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; bees

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ctgb

Board for the Authorisation of plant protection products and biocides

Chapter 7 Ecotoxicology; terrestrial; bees

Category: Plant Protection Products

Changes in the Evaluation Manual

Evaluation manual PPP EU part Chapter 7 Terrestrial; bees			
Version	**Date**	**Paragraph**	**Changes**
2.1	October 2016		New situation in the updated E.M.
			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.
			Formatting changes. Updating references to Regulation (EC) No 1107/2009
			More detailed information about the risk assessment.
2.2	January 2020		Update to discuss the new EU MRL honey guidance and give guidance on how to use chronic data in the risk assessment of products.
		1	Sentence included on the administrative EFSA guidance
2.3	July 2021	1.3	Note on active substances with a mode of action aimed at suffocation of the target organisms included.
2.4	February 2022	1.3	Note on active substances with a mode of action aimed at suffocation of the target organisms removed (until further guidance is available).

GENERAL INTRODUCTION

This chapter briefly describes the data requirements for estimation of the effects on bees 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.

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 bees. Honeybees are economically important and they are also an important indicator of negative effects on the environment. This means that, apart from a clear economic purpose, the risk assessment for bees also serves to avoid allowing products which present an unacceptable risk to the environment to reach the market. The risk to bees must be evaluated if there is a chance of exposure of these organisms.

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 of the Evaluation Manual (§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 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.

Guidelines for the risk evaluation for bees are given in the Guidance Document on Terrestrial Ecotoxicology (Sanco/10329/2002 rev 2 final). This document refers to EPPO guidelines. The most recent version of this concerning tests on bees is the standard on the conduct of trials for the evaluation of side-effects of plant protection products on honeybees (PP1/170) (first published in 1991, the latest revision in 2010).

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 bees are described in point 8.3.1 (effects on bees) of part A (for chemical active substances) of Commission Regulation (EU) No 283/2013.

Point 8.3.1 consists of the following data requirements:
8.3.1. Effects on bees
8.3.1.1. Acute toxicity to bees
8.3.1.1.1. Acute oral toxicity
8.3.1.1.2. Acute contact toxicity
8.3.1.2. Chronic toxicity to bees
8.3.1.3. Effects on honeybee development and other honeybee life stages
8.3.1.4. Sub-lethal effects

These points should always be addressed for honeybees. Tests on other bee species may be submitted as well.

Several bee testing guidelines have recently been developed under the auspices of the OECD, e.g. on bumblebee acute toxicity (OECD Test No. 246 and 247), chronic toxicity to adult honeybees (OECD Test no. 245) and honeybee larval toxicity. For larvae, the multiple exposure test (OECD unclassified Guidance Document No. 239) is preferred over the single exposure test (OECD Test No. 237). Acute test guideline development on the solitary bee *Osmia* spp. is underway and a draft guideline is expected to be available on the OECD website in the near future. Where final (harmonized) versions are available, these should be used. Tests performed according to draft versions may be accepted for the risk assessment as long as the deviations from the final guideline are not expected to have severely impacted the outcome of the test (to be determined on a case-by-case basis).

1.2.2 Data requirements for the product

The data requirements regarding the risk of the plant production product for bees are described in point 10.3.1 (effects on bees) of part A (for plant protection products) of Commission Regulation (EU) No 284/2013.

Point 10.3.1 consists of the following data requirements:
10.3.1. Effects on bees
10.3.1.1 Acute toxicity to bees
10.3.1.1.1 Acute oral toxicity
10.3.1.1.2 Acute contact toxicity
10.3.1.2 Chronic toxicity to bees
10.3.1.3 Effects on honey bee development and other honey bee life stages
10.3.1.4 Sub-lethal effects
10.3.1.5 Cage and tunnel tests
10.3.1.6 Field tests with honeybees

These points should always be addressed for honeybees. Tests on other bee species may be submitted as well.

Several bee testing guidelines have recently been developed under the auspices of the OECD, e.g. on bumblebee acute toxicity (OECD Test No. 246 and 247), chronic toxicity to adult honeybees (OECD Test no. 245) and honeybee larval toxicity. For larvae, the multiple exposure test (OECD unclassified Guidance Document No. 239) is preferred over the single exposure test (OECD Test No. 237). Acute test guideline development on the solitary bee *Osmia* spp. is underway and a draft guideline is expected to be available on the OECD website in the near future. Where final (harmonized) versions are available, these should be used. Tests performed according to draft versions may be accepted for the risk assessment as long as the deviations from the final guideline are not expected to have severely impacted the outcome of the test (to be determined on a case-by-case basis).

