CONCLUSION ON PESTICIDE PEER REVIEW

Conclusion on the peer review of the pesticide risk assessment of the active substance hexythiazox[1]

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SUMMARY

Hexythiazox is one of the 79 substances of the third stage part A of the review programme covered by Commission Regulation (EC) No 1490/2002[3] , as amended by Commission Regulation (EC) No 1095/2007[4] . In accordance with the Regulation, at the request of the Commission of the European Communities (hereafter referred to as 'the Commission'), the EFSA organised a peer review of the initial evaluation, i.e. the Draft Assessment Report (DAR), provided by Finland being the designated rapporteur Member State (RMS). The peer review process was subsequently terminated following the applicant's decision, in accordance with Article 11e, to withdraw support for the inclusion of hexythiazox in Annex I to Council Directive 91/414/EEC.

Following the Commission Decision of 5 December 2008 (2008/934/EC)[5] concerning the non-inclusion of hexythiazox in Annex I to Council Directive 91/414/EEC and the withdrawal of authorisations for plant protection products containing that substance, the applicant Nisso Chemicals Europe GmbH made a resubmission application for the inclusion of hexythiazox in Annex I in accordance with the provisions laid down in Chapter III of Commission Regulation (EC) No. 33/2008[6]. The resubmission dossier included further data in response to the issues identified in the DAR.

In accordance with Article 18 of Commission Regulation (EC) No. 33/2008, Finland being the designated RMS, submitted an evaluation of the additional data in the format of an Additional Report. The Additional Report was received by the EFSA on 20 October 2009.

In accordance with Article 19 of Commission Regulation (EC) No. 33/2008, the EFSA distributed the Additional Report to Member States and the applicant for comments on 21 October 2009. The EFSA collated and forwarded all comments received to the Commission on 18 January 2010.

In accordance with Article 20, following consideration of the Additional Report, the comments received, and where necessary the DAR, the Commission requested the EFSA to conduct a focused peer review in the areas of mammalian toxicology and ecotoxicology and deliver its conclusions on hexythiazox.

[1] On request from the European Commission, Question No EFSA-Q-2010-00115, issued on 7 September 2010.
[2] Correspondence: praper@efsa.europa.eu
[3] OJ L224, 21.08.2002, p.25
[4] OJ L 246, 21.9.2007, p. 19
[5] OJ L 333, 11.12.2008, p.11
[6] OJ L 15, 18.01.2008, p.5

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The conclusions laid down in this report were reached on the basis of the evaluation of the representative uses of hexythiazox as an acaricide on apples, grapes and citrus, as proposed by the applicant. Full details of the representative uses can be found in Appendix A to this report.

No data gaps or areas of concern were identified in the section identity, physical and chemical properties and analytical methods.

No critical areas of concern were identified in the mammalian toxicology section. Nevertheless data gaps were identified in order to address the toxicological properties of metabolite PT-1-3 and the preferential metabolism of each isomer in animals and their impact on the toxicity and re-entry worker risk assessment.

Based on the metabolism studies conducted in fruit crops and tea, the residue was defined as hexythiazox alone for monitoring and risk assessment. MRLs were proposed for pome fruits, citrus and grape. Data gaps were identified regarding the possible presence of the metabolite PT-1-3 in processed commodities and the possible impact of a preferential metabolism/degradation of each constituent isomer on the overall consumer risk assessment.

The data available on fate and behaviour in the environment are sufficient to carry out the required environmental exposure assessments at the EU level for representative uses. The potential for groundwater contamination consequent to these uses from hexythiazox or the metabolites PT-1-2, PT-1-3 and PT-1-9 above the parametric drinking water limit of 0.1µg/L was assessed as low.

Hexythiazox is very toxic to aquatic organisms, however the risk was assessed as low for the use in grapes and risk mitigation measures are needed for the representative use in citrus. Risk mitigation measures comparable to a 20 m no-spray buffer zone including run-off mitigation were not sufficient to achieve TERs above the trigger for the use in apples indicating a high risk. A high risk to bees cannot be excluded for all representative uses because of the potential adverse effects on bee brood. The risk to birds and mammals, non-target arthropods, soil macro- and micro-organisms, non-target plants and biological methods of sewage treatment was assessed as low.

KEY WORDS

hexythiazox, peer review, risk assessment, pesticide, acaricide

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BACKGROUND

Legislative framework

Commission Regulation (EC) No 1490/2002[7], as amended by Commission Regulation (EC) No 1095/2007[8] lays down the detailed rules for the implementation of the third stage of the work programme referred to in Article 8(2) of Council Directive 91/414/EEC. This regulates for the European Food Safety Authority (EFSA) the procedure for organising, upon request of the Commission of the European Communities (hereafter referred to as 'the Commission'), a peer review of the initial evaluation, i.e. the Draft Assessment Report (DAR), provided by the designated rapporteur Member State.

Commission Regulation (EC) No 33/2008[9] lays down the detailed rules for the application of Council Directive 91/414/EEC for a regular and accelerated procedure for the assessment of active substances which were part of the programme of work referred to in Article 8(2) of Council Directive 91/414/EEC but which were not included in Annex I. This regulates for the EFSA the procedure for organising the consultation of Member States and the applicant(s) for comments on the Additional Report provided by the designated RMS, and upon request of the Commission the organisation of a peer review and/or delivery of its conclusions on the active substance.

Peer review conducted in accordance with Commission Regulation (EC) No 1490/2002

Hexythiazox is one of the 79 substances of the third stage part A of the review programme covered by Commission Regulation (EC) No 1490/2002, as amended by Commission Regulation (EC) No 1095/2007. In accordance with the Regulation, at the request of the Commission, the EFSA organised a peer review of the DAR provided by the designated rapporteur Member State, Finland, which was received by the EFSA on 27 January 2006 (Finland 2006).

The peer review was initiated by dispatching the DAR to Member States on 9 June 2006 and to the applicant Nisso Chemicals Europe GmbH on 18 May 2006 for consultation and comments. In addition, the EFSA conducted a public consultation on the DAR. The comments received were collated by the EFSA and forwarded to the RMS for compilation and evaluation in the format of a Reporting Table. The Reporting Table containing the RMS' evaluation of the comments in column 3 was further considered by the EFSA, resulting in a conclusion in column 4.

The peer review process was subsequently terminated following the applicant's decision, in accordance with Article 11e, to withdraw support for the inclusion of hexythiazox in Annex I to Council Directive 91/414/EEC.

Peer review conducted in accordance with Commission Regulation (EC) No 33/2008

Following the Commission Decision of 5 December 2008 (2008/934/EC)[10] concerning the non-inclusion of hexythiazox in Annex I to Council Directive 91/414/EEC and the withdrawal of authorisations for plant protection products containing that substance, the applicant Nisso Chemical Europe GmbH made a resubmission application for the inclusion of hexythiazox in Annex I in accordance with the provisions laid down in Chapter III of Commission Regulation (EC) No. 33/2008. The resubmission dossier included further data in response to the issues identified in the DAR.

In accordance with Article 18, Finland being the designated RMS, submitted an evaluation of the additional data in the format of an Additional Report. The Additional Report was received by the EFSA on 20 October 2009 (Finland 2009).

[7] OJ L224, 21.08.2002, p.25
[8] OJ L246, 21.9.2007, p.19
[9] OJ L 15, 18.01.2008, p.5
[10] OJ L 333, 11.12.2008, p.11

In accordance with Article 19, the EFSA distributed the Additional Report to Member States and the applicant for comments on 21 October 2009. In addition, the EFSA conducted a public consultation on the Additional Report. The EFSA collated and forwarded all comments received to the Commission on 18 January 2010. At the same time, the collated comments were forwarded to the RMS for compilation in the format of a Reporting Table. The applicant was invited to respond to the comments in column 3 of the Reporting Table. The comments and the applicant's response was evaluated by the RMS in column 3.

In accordance with Article 20, following consideration of the Additional Report, the comments received, and where necessary the DAR, the Commission decided to further consult the EFSA. By written request, received by the EFSA on 17 February 2010 the Commission requested the EFSA to arrange a consultation with Member State experts as appropriate and deliver its conclusions on hexythiazox within 6 months of the date of receipt of the request, subject to an extension of a maximum of 90 days where further information were required to be submitted by the applicant in accordance with Article 20(2).

The scope of the peer review and the necessity for additional information, not concerning new studies, to be submitted by the applicant in accordance with Article 20(2), was considered in a telephone conference between the EFSA, the RMS, and the Commission on 12 March 2010 the applicant was also invited to give its view on the need for additional information. On the basis of the comments received, the applicant's response to the comments, and the RMS' subsequent evaluation thereof, it was concluded that the EFSA should organise a consultation with Member State experts in the areas of mammalian toxicology and ecotoxicology and that further information should be requested from the applicant in the area of 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 consultation with Member State experts, and the additional information to be submitted by the applicant, were compiled by the EFSA in the format of an Evaluation Table.

The conclusions arising from the consideration by the EFSA, and as appropriate by the RMS, of the points identified in the Evaluation Table, together with the outcome of the expert discussions where these took place, was 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 August 2010.

This conclusion report summarises the outcome of the peer review of the risk assessment on the active substance and the representative formulation evaluated on the basis of the representative uses as a acaricide on rapes, apples and citrus as proposed by the applicant. A list of the relevant end points for the active substance as well as the formulation is provided in Appendix A. In addition, a key supporting document to this conclusion is the Peer Review Report, 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 (EFSA 2010) comprises the following documents:

- the comments received,
- the Reporting Table (DAR) (revision 1-1; 17 March 2010)
- the Reporting Table (AR) (revision 1-1; 17 March 2010
- the Evaluation Table (07 September 2010)

- the report(s) of the scientific consultation with Member State experts (where relevant).

Given the importance of the DAR and the Additional Report including its addendum (compiled version of August 2010 containing all individually submitted addenda, Finland 2010) and the Peer Review Report, both documents are considered respectively as background documents A and B to this conclusion.

THE ACTIVE SUBSTANCE AND THE FORMULATED PRODUCT

Hexythiazox is the ISO common name for (4*RS*,5*RS*)-5-(4-chlorophenyl)-*N*-cyclohexyl-4-methyl-2-oxo-1,3-thiazolidine-3-carboxamide (IUPAC).

The representative formulated product for the evaluation was 'Nissorun' a wettable powder formulation (WP) containing 100 g/kg hexythiazox, registered under different trade names in Europe.

The representative uses evaluated comprise foliar spraying against spider mites in apple, grape and citrus. Full details of the GAP can be found in the list of end points in Appendix A.

CONCLUSIONS OF THE EVALUATION

It must be noted that hexythiazox is a racemic mixture of enantiomers (4*R*,5*R*) and (4*S*,5*S*), but the possible preferential metabolism/degradation of each isomer in animals, plants and the environment was not investigated and not considered during this peer review. Moreover, the analytical methods used in the studies reported through all sections were not stereo-selective and all values mentioned as "hexythiazox" have to be considered as "sum of enantiomers". The possible impact of each individual enantiomer on the toxicity, the worker and consumer risk assessment and the environment was not evaluated. Data gaps were identified to address the impact in sections 2, 3, 4 and 5 of a possible change in the isomeric composition.

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

The minimum purity of hexythiazox technical material is 976 g/kg. No FAO specifications exists.

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 hexythiazox or the respective formulation. The main data regarding the identity of hexythiazox and its physical and chemical properties are given in appendix A.

Adequate analytical methods are available for the determination of hexythiazox in the technical material and in the representative formulation. Hexythiazox residues in plant commodities with high acid content and high water content can be determined by multi-residue method or single methods. No MRLs for hexythiazox in foodstuffs of animal origin are established, and therefore no method for food/feed of animal origin is needed. Adequate analytical methods are available to monitor hexythiazox residues in the environmental matrices. Since hexythiazox is not classified as acute toxic or very toxic, analytical methods for the determination of residues of hexythiazox in body fluids and/or tissues are not required.

2. Mammalian toxicity

Hexythiazox is a racemic mixture of enantiomers (4*R*,5*R*) and (4*S*,5*S*). The possible preferential metabolism of each isomer in animals, the behaviour of each of the individual hexythiazox stereoisomers in the environment (see section 4) and the possible impact of each individual enantiomer on the toxicity and risk assessment for re-entry workers are not known. Therefore, a data gap and an issue that could not be finalized have been identified.

The toxicological batches cover the agreed technical specification.

Absorption, distribution and excretion of hexythiazox were rapid. Oral absorption was estimated at 30%. There was no evidence for accumulation. The main metabolic pathway identified was oxidation of the cyclohexane ring to form the major metabolite PT-1-8 (*cis*). The acute toxicity of hexythiazox to rats was low by the oral, dermal and inhalation routes. It is not a skin or eye irritant or a skin sensitizer. After short-term exposure the critical effects were found in the liver (increased liver weights in mice and rats) and adrenals (fatty degeneration in rats and adrenocortical hypertrophy in dogs). Non-specific critical effects such as reduced body weight gain were also observed in rats and

mice. The dog was the most sensitive species. The relevant short-term toxicity NOAEL is 2.87 mg/kg bw/day found in the 1-year dog study. In the long-term toxicity studies, reduced body weight gain and adrenals changes (fatty changes in rats and increase absolute and relative weight in mice) were observed. Changes in haematology and clinical chemistry and increased organ weight with increased incidence of proteinaceous casts in kidney were also observed in mice. The relevant long-term toxicity NOAEL is 3.20 mg/kg bw/day in the 2-year rat study. The weight of evidence suggests that hexythiazox is not genotoxic. With regard to the carcinogenic properties, tumours were observed at high dose levels in mice and rats. In mice, hepatoblastoma in both sexes and liver adenomas in females were observed at 267 mg/kg bw/day. In male rats, thyroid parafollicular cell adenoma and fibroadenoma of mammary gland were observed at 163 mg/kg bw/day. The RMS did not propose classification and labelling with R40, Carc. Category 3, but some concerns were raised by some MS with regard to the potential classification (further details are given in the reporting table point A2(9)). The final decision has to be taken at ECHA. No effect was seen on the reproductive performance and parameters; no developmental effects were observed either in rats and rabbits. No potential for neurotoxicity was observed.

The metabolite PT-1-3 possibly present in significant levels in processed commodities (see section 3) is a minor rat metabolite. An Ames test gave negative results. According to oral acute toxicity PT-1-3 (LD_{50}=341 mg/kg bw) could be considered of higher toxicity than the parent (LD_{50}>5000 mg/kg bw). Nevertheless, no conclusion can be drawn on this metabolite based on the available data (data gap).

The references values for hexythiazox are the following: the Acceptable Daily Intake (ADI) is 0.03 mg/kg bw/day; the Acceptable Operator Exposure Level (AOEL) is 0.009 mg/kg bw/day; no Acute Reference Dose (ARfD) is allocated, not necessary. It is noted that there is a margin of safety higher than 8000 and 5000 with regard to the ADI and the levels where tumours were found in mice and rats, respectively.

Operator exposure was estimated considering tractor-mounted and hand-held spraying in apples, grapes and citrus. Results indicated operator exposure levels below the AOEL in tractor-mounted air-assisted applications for citrus (German and UK POEM models), apples (German model) and grapes (German Model) when appropriate PPE is used. With the hand-held spraying method the operator exposure is below the AOEL even without the use of PPE (German model). Worker exposure is considered inconclusive as the possible impact of each individual enantiomer on the toxicity and risk assessment of re-entry worker are not known. Bystander exposure estimates were below the AOEL.

3. Residues

It must be noted that hexythiazox is a racemic mixture of enantiomers, but the possible preferential metabolism/degradation of each constituent isomer in plants was not investigated and not considered during this peer review. Therefore, a data gap was identified to address the impact of the isomeric composition on the toxicity and the overall consumer risk assessment.

Metabolism in plants was investigated in the fruit plant group (on grape, citrus, pear and apple) and in tea, using foliar applications of ^{14}C-hexythiazox labelled on the thiazolidine moiety and experimental designs representative of the supported uses. The metabolism was similar in all crops investigated and hexythiazox was seen to undergo a limited metabolism in plants. Translocation within the treated fruits was minimal, most of the radioactivity being recovered in the surface washes. The parent hexythiazox was by far the most predominant component of the residues at harvest, accounting for more than 60% of the TRR 60 days after application. Although all of these studies were conducted with a single ^{14}C-label, additional labelling was not considered necessary, having regard to the limited degradation of the parent compound. Based on these studies, the residue definition for monitoring and risk assessment was limited to the parent hexythiazox only.

A sufficient number of supervised residue trials was provided to derive MRLs for grape, apple and citrus. These results are supported by the storage stability studies showing hexythiazox residues to be stable, in water containing matrices at -20°C, for up to 2 years. Processing studies were provided and

processing factors were calculated for the parent compound in citrus and grape commodities. However, little information was provided on the transfer of the metabolite PT-1-3, seen to be the major compound of the residues under sterilisation conditions (48% TRR). Considering that PT-1-3 is more acutely toxic than the parent (LD_{50} = 341 mg/kg bw, parent >5000 mg/kg bw, see section 2), additional toxicological information is required on its toxicological relevance and on its possible transfer and level in processed commodities.

Livestock metabolism and feeding studies were provided but no residue definitions were finally proposed for products of animal origin, since the supported crops are not used to feed poultry and the calculated intake by ruminants is just below the threshold level of 0.10 mg/kg DM. Moreover, when considering the available metabolism and feeding studies, residue levels in all ruminant matrices are expected to be far below 0.01 mg/kg when considering the residue intake resulting from the supported uses. This point should be reconsidered if further uses significantly increase the intake by animals.

Rotational crop studies were provided, although such information is not required when considering the representative uses on fruit crops. This point should be reconsidered if further additional uses are envisaged on plants included in crop rotations.

The highest intake estimated using the EFSA PRIMo model and the proposed MRLs is 9% of the ADI (DE Child). It is therefore possible to conclude on the absence of chronic risks for consumers, even if the isomeric composition of the residues was not addressed. No ARfD was allocated and therefore, an acute risk assessment was not necessary.

4. Environmental fate and behaviour

As already discussed, the regulatory dossier provides no information on the behaviour of each of the individual hexythiazox stereoisomer in the environment. This is also true for the metabolites that have chiral carbon atoms. As chiral chromatographic techniques were not employed in any of the fate and behaviour investigations it is not known if any enantiomer is degraded more quickly than the other, or if any other conversion may occur in the environmental matrices studied. Consequently a data gap was identified .References made to hexythiazox or the breakdown products in section 4 therefore relate to the sum of the stereoisomers (enantiomers)[11].

