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

EU part

Plant protection products

Chapter 8 Efficacy

version 2.2 March 2019

ctgb

Board for the Authorisation of plant protection products and biocides

Chapter 8 Efficacy

Category: Plant Protection Products

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

Evaluation manual PPP NL part Chapter 8: Efficacy			
Version	**Date**	**Paragraph**	**Changes**
2.0	January 2014		None. Original document.
2.1	October 2016	entire document	There are no major changes regarding requirements for the efficacy dossier, but the document has been rewritten for clarity, and has been updated with links to relevant external guidance.
2.2	March 2019	1.6.1 also Updated hyperlinks in other parts of the document.	Implementation of new EPPO standards (PP1/306 and PP1/307) Clarified the introduction of Leaf Wall Area.
			Updated hyperlinks in other parts of the document.

GENERAL INTRODUCTION

This chapter describes the data requirements for estimation of the efficacy of a plant protection product and its active substance and the evaluation methods used in the EU framework (§1 - §1.5) 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 under §1.3.
The procedures for the evaluation of plant protection products are described under §1.4-1.6.

1.1. Introduction

The efficacy must be determined to prevent non-effective product from reaching the market and to ensure that the effective products have no undesirable effects on plants or plant products. When a product is insufficiently effective there is a real risk that the user will use the product at a higher dose or frequency which results in a higher exposure of humans and the environment to the product /the active substance, possibly with undesirable effects.

Data requirements, evaluation methodologies and criteria for the Netherlands that deviate from, or further elaborate, the provisions under EU framework (§1), are described in the NL part of this evaluation manual.

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 representative product.

Experiments carried out after the 1st January 1998 must have been carried out under GEP (Good Experimental Practice). If non-GEP studies are submitted, a justification for their use should be included.

If 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.

1.3. Data requirements for the active substance

This chapter aims to give procedures for the approval of active substances in Commission Implementing Regulation (EU) No 540/2011.

The data requirements concerning the efficacy of the active substance are described in Commission Regulation (EU) No 283/2013, section 3 (Further information on the active substance).

Approval of new active substances and renewals differ in their efficacy requirements. Below are the requirements for each type of dossier.

1.3.1. New active substances

Regulation (EC) No 1107/2009 Annex II point 3.2 states that ‘an active substance alone or associated with a safener or synergist shall only be approved where it has been established for one or more representative uses that the plant protection product, consequent on application consistent with good plant protection practice and having regard to realistic conditions of use is sufficiently effective.’

The Data requirements for efficacy for the approval of new active substances are described in guidance document SANCO/10054/2013: *Guidance document on data requirements on efficacy for the dossier to be submitted for the approval of new active substances contained in plant protection products.*
The principal objective of the efficacy evaluation of an active substance is to confirm that the dose rates that are included in the GAP are realistic for the risk evaluation and approval, and representative for all subsequent authorisations, and that a summary dossier should be submitted.

If efficacy trials are performed, these should follow PP1 EPPO standards(The EU and OECD guidelines for the execution of experiments in Commission Communications 2013/C 95/01 refer to EPPO standards for areas where efficacy is concerned.)

If 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. Similarly, for deviations from EPPO standards a justification should be provided.

1.3.2. Renewal of active substances

For the renewal of active substances the efficacy requirements are described in paragraph 4.5 of SANCO/2012/11251: *Guidance document on the renewal of active substances to be assessed in compliance with Regulation (EU) No 844/2012 (the Renewal Regulation.*

Considering that the substance is already approved, and authorisations of plant protection products have already been evaluated according to uniform principles, the data package required for renewals is very limited. It consists mainly of an overview of efficacy information concerning the representative and currently authorized uses of the product.

1.4. Data requirements for the product

The data requirements regarding the efficacy of the plant protection product are described in Commission Regulation (EU) No 284/2013, section 3 (Data on application) and section 6 (efficacy data).

This section provides information on subjects that do not fit under a specific data requirement, or that are relevant for multiple requirements. Discussion on specific data requirements as listed in Sections 3 and 6 in Commission Regulation (EU) No 284/2013 is discussed the relevant sections.

