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

EU part

Plant protection products

Chapter 7 Ecotoxicology; terrestrial; non target arthropods and plants

version 2.2; January 2020

ctgb

Board for the Authorisation of plant protection products and biocides

Chapter 7 Ecotoxicology; terrestrial; non target arthropods and plants

Category: Plant Protection Products

Changes in the Evaluation Manual

Evaluation manual PPP EU part Chapter 7 Non targets arthropods and plants			
Version	**Date**	**Paragraph**	**Changes**
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 1.3	Further elaboration or clarification on risk assessment issues that are used by Ctgb included in the text of 1.3: Herbicide application in orchards No use of MAF in case of EU (active substance) assessments for non-target terrestrial plants
		Appendix 1, Point 4	Note on correction factor 0.5 from ESCORT 2 for the in field exposure calculation for orchards and vineyards included.
		Appendix 2, Point 5	Criterion included for acceptance of data normality in case of the SSD approach
2.2	January 2020	Chapter 1.3 Non-target arthropods	Conclusions from the Pesticides Peer review Meeting 185 on Recurring Issues on Ecotoxicology (EFSA Supporting publication 2019:EN-1673)
		Chapter 1.3 (non-target plants)	Endpoint based on phytotoxicity
		I.1 and II.1	Sentence included on the administrative EFSA guidance

GENERAL INTRODUCTION

This chapter describes the data requirements for estimation of the effects on non target arthropods and plants of a plant protection product and its active substance 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 non-target arthropods (I) and a part about non-target plants (II).

I NON TARGET ARTHROPODS

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.

Notifiers preparing an assessment report for active substances need to comply with the relevant guidance, instructions and format laid down in the EFSA Administrative guidance on submission of dossiers and assessment reports for the peer-review of pesticide active substances.

1.1 Introduction

This chapter describes the risk assessment of plant protection products for non-target arthropods.

Non-target arthropods play a vital role in the ecosystem. For this reason plant protection products should cause no unacceptable and prolonged effects on populations of non-target arthropods, not in the treated part and not beyond. An agricultural purpose is served at the same time: the protection of natural enemies in integrated pest control. The risk to non-target arthropods must be assessed in case there is a chance of exposure of these organisms.

Guidelines for the risk assessment for non-target arthropods are given in the Guidance Document on Terrestrial Ecotoxicology (Sanco/10329/2002 rev 2 final) in which the testing procedure is described as elaborated in the report written on the basis of the SETAC/ESCORT 2 workshop [1]

A decision tree with corresponding explanatory notes is presented in Appendix 1. This decision tree summarises the decision scheme for arthropods in non-integrated pest management systems.

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 of an active substance in Commission Implementing Regulation (EU) No 540/2011 [2] a dossier that meets the provisions laid down in Commission Regulation (EU) No 283/2013 and 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 data requirements regarding the risk of the active substance for non-target arthropods are described in Commission Regulation (EU) No 283/2013 , point 8.3.2 (Effects on non-target arthropods other than bees).

Point 8.3.2 consists of the following data requirements:
8.3.2.1 Effects on Aphidius rhopalosiphi
8.3.2.2 Effects on Typhlodromus pyri

1.2.2 Data requirements for the product

The data requirements regarding the risk of the plant protection product for non-target arthropods are described in Commission Regulation (EU) No 284/2013, point 10.3.2 (Effects on non-target arthropods other than bees).

Point 10.3.2 consists of the following data requirements:
10.3.2.1 Standard laboratory testing for non-target arthropods
10.3.2.2 Extended laboratory testing, aged residue studies with non-target arthropods
10.3.2.3 Semi-field studies with non-target arthropods
10.3.2.4 Field studies with non-target arthropods
10.3.2.5 Other routes of exposure for non-target arthropods

1.2.3 Data requirements for metabolites

Except for the active substance and the product, data are also required for metabolites to which non-target arthropods may be exposed. Arthropods may be exposed to metabolites in/on plants and to metabolites in the soil. For metabolites in vegetation, standard laboratory tests are normally not required. Metabolites that are the actually active molecule may be exceptions.

General guidance is given in the general part about metabolites as described under ‘birds and mammals’ (§1.2.3). Where higher tier studies (cage/tent/tunnel or field tests) have been carried out with the pesticide under realistic exposure conditions it can be assumed that the potential risk of metabolites has been taken into account. Soil metabolites: when relevant these are tested with soil meso- and macro-organisms (data point 8.4.2); tests with surface dwelling soil arthropods are therefore not required.

1.3 Risk assessment

The risk assessment methodology for non-target arthropods has in EU context been elaborated in the Guidance Document on Terrestrial Ecotoxicology (Sanco/10329/2002 rev 2 final), which follows the recommendations of the ESCORT 2 workshop [1].

Each study is summarised and analysed separately. The final conclusion and the endpoint per aspect (such as LR_{50}) are presented in a list of endpoints. The risk is assessed against these endpoints.

In Appendix 1 to this chapter, a risk assessment scheme for non-target arthropods in non-

integrated pest management systems is included. This decision scheme follows the ESCORT 2 guidance [1], with additions and clarifications such as they have evolved in risk assessment practice over the years. Since these additions and clarifications are in line with what is currently commonly accepted (and required) during EU-reviews, they are included in the EU-part of this chapter. The scheme for integrated pest management systems is included in Appendix 1 to the NL-part of this chapter.

In addition, the following approach is used by Ctgb for herbicide application to bare soil strips under trees in orchards:

In the first tier, foliar dwelling arthropods have to be considered for the treated area. When a risk is identified, refinement is possible by taking into account in-field drift to the grass strips, and performing the refined risk assessment for the foliar dwelling arthropods in the grass strips.The exposure in this scenario should be 10% (due to drift from application to the bare soil beneath the trees).

Pesticides Peer review Meetings on Recurring Issues on Ecotoxicology

In the Pesticides Peer review Meeting 185 on Recurring Issues on Ecotoxicology (EFSA Supporting publication 2019:EN-1673), the agreements that were reached are presented below. These agreements apply to EU active substance dossiers submitted from 7 July 2019 and national product assessment submitted from 1 january 2020:

- Vegetation distribution factor (VDF):
  The experts agreed that the VDF value should be changed as better data are now available. It was recommended that a VDF value of 5 is applied for all the tiers of the assessment as an interim solution. Such an interim solution should be reflected in the (European Commission, 2002) document and its implementation should be further considered.

- Substrate in aged residue studies:
  It was agreed that until further guidance is developed, the substrate used in the aged residue studies does not need to be relevant for the crop under assessment.