In soil laboratory incubations under aerobic conditions in the dark hexythiazox exhibits low to medium persistence forming the major (>10% applied radioactivity (AR)) metabolites PT-1-2 (max. 39.5%AR, exhibiting moderate to high persistence) and PT-1-9 (max. 21.1%AR, exhibiting low to moderate persistence). The metabolite PT-1-3 also triggered consideration for groundwater exposure assessment[12] (max. 9.2%AR, exhibiting moderate to medium persistence). Mineralisation of the thiazolidine ring and cyclohexyl ring radiolabels to carbon dioxide accounted for 6 to 8 % AR and 31.3 % AR after 90 days respectively. The formation of unextractable residues (not extracted using methanol, then methanol:water or acetone) for these radiolabels accounted for 15-21% AR and 8.9%AR after 90 days respectively. In anaerobic laboratory incubations hexythiazox was more persistent than under aerobic conditions and no metabolite accounted for >10%AR when these conditions were maintained up to 120 days. Hexythiazox is considered immobile in soil. PT-1-2, PT-1-9 and PT-1-3 all exhibited medium to low soil mobility. It was concluded that the adsorption of hexythiazox, PT-1-2, PT-1-9 and PT-1-3 was not pH dependent.

In field dissipation studies carried out at 4 sites in Germany (spray application to the soil surface on bare soil plots in May, with limited numbers of sampling points) hexythiazox exhibited a comparable pattern of persistence to that exhibited in the laboratory incubations. Sample analyses were carried out

[11] The breakdown products PT-1-8 and PT-1-6 that occurred in environmental matrices at concentrations that did not trigger further assessment (so fate and behaviour information is only presented in appendix A of this conclusion), contain two chiral centres, and therefore; have the potential for 4 stereoisomers (2 diastereoisomer pairs).

[12] According to European Commission (2003), as this metabolite exceeded 5%AR at more than 2 consecutive sampling times.

for parent hexythiazox and using a common moiety method that nominally quantified all residues that contained the 5-(4-chlorophenyl)-4-methyl-2oxothiazolidone moiety.

In laboratory incubations in dark aerobic natural sediment water systems (4 systems investigated), hexythiazox exhibited moderate to high persistence forming the major metabolite PT-1-2, (max. ca. 12.8%AR and 19.4%AR in water and sediment respectively), with this maximum being at the end of the investigations (100 days). The unextractable sediment fraction (not extracted using methanol:water, then methanol or acetone) was a major sink for the thiazolidine C^{14} ring radiolabel (accounting for 26-28%AR at 100 days) but less significant for cyclohexyl C^{14} ring radiolabel (accounting for only 2.6-5.4% AR at 100 days). Mineralisation of these radiolabels accounted for only 2.5-6 % AR at 100 days. The available data indicated that sterile hydrolysis or sterile aqueous photolysis are not expected to contribute to the breakdown of hexythiazox in surface water environments.

For the representative uses assessed, the necessary surface water and sediment exposure assessments (Predicted environmental concentrations (PEC)) were carried out for the metabolites PT-1-2, PT-1-3 and PT-1-9 using the FOCUS (2001) step 1 and step 2 approach (version 1.1 of the Steps 1-2 in FOCUS calculator). For the active substance hexythiazox, appropriate Step 3 (FOCUS, 2001) and Step 4 calculations were available[13]. The step 4 calculations appropriately followed the FOCUS (2007) guidance with no-spray buffer zones of up to 20m being implemented for drainage scenarios (20m represents *ca.* an 88-89% spray drift reduction for apples and 15m represents *ca.* an 89-91% spray drift reduction for citrus) and combined no-spray buffer zones with vegetative buffer strips of up to 20m (reducing solute flux in runoff by up to 80% and erosion runoff by up to 95%), being implemented for the runoff scenarios.

The necessary groundwater exposure assessments were appropriately carried out using FOCUS (2000) scenarios and the models PEARL 3.3.3 and PELMO 3.3.2[14] for the active substance hexythiazox and the metabolites PT-1-2, PT-1-3 and PT-1-9. The potential for groundwater exposure from the representative uses assessed, by hexythiazox or these metabolites above the parametric drinking water limit of 0.1 µg/L, was concluded to be low in geoclimatic situations that are represented by all 9 FOCUS groundwater scenarios.

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

5. Ecotoxicology

The regulatory dossier provides no information on ecotoxicity and the environmental behaviour of each of the individual hexythiazox stereoisomers or the metabolites that have chiral carbon atoms. Consequently a data gap was identified.

Hexythiazox is very toxic to aquatic organisms. The solubility of hexythiazox in water is low (0.1 mg/L). Analytical verification of test concentrations showed that measured concentrations were always more than 20% less than the nominal concentrations. Therefore only endpoints based on analytically verified mean measured concentrations were used for the risk assessment. Tests where solvents were used to achieve higher test concentrations of hexythiazox showed that acute effect concentrations for fish and invertebrates as well as the E_bC_{50}/E_rC_{50} for algae were above the water solubility of hexythiazox. Tests with the formulation and fish, daphnids and algae showed that formulated hexythiazox was of lower toxicity to the tested aquatic organisms and therefore the risk assessment is based on endpoints for the technical active substance.

[13] Simulations correctly utilised the agreed Q10 of 2.58 (following EFSA (2007)) and Walker equation coefficient of 0.7.
[14] Simulations complied with EFSA (2004) and correctly utilised the agreed Q10 of 2.58 (following EFSA (2007)) and Walker equation coefficient of 0.7

The lowest endpoints driving the aquatic risk assessment were observed in the acute and chronic studies with daphnids. The TERvalues exceeded the Annex VI trigger value with FOCUS Step 3 PECsw for the use in grapes. A no-spray buffer zone of 15 m was required for the use in citrus to achieve TERs above the Annex VI trigger. No FOCUS Step 4 scenario including a no-spray buffer zone of 20m resulted in TERs above the Annex VI triggers for the use in apples. The RMS suggested refining the risk assessment with 21-d twa PECsw values. However the most sensitive endpoint is mortality and from the underlying data it seems that the time to onset of effects is less than 21 days. Therefore EFSA is of the opinion that the aquatic risk assessment for the use in apples needs to be refined further. The tocixicity of metabolites PT-1-2, PT-1-3 (minor) and PT-1-9 (minor) was always more than 10 times less toxic to Dapnia than the parent substance. The TERs for the metabolites PT-1-2, PT-1-3 and PT-1-9 were well above the Annex VI triggers of 100 and 10 with FOCUS step2 PECsw values.
Two bioconcentration studies with bluegill sunfish (*Lepomis macrochirus*) and carp (*Cyprinus carpio*) were conducted although the log P_{ow} of hexythiazox was < 3 . The study with carp was assessed as not valid. The whole fish BCF ()bioconcentration factor) was determined as 1100 for bluegill sunfish. However, hexythiazox was transformed rapidly into metabolites and the depuration was rapid. 89 to 94% of the applied radioactivity depurated within 14 days after exposure. The risk from bioaccumulation is considered to be low. The log P_{ow} of the major metabolite PT-1-2 was 2.44 and therefore no bioconcentration study was triggered.

The oral and contact HQ values for bees indicated a low risk. However, concerns were raised during the peer-review that bee-brood may be at risk since hexythiazox is effective against eggs and larval stages of mites. A bee brood study was submitted by the applicant and discussed in a teleconference (PRAPeR TC 35) in June 2010. Several drawbacks of the study were identified during the discussion, e.g. no toxic standard was used in the study; the development of individual bees was not followed and therefore it was not possible to assess effects on larvae development; the observation period might have been too short to identify effects on brood development. In addition, the relation between the application rate in the study and data from residue trials was unclear. A data gap was set to further address the risk to bee brood.

The risk to birds and mammals, non-target arthropods, earthworms, soil non-target macro-organisms (litterbag-test), soil micro-organisms, non-target plants and biological methods of sewage treatment was assessed as low.

6. Overview of the risk assessment of compounds listed in residue definitions triggering assessment of effects data for the environmental compartments

6.1. Soil

Compound (name and/or code)	Persistence	Ecotoxicology
hexythiazox	low to medium persistence Single first order DT_{50} 8-75 days (15-25°C, 40-50 %MWHC soil moisture)	The risk to earthworms, soil-dwelling macro- and micro-organisms was assessed as low.
PT-1-2	moderate to high persistence Single first order DT_{50} 15-264 days (15-25°C, 45-50 %MWHC soil moisture)	The risk to earthworms, soil-dwelling macro- and micro-organisms was assessed as low. The acute TERs for earthworms were more than 1 order of magnitude greater than for hexythiazox.
PT-1-3	moderate to medium persistence Single first order DT_{50} 17-54 days (15-25°C, 45-50%MWHC soil moisture)	The risk to earthworms, soil dwelling macro- and micro-organisms was assessed as low. The acute TER for earthworms were more than 1 order of magnitude greater than for hexythiazox.
PT-1-9	low to moderate persistence Single first order DT_{50} 8-39 days (15-25°C, 40-50 %MWHC soil moisture)	The risk to earthworms, soil-dwelling macro- and micro-organisms was assessed as low. The acute TER for earthworms were more than 1 order of magnitude greater than for hexythiazox.

6.2. Ground water

Compound (name and/or code)	Mobility in soil	>0.1 µg/L 1m depth for the representative uses (at least one FOCUS scenario or relevant lysimeter)	Pesticidal activity	Toxicological relevance	Ecotoxicological activity

hexythiazox	immobile K_{Foc} 8714-12823 mL/g	No	Yes	Yes	Yes
PT-1-2	medium to low mobility K_{Foc} 274-561 mL/g	No	No data submitted No data needed	No assessment required. (LD_{50}=1079 mg/kg bw. Ames test negative.)	The risk to aquatic organisms in surface water was assessed as low.
PT-1-3	medium to low mobility K_{Foc} 296-674 mL/g	No	No data submitted No data needed	No assessment required. (Acutely more toxic than hexythiazox: LD_{50}=341 mg/kg bw. Ames test negative.)	The risk to aquatic organisms in surface water was assessed as low.
PT-1-9	medium to low mobility K_{Foc} 402-922 mL/g	No	No data submitted No data needed	No assessment required. (LD_{50}>5000 mg/kg bw. Ames test negative.)	The risk to aquatic organisms in surface water was assessed as low.

6.3. Surface water and sediment

Compound (name and/or code)	Ecotoxicology
hexythiazox	Very toxic to aquatic organisms. The risk was assessed as low with FOCUS step3 PECsw values for the use in grapes. Risk mitigation such as a 15 m and 20 m no spray buffer zones including run-off mitigation were required for the uses in citrus and apples, respectively.
PT-1-2	Harmful to aquatic organisms.
PT-1-3	Harmful to aquatic organisms.
PT-1-9	Harmful to aquatic organisms

6.4. Air

Compound (name and/or code)	Toxicology
hexythiazox	Low acute toxicity (Rat LC50 inhalation .2.0 mg/L, 4h; whole body exposure).

LIST OF STUDIES TO BE GENERATED, STILL ONGOING OR AVAILABLE BUT NOT PEER REVIEWED

- Hexythiazox consists of two enantiomers. Information on the preferential metabolism of each isomer in animals are required and its possible impact on the toxicity and the re-entry worker risk assessment need to be addressed (relevant for all representative uses evaluated; data gap identified by EFSA after the commenting phase; no submission date proposed; see section 2).

- Hexythiazox consists of two enantiomers. Information on the preferential metabolism/degradation of each isomer in plants is required and the possible impact on the toxicity and the consumer risk assessment need to be addressed (relevant for all representative uses evaluated; data gap identified by EFSA after the commenting phase; no submission date proposed; see section 3).

- Processing studies where samples are analysed for the parent and the metabolite PT-1-3 should be provided, with a special attention to fractions subject to a heating step (relevant for all representative uses evaluated; submission date proposed by the applicant; unknown, see section 3)

- Toxicological information to address the toxicity of the metabolite PT-1-3, possibly present in significant levels in processed commodities (relevant for all representative uses evaluated; submission date proposed by the applicant; unknown, see section 2 and 3).

- The exposure patterns and consequent risk assessment to wild non target organisms needs to be characterised further, in relation to the impact that the potentially varying enantiomer ratio of hexythiazox or the chiral breakdown products may have on the risks assessed and the extent of risk mitigation required (relevant for all the representative uses evaluated; submission date proposed by the applicant: unknown, see sections 4 and 5).

- The risk assessment for aquatic organisms needs to be refined further (relevant for the use in apples; submission date proposed by the applicant: none; see section 5)

- The risk to bee brood needs to be addressed (relevant for all representative uses evaluated; submission date proposed by the applicant: none; see section 5)

PARTICULAR CONDITIONS PROPOSED TO BE TAKEN INTO ACCOUNT TO MANAGE THE RISK(S) IDENTIFIED

- Results indicated operator exposure levels below the AOEL in tractor-mounted air-assisted applications for citrus (German and UK POEM models), apples (German model) and grapes (German Model) when appropriate PPE is used (gloves during mixing and loading and application according to the UK POEM and German model and protective clothes and sturdy footwear during application according to the German model).

- Risk mitigation comparable to no spray buffer zones and run-off mitigation of 15m are needed for the representative uses in citrus to protect the aquatic environment.

ISSUES THAT COULD NOT BE FINALISED

- Worker exposure is considered inconclusive as the possible impact of each individual enantiomer on the toxicity, the preferential metabolism of each isomer in animals and the behaviour of each of the individual hexythiazox stereoisomer in the environment are not known (see section 2).

- The residue definition for risk assessment for processed commodities, with regard to the possible presence of the metabolite PT-1-3, could not be finalised

- A high risk to the aquatic environment was indicated for the use in apples. Risk mitigation comparable to a 20m no-spray buffer zone would not be sufficient to achieve TERs above the trigger.

CRITICAL AREAS OF CONCERN

- A high risk to bees cannot be excluded for all representative uses evaluated, because of the potential adverse effects on the bee brood.

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[15] For further guidance documents see http://ec.europa.eu/food/plant/protection/resources/publications_en.htm#council (EC) or http://www.oecd.org/document/59/0,3343,en_2649_34383_1916347_1_1_1_1,00.html (OECD)

APPENDICES

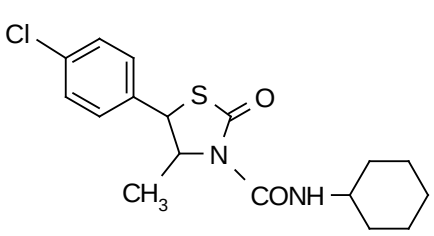
APPENDIX A – LIST OF END POINTS FOR THE ACTIVE SUBSTANCE AND THE REPRESENTATIVE FORMULATION

Identity, Physical and Chemical Properties, Details of Uses, Further Information

Active substance (ISO Common Name)	Hexythiazox
Function (*e.g.* fungicide)	Acaricide

Rapporteur Member State	FINLAND
Co-rapporteur Member State	-

Identity (Annex IIA, point 1)

Chemical name (IUPAC)	(4*RS*,5*RS*)-5-(4-chlorophenyl)-*N*-cyclohexyl-4-methyl-2-oxo-1,3-thiazolidine-3-carboxamide
Chemical name (CA)	*trans*-5-(4-chlorophenyl)-*N*-cyclohexyl-4-methyl-2-oxo-3-thiazolidinecarboxamide
CIPAC No	439
CAS No	78587-05-0
EC No (EINECS or ELINCS)	None
FAO Specification (including year of publication)	None
Minimum purity of the active substance as manufactured	976 g/kg (1:1 mixture of (4*R*, 5*R*) and (4*S*, 5*S*)
Identity of relevant impurities (of toxicological, environmental and/or other significance) in the active substance as manufactured	None
Molecular formula	$C_{17}H_{21}ClN_2O_2S$
Molecular mass	352.9 g/mol
Structural formula	

Physical-chemical properties (Annex IIA, point 2)

Melting point (state purity)	105.4 °C (>99.9 %)
Boiling point (state purity)	222 °C (99.9 %)
Temperature of decomposition (state purity)	> 300 °C (99.9 %)
Appearance (state purity)	Pure material: White odourless powder Technical material: Pale yellow odourless powdery crystal (98.9 %)
Vapour pressure (state temperature and purity)	< 1.33 x 10^{-6} Pa at 25 °C (99.8 %)
Henry's law constant	1.19 x 10^{-2} Pa x m^3 x mol^{-1} at 20 °C vapour pressure: 3.38 x 10^{-6} Pa at 20 °C (99.4 %) water solubility: 0.1 mg/l at 20 °C (99.6 %)
Solubility in water (state temperature, purity and pH)	pH 5: 0.1 mg/l at 20 °C (99.6 %) pH 7: 0.1 mg/l at 20 °C (99.6 %) pH 9: 0.1 mg/l at 20 °C (99.6 %)
Solubility in organic solvents (state temperature and purity)	acetone 159 g/l acetonitrile 34 g/l dichloromethane 619 g/l ethanol 22 g/l ethyl acetate 148 g/l n-heptane 4.6 g/l n-hexane 4.6 g/l methanol 17 g/l toluene 233 g/l xylene 230 g/l all at 20 °C (99.7 %)
Surface tension (state concentration, temperature and purity)	71.8 mN/m, 90 % saturated aq. solution, at 20 °C (99.7 %)
Partition co-efficient (state temperature, pH and purity)	log P_{ow} = 2.67 at 25 °C, unbuffered solution, (>99 %) Effect of pH not required, does not dissociate.
Dissociation constant (state purity)	Does not dissociate in water. (>99.9 %)

UV/VIS absorption (max.) incl. ε (state purity and pH)	Maximum absorption at neutral: λ_{max} = 202.0 nm ε = 24220 l · mol^{-1} · cm^{-1} λ_{max} = 225.0 nm ε = 18390 l · mol^{-1} · cm^{-1} acid: λ_{max} = 225.5 nm ε = 18310 l · mol^{-1} · cm^{-1} basic: λ_{max} = 224.5 nm ε = 16990 l · mol^{-1} · cm^{-1} No absorption above 290 nm. (>99.9 %)
Flammability (state purity)	Not flammable (99.7 %)
Explosive properties (state purity)	Non explosive (99.7%)
Oxidising properties (state purity)	Non oxidising (99.7 %)

Summary of representative uses evaluated (Hexythiazox)

Crop and/ or situation (a)	Member State, Country or Region	Product name	F G or I (b)	Pests or Group of pests controlled (c)	Preparation		Application				Application rate per treatment (for explanation see the text in front of this section)			PHI (days) (m)	Remarks
					Type (d-f)	Conc. of as (i)	method kind (f-h)	growth stage & season (j)	number min/ max (k)	interval between applications (min)	kg as/hL (l) min – max	water L/ha min–max	kg as/ha(l) min–max		
Apples	NE	Nissorun	F	Spidermites	WP	100 g/kg	Spraying	Spring or when pests appear	1	na	0.0067	1500	0.100	28	(1) (2) (3) (4)
Apples	SE	Nissorun	F	Spidermites	WP	100 g/kg	Spraying	Spring or when pests appear	1	na	0.0067	1500	0.100	28	(1) (2) (3) (4)
Grapes	NE	Nissorun	F	Spidermites	WP	100 g/kg	Spraying	Spring or when pests appear	2	30 d	0.008	1000	0.080	21	(1) (2) (3)
Grapes	SE	Nissorun	F	Spidermites	WP	100 g/kg	Spraying	Spring or when pests appear	2	30 d	0.008	1000	0.080	21	(1) (2) (3)
Citrus (oranges, mandarins)	SE	Nissorun	F	Spidermites	WP	100 g/kg	Spraying	1. BBCH 69 2. BBCH 74 3. 14 d PHI	3	17 d	0.002	4000	0.080	14	(1) (2) (3)

(1) A high risk to bees cannot be excluded because of the potential adverse effects on bee brood.
(2) The worker exposure risk assessment could not be finalized.
(3) The residue definition for the risk assessment for processed commodities could not be finalized.
(4) High risk to aquatic organisms.