EU and OECD guidelines do not offer detailed guidance on the setup for efficacy trials, or the data requirements for an efficacy dossier.

For this Commission Communication 2013/C 95/02 refers to the European and Mediterranean Plant Protection Organization (EPPO).

The relevant guidance can be found in the PP1 EPPO standards. A large number of PP1 EPPO guidance documents are available. These range from general standards that explain the basics of an efficacy evaluation and standards dealing with specific data requirements to EPPO standards that provide information on specific pathogens, crops, and/or situations. When creating an efficacy dossier for a new product, an important step is to look at which EPPO standards are available that are relevant for the claimed uses. Relevant EPPO standards should be followed.

If 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. Similarly, for deviations from

EPPO standards a justification should be provided.

This document will not repeat the guidance provided by the EPPO, but will try to give information on the areas that are most likely to present problems during the creation of an efficacy dossier, and provide guidance on which standards or other guidance documents to refer to for those specific cases.

Zonal efficacy assessments
Climate is an important factor that can influence the efficacy of a product. This issue has been addressed by defining zones with comparable climates. EPPO Standard PP 1/241 *Guidance on comparable climate*s explains these EPPO climatic zones. It should be noted that these zones differ from the EU regulation zones.

The EPPO website on Zonal Efficacy Assessments provides further information on data requirements for zonal dossiers. This website also provides examples of zonal efficacy evaluations to assist applicants and evaluators to interpret the EPPO standards. Reference should also be made to EPPO standard pp1/278(1) *Principles of zonal data production and evaluation.*

On EPPO website, guidance is also available that indicates which areas of the efficacy data requirements that should be considered as part of the core zonal dossier, and what relevant issues may need to be addressed under national addenda (SANCO/10055/2013 Rev. 4)

Low risk products
Please refer to the CTGB evaluation manual for biopesticides.

Extrapolation possibilities
In some cases it is possible to register new uses with a reduced, or no data package if efficacy and crop safety can be extrapolated from already authorised or tested uses. The EPPO includes information on extrapolations for minor uses on their website. This page also lists extrapolation tables both for efficacy and for crop safety.

All extrapolations should be viewed on a case-by-case manner and expert judgment should always be applied when employing these tables.

Further information is available in EPPO standard PP1/224 *Principles of efficacy evaluation for minor uses*, and standard PP1/257 *Efficacy and crop safety extrapolations for minor uses.*

Crops that are minor in one country could be major in another, reference is therefore also made to the NL evaluation manual. It should also be mentioned that extrapolations are different from minor use extensions under article 51 of regulation (EC) No 1107/2009.

1.5. Data on application
Section 3 in Commission Regulation (EU) No 284/2013, explains how the data points related to “data on application” should be handled.

1.6. Efficacy Data
Section 6 in Commission Regulation (EU) No 284/2013, lists the efficacy data requirements. In this evaluation manual the different efficacy-related subjects are listed in the same order as in Commission Regulation (EU) No 284/2013. It should be noted that this differs from the order in the Draft Registration Report (DRR) format. Please note that a version of the DRR

format with information and advice on what is needed for the different sections is available from the website of the European commission.

1.6.1. Preliminary trials

(284/2013; 6.1)
Commission Regulation (EU) No 284/2013, paragraph 6.1 provides information on preliminary trials. For products with more than one active substance a justification ofthe co-formulation should also be included in this section. Formulation changes may be addressed here as well, however depending on the nature of the submitted data (justification or trials) evaluation of associated efficacy trials may be performed in the efficacy section instead.(1.6.2)

Co-formulation
For co-formulated mixtures an EPPO standard is available PP1/306 (*General principles for the development of co-formulated mixtures of plant protection products*).

Formulation changes.
In the case of a formulation change it may be possible to claim that efficacy and crop safety of a formulation is comparable to an existing formulation. The amount of trials or other supporting data that is needed depends on the nature and magnitude of the formulation change.

