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Evaluation biologique des produits phytosanitaires
Efficacy evaluation of plant protection products

PP 1/214 (4) Principles of acceptable efficacy

Specific scope

This Standard describes the principles for determining whether the efficacy of a plant protection product is acceptable for the purposes of registration. More specific guidance is provided in other general and specific Standards in the series PP 1. Where registration across several countries is being considered and a single biological dossier is intended by the applicant, the submission (and subsequent evaluation by the competent authority) should consider the conditions and factors that affect performance arising across that area. These requirements are elaborated in PP 1/278 *Principles of zonal data production and evaluation*.

Specific approval and amendment

First approved in 2000-09.
Revision mainly to reflect zonal assessment approved in 2012-09.
Revision approved in 2014-09 and 2017-09.

1. Introduction

In order to decide whether a particular plant protection product should be sold and used, national registration authorities have the responsibility of ensuring that there is no unnecessary risk to the environment, to the person(s) applying the product or to the end-users of the crop (either humans or domestic animals) from its use. There is often some risk attached to the use of plant protection products and it is thus necessary to decide if the benefits from the use of the plant protection product outweigh any disadvantages. Most countries therefore require that the efficacy of the plant protection product be evaluated in order to establish that there really is a benefit (in terms of pest control and consequent yield improvement) from the application of the product. EC Regulation 1107/2009 concerning the placing of plant protection products on the market (EC, 2009) expresses this requirement by declaring that any plant protection product should be 'sufficiently effective', but without explaining what is meant by this term.

The object of this document is to explain which factors should be taken into account during a registration evaluation to decide whether the efficacy that has been assessed in relation to the intended use is acceptable for the purposes of registration. For the final decision on registration, other criteria (such as effects on the environment, public health, etc.) will be taken into account, but these decisions go beyond the scope of this document.

2. Definition of efficacy

In practice a particular plant protection product is applied with a specific purpose in mind, that is the control of one or more pests (e.g. insects, fungi, weeds, rodents) or the modification of plant growth (e.g. growth regulation). The quantification of this direct effect can be termed 'direct efficacy' or 'effectiveness'. However, as there should be a benefit from the use of the product, it is clear that the measure of efficacy required for registration covers more than just this direct efficacy. The efficacy of a plant protection product can be defined as a measure of the overall effect of its application on the agricultural system in which it is used.

Efficacy can be considered to be a balance between:

(a) The positive effects of treatment in performing the desired plant protection activity, that is controlling the target pest or modifying crop growth in order to achieve improvement in the quantity and/or quality of crop yield or premature or delayed ripening;
(b) The negative effects (such as development of resistance, phytotoxicity, reduction of quality or quantity of yield, taint, transformation processes, damage to beneficial organisms, damage to succeeding or adjacent crops,); and
(c) Other aspects of efficacy which, depending on the product, can be either positive or negative; these include effects on other non-target pests, the length of time for which the plant protection product continues to be active, its ease of use, and compatibility with other cultural practices and crop protection measures.

The net result of the positive and negative effects should be a sufficient overall agricultural benefit to justify the use of the plant protection product.

3. Assessment of efficacy

Efficacy is assessed by the consideration of data from several different sources. Direct efficacy (effectiveness) is evaluated in specific trials. Information on phytotoxicity, effects on non-target pests and beneficial organisms and damage to succeeding or adjacent crops can come from observations made during efficacy evaluation trials, but may also need specific trials, some of which may be performed as part of the evaluation of risk to the environment. Data on resistance comes from separate data sets within the registration dossier. Other information on, for example, ease of use and compatibility with other practices is obtained from data on use pattern(s).

4. Evaluation of direct efficacy (effectiveness)

Direct efficacy is evaluated under conditions as near as possible to the conditions of practical use of the product; this means, in general, evaluation by means of trials under field or glasshouse conditions. The EPPO Standards from the series PP 1 on *Efficacy evaluation of plant protection products* explain how field or glasshouse trials should be conducted and attempt to define the minimum requirements necessary to assess the direct efficacy of a particular plant protection product for a particular purpose in a particular crop. The systematic assessments made during the trial only provide information on direct efficacy, apart from specific selectivity trials where phytotoxicity to the crop is assessed (see Appendix 1). The number, design, lay-out and execution of the trials, as presented in the EPPO Standards, have been chosen so that the result of the direct efficacy evaluation (alone) can be statistically analysed, considering an adequate measure of probability. Information on the other elements within the overall definition of efficacy, described above, are normally derived from observations made during the trial, with the understanding that if these observations indicate significant effects, then more systematic evaluation or possibly other trials will be needed. These observations can also include aspects that do not come under direct efficacy, such as effects on wildlife. In principle, yield data (on quantity or quality) should always be recorded to ensure that the observed effect on the target pest is translated into a positive effect on yield. However, in many cases, for example when the correlation between the pest population and yield is well known and unequivocal or where the pest is known to have no effect on yield in the present season, yield data is not required (see specific Standards from the series PP 1 on *Efficacy evaluation of plant protection products*).

