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

EU part

Plant protection products

Chapter 8 Efficacy

version 1.0; January 2013

ctgb

Board for the Authorisation of plant protection products and biocides

Chapter 8 Efficacy

Category: Plant Protection Products

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) under Regulation (EC) No 1107/2009 [1].

Substances that are approved under Regulation (EC) No 1107/2009 and were approved under Directive 91/414/EEC [2] are included in Commission Implementing Regulation (EU) No 540/2011 [3].

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 [3].

1.1. Introduction

The efficacy must be determined to prevent that non-effective products reach the market and to ensure that the effective products have no undesirable effects on plants or plant products. Where a product is not or 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, criteria and trigger values that deviate from, or further elaborate, the provisions under EU framework (§1), are described in the NL part (§2 - §2.5). The further provisions on national level can also be used for inclusion of an active substance in Commission Implementing Regulation (EU) No 540/2011 [3].

1.2. Data requirements

In order to qualify for inclusion of an active substance in Commission Implementing Regulation (EU) No 540/2011 [3] a dossier that meets the provisions laid down in Commission Regulation (EU) No 544/2011 [4] and Commission Regulation (EU) No 545/2011 of Regulation (EC) No 1107/2009 [5] must be submitted for the active substance as well as for the product.

Generally, EU guidelines for the execution of experiments are mentioned in Commission Regulation (EU) No 544/2011[4] and in Commission Regulation (EU) No 545/2011[5]. Where available, an equivalent OECD/EPPO guideline can be used as well.
The text in Commission Regulation (EU) No 544/2011 and Commission Regulation (EU) No 545/2011 of Regulation (EC) No 1107/2009 is outdated, the studies must always be carried out in accordance with the most recent version of the EU guideline or the OECD/EPPO guideline.

Commission Regulation (EU) No 544/2011 and Commission Regulation (EU) No 545/2011 of Regulation (EC) No 1107/2009 have not yet been brought in line with the most recent versions of the guidance documents. This means that some differences may exist between the data requirements described in Commission Regulation (EU) No 544/2011 and Commission Regulation (EU) No 545/2011 of Regulation (EC) No 1107/2009 and those in the guidance documents.

It is therefore strongly recommended to consult the guidance documents as well; the guidance documents are applicable where differences exist.

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.

Experiments carried out after the 1st January 1998 must have been carried out under GEP (Good Experimental Practice).

1.2.1. Data requirements for the active substance

The text below in grey frames has been taken from Commission Regulation (EU) No 544/2011. The numbering in these grey frames follows the section numbering in this Commission Regulation. Any necessary additions to the text have been added below the grey frames. Question numbers (NL as well as EU) are given below the headings.
The endpoints of the study are given as well, if relevant.
The data requirements concerning the efficacy of the active substance are described in Commission Regulation (EU) No 544/2011, point 3 (Further information on the active substance).
In Commission Regulation (EU) No 544/2011 no further data requirements on efficacy of the active substance are mentioned. It is therefore recommended to consult the Sanco document "*data requirements on efficacy for the dossier to be submitted for the approval of new active substances contained in plant protection products"* or other relevant guidance documents.

Further information on the active substance

3. Further information on the active substance

(i) The information provided must describe the intended purposes for which preparations containing the active substance are used, or are to be used and the dose and manner of their use or proposed use.
(ii) The information provided must specify the normal methods and precautions to be followed, in the handling, storage and transport of the active substance.
(iii) The studies, data and information submitted, together with other relevant studies, data and information, must both specify and justify the methods and precautions to be followed in the event of fire. The possible products of combustion in the event of fire shall be estimated, based on the chemical structure and the chemical and physical properties of the active substance.
(iv) The studies, data and information submitted, together with other relevant studies, data and information, must demonstrate the suitability of measures proposed for use in emergency situations.
(v) The information and data referred to are required for all active substances, except where otherwise specified.

Function, e.g. fungicide, herbicide, insecticide, repellent, plant growth regulator

3.1. Function, e.g. fungicide, herbicide, insecticide, repellent, growth regulator

The function must be specified from among the following:

- acaricide
- bactericide
- fungicide
- herbicide
- insecticide
- molluscicide
- nematicide
- plant growth regulator
- repellent
- rodenticide
- semio-chemicals
- talpicide
- viricide
- other (must be specified)

Effects on harmful organisms, e.g. contact poison, inhalation poison, stomach poison, fungitoxic or fingistatic, etc., systematic or not in plants

3.2. Effects on harmful organisms, e.g. contact poison, inhalation poison, stomach poison, fungitoxic, etc., systematic or not in plants

3.2.1. The nature of the effects on harmful organisms must be stated:
- contact action
- stomach action
- inhalation action
- fungitoxic action
- fungistatic action
- desiccant
- reproduction inhibitor
- other (must be specified)

3.2.2. It must be stated whether or not the active substance is translocated in plants and where relevant whether such translocation is apoplastic, symplastic or both.