- Risk assessment for non-target arthropods when oral exposure is relevant:
  It was agreed that, until guidance is developed and adopted, data for herbivorous species should not be requested. In cases where a concern is raised (e.g. based on the mode of action of the active substance), then this should be highlighted in the risk assessment and acknowledged in the EFSA conclusion.

- Minimum detectable difference in higher tier field studies:
  It was overall considered premature to recommend calculating the MDD for higher tier studies with NTA, as criteria to help interpret these MDD values are currently lacking (e.g. classes of MDD, minimum number of taxa with an acceptable MDD). According to Ctgb, this agreement does not exclude the possibility that an MDD analysis could provide useful information on a case-by-case basis.

- Evaluation of NTA field studies:
  The experts at the meeting acknowledged that using the guidance by de Jong et al. (2010) is useful and that some aspects of the guidance should be used for EU-level assessments until further guidance for the evaluation of NTA field studies is available.

The elements agreed upon have been in included in a template in Appendix H from the report of the meeting (EFSA Supporting publication 2019:EN-1673) and are included below (sections copied from the EFSA report are marked in grey). It was recommended by the meeting that this template is followed when reporting the studies in the RARs/DARs. It should be noted that the template contains some modifications as compared to the report from de Jong et al. (2010).

Table H1: For each item proposed for the evaluation, recommendations are provided on issues to consider when evaluating different relevant items of field studies with arthropods

No	Test item	Recommendations
1	Substance (formulation, toxic reference, etc.)	Information about the applied substance (active substance or formulation) and the toxic reference (if used) should be reported. The guidance specifies that the same test item can be a reference when used at a higher application rate (able to cause 50 % effects): Clear effects should be found in the toxic reference, at least a 50 % effect on at least one sampling date, for at least 10 % of the taxa for which statistical evaluation is possible, and when these criteria are not met the test is not reliable. When no reference item is included, the highest application rate of the test item could act as such, and in that case the same criteria are used for the highest treatment rate as for the reference item. In the case that a toxic reference item is not included, high enough rates of the test item should be applied to cause clear effects as a toxic reference, unless effects were clearly seen with the test item at the 'target' application rate(s). If not, the study should be classified as 'unreliable'. This is in agreement with what is written in the guidance. It should be noted that the test with a toxic reference item is a validation tool. The use class (e.g. insecticide, herbicide) and mode of action (e.g. contact, systemic, cholinesterase inhibitor) of the test item should be reported.
2	Test site	The history of the test site at least two years before the start of the experiment should be available (e.g. previous cropping history, application of pesticides, mineral fertilisers, establishment of orchards, crop rotation for arable crops, etc.). Treatments applied to maintain the health of the crop, e.g. fungicides, must be applied to the whole test site. When the results of a field study should be used for assessment of the potential impact on the off-crop fauna, the off-crop area is considered to be an undisturbed area (use of other pesticides is not acceptable).
3	Application	Data about the application are relevant in order to evaluate whether the application in terms of mode of application, dosage, number of applications and interval between applications, reflects the GAP. Information on the climatic conditions in the period before, during and after the application as well as information about artificial irrigation should also be reported. The field study should preferably be conducted in the season of the proposed use of the substance. The above are important to evaluate the correct exposure of NTAs to the tested substance.
4	Experimental design	Random plot design, Latin square, plot size (a minimum plot size of 1 ha for arable land and 0.2 ha for orchards is recommended), number of replicates, number of samples. Recovery could differ for off-crop and in-crop sites. In terms of recovery, the scale of the study should be considered when comparing it with the scale of the field under the proposed use.

		The duration of the study should be long enough in order to assess the recovery within the test period. Recovery is assessed for different taxonomic levels, from population to community. Delayed effects may occur after recovery has been demonstrated and after the test period. This is relevant for sensitive life stages and should be addressed in the study report. It should be noted that regarding the issue of whether the potential for recovery/recolonisation should be demonstrated to be below one year, more criteria are needed. An increasing number of field studies are conducted under the principles of good laboratory practice. For new studies this is a requirement.
5	Biological system	For the time being, a quite extensive and detailed list of taxa is provided in Table 4 of the de Jong et al. (2010) guidance for reliability assessment and is agreed as a minimum requirement for arable crops, orchards and off-field. Thus an updated version of Table 4, including the previously missing footnotes, should be used as a reference for the reliability assessment, as is included in the meeting technical report. In agreement with the de Jong et al. (2010) guidance, the desired taxa level of identification is provided in this table; about 50–80 taxa are available to allow for statistical analysis with sufficient power in a typical field study. Also, the minimum number of individuals should fulfil the requirements of statistical analysis. It should be noted that if the listed taxa are lacking, a study is not invalidated, hence the evaluator should clarify the issue; e.g. seek a justification for the lacking/not measured or additionally reported taxa under local conditions. The biological system should be summarised (e.g. dominant groups, the frequency of species found, etc.).
6	Sampling	Sampling method, scheme, area, etc. Some general guidance is given in Candolfi et al. (2000a). In the study report it should be clearly indicated which sampling method is used for each group of species. Given the (sometimes) large variability of a population over time, the pre-treatment monitoring of the community should be conducted not too long before treatment. Pre-treatment sampling, preferably shortly (< 5 days) before the first application, is desired in order to assess the variation between plots and the taxa exposed. In some cases (e.g. application early in the growing season or in the winter) this is not useful or possible because certain organisms are not yet present in sufficient numbers. Weather conditions in the period before sampling should be recorded. For off-crop risk assessment the populations of organisms living on the soil surface should be recorded as well.
7	Results in terms of application	According to the guidance, it should be possible to check whether the right amount of the substance studied was applied in the test: e.g. by measuring the compound in the spray solution and controls of the spray pattern. The weather conditions during the test should be considered, and attention should be paid to deviations from the average conditions of the test site (e.g. heavy rainfall or unusually low or high temperatures on the day of application that could influence exposure of the NTA fauna).
8	Endpoints	Population level effects should be reported. The population effect on each taxon including sensitive life stages and, where possible, recovery with time to recovery, compared to controls should be

