Evaluation Manual for the Authorisation of plant protection products according to Regulation (EC) No 1107/2009

EU part

Plant protection products

Chapter 7 Ecotoxicology; aquatic

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Board for the Authorisation of plant protection products and biocides

Chapter 7 Ecotoxicology; aquatic

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Important changes with the last version of the E.M.

Evaluation manual PPP EU part Chapter 7 Aquatic Version 2.0; January 2014		Evaluation manual PPP EU part Chapter 7 Aquatic Version 2.1; October 2016	
		Chapter 1.2	Text from data requirements deleted from the Manual, replaced with reference/links to Regulations (EU) No 283/2013 and 284/2013. Short list of data requirements included in the text.
		Chapter 1.2.3	Criteria for relevant metabolites are adjusted
		Chapter 1.3	Further elaboration or clarification on risk assessment issues that are used by Ctgb included in the text of 1.3: - Points of attention regarding the use of NOEC or NOEAEC from micro-/mesocosmstudies - Expression of the endpoints from aquatic studies - Algae (Methodology for calculating the section-by-section coefficient of variation in algal studies (OECD 201) - PECsw-twa - Further elaborations of the criteria reported in the EFSA guidance document on aquatic risk assessment - With respect to SSD and micro-/mesocosm studies reference is made now to EFSA aquatic GD

GENERAL INTRODUCTION

This chapter describes the data requirements for estimation of the effects of a plant protection product and its active substance on the aquatic environment and STP, and how reference values are derived in the EU framework (§1 - §1.5) under Regulation (EC) No 1107/2009.

This chapter consists of two parts: a part about effects on aquatic and sediment dwelling organisms (I), and a part about effects on sewage treatment plants (STPs) (II),

I AQUATIC AND SEDIMENT DWELLING ORGANISMS

1. EU FRAMEWORK

In this document, the procedures for the evaluation and re-evaluation of active substances as laid down in the EU are described; the NL procedure for evaluation of a substance is reverted to when no EU procedure has been laid down. The NL-procedure for the evaluation of a substance is described in §2 - §2.5 of part 2 of the Evaluation Manual (plant protection products). This document aims to give procedures for the approval of active substances and inclusion in Commission Implementing Regulation (EU) No 540/2011.

1.1. Introduction

This chapter describes the risk assessment of plant protection products for aquatic and sediment dwelling organisms.

This chapter is related to Chapter 6 Fate and behaviour in the environment; behaviour in surface water, sediment and sewage treatment plant (STP). That chapter describes the determination of estimated or measured concentrations in the sediment.

Guidelines for the risk assessment for aquatic organisms are described in the Guidance on tiered risk assessment for plant protection products for aquatic organisms in edge-of-field surface waters (EFSA Journal 2013; 11(7):3290).

For sediment organisms these guidelines can be found in Guidance Document on Aquatic Ecotoxicology (SANCO/3268/2001).

Data requirements, evaluation methodologies, criteria and trigger values that deviate from, or further elaborate, the provisions under EU framework (§1), are described in the NL part (§2 - §2.5). The national further provisions can also be used for inclusion of an active substance in Commission Implementing Regulation (EU) No 540/2011.

1.2. Data requirements

In order to qualify for inclusion in Commission Implementing Regulation (EU) No 540/2011 a dossier that meets the provisions laid down in Commission Regulation (EU) No 283/2013and Commission Regulation (EU) No 284/2013 of Regulation (EC) No 1107/2009 must be submitted for the active substance as well as for the product,.

Generally, EU and OECD guidelines for the execution of experiments are mentioned in Commission Communication 2013/C 95/01.

When according to the applicant a certain study is not necessary, a relevant scientific justification can be provided for the non-submission of the particular study.

1.2.1. Data requirements for the active substance

The date requirements regarding the risk of the active substance for aquatic organisms are described in part A of Commission Regulation (EU) No 283/2013, point 8.2 (effects on aquatic organisms).

Point 8.2 consists of the following data requirements:

8.2.1:	Acute toxicity to fish
8.2.2:	Long-term and chronic toxicity to fish
8.2.2.1:	Fish early life stage test
8.2.2.2:	Fish full life cycle test
8.2.2.3:	Bioconcentration in fish
8.2.3:	Endocrine disrupting properties
8.2.4:	Acute toxicity to aquatic invertebrates
8.2.4.1:	Acute toxicity to *Daphnia magna*
8.2.4.2:	Acute toxicity to additional aquatic invertebrate species
8.2.5:	Long-term and chronic toxicity to aquatic invertebrates
8.2.5.1:	Reproductive and developmental toxicity to *Daphnia magna*
8.2.5.2:	Reproductive and developmental toxicity to an additional aquatic invertebrate species
8.2.5.3:	Development and emergence in *Chironomus riparius*
8.2.5.4:	Sediment dwelling organisms
8.2.6:	Effects on algal growth
8.2.6.1:	Effects on growth of green algae
8.2.6.2:	Effects on growth of an additional algal species
8.2.7:	Effects on aquatic macrophytes
8.2.8:	Further testing on aquatic organisms

1.2.2. Data requirements for the product

The date requirements regarding the risk of the plant protection product for aquatic and sediment dwelling organisms are described in Commission Regulation (EU) No 283/2013, point 10.2 (effects on aquatic organisms).