EPPO PP1/307 (*Efficacy considerations and data generation when making changes to the chemical composition or formulation type of plant protection products)* provides guidance on the steps that need to be followed. It should be kept in mind that if data from another formulation is used or referred to in a dossier, appropriate data access to this formulation should be available. In a zonal dossier the availability of accessible data and the extent of label claims that can be supported may differ between member states.

The Zonal rapporteur Member State will assess the relevance of the submitted dossier and whether comparability to the authorised formulation has been demonstrated. Only individual concerned Member States can determine the data protection status and data access to that authorized product, and can draw final conclusions.

Result of the preliminary trials section:
Preliminary indication of the dose rate. If relevant, a justification of the co-formulation and formulation changes.

1.6.2. Efficacy

Minimum effective dose
Guidance for trials on minimum effective dose is addressed in EPPO standard PP1/225(2).

Result:
The minimum effective dose rates of the proposed label claims for the product.

Dose rates in high crops:
Because of historical reasons, many different dose rate systems exist on national labels for high growing crops, this greatly complicates the writing and evaluation of dossiers.
EPPO standard PP1/239 “dose expression for plant protection products” states that “per treated leaf wall area” (LWA) is becoming the common dose expression for high growing crops.

For the **central registration zone** dates have been set for introduction of LWA as the

mandatory dose expression system in pomefruits, grapevine and high growing (fruiting) vegetables. All trials carried out in these crops after 1-1-2018 must be planned and carried out on the basis of LWA. Furthermore, per 1-1-2020 all dossiers submitted under article 33 must be supported by trials planned and carried out based on LWA as the efficacy unit of dose expression.

The dose rate in LWA should be included in the GAP table. It is important to note that the rate per unit of surface area (e.g. kg/ha) should always be included as well, as it is required for risk assesments. The dose rate in LWA is needed for the efficacy section only.

Efficacy
In the Commission Regulation (EU) No 284/2013, paragraph 6.2 provides an overview of efficacy testing requirements, reference is made to the PP1 EPPO standards for detailed guidance.

A large number of PP1 EPPO standards have been written that are relevant for this section. When writing an efficacy dossier, the relevant EPPO standards should be identified and followed, including the general standards that address trial setup and dossier requirements, as well as the specific standards on certain crops and pathogens.

The EPPO website on zonal efficacy assessments has several examples that are intended to help with interpretation of the EPPO standards.

Result:
Level of effectiveness of the proposed product. Depending on the results, label claims may be authorized or rejected. Additional label advice or recommendations may be needed to ensure that the product is properly applied to achieve the desired effect.

1.6.3. Information on the occurrence or possible occurrence of the development of resistance

Commission Regulation (EU) No 284/2013, paragraph 6.3 provides information on the requirements concerning the occurrence or possible occurrence of resistance.

EPPO standard PP1/213 *Resistance risk analysis* describes how the risk of resistance to plant protection products can be assessed, and provides guidance on resistance management.

Fungicides, herbicides and insecticides active substances have been grouped according to their mode of action (MoA) by the resistance action committees. Active substances with the same mode of action often show cross resistance and/or similar risks for resistance development. Information about resistance and resistance management can be found at the web pages of the different resistance action committees:

Fungicide Resistance Action Committee (FRAC). FRAC MoA classification
Herbicide Resistance Action Committee (HRAC). HRAC MoA classification
Insecticide Resistance Action Committee (IRAC). IRAC MoA classification

Mode of action classifications for these three groups are updated on a regular basis, the latest available version should be used. The hyperlinks to MoA classifications included above were the most recent versions in early 2019.

The evaluation of the provided information on the possible development of resistance and

resistance management will be performed in the core dossier. Resistance risk and occurrence can vary between member states. The same is true for availability of alternatives and for agricultural practices that may influence resistance risk.

Therefore, specific warning sentences and resistance management advice that should be provided on the labels has to be determined on a national level by the concerned member state(s), based on the evaluation in the core dossier.

Result:
Advice and instructions on resistance management. In some cases label restrictions may have to be included for an acceptable use pattern.

1.6.4. Adverse effects on treated crops

Commission Regulation (EU) No 284/2013, paragraph 6.4 provides information on the requirements concerning adverse effects on treated crops.