Field of use envisaged, e.g. field, protected crops, storage of plant products, home gardening

3.3. Field of use envisaged, e.g. field, protected crops, storage of plant products, home gardening
The field(s) of use, existing and proposed, for preparations containing the active substance must be specified from among the following:
- Field use, such as agriculture, horticulture, forestry and viticulture
- Protected crops
- Amenity
- Weed control on non-cultivated areas
- Home gardening
- House plants
- Plant products storage practice
- Other (specify)

Harmful organisms controlled and crops or products protected or treated

3.4. Harmful organisms controlled and crops or products protected or treated

3.4.1. Details of existing and the intended use in terms of crops, groups of crops, plants, or plant products treated and where relevant protected, must be provided.

3.4.2. Where relevant, details of harmful organisms against which protection is afforded, must be provided.

3.4.3 Where relevant, effects achieved e.g. sprout suppression, retardation of ripening, reduction in stem length, enhanced fertilization etc., must be reported.

Mode of action

3.5. Mode of action

3.5.1. To the extent that is has elucidated, a statement must be provided as to the mode of action of the active substance in terms, where relevant, of the biochemical and physiological mechanism(s) and biochemical pathway(s) involved. Where available, the results of relevant experimental studies must be reported.

3.5.2. Where it is known that to exert its intended effect, the active substance must be converted to a metabolite or degradation product following application or use of preparations containing it, the following information, cross referenced to and drawing on information provided in the context of paragraphs 5.6, 5.11, 6.1, 6.2, 6.7, 7.1, 7.2 and 9, where relevant, must be provided for active metabolite or degradation product:
- chemical name according to IUPAC and CA nomenclature,
- ISO common name or porposed common name,
- CAS EC-number EC (Einecs or ELINCS) number, and CIPAC number if available,
- empirical and structural formula, and
- molecular mass.

3.5.3. Available information relating to the formation of active metabolites and degradation products, must be provided, to include:
- the processes, mechanisms and reactions involved,
- kinetic and other data concerning the rate of conversion and if known the rate limiting step,
- environmental and other factors effecting the rate and extent of conversion.

Information on the occurrence or possible occurrence of the development of resistance and appropriate management strategies

3.6. Information on the occurrence or possible occurrence of the development of resistance and appropriate management strategies

Where available information on possible occurrence of the development of resistance or cross-resistance must be provided.

1.2.2. Data requirements for the product

The text below in grey frames has been taken from Commission Regulation (EU) No 545/2011.

The numbering in these grey frames follows the section numbering in this Commission Regulation. Any necessary additions to the text have been added below the grey frames. Question numbers (NL as well as EU) are given below the headings.
The endpoints of the study are given as well, if relevant.

The date requirements regarding the efficacy of the plant protection product are described in Commission Regulation (EU) No 545/2011, point 4 (further information on the plant protection product) and 6 (efficacy data).

Further information on the plant protection product

4. Further information on the plant protection product

Necessary waiting periods or other precautions to protect man, livestock and the environment

4.3. Re-entry periods, necessary waiting periods or other precautions to protect man, livestock and the environment

The information provided must follow from and be supported by the data provided for the active substance(s) and that provided under Sections 7 and 8.

4.3.1. Where relevant pre-harvest intervals, re-entry periods or withholding periods necessary to minimize the presence of residues in or on crops, plants and plant products, or in treated areas or spaces, with a view to protecting man or livestock, must be specified e.g.:
- pre-harvest interval (in days) for each relevant crop,
- re-entry period (in days) for livestock, to areas to be grazed,
- re-entry period (in hours or days) for man to crops, buildings or spaces treated,
- withholding period (in days) for animal feedingstuffs,
- waiting period (in days), between application and handling treated products, or
- waiting period (in days), between last application and sowing or planting succeeding crops.

4.3.2. Where necessary, in the light of the test results, information on any specific agricultural, plant health or environmental conditions under which the preparation may or may not be used must be provided.