These main trial results may be influenced, positively or negatively, by a number of other factors which, according to the Standard, should be recorded during the trial:

(a) Suitability of crop (including cultivar, growth stage);
(b) Suitability of test organism (strain, life stage, population density);
(c) Suitability of trial site;
(d) Reliability of equipment;
(e) Correct dosage;
(f) Influence of other plant protection products applied;
(g) Climate;
(h) Soil type and condition.

Expert judgement is needed to decide if any of these factors could have influenced the efficacy and whether the effect was an apparent increase or decrease of direct efficacy. In addition, the expert assessor may be able to recognize other possible influences on direct efficacy from an examination of the data set presented for registration; for example, mode of action, formulation or development of resistance may influence the trial results. By studying these factors, the expert may also be able to develop conditions and limitations of use that would improve direct efficacy, prevent negative effects or allow control of a pest or the attainment of a protective purpose even under unfavourable conditions.

An untreated control is evaluated in the trial to check that the population of the target organism (or plant growth) behaves in the expected manner during the period of the trial. It is thus used to detect any external influence on efficacy. The untreated control can also be a point of reference when deciding on the acceptability of a certain level of efficacy (see below).

A reference product is included in nearly every efficacy evaluation trial. Because of the variability of the conditions under which plant protection products are used, the inclusion of a reference is necessary in order to allow a meaningful evaluation of efficacy under the conditions of the trial and to permit comparison between different trials in a series. In addition, the presence of a reference product allows comparison with other plant protection products not included in the trial series. The reference product should be a product known to be satisfactory in practice and, preferably, with a mode of action that is the same as or similar to that of the test product. The reference product also serves as a means of comparing the test product with a control measure with known characteristics in practice.

EPPO recommends that, if possible, every trial on efficacy evaluation should include a reference product and, because the consideration of acceptable efficacy should generally be related to it, then the reference product should, as far as possible, be a product registered for the intended use in the country in which the trial is performed. However, a non-registered product could be used provided that it is known to be satisfactory in practice. This product may have previously been registered in the country or may be registered in another country. There may be other reasons why

the product is not registered for general use in a country, but its use in a field trial may be acceptable. In some countries, special official permission should be obtained for the use of a non-registered product in a trial.

In general, the choice of reference product is left to the applicant, but it may be advisable for the applicant to consult the registration authority as to the acceptability of the reference product chosen. This is particularly important where trials are being conducted across a number of countries and where it is unlikely that the same products will be registered.

In cases in which no reference product is available (for example, when the type of product or its use are new or when all potential reference products have been withdrawn from use), the first consideration should be to determine whether a non-chemical method might be used as a reference. If this is not possible, it should be accepted that the trial can continue without a reference product and a comparison with the untreated control is the only option.

5. Evaluation of other elements of efficacy

As mentioned above, other elements having an impact on overall efficacy are recorded if they are observed during a field trial on efficacy evaluation but not specifically targeted by the trial guidelines. However, if any effects other than on direct efficacy are observed, additional trials on these effects may be required.

5.1 Development of resistance

EPPO Standard PP 1/213 *Resistance risk analysis* indicates what information should be provided in the registration dossier to indicate whether resistance is likely to occur during practical use of the plant protection product.

5.2 Phytotoxicity

If phytotoxic effects are observed on the crop during the efficacy evaluation trial, the symptoms should be accurately described. EPPO Standard PP 1/135 *Phytotoxicity assessment* gives detailed information on how such assessment should be performed. Apart from the efficacy evaluation of herbicides, plant growth regulators, seed treatments and crops grown under protected conditions, specific trials are usually not required (see Appendix 1).

