>R5</b>	2,4,5-trichloro-3-cyano-6-hydroxybenzamide O=C(N)C1 = C(O)C(Cl)=C(Cl)C(C#N)=C1Cl	
<b>R611553</b> <b>R4</b> <b>Compound 9</b> <b>CSCC926922</b>	2,3,5-trichloro-4,6-dicyanobenzene-1-sulfonic acid <chem>O=S(C1 = C(Cl)C(Cl)=C(C#N)C(Cl)=C1C#N)(O)=O</chem>	
<b>R613636</b> <b>SDS-47525</b> <b>M14</b> <b>SDS-19221</b> <b>R2</b> <b>Compound 3</b> <b>CSCC548417</b>	2,3,4,6-tetrachloro-5-cyanobenzamide <chem>O=C(N)C1 = C(Cl)C(Cl)=C(Cl)C(C#N)=C1Cl</chem>	
<b>R613800</b> <b>C15</b>	2,5-dichloro-4,6-bis(sulfanyl)benzene-1,3-dicarbonitrile <chem>N#CC1 = C(S)C(Cl)=C(S)C(C#N)=C1Cl</chem>	

Code/trivial name	Chemical name/SMILES notation	Structural formula
<b>SDS-3316</b>	5-chloro-2,4,6-trimethoxybenzene-1,3-dicarbonitrile <chem>N#CC1 = C(OC)C(Cl)=C(OC)C(C#N)=C1OC</chem>	
<b>R613801</b> <b>PD2</b> <b>SDS 005473</b> <b>MM230</b> <b>C-1</b> <b>CSAA509968</b> <b>AGR359-025</b> <b>CNIL/14</b>	2,4,5-trichlorobenzene-1,3-dicarbonitrile <chem>N#CC1 = CC(Cl)=C(Cl)C(C#N)=C1Cl</chem>	
<b>R611967</b> <b>SDS 47524</b> <b>Compound 6</b>	2,3,6-trichloro-5-cyanobenzamide <chem>O=C(N)C1 = C(Cl)C(Cl)=CC(C#N)=C1Cl</chem>	
<b>SYN546671</b> <b>R613803</b> <b>C6</b>	2,4,5-trichloro-6-sulfanylbenzene-1,3-dicarbonitrile <chem>N#CC1 = C(S)C(Cl)=C(Cl)C(C#N)=C1Cl</chem>	
<b>SYN546872</b> <b>VIS-02, R3</b>	2,4,5,6-tetrachlorobenzene-1,3-dicarboxamide <chem>O=C(C1 = C(Cl)C(Cl)=C(Cl)C(C(N)=O)=C1Cl)N</chem>	
<b>SYN546934</b> <b>MM196</b>	4,5-dichloro-1,3-dicyanobenzene <chem>N#CC1 = CC(C#N)=CC(Cl)=C1Cl</chem> or 4,6-dichloro-1,3-dicyanobenzene <chem>N#CC1 = CC(C#N)=C(Cl)C=C1Cl</chem> or 2,4-dichloro-1,3-dicyanobenzene <chem>N#CC1 = C(Cl)C(C#N)=CC=C1Cl</chem> or 5,6-dichloro-1,3-dicyanobenzene <chem>N#CC1 = CC(C#N)=C(Cl)C(Cl)=C1</chem> or 2,5-dichloro-1,3-dicyanobenzene <chem>N#CC1 = C(Cl)C(C#N)=CC(Cl)=C1</chem>	

Code/trivial name	Chemical name/SMILES notation	Structural formula
<b>R613841</b> <b>SDS67042, compound 8</b>	4,6,7-trichloro-3-oxo-2,3-dihydro-1,2-benzothiazole-5-carbonitrile <chem>Clc2c1SNC(=O)c1c(Cl)c(C#N)c2Cl</chem>	
<b>R613842</b> <b>SDS67042-sulfoxide</b>	4,6,7-trichloro-1,3-dioxo-2,3-dihydro-1H-1,2-benzothiazole-5-carbonitrile <chem>Clc1c2c(c(Cl)c(C#N)c1Cl)C(=O)NS2 = O</chem>	
<b>M7</b>	Unknown	
<b>M10</b>	Unknown	
<b>PD1</b> <b>R613911</b>	2,5-dichlorobenzene-1,3-dicarbonitrile <chem>Clc1 cc(C#N)c(Cl)c(c1)C#N</chem>	
<b>PD3</b>	Unknown	
<b>PD4</b>	Unknown	
<b>PD5</b> <b>SYN549430</b>	4,6,7-Trichloro-3-oxo-1,2-benzoxazole-5-carbonitrile <chem>Clc1c(Cl)c(C#N)c(Cl)c2C(=O)Noc12</chem>	
<b>R950097</b> <b>4-amino-2,5,6-trichloroiso-phthalonitrile</b>	4-amino-2,5,6-trichlorobenzene-1,3-dicarbonitrile <chem>Clc1c(C#N)c(Cl)c(C#N)c(N)c1Cl</chem>	
<b>U38, Unknown 38 mins</b> <b>U40</b> <b>Unknown 40 mins</b>	4,6-dichloro-7-hydroxy-3-oxo-2,3-dihydrobenzo[d]isothiazole-5-carbonitrile 1-oxide <chem>Oc1c(Cl)c(C#N)c(Cl)c(C(N2)=O)c1S2 = O</chem> or 4,7-dichloro-6-hydroxy-3-oxo-2,3-dihydrobenzo[d]isothiazole-5-carbonitrile 1-oxide <chem>Clc1c(O)c(C#N)c(Cl)c(C(N2)=O)c1S2 = O</chem> or 6,7-dichloro-4-hydroxy-3-oxo-2,3-dihydrobenzo[d]isothiazole-5-carbonitrile 1-oxide <chem>Clc1c(Cl)c(C#N)c(O)c(C(N2)=O)c1S2 = O</chem>	

Code/trivial name	Chemical name/SMILES notation	Structural formula
<b>U44</b> <b>Unknown 44 mins</b>	2,4-dichloro-5-hydroxyisophthalonitrile <chem>N#CC1 = CC(O)=C(C(C#N)=C1Cl)Cl</chem> or 2,5-dichloro-4-hydroxyisophthalonitrile <chem>N#CC1 = CC(Cl)=C(C(C#N)=C1Cl)O</chem> Or 4,5-dichloro-2-hydroxyisophthalonitrile <chem>N#CC1 = CC(Cl)=C(C(C#N)=C1O)Cl</chem>	
<b>SYN546677</b>	(2 <i>R</i> )-2-acetamido-3-[3,5-bis[[ <i>(2R)</i> ]-2-acetamido-3-hydroxy-3-oxo-propyl]sulfanyl]-4-chloro-2,6-dicyano-phenyl]sulfanyl-propanoic acid <chem>CC(=O)N[C@@H](CSc1c(Cl)c(SC[C@H](NC(=O)C)C(=O)O)c(C#N)c(SC[C@H](NC(=O)C)C(=O)O)c1C#N)C(=O)O</chem>	
<b>SYN546673</b>	(2 <i>S</i> )-2-amino-5-[[ <i>(1R)</i> ]-2-(carboxymethylamino)-2-oxo-1-[(2,3,5-trichloro-4,6-dicyano-phenyl)sulfanylmethyl]ethyl]amino]-5-oxo-pentanoic acid <chem>N[C@@H](CCC(=O)N[C@@H](CSc1c(Cl)c(Cl)c(C#N)c(Cl)c1C#N)C(=O)NCC(=O)O)C(=O)O</chem>	

SMILES: simplified molecular-input line-entry system.