Efficacy data

6. Efficacy data

General

General

The data supplied must be sufficient to permit an evaluation of the plant protection product to be made. In particular it must be possible to evaluate the nature and extent of benefits that accrue following use of the preparation, where they exist in comparison to suitable reference products and damage thresholds, and to define its conditions of use.

The number of trials to be conducted and reported depends mainly on factors such as the extent to which the properties of the active substance(s) it contains are known and on the range of conditions that arise, including variability in plant health conditions, climatic differences, the range of agricultural practices, the uniformity of the crops, the mode of application the type of harmful organism and the type of plant protection product.

Sufficient data must be generated and submitted to confirm that patterns determined hold for the regions and the range of conditions, likely to be encountered in the regions concerned, for which its use is to be recommended. Where an applicant claims that tests in one or more of the proposed regions of use are unnecessary because conditions are comparable with those in other regions where tests have been carried out, the applicant must substantiate the claim for comparability with documentary evidence.

In order to assess seasonal differences, if any, sufficient data must be generated and submitted to confirm the performance of the plant protection product in each agronomically and climatically different region for each particular crop (or commodity)/harmful organism combination. Normally trials on effectiveness or phytotoxicity, where relevant, in at least two growing seasons must be reported.

If to the opinion of the applicant the trials from the first season adequately confirm the validity of claims made on the basis of extrapolation of results from other crops, commodities or situations or from tests with closely similar preparations, a justification, which is acceptable to the competent authority for not carrying out a second season's work must be provided. Conversely, where, because of climatic or plant health conditions or other reasons the data obtained in any particular season are of limited value for the assessment of performance, trials in one or more further seasons must be conducted and reported.

Preliminary tests
(545/20116.1)

6.1. Preliminary tests
Reports in summary form of preliminary tests, including glasshouse and field studies, used to assess the biological activity and dose range finding of the plant protection product and of the active substance(s) it contains, must be submitted when requested by the competent authority. These reports will provide additional information for the competent authority when it evaluates the plant production product. Where this information is not submitted a justification which is acceptable to the competent authority must be provided.

Result
→ proposed dose

Testing effectiveness
(545/20116.2)

6.2. Testing effectiveness
Aim of the tests
The tests shall provide sufficient data to permit an evaluation of the level, duration and consistency of control or protection or other intended effects of the plant protection product in comparison to suitable reference products, where they exist.

Test conditions

Normally a trial consists of three components: test product, reference product and untreated control.
The performance of the plant protection product must be investigated in relation to suitable reference products, where they exist. A suitable reference product is defined as an authorized plant protection product which has proved a sufficient performance in practice under the agricultural, plant health and environmental (including climatic) conditions in the area of proposed use. In general, formulation type, effects on the harmful organisms, working spectrum and method of application should be close to those of the tested plant protection product.

Plant protection products must be tested in circumstances where the target harmful organism has been shown to have been present at a level causing or known to cause adverse effects (yield, quality, operational benefit) on an unprotected crop or area or on plants or plant products which have not been treated or where the harmful organism is present at such a level that an evaluation of the plant protection product can be made.

Trials to provide data on plant protection products for control of harmful organisms must show the level of control of the species of harmful organisms concerned or of species representative of groups for which claims are made. Trials must include the different stages of growth of life cycle of the harmful species, where this is relevant and the different strains or races, where these are likely to show different degrees of susceptibility.

Similarly, trials to provide data on plant protection products which are plant growth regulators, must how the level of effects on the species to be treated, and include investigation of differences in the response of a representative sample of the range of cultivars on which its use is proposed.

In order to clarify the dose response, dose rates lower than the recommended one must be included in some trials in order to enable to assess whether the recommended rate is the minimum necessary to achieve the desired effect.

The duration of the effects of treatment must be investigated in relation to the control of the target organism or effect on the treated plants or plant products, as appropriate. When more than one application is recommended, trials must be reported which establish the duration of the effects of an application, the number of applications necessary and the desired intervals between them.

Evidence must be submitted to show that the dose, timing and method of application recommended give adequate control, protection or have the intended effect in the range of circumstances likely to be encountered in practical use.

Unless there are clear indications that the performance of the plant protection production is unlikely to be affected to a significant degree by environmental factors, such as temperature or rain, an investigation of the effects of such factors on performance must be carried out and reported, particularly where it is known that the performance of chemically related products is so affected.

Where proposed label claims include recommendations for the use of the plant protection product with other plant protection product(s) or adjuvant(s) information on the performance of the mixture must be provided.