Point 10.2 consists of the following data requirements:

10.2.1:	Acute toxicity to fish, aquatic invertebrates or effects on algal growth and macrophytes
10.2.2:	Additional long-term and chronic toxicity on fish, aquatic invertebrates and sediment dwelling organisms
10.2.3:	Further testing on aquatic organisms

1.2.3. Data requirements for metabolites

Metabolites in the water phase

For metabolites that are formed at more than 10 % at any timepoint or between 5 and 10 % at two or more occasions or at more than 5 % at the end of the study, a risk assessment (RA) is needed. In general, RA for metabolites formed below 5 % or below 10 % (observed at a single occasion) is not considered necessary. However, if there is reason to believe that a metabolite formed at < 5 % has intrinsic properties comparable to the parent substance in terms of its biological target activity, or that it has certain structural properties indicating high reactivity (i.e. mutagenicity) or endocrine disrupting properties or that it has unacceptable toxicological properties, then that metabolite may be ecotoxicologically relevant and a RA is needed. Data on transformation rate, bioconcentration and acute toxicity to algae, invertebrates and fish are required for such metabolites.

Metabolites in the sediment phase
Major metabolites in the sediment phase are metabolites of which in the laboratory study into the transformation in a water/sediment system the concentration in the sediment phase after 14 days is higher than or equal to 10% of the added amount of active substance.

Data on the toxicity to sediment dwelling organisms are required for such metabolites.
Minor metabolites (formed in a concentration lower than 10% of the amount of added active substance) should be taken into consideration as well, because they may well be ecotoxicologically relevant. Hence, all available information and expert judgement should be used to assess if metabolites <10% give rise to particular concern..

The data requirements mentioned in these sections do not always need to be met by means of experimental studies. Applicants may also answer the open questions by means of other available information in support of a scientific and rational risk assessment.

Valuable sources of information are e.g.:

- consideration of molecular structure of the metabolite (active part intact?);
- the occurrence of metabolites in the medium in existing tests with the active substance or major metabolites;
- general knowledge on the relationship between the toxicity of the metabolite and its parent substance (e.g. from the aquatic base set (fish, daphnia, algae);
- information on pesticidal activity from biological screening data;
- available knowledge on related compounds;

Further information is given in the Guidance on tiered risk assessment for plant protection products for aquatic organisms in edge-of-field surface waters (EFSA Journal 2013; 11(7):3290) with respect to the water phase and in the Guidance Document on Aquatic Ecotoxicology (SANCO/3268/2001) regarding the sediment phase.

1.3. Risk assessment

Aquatic organisms
The risk assessment methodology for aquatic organisms has in EU context been elaborated in the Guidance on tiered risk assessment for plant protection products for aquatic organisms in edge-of-field surface waters (EFSA Journal 2013; 11(7):3290). Each study is analysed and evaluated separately. The final conclusion and the endpoint per aspect (such as LC_{50} fish and NOECecosystem) are presented in a list of endpoints.

Risk assessment is based on comparison with endpoints. The risk evaluation for aquatic organisms follows a tiered approach. The first tier is based on model data as regards exposure and on laboratory data as regards toxicity. This is a general conservative evaluation of the behaviour and toxicity of the substance in the environment.
Where the criteria of the first tier of the evaluation are not met, there is the possibility to submit supplementary data for conducting a refined risk evaluation (higher tier).

Further information about the method to determine the exposure concentration is given in Chapter 6 Fate and behaviour in the environment; Behaviour in surface water, sediment and sewage treatment plant (STP), §1.3. The estimated exposure concentration is then compared with the toxicity data for the different aquatic organisms.

Sediment dwelling organisms
The risk assessment methodology for sediment dwelling organisms has in EU context been elaborated in the Guidance Document on Aquatic Ecotoxicology (SANCO/3268/2001).

What is written above for aquatic organisms about endpoints, risk assessment, higher tier and exposure concentrations also applies to sediment dwelling organisms.

In addition, further elaboration or clarification on risk assessment issues that are used by Ctgb are included in the text below:

A. Issues EFSA aquatic guidance document

Certain parts of the aquatic guidance document (EFSA, 2013) are still under discussion, e.g. the relevant endpoints for algae and aquatic plants and the geomean approach. Many Member States commented on these parts and expressed their concerns. The actual situation is that there is no agreement between the Member States about the approach to follow on these points. Member States asked for an update of the Guidance Document to deal with the concerns. It is decided by EFSA that a corrigendum of the aquatic GD is necessary on these issues; as long as such a corrigendum is not performed, Member States follow their own approach.

A.1 Relevant endpoints for algae and macrophytes

In the EFSA aquatic guidance document (see EFSA Journal 2013;11(7):3290) it is strongly recommended to use the ErC50 value as the endpoint for algae/macrophytes in risk assessment. In the former guidance (SANCO) the lowest endpoint (EbC50, EyC50, ErC50) had to be selected for the risk assessment. Because the ErC50 value is in most cases higher than the EC50 based on biomass or yield the protection level for algae and macrophytes will be lower when following the recommendation of the new guidance document.

For EU-dossiers it was decided to use the ErC50 in the risk assessment and to mention all endpoints (ErC50, EbC50 and EyC50) in the LoEP (EFSA technical report: Outcome of the pesticides peer review meeting on general recurring issues in ecotoxicology, December 2015), so that for the product assessment MSs can choose the endpoints they consider most appropriate. For the zonal assessments there is no decision yet taken by the Central Zone Steering Committee (CZSC).

The standard test duration of algae tests is 72 hours, according to the relevant OECD guideline. However, also tests with a duration of 96 hours and 120 hours are available. According to the new aquatic GD of EFSA (2013), algae tests with a test duration of 72-h and 96-h are acceptable. If endpoints are available at 72-h as well as 96-h the lowest of the two should be used for risk assessment.