Remarks:

(a) For crops, the EU and Codex classifications (both) should be taken into account; where relevant, the use situation should be described (e.g. fumigation of a structure)	(i) g/kg or g/L.
(b) Outdoor or field use (F), greenhouse application (G) or indoor application (I)	(j) Growth stage at last treatment (BBCH Monograph, Growth Stages of Plants, 1997, Blackwell, ISBN 3-8263-3152-4), including where relevant, information on season at time of application
(c) *e.g.* biting and suckling insects, soil born insects, foliar fungi, weeds	(k) Indicate the minimum and maximum number of application possible under practical conditions of use
(d) *e.g.* wettable powder (WP), emulsifiable concentrate (EC), granule (GR)	(l) The values should be given in g or kg whatever gives the more manageable number (e.g. 200 kg/ha

(e) GCPF Codes - GIFAP Technical Monograph No 2, 1989 (f) All abbreviations used must be explained (g) Method, e.g. high volume spraying, low volume spraying, spreading, dusting, drench (h) Kind, *e.g.* overall, broadcast, aerial spraying, row, individual plant, between the plant- type of equipment used must be indicated	instead of 200 000 g/ha or 12.5 g/ha instead of 0.0125 kg/ha (m) PHI - minimum pre-harvest interval

Methods of Analysis

Analytical methods for the active substance (Annex IIA, point 4.1)

Technical as (analytical technique)	HPLC-UV
Impurities in technical as (analytical technique)	HPLC-UV Karl-Fischer titration
Plant protection product (analytical technique)	HPLC-UV

Analytical methods for residues (Annex IIA, point 4.2)

Residue definitions for monitoring purposes

Food of plant origin		hexythiazox
Food of animal origin		none
Soil		hexythiazox
Water	surface	hexythiazox
	drinking/ground	hexythiazox
Air		hexythiazox

Monitoring/Enforcement methods

Food/feed of plant origin (analytical technique and LOQ for methods for monitoring purposes)	HPLC-UV; LOQ: 0.05 mg/kg hexythiazox, for fruits with high acid content and commodities with high water content. Multi-method (DFG S 19 extended revision): GC-ECD; LOQ: 0.05 mg/kg hexythiazox, for fruits with high acid content and commodities with high water content.
Food/feed of plant origin (analytical technique and LOQ for methods for monitoring purposes)	No MRL proposed
Soil (analytical technique and LOQ)	HPLC-UV; LOQ: 0.01 mg/kg hexythiazox
Water (analytical technique and LOQ)	LC-MS/MS; LOQ: 0.05 µg/kg hexythiazox for surface and tap water.
Air (analytical technique and LOQ)	HPLC-UV; LOQ: 0.9 µg/m^3 hexythiazox
Body fluids and tissues (analytical technique and LOQ)	No analytical method is required since hexythiazox is not classified as toxic or very toxic.

Classification and proposed labelling with regard to physical and chemical data (Annex IIA, point 10)

	RMS/peer review proposal
Active substance	Not classified

Impact on Human and Animal Health

Absorption, distribution, excretion and metabolism (toxicokinetics) (Annex IIA, point 5.1)

Rate and extent of oral absorption ‡	About 30 % absorbed within 72 h, based on urinary excretion data and the amount recovered in tissues and carcass. Absorption was lower (11 % within 96 h) at a high dose level.
Distribution ‡	1-10 % of the administered dose detected in tissues and carcass at 72 or 96 h after dosing. Highest levels were observed in fat followed by adrenals and liver. Residue levels in fat were generally two-fold higher in females than in males.
Potential for accumulation ‡	No evidence of accumulation.
Rate and extent of excretion ‡	> 90 % excreted within 72 h. About 30 % excreted in urine and > 60 % in faeces.
Metabolism in animals ‡	Almost 20 % of administered dose was excreted as parent in faeces; about 0.5 % was excreted in urine. Hexythiazox was mainly oxidised in the cyclohexane ring to form PT-1-8 (cis) (about 8% of the administered dose in faeces, 0.5 % in urine) and PT-1-8 (trans) (1 % of the administered dose in faeces, 0.4 % in urine). 60 % of the radioactivity in urine and faeces was not identified as metabolites.
Toxicologically relevant compounds ‡ (animals and plants)	Hexythiazox; metabolite PT-1-3 (toxicological data insufficient) in processed commodities
Toxicologically relevant compounds ‡ (environment)	Hexythiazox

Acute toxicity (Annex IIA, point 5.2)

Rat LD_{50} oral ‡	> 5000 mg/kg bw	
Rat LD_{50} dermal ‡	> 5000 mg/kg bw	
Rat LC_{50} inhalation ‡	> 2.0 mg/l/4 h (whole body exposure)	
Skin irritation ‡	Non-irritant	
Eye irritation ‡	Non-irritant	
Skin sensitisation ‡	Non-sensitiser (Magnusson-Kligman maximisation test)	

Short term toxicity (Annex IIA, point 5.3)

Target / critical effect ‡	Liver toxicity and reduced body weight gain, mouse Changes in clinical chemistry, increased liver weights, fatty degeneration of adrenal cortex, and

	reduced body weight gain, rat Adrenocortical hypertrophy, dog	
Relevant oral NOAEL ‡	28 day mouse: 55.1 mg/kg bw/day 90 day rat: 5.4 mg/kg bw/day 1 year dog: 2.87 mg/kg bw/day	
Relevant dermal NOAEL ‡	No study submitted – not required.	
Relevant inhalation NOAEL ‡	No study submitted – not required.	

Genotoxicity ‡ (Annex IIA, point 5.4)

The weight of evidence suggests that hexythiazox is not genotoxic.	

Long term toxicity and carcinogenicity (Annex IIA, point 5.5)

Target/critical effect ‡	Adrenal fatty changes and reduced body weight gain, rat Changes in haematology and clinical chemistry, increased adrenal weights, increased organ weight with increased incidence of proteinaceous casts in kidney and reduced body weight gain, mouse	
Relevant NOAEL ‡	2 year rat: 3.20 mg/kg bw/day 2 year mouse: 6.72 mg/kg bw/day	
Carcinogenicity ‡	Hepatoblastoma in male and female mice and liver adenomas in female mice at 267 mg/kg bw/day. Thyroid parafollicular cell adenoma and fibroadenoma of mammary gland in male rats at 163 mg/kg bw/day.	

Reproductive toxicity (Annex IIA, point 5.6)

Reproduction toxicity

Reproduction target / critical effect ‡	Parental: increased organ weights, decreased body weight and food consumption Reproductive: No reproductive toxicological effects. Offspring: decreased body weight	
Relevant parental NOAEL ‡	3.75 mg/kg bw/day	
Relevant reproductive NOAEL ‡	136 mg/kg bw/day	
Relevant offspring NOAEL ‡	3.75 mg/kg bw/day	

Developmental toxicity

Developmental target / critical effect ‡	Rat Maternal: decreased body weight gain, increased organ weights Developmental: No developmental toxicity Rabbit Maternal: No toxicity was observed. Developmental: No developmental toxicity	
Relevant maternal NOAEL ‡	Rat: 240 mg/kg bw/day Rabbit: ≥ 1080 mg/kg bw/day	
Relevant developmental NOAEL ‡	Rat: ≥ 2160 mg/kg bw/day Rabbit: ≥ 1080 mg/kg bw/day	

Neurotoxicity (Annex IIA, point 5.7)

Acute neurotoxicity ‡	No data available - no concern from other studies.	
Repeated neurotoxicity ‡	No data available - no concern from other studies.	
Delayed neurotoxicity ‡	No data available - no concern from other studies.	

Other toxicological studies (Annex IIA, point 5.8)

Mechanism studies ‡	No data available – not required.

Studies performed on metabolites or impurities ‡	
Acute oral toxicity of metabolites	PT-1-4, PT-1-5, PT-1-6, PT-1-8(cis), PT-1-8(trans) and PT-1-9 LD_{50} > 5000 mg/kg bw PT-1-2 LD_{50} = 1079 mg/kg bw; **R22** PT-1-3 LD_{50} = 341 mg/kg bw; **R22**
Reverse mutation study of metabolites (PT-1-2, PT-1-3, PT-1-4(trans-2), PT-1-5(1), PT-1-6(trans-2), PT-1-8(cis), PT-1-8(trans) and PT-1-9)	Negative
General pharmacology study of hexythiazox	Effects on central nervous system, cardiovascular and respiratory system, skeletal muscle, isolated smooth muscle, intestinal motility, gastric secretion and blood coagulation rather mild.

Medical data ‡ (Annex IIA, point 5.9)

Medical surveillance on manufacturing plant personnel	No effects in manufacturing during a 3-year examination. No adverse health effects were found in a 10-year follow-up period on the plant employees manufacturing hexythiazox.
Clinical cases, poisoning incidents and exposure of the general population	According to the notifier and a brief literature search, no poisoning is known. No clinical cases or poisoning incidents related to the use or production of hexythiazox were found in a new comprehensive literature search.

Summary (Annex IIA, point 5.10)

	Value	Study	Safety factor
ADI ‡	0.03 mg/kg bw/day	2 year rat	100
AOEL ‡	0.009 mg/kg bw/day	1 year dog	100; (bioavailability 30 %)
ARfD ‡	Not allocated		

Dermal absorption ‡ (Annex IIIA, point 7.3)

Formulation (Nissorun 10 % WP)	Concentrate: 1 % Spray dilutions: 10 % Rat *in vivo*

Exposure scenarios (Annex IIIA, point 7.2)

Operator	**Apple** Tractor mounted air assisted sprayer Above the AOEL without PPE (167-244% AOEL, German-UK POEM models) Below the AOEL with PPE (33%, German Model, gloves during mixing/loading and application, coverall and sturdy footwear during application) Hand-held equipment Below the AOEL without PPE (89%, German Model). **Grapes** Tractor mounted air assisted sprayer Above the AOEL without PPE (133-256%, German-UK POEM models) Below the AOEL with PPE (22%,German Model, gloves during mixing/loading and application, coverall and sturdy footwear during application) Hand-held equipment Below the AOEL without PPE (67%, German Model) **Citrus** Tractor mounted air assisted sprayer Above the AOEL without PPE (133-122% AOEL, German-UK POEM models) Below the AOEL with PPE (22% with gloves during mixing/loading and application, coverall and sturdy footwear during application – German model; 78% with gloves during mixing/loading and application - UK POEM) Hand-held equipment Below the AOEL without PPE (67-78%, German - UK POEM models, respectively)
Workers	Inconclusive. Further data are needed.

Bystanders	Bystander exposure below the AOEL in all scenarios (Europoem 2, Bystander Working Group Report, December 2002).

Classification and proposed labelling with regard to toxicological data (Annex IIA, point 10)

	Peer review proposal
Substance classified (hexythiazox)	No classification

Residues

Metabolism in plants (Annex IIA, point 6.1 and 6.7, Annex IIIA, point 8.1 and 8.6)

Plant groups covered	Fruit crops (grapes, citrus, pears and apples) and tea. (foliar and fruit treatments)
Rotational crops	Lettuce, turnip and cereals
Metabolism in rotational crops similar to metabolism in primary crops?	Not relevant considering the supported uses. Study indicates PT-1-2 to be the metabolite of concern in rotational crops.
Processed commodities	Standard hydrolysis study
Residue pattern in processed commodities similar to residue pattern in raw commodities?	Hexythiazox degraded to PT-1-3 (48% TRR) under sterilisation conditions (120°C, pH 6, 20 min).
Plant residue definition for monitoring	Hexythiazox
Plant residue definition for risk assessment	Hexythiazox
Conversion factor (monitoring to risk assessment)	None

Metabolism in livestock (Annex IIA, point 6.2 and 6.7, Annex IIIA, point 8.1 and 8.6)

Animals covered	Lactating ruminant (goat), poultry (hen)
Time needed to reach a plateau concentration in milk and eggs	Milk: plateau below LOQ in a 28-day study Eggs: levels steadily increasing in a 6-day study
Animal residue definition for monitoring	Not discussed. Not proposed and not required considering the supported uses
Animal residue definition for risk assessment	No residues expected
Conversion factor (monitoring to risk assessment)	No
Metabolism in rat and ruminant similar (yes/no)	Not discussed
Fat soluble residue: (yes/no)	Not discussed

Residues in succeeding crops (Annex IIA, point 6.6, Annex IIIA, point 8.5)

Not relevant considering the supported uses

Stability of residues (Annex IIA, point 6 introduction, Annex IIIA, point 8 Introduction)

Hexythiazox residues stable up to: - 2 years in water containing matrices (strawberry, apple) when stored at -20°C; - 1 year in acid (mandarin) and water containing matrices (apple, pear) when stored at -30°C.

Stability data for animal products not provided and not required.

Residues from livestock feeding studies (Annex IIA, point 6.4, Annex IIIA, point 8.3)

	Ruminant:	Poultry:	Pig:
	Conditions of requirement of feeding studies		
Expected intakes by livestock ≥ 0.1 mg/kg diet (dry weight basis) (yes/no - If yes, specify the level)	No	No	No
Potential for accumulation (yes/no):	No	Not relevant	Not relevant
Metabolism studies indicate potential level of residues ≥ 0.01 mg/kg in edible tissues (yes/no)	No	Not relevant	Not relevant
	Feeding studies (Specify the feeding rate in cattle and poultry studies considered as relevant) Residue levels in matrices : Mean (max) mg/kg		
Muscle	-	-	-
Liver	-	-	-
Kidney	-	-	-
Fat	-	-	-
Milk	-		
Eggs		-	

Summary of residues data according to the representative uses on raw agricultural commodities and feedingstuffs (Annex IIA, point 6.3, Annex IIIA, point 8.2)

Crop	Northern/ Southern Region field or/ glasshouse	Trials results relevant to the representative uses (a)	Recommendation/comments	MRL estimated from trials according to the representative use	HR (c)	STMR (b)
Pome fruit	NE	<0.01, 7× 0.05, 0.06, 0.08	PHI 27 – 29 days R_{max}: 0.10 R_{ber}: 0.10 (calculated on NE + SE data)	**0.1**	0.08	0.05
	SE	3× <0.01, 6× 0.05, 0.08			0.08	0.05
Grapes	NE	2× 0.06, 0.09, 0.12, 0.13, 0.16, 0.18, 0.19	PHI 20 – 22 days R_{max}: 0.22 R_{ber}: 0.29 (calculated on NE + SE data)	**0.5**	0.19	0.13
	SE	2× <0.05, 3× 0.09, 0.10, 0.12, 0.14			0.14	0.09
Orange	SE	Whole fruit: 5× <0.05, 2× 0.07, 0.08 Peel: < 0.05, 0.08, 0.17, 0.18, 2× 0.19 Pulp: 7× <0.01, <0.05	PHI 13 – 15 days MRL for citrus calculated on orange + mandarin data: R_{max}: 0.10 R_{ber}: 0.14 (calculated on NE + SE data)	**0.2** (citrus)	0.08	Whole fruit: 0.05 Pulp: <0.01
Mandarin	SE	Whole fruit: 5× <0.05, 0.07, 0.08, 0.09 Peel: <0.05, 0.08, 0.10, 0.14, 0.15, 0.2, 0.21, 0.28 Pulp: 6× <0.01, 2× <0.05			0.09	Whole fruit: 0.05 Pulp: <0.01

(a) Numbers of trials in which particular residue levels were reported *e.g.* 3 x <0.01, 1 x 0.01, 6 x 0.02, 1 x 0.04, 1 x 0.08, 2 x 0.1, 2 x 0.15, 1 x 0.17
(b) Supervised Trials Median Residue *i.e.* the median residue level estimated on the basis of supervised trials relating to the representative use
(c) Highest residue

Consumer risk assessment (Annex IIA, point 6.9, Annex IIIA, point 8.8)

ADI	0.03 mg/kg bw/day
TMDI (% ADI) according to EFSA PRIMo rev.2 model	Maximum: 9% ADI (DE Child)
TMDI (% ADI) according to national (to be specified) diets	4% (Schoolchild diet, German BBA model), 4% (European diet, WHO/GEMS Food model)
IEDI (WHO European Diet) (% ADI)	0.96% (adult)
NEDI (specify diet) (% ADI)	
Factors included in IEDI and NEDI	None
ARfD	Not allocated and not required
IESTI (% ARfD)	Not relevant
NESTI (% ARfD) according to national (to be specified)	Not relevant
Factors included in IESTI and NESTI	Not relevant

Processing factors (Annex IIA, point 6.5, Annex IIIA, point 8.4)

Crop/ process/ processed product	Number of studies	Processing factors		Amount transferred (%) (Optional)
		Transfer factor	Yield factor	
Grapes				
Gape juice processing	2 balance and 2 follow up			
Pomace, wet		2**	-	
Lees		11.3**	-	
Juice, final		0.25	-	
Grape wine processing	2 balance and 2 follow up			
Must		0.25**	-	
Wine (after alcoholic fermentation)		0.09**	-	
Pomace, wet		10.0**	-	
Pomace, dry		16.5*	-	
Wine (after malolactic fermentation)		0.02*	-	
Lees		0.53**	-	
Wine (final)		0.04		
Raisins processing	2 balance and 2 follow up			
Dipping solution		0.53**	-	
Raisins		1.75	-	
Citrus (Oranges, Mandarins)				
Canned fruit processing	2 balance and 4 follow up			
Peel		3.6**	-	
Fruit, peeled		0.24**	-	
Fruit, canned		0.14	-	

Marmalade processing	4 balance			
Marmalade		0.21	-	
Juice processing	2 balance and 4 follow up			
Waste, sieving		0.22	-	
Juice, raw		0,44	-	
Pomace, wet (large variation, 1.50 taken as provisional value)		1,06** (0.61 & 1.5)	-	
Pomace, dry		5,08**	-	
Juice, final		0,25	-	

**: Figure relying on two studies only
*: Figure relying on 1 study only

Proposed MRLs (Annex IIA, point 6.7, Annex IIIA, point 8.6)

Apples	0.1 mg/kg
Grapes	0.5 mg/kg
Citrus (oranges, mandarins)	0.2 mg/kg

When the MRL is proposed at the LOQ, this should be annotated by an asterisk (*) after the figure.