1.6.4.1. Phytotoxicity to target plants (including different cultivars), or to target plant products

EPPO standard PP1/135 on phytotoxicity assessment should be followed. In addition, the EPPO page on minor uses of plant protection products and extrapolation tables includes a number of extrapolation tables for crop safety.

Phytotoxicity assessment can be especially challenging for crop groups like ornamentals that are not only diverse, but also have low tolerance for phytotoxic effects. An EPPO example of an evaluation of an insecticide in protected ornamentals is available on the EPPO website. This example specifies the requirements for phytotoxicity assessment.

1.6.4.2. Effects on the yield of treated plants or plant products

This paragraph concerns the evaluation of the possibleeffect of the plant protection product on yield reduction or loss in storage of treated plants or plant products.

The general EPPO standard on phytotoxicity assessment (PP1/135(4)) provides information on the effects on yield. One of the conclusions in this standard is that the criteria for assessing quantity and quality of yield are generally crop-specific. A more detailed guidance on requirements for yield or yield quality data reference is made to specific EPPO PP1 standards for the relevant crops or situations.

1.6.4.3. Effects on the quality of plants or plant products

The general EPPO standard on phytotoxicity assessment (PP1/135(4)) provides information on the effects on yield. One of the conclusions in this standard is that the criteria for assessing quantity and quality of yield are generally crop-specific. For more detailed guidance on requirements for yield or yield quality data reference is made to specific EPPO PP1 standards for the relevant crops or situations.

Taint testing
Taint refers to an unpleasant taste or smell of the harvested or processed plant product that may be caused by treatment with a plant protection product. For certain types of treatments it is required to provide evidence that the product produces no taint.

The relevant standard for taint testing is EPPO standard PP1/242 *Taint tests.*

Result:
Warnings concerning effects quality of yield, or flavour and taste. In case of unacceptable

effects, the label claim may be rejected.

1.6.4.4. Effects on transformation processes

Where relevant, tests for effects on transformation processes must be conducted.

EPPO standard PP1/243 *Effects of plant protection products on transformation processes* provides general guidance on the need for data on possible adverse effects of plant protection products on processes for the transformation of harvested crops.

Specific guidance for wine making is available in EPPO standard PP1/268 *Study of unintentional effects of plant protection products on fermentation processes and characteristics of wine.*

Result:
Warnings concerning effects on transformation processes. In case of unacceptable effects, the label claim may be rejected.

1.6.4.5. Impact on treated plants or plant products to be used for propagation

The general EPPO standard on phytotoxicity assessment (PP1/135), paragraph 9 provides information on data requirements concerning the impact on treated plants or plant products used for propagation.

Result:
Advice on effects and where appropriate warnings for losses or aberrations.

1.6.5. Observations on other undesirable or unintended side-effects

Commission Regulation (EU) No 284/2013, paragraph 6.5 provides information on the requirements concerning other undesirable or unintended side-effects.

1.6.5.1. Impact on succeeding crops

Guidance on the data requirements for succeeding crops can be found in EPPO standard PP1/207 *Effects on succeeding crops*.

Result:
Advice and instructions to prevent or restrict effects on succeeding crops. Warnings and possible restrictions on use.

1.6.5.2. Impact on other plants, including adjacent fields

Guidance on the data requirements for adjacent crops can be found in EPPO standard PP1/256 *Effects on adjacent crops*.

Result:
Advice and instructions to prevent or restrict effects on adjacent crops. Warnings and possible restrictions on use.

1.6.5.3. Effects on beneficial and other non-target organisms

Commission Regulation (EU) No 284/2013, paragraph 6.5.3 provides information on the requirements concerning effects on beneficial and other non-target organisms.

For this section, reference is often made to the ecotoxicological section.

1.7. Approval

1.7.1. Approval of the active substance

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

1.7.2. Evaluation of plant protection products

The principles for evaluation of efficacy are presented in Commission Regulation (EU) No 546/2011. These are the relevant sections of the introductory principles, the general principles and the specific principles efficacy and absence of unacceptable effects on plants or plant products.