5.3 Taint and transformation processes

EPPO Standard PP 1/242 *Taint tests* provides general guidance on the requirements for testing whether harvested plants or plant products are tainted by plant protection products. Plant products which are so transformed that they are totally different in nature from the raw crop (e.g. bread, beer, wine) are covered by EPPO Standards PP 1/243 *Effects of plant protection products on transformation processes* and PP 1/268 *Study of unintentional effects of plant protection products on fermentation processes and characteristics of wine.*

5.4 Damage to succeeding or adjacent crops

EPPO Standard PP 1/207 *Effects on succeeding crops* provides guidance on whether and how information should be obtained on possible long-term effects resulting from treatment with the plant protection product. Generally, the need for such information will be triggered by data on fate and behaviour in soil, and/or biological activity in soil against germination or growth. EPPO Standard PP 1/256 *Effects on adjacent crops* provides guidance on whether and how information should be obtained on the risk to adjacent crops from an application of a plant protection product.

5.5 Effects on other pests

Any positive or negative effects on pests other than the target pest(s) are recorded during the efficacy evaluation trials, but no other data is systematically required.

5.6 Effects on other non-target organisms

The observation of effects on naturally occurring or introduced pollinators or natural enemies in the treated crop during the trial should trigger the requirement for additional specific information. In order to determine the nature of that information, EPPO Standard PP 3 *Environmental risk assessment scheme of plant protection products* should be consulted, particularly Chapter 9 'Non-target terrestrial arthropods'.

6. Decision on acceptable efficacy

If efficacy is acceptable, then the use of a plant protection product shows a satisfactory effect in relation to its aim. What is meant by 'satisfactory' is the key point in this issue. Two major criteria of acceptable efficacy can be presented, but it should be stressed that expert judgement is an essential element in the final decision.

The primary criterion of acceptable efficacy is that the product should show results that are significantly superior to those recorded in the untreated control, i.e. that the use of the product is better than no use. The product should show a consistent, well-defined benefit to the user. Where no reference product is available, such a comparison with the untreated control is the only criterion of acceptable efficacy.

A secondary criterion is how the performance of the test product compares with that of a reference product. The general intention is to prevent the use of products that have distinctly lower effectiveness than products that are already available on the market for the same use. However, if the test product is markedly less effective against the target pest or in modifying plant growth than that of the reference product, it may still be possible to regard this as acceptable

if other characteristics of the test product have advantages over the reference product. The following characteristics could influence the interpretation of acceptable efficacy:

(a) Use over a wider range of growth stages of the crop or use in a wider range of crops, including minor crops.
(b) Effects against more pest stages;
(c) Lesser influence of climatic factors or soil type;
(d) Greater compatibility with cultural practices or other plant protection measures;
(e) Lower probability of resistance or important as part of a resistance management strategy;
(f) Effects against other pests;
(g) Fewer undesirable effects (on beneficial organisms, other crops etc.).

Furthermore, when direct efficacy has *not* been shown to be acceptable, it may be possible to envisage management options (e.g. use limitations) that would improve it to a sufficient level.

Reference

EC (2009) Regulation (EC) No 1107/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market and repealing Council Directive 79/117/EEC and 91/414/EEC. *Official Journal of the European Union L* **309**, 1–50.

Appendix 1 – Special note for specific crop safety/selectivity trials

Safety to the treated crop is considered to be as important as direct efficacy.

(a) For herbicides, according to EPPO Standards, specific trials are set up where weed populations are low and specific crop safety assessments are made and yield is measured. Doses higher than those recommended are applied to provide information on the margin of crop safety. With plant growth regulators, detailed assessments are made during effectiveness trials to determine whether there are any unwanted effects on growth of the plants. Effects on succeeding and adjacent crops are also important considerations.
(b) In protected crops, plant protection products can be applied throughout the year, including periods when the crop is most sensitive to these treatments, and can give (unacceptable) phytotoxic effects. If the risk of phytotoxicity is expected, or if symptoms of phytotoxicity appear in effectiveness trials, separate phytotoxicity trials may be conducted to establish the margin of selectivity (see PP 1/135 *Phytotoxicity assessment*).

The balance between direct efficacy (effectiveness) and any negative effects should be considered as detailed in the section 'Definition of efficacy'. Situations where crop safety is compromised should be specified on the label, for example weather conditions or certain soil types. It is possible that, where effectiveness is very important (for example novel activity against an important weed), a lower margin of crop safety may be acceptable. In these circumstances, clear warnings of the balance between positive and negative aspects should appear on the label. The types of circumstance where a lower margin of crop safety can be allowed are similar to those that apply to a lower margin of direct efficacy for other products (see section 'Evaluation of direct efficacy (effectiveness)').