Fate and Behaviour in the Environment

Route of degradation (aerobic) in soil (Annex IIA, point 7.1.1.1.1)

Mineralization after 100 days	at 15°C: 4-8 % AR after 98 d, 5-9 % AR after 112 d (n=2); at 20°C: 6-8 % AR after 90 d, 8-10 % AR after 122 d (n=2); at 20°C: 36 % AR after 118 days (n=1)*; 31.3 % AR after 90 d* at 25°C: 9-19 % AR after 84 d (n=2)
Non-extractable residues after 100 days	at 15°C: 36-51 % AR after 98 d, 34-50 % AR after 112 d (n = 2); at 20°C: 15-21 % AR after 90 d, 17-20 % AR after 122 d (n = 2); at 20°C: 10 % AR after 118 days (n=1)*; 8.9 % AR after 90 d* at 25°C: 42-48 % AR after 84 d (n = 2)
Metabolites that may require further consideration - name and/or code, % of applied (range and maximum)	**PT-1-9** [5-(4-chlorophenyl)-N-(4-oxocyclohexyl)-4-methyl-2-oxothiazolidine-3-carboxamide]: maximum 21.1 % AR at day 14 (15°C); **PT-1-2** [Trans-5-(4-chlorophenyl)-4-methyl-2-oxothiazolidine-3-carboxamide]: maximum 39.5 % AR at day 122 (20°C); **PT-1-3** [Trans-5-(4-chlorophenyl)-4-methyl-2-oxothiazolidine]: maximum 9.2 % AR at day 90 (20°C)

*^{14}C-cyclohexyl labelled Hexythiazox
The values without the asterisk relate to the thiazolidine label

Route of degradation in soil - Supplemental studies (Annex IIA, point 7.1.1.1.2)

Anaerobic degradation	
Non-extractable residues after 100 days	9.7 % AR after 120 days and 7.9 % AR after 360 days (n = 1)
Metabolites that may require further consideration - name and/or code, % of applied (range and maximum)	**PT-1-2**: max. 21.0 % AR at day 360; cyclohexane-hydroxylated compounds (**PT-1-4**, **PT-1-6**, **PT-1-8**): sum of all max. 14.9 % AR at day 360
Soil photolysis	DT_{50} = 116 days
Non-extractable residues	max. 15.4 % AR after 62 days (n = 1)
Metabolites that may require further consideration - name and/or code, % of applied (range and maximum)	None

Rate of degradation in soil (Annex IIA, point 7.1.1.2, Annex IIIA, point 9.1.1)

Laboratory studies

Hexythiazox	Aerobic conditions						
Soil type	X	pH	Temperature °C / % MWHC	DT_{50} /DT_{90} (days)	DT_{50} (d) 20°C pF2/10kPa)*)	χ^2 error (%)	Method of calculation
Sand		6.7	20 °C / 40 %	35.3 / 117.2	32.5	4.9	SFO
Sandy loam		6.2	20 °C / 40 %	32.2 / 107.1	27.4	7.4	SFO
Clay loam		7.4	15 °C / 50 %	18.3**)/ 60.8	7.8	6.4	**)
Light clay		5.6	15 °C / 50 %	31.5 / 104.5	14.4	6.8	SFO
Clay loam		7.4	25 °C / 50 %	9.6**)/ 32.2	10.3	2.8	**)
Light clay		5.6	25 °C / 50 %	16.5 / 54.8	18.9	8.6	SFO
Silt loam		6.3	20 °C / 40 %	74.6 / 247.8	56.0	3.8	SFO
Geometric mean					23.7 (n=5)		

*) Q_{10} of 2.58 and Walker equation coefficient of 0.7
**) DT_{50} derived from the DT_{90} value based on FOMC kinetics divided by the factor of 3.32 (pseudo-first-order DT_{50})

PT-1-9	Aerobic conditions							
Soil type	X	pH	Temperature °C / % MWHC	DT_{50}/ DT_{90} (days)	f. f. *) k_{dp}/k_f	DT_{50} (d) (20°C pF2/10kPa)***)	χ^2 error (%)	Method of calculation
Sand		6.7	20 °C / 40%	17.0 / 56.3	0.64	15.6	11.9	SFO
Sandy loam		6.2	20 °C / 40%	7.7 / 25.7	0.80	6.6	11.5	SFO
Clay loam		7.4	15 °C / 50 %	19.7***)/ 65.4	0.44	8.4	15.6	FOMC
Light clay		5.6	15 °C / 50 %	39.1 / 129.7	0.44	17.9	5.8	SFO
Clay loam		7.4	25 °C / 50 %	7.9***)/ 26.2	0.44	8.4	20.8	FOMC
Light clay		5.6	25 °C / 50 %	21.9 / 72.7	0.42	25.0	4.3	SFO
Geometric mean						11.7 (n=4)		

*) The formation fraction from hexythiazox (the arithmetic mean formation fraction is 0.58).
**) Q_{10} of 2.58 and Walker equation coefficient of 0.7
***) DT_{50} derived from the DT_{90} value based on FOMC kinetics divided by the factor of 3.32 (pseudo-first-order DT_{50}).

PT-1-2	Aerobic conditions							
Soil type	X	pH	Temperature °C / % MWHC	DT_{50}/ DT_{90} (days)	f. f. k_{dp}/k_f	DT_{50} (d) 20°C pF2/10kPa)*)	χ^2 error (%)	Method of calculation

Sandy loam		7.2	20 ºC / 45 %	153.9 / 511.3	-	153.9	2.7	SFO
Sandy loam		5.2	20 ºC / 45 %	264.2 / 877.5	-	264.2	1.5	
Clay loam		8.0	20 ºC / 45 %	43.1 / 143.1	-	43.1	8.8	
Clay loam		7.4	15 ºC / 50 %	21.4 / 71.0	-	9.1	4.9	
Light clay		5.6	15 ºC / 50 %	35.9 / 119.1	-	16.4	5.9	
Clay loam		7.4	25 ºC / 50 %	15.2 / 50.4	-	16.2	4.0	
Light clay		5.6	25 ºC / 50 %	22.7 / 75.5	-	26.0	7.8	
Geometric mean						54.3 (n=5)		

*) Q_{10} of 2.58 and Walker equation coefficient of 0.7

PT-1-3	Aerobic conditions							
Soil type	X	pH	Temperature ºC / % MWHC	DT_{50}/ DT_{90} (days)	f. f. k_{dp}/k_f	DT_{50} (d) 20°C pF2/10kPa)*)	χ^2 error (%)	Method of calculation
Sandy loam		7.2	20 ºC / 45 %	46.0 / 152.8	-	46.0	5.6	SFO
Sandy loam		5.2	20 ºC / 45 %	54.1 / 179.6	-	54.1	10.4	
Clay loam		8.0	20 ºC / 45 %	24.9 / 82.8	-	24.9	11.4	
Clay loam		7.4	15 ºC / 50 %	25.1 / 83.2	-	10.7	3.4	
Light clay		5.6	15 ºC / 50 %	31.1 / 103.4	-	14.3	4.7	
Clay loam		7.4	25 ºC / 50 %	17.3 / 57.4	-	18.4	6.3	
Light clay		5.6	25 ºC / 50 %	21.3 / 70.8	-	24.4	3.8	
Geometric mean						28.1 (n=5)		

*) Q_{10} of 2.58 and Walker equation coefficient of 0.7

Field studies

Hexythiazox	Aerobic conditions							
Soil type	Location	X^1	pH	Depth (cm)	$DisT_{50}$ (days)	$DisT_{90}$ (days)		
Silty loam (bare)	Germany		5.8	25-100	n.d.	around 58*		
Loamy sand (bare)	Germany		4.8	25-100	n.d.	around 16*		

Sandy loam (bare)	Germany		7.0	25-100	n.d.	around 97*		
Sandy loam (bare)	Germany		6.9	25-100	n.d.	around 29*		

n.d. Not determined because not enough data points above the detection limit of 0.01 mg/kg were available

* The estimate of $DisT_{90}$ indicates the sampling time when the Hexythiazox residues in soil were first time detected to be below the detection limit of 0.01 mg/kg

pH dependence (yes / no) (if yes type of dependence)	No

Soil adsorption/desorption (Annex IIA, point 7.2.1)

Hexythiazox							
Soil Type	OC %	Soil pH (Ca)	K_d	K_{oc}	K_f	K_{foc}	1/n
Sandy loam	1.0	5.5			128	12823	0.94
Silt loam	1.2	6.3			134	11164	0.96
Clay loam	3.9	5.6			340	8714	0.95
Sandy loam	1.2	7.2			110	9143	1.04
Mean						10461	0.98
pH dependence, Yes or No			No				

Metabolite **PT-1-2**							
Soil Type	OC %	Soil pH (w)	K_d	K_{oc}	K_f	K_{foc}	1/n
Clay loam	4.6	8.0	16.1	350	12.6	274	0.90
Silt loam	2.8	7.0	16.3	581	12.4	443	0.89
Sandy loam	0.8	5.0	5.1	638	4.5	561	0.93
Mean				523		426	0.91
pH dependence (yes or no)			No				

Metabolite **PT-1-3**							
Soil Type	OC %	Soil pH (w)	K_d	K_{oc}	K_f	K_{foc}	1/n
Clay loam	4.6	8.0	17.4	378	13.6	296	0.90
Silt loam	2.8	7.0	19.0	678	14.2	508	0.89
Sandy loam	0.8	5.0	7.0	873	5.4	674	0.86
Mean				643		493	0.88
pH dependence (yes or no)			No				

Metabolite **PT-1-9**							
Soil Type	OC %	Soil pH (w)	K_d	K_{oc}	K_f	K_{foc}	1/n
Clay loam	4.6	8.0	25.0	544	18.5	402	0.89
Silt loam	2.8	7.0	24.8	886	17.7	631	0.87
Sandy loam	0.8	5.0	9.8	1221	7.4	922	0.88
Mean				884		652	0.88
pH dependence (yes or no)			No				

Mobility in soil (Annex IIA, point 7.1.3, Annex IIIA, point 9.1.2)

Column leaching	Eluation: 10 mL/h (distilled water) Time period: 4 days
	Leachate: < 0.1 % AR in leachate > 92 % AR retained in top 5 cm
Aged residues leaching	Aged for: 10 days Time period: 4 days Eluation: 10 mL/h (distilled water)
	Analysis of soil residues post ageing: 45.2 % active substance; 9.5 % PT-1-2; 4.2 % PT-1-3; 8.5 % PT-Cy-O (PT-1-5 and PT-1-9); 2.6 % PT-Cy-OH (PT-1-4 and PT-1-8) Leachate: < 0.1 % AR in leachate
	Leachate: < 0.1 % AR in leachate 49.1 % active substance; 6.9 % PT-1-2; 3.7 % PT-1-3; 12.2 % PT-Cy-O (PT-1-5 and PT-1-9) > 87 % AR retained in top 5 cm
Lysimeter/field leaching studies	Not required

PEC (soil) (Annex IIIA, point 9.1.3)

Hexythiazox	DT_{50} (d): 74.6 days Kinetics: SFO Representative worst case laboratory degradation
Method of calculation Application data	Crop: apples, grapes, citrus Depth of soil layer: 5 cm % plant interception: 50 % (apples), 40 % (grapes), 70 % (citrus) Number of applications and application rates: 1 × 0.10 kg ai/ha in apples 2 × 0.08 kg ai/ha in grapes 3 × 0.08 kg ai/ha in citrus Interval between applications: 30 days

$PEC_{(s)}$	Apples (1 × 0.10 kg ai/ha)		Grapes (2 × 0.08 kg ai/ha)		Citrus (3 × 0.08 kg ai/ha)	
		Time		Time		Time

(mg/kg)	Actual	weighted average	Actual	weighted average	Actual	weighted average
Initial*	0.0667	-	0.1124	-	0.0745	-

* As only initial worst case PEC_s values were used in risk assessment, no short-term, long-term or plateau concentrations are shown.

Metabolite **PT-1-2**	Molecular weight relative to parent: 0.77
Method of calculation	DT_{50} (d): 264 days Kinetics: SFO Representative worst case laboratory degradation
Application data	Application rate assumed: 1 × 0.0395 kg/ha in apples 2 × 0.0316 kg/ha in grapes 3 × 0.0316 kg/ha in citrus (assumed PT-1-2 is formed at a maximum of 39.5 % of the applied dose)

	Apples		Grapes		Citrus	
$PEC_{(s)}$ (mg/kg)	Actual	Time weighted average	Actual	Time weighted average	Actual	Time weighted average
Initial*	0.0203	-	0.0375	-	0.0270	-
Plateau conc.	0.0329		0.0608		0.0438	

Metabolite **PT-1-3**	Molecular weight relative to parent: 0.65
Method of calculation	DT_{50} (d): 54 days Kinetics: SFO Representative worst case laboratory degradation
Application data	Application rate assumed: 1 × 0.0092 kg/ha in apples 2 × 0.0074 kg/ha in grapes 3 × 0.0074 kg/ha in citrus (assumed PT-1-3 is formed at a maximum of 9.2 % of the applied dose)

	Apples		Grapes		Citrus	
$PEC_{(s)}$ (mg/kg)	Actual	Time weighted average	Actual	Time weighted average	Actual	Time weighted average
Initial*	0.0040	-	0.0064	-	0.0041	-

*As only initial worst case PEC_s values were used in risk assessment, no short-term, long-term or plateau concentrations are shown.

Metabolite **PT-1-9**	Molecular weight relative to parent: 1.05
Method of calculation	DT_{50} (d): 39 days Kinetics: SFO Representative worst case laboratory degradation
Application data	Application rate assumed: 1 × 0.0211 kg/ha in apples 2 × 0.0169 kg/ha in grapes 3 × 0.0169 kg/ha in citrus (assumed PT-1-9 is formed at a maximum of 21.1 % of the applied dose)

$PEC_{(s)}$ (mg/kg)	Apples		Grapes		Citrus	
	Actual	Time weighted average	Actual	Time weighted average	Actual	Time weighted average
Initial*	0.0148	-	0.0225	-	0.0137	-

* As only initial worst case PEC_s values were used in risk assessment, no short-term, long-term or plateau concentrations are shown.

Route and rate of degradation in water (Annex IIA, point 7.2.1)

Hydrolysis of active substance and relevant metabolites (DT_{50}) (state pH and temperature)	pH 5: stable at 22°C, DT_{50} = 2608 days at 50°C and 315 days at 70°C pH 7: stable at 22°C, DT_{50} = 203 days at 50°C and 12 days at 70°C pH 9: DT_{50} = 504 days at 22°C, 3.4 days at 50°C and 0.2 days at 70°C
	Metabolites: PT-1-3 max. 91.9 % at pH 9, 70°C after 27 days PT-1-3 max. 7.0 % at ambient (22°C) temperature at pH 9 after 57 days
Photolytic degradation of active substance and relevant metabolites	Xenon arc lamp, distilled water and river water, 25°C DT_{50} in distilled water: 168 days DT_{50} in river water: 147 days Indirectly phototransformed by water radicals generated from irradiation of artificial sunlight. Several metabolites but none of them exceeded 4.3 %.
Readily biodegradable (yes/no)	No

Degradation in water / sediment

Hexythiazox	Distribution (Max. in water 74-86 % AR after day 0 and in sed. 71-72 % AR after day 7)

Water / sediment system	pH (w)	pH (sed)	temp °C	$DegT_{50}$-$DegT_{90}$ whole syst.	χ^2 error (%)	DT_{50}-DT_{90} water	St. (r^2) χ^2 error (%)	DT_{50}-DT_{90} sed.	St. (r^2) χ^2 error (%)	Method of calculation
System I*), Krempe (sandy loam)	7.8	7.0	20	38 - 128	5.2	0.5 – 1.5	15.3	42 - 138	4.5	SFO[1]
System II*), Ohlau (sand)	7.4	6.2	20	33 - 109	6.1	0.6 -1.8	10.6	37 - 123	10.4	
System III**), Wenne (sandy)	7.6	7.4	20	156 - 519	5.1	11-38	7.3	n.d.	-	
System IV**), Schmallenberg – Graftschaft (loamy)	7.5	7.0	20	135 - 449	6.5	4 - 13	7.3	n.d.	-	
Geometric mean				72 - 239		1.9 – 6.0		39 - 130		

Metabolite PT-1-2	Distribution: Max. in water 12.8 % AR after 100 d. Max. in sed 19.4 % AR after 100 d
Metabolite PT-1-9	Distribution: Max. in water 8.7 % AR after 125 d. Max. in sed 8.7 % AR after 61 d
Metabolite PT-1-8-c	Distribution: Max. in water 9.1% AR after 14 & 28 d. Max. in sed. 7.4% AR after 125 d
Metabolite PT-1-8-t	Distribution: Max. in water 7.1 % AR after 28 d. Max. in sed. 8.7 % AR after 59 d

Mineralization and non extractable residues

Water / sediment system	pH (w)	pH (sed)	Mineralization % after 100 days (end of the study).	Non-extractable residues in sediment. Max % after x days
System I*), Krempe	7.8	7.0	2.5 (100 days)	26.4 % (100 days)
System II*), Ohlau	7.4	6.2	6.0 (100 days)	27.9 (100 days)
System III**), Wenne	7.6	7.4	2.7 (100 days)	2.6 (100 days)
System IV**), Schmallenberg – Graftschaft	7.5	7.0	4.8 (100 days)	5.4 (100 days)

[1]Calculated with the KinGUI vers. 1.1
n.d. not determined due to slow dissipation in this phase
$DegT_{50/90}$ for degradation
$DT_{50/90}$ for dissipation
*) Thiazolidine ring labelled a.s.
**) Cyclohexyl labelled a.s.