		reported. Number of arthropod species/taxa and individuals and community groups (e.g. Aranae, Insecta, etc.; juveniles and adults, separately). Total biomass of all arthropod and community groups (e.g. Aranae, Insecta, etc.; juveniles and adults, separately). Numbers and biomass of at least the two most abundant species/taxa (juveniles and adults, separately). Functional endpoints: e.g. parasitism rates. Indirect effects: e.g. prey items counted to interpret the importance of food/prey removal. Depending on the test design, an assessment endpoint could be derived (no observed effects rate, no observed ecological adverse effects rate, lowest observed ecological adverse effect rate).
9	Elaboration of the results	Statistical analysis Multivariate or univariate (ANOVA) techniques can be used. It is recommended that a power analysis is always provided for the endpoints investigated in the study. When elaborating the results, consideration should be given to biological relevance vs statistical significance of observed effects. The concept of MDD refers to the magnitude of the effect that needs to exist in the treatment population in relation to the control in order to obtain a statistically significant difference in hypothesis testing. The MDD concept is potentially very beneficial for the interpretation of the field studies, but further criteria need to be developed specifically for NTAs in order to fruitfully use this information in the assessment. Community analysis tools such as principal response curve could be used but should not be specifically requested (optional). Summary Table 2 in de Jong et al. (2010) is useful for a quick overview of effects and should be included. However, more details in a less aggregated form have been provided in the study summary in order to allow for a transparent evaluation.
10	Effect classification	For the effects, a classification is recommended on page 25, Table 5 of de Jong et al. (2010). However, the effect classes are not considered for the time being. It is optional to report them but if they are missing from the report it would not lead to a lowering of the reliability score. The proposal of using effect classes can be further considered in future development activities. (e.g. EFSA PPR Panel, 2015).

In addition, the following information was included in Appendix H from the EFSA report (EFSA Supporting publication 2019:EN-1673):

Footnotes and legend to Table 4 on page 22 of the guidance by de Jong et al. (2010):
The footnotes and legend for Table 4 on p. 22 are missing from the de Jong et al. (2010) guidance document. The information was received from the authors of the guidance. In order to facilitate the use of Table 4 of the guidance it is provided below:

* For Coccinellidae the remark has to be made that species from this taxon can populate a certain area relatively quickly as a result of the presence of aphids. When aphids are not present and abundant, Coccinellidae will not appear; this does not render the test directly unreliable, however this phenomenon should be taken into account when evaluating the study.
Legend:

'+' means that the taxon should be present and identified at the level specified, else the test is not sufficiently comprehensive to be of general validity. When '+' taxa are lacking in the specified agro-ecosystem addition of appropriate data, for example from other (laboratory) studies is needed to make the test reliable, otherwise the test is considered unreliable.
A '+/-' means that a taxon should be present in the south of Europe, but not necessarily in the north of Europe.
A '0' means that the test is less reliable (Ri 2) when sufficiently robust data at the indicated level of taxonomic precision are missing, but additional data are not required.
A '-' indicates that a specified taxon is generally not relevant for the specified cropping system(s).
'Off-crop' means non-cropped lands in the vicinity of agricultural fields, e.g. meadows or woodlands.

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 evaluation for non-target arthropods are included in Part B Evaluation, point 2.5.2 Impact on non-target species, point 2.5.2.4.

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 non-target arthropods are included in Part C Decision making, point 2.5.2 Impact on non-target species, point 2.5.2.4.

1.5 Developments

In March 2010 a follow-up of ESCORT II was organised, the ESCORT III workshop. It is expected that the risk assessment will change on certain points. The report from this workshop is expected to be input for the revision of the Guidance Document on Terrestrial Ecotoxicology (Sanco/10329/2002). This revision is taking place at this moment (by EFSA), and the following EFSA opinion was published on the science behind the upcoming revison: Scientific opinion addressing the state of the science on risk assessment of plant protection products for non-target arthropods (EFSA Journal 2015; 13(2):3996) .

II NON TARGET PLANTS

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 .

Notifiers preparing an assessment report for active substances need to comply with the relevant guidance, instructions and format laid down in the EFSA Administrative guidance on submission of dossiers and assessment reports for the peer-review of pesticide active substances.

1.1 Introduction

This chapter describes the risk assessment of plant protection products for terrestrial non-target plants. Terrestrial non-target plants are plants positioned outside the treated field without being a crop.

Terrestrial non-target plants play an important role in the ecosystem. This is why plant protection products should cause no unacceptable and prolonged effects on terrestrial non-target plants. The risk to terrestrial non-target plants must be evaluated if there is a chance of exposure of such plants.

Guidelines for the evaluation of the risk to terrestrial non-target plants are given in the Guidance Document on Terrestrial Ecotoxicology (Sanco/10329/2002 rev 2 final) .

The decision tree with corresponding explanatory notes is presented in Appendix 2. These decision trees summarise the decision scheme for terrestrial non-target plants.

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 [2] a dossier that meets the provisions laid down in Commission Regulation (EU) No 283/2013 and 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 data requirements regarding the risk of the active substance for non-target plants are described in Commission Regulation (EU) No 283/2013, point 8.6 (effects on terrestrial non-target higher plants).

Point 8.6 consists of the following data requirements:
8.6.1: Summary of screening data
8.6.2: Testing on non-target plants

1.2.2 Data requirements for the product

The data requirements regarding the risk of the plant protection product for non-target plants are described in Commission Regulation (EU) No 284/2013, point 10.6 (available data from biological primary screening in summary form).

Point 10.6 consists of the following data requirements:
10.6.1: Summary of screening data
10.6.2: Testing on non-target plants
10.6.3: Extended laboratory studies on non-target plants
10.6.4: Semi-field and field studies on non-target plants

1.2.3 Data requirements for metabolites

Standard laboratory tests are normally not required for metabolites. Exceptions may be formed by metabolites that are the actually active molecule. See the general part about metabolites as described in §1.2.3 of Chapter 7 Ecotoxicology; Terrestrial; Birds and mammals for general guidance. Where higher tier studies have been carried out with the pesticide under realistic exposure conditions, it may be assumed that the potential risk of metabolites has been taken into account.

1.3 Risk assessment

The risk assessment methodology for non-target plants has in EU context been elaborated in the Guidance Document on Terrestrial Ecotoxicology (Sanco/10329/2002 rev 2 final) .

Each study is summarised and analysed separately. The final conclusion and the endpoint per aspect (such as ER_{50}) are presented in a list of endpoints. Risk is assessed against these endpoints.

In Appendix 2 to this chapter, a risk assessment scheme for non-target terrestrial plants is included.