Test guideline

Trials must be designed to investigate specified issues, to minimise the effects of random variation between different parts of each site and to enable statistical analysis to be applied to results amenable to such analysis. The design, analysis and reporting of trials must be in accordance with European and Mediterranean Plant Protection Organisation (EPPO) guidelines 152 and 181. The report shall include a detailed and critical assessment of the data.

The trials must be carried out in accordance to specific EPPO guidelines, where available, or when a member state requires so and when the test is carried out on the territory of this, with guidelines satisfying at least the requirements of the corresponding EPPO guideline.
A statistical analysis of results amenable to such analysis must be carried out; where necessary the test guideline used must be adapted to enable such analysis.

Result
→ effective or not

Information on the occurrence or possible occurrence of resistance
(545/20116.3)

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

Laboratory data and where it exists, field information relating to the occurrence and development of resistance or cross-resistance in populations of harmful organisms to the active substance(s), or to related active substances, must be provided. Where such information is not directly relevant to the uses for which authorization is ought or to be renewed (different species of harmful organism or different crops), it must, if available, nevertheless be provided, as it may provide and indication of the likelihood of resistance developing in the target population.

Where there is evidence or information to suggest that, in commercial use, the development of resistance is likely, evidence must be generated and submitted as to the sensitivity of the population of the harmful organism concerned to the plant protection product. In such cases a management strategy designed to minimize the likelihood of resistance or cross-resistance developing in target species must be provided.

Result
→ advice and instructions resistance management in accordance with guidelines resistance action committees (IRAC, FRAC, HRAC) and guideline 2003/82/EC.

Effects on the yield of treated plants or plant products in terms of quantity and/or quality

6.4. Effects on the yield of treated plants or plant products in terms of quantity and/or quality

Effects on the quality of plants or plant products
(545/20116.4.1)

6.4.1. Effects on the quality of plants or plant product

Aim of the tests
The tests shall provide sufficient data to permit an evaluation of the possible occurrence of taint or odour or other quality aspects of plants or plant products after treatment with

the plant protection product.

Circumstances in which required
The possibility of the occurrence of taint or odour in food crops must be investigated and be reported where:
- the nature of the products or its use is such that a risk of occurrence of taint or odour might be expected,
or
- other products based on the same or a closely similar active ingredient have been shown to present a risk of occurrence of taint or odour.

The effects of plant protection products on other quality aspects of treated plants or plant products must be investigated and reported where:
- the nature of the plant protection product or it use could have an adverse influence on other quality aspects (for example in the case of use of plant growth regulators close or harvest), or
- other products based on the same or a closely similar active ingredient have been shown to have an adverse influence on the quality.

Testing should be conducted initially on the main crops on which the plant protection product is to be used, at twice the normal rates of application and using, where relevant, the main methods of processing. Where effects are observed it is necessary to perform testing at the normal rate of application.
The extent of investigation necessary on other crops will depend on their degree of similarity of the main crops already tested, the quantity and quality of data available on those main crops and how far the manner of use of the plant protection product and methods of processing the crops, are similar. It is generally sufficient to perform the test with the main formulation type to be authorised.

Result
→ Warnings concerning effects on flavour and taste, where appropriate in case of unacceptable effects not honouring the claim.

Effects on transformation processes
(545/20116.4.2)

6.4.2. Effects on transformation processes

Aim of the tests
The tests shall provide sufficient data to permit an evaluation of the possible occurrence of adverse effects after treatment with the plant protection product on transformation processes or on the quality of their products.

Circumstances in which required:
When the treated plants or plant products are normally intended for use in transformation process such as wine making, brewing or bread making and when at harvest significant residues are present, the possibility of the occurrence of adverse effects must be investigated and reported where:

- there are indications that the use of the plant protection product could have an influence on the processes involved (for example in the case of use of plant growth regulators or fungicides close to harvest),
or
- other products based on the same or a closely similar active ingredient have been shown to have an adverse influence on these processes or its products.
It is generally sufficient to perform the test with the main formulation type to be authorised.

Result
→ Warnings concerning effects on transformation processes, where appropriate in case of unacceptable effects not honouring the claim.

Effects on the yield of treated plants or plant products

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

Aim of the tests
The test shall provide sufficient data to permit an evaluation of the performance of the plant protection product and of possible occurrence of yield reduction or loss in storage of treated plants or plant products.

Circumstances in which required
The effects of plant protection products on the yield or yield components of treated plant products must be determined where relevant. When treated plants or plant products are likely to be stored the effect on the yield after storage, including data on starage life must be determined where relevant.
This information will normally be available from the tests required in point 6.2.