With respect to the endpoints from 120-h tests the endpoints at 72-h and 96-h should be determined, if possible. The lowest of the two should be used for risk assessment. If it is not possible to determine the endpoints at 72-h and/or 96-h, the 120-h endpoint is used for risk assessment.

The standard test duration of Lemna tests is 7 days, according to the relevant guideline. However, also 14-day endpoints are sometimes available. If the last endpoint is lower than the 7-d endpoint, the 14-d endpoint should be used for risk assessment, because there is no reason to assume that the endpoint at 14 days is less reliable (in consultation with Gertie Arts from WUR Environmental Research).

A.2 Geomean approach

For using the geometric mean in risk assessment additional data than the ones defined in the data requirements are needed. However, in some cases, two endpoints are sufficient for carrying out the geomean approach.

For using the geomean approach, the endpoints should be derived by highly comparable tests (including duration of the tests and how these tests cover the life cycle of the tested species).

At the zonal harmonisation workshop in Vienna (2015) it was decided that the geomean is only accepted for the acute risk assessment. The geomean is accepted for the chronic risk assessment of algae and *Lemna* (not *Myriophyllum*) but not for fish and invertebrates. However, there is a concern that the level of protection is not sufficient for each single active substance and PPP. Germany has made a proposal for a decision scheme in which it is decided whether the lowest endpoint or a geomean should be used. However, no final Central Zone decision is yet made on the proposal of Germany.

B. Other issues

B.1 Points of attention regarding the use of NOEC or NOEAEC from micro-/mesocosmstudies

B.1.1 Total period of effects

When extrapolating the results from a mesocosm study to a proposed application regime for a product, it has to be kept in mind that the total period of effects in the whole season may not be longer than 8 weeks, if the NOEAEC (based on recovery) is used for risk assessment. It must also be kept in mind that for certain compounds like Insect Growth Regulators the effects can appear later in the study. The period before the appearance of the effects is in that case not taken into account.

In certain cases it is not clear from the GAP how many crop-cycles are possible in a growing season (GAP only presents the uses for one crop-cycle). It is important to have the right information in order to be able to apply the right endpoint from the micro-/mesocosm study. In cases that the NOEAEC value cannot be used because the total period of effects is greater than 8 weeks, the NOEC (based on class 1 effects) from the micro-/mesocosm study may be used for risk assessment, if there is no accumulation of the substance in the water-phase. If there is a build-up of the active substance in the water, the mesocosm study is in principle not appropriate to use in the risk assessment, because the number of applications and therefore the maximum concentration in practice is higher than in the mesocosm study.

B.1.2 Product with two or more active substances

Another issue is the question which endpoint to use from a micro-/mesocosm study if it concerns a product with two or more active substances and a mesocosm study is only available for one or more of the active substances separately, but not for the product. In that case the recovery endpoint (NOEAEC) cannot be used for risk assessment, because the presence of the other active substance(s) in the product can hamper the recovery of the affected species. Hence, in these cases the NOEC (based on class 1 effects) should be used for risk assessment.

B.1.3 ERO-RAC or ETO-RAC

With regard to core assessments, it was agreed during the harmonization meeting in Vienna (2015) to use the ETO-RAC, if available. The Central Zone Steering Committee decided that the ERO-option should be applied in case no ETO (NOEC) is reported in the LoEP (Warsaw, May 2015). However, meanwhile DE started a discussion on a third option on CIRCABC. This point therefore remains open.

B.2 Expression of the endpoints

In the EFSA technical report: Outcome of the pesticides peer review meeting on general recurring issues in ecotoxicology, December 2015, the following is mentioned regarding the

expression of the endpoints from tests with aquatic organisms:

EFSA proposal
It was considered that the way to express the toxicity endpoint for tier 1 studies (i.e. mean measured, nominal or initial measured), should not depend on the study design, on the physical chemical or environmental fate parameters, on technical difficulties when testing, and on how the endpoint will be used in the first tier risk assessment. The choice must depend on the actual exposure throughout the whole exposure period of that particular test. Where a suitable exposure throughout the whole period was not demonstrated, none of the endpoints must be used in first tier risk assessments.

This means that:
1) **Nominal concentrations** can be used to express the toxicity from any kind of test if the test concentrations were maintained ± 20 % of the nominal at all times throughout the test including the study end sampling. Mean measured is also an option for this situation.

2) **Initial measured concentrations** can be used to express the toxicity from any kind of test if the initial test concentrations were below 80 % of the nominal and this concentration was maintained throughout the test (within ± 20 % of the initial) including the final sampling. Mean measured is also an option for this situation.

3) **Mean measured concentrations** must be used to express the toxicity from any kind of test when the test concentrations were not maintained within the range of ± 20 % of the nominal or initial measured, but significant concentrations of the test item were still present at the end of the exposure period (or at the end of the renewal period for semi-static design).

4) When the test concentrations were not maintained and significant residues were not present at the end of the exposure period (or at the end of the renewal period for semi-static design), the **validity of the study should be questioned**.

Conclusion
The experts acknowledged the relevance of the way to express the toxicity endpoint from standard toxicity tests. The EFSA's proposals were not considered contradictory to those of the European Commission (2002a) guidance document. Therefore, the EFSA proposals listed above were agreed. However, further clarification should be provided in the EFSA aquatic guidance document (EFSA, 2013).