There are a few issues which need some more explanation, because it is not described clearly in the Guidance Document on Terrestrial Ecotoxicology:

- *Use of MAF*
  In the EFSA technical report: Outcome of the pesticides peer review meeting on general recurring issues in ecotoxicology, December 2015, the following is agreed regarding the use of a MAF in the risk assessment for Non-target Terrestrial Plants. Note that this is only valid for EU assessments (DAR/RAR):

  It was agreed that, from a scientific point of view, there is a logical reason to account for multiple applications in the risk assessment for NTTP. There were various approaches as to how this could be considered (i.e. foliar or soil default values of ESCORT II or EFSA PPR Panel (2014)). However, the experts could not agree which approach should be applied to the risk assessment and it was noted that currently different MAF values were being used by different RMS's (i.e. no harmonised approach). Therefore, it was agreed that for the risk assessment of active substances, no MAF values should be used by default, until a guidance document is developed.

- *Species Sensitivity Distribution: Acceptability criteria HC5*
  If an SSD is run, the data normality must be accepted at no less than 0.05 significance level to be acceptable for use in RA (look under "goodness-of-fit"). Modelling which does not pass at least this level (i.e. only passes at 0.025 or 0.01) indicates a poor fit for the data and a less reliable outcome[1]. This also in line with the current agreement in the draft NTP guidance.

  - *Phytotoxicity*
    In the EFSA technical report…….. the issue of phytotoxicity was raised. In addition to seedling emergence, OECD T 208 (OECD 2006a) and vegetation and vigour, OECD TG 227 (OECD 2006b), other variables, such as visual phytotoxicity, and sometimes shoot length, are evaluated according to these respective guidelines. ERX values for visual observations (also referred to as 'visible detrimental effects' or 'visual injury', such as chlorosis, necrosis, wilting, leaf and stem deformation) could be determined, where a dose–response relationship is available, but this is not often the case. The experts at the meeting discussed the relevance of using this endpoint in the Tier 1 risk assessment. The experts considered that effects on growth may also cover the phytotoxicity endpoint, which may be subjective being based on visual assessment. However, it was noted that the EFSA PPR Panel (2014) reported that for a significant number of cases this endpoint was reported as being lower than the others. Therefore, considering that the endpoint is part of the test guidelines and that the data requirements do not specify the parameters to define the endpoint for risk assessment, the experts concluded that the ECX based on phytotoxicity should be reported in the study summary and in the list of endpoints. Where the derived endpoint is the lowest of those available, it should be considered for the Tier 1 risk assessment. Such an interim solution should be reflected in the (European Commission, 2002) document and its implementation should be further considered.

Further elaborations of the EU evaluation methodology:

Combination toxicity

Combination toxicity must be determined when plant protection products contain several active substances. The issue of combined toxicity is further described in Appendix A.

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] As the significance level decreases (and the critical value increases), it becomes less and less probable that the sample derives from a normal distribution.

1.4.2 Evaluation of plant protection products

The evaluation, as applied for the risk assessment for non-target plants, has been elaborated in the Guidance Document on Terrestrial Ecotoxicology (Sanco/10329/2002 rev 2 final).

1.4.3 Decision making for plant protection products

Decision making, as applied in the risk assessment for non-target plants, has been elaborated in the Guidance Document on Terrestrial Ecotoxicology (Sanco/10329/2002 rev 2 final).

1.5 Developments

Revision of the Guidance Document on Terrestrial Ecotoxicology (Sanco/10329/2002 rev 2 final) is taking place at this moment (by EFSA), and the following EFSA opinion was published on the science behind the upcoming revision: Scientific Opinion addressing the state of the science on risk assessment of plant protection products for non-target terrestrial plants (EFSA Journal 2014; 12(7): 3800).

2 REFERENCES

1. Candolfi MP, Barrett KL, Campbell PJ, Forster R, Grandy N, Huet MC, Lewis G, Oomen PA, Schmuck R and Vogt H (eds) (2001): Guidance document on regulatory testing and risk assessment procedures for plant protection products with non-target arthropods. From the ESCORT 2 workshop. SETAC, Pensacola, 46 p

2. De Jong et al. (2010). Guidance for summarising and evaluating field studies with non-target arthropods. RIVM report 601712006.

3 APPENDICES

Appendix 1 Explanatory notes decision tree risk to non-target arthropods

1) A distinction is made between integrated and non-integrated pest management systems because the evaluation for non-target arthropods for these two types of systems is essentially different. In the case of integrated pest management systems natural enemies are deliberately brought into the cropping system to control pests. In the case of non-integrated pest management systems the risk is estimated for non-target arthropods that are present by nature. The scheme for non-integrated systems is dealt with in this chapter. The scheme for integrated pest management systems is included in Appendix 1 to the NL-part of this chapter.

2) The applicant should always submit data about the risk to non-target arthropods if there is a chance of exposure of these organisms (question 283/2013 8.3.2 and 284/2013 10.3.2). In case of applications on the soil and on crops there is practically always chance of exposure. It should be noted that some species have overwintering larvae in the soil, which, if relevant, must be taken into account in the risk assessment as well.
The chance of exposure is low in case of application of products for sealing and healing of pruning wounds.

3) The first step consists of the performance of glass plate tests with the standard test organisms *Aphidius rhopalosiphi* and *Typhlodromus pyri*, preferably dose-response tests so that an LR50 value can be established. When, however, a low toxicity is expected, limit tests can also be carried out with a dose that is equal to the maximum use dose multiplied by the Multiple Application Factor (MAF). These tests should normally be carried out with the formulation. For determination of the MAF reference is made to the ESCORT 2 report [1].

4) The standard species mentioned above are not suitable for formulations such as granules, seed dressings, baits and IGRs (Insect Growth Regulators) in view of:
   - technical reasons: laboratory glass plate tests with the two standard species cannot be carried out with granular formulations, seed dressings and baits;
   - the fact that effects cannot be detected in a standard laboratory test with the standard species as result of a different mode of action (e.g. an acute laboratory test with an Insect Growth regulator (IGR) on *A. rhopalosiphi* will probably not show any effect).

   The approach described in the Guidance Document on Terrestrial Ecotoxicology (Sanco/10329/2002 rev 2 final) is followed for these types of products:
   - for products which are applied into the soil (e.g. granules, seed dressings, baits) studies should be carried out with *Hypoaspis aculeifer* or *Folsomia candida*. When considered suitable, studies can be carried out with *Aleochara sp.* (N.B. test compound should be mixed into the soil).
   - For products which are applied on (bare) soil, tests with several soil (surface) dwelling species are acceptable (e.g. *Hypoaspis aculeifer*, *Folsomia candida, Aleochara bliineata, Poecilus cupreus, Pardosa sp.).*
   - For IGRs and other plant protection products with a special mode of action the tests should be concentrated on those stages of non-target arthropods that are sensitive to the plant protection product in question (e.g. juvenile stages) while taking relevant absorption routes into account. Tests must be carried out with *Typhlodromus pyri* and one other species (e.g. *Coccinella septempunctata*, *Orius laevigatus* or *Chrysoperla carnea*).