PEC (surface water) and PEC sediment (Annex IIIA, point 9.2.3)

Hexythiazox

Parameters used in $FOCUS_{sw}$ 2	Molecular weight (g/mol): 352.88 Water solubility (mg/L): 0.4 Koc/Kom (L/kg): 10461 / 6068 DT_{50} soil (d): 23.71 days (Geomean of 5 soils, laboratory values in accordance with FOCUS SFO) Normalisation to 10 kPa/ pF2 and 20 °C with Q10 of 2.58 and Walker equation coefficient of 0.7 DT_{50} water/sediment system (d): 1000 days (Default worst case by FOCUS) DT_{50} water (d): 71.84 days (Geomean of the total systems) DT_{50} sediment (d): 1000 days (Default worst case by FOCUS) Crop interception (%): Apples 40 %, Grapes 50 %, Citrus 70 %
Parameters used in $FOCUS_{sw}$ step 3	Vapour pressure: 3.4×10^{-6} Pa Kom/Koc: 6068 / 10461 1/n: 0.9745 (Freundlich exponent, mean value)
Application rate	Crop: Apples, Grapes, Citrus Number of applications and application rates (g as/ha): 1 × 100 g ai/ha in apples 2 × 80 g ai/ha in grapes 3 × 80 g ai/ha in citrus Interval (d): 30 days Depth of water body: 30 cm Application in Southern Europe and early application scenarios (worst case for run-off/drainage inputs)
Main routes of entry	Drift, drainage, run-off The used areic mean deposition rates for the Step 4 assessment are as follows: - Apples (20 m no spray zone): ditch 2.6 %; stream 3.12 % -Citrus (15 m no spray zone): ditch 2.52 % and 1.109 % (90th and 77th percentiles); stream 3.03 %

and 1.109 % (90th and 77th percentiles). For the mitigation of runoff following mitigation values were used: - Apples (20 m): 80 % runoff volume and flux, 95 % erosion mass and flux - Citrus (15 m): 60 % runoff volume and flux, 85 % erosion mass and flux

Step 2 scenarios,
Hexythiazox (only initial PEC_{sw} values used in risk assessment are included; full results are available in DAR)

PEC_{sw} (µg/L)	Apples (1 × 0.10 kg ai/ha)		Grapes* (2 × 0.08 kg ai/ha)		Citrus** (3 × 0.08 kg ai/ha)	
	Actual	TWA	Actual	TWA	Actual	TWA
0d	9.732	-	0.7263	-	4.1933	-

*based on 82nd percentile spray drift values
**based on 90th percentile spray drift values

Step 3 scenarios, Hexythiazox:

PEC_{sw} (µg/L)	Step 3 scenarios: Pome fruit (apples)							
	D3: Vreedepeel, ditch		D4: Skousbo, pond		D4: Skousbo, stream		D5: La Jailliere, pond	
	Actual	TWA	Actual	TWA	Actual	TWA	Actual	TWA
0d	7.689	-	0.467	-	7.480	-	0.467	-
1d	3.488	5.896	0.450	0.458	0.000	0.485	0.449	0.458
2d	0.397	3.752	0.434	0.450	0.000	0.242	0.432	0.449
4d	0.025	1.926	0.406	0.435	0.000	0.121	0.403	0.433
7d	0.019	1.110	0.370	0.414	0.000	0.069	0.367	0.412
14d	0.012	0.563	0.309	0.376	0.000	0.035	0.308	0.373
21d	0.008	0.378	0.265	0.346	0.000	0.023	0.268	0.345
28d	0.006	0.285	0.235	0.322	0.000	0.017	0.237	0.321
42d	0.003	0.192	0.194	0.286	0.000	0.012	0.193	0.285
50d	0.003	0.162	0.175	0.269	0.000	0.010	0.175	0.269
100d	0.001	0.082	0.102	0.202	0.000	0.005	0.106	0.203

Step 3 scenarios, Hexythiazox:

PEC_{sw} (µg/L)	Step 3 scenarios: Pome fruit (apples)							
	D5: La Jailliere, stream		R1: Weiherbach, pond		R1: Weiherbach, stream		R2: Porto, stream	
	Actual	TWA	Actual	TWA	Actual	TWA	Actual	TWA
0d	7.455	-	0.467	-	6.221	-	8.242	-
1d	0.000	0.282	0.449	0.458	0.000	1.074	0.000	0.700
2d	0.000	0.141	0.432	0.449	0.000	0.537	0.000	0.350
4d	0.000	0.071	0.402	0.433	0.000	0.269	0.000	0.175
7d	0.000	0.040	0.364	0.411	0.000	0.154	0.000	0.100
14d	0.000	0.020	0.298	0.370	0.000	0.077	0.023	0.051
21d	0.000	0.014	0.254	0.338	0.000	0.051	0.000	0.034
28d	0.000	0.010	0.223	0.313	0.000	0.039	0.000	0.026
42d	0.000	0.007	0.177	0.275	0.000	0.026	0.000	0.017
50d	0.000	0.006	0.157	0.258	0.000	0.022	0.000	0.014
100d	0.000	0.003	0.082	0.186	0.000	0.011	0.000	0.007

Step 3 scenarios, Hexythiazox:

PEC_{sw} (µg/L)	Step 3 scenarios: Pome fruit (apples)			
	R3: Bologna, stream		R4: Roujan, stream	
	Actual	TWA	Actual	TWA
0d	8.803	-	6.223	-
1d	0.011	2.827	0.000	1.080
2d	0.003	1.415	0.000	0.540
4d	0.002	0.709	0.000	0.270
7d	0.002	0.406	0.000	0.155
14d	0.001	0.204	0.000	0.077
21d	0.001	0.140	0.000	0.052
28d	0.000	0.105	0.000	0.039
42d	0.000	0.070	0.000	0.027
50d	0.000	0.059	0.000	0.023
100d	0.000	0.030	0.016	0.013

Step 3 scenarios, Hexythiazox:

PECsw (µg/L)	Step 3 scenarios: Vine					
	D6: Thiva, ditch**		R1: Weiherbach, pond*		R1: Weiherbach, stream**	
	Actual	TWA	Actual	TWA	Actual	TWA
0d	0.441	-	0.018	-	0.326	-
1d	0.006	0.173	0.017	0.017	0.000	0.054
2d	0.000	0.087	0.017	0.017	0.000	0.027
4d	0.000	0.044	0.016	0.017	0.000	0.014
7d	0.000	0.025	0.014	0.016	0.000	0.008
14d	0.000	0.013	0.012	0.015	0.000	0.004
21d	0.000	0.009	0.011	0.014	0.000	0.003
28d	0.000	0.007	0.009	0.013	0.000	0.002
42d	0.000	0.004	0.007	0.011	0.000	0.002
50d	0.000	0.004	0.007	0.011	0.000	0.002
100d	0.000	0.002	0.004	0.009	0.000	0.001

*based on 82nd percentile spray drift values
**based on 90th percentile spray drift values

Step 3 scenarios, Hexythiazox:

PECsw (µg/L)	Step 3 scenarios: Vine					
	R2: Porto, stream**		R3: Bologna, stream**		R4: Roujan, stream**	
	Actual	TWA	Actual	TWA	Actual	TWA
0d	0.433	-	0.462	-	0.326	-
1d	0.000	0.036	0.000	0.140	0.000	0.054
2d	0.000	0.018	0.000	0.070	0.000	0.037
4d	0.000	0.009	0.000	0.035	0.000	0.019
7d	0.000	0.005	0.000	0.020	0.000	0.011
14d	0.018	0.003	0.000	0.010	0.000	0.005
21d	0.000	0.002	0.000	0.010	0.000	0.004
28d	0.000	0.002	0.000	0.007	0.000	0.003
42d	0.000	0.001	0.000	0.005	0.000	0.002
50d	0.000	0.001	0.000	0.004	0.000	0.002
100d	0.000	0.001	0.000	0.002	0.000	0.001

*based on 82nd percentile spray drift values
**based on 90th percentile spray drift values

Step 3 scenarios, Hexythiazox:

PEC_{sw} (µg/L)	Step 3 scenarios: Citrus			
	D6: Thiva, ditch**		R4: Roujan, stream**	
	Actual	TWA	Actual	TWA
0d	2.927	-	2.213	-
1d	2.634	2.774	0.000	0.359
2d	2.382	2.638	0.000	0.180
4d	1.864	2.385	0.000	0.090
7d	0.963	1.965	0.000	0.051
14d	0.222	1.215	0.000	0.026
21d	0.129	0.865	0.000	0.017
28d	0.089	0.676	0.000	0.013
42d	0.003	0.458	0.000	0.009
50d	0.005	0.385	0.000	0.007
100d	0.009	0.198	0.000	0.004

*based on 77th percentile spray drift values
**based on 90th percentile spray drift values

Step 4 scenarios, Hexythiazox:

PEC_{sw} (µg/L)	Step 4 scenarios: Pome fruit (apples), 20 m buffer zone							
	D3: Vreedepeel, ditch		D4: Skousbo, pond		D4: Skousbo, stream		D5: La Jailliere, pond	
	Actual	TWA	Actual	TWA	Actual	TWA	Actual	TWA
0d	0.848	-	0.093	-	0.902	-	0.093	-
1d	0.385	0.650	0.090	0.091	0.000	0.058	0.090	0.091
2d	0.044	0.414	0.087	0.090	0.000	0.029	0.086	0.090
4d	0.003	0.212	0.081	0.087	0.000	0.015	0.080	0.086
7d	0.002	0.122	0.074	0.083	0.000	0.008	0.073	0.082
14d	0.001	0.062	0.062	0.075	0.000	0.004	0.061	0.074
21d	0.001	0.042	0.053	0.069	0.000	0.003	0.053	0.069
28d	0.001	0.031	0.047	0.064	0.000	0.002	0.047	0.064
42d	0.000	0.021	0.038	0.057	0.000	0.001	0.038	0.057
50d	0.000	0.018	0.035	0.053	0.000	0.001	0.035	0.053
100d	0.000	0.009	0.020	0.040	0.000	0.001	0.021	0.040

Step 4 scenarios, Hexythiazox:

PEC_{sw} (µg/L)	Step 4 scenarios: Pome fruit (apples), 20 m buffer zone							
	D5: La Jailliere, stream		R1: Weiherbach, pond		R1: Weiherbach, stream		R2: Porto, stream	
	Actual	TWA	Actual	TWA	Actual	TWA	Actual	TWA
0d	0.899	-	0.093	-	0.750	-	0.994	-
1d	0.000	0.034	0.090	0.091	0.000	0.129	0.000	0.084
2d	0.000	0.017	0.086	0.090	0.000	0.065	0.000	0.042
4d	0.000	0.009	0.080	0.086	0.000	0.032	0.000	0.021
7d	0.000	0.005	0.072	0.082	0.000	0.019	0.000	0.012
14d	0.000	0.002	0.059	0.074	0.000	0.009	0.005	0.006
21d	0.000	0.002	0.050	0.067	0.000	0.006	0.000	0.004
28d	0.000	0.001	0.044	0.062	0.000	0.005	0.000	0.003
42d	0.000	0.001	0.035	0.055	0.000	0.003	0.000	0.002
50d	0.000	0.001	0.031	0.051	0.000	0.003	0.000	0.002
100d	0.000	0.000	0.016	0.037	0.000	0.001	0.000	0.001

Step 4 scenarios, Hexythiazox:

PEC_{sw} (µg/L)	Step 4 scenarios: Pome fruit (apples), 20 m buffer zone			
	R3: Bologna, stream		R4: Roujan, stream	
	Actual	TWA	Actual	TWA
0d	1.061	-	0.750	-
1d	0.001	0.341	0.000	0.130
2d	0.000	0.171	0.000	0.065
4d	0.000	0.086	0.000	0.033
7d	0.000	0.049	0.000	0.019
14d	0.000	0.025	0.000	0.009
21d	0.000	0.017	0.000	0.006
28d	0.000	0.013	0.000	0.005
42d	0.000	0.009	0.000	0.003
50d	0.000	0.007	0.000	0.003
100d	0.000	0.004	0.004	0.002

Step 4 scenarios, Hexythiazox:

PEC_{sw} (µg/L)	Step 4 scenarios: Citrus, 15 m buffer zone			
	D6: Thiva, ditch**		R4: Roujan, stream**	
	Actual	TWA	Actual	TWA
0d	0.445	-	0.390	-
1d	0.401	0.422	0.000	0.063
2d	0.362	0.401	0.000	0.032
4d	0.283	0.363	0.000	0.016
7d	0.145	0.298	0.000	0.009
14d	0.033	0.184	0.000	0.005
21d	0.019	0.131	0.000	0.003
28d	0.014	0.102	0.000	0.002
42d	0.000	0.069	0.000	0.002
50d	0.001	0.058	0.000	0.001
100d	0.001	0.030	0.000	0.001

*based on 77th percentile spray drift values
**based on 90th percentile spray drift values

Metabolites

Metabolite **PT-1-2** Parameters used in $FOCUS_{sw}$ step 2	Molecular weight (g/mol): 270.74 Water solubility (mg/L): 28.9 K_{oc} (L/kg): 426 DT_{50} soil (d): 54.26 days DT_{50} in sediment/water system, in water and in sediment (d): 1000 days (FOCUS default worst case) Maximum occurrence observed: In water/sediment 32.2 %, in soil 39.5 %
Metabolite **PT-1-3** Parameters used in $FOCUS_{sw}$ step 2	Molecular weight (g/mol): 227.71 Water solubility (mg/L): 28.8 K_{oc} (L/kg): 493 DT_{50} soil (d): 28.08 days DT_{50} in sediment/water system, in water and in sediment (d): 1000 days (FOCUS default worst case) Maximum occurrence observed: In water/sediment 4.5 %, in soil 9.2 %

Metabolite **PT-1-9** Parameters used in $FOCUS_{sw}$ step 2	Molecular weight (g/mol): 366.86 Water solubility (mg/L): 7.9 K_{oc} (L/kg): 652 DT_{50} soil (d): 11.66 days DT_{50} in sediment/water system, in water and in sediment (d): 1000 days (FOCUS default worst case) Maximum occurrence observed: In water/sediment 12.7 %, in soil 21.1 %

Step 2 scenarios, degradation products:

Initial PEC_{sw} (µg/L)	Apples (1 × 0.10 kg ai/ha)	Grapes* (2 × 0.08 kg ai/ha)	Citrus** (3 × 0.08 kg ai/ha)
PT-1-9	1.552	0.686	1.074
PT-1-2	3.209	1.885	2.809
PT-1-3	0.456	0.282	0.351

*based on 82nd percentile spray drift values
**based on 77th percentile spray drift values

PEC (sediment)

Method of calculation	Stepwise approach based on recommendations given in SANCO/4802/2001-rev.2. by the FOCUS Surface Water Scenarios Working Group
Application rate	1 x 0.10 kg ai/ha in apples 2 x 0.08 kg ai/ha in grapes 3 x 0.08 kg ai/ha in citrus Interval between applications: 30 days

Step 2 scenarios, Hexythiazox:
(only initial PEC_{sed} values used in risk assessment are included; full results are available in AR)

PEC_{sed} (µg/kg)	Apples (1 x 0.10 kg ai/ha)		Grapes*) (2 x 0.08 kg ai/ha)		Citrus**) (3 x 0.08 kg ai/ha)	
	Actual	TWA	Actual	TWA	Actual	TWA
0d	117.170	---	55.995	---	89.897	---

*based on 82nd percentile spray drift values
**based on 77th percentile spray drift values

Step 2 scenarios, degradation products:

Initial PEC_{sed} (µg/kg)	Apples (1 x 0.10 kg ai/ha)	Grapes*) (2 x 0.08 kg ai/ha)	Citrus**) (3 x 0.08 kg ai/ha)
PT-1-9	9.288	4.430	6.267
PT-1-2	12.766	7.902	11.152
PT-1-3	2.117	1.373	1.615

*based on 82nd percentile spray drift values
**based on 77th percentile spray drift values

Step 3 scenarios, Hexythiazox:
(only initial PEC_{sed} values used in risk assessment are included; full results are available in AR)

PEC_{sed} (µg/kg)	Step 3 scenarios: Pome fruit (apples)				
	D4: ditch	D4: pond	D4: stream	D5: pond	D5: stream
0d	5.388	4.388	0.354	4.399	0.199

PEC_{sed} (µg/kg)	Step 3 scenarios: Pome fruit (apples)				
	R1: pond	R1: stream	R2: stream	R3: stream	R4: stream
0d	4.078	0.805	0.559	2.102	0.810

PEC_{sed} (µg/kg)	Step 3 scenarios: Grapes*)					
	D6: ditch	R1: pond	R1: stream	R2: stream	R3: stream	R4: stream
0d	0.284	0.234	0.173	0.417	0.196	0.659

*based on 82nd percentile spray drift values

PEC_{sed} (µg/kg)	Step 3 scenarios: Citrus	
	D6: ditch	R4: stream
0d	8.915*)	0.550**)

*based on 90th percentile spray drift values
**based on 77th percentile spray drift values

PEC (ground water) (Annex IIIA, point 9.2.1)

Hexythiazox Method of calculation and type of study (*e.g.* modelling, field leaching, lysimeter)	Modeling using FOCUS model(s), with appropriate FOCUS gw scenarios, according to FOCUS guidance. Models used: FOCUS PELMO 3.3.2 and FOCUS PEARL 3.3.3. pesticide leaching models Scenarios for crops (list of names): For Apples: Châteaudun, Hamburg, Jokioinen, Kremsmünster, Okehampton, Piacenza, Porto, Sevilla, Thiva. For Grapes: Châteaudun, Hamburg, Kremsmünster, Piacenza, Porto, Sevilla, Thiva. For Citrus: Piacenza, Porto, Sevilla, Thiva. Degradation: DT_{50} 23.71 days (geomean for 5 soils in laboratory, normalisation to 10 kPa/ pF2 and 20 °C with Q10 of 2.58 and Walker equation coefficient of 0.7) K_{oc}: 10461, $^1/_n$= 0.9745 (mean of 4 European soils).