Additional important points concerning expression of endpoints
Furthermore, the following additional points were noted:

- The recommendations of the test-guideline should be followed when the European Commission (2002a) and the EFSA proposals cannot be applied;
- In line with the recommendations of OECD 23, for flow-through studies only, the arithmetic mean can be used to calculate the mean measured concentration; otherwise geometric mean measured concentrations should be used.
- If peak or initial measured concentrations are used to express the endpoint, and concentrations were not maintained, then such endpoint should only be considered in the context of a higher tier risk assessment, ensuring that the exposure in the study is sufficiently representative of the predicted exposure profile.
- The final measured concentrations for expression of the toxicity endpoint can be used when this is worst-case.
- Concentrations of the test item in algae studies must also be maintained as for other test organisms. The issue that the chemical might be taken up by the algal cells is partially covered by the OECD 201. However, clarification and/or targeted

measurements would be needed to prove the concentration levels that the test organisms were exposed to for the study duration.

- Study summaries presented in assessment reports (DAR/RAR) should include sufficient information on the analytics to understand the fate and behaviour of the test item in the test water throughout the study. In general a small table with the measured values is preferred. However, in straightforward cases (i.e. very stable test item) the tabular form is not essential. The lowest value measured during the exposure period, should always be reported. The values expressed as percentage of the nominal or initial measured are equally appropriate.
- It is essential that the list of endpoints accurately reflects the conditions of the study i.e. the study duration should reflect the length of exposure (e.g. if the test concentrations were not maintained by the end of the study, but the study is reported in the list of endpoints, the entry under the 'time-scale' should be carefully considered; if the analytical measurements express the sum of the active substance and its metabolites, this should be clearly indicated).
- The appropriateness of LOD or half of the LOQ, foreseen in OECD 23 for difficult substances, was also considered during the meeting. The experts considered that this approach could be used when intermediate measurements (e.g. more than one intermediate point or other information) are available. This information may allow using the LOD or half of the LOQ, to calculate a geometric mean concentration. When only initial and final measurements are available and no concentrations were detected at study end, the use of the LOD or half of LOQ is not supported. This is because it is not known when the concentrations decreased to practically zero (<LOD). The usefulness of such studies in first tier risk assessments should be questioned. It was noted that the text in OECD 23 is not explicit.

In general the same line is followed for the national product assessments. For detailed agreements made on national level, reference is made to the NL part of the aquatic part of the Evaluation Manual.

B.3 Other issues discussed between Member States

The following issues from the EFSA technical report: Outcome of the pesticides peer review meeting on general recurring issues in ecotoxicology, December 2015 are also relevant:

B.3.1 Algae (Methodology for calculating the section-by-section coefficient of variation in algal studies (OECD 201).

Based on the clarification provided at the meeting, it was clear that the methodology to be used for calculating the CV for section-by-section specific growth rates is the following: calculate specific growth rates for first control replicate for day 0-1, 1-2 and 2-3 and then calculate CV for first control replicate. Use the same approach to calculate CV values also for 2nd and 3rd control replicates. Then calculate the mean CV.

B.3.2 PECsw-twa – Further elaborations of the criteria reported in the EFSA guidance document on aquatic risk assessment

The experts at the meeting considered there is a need to have further clarifications and corrections on the EFSA aquatic guidance document regarding the application of the PECsw;twa. The main issues identified were 1) identification of organisms for which the reciprocity appraoch is applicable (e.g. fish, *Lemna, Daphnia,* all); 2) indication of the duration over which linear reciprocity needs to be determined (e.g. entire study, part of the study); 3) recommendation on how to express the endpoint (all study or just the linear part?) in case reciprocity is only determined for a part of the study; 4) clarification regarding the criteria to assess linearity (e.g. R^2 value, p-value of the regression, etc.); 5) clarification on the assessment of the latency.

It was agreed that until further guidance on reciprocity and latency of effects is available, then the use of TWA approaches are unlikely to be sufficiently robust to be used in regulatory risk assessment.

Decision-scheme
A decision scheme with corresponding explanatory notes is presented in Appendix 1.
This decision tree summarises the decision scheme for aquatic and sediment dwelling organisms.

1.4. Approval

This section describes the approval criteria for active substances (section 1.4.1) and plant protection products (section 1.4.2 and 1.4.3). For the EU approval procedure of active substances a representative formulation has to be included in the dossier. Therefore section 1.4.1 to 1.4.3 apply. For the zonal applications of plant protection products only section 1.4.2 and 1.4.3 apply.

1.4.1. Approval of the active substance

Annex II of Regulation (EC) No 1107/2009 provides the procedure and criteria for the approval of an active substances, safeners and synergists.

Point 3 of Annex II of Regulation (EC) No 1107/2009 gives the criteria for the approval of an active substance.

1.4.2. Evaluation of plant protection products

The principles for the evaluation regarding the effects on the environment are presented in Commission Regulation (EU) No 546/2011 (i.e. the Uniform Principles).

The specific principles for decision making for aquatic organisms are included in Part B Evaluation, point 2.5.2.2.

1.4.3. Decision making for plant protection products

The principles for the decision-making regarding the effects on the environment are presented in Commission Regulation (EU) No 546/2011 (i.e. the Uniform Principles).

The specific principles for decision making for aquatic organisms are included in Part C Decision making, point 2.5.2.2.

1.5. Developments

Hormone-disturbing substances
It is known that substances may disturb endocrine systems of organisms.
Endocrine substances may in an early life stage cause damage of which the effects only manifest themselves later, possibly only in a next generation. It is recognised that the current available chronic toxicity tests are not adequate to demonstrate potential endocrine effects. This is why in an international programme, organised by OECD, toxicity tests (including fish) are being developed to identify endocrine-disturbing substances. For the time being, data on mammals may give an indication.