There are several examples of special applications such as drenching treatments, application via drip irrigation, etc. Such cases should be dealt with pragmatically, which means that it should be considered case by case which types of organisms are exposed and in which way the test can be conducted.

Except for the active substance and the product, data are also required for metabolites to which non-target arthropods may be exposed. Arthropods may be exposed to metabolites in/on plants and to metabolites in the soil. For metabolites in vegetation standard laboratory tests are normally not required. Metabolites that are the actually active molecule may be exceptions. General guidance is given in the general part about metabolites as described under 'birds and mammals'.
Where higher tier studies (cage/tent/tunnel or field tests) have been carried out with the pesticide under realistic exposure conditions it can be assumed that the potential risk of metabolites has been taken into account.
Soil metabolites are tested with soil organisms; tests with surface dwelling soil arthropods are therefore not required.

5) A Hazard Quotient (HQ) must be calculated for both standard species and both the 'in-field' risk as well as the 'off-field' risk are taken into account. For the method according to which the 'in-field' and 'off-field' exposure must be calculated we refer to the Guidance Document on Terrestrial Ecotoxicology, on the understanding that for national risk assessments NL-specific drift figures are used for calculating the 'off-field' exposure, for which we refer to §2.3 (NL-part).

Note on correction factor 0.5 from ESCORT 2 for the in field exposure calculation for orchards and vineyards:

- This correction factor can be used in the exposure calculation for the HQ when the effect endpoint is based on a 2D-test (i.e. glass plate or leaf disc). If the test is in a '3D-system', i.e. spraying of whole plants, the correction factor is not applicable.
- This factor can only be used for orchards and vineyards (but not other '3D crops' such as e.g. tomatoes).

Note on VDF (vegetation distribution factor) for the off-field exposure calculation:
In the Pesticides Peer review Meeting on Recurring Issues on Ecotoxicology held in 2019 (EFSA Supporting publication 2019:EN-1673), the experts agreed that the VDF value should be changed as better data are now available. It was recommended that a VDF value of 5 is applied for all the tiers of the assessment as an interim solution. (This applies to EU active substance dossiers submitted from 7 July 2019 and national product assessment submitted from 1 january 2020.)

The criterion for both HQ values is that these should be lower than 2 (or effects in limit tests <50%). This criterion is based on available (semi-) field data where lethal, sublethal and reproduction endpoints have been measured for a considerable number of types of substances and species. This means that this first step in the evaluation (in which the criterion HQ < 2 is applied) also covers sublethal and reproduction effects and it is not necessary to separately consider sublethal and reproduction endpoints in the first step of the evaluation.

Where also other species than *Aphidius rhopalosiphi* and *Typhlodromus pyri* have been tested in first tier laboratory tests, these cannot be tested against the HQ trigger of 2 because this trigger has only been validated for Aphidius and Typhlodromus.
The results of these tests will be assessed against the criterion of 50% effect (or HQ of 1,

if LR50 and ER50 values are available).

When it concerns tests with the soil organisms *Hypoaspis aculeifer* and *Folsomia candida*, the NOEC (mg/kg soil) is the relevant endpoint. For risk assessment a safety factor of 5 is applied. In the case that artificial soil is used in the test, correction for the percentage of organic matter is necessary (if log Kow > 2).

Off-crop interception:
In cases that only exposure of soil dwelling species is relevant (for example when a reasoned case is made that soil surface spiders are the most sensitive species), interception by the off-crop vegetation may be taken into account in the off-field risk assessment.
For the time being the following interception percentages are applied - till better underpinned percentages come available - which are considered realistic worst-case:
- December – February: 20%
- March: 30%
- April: 40%
- May – September: 50%
- October: 40%

It should be noted that when these percentages are taken into account, the vegetation distribution factor cannot be used in the HQ-calculation (off-field).

6) Where the HQ values are $\geq$ 2 and suitable or desirable risk reduction measures 'in-field' and/or 'off-field' are not possible, higher tier tests must be carried out. First, the sensitive species for which the HQ value is $\geq$ 2 should be studied in such a higher tier test where extra species are tested: in case that only the HQ for the 'in-field' risk estimate is exceeded, one extra species must be tested; in case the HQ for 'in-field' as well as 'off-field' is exceeded, two extra species. The preferred species are: *Orius laevigatus*, *Chrysoperla carnea*, *Coccinella septempunctata* and *Aleochara bilineata* in view of the fact that the available data indicate that these organisms are relatively sensitive and that good test methods are available. The species *Aleochara bilineata* should in any case be used for products that are applied early in the season and where products are applied on the soil.

Higher tier tests concern extended laboratory tests (with natural substrate) and (semi) field tests. 'Aged-residue' tests also come under the higher tier tests. These tests can be used for establishing the duration of the effect in view of the possible recovery of populations by recolonisation. See also note 7) below.

If the only available data are extended laboratory tests with *A. rhopalosiphi* and *T. pyri*, tests with two additional species will be required, irrespective of the acceptability of the risk for *A. rhopalosiphi* and *T. pyri.* The reason for this is that in this case no first tier risk assessment can be performed to establish the requirements for additional species.

It should be noted that generally, in-crop field studies are considered not acceptable to address off-crop risks. When a field study is chosen as approach to address the off-crop risk to non-target arthropods, it should be demonstrated in this study that no unacceptable effects on a non-target arthropod community that is representative for fauna of off-crop habitats in The Netherlands (e.g. meadow, hay field or (agricultural) verge) will occur as a result from drift exposure. Studies conducted in e.g. Northern France and Germany are also considered representative for The Netherlands. Preferably a multi-dose rate (NOEC) design is used. Before such a study is undertaken, the study protocol may

be discussed with the Ctgb.

If an in-crop field test is performed to address an in-crop risk, and *A. rhopalosiphi* and *T. pyri* do not occur in the crop of concern, it is acceptable that these species are not present in the study, as long as a representative fauna for this crop is present.

Further guidance on the evaluation of arthropod field studies can be found in De Jong et al. (2010) (Guidance for summarising and evaluating field studies with non-target arthropods. RIVM report 601712006/2010).

For 'in-field' and 'off-field' the following risk reducing measures are among the options:

'in-field':
- reduction of the dose level;
- changes in application frequency and application interval;
- changes in timing of the application.