Result
→ advice on effects and where appropriate warnings for losses or aberrations.

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

6.5. Phytotoxicity to target plants (including different cultivars), or to target plant products (545/20116.5)

Aim of the tests
The test shall provide sufficient data to permit an evaluation of the performance of the plant protection product and of the possible occurrence of phytotoxicity after treatment with the plant protection product.

Circumstances in which required
For herbicides and for other plant protection products for which adverse effects, however transitory, are seen during the trials, performed in accordance to point 6.2, the margins of selectivity on target crops must be established, using twice the recommended rate of application. Where serious phytotoxic effects are seen, an intermediate application rate must also be investigated.
Where adverse effects occur, but are claimed to be unimportant in comparison with the benefits of use or transient, evidence to support this claim is required.

If necessary yield measurement must be submitted.
The safety of a plant protection product to the main cultivars of the main crops for which it is recommended must be demonstrated, including effects of crop growh stage, vigour, and other factors which may influence suspectibility to damage or injury.
The extent of investigation necessary on other crops will depend on their degree of similarity to the main crops already tested, the quantity and quality of data available on those main crops and how far the manner of use of the plant protection product, if relevant, is similar. It is generally sufficient to perform the test with the main formulation type to be authorized.
Where proposed label claims include recommendations for the use of the plant protection product with other plant protection product(s), the provisions of the previous paragraphs apply for the mixture.

Test guideline
Observations concerning phytotoxicity must be performed in the tests provided for in point 6.2.
Where phytotoxic effects are seen, they must be accurately assessed and recorded in accordance with EPPO guideline 135 or when a Member State requires so and when the test is carried out on the territory of this Member State, with guidelines satisfying at least the requirements of this EPPO guideline.
A statistical analysis of results amenable to such analysis must be carried out, where necessary the test guideline used must be adapted to enable such analysis.

Result
→ Advice and instructions about presence and occurrence of phytotoxicity. The claim is not honoured in case of unacceptable phytotoxicity.

Observations on undesirable or unintended side-effects, e. g. on beneficial and other non-target organisms, on succeeding crops, other plants or parts of treated plants used for propagating purposes (e. g. seeds, cuttings, runners)

6.6. *Observations on undesirable or unintended side-effects, e. g. on beneficial and other non-target organisms, on succeeding crops, other plants or parts of treated plants used for propagating purposes (e. g. seeds, cuttings, runners).*

Impact on succeeding crops

6.6.1. Impact on succeeding crops

Aim of the information required
Sufficient data must be reported to permit an evaluation of possible adverse effects of a treatment with the plant protection product on succeeding crops.

Circumstances in which required
Where data, generated in accordance with point 9.1, shows that significant residues of the active substance, its metabolites or degradation products, which have or may have biological activity on succeeding crops, remain in soil or in plant materials, such as straw or organic material up to sowing or planting time of possible succeeding crops, observations must be submitted on effects on the normal range of succeeding crops.

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

Impact on other plants, including adjacent fields

6.6.2. Impact on other plants, including adjacent crops

Aim of the information required
Sufficient data must be reported to permit an evaluation of possible adverse effects of a treatment with the plant protection product on other plants, including adjacent crops.

Circumstances in which required
Observations must be submitted on adverse effects on other plants, including the normal range of adjacent crops, when there are indications that the plant protection product could affect these plants via vapour drift.

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

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

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

Aim of the information required
Sufficient data must be reported to permit an evaluation of possible adverse effects of a treatment with the plant protection product on plants or plant products ot be used for propagation.

Circumstances in which required
Observations must be submitted on the impact of plant protection products on plant parts used for propagation except where the proposed uses preclude use on crops intended for production of seeds, cuttings, runners or tubers for planting, as appropriate.
(i) for seeds - viability, germination and vigour;
(ii) cuttings - rooting and growth rates;
(iii) runners - establishment and growth rates;
(iv) tubers - sprouting and normal growth.

Test guideline
Seeds testing shall be done according to ISTA Methods (1).

1) International Rules for Seed Testing, 1985. Proceedings of the International Seed Testing Association, Seed Science and Technology, Volume 13, Number 2, 1985.

Result
→ Advice and instructions to prevent or restrict effects on propagation material. Warnings and possible restrictions on use.

Side-effects on beneficial and other non-target organisms

6.6.4. Effects on beneficial and other non-target organisms (545/20116.6.4)
Any effects, positive or negative, on the incidence of other harmful organisms, observed in the tests performed in accordance with the requirements of this section, shall be reported. Any observed environmental effects must also be reported, especially effects on wildlife and/or beneficial organisms.