Application rate	No. of applications and application rates: 1 × 0.10 kg ai/ha in apples 2 × 0.08 kg ai/ha in grapes 3 × 0.08 kg ai/ha in citrus Time of application: Early application at time of leaf emergence Crop interception: 50 % for apples, 40 % for grapes, 70 % for citrus
PT-1-2	Degradation: DT_{50} 54.26 days (geomean degradation rate in 5 soils in laboratory, normalisation to 10 kPa/ pF2 and 20 °C with Q10 of 2.58 and Walker equation coefficient of 0.7). K_{oc}: 426, mean of 3 soils, $^1/_n$= 0.904. Formation fraction: 0.42 (from Hexythiazox) and 1.0 (from PT-1-9)
PT-1-3	Degradation: DT_{50} 28.08 days (geomean degradation rate in 5 soils in laboratory, normalisation to 10 kPa/ pF2 and 20 °C with Q10 of 2.58 and Walker equation coefficient of 0.7). K_{oc}: 493, mean of 3 soils, $^1/_n$= 0.882. Formation fraction: 1.0 (from PT-1-2)
PT-1-9	Degradation: DT_{50} 11.66 days (geomean degradation rate in 4 soils in laboratory, normalisation to 10 kPa/ pF2 and 20 °C with Q10 of 2.58 and Walker equation coefficient of 0.7). K_{oc}: 652, mean of 3 soils, $^1/_n$= 0.880. Formation fraction: 0.58 (from Hexythiazox)

PEC(gw) - FOCUS modelling results (80th percentile annual average concentration at 1m)

Maximum concentration	Not relevant
Average annual concentration	80th percentile annual average concentration for both FOCUS models and for all scenarios Hexythiazox: < 0.001 µg/L PT-1-9: < 0.001 µg/L PT-1-2: < 0.001 µg/L PT-1-3: < 0.001 µg/L

Fate and behaviour in air (Annex IIA, point 7.2.2, Annex III, point 9.3)

Direct photolysis in air	Not studied - no data requested
Quantum yield of direct phototransformation	No adsorption > 290 nm
Photochemical oxidative degradation in air	DT_{50} of 3.62 hours derived by the Atkinson method of calculation

Volatilisation	From plant surfaces (BBA guideline): negligible
	From soil surfaces (BBA guideline): negligible

PEC (air)

The volatility of Hexythiazox is negligible. Moreover, its reactivity with OH radicals in the troposphere is predicted to be extremely rapid. Thus it is concluded that it is unlikely that significant residues will occur in the air.

Residues requiring further assessment

Environmental occurring metabolites requiring further assessment by other disciplines (toxicology and ecotoxicology) or for which a groundwater exposure assessment is triggered.	Soil: Hexythiazox, PT-1-2, PT-1-3 and PT-1-9 Surface Water: Hexythiazox, PT-1-2, PT-1-3 and PT-1-9 Sediment: Hexythiazox, PT-1-2, PT-1-3 and PT-1-9 Groundwater: Hexythiazox, PT-1-2, PT-1-3 and PT-1-9 Air: Hexythiazox

Monitoring data, if available (Annex IIA, point 7.4)

Soil	No data provided - none requested
Surface water	No data provided - none requested
Ground water	No data provided - none requested
Air	No data provided - none requested

Points pertinent to the classification and proposed labelling with regard to fate and behaviour data

Not readily biodegradable (candidate for R53).

Effects on Non-target Species

Effects on terrestrial vertebrates (Annex IIA, point 8.1, Annex IIIA, points 10.1 and 10.3)

Species	Test substance	Time scale	Endpoint (mg/kg bw/d)	Endpoint (mg/kg feed)
Birds				
Mallard duck	Hexythiazox	Acute	>2000 mg/kg bw	
Mallard duck	Hexythiazox	Short-term	>523 mg/kg bw/d	
Bobwhite quail	Hexythiazox	Long-term	100 mg/kg bw/d	
Mammals				
Rat, mouse, dog	Hexythiazox	Acute	> 5000 mg/kg bw	
Rat	Hexythiazox	Long-term	23.5 mg/kg bw/d	
Additional higher tier studies: None				

Toxicity/exposure ratios for terrestrial vertebrates (Annex IIIA, points 10.1 and 10.3)

Apple, application rate 0.1 kg ai/ha. Represent worst case and covers also grapes and citrus.

Indicator species/Category[2]	Time scale	ETE (mg/kg bw/d)	TER[1]	Annex VI Trigger[3]
Tier 1 (Birds)				
Insectivorous bird	Acute	5.41	> 370	10
Insectivorous bird	Short-term	3.02	> 173	10
Insectivorous bird	Long-term	3.02	33.2	5

Apple 0.1 kg ai/ha, Grape 2 × 0.08 kg ai/ha, Citrus 3 × 0.08 kg ai/ha.

Tier 1 (Mammals)				
Small herbivorous mammal	Acute	11.8 (Apple) 11.3 (Grapes) 12.3 (Citrus)	> 424 > 441 > 407	10
Small herbivorous mammal	Long-term	3.4 (Apple) 3.0 (Grapes) 3.5 3.8 (Citrus)	6.9 7.8 6.2	5

[1] Risk assessment according to SANCO/4145/2000

Apple 1 × 0.1 kg ai/ha, Grape 2 × 0.08 kg ai/ha, Citrus 3 × 0.08 kg ai/ha.

Crop	Indicator species	Time scale	Defined daily dose (mg/kg bw)	TER[1]	Annex VI Trigger
Screening step (Birds)					
Apples	Small insectiv. bird	Acute	4.7	715	10
Grapes	Small omniv. bird	Acute	9.1	366	10
Citrus	Small insectiv. bird	Acute	6.0	559	10
Apples	Small insectiv. bird	Long-term	1.8	55	5
Grapes	Small omniv. bird	Long-term	4.4	23	5
Citrus	Small insectiv. bird	Long-term	2.2	46	5
Screening step (Mammals)					
Apples	Small herbivorous mammal	Acute	13.6	367	10
Grapes			13.1	382	10
Citrus			17.5	286	10
Apples	Small herbivorous mammal	Long-term	7.2	0.75	5
Grapes			8.1	0.67	5
Citrus			8.7	0.62	5
Tier 1 Step (Mammals)					
Apples	Generic focal species: Dormouse, Shrew, Vole, Lagomorph, Mouse	Long-term	0.03-3.13	≥ 7.8	5
Grapes			0.03-2.82	≥ 8.6	5
Citrus			0.03-3.51	≥ 6.9	5

[1] Risk assessment according to Guidance document "PPR panel opinion on the science behind the guidance document on risk assessment for birds and mammals (The EFSA Journal (2008) 734:1-181)"

Drinking water exposure for terrestrial vertebrates (Annex IIIA, points 10.1 and 10.3)

Crop	Application rate [g ai/L]	DWR [L ai/d]	PEC puddle [g ai/L]	Daily dose [mg ai/kg bw]	LD_{50} [mg ai/kg bw]	TER[1]
Birds						
Acute						
Apples	0.067	0.003	0.013	3.9	> 2000	> 513
Grapes	0.08		0.016	4.8		> 417
Citrus	0.02		0.004	1.2		> 1667
Short-term						
Apples	0.067	0.003	0.013	3.9	> 523	> 134
Grapes	0.08		0.016	4.8		> 109
Citrus	0.02		0.004	1.2		> 436
Long-term						
Apples	0.067	0.003	0.013	3.9	100	26
Grapes	0.08		0.016	4.8		21
Citrus	0.02		0.004	1.2		83
Mammals						
Acute						
Apples	0.067	0.004	0.013	2.08	> 5000	> 2404
Grapes	0.08		0.016	2.56		> 1953
Citrus	0.02		0.004	0.64		> 7813
Long-term						
Apples	0.067	0.004	0.013	2.08	23.5	11.30
Grapes	0.08		0.016	2.56		9.18
Citrus	0.02		0.004	0.64		36.72

[1] Risk assessment according to SANCO/4145/2000

Crop	Application rate [g ai/ha]	PEC puddle [mg ai/L]	Daily dose [mg ai/kg bw]	LD_{50} / NOAEL [mg ai/kg bw]	TER[2]
Birds					
Acute					
Apples	100	1.74	0.801	3347	4181
Grapes	112*	1.95	0.897		3733
Citrus	120*	2.09	0.961		3484
Reproduction					
Apples	100	1.74	0.801	100	125
Grapes	112*	1.95	0.897		112
Citrus	120*	2.09	0.961		104
Mammals					
Acute					
Apples	100	1.74	0.418	5000	11970
Grapes	112*	1.95	0.468		10687
Citrus	120*	2.09	0.501		9975
Reproduction					
Apples	100	1.74	0.418	5.4	12.9
Grapes	112*	1.95	0.468		11.5
Citrus	120*	2.09	0.501		10.8

[2] Risk assessment according to Guidance document "PPR panel opinion on the science behind the guidance document on risk assessment for birds and mammals (The EFSA Journal (2008) 734:1-181)"

* application rate multiplied by mean MAF

Food chain exposure for terrestrial vertebrates (Annex IIIA, points 10.1 and 10.3)

Food chain from earthworm to earthworm-eating birds and mammals

	BCF_{WORM}	PEC_{SOIL} [mg ai/kg]	PEC_{WORM} [mg ai/kg]	Daily dose [mg/kg bw]	TER[1]
Birds	0.097	0.0952	0.0092	0.0102	9804
Mammals	0.097	0.0952	0.0092	0.0129	1822

Food chain from fish to fish-eating birds and mammals

	BCF_{FISH}	PEC_{SW} [µg ai/L]	PEC_{FISH} [mg ai/kg]	Daily dose [mg/kg bw]	TER[1]
Birds	1600	1.480	2.368	0.497	201
Mammals	1600	1.480	2.368	0.308	76

[1] Risk assessment according to SANCO/4145/2000

Food chain from earthworm to earthworm-eating birds and mammals

Crop	BCF_{WORM}	PEC_{SOIL} [mg ai/kg]	PEC_{WORM} [mg ai/kg]	Exposure [mg/kg bw]	TER[2]
Birds					
Apples	0.115	0.0667	0.0077	0.0080	12443
Grapes	0.115	0.1081	0.0124	0.0130	7678
Citrus	0.115	0.0693	0.008	0.0083	11976
Mammals					
Apples	0.115	0.0667	0.0077	0.0098	551
Grapes	0.115	0.1081	0.0124	0.016	340
Citrus	0.115	0.0693	0.008	0.0102	531

Food chain from fish to fish-eating birds and mammals

	BCF_{FISH}	PEC_{SW} [µg ai/L]	PEC_{FISH} [mg ai/kg]	Exposure [mg/kg bw]	TER[2]
Birds	1600	1.480	2.368	0.485	206
Mammals	1600	1.480	2.368	0.324	17

[2] Risk assessment according to Guidance document "PPR panel opinion on the science behind the guidance document on risk assessment for birds and mammals (The EFSA Journal (2008) 734:1-181)"

Toxicity data for aquatic species (most sensitive species of each group) (Annex IIA, point 8.2, Annex IIIA, point 10.2)

Group	Test substance	Time-scale (Test type)	Endpoint	Toxicity[1] (mg ai/L)
Laboratory tests				
Fish				
Lepomis macrochirus	Hexythiazox	96 hr (static)	Mortality, LC_{50}	3.2 mg/L ($_{mm}$)
Oncorhynchus mykiss	Hexythiazox	28 d (semi-static)	Growth, NOEC	0.04 mg/L ($_{mm}$)
Oncorhynchus mykiss	Metabolite **PT-1-2**	96 hr (static)	Mortality, LC_{50}	1.46 mg/L ($_{mm}$)
Oncorhynchus mykiss	Metabolite **PT-1-9**	96 hr (static)	Mortality, LC_{50}	1.22-2.41 mg/L ($_{mm}$)
Aquatic invertebrate				
Daphnia magna	Hexythiazox	48 h (static)	Mortality, EC_{50}	~~> 0.47~~ 0.36 mg/L ($_{mm}$)
Daphnia magna	Hexythiazox	21 d (flow-through)	Reproduction and mortality, NOEC	0.0061 mg/L ($_{mm}$)
Daphnia magna	Metabolite **PT-1-2**	48 h (static)	Mortality, EC_{50}	14 mg/L ($_{mm}$)
Daphnia magna	Metabolite **PT-1-3**	48 h (static)	Mortality, EC_{50}	13.6 mg/L ($_{nom}$)
Daphnia magna	Metabolite **PT-1-9**	48 h (static)	Mortality, EC_{50}	4.2 mg/L ($_{mm}$)
Sediment dwelling organisms				
Chironomus riparius	Hexythiazox	21 d (static)	Emergence, NOEC	1.7 mg/L ($_{mm}$)
Algae				
Scenedesmus subspicatus	Hexythiazox	72 h (static)	Biomass: E_bC_{50} Growth rate: E_rC_{50}	> 0.4 mg/L ($_{mm}$) > 0.4 mg/L ($_{mm}$)
Pseudokirch subcapitata	Metabolite **PT-1-2**	72 h (static)	Biomass: E_bC_{50}	8.67 mg/L ($_{nom}$)
Pseudokirch subcapitata	Metabolite **PT-1-9**	72 h (static)	Biomass: E_bC_{50}	11.9 mg/L ($_{mm}$)
Higher plant: not required				
Microcosm or mesocosm tests: not required				

Based on nominal ($_{nom}$) or mean measured concentrations ($_{mm}$).

Toxicity/exposure ratios for the most sensitive aquatic organisms (Annex IIIA, point 10.2)

FOCUS Step 2

Apples, 1 × 0.1 kg ai/ha, leaf emergence as growth stage

Test substance	N/S[1]	Organism	Toxicity endpoint (mg/L)	Time scale	PEC[2]	TER	Annex VI Trigger[3]
Hexythiazox	S	Fish	3.2	Acute	9.732 (max)	329	100
Hexythiazox	S	Fish	0.04	Chronic	$9.732_{(max)}$	**4.11**	10
Hexythiazox	S	Aquatic invertebrates	0.36	Acute	9.732 (max)	**37**	100
Hexythiazox	S	Aquatic invertebrates	0.0061	Chronic	$9.732_{(max)}$	**0.63**	10
Hexythiazox	S	Algae	>0.4	Chronic	9.732 (max)	>41	10
Hexythiazox	S	Sediment-dwelling organisms[4]	1.7	Chronic	9.732 (max) (PEC_{sw})	175	10
PT-1-2	S	Fish	1.46	Acute	$3.209_{(max)}$	455	100
PT-1-2	S	Aquatic invertebrate	14	Acute	$3.209_{(max)}$	4363	100
PT-1-2	S	Algae	8.67	Acute	$3.209_{(max)}$	2702	100
PT-1-3	S	Aquatic invertebrate	13.6	Acute	$0.456_{(max)}$	29825	100
PT-1-9	S	Fish	1.22	Acute	$1.552_{(max)}$	786	100
PT-1-9	S	Aquatic invertebrate	4.2	Acute	$1.552_{(max)}$	2706	100
PT-1-9	S	Algae	11.9	Acute	$1.552_{(max)}$	7668	100

Grapes, 2 × 0.08 kg ai/ha, leaf emergence as growth stage

Test substance	N/S[1]	Organism	Toxicity endpoint (mg/L)	Time scale	PEC[2]	TER	Annex VI Trigger[3]
Hexythiazox	S	Fish	3.2	Acute	$0.726_{(max)}$	4406	100
Hexythiazox	S	Fish	0.04	Chronic	$0.726_{(max)}$	55	10
Hexythiazox	S	Aquatic invertebrates	0.36	Acute	$0.726_{(max)}$	496	100
Hexythiazox	S	Aquatic invertebrates	0.0061	Chronic	$0.726_{(max)}$	**8.40**	10
Hexythiazox	S	Algae	>0.4	Chronic	$0.726_{(max)}$	>551	10
Hexythiazox	S	Sediment-dwelling organisms[4]	1.7	Chronic	$0.726_{(max)}$ (PEC_{sw})	2341	10
PT-1-2	S	Fish	1.46	Acute	$1.885_{(max)}$	775	100
PT-1-2	S	Aquatic invertebrate	14	Acute	$1.885_{(max)}$	7427	100
PT-1-2	S	Algae	8.67	Acute	$1.885_{(max)}$	4599	100
PT-1-3	S	Aquatic invertebrate	13.6	Acute	$0.282_{(max)}$	48227	100
PT-1-9	S	Fish	1.22	Acute	$0.686_{(max)}$	1778	100
PT-1-9	S	Aquatic invertebrate	4.2	Acute	$0.686_{(max)}$	6122	100
PT-1-9	S	Algae	11.9	Acute	$0.686_{(max)}$	17347	100

Citrus, 3 × 0.08 kg ai/ha, Growth stages: BBCH 69, BBCH 74 and 14 days before harvest.

Test substance	N/S[1]	Organism	Toxicity endpoint (mg/L)	Time scale	PEC[2]	TER	Annex VI Trigger[3]
Hexythiazox	S	Fish	3.2	Acute	$4.193_{(max)}$	763	100
Hexythiazox	S	Fish	0.04	Chronic	$4.193_{(max)}$	**9.54**	10
Hexythiazox	S	Aquatic invertebrates	0.36	Acute	$4.193_{(max)}$	**86**	100
Hexythiazox	S	Aquatic invertebrates	0.0061	Chronic	$4.193_{(max)}$	**1.45**	10
Hexythiazox	S	Algae	>0.4	Chronic	$4.193_{(max)}$	>95	10
Hexythiazox	S	Sediment-dwelling organisms[4]	1.7	Chronic	$4.193_{(max)}$	405	10
PT-1-2	S	Fish	1.46	Acute	$2.806_{(max)}$	520	100
PT-1-2	S	Aquatic invertebrate	14	Acute	$2.806_{(max)}$	4989	100
PT-1-2	S	Algae	8.67	Acute	$2.806_{(max)}$	3090	100
PT-1-3	S	Aquatic invertebrate	13.6	Acute	$0.351_{(max)}$	38746	100
PT-1-9	S	Fish	1.22	Acute	$1.074_{(max)}$	1136	100
PT-1-9	S	Aquatic invertebrate	4.2	Acute	$1.074_{(max)}$	3911	100
PT-1-9	S	Algae	11.9	Acute	$1.074_{(max)}$	11080	100

[1] Northern (N) or Southern (S)

Note: TER values in bold indicate unacceptable risk

Refined aquatic risk assessment using higher tier FOCUS modelling.