'off-field':
- measures that reduce the amount of drift to the area outside the crop such as:
. buffer zones;
. wind hedges:
. drift-reducing application techniques.

7) The risk is unacceptable if the effects found in the extended laboratory tests are equal to or higher than the trigger value (trigger value is 50%[2]) and there is no potential (rapid) recovery or recolonisation. When risk-mitigating measures neither lead to an acceptable risk to non-target arthropods, the product cannot be authorised.

The criterion for (potential) recovery or recolonisation for 'in-field' is that this must be the case before the following spraying season. The period for 'off-field' is shorter, for the time being without a specific definition. The Guidance Document on Terrestrial Ecotoxicology (Sanco/10329/2002 rev 2 final) mentions an ecologically relevant period. It should be noted however, that under the new data requirements, aged residue tests can no longer be used for the off-field risk assessment. This means that for the off-field risk assessment, off-field field studies demonstrating no effects or actual recovery should be provided. Ctgb is of the opinion that the 'ecologically relevant period' should be very short, because the off-crop area is important for recolonisation of species into the in-field area. Hence, a relatively undisturbed off-crop area is necessary to make recolonisation possible (recolonisation of the in-field area from the off-crop area can cause source-sink effects, which is an additional stress-factor tot the off-crop area).

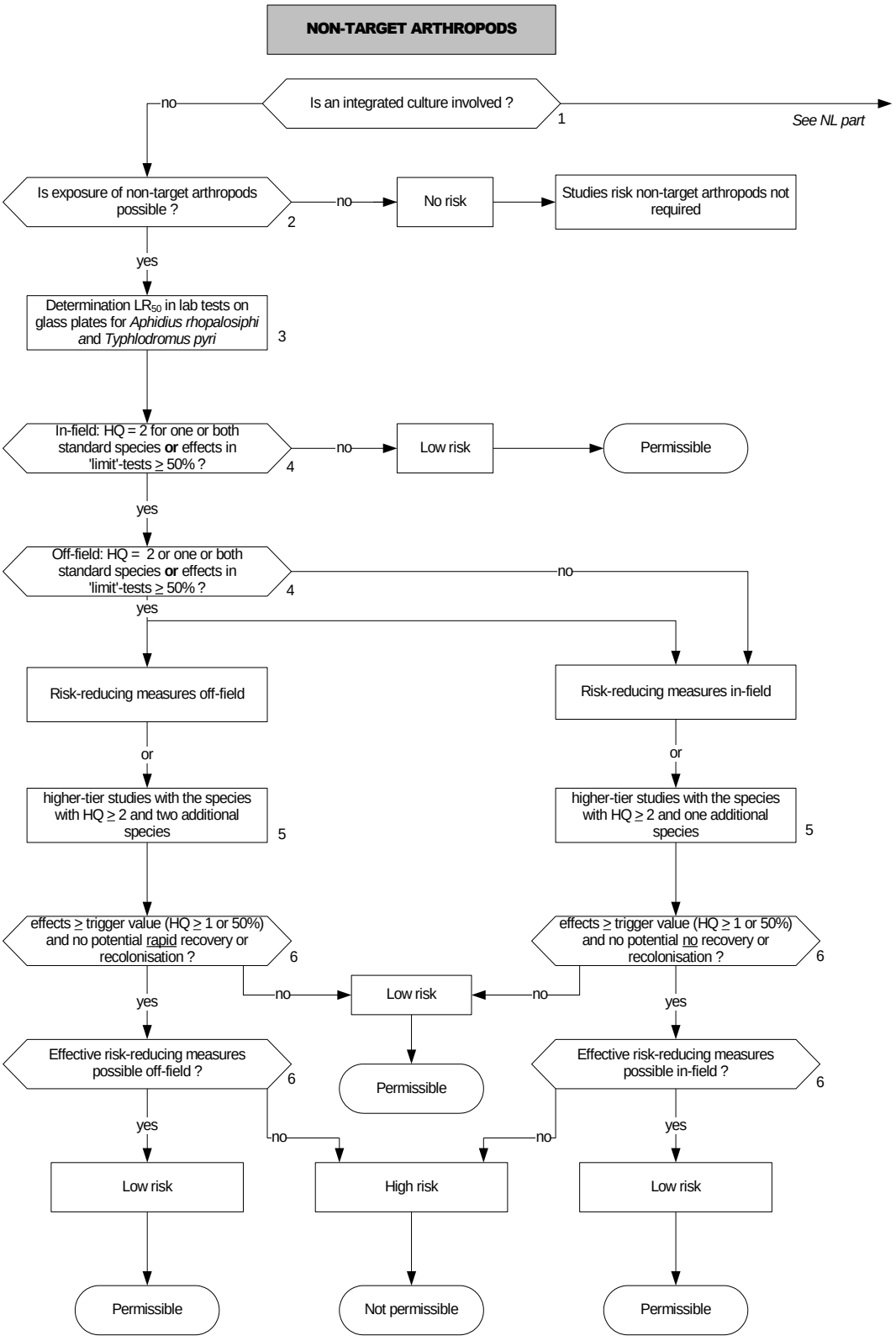
For field tests, ESCORT 2 does not provide fixed trigger values for acceptability of effects. As clear guidance on the use of the endpoints from this type of studies is currently lacking, the recommendation in the proceedings from the ESCORT 3 workshop (2010) is followed for the off-field risk assessment:
At the level of field studies, the no observed effect rate (NOER) community and the no observed ecologically adverse effect rate (NOEAER) population (effects of limited magnitude and duration) should be used for the off-field risk assessment.

[2] The trigger value of 50% can be considered equal to an HQ value of 1, provided that only mortality effects occur and no sublethal effects. In case sublethal effects are found, ER50 can be determined and tested against the HQ trigger of 1.

To further specify ‘effects of limited magnitude and duration’, Ctgb considers this to be ‘slight and transient effects’ cf. Effect Class 2 in the Guidance for summarising and evaluating field studies with non-target arthropods (De Jong et al. , 2010) [2], taking into account what is said above about the duration of the ecologically relevant period. In De Jong et al. (2010), Class 2 effects are defined as: Quantitatively restricted response of one or a few taxa and only observed on one sampling occasion.

For the in-field risk assessment, if in- field field studies are available, recovery before the start of the next spraying season should be demonstrated. This applies to Effect Class 6 or lower from de Jong et al. (2010).