1.2.3 Data requirements for metabolites

Standard laboratory tests are normally not required for metabolites. Exceptions may be cases where for example the metabolite is the pesticidal active molecule. See the general section about metabolites as described in §1.2.3 of Chapter 7 Ecotoxicology; terrestrial; Birds and mammals for general guidance. Where higher tier studies (cage/tent/tunnel or field tests) 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 bees has in EU context been elaborated in the Guidance Document on Terrestrial Ecotoxicology (Sanco/10329/2002 rev 2 final). This document refers to EPPO guidelines. The most recent version of this concerning the risk assessment for bees is EPPO Series PP 3 Environmental Risk Assessment Scheme for Plant Protection products – Chapter 10: Honeybees (first published in 1993, the latest revision in 2010). This is used by Ctgb for the risk assessment of active substances and plant protection products.

In addition, active substances for which the dossier is submitted after September 2015 will be evaluated according to the first tier of the EFSA Guidance Document on the risk assessment of plant protection products on bees (*Apis mellifera, Bombus* spp. and solitary bees) (EFSA Journal 2013;11(7):3295). This was agreed in a general ecotoxicology meeting, Pesticide Peer Review Meeting 133 which took place from 23 to 25 September 2015. The EFSA guidance document on bees has not been noted at the EU level yet. Nevertheless, as explained in the report of the meeting, the current guidance documents do not cover honeybee larvae and chronic adult honeybee toxicity, while endpoints for these are available following the current data requirements. “In the absence of alternative approaches taken note by risk managers, it was recommended that the risk assessment to honeybees should be performed (first tier) according to EFSA (2013). For higher tier, the studies should be critically evaluated and considered in light of the issues raised in EFSA PPR Panel (2012) and EFSA (2013) with regard to the methodologies used. On the basis of all the available information, a conclusion should be drawn with regard to the risk to honeybees. For bumblebees and solitary bees, it was agreed that if any data are submitted, they should be evaluated. However, currently it cannot be recommended to routinely perform a risk assessment. Where data are not available and no risk assessment can be performed, this issue will be reflected in the EFSA conclusion.” As long as no further decisions have been taken at the risk management level on the relevant guidance for bees, Ctgb will follow this agreement for active substance evaluation (both for first evaluation and renewal) and will present two first tier risk assessments based on the two different guidance documents. However, we will not perform a risk assessment according to the new Guidance for larval toxicity in instances when only a one dose test is available, as the trigger value for larval toxicity in the new guidance is based upon an assumption of multiple exposures, and we therefore do not consider it appropriate to compare the single dose toxicity value with the multiple dose trigger.

For product assessments, the Ctgb follows a stepwise approach with regard to the chronic data:

1) The adult acute oral endpoint is compared with the chronic adult and larval endpoints (all LD(D)50-values, and all expressed *per day* taking into account the number of *exposure* days in the studies (i.e. not the study duration). If there is ≤5x difference, there is no indication of increased toxicity. If the difference is >5 or cannot be properly assessed due to >-endpoints, go to 2.
2) Are there higher tier data, and do these cover the chronic and larval exposure? If so, the risk assessment is based on the higher tier data and there is no need for exposure/toxicity calculations with the first tier endpoints. If not, or not adequate, go to

3).

3) a) For a seed or soil treatment, use the EPPO (2010) guidance to perform the chronic and larval risk assessments.
b) For spray treatments, calculate the chronic and/or larval risk according to the EFSA (2013, update 2014) Guidance for the bee species that you have data available for (normally honeybees only). While it is not yet noted, this guidance does give a conservative indication of the potential risk of the possible exposure routes. The outcome of this first tier assessment will be taken into account by Ctgb in a context-based approach to see if further data are necessary. The risk assessment should describe the relevance of the different routes for this particular crop in the Netherlands. The conclusion of the risk assessment will be based on a weight-of-evidence approach taking all the available data and information into account.

Each study is summarized and analyzed separately. The final conclusion and the endpoint per aspect (such as LD_{50}(oral)) are presented in a list of endpoints. The risk assessment is based on a comparison of exposure and toxicity, using a relevant trigger value.

Combination toxicity
Combination toxicity must be determined when plant protection products contain several active substances, and for tankmixes that are specified on the label. The issue of combined toxicity is further described in Appendix A.

Exposure routes
The risk assessment considers the potential risk to bees from exposure resulting from the use of the plant protection product according to the GAP. This clearly concerns exposure via the crop itself (from direct overspray and systemic uptake), but other exposure routes may also be relevant. The main exposure routes are highlighted below.