FOCUS Step 3

Apples, 1 × 0.1 kg ai/ha

Test substance	Scenario[1]	Water body type[2]	Test organism[3]	Time scale	Toxicity endpoint (mg/L)	PEC[4]	TER	Annex VI trigger
Hexythiazox	D3	Ditch	Aquatic invert.	Acute	0.36	$7.689_{(max)}$	**47**	100
Hexythiazox	D4	Pond	Aquatic invert.	Acute	0.36	$0.467_{(max)}$	711	100
Hexythiazox	D4	Stream	Aquatic invert.	Acute	0.36	$7.480_{(max)}$	**48**	100
Hexythiazox	D5	Pond	Aquatic invert.	Acute	0.36	$0.467_{(max)}$	771	100
Hexythiazox	D5	Stream	Aquatic invert.	Acute	0.36	$7.455_{(max)}$	**48**	100
Hexythiazox	R1	Pond	Aquatic invert.	Acute	0.36	$0.467_{(max)}$	771	100
Hexythiazox	R1	Stream	Aquatic invert.	Acute	0.36	$6.221_{(max)}$	**58**	100
Hexythiazox	R2	Stream	Aquatic invert.	Acute	0.36	$8.242_{(max)}$	**44**	100
Hexythiazox	R3	Stream	Aquatic invert.	Acute	0.36	$8.803_{(max)}$	**41**	100
Hexythiazox	R4	Stream	Aquatic invert.	Acute	0.36	$6.223_{(max)}$	**58**	100

[1] drainage (D1-D6) and run-off (R1-R4)
[2] ditch/stream/pond
[3] only critical groups failed at Step 2 are included.
[4] initial maximum value

Apples, 1 × 0.1 kg ai/ha

Test substance	Scenario[1]	Water body type[2]	Test organism[3]	Time scale	Toxicity endpoint (mg/L)	PEC[4]	TER	Annex VI trigger
Hexythiazox	D3	Ditch	Aquatic invert.	Chronic	0.0061	$7.689_{(max)}$	**0.79**	10
Hexythiazox	D4	Pond	Aquatic invert.	Chronic	0.0061	$0.467_{(max)}$	13	10
Hexythiazox	D4	Stream	Aquatic invert.	Chronic	0.0061	$7.480_{(max)}$	**0.82**	10
Hexythiazox	D5	Pond	Aquatic invert.	Chronic	0.0061	$0.467_{(max)}$	13	10
Hexythiazox	D5	Stream	Aquatic invert.	Chronic	0.0061	$7.455_{(max)}$	**0.82**	10
Hexythiazox	R1	Pond	Aquatic invert.	Chronic	0.0061	$0.467_{(max)}$	13	10
Hexythiazox	R1	Stream	Aquatic invert.	Chronic	0.0061	$6.221_{(max)}$	**0.98**	10
Hexythiazox	R2	Stream	Aquatic invert.	Chronic	0.0061	$8.242_{(max)}$	**0.74**	10
Hexythiazox	R3	Stream	Aquatic invert.	Chronic	0.0061	$8.803_{(max)}$	**0.69**	10
Hexythiazox	R4	Stream	Aquatic invert.	Chronic	0.0061	$6.223_{(max)}$	**0.98**	10
Hexythiazox	D3	Ditch	Fish	Chronic	0.04	$7.689_{(max)}$	**5.20**	10
Hexythiazox	D4	Pond	Fish	Chronic	0.04	$0.467_{(max)}$	86	10
Hexythiazox	D4	Stream	Fish	Chronic	0.04	$7.480_{(max)}$	**5.35**	10
Hexythiazox	D5	Pond	Fish	Chronic	0.04	$0.467_{(max)}$	86	10
Hexythiazox	D5	Stream	Fish	Chronic	0.04	$7.455_{(max)}$	**5.37**	10
Hexythiazox	R1	Pond	Fish	Chronic	0.04	$0.467_{(max)}$	86	10
Hexythiazox	R1	Stream	Fish	Chronic	0.04	$6.221_{(max)}$	**6.43**	10
Hexythiazox	R2	Stream	Fish	Chronic	0.04	$8.242_{(max)}$	**4.85**	10
Hexythiazox	R3	Stream	Fish	Chronic	0.04	$8.803_{(max)}$	**4.54**	10
Hexythiazox	R4	Stream	Fish	Chronic	0.04	$6.223_{(max)}$	**6.43**	10

Grapes, 2 × 0.08 kg ai/ha

Test substance	Scenario[1]	Water body type	Test organism[2]	Time scale	Toxicity endpoint (mg/L)	PEC[3] (µg/L)	TER	Annex VI trigger
Hexythiazox	D6	Ditch	Aquatic invert.	Chronic	0.0061	$0.441_{(max)}$	14	10
Hexythiazox	R1	Pond	Aquatic invert.	Chronic	0.0061	$0.018_{(max)}$	339	10
Hexythiazox	R1	Stream	Aquatic invert.	Chronic	0.0061	$0.326_{(max)}$	19	10
Hexythiazox	R2	Stream	Aquatic invert.	Chronic	0.0061	$0.433_{(max)}$	14	10
Hexythiazox	R3	Stream	Aquatic invert.	Chronic	0.0061	$0.462_{(max)}$	13	10
Hexythiazox	R4	Stream	Aquatic invert.	Chronic	0.0061	$0.326_{(max)}$	19	10

Citrus, 3 × 0.08 kg ai/ha

Test substance	Scenario[1]	Water body type	Test organism[2]	Time scale	Toxicity endpoint (mg/L)	PEC[3] (µg/L)	TER	Annex VI trigger
Hexythiazox	D6	Ditch	Aquatic invert.	Acute	0.36	$2.927_{(max)}$	123	100
Hexythiazox	R4	Stream	Aquatic invert.	Acute	0.36	$2.213_{(max)}$	163	100
Hexythiazox	D6	Ditch	Aquatic invert.	Chronic	0.0061	$2.927_{(max)}$	**2.08**	10
Hexythiazox	R4	Stream	Aquatic invert.	Chronic	0.0061	$2.213_{(max)}$	**2.76**	10
Hexythiazox	D6	Ditch	Fish	Chronic	0.04	$2.927_{(max)}$	14	10
Hexythiazox	R4	Stream	Fish	Chronic	0.04	$2.213_{(max)}$	18	10

[1] drainage (D1-D6) and run-off (R1-R4)
[2] only critical groups failed at Step 2 are included.
[3] initial maximum value
Note: TER values in bold indicate unacceptable risk

FOCUS Step 4

Apples, 1 × 0.1 kg ai/ha

Scenario[1]	Water body type	Test organism[2]	Time scale	Toxicity endpoint (mg/L)	Buffer zone distance (m)	PEC[3] (µg/L)	TER	Annex VI trigger
D3	Ditch	Aquatic invert.	Acute	0.36	20	$0.848_{(max)}$	425	100
D4	Stream	Aquatic invert.	Acute	0.36	20	$0.902_{(max)}$	399	100
D5	Stream	Aquatic invert.	Acute	0.36	20	$0.899_{(max)}$	400	100
R1	Stream	Aquatic invert.	Acute	0.36	20	$0.750_{(max)}$	480	100
R2	Stream	Aquatic invert.	Acute	0.36	20	$0.994_{(max)}$	362	100
R3	Stream	Aquatic invert.	Acute	0.36	20	$1.061_{(max)}$	339	100
R4	Stream	Aquatic invert.	Acute	0.36	20	$0.750_{(max)}$	480	100
D3	Ditch	Aquatic invert.	Chronic	0.0061	20	$0.848_{(max)}$	**7.19**	10
D4	Stream	Aquatic invert.	Chronic	0.0061	20	$0.902_{(max)}$	**6.76**	10
D5	Stream	Aquatic invert.	Chronic	0.0061	20	$0.899_{(max)}$	**6.79**	10
R1	Stream	Aquatic invert.	Chronic	0.0061	20	$0.750_{(max)}$	**8.13**	10
R2	Stream	Aquatic invert.	Chronic	0.0061	20	$0.994_{(max)}$	**6.14**	10
R3	Stream	Aquatic invert.	Chronic	0.0061	20	$1.061_{(max)}$	**5.75**	10
R4	Stream	Aquatic invert.	Chronic	0.0061	20	$0.750_{(max)}$	**8.13**	10
D3	Ditch	Fish	Chronic	0.04	20	$0.848_{(max)}$	47	10
D4	Stream	Fish	Chronic	0.04	20	$0.902_{(max)}$	44	10
D5	Stream	Fish	Chronic	0.04	20	$0.899_{(max)}$	44	10
R1	Stream	Fish	Chronic	0.04	20	$0.750_{(max)}$	53	10
R2	Stream	Fish	Chronic	0.04	20	$0.994_{(max)}$	40	10
R3	Stream	Fish	Chronic	0.04	20	$1.061_{(max)}$	38	10
R4	Stream	Fish	Chronic	0.04	20	$0.750_{(max)}$	53	10

Citrus, 3 × 0.08 kg ai/ha

Scenario[1]	Water body type	Test organism[2]	Time scale	Toxicity endpoint (mg/L)	Buffer zone distance (m)	PEC[3] (µg/L)	TER	Annex VI trigger
D6	Ditch	Aquatic invert.	Chronic	0.0061	15	$0.445_{(max)}$	14	10
R4	Stream	Aquatic invert.	Chronic	0.0061	15	$0.390_{(max)}$	16	10

[1] drainage (D1-D6) and run-off (R1-R4)
[2] only critical groups failed at Step 3 are included.
[3] initial maximum (max) or 21 d time weighed average (twa) value
Note: TER values in bold indicate unacceptable risk

Bioconcentration

	Hexythiazox
logPow	
Bioconcentration factor (BCF)*	1100 (lower exposure conc.), 850 (higher exposure conc.) Mean BCF 975
Annex VI Trigger for the bioconcentration factor	1000
Clearance time (days) (CT_{50})	< 1 day
(CT_{90})	< 14 days
Level and nature of residues (%) in organisms after the 14 day depuration phase	11 and 6 % ^{14}C-residues left at two concentrations. 2-23 % of total residues as Hexythiazox after 28 days.

* based on total ^{14}C determined from whole fish

Effects on honeybees (Annex IIA, point 8.3.1, Annex IIIA, point 10.4)

Test substance	Acute oral toxicity, LD_{50} (µg/bee)	Acute contact toxicity, LD_{50} (µg/bee)
Hexythiazox	> 112.2	> 200
Field or semi-field tests: Not required		

Hazard quotients for honey bees (Annex IIIA, point 10.4)

Test substance	Route	Hazard quotient	Annex VI Trigger
Apples, 1 × 0.1 kg ai/ha			
Hexythiazox	Contact	< 0.5	50
Hexythiazox	Oral	< 0.9	50

Test substance	Route	Hazard quotient	Annex VI Trigger
Grapes, 2 × 0.08 kg ai/ha			
Hexythiazox	Contact	< 0.4	50
Hexythiazox	Oral	< 0.7	50
Citrus, 3 × 0.08 kg ai/ha			
Hexythiazox	Contact	< 0.4	50
Hexythiazox	Oral	< 0.7	50

Effects on other arthropod species (Annex IIA, point 8.3.2, Annex IIIA, point 10.5)

Tier I laboratory tests with sensitive standard species

Species	Test Substance	Endpoint	Effect: (LR_{50}, Mortality %)
*Aphidius matricariae** (Parasitoid)	Ordoval (10.5 % WP formulation)	Mortality, reproduction	LR_{50} > 157.5 g as/ha (mortality 33.3 %), No effect on reproduction
Typhlodromus pyri (Predatory mite)	No Tier-1 data available. Tier-2 test provided.		

*Similar sensitivity of *A. matricariae* and *A. rhopalosiphi* has been shown in Tier-2 tests

Tier I risk assessment on *A. matricariae* based on HQ-method

Crop	LR_{50} [g ai/ha]	Drift value [%]	Application rate [g ai/ha]	MAF	HQ in-field	HQ off-field	Trigger
Apples	> 157.5 g	29.2	100	1	< 0.63	< 0.19	2
Grapes	> 157.5 g	7.23	80	1.3	< 0.66	< 0.05	2
Citrus	> 157.5 g	11.01	80	1.3	< 0.66	< 0.07	2

Further laboratory studies with other non-target arthropod species

Species	Life stage	Test substance, substrate and duration	Dose (g ai/ha)	Endpoint	% adverse effect	Trigger
Poecilus cupreus (Foliage dwelling predator)	Adult	BAS 9075 1 I (10.5 % WP formulation), quartz sand, 14 d	155 and 309	Mortality, food consumption	0 % (Mortality) No effect on feeding	50 %
Coccinella septempunctata (Foliage dwelling predator)	Adult	Ordoval (10.5 % WP formulation), glass plates, 14 d (mortality) + 21 d (reproduction)	157.5	Mortality, reproduction	0 % (Mortality) 43 % (No. of eggs) 45 % (No. of larvae) 3 % (Hatching)	50 %
Pardosa sp. (Ground dwelling predator)	Adult	BAS 9075 1 I (10.5 % WP formulation), quartz sand, 14 d	155 and 309	Mortality, food consumption	3.9 % (Mortality) No effect on feeding	50 %

Tier II extended laboratory studies

Species	Life stage	Test substance, substrate and duration	Dose (g ai/ha)	Endpoint	% adverse effect	Trigger
Typhlodromus pyri (Predatory mite)	Adult	Hexythiazox 10 WP (10.4 % WP formulation), bean leaves, 14 d	5, 12, 29, 74 and 184	Mortality, reproduction (No. of eggs)	Mortality ≤ 3 %, ≤ 2%* (day 7) and ≤ 17 % (day 14) Effects on reproduction ≤ 5.2 % (day 14). No dose response	50 %
Typhlodromus pyri (Predatory mite)	Juvenile	BAS 9075 1 I (10.3 % WP formulation), bean leaves, 7 d	0.8, 2.4, 7.3, 21.9 and 65.9	Mortality	Mortality ≤ 45 %, ≤ 36 %*	50 %
Aphidius rhopalosiphi (Parasitoid)	Adult	BAS 9075 1 I (10.3 % WP formulation), vine leaves, 2 d (mortality) + 9-10 d (reproduction)	100, 150, 200, 250 and 300	Mortality, reproduction (No. of parasitized aphid mummies)	Mortality ≤ 3 %* No adverse effects on reproduction	50 %

Species	Life stage	Test substance, substrate and duration	Dose (g ai/ha)	Endpoint	% adverse effect	Trigger
Aphidius matricariae (Parasitoid)	Adult	BAS 9075 1 I (10.3 % WP formulation), vine leaves, 2 d (mortality) + 9-10 d (reproduction)	150 and 300	Mortality, reproduction (No. of parasitized aphid mummies)	No mortality No adverse effects on reproduction	50 %
*Coccinella septempunctata*** (Foliage dwelling predator)	Larvae to adult	BAS 9075 1 I (10.3 % WP formulation), bean seedling, 15 days (mortality) + ≥ 38 days (reproduction)	65.9, 154.5 and 309	Mortality, reproduction (No. of fertile eggs / female / day)	Mortality ≤ 55 %, ≤ 35 %* Reduction in reproductive capacity 30, 5 and 56 % at the test doses	50 %
Orius majusculus (Foliage dwelling predator)	Nymph	Ordoval (10.5 % WP formulation), bean leaf, 15 days (mortality) + 43 days (reproduction)	157.5	Mortality, reproduction (No. of eggs per female, hatching rate)	Mortality 27 %, 17 %* No adverse effects on reproduction	50 %

* Mortality corrected for control mortality
** The beetles used in the study were infected with a unicellular pathogen possibly reducing the fitness of test organisms

Semi-field and field tests

Species	Life stage	Test substance, substrate and duration	Dose (g ai/ha)	Endpoint	% adverse effect	Trigger
Aphidius matricariae (Parasitoid)	Adult	BAS 9075 1 I (10.5 % WP formulation), wheat seedlings under semi-field conditions in a tent of gauze, 15 d	157.5	Reproduction (No. of parasitized aphids) Mortality was not assessed	39 % reduction in reproductive capacity	50 %
Typhlodromus pyri (Predatory mite)	All stages	BAS 9075 1 I (WP formulation), efficacy field trial in grapes, 36 d	2 × 80	Mortality (reduction in number of living mites compared to initial value)	75 % (8 d after 1st application) 65 % (8 d after 2nd application) 50 % (28 d after 2nd application)	50 %

Effects on earthworms, other soil macro-organisms and soil micro-organisms (Annex IIA points 8.4 and 8.5. Annex IIIA, points, 10.6 and 10.7)

Test organism	Test substance	Time scale	Endpoint[1]
Earthworms[2]			
Eisenia foetida	BAS 9075 1 I (10.5% hexythiazox)	Acute 14 days	LC_{50} > 105 mg ai/kg dry soil LC_{50corr} > 52.5 mg ai/kg dry soil[1]
Eisenia foetida	Metabolite PT-1-2	Acute 14 days	LC_{50} > 1000 mg/kg dry soil LC_{50corr} > 500 mg ai/kg dry soil[1]
Eisenia foetida	Metabolite PT-1-3	Acute 14 days	LC_{50} > 62.5 mg/kg dry soil LC_{50corr} > 31.3 mg ai/kg dry soil[1]
Eisenia foetida	Metabolite PT-1-9	Acute 14 days	LC_{50} > 62.5 mg/kg dry soil LC_{50corr} > 31.3 mg ai/kg dry soil[1]
Eisenia foetida	Metabolite PT-1-2	Chronic 8 weeks	NOEC 15.6 mg/kg dry soil $NOEC_{corr}$ 7.8 mg ai/kg dry soil[1]
Eisenia foetida	Metabolite PT-1-3	Chronic 8 weeks	NOEC 62.5 mg/kg dry soil $NOEC_{corr}$ 31.3 mg ai/kg dry soil[1]
Eisenia foetida	Metabolite PT-1-9	Chronic 8 weeks	NOEC 62.5 mg/kg dry soil $NOEC_{corr}$ 31.3 mg ai/kg dry soil[1]
Other soil macro-organisms: Not required			
Soil micro-organisms			
Nitrogen mineralisation	Hexythiazox	28 days	-0.5 to +6 % effect at day 28 at 0.20, 0.40 and 1.07 mg ai/kg dw soil
Nitrogen mineralisation	WP formulation containing 10.5% hexythiazox	42 days	-3 to +28 % effect at day 28 at 0.17 and 1.7 mg ai/kg dw soil -5% to +16% effect at day 42 at 0.17 and 1.7 mg ai/kg dw soil
Nitrogen mineralisation	Metabolite PT-1-2	28 days	-0.5 to +6% effect at day 28 at 0.41 and 2.05 mg/kg dw soil
Nitrogen mineralisation	Metabolite PT-1-3	28 days	-0.1 to +14% effect at day 28 at 0.345 to 1.72 mg/kg dw soil
Nitrogen mineralisation	Metabolite PT-1-9	28 days	-2% effect at day 28 at 0.559 and 2.79 mg/kg dw soil

Carbon mineralisation	Hexythiazox	28 days	-4 to +0.1 % effect at day 28 at 0.20, 0.40 and 1.07 mg ai/kg dw soil
Carbon mineralisation	WP formulation containing 10.5% hexythiazox	14 days	- 6 to +15% effect at day 14 at 0.17 and 1.7 mg ai/kg dw soil
Carbon mineralisation	Metabolite PT-1-2	28 days	+0.8 to +2 % effect at day 28 at 0.41 and 2.05 mg/kg dw soil
Carbon mineralisation	Metabolite PT-1-3	28 days	-3 to 5% effect at day 28 at 0.345 and 1.72 mg/kg dw soil
Carbon mineralisation	Metabolite PT-1-9	28 days	+1 to +3 % effect at day 28 at 0.559 and 2.79 mg/kg dw soil
Field studies: Not required Litterbag study was performed with PT-1-2 using two applications of 41 and 72 g PT-1-2/ha at 15 days interval. The nominal cumulative PT-1-2 concentration in soil was 0.0755 mg/kg soil dw and the mean measured concentration after the second application was 0.099 mg/kg soil dw, which is 131 % of the nominal. After twelve months no significant differences were seen in the decomposition rates as the mass loss in the litterbags were 55.3 % in control and 60.9 % in the PT-1-2 treatment.			