However, it is noted that in the Pesticides Peer review Meeting on Recurring Issues on Ecotoxicology held in 2019 (EFSA Supporting publication 2019:EN-1673), the experts concluded that the effect classes from De Jong et al. (2010) are not considered for the time being. It is optional to report them but if they are missing from the report it would not lead to a lowering of the reliability score. The proposal of using effect classes can be further considered in future development activities. (e.g. EFSA PPR Panel, 2015).


NON-TARGET ARTHROPODS
Is an integrated culture involved ?
1
no
See NL part
Is exposure of non-target arthropods possible ?
2
no
No risk
Studies risk non-target arthropods not required
yes
Determination LR50 in lab tests on glass plates for Aphidius rhopalosiphi and Typhlodromus pyri
3
In-field: HQ = 2 for one or both standard species or effects in 'limit'-tests ≥ 50% ?
4
no
Low risk
Permissible
yes
Off-field: HQ = 2 or one or both standard species or effects in 'limit'-tests ≥ 50% ?
4
no
yes
Risk-reducing measures off-field
Risk-reducing measures in-field
or
or
higher-tier studies with the species with HQ ≥ 2 and two additional species
5
higher-tier studies with the species with HQ ≥ 2 and one additional species
5
effects ≥ trigger value (HQ ≥ 1 or 50%) and no potential rapid recovery or recolonisation ?
6
effects ≥ trigger value (HQ ≥ 1 or 50%) and no potential no recovery or recolonisation ?
6
no
Low risk
no
yes
yes
Effective risk-reducing measures possible off-field ?
6
Permissible
Effective risk-reducing measures possible in-field ?
6
yes
no
no
yes
Low risk
High risk
Low risk
Permissible
Not permissible
Permissible

Appendix 2 Explanatory notes decision tree risk to terrestrial non-target plants

1) Definition: terrestrial non-target plants are plants positioned outside the field to be treated without being a crop.

2) Data on the risk to terrestrial non-target plants are not always required. Where exposure is negligible, no data need to be submitted, e.g., in the case of:
   - Rodenticides
   - Seed treatments
   - Granules
   - Bulb dipping
   - Drenching treatment
   - Substances used to cover and cure pruning wounds
   - Substance that are used in stored products

3) This step is based on the already available data, with a preference for screening data. Data on at least 6 species of different taxa tested with the highest nominal dose (1x) should be available. These species should cover monocotyledonous as well as dicotyledonous species. Besides these data, further information available in the biological dossier or obtained from various field experiments such as efficacy studies, residue studies, environmental-behavioural and ecotoxicological studies about efficacy, selectivity, phytotoxicity etc. can be provided.
   This first step can be skipped for herbicides and plant growth regulators because these substances will as result of their envisaged effect on plants always reach the second step.

   The criterion is that the risk can be considered as acceptable where no data indicate that one or more species experience more than 50% phytotoxic effects at the maximum dose level. If the results show that there is more than 50% effect for one species or that there are clear indications of effects on more than one species, additional research needs to be carried out.

4) Where a potential risk is identified (more than 50% effect for one or more species at the maximum dose), specific information must be submitted about the toxicity of the substance for terrestrial plants. These are laboratory experiments on a selection of plants. It is strongly recommended to conduct dose-response tests with 6 –10 plant species representing families for which significant herbicidal effect is claimed.
   These tests should resemble realistic exposure conditions as much as possible. For applications on leaves, e.g., the tests must be carried out by spraying the pesticide on the plant. Application on soil should be carried out where this is more suitable in view of the mode of action.

   Tests must be carried out with the formulations.
   Suitable test protocols are available: OECD guideline 208 (Seedling emergence and seedling growth test) and OECD guideline 227 (Vegetative vigour test).

5) This step consists of a quantitative risk assessment according to the exposure/effect approach. Exposure as well as effect are expressed in application dose (g/ha).
ER50 values (ER50 = the dose at which 50% effect is observed) are available from the plant tests as mentioned under step 2 of the data requirements. There are two possible approaches for the risk assessment: the deterministic approach and the probabilistic approach. The most suitable approach depends on the dataset.

Deterministic approach
In the deterministic approach the toxicity of the most sensitive species is taken as starting point for the effect. Where the ratio toxicity/exposure is higher than 5, the risk is considered acceptable. This trigger value of 5 is valid where data on at least 6 plant species are available. In case data on significantly more than 6 plant species are available, this trigger value may –where appropriate – be adjusted slightly upward (expert judgement).

Probabilistic approach
Probabilistic methods in which the 'species sensitivity distribution' (SSD) is used may in principle be applied because data on 6 – 10 species are available. This approach requires a log-normal or a differently defined type of distribution of the data. If a SSD is run, the data normality must be accepted at no less than 0.05 significance level to be acceptable for use in RA (look under "goodness-of-fit"). Modelling which does not pass at least this level (i.e. only passes at 0.025 or 0.01) indicates a poor fit for the data and a less reliable outcome[3]. This also in line with the current agreement in the draft NTP guidance. In case the ER50 for at least 95% of the species (HR5) is above the highest estimated exposure level, the risk to terrestrial non-target plants is considered acceptable. If not, the risk is high.

The initial exposure of non-target plants should be determined at the following distances from the centre of the last crop row:
- field crops (including "soft fruit" and bush and hedge shrubbery) and soil applications, as in the case of herbicides: 2 m (1 m from the edge of the parcel) (evaluation zone 1.5 – 2.5 m);
- 3 m for large fruit (evaluation zone 2.5 – 3.5 m);
- 5 m for lane trees (evaluation zone 4.5 – 5.5 m).

For these distances the following drift percentages apply in the Netherlands:
- outdoor field cultures and soil applications: 4.7%;
- large fruit: 37% before 1 May; 15.9% after 1 May (the latter value (15.9%) is also used for grapes and small fruit (irrespective of application time).;
- lane trees: high lane trees: 11.9%; spindle trees ('spillen') (closely spaced): 1.8% and transplanted trees ('opzetters') (widely spaced): 6.3%. These percentages are in case of a crop-free zone of 5 m (LOTV)).

Where the crop free zones exceed the standard distances from the centre of the last crop row mentioned here, the 'off-field' area only starts after the crop-free zone and the drift percentage must be determined at a distance as large as the crop-free zone.
Where natural objects have been placed to reduce the amount of drift (e.g. a wind hedge) this object should not be considered as part of the off-field area that needs to be protected. It must be kept in mind that those crop-free zones and natural objects in many cases are only applied on those parts of parcels which borders watercourses. Protection

[3] As the significance level decreases (and the critical value increases), it becomes less and less probable that the sample derives from a normal distribution.

of non-target terrestrial plants is needed for all sides of a parcel.