In the process of revision of 544/2011 and 545/2011 data requirements regarding endocrine disruption will be taken into account by setting several data requirements.

Organisms in groundwater
Studies of the biological groundwater ecosystem have led to the notion that the groundwater ecosystem is a system as such which needs protection [1,2]. Active substances and/or

metabolites should for this reason be evaluated for their effects on the groundwater ecosystem in the future.

In the absence of more specific information and harmonised test guidelines, it may be assumed that groundwater organisms have the same sensitivity as taxonomically and physiologically related organisms in surface water. Crustaceans represent the most important groundwater taxa and – from a provisional scientific point of view – data on crustaceans in surface water are considered as suitable and adequate to cover the risk to groundwater organisms. Recovery observed in higher tier tests, however, is possibly not relevant for organisms in groundwater. Currently, harmonised schemes for exposure and risk assessment are not available. Further research should therefore be carried out in this field.

Ecological modelling
Reference is made to the Guidance on tiered risk assessment for plant protection products for aquatic organisms in edge-of-field surface waters (EFSA Journal 2013; 11(7):3290).
Section 11.3 of this document gives information about the state-of-the-art of the use of mechanistic effect models in regulatory environmental risk assessment.

In the near future, the PPR Panel will elaborate scientific opinions on good modelling practice and more specifically on modelling within the aquatic RA. Since there is a lack of experience and guidance for these approaches in RA, the use of mechanistic modelling within the authorisation of PPPs has to be evaluated carefully and case-by-case until special guidance becomes available.

Risks of fungicides to aquatic fungi
Almost no information is available concerning the potential risks of fungicides (or PPPs in general) to aquatic fungi. Maltby *et al.* (2009)[3] compiled aquatic ecotoxicity data for a series of fungicides. The dataset included acute single-species data for 42 fungicides, semi-field data for 12 fungicides and covered seven modes of action and different exposure regimes. SSDs were constructed for separate taxonomic groups (*i.e.* fish, invertebrates, and primary producers) and for all groups together. They conclude that there is no evidence to suggest that derived threshold values based on hazardous concentrations (HC_p) from acute aquatic SSDs would pose a risk to aquatic hyphomycetes. However, laboratory toxicity data on fungi were not included in the datasets, since they were not available. In the micro/mesocosm studies reviewed, only functional responses of micro-organisms in the form of litter decomposition received attention. None of the semi-field studies specifically studied structural endpoints of fungi. Maltby *et al* (2009)[3] therefore also concluded that the underlying data is limited in number and that further research on nontarget fungi should be conducted. The relevance of further research into the sensitivity of aquatic fungi was demonstrated recently in screening studies by Dijksterhuis *et al.* (2009, 2011)[4, 5] and CBS (2009)[6]. Their data indicate that HC_5 concentrations derived by Maltby *et al*. (2009)[3] for ergosterol inhibitors may show an effect on aquatic fungi. Further research is needed to address the relevance of aquatic fungi as additional non-target groups in the risk assessment of PPPs. Special attention should be paid to the selection of appropriate test species, given the enormous diversity within the kingdom of fungi. When these data are collated, it will be a risk manager decision to set the specific protection goal for aquatic fungi (e.g. structure and/or function).

Sediment organisms
Regarding sediment organisms the following EFSA Opinion was published:
EFSA PPR Panel (EFSA Panel on Plant Protection Products and their Residues), 2015. Scientific Opinion on the effect assessment for pesticides on sediment organisms in edge-of-

field surface water. EFSA Journal 2015;13(7):4176, 145pp. doi:10.2903/j.efsa.2015.4176.
This opinion is assumed to be input for future guidance.

Multiple stress and mixture toxicity
In many crops during the growing season more than one compound will be used. In some crops this can add up to more than 50 applications and some of these compounds will be applied together, e.g. an herbicide together with an insecticide and/or fungicide. Sometimes even two or three herbicides or two or three fungicides or two insecticides may be applied simultaneously, up to 5 or 6 compounds at the same time. When these combinations (e.g. tank mixes) are not sold as a formulation the legislative process does not take account for the potential combined effects of the use of these tank mixes. Neither does the legislative process take into account that different compounds of the same group (e.g. insecticides) or of different groups (e.g. insecticides, herbicides, fungicides) are used over time in the same growing season.

When a compound is allowed on the market this decision is sometimes based on the potential of recovery. Whether under different crop scenarios the recovery option is appropriate to use in the derivation of the RAC needs to be evaluated from an ecological point of view, since during the growing season drainage ditches may be affected multiple times by the use of plant protection products. EFSA is planning to take this topic into account.

II EFFECTS ON A SEWAGE TREATMENT PLANT (STP)

1. EU FRAMEWORK

In this document, the procedures for the evaluation and re-evaluation of active substances as laid down in the EU are described; the NL procedure for evaluation of a substance is reverted to when no EU procedure has been laid down. The NL-procedure for the evaluation of a substance is described in §2 - §2.5 of part 2 of the Evaluation Manual (plant protection products). This document aims to give procedures for the approval of active substances and inclusion in Commission Implementing Regulation (EU) No 540/2011.

1.1. Introduction

This chapter serves to estimate the risk to micro-organisms in the STP.

This chapter is related to Chapter 6 Fate and behaviour in the environment; behaviour in surface water, sediment and sewage treatment plant (STP).

Data requirements, evaluation methodologies, criteria and trigger values that deviate from, or further elaborate, the provisions under EU framework (§1), are described under NL framework (§2 - §2.5). The national further provisions can also be used for inclusion of an active substance in Commission Implementing Regulation (EU) No 540/2011.