Result
→ Warnings and possible restrictions, especially aimed at inclusion of the requested product in a system of integrated pest management.

Summary and evaluation of data presented under 6.1 to 6.6

6.7. Summary and evaluation of data presented under 6.1 to 6.6 (545/20116.7)

A summary of all data and informations provided under points 6.1 to 6.6 must be provided, together with a detailed and a critical assessment of the data, with particular reference to the benefits that the plant protection product offers, adverse effects that do or may arise and measures necessary to avoid or minimize adverse effects.'

Result
→ Biological Assessment Dossier.

1.3. Assessment
Each study or cluster of studies (see §1.2.1 and 1.2.2) is summarised and evaluated separately.
The data submitted in the context of the application are for efficacy tested against the criteria given in § 1.4. It is investigated for each sub-aspect whether there is an effect and to what extent. The extent of this effect is then compared with and measured against known effects of a set of adequate reference products (including, if available, a standard product). Finally, the effects of the different part aspects are weighed against each other to arrive at a final judgement about efficacy. This weighing includes the study data as well as, if available, laboratory and field data and, if available, literature data. Studies abroad must also have been conducted by official or officially recognised bodies.

1.4. Approval
Regulation (EC) No 1107/2009 Annex II Directive 91/414/EEC provides the procedure and criteria for the approval of active substances, safeners and synergists pursuant to Chapter II of Regulation (EC) No 1107/2009.

Point 3 of Annex II of Regulation (EC) No 1107/2009 gives the criteria for the approval of an active substance. The texts specifically applicable to the aspect efficacy are presented below.

3. Criteria for the approval of an active substance

3.2. Efficacy

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. This requirement shall be evaluated in accordance with the uniform principles for evaluation and authorisation of plant protection products referred to in Article 29(6).

1.4.1. Evaluation

The principles for evaluation of efficacy are presented in Commission Regulation (EU) No 546/2011 [6]. 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 as well as Impact on vertebrates to be controlled. The specific principles Efficacy and Absence of unacceptable effects on plants or plant products as well as Impact on vertebrates to be controlled are in the text below printed in a grey frame. This text, including numbering, is the literal text from Commission Regulation (EU) No 546/2011.

2.1. Efficacy

2.1.1. Where the proposed use concerns the control of or protection against an organism, Member States shall evaluate the possibility that this organism could be harmful under the agricultural, plant health and environmental (including climatic) conditions in the area of the proposed use.

2.1.2. Where the proposed use concerns an effect other than the control of or protection against an organism, Member States shall evaluate whether significant damage, loss or inconvenience could occur under the agricultural, plant health and environmental (including climatic) conditions in the area of proposed use if the plant protection product were not used.

2.1.3. Member States shall evaluate the efficacy data on the plant protection product as provided for in the Annex to Regulation (EU) No 545/2011 having regard to the degree of control or the extent of the effect desired and having regard to the relevant experimental conditions such as:
- the choice of the crop or cultivar,
- the agricultural and environmental (including climatic) conditions,
- the presence and density of the harmful organism,
- the development stage of crop and organism,
- the amount of the plant protection product used,
- if required on the label, the amount of adjuvant added,
- the frequency and timing of the applications,
- the type of application equipment.

2.1.4. Member States shall evaluate the performance of the plant protection product in a range of agricultural, plant health and environmental (including climatic) conditions likely to be encountered in practice in the area of proposed use and in particular:
(i) the level, consistency and duration of the effect sought in relation to the dose in comparison with a suitable reference product or products and an untreated control;
(ii) where relevant, effect on yield or reduction of loss in storage, in terms of quantity and/or quality, in comparison with a suitable reference product or products and an untreated control.
Where no suitable reference product exists, Member States shall evaluate the

performance of the plant protection product to determine whether there is a consistent and defined benefit under the agricultural, plant health and environmental (including climatic) conditions in the area of proposed use.

2.1.5. Where the product label includes requirements for use of the plant protection product with other plant protection products and/or with adjuvants as a tank mix, Member States shall make the evaluations referred to in points 2.1.1 to 2.1.4 in relation to the information supplied for the tank mix.
Where the product label includes recommendations for use of the plant protection product with other plant protection products and/or with adjuvants as a tank mix, Member States shall evaluate the appropriateness of the mix and of its conditions of use.