In cases that only exposure by the soil is relevant (e.g. when an active substance has only adverse effects on pre-emergence stadia of non-target plants), some interception by the off-crop vegetation may be taken into account. For the time being the following interception percentages are applied - till better underpinned percentages come available - which are considered realistic worst-case:
- December – February: 20%
- March: 30%
- April: 40%
- May – September: 50%
- October: 40%

If a plant protection product contains several active substances, the combination toxicity must be determined as well as for combinations of plant protection products of which the combination (tank mix) is recommended in the directions for use.

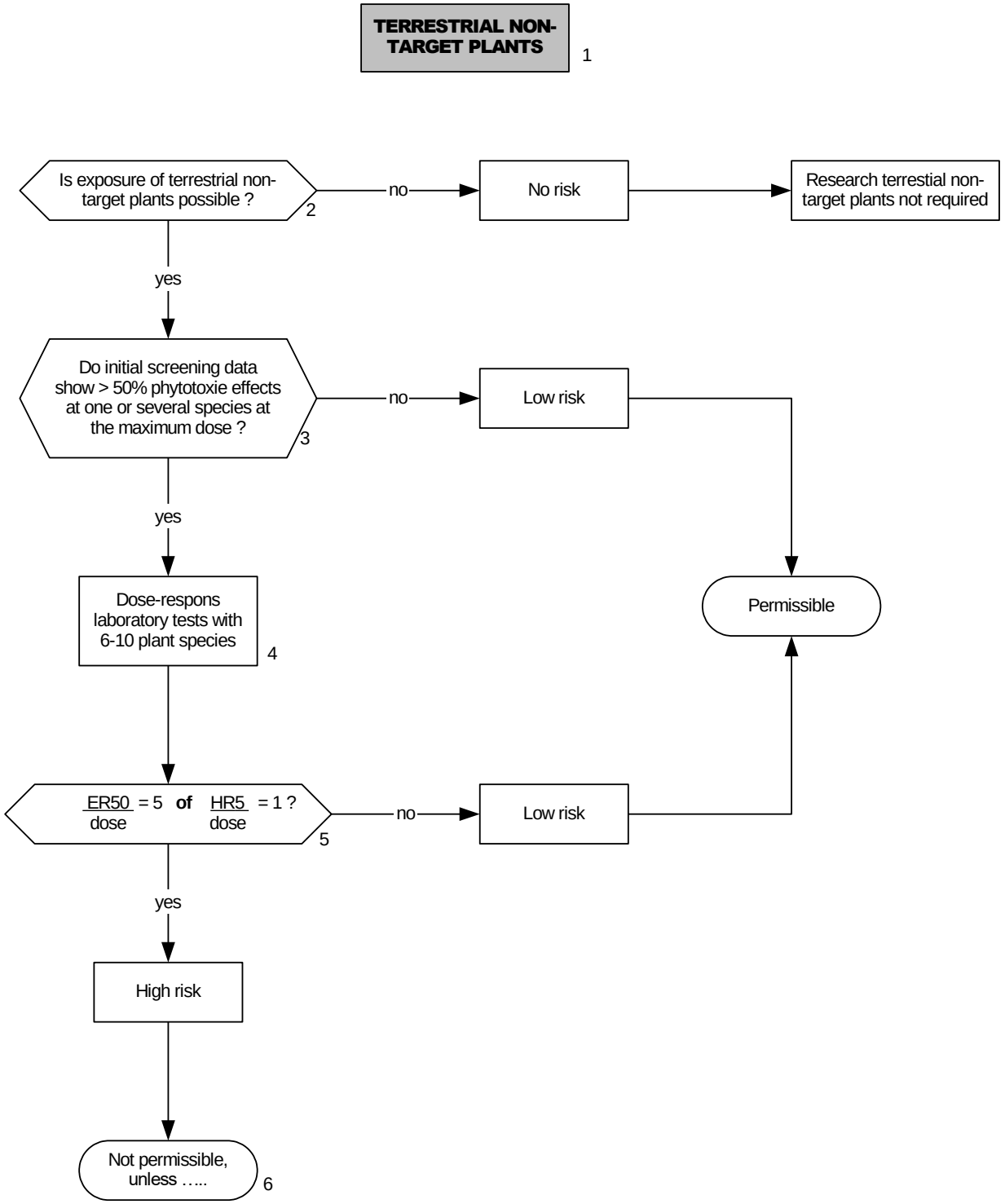
For the acute risk assessment, the combination toxicity on the basis of the tests with the product are compared with the combination toxicity on the basis of toxicity research with the separate active substances. The risk of combination products is determined on the basis of the lowest TER as calculated based on the toxicity of the separate active substances or the toxicity of the product.

The combination toxicity is determined on the basis of concentration addition. For the calculation method see Appendix A.

6) Where on the basis of the previous step a high risk is concluded to exist, the use is not permissible unless it can be demonstrated by means of adequate risk evaluation that there are no unacceptable direct or indirect effects for terrestrial non-target plants.

An adequate risk evaluation may consist of the performance of a (semi) field study to investigate the effects on non-target plants under realistic application conditions. Because such studies take a long time and are expensive, it is recommended to investigate whether options exist for refinement of the exposure and/or effects. In addition, (semi) field studies are not required if the risk identified in step 2 can sufficiently be reduced by means of risk-mitigating measures.
Field and semi-field studies with non-target plants have not been standardised.
It is therefore recommended to contact the Ctgb beforehand to discuss the protocol.
Generally, it can be stated that in such tests effects on plant abundance and biomass production at different distances from the crop or at exposure levels representing exposure at different distances from the crop, need to be analysed.

Because the exposure of terrestrial non-target plants is mainly caused by drift of pesticides, possible measures to reduce the risk to these plants are based on reduction of the amount of drift. In principle, all already existing drift-mitigating measures can be applied. The drift reduction of drift reducing measures, which are easy to realise in practice are mentioned in paragraph 2.3 of the NL part.


TERRESTRIAL NON-TARGET PLANTS
1
Is exposure of terrestrial non-target plants possible ?
2
no
No risk
Research terrestial non-target plants not required
yes
Do initial screening data show > 50% phytotoxie effects at one or several species at the maximum dose ?
3
no
Low risk
yes
Dose-respons laboratory tests with 6-10 plant species
4
Permissible
ER50 / dose = 5 of HR5 / dose = 1 ?
5
no
Low risk
yes
High risk
Not permissible, unless …..
6