1.2. Data requirements

In order to qualify for inclusion in Commission Implementing Regulation (EU) No 540/2011 a dossier that meets the provisions laid down in Commission Regulation (EU) No 283/2013and Commission Regulation (EU) No 284/2013 of Regulation (EC) No 1107/2009 [must be submitted for the active substance as well as for the product.

Generally, EU and OECD guidelines for the protocol of experiments are mentioned in Commission Communication 2013/C 95/01 and Commission Communication 2013/C 95/02.

When according to the applicant a certain study is not necessary, a relevant scientific justification can be provided for the non-submission of the particular study.

1.2.1. Data requirements for the active substance

The date requirements regarding the effects of the active substance on sewage treatment plants (STPs) are described in Commission Regulation (EU) No 283/2013, point 8.8 (effects on biological methods for sewage treatment).

Point 8.8 consists of the following data requirements:
8.8: Effects on biological methods for sewage treatment

1.2.2. Data requirements for the product

According to Commission Regulation (EU) No 284/2013, no data are required for the risk assessment for an STP.

1.3. Risk assessment

Risk assessment is carried out as described in §1.3 of Chapter 6 Fate and behaviour in the environment; behaviour in surface water, sediment and sewage treatment plant (STP).

1.4. Approval

This section describes the approval criteria for active substances (section 1.4.1) and plant protection products (section 1.4.2 and 1.4.3). For the EU approval procedure of active

substances a representative formulation has to be included in the dossier. Therefore section 1.4.1 to 1.4.3 apply. For the zonal applications of plant protection products only section 1.4.2 and 1.4.3 apply.

1.4.1 Approval of the active substance

Annex II of Regulation (EC) No 1107/2009provides the procedure and criteria for the approval of an active substances, safeners and synergists.

Point 3 of Annex II of Regulation (EC) No 1107/2009 gives the criteria for the approval of an active substance.

1.4.2 Evaluation of plant protection products

Commission Regulation (EU) No 546/2011 (i.e. the Uniform Principles), contains no specific criteria for risk assessment as regards sewage treatment.

1.4.3 Decision making for plant protection products

Commission Regulation (EU) No 546/2011 (i.e. the Uniform Principles), contains no specific criteria for decision making as regards sewage treatment. However, for the national assessment the threshold level used for risk assessment is 0.1 * EC50 STP value.

1.5. Developments

None.

2. APPENDICES

Appendix 1 Explanatory notes decision tree Risk to aquatic and sediment dwelling organisms based on Regulation (EC) 1107/2009

1) For each active substance, information concerning toxicity to aquatic organisms (Commission Regulation (EU) No 283/2013: point 8.2) must be provided, unless it can be demonstrated that it can be ruled out that the substance reaches surface water during good (agricultural) use of the product, in compliance with the WG/GA (Statutory Use Instructions/Directions for Use). For the purposes of labelling in the European framework, data concerning acute toxicity of the active substance to algae, aquatic invertebrates and fish, and the ready biodegradability of the active substance must always be provided. For each product in principle data concerning toxicity to aquatic organisms must be provided if the toxicity of the plant protection product cannot be predicted on the basis of the data for the active substance (Commission Regulation (EU) No 284/2013, point 10.2).

2) The acute toxicity research (283/2103 point 8.2.1/8.2.4/A8.2.6) must be carried out in accordance with standardised methods with representatives of at least 3 different trophic levels, i.e., algae, aquatic invertebrates and fish.
For fish acute toxicity data are always required for rainbow trout (*Oncorhynchus mykiss*). Seven fish should be used, also in a limit test.
For herbicides and growth regulators a standard test with higher aquatic plants must be submitted (283/2013 point 8.2.7) as well as a test with a second algal species from a different taxonomic group.
For pesticides with an insecticidal mode of action data are required for *Daphnia* sp. (*D. magna* preferred) and an additional arthropod (preferably a *Chironomus* test, if data on *Americamysis bahia* are not already available).
If a long-term/chronic study on insects is already available there is no need to require additionally an acute one.
Except for the active substance and the product, data about metabolites formed in the water and sediment phase of water/sediment systems are required as well. For metabolites that are formed at more than 10 % or between 5 and 10 % at two or more occasions or at more than 5 % at the end of the study, data is needed. In general, data for metabolites formed below 5 % or below 10 % (observed at a single occasion) is not considered necessary. However, if there is reason to believe that a metabolite formed at < 5 % has intrinsic properties comparable to the parent substance in terms of its biological target activity, or that it has certain structural properties indicating high reactivity (i.e. mutagenicity) or endocrine disrupting properties or that it has unacceptable toxicological properties, then that metabolite may be ecotoxicologically relevant and data is needed.Data on transformation rate, bioconcentration and acute toxicity to algae, aquatic invertebrates and fish are required for such metabolites.
Metabolites should in general also be tested with *Lemna*, *Chironomus* or other species if these taxa have been the most sensitive with the active substance. If it can be demonstrated that certain taxonomic groups are clearly less sensitive to the active substance (by a factor of 100) than other groups, testing can be limited to those which are the most sensitive ones. If testing reveals that the toxicity of the metabolite to one taxonomic group is similar to the parent or higher then testing may be required on all taxonomic groups.
Major metabolites in the sediment phase are metabolites of which in the laboratory study into the transformation in a water/sediment system the concentration in the sediment phase after 14 days is higher than or equal to 10% of the added amount of active substance. Data on the toxicity to sediment dwelling organisms are required for such metabolites.