2.2. Absence of unacceptable effects on plants or plant products

2.2.1. Member States shall evaluate the degree of adverse effects on the treated crop after use of the plant protection product according to the proposed conditions of use in comparison, where relevant, with a suitable reference product or products, where they exist, and/or an untreated control.
(a) This evaluation will take into consideration the following information:
(i) the efficacy data provided for in the Annex to Regulation (EU) No 545/2011;
(ii) other relevant information on the plant protection product such as nature of the preparation, dose, method of application, number and timing of applications;
(iii) all relevant information on the active substance as provided for in of the Annex to Regulation (EU) No 544/2011, including mode of action, vapour pressure, volatility and water solubility.
(b) This evaluation will include:
(i) the nature, frequency, level and duration of observed phytotoxic effects and the agricultural, plant health and environmental (including climatic) conditions that affect them;
(ii) the differences between main cultivars with regard to their sensitivity to phytotoxic effects;
(iii) the part of the treated crop or plant products where phytotoxic effects are observed;
(iv) the adverse impact on the yield of the treated crop or plant products in terms of quantity and/or quality;
(v) the adverse impact on treated plants or plant products to be used for propagation, in terms of viability, germination, sprouting, rooting and establishment;
(vi) where volatile products are concerned, the adverse impact on adjacent crops.

2.2.2. Where the available data indicate that the active substance or significant metabolites, degradation and reaction products persist in soils and/or in or on plant substances in significant quantities after use of the plant protection product according to the proposed conditions of use, Member States shall evaluate the degree of adverse effects on subsequent crops. This evaluation will be carried out as specified in point 2.2.1.

2.2.3. Where the product label includes requirements for use of the plant protection product with other plant protection products or with adjuvants as a tank mix, the evaluation as specified in point 2.1.1 will be carried out in relation to the information supplied for the tank mix.

2.3. *Impact on vertebrates to be controlled*
Where the proposed use of the plant protection product aims to have an effect on vertebrates, Member States shall evaluate the mechanism by which this effect is obtained and the observed effects on the behaviour and health of the target animals; when the intended effect is to kill the target animal they shall evaluate the time necessary to obtain the death of the animal and the conditions under which death occurs.
This evaluation will take into consideration the following information:
(i) all relevant information as provided for in the Annex to Regulation (EU) No 544/2011 and the results of the evaluation thereof, including the toxicological and metabolism studies;
(ii) all relevant information on the plant protection product as provided for in the Annex to Regulation (EU) No 545/2011, including toxicological studies and efficacy data.

1.4.2. Decision making

The principles for decision making as regards 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 as well as Impact on vertebrates to be controlled.
The specific principles Efficacy and Absence of unacceptable effects on plants or plant products as well as Impact on vertebrates to be controlled are in the text below printed in a grey frame. This text, including numbering, is the literal text from Commission Regulation (EU) No 546/2011.

2.1. Efficacy

2.1.1. Where the proposed uses include recommendations for the control of or protection against organisms which are not considered to be harmful on the basis of experience acquired or scientific evidence under normal agricultural, plant health and environmental (including climatic) conditions in the areas of proposed use or where the other intended effects are not considered to be beneficial under those conditions, no authorisation shall be granted for those uses.

2.1.2. The level, consistency and duration of control or protection or other intended effects must be similar to those resulting from the use of suitable reference products. If no suitable reference product exists, the plant protection product must be shown to give a defined benefit in terms of the level, consistency and duration of control or protection or other intended effects under the agricultural, plant health and environmental (including climatic) conditions in the area of proposed use.

2.1.3. Where relevant, yield response when the product is used and reduction of loss in storage must be quantitatively and/or qualitatively similar to those resulting from the use of suitable reference products. If no suitable reference product exists, the plant protection product must be shown to give a consistent and defined quantitative and/or qualitative benefit in terms of yield response and reduction of loss in storage under the agricultural, plant health and environmental (including climatic) conditions in the area of proposed use.

2.1.4. Conclusions as to the performance of the preparation must be valid for all areas of the Member State in which it is to be authorized, and must hold for all conditions under which its use is proposed, except where the proposed label specifies that the preparation is intended for use in certain specified circumstances (e.g. light infestations, particular soil types or particular growing conditions).

2.1.5. Where proposed label claims include requirements for use of the preparation with other specified plant protection products or adjuvants as a tank mix, the mixture must achieve the desired effect and comply with the principles referred to in points 2.1.1 to 2.1.4.
Where proposed label claims include recommendations for use of the preparation with specified plant protection products or adjuvants as a tank mix, Member States shall not accept the recommendations unless they are justified.