[1] endpoint has been corrected due to log Pow >2.

Toxicity/exposure ratios for soil organisms

Test organism	Crop	Test substance	Time scale	Soil PEC[1] (mg/kg)	TER	Trigger
Earthworms						
Eisenia foetida	Apples	BAS 9075 1 I (10.5% hexythiazox)	Acute 14 days	0.0667	787	10
	Grape			0.1124	467	
	Citrus			0.0745	705	
Eisenia foetida	Apples	Metabolite PT-1-2	Acute 14 days	0.0203 0.0329*	>24631 >15198	10
	Grape			0.0375 0.0608*	> 13333 > 8224	
	Citrus			0.0270 0.0438*	> 18519 > 11416	
Eisenia foetida	Apples	Metabolite PT-1-3	Acute 14 days	0.0040	> 7825	10
	Grape			0.0064	> 4891	
	Citrus			0.0041	> 7634	
Eisenia foetida	Apples	Metabolite PT-1-9	Acute 14 days	0.0148	> 2115	10
	Grape			0.0225	> 1391	
	Citrus			0.0137	2285	

Eisenia foetida	Apples	Metabolite PT-1-2	Chronic 8 weeks	0.0203 0.0329*	384 237	5
	Grape			0.0375 0.0608*	208 128	
	Citrus			0.0270 0.0438*	289 178	
Eisenia foetida	Apples	Metabolite PT-1-3	Chronic 8 weeks	0.004	7825	5
	Grape			0.0064	4891	
	Citrus			0.0041	7634	
Eisenia foetida	Apples	Metabolite PT-1-9	Chronic 8 weeks	0.0148	2115	5
	Grape			0.0225	1391	
	Citrus			0.0137	2285	

* maximum plateau PEC soil value (the value is given as the DT_{90} exceeds 365 days)

Effects on non target plants (Annex IIA, point 8.6, Annex IIIA, point 10.8)

Vegetative vigour screening test data

Species	ER_{50} (g ai/ha) vegetative vigour	MAF	Drift value[1] (%)	Exposure (g ai/ha)	TER
Apples 1 × 0.10 kg ai/ha					
Cabbage *Brassica oleracea*	> 750 g ai/ha	1	29.2	29.2	> 26
Carrot *Daucus carota*					
Pea *Pisum sativum*					
Maize *Zea mays*					
Oats *Avena sativa*					
Onion *Allium cepa*					
Grapes 2 × 0.08 kg ai/ha					
Cabbage *Brassica oleracea*	> 750 g ai/ha	1.7	7.23	9.83	> 76
Carrot *Daucus carota*					
Pea *Pisum sativum*					
Maize *Zea mays*					
Oats *Avena sativa*					
Onion *Allium cepa*					

Citrus 3 × 0.08 kg ai/ha					
Cabbage *Brassica oleracea*	> 750 g ai/ha	2.3	11.01	20.26	> 37
Carrot *Daucus carota*					
Pea *Pisum sativum*					
Maize *Zea mays*					
Oats *Avena sativa*					
Onion *Allium cepa*					

[1] Drift value according to BBA (2000)

Effects on biological methods for sewage treatment (Annex IIA 8.7)

Test type/organism	O_2 consumption
Dose-response/*Pseudomonas putida* (1 – 100 mg ai/L)	-5 to +7 % inhibition compared to control
Limit test / Activated sludge (100 mg ai/L)	- 3.46 % effect in O_2 consumption compared to control

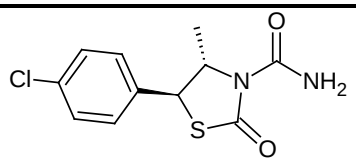
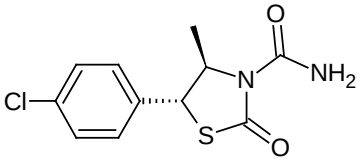
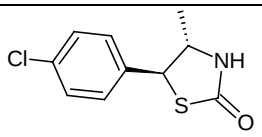
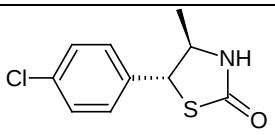
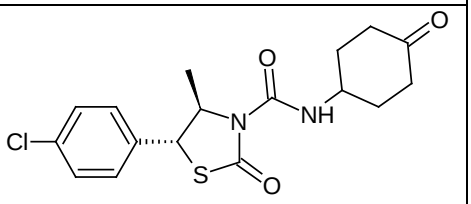
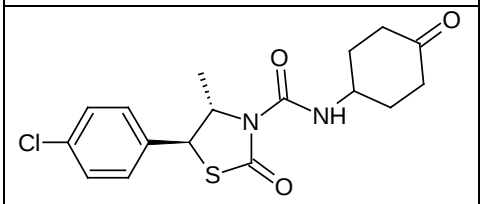
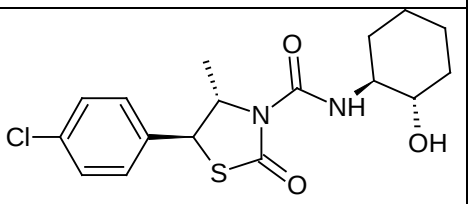
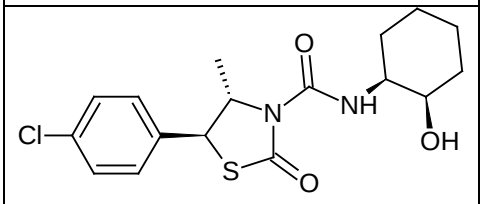
Ecotoxicologically relevant compounds (all parent and all relevant metabolites requiring further assessment from the fate section)

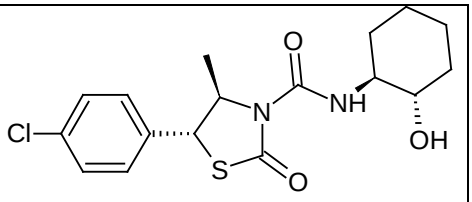
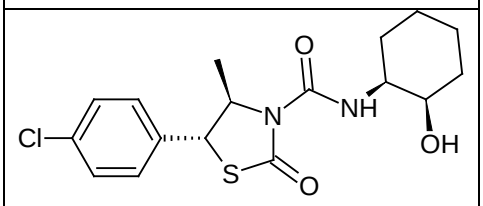
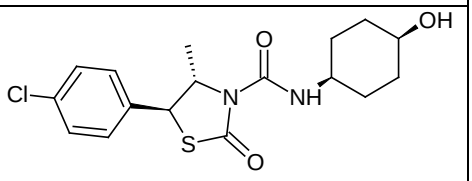
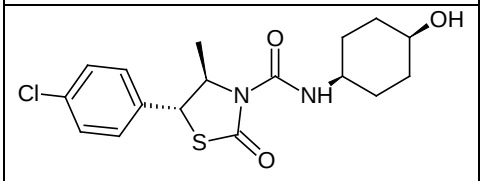
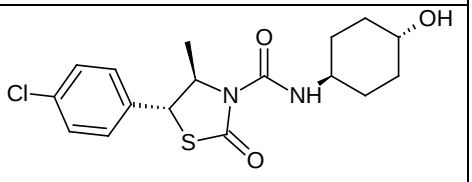
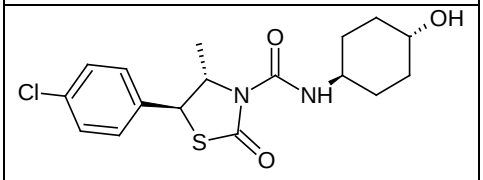
Compartment	
soil	Hexythiazox, PT-1-2, PT-1-3 and PT-1-9
water	Hexythiazox, PT-1-2, PT-1-3 and PT-1-9
sediment	Hexythiazox, PT-1-2, PT-1-3 and PT-1-9
groundwater	Hexythiazox, PT-1-2, PT-1-3 and PT-1-9
air	Hexythiazox

Classification and proposed labelling with regard to ecotoxicological data (Annex IIA, point 10 and Annex IIIA, point 12.3)

	RMS/peer review proposal
Hexythiazox	R50/53

APPENDIX B – USED COMPOUND CODE(S)

Code/Trivial name*	Chemical name**	Structural formula**
PT-1-2	(4*S*,5*S*)-5-(4-chlorophenyl)-4-methyl-2-oxo-1,3-thiazolidine-3-carboxamide	
	(4*R*,5*R*)-5-(4-chlorophenyl)-4-methyl-2-oxo-1,3-thiazolidine-3-carboxamide	
PT-1-3	(4*S*,5*S*)-5-(4-chlorophenyl)-4-methyl-1,3-thiazolidin-2-one	
	(4*R*,5*R*)-5-(4-chlorophenyl)-4-methyl-1,3-thiazolidin-2-one	
PT-1-9	(4*R*,5*R*)-5-(4-chlorophenyl)-4-methyl-2-oxo-*N*-(4-oxocyclohexyl)-1,3-thiazolidine-3-carboxamide	
	(4*S*,5*S*)-5-(4-chlorophenyl)-4-methyl-2-oxo-*N*-(4-oxocyclohexyl)-1,3-thiazolidine-3-carboxamide	
PT-1-6	(4*S*,5*S*)-5-(4-chlorophenyl)-*N*-[(1*S*,2*S*)-2-hydroxycyclohexyl]-4-methyl-2-oxo-1,3-thiazolidine-3-carboxamide	
	(4*S*,5*S*)-5-(4-chlorophenyl)-*N*-[(1*S*,2*R*)-2-hydroxycyclohexyl]-4-methyl-2-oxo-1,3-thiazolidine-3-carboxamide	

PT-1-6	(4*R*,5*R*)-5-(4-chlorophenyl)-*N*-[(1*S*,2*S*)-2-hydroxycyclohexyl]-4-methyl-2-oxo-1,3-thiazolidine-3-carboxamide	
	(4*R*,5*R*)-5-(4-chlorophenyl)-*N*-[(1*S*,2*R*)-2-hydroxycyclohexyl]-4-methyl-2-oxo-1,3-thiazolidine-3-carboxamide	
PT-1-8-*cis*	(4*S*,5*S*)-5-(4-chlorophenyl)-*N*-(*cis*-4-hydroxycyclohexyl)-4-methyl-2-oxo-1,3-thiazolidine-3-carboxamide	
	(4*R*,5*R*)-5-(4-chlorophenyl)-*N*-(*cis*-4-hydroxycyclohexyl)-4-methyl-2-oxo-1,3-thiazolidine-3-carboxamide	
PT-1-8-*trans*	(4*R*,5*R*)-5-(4-chlorophenyl)-*N*-(*trans*-4-hydroxycyclohexyl)-4-methyl-2-oxo-1,3-thiazolidine-3-carboxamide	
	(4*S*,5*S*)-5-(4-chlorophenyl)-*N*-(*trans*-4-hydroxycyclohexyl)-4-methyl-2-oxo-1,3-thiazolidine-3-carboxamide	

* The metabolite name in bold is the name used in the conclusion.

** ACD/ChemSketch, Advanced Chemistry Development, Inc., ACD/Labs Release: 12.00 Product version: 12.00 (Build 29305, 25 Nov 2008)

ABBREVIATIONS

1/n	slope of Freundlich isotherm
ε	decadic molar extinction coefficient
°C	degree Celsius (centigrade)
µg	microgram
µm	micrometer (micron)
a.s.	active substance
AChE	acetylcholinesterase
ADE	actual dermal exposure
ADI	acceptable daily intake
AF	assessment factor
AOEL	acceptable operator exposure level
AP	alkaline phosphatase
AR	applied radioactivity
ARfD	acute reference dose
AST	aspartate aminotransferase (SGOT)
AV	avoidance factor
BCF	bioconcentration factor
BUN	blood urea nitrogen
bw	body weight
CAS	Chemical Abstract Service
CFU	colony forming units
ChE	cholinesterase
CI	confidence interval
CIPAC	Collaborative International Pesticide Analytical Council Limited
CL	confidence limits
d	day
DAA	days after application
DAR	draft assessment report
DAT	days after treatment
DM	dry matter
DT_{50}	period required for 50 percent disappearance (define method of estimation)
DT_{90}	period required for 90 percent disappearance (define method of estimation)
dw	dry weight
EbC_{50}	effective concentration (biomass)
EC_{50}	effective concentration
ECHA	European Chemical Agency
EEC	European Economic Community
EINECS	European Inventory of Existing Commercial Chemical Substances
ELINCS	European List of New Chemical Substances
EMDI	estimated maximum daily intake
ER_{50}	emergence rate/effective rate, median
ErC_{50}	effective concentration (growth rate)
EU	European Union
EUROPOEM	European Predictive Operator Exposure Model
f(twa)	time weighted average factor
FAO	Food and Agriculture Organisation of the United Nations
FIR	Food intake rate
FOB	functional observation battery
FOCUS	Forum for the Co-ordination of Pesticide Fate Models and their Use
g	gram
GAP	good agricultural practice
GC	gas chromatography
GCPF	Global Crop Protection Federation (formerly known as GIFAP)

GGT	gamma glutamyl transferase
GM	geometric mean
GS	growth stage
GSH	glutathion
h	hour(s)
ha	hectare
Hb	haemoglobin
Hct	haematocrit
hL	hectolitre
HPLC	high pressure liquid chromatography or high performance liquid chromatography
HPLC-MS	high pressure liquid chromatography – mass spectrometry
HQ	hazard quotient
IEDI	international estimated daily intake
IESTI	international estimated short-term intake
ISO	International Organisation for Standardisation
IUPAC	International Union of Pure and Applied Chemistry
JMPR	Joint Meeting on 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_{doc}	organic carbon linear adsorption coefficient
kg	kilogram
K_{Foc}	Freundlich organic carbon adsorption coefficient
L	litre
LC	liquid chromatography
LC_{50}	lethal concentration, median
LC-MS	liquid chromatography-mass spectrometry
LC-MS-MS	liquid chromatography with tandem mass spectrometry
LD_{50}	lethal dose, median; dosis letalis media
LDH	lactate dehydrogenase
LOAEL	lowest observable adverse effect level
LOD	limit of detection
LOQ	limit of quantification (determination)
m	metre
M/L	mixing and loading
MAF	multiple application factor
MCH	mean corpuscular haemoglobin
MCHC	mean corpuscular haemoglobin concentration
MCV	mean corpuscular volume
mg	milligram
mL	millilitre
mm	millimetre
MRL	maximum residue limit or level
MS	mass spectrometry
MSDS	material safety data sheet
MTD	maximum tolerated dose
MWHC	maximum water holding capacity
NESTI	national estimated short-term intake
ng	nanogram
NOAEC	no observed adverse effect concentration
NOAEL	no observed adverse effect level
NOEC	no observed effect concentration
NOEL	no observed effect level
OM	organic matter content
Pa	Pascal

PD	proportion of different food types
PEC	predicted environmental concentration
PEC_{air}	predicted environmental concentration in air
PEC_{gw}	predicted environmental concentration in ground water
PEC_{sed}	predicted environmental concentration in sediment
PEC_{soil}	predicted environmental concentration in soil
PEC_{sw}	predicted environmental concentration in surface water
pH	pH-value
PHED	pesticide handler's exposure data
PHI	pre-harvest interval
PIE	potential inhalation exposure
pK_a	negative logarithm (to the base 10) of the dissociation constant
P_{ow}	partition coefficient between *n*-octanol and water
PPE	personal protective equipment
ppm	parts per million (10^{-6})
ppp	plant protection product
PT	proportion of diet obtained in the treated area
PTT	partial thromboplastin time
QSAR	quantitative structure-activity relationship
r^2	coefficient of determination
RPE	respiratory protective equipment
RUD	residue per unit dose
SC	suspension concentrate
SD	standard deviation
SFO	single first-order
SSD	species sensitivity distribution
STMR	supervised trials median residue
$t_{1/2}$	half-life (define method of estimation)
TER	toxicity exposure ratio
TER_A	toxicity exposure ratio for acute exposure
TER_{LT}	toxicity exposure ratio following chronic exposure
TER_{ST}	toxicity exposure ratio following repeated exposure
TK	technical concentrate
TLV	threshold limit value
TMDI	theoretical maximum daily intake
TRR	total radioactive residue
TSH	thyroid stimulating hormone (thyrotropin)
TWA	time weighted average
UDS	unscheduled DNA synthesis
UV	ultraviolet
W/S	water/sediment
w/v	weight per volume
w/w	weight per weight
WBC	white blood cell
WG	water dispersible granule
WHO	World Health Organisation
wk	week
yr	year