Minor metabolites should be taken into consideration as well.
The data requirements mentioned in this section do not always need to be met by means of experimental studies.
Applicants may also answer the open questions by means of other available information in support of a scientific and rational risk assessment. Valuable sources of information are e.g.:

- consideration of molecular structure of the metabolite (active part intact?);
- the occurrence of metabolites in the medium in existing tests with the active substance or major metabolites;
- general knowledge on the relationship between the toxicity of the metabolite and its parent substance (e.g. from the aquatic base set (fish, daphnia, algae);
- information on pesticidal activity from biological screening data;
- available knowledge on related compounds;

Further information is given in the Guidance on tiered risk assessment for plant protection products for aquatic organisms in edge-of-field surface waters (EFSA Journal 2013; 11(7):3290).

3) Also chronic toxicity data (283/2013 point 8.2.2/8.2.5) must be submitted , unless there is 90% or more loss of the original substances over 24 hours via hydrolysis.

4) A chronic study with fish and *Daphnia* sp. is required. For fish this should be a Early life-stage test, unless a fish full life-cycle (FFLC) test is provided. An FFLC may be required depending on the persistence and bioaccumulative potential of the substance; the following critera applies: BCF > 1000 ánd the elimination during the 14 day depuration phase in the bioconcentration study <95% ánd the substance is stable in water or sediment ($DegT_{90}$ > 100 days).
For pesticides with an insecticidal mode of action preferably the most sensitive standard test arthropods (*Daphnia, Chironomus, Americamysis*) from the acute Tier 1 data set should be selected as test species in the chronic effect assessment. If in the acute assessment a certain standard test arthropod is a factor of 10 more sensitive a chronic test with this arthropod should be performed.

5) Where in a water/sediment study (283/2013 point 7.2.2.3.) at or after 14 days (283/2013 point 8.2.7) ≥ 10% of the active substance and/or metabolite is found in the sediment or when the substance interferes with moulting hormones (e.g. insect growth regulators), a chronic toxicity test with sediment dwelling organisms (*Chironomus sp*.) (283/2013 point 8.2.7) must be provided unless the EC10/NOEC from the chronic daphnia test (or a comparable study with aquatic insects if this group of organisms is more sensitive) ≥ 0.1 mg a.s./L.

6) Further information on the calculation and determination of the PEC is given in Chapter 6 Behaviour and fate in the environment; behaviour in surface water, sediment and sewage treatment plant (STP).

7) The following criteria must be met:
An active substance and each of its transformation products have in surface water a concentration lower than:

- 0.01 of the LC_{50} for acute toxicity to fish
- 0.01 of the EC_{50} for acute toxicity to aquatic invertebrates
- 0.1 of the EC50 for algae
- 0.1 of the EC50 for aquatic plants

- 0.1 of the NOEC for long-term toxicity to fish and aquatic invertebrates
- 0.1 of the NOEC for long-term toxicity to sediment dwelling organisms

The risk is low if these criteria are met. The product can be authorised in as far as the risk to aquatic and sediment dwelling organisms is concerned.

8&9)A risk is present if the criteria as given under 6) are not met. Such a use is considered as not permissible, unless a further (adequate) risk evaluation shows that there are no unacceptable direct or indirect effects for aquatic and sediment dwelling organisms and organisms that depend on aquatic ecosystems (higher tier). The higher tier risk assessment is performed according to Regulation (EC) 1107/2009 and hence the Guidance on tiered risk assessment for plant protection products for aquatic organisms in edge-of-field surface waters (EFSA Journal 2013; 11(7):3290).

10) Research is requested to determine species accumulation and elimination, i.e., the extent to which the substances in question are directly absorbed from the water, retained (bioconcentration factor BCF), and excreted by the organism.
The octanol/water partition coefficient (Kow) (283/2013 point 2.7) of a substance gives information about the bioaccumulating capacity of a substance. Where the logKow of a substance < 3, experimental research is not required. For such organic substances sufficient insight into the bioaccumulating capacity can be obtained from the octanol/water partition coefficient (Kow) (283/2013 point 2.7), for which the following formula (Veith et al., 1979[1]) is used:

logBCF = 0.85*logKow - 0.70 (L/kg)

Experimental research with fish is required for substances with a logKow > 3 (283/2013 point 8.2.2.3), unless the substance is considered not stable, i.e. , more than 90% loss of the original substance over 24 h via hydrolysis. BCF_k (kinetic bioconcentration factor) values should be reported as growth-corrected and as lipid-normalised values (default 5% lipid content).

11) An active substance of a plant protection product and each of its transformation products have a maximum bioconcentration factor lower than:
a. 1000 for readily biodegradable active substances, or
b. 100 for active substances that are not readily biodegradable.

12) Where this is not the case, a risk is present and the use is not permissible, unless a further (adequate) risk evaluation shows that there are no unacceptable direct or indirect effects for aquatic and sediment dwelling organisms and organisms that depend on aquatic ecosystems (higher tier). The higher tier risk assessment is performed according to Regulation (EC) 1107/2009 and hence the Guidance on tiered risk assessment for plant protection products for aquatic organisms in edge-of-field surface waters (EFSA Journal 2013; 11(7):3290).