2.2. Absence of unacceptable effects on plants or plant products

2.2.1. There must be no relevant phytotoxic effects on treated plants or plant products except where the proposed label indicates appropriate limitations of use.

2.2.2. There must be no reduction of yield at harvest due to phytotoxic effects below that which could be obtained without the use of the plant protection product, unless this reduction is compensated for by other advantages such as an enhancement of the quality of the treated plants or plant products.

2.2.3. There must be no unacceptable adverse effects on the quality of treated plants or plant products, except in the case of adverse effects on processing where proposed label claims specify that the preparation should not be applied to crops to be used for processing purposes.

2.2.4. There must be no unacceptable adverse effects on treated plants or plant products used for propagation or reproduction, such as effects on viability, germination, sprouting, rooting and establishment, except where proposed label claims specify that the preparation should not be applied to plants or plant products to be used for propagation or reproduction.

2.2.5. There must be no unacceptable impact on succeeding crops, except where proposed label claims specify that particular crops, which would be affected, should not be grown following the treated crop.

2.2.6. There must be no unacceptable impact on adjacent crops, except where proposed label claims specify that the preparation should not be applied when particular sensitive adjacent crops are present.

2.2.7. Where proposed label claims include requirements for use of the preparation with other plant protection products or adjuvants, as a tank mix, the mixture must comply with the principles referred to in points 2.2.1 to 2.2.6.

2.2.8. The proposed instructions for cleaning the application equipment must be both practical and effective so that they can be applied with ease so as to ensure the removal of residual traces of the plant protection product which could subsequently cause damage.

2.3. Impact on vertebrates to be controlled
An authorization for a plant protection product intended to eliminate vertebrates shall be granted only when:
- death is synchronous with the extinction of consciousness, or
- death occurs immediately, or
- vital functions are reduced gradually without signs of obvious suffering.
For repellent products, the intended effect shall be obtained without unnecessary

suffering and pain for the target animals.

1.5. Developments

- EPPO (European and Mediterranean Plant Protection Organisation) is working on guidance documents for the zonal evaluation of the aspect efficacy (see Eppo Website for the most updated documents).
- A guidance document on efficacy requirements for new active substances was in development when this evaluation manual was written, a draft version was already available: Sanco E3 working document. Data requirements on efficacy for the dossier to be submitted for the approval of new active substances (as defined under Regulation (EC) No 1107/2009) contained in plant protection products.

2. APPENDICES

None.

3. REFERENCES

1 Regulation (EC) No 1107/2009, http://eur-lex.europa.eu/Notice.do?checktexts=checkbox&val=504604%3Acs&pos=1&page=1&lang=en&pgs=10&nbl=1&list=504604%3Acs%2C&hwords=&action=GO&visu=%23texte

2 Directive 91/414/EEC, http://eur-lex.europa.eu/Notice.do?checktexts=checkbox&val=172911%3Acs&pos=3&page=1&lang=en&pgs=10&nbl=3&list=447073%3Acs%2C185439%3Acs%2C172911%3Acs%2C&hwords=&action=GO&visu=%23texte

3 Commission Implementing Regulation (EU) No 540/2011, http://eur-lex.europa.eu/Notice.do?checktexts=checkbox&val=574460%3Acs&pos=6&page=1&lang=en&pgs=10&nbl=6&list=646199%3Acs%2C628324%3Acs%2C615541%3Acs%2C607847%3Acs%2C607130%3Acs%2C574460%3Acs%2C&hwords=&action=GO&visu=%23texte

4 Commission Regulation (EU) No 544/2011 of Regulation (EC) No 1107/2009, http://eur-lex.europa.eu/Notice.do?checktexts=checkbox&val=574584%3Acs&pos=2&page=1&lang=en&pgs=10&nbl=2&list=607696%3Acs%2C574584%3Acs&hwords=&action=GO&visu=%23texte

5 Commission Regulation (EU) No 545/2011 of Regulation (EC) No 1107/2009, http://eur-lex.europa.eu/Notice.do?checktexts=checkbox&val=574590%3Acs&pos=2&page=1&lang=en&pgs=10&nbl=2&list=607698%3Acs%2C574590%3Acs%2C&hwords=&action=GO&visu=%23texte

6 Commission Regulation (EU) No 546/2011, http://eur-lex.europa.eu/Notice.do?checktexts=checkbox&val=574598%3Acs&pos=2&page=1&lang=en&pgs=10&nbl=2&list=607713%3Acs%2C574598%3Acs%2C&hwords=&action=GO&visu=%23texte