Exposure via flowering crops
On national level, an overview is given of the attractiveness of agricultural crops for honeybees for the collection of nectar and/or pollen (hereafter named the NL Bee List; see the NL part of Evaluation Manual for bees, appendix II-1). This document is used for identification of relevant crops for honeybee risk assessment. Moreover, this document is valuable for the understanding of risk mitigation sentences in which the phrase ‘bee-attractive crops’ is mentioned.
It is noted that per January 1st 2020, the guidance for determining the magnitude of pesticide residue levels in honey and setting Maximum Residue Levels in honey (SANTE/11956/2016 Rev. 9) is in force. While this guidance document is aimed at protecting humans from exposure to pesticides in honey, it has a link with the risk assessment for bees, in that it contains a list of melliferous crops (Appendix II of the honey MRL guidance, hereafter named MRL honey list).
The Ctgb has compared the two lists and found that, generally, the lists are in line: they either deem a crop attractive or not attractive to honeybees. Differences between the lists can usually be explained by one or more of the following:

a) The MRL honey list covers all crops for which an MRL is needed (according to Annex I Reg (EC) No 396/2005)), including imported crops (such as citrus and almond). The NL Bee List only contains crops which are grown in the Netherlands.
b) Crops grown for seed production are flowering per definition. The MRL honey list mentions per crop if it is considered attractive only when grown for seed production, while the bee list contains a specific category for seed production (‘Plant breeding crops and basic seed production for arable, vegetable and fruit crops, herbs and ornamental crops’).

c) Certain crops do not produce nectar, and are thus not relevant for honey production, but are still attractive to honeybees for their pollen.

Two differences cannot be easily explained: In the NL Bee List, rose is considered attractive to honeybees both for nectar and pollen, but it is not considered to be a melliferous crop in the MRL honey list. Conifer is not considered attractive to honeybees in the NL Bee List, but is considered to have melliforous capacity in the MRL honey list. These differences will be investigated. Until further notice, Ctgb will use the NL Bee List as published in the NL part of this Evaluation Manual as a basis for the risk assessment for bees.

Exposure via flowering weeds
In the first tier, it is assumed that bees may fly on flowering weeds in the field. In higher tier, information can be used about the likelihood of a large amount of flowering weeds in a crop under normal agricultural practice. If relevant, applicants should address this for all countries relevant for their application.

Off-field risk
Spray applications: In cases where in-field risk to bees has been determined, an off-field risk should be calculated using the drift values as used for the off-field risk assessment for non-target arthropods (see §1.3 of the EU part of Chapter 7 Ecotoxicology: terrestrial; non target arthropods). Seed treatments: A list indicating whether there is potential risk to bees from dust drift during sowing of treated seeds was developed in 2010 and is attached to the NL part of this Evaluation Manual.

Succeeding crops
Persistent and systemic substances may be present in nectar and/or pollen of succeeding flowering crops (including replacement crops). See §2.3.

Risk mitigation measures
If a potential risk is indicated, this may be addressed with additional data. Alternatively, it is often possible to address a potential risk with a restriction sentence on the instructions for use. As these sentences are member state specific, the Ctgb will mention only the generic intention of the sentences in the EU evaluation or the core dossier.

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 bees are included in Part B Evaluation, point 2.5.2.3.

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 bees are included in Part C Decision making, point 2.5.2.3.

1.5 Developments

In May 2012, the EFSA published their Scientific Opinion on the science behind the development of a risk assessment of Plant Protection Products on bees (*Apis mellifera*, *Bombus* spp. and solitary bees). A Guidance document for bees based on this scientific opinion was published by EFSA in 2013 and updated in 2014. To date, this guidance document has not been noted by the Standing Committee on Plants, Animals, Food and Feed (SCOPaFF) and it is thus not part of the official list from the European Commission of guidelines to be used for active substance and plant protection product approval. EFSA has received a mandate from the European Commission to revise certain parts of the Guidance Document and has published a work plan. The revision is ongoing and expected to be finalised in March 2021.

Ctgb notes that EFSA has published the document "Collection and analysis of pesticide residue data for nectar and pollen" which is expected to be incorporated in the revised guidance document.

While waiting for harmonized EU guidance, the NL has collated information to aid in the risk assessment for bees in the Netherlands, including:

- A list for all crops indicating whether they are attractive to honeybees was developed in 2011 and revised in 2015, and is attached to the NL part of this Evaluation Manual.

- A list indicating whether there is potential risk from dust drift during sowing of treated seeds was developed in 2010 and is attached to the NL part of this Evaluation Manual.

- A list indicating for which crops exposure via honeydew should be considered in the risk assessment was developed in 1997 and revised in 2018, and is attached to the NL part of this Evaluation Manual.

In early 2015 EFSA launched a major project with the aim of developing a holistic approach to the risk assessment of multiple stressors (including pesticides) in honeybees (MUST-B).