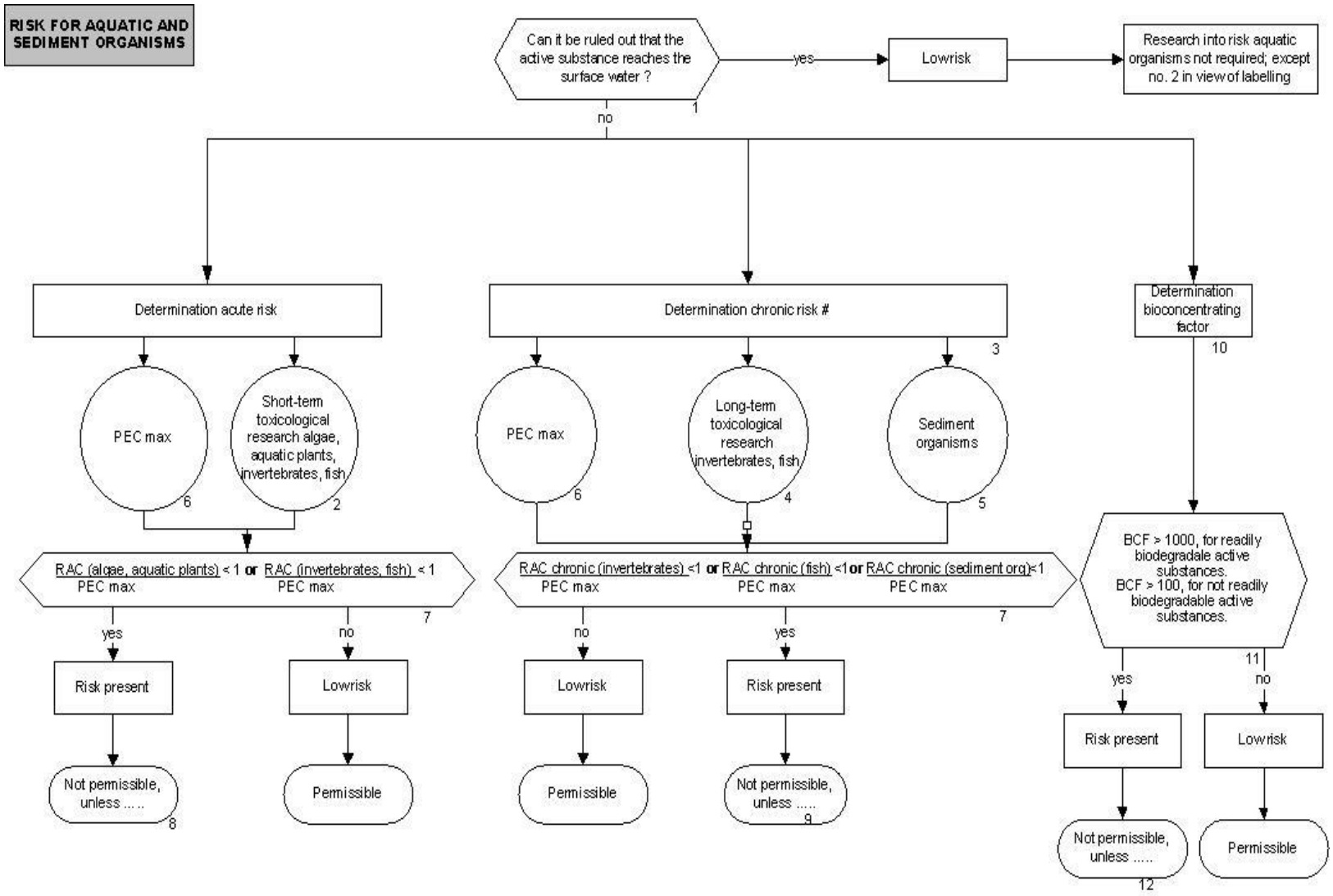
For the higher tier risk assessment triggered by exceeding of the first tier TER values several possibilities exist, e.g.:
- geomean approach;
- SSD approach;
- modified exposure tests;

[1] Veith, G.D., D.L. Defoe and B.V. Bergstedt. 1979. Measuring and estimating the bioconcentration factor of chemicals on fish. J. Fish. Res. Board Can. 36: 1040-1048.

- micro-/mesocosm studies.

For more information about these studies and approaches reference is made to the Guidance on tiered risk assessment for plant protection products for aquatic organisms in edge-of-field surface waters (EFSA Journal 2013; 11(7):3290).

A TER is calculated based on the relevant higher tier Regulation (EC) 1107/2009 toxicity endpoint and the relevant PEC in the edge-of-field ditch. The toxicity endpoint depends on the higher tier approach which is chosen; modified exposure studies are directed on taking into account fate processes under natural conditions; the endpoint will change but in principle the same safety factor will be applied as in the first tier risk assessment. The SSD approach yields an endpoint which is the mean HC5 value with a certain safety factor. More information can be found in the EFSA aquatic guidance.
A micro-/mesocosm study yields a NOEC or NOEAEC. For risk assessment a safety factor is applied (trigger value). The safety factor depends on the endpoint and on the number of studies available. For more information see the EFSA aquatic guidance.
If the TER is lower than the trigger value, a risk is still present; drift reduction measures may be applied. If these are sufficient the risk in the edge-of-field ditch is acceptable.



Unless there is 90% or more loss of the original substance over 24 hours via hydrolysis

3. REFERENCES

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4 Dijksterhuis J, Van Doorn T, Postma J. 2009. De gevoeligheid van oppervlaktewaterschimmels blootgesteld aan azolen en strobilurines die worden toegepast in de landbouw. Centraal Bureau voor Schimmelcultures / Ecofide, Utrecht, Weesp, 32 pp.

5 Dijksterhuis J, Van Doorn T, Postma J. 2011. Effects of seven fungicides on non-target aquatic fungi. *Wat Air Soil Pollut* DOI 10.1007/s11270-011-0836-3.

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