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European and Mediterranean Plant Protection Organization
Organisation Européenne et Méditerranéenne pour la Protection des Plantes PP 1/226 (3)

Evaluation biologique des produits phytosanitaires
Efficacy evaluation of plant protection products

PP 1/226 (3) Number of efficacy trials

Specific scope

This Standard provides guidance on the number of trials in target crops needed to demonstrate the efficacy of a plant protection product at the recommended dose.

Specific approval and amendment

First approved in 2003-09.

Revision mainly to reflect zonal assessment approved in 2012-09.

Revision in 2018-09 following the adoption of EPPO Standard PP 1/307 *Efficacy considerations and data generation when making changes to the chemical composition or formulation type of plant protection products.*

Introduction

Evaluation of the efficacy of a plant protection product is a prerequisite for authorization of that product by a national regulatory authority so that it can be sold and used. Efficacy is demonstrated by conducting trials with the product, both to evaluate its performance against the pest (or its activity in the case of a plant growth regulator) and to demonstrate the nature and extent of any adverse effects on the crop or on the produce derived from that crop, as well as on succeeding or adjacent crops (see EPPO Standard PP 1/214 *Principles of acceptable efficacy*).

Guidance is available, in the form of specific standards for the efficacy evaluation of plant protection products, to provide an appropriate and accepted method for the conduct of efficacy testing. These standards are available for a large number of pests. Further guidance is available on the provision of appropriate methodology for testing of adverse effects (e.g. EPPO Standards PP 1/135 *Phytotoxicity assessment* and PP 1/207 *Effects on succeeding crops*).

To demonstrate the performance of a plant protection product it is necessary to conduct a number of trials in different regions with distinct environmental conditions, and normally in different years and growing seasons, as indicated in the individual EPPO Standards for efficacy evaluation. Thus a trial series is conducted in which product performance is evaluated. EPPO Standard PP 1/181 *Conduct and reporting of efficacy evaluation trials including good experimental practice* provides an indication of the factors influencing the number of trials that are necessary to form part of a trial series.

For the purposes of this Standard, a region might be considered as a country or countries with some differences in climatic, agronomic and edaphic conditions. When the region becomes larger and the conditions more diverse, a broader consideration of the number of trials is required. This is particularly so where there is more diversity in the agronomy of the crop, as well as in the severity of pest pressure and sensitivity to plant protection products. In such situations reference should be made to EPPO Standard PP 1/278 *Principles of zonal data production and evaluation*.

For recommendations on the number of trials for similar formulations see EPPO Standard PP 1/307 *Efficacy considerations and data generation when making changes to the chemical composition or formulation type of plant protection products*.

Number of trials in a trial series

The purpose of this document is to provide further information and some guiding principles on the number of trials that should be done to evaluate the performance of a plant protection product, both for direct efficacy (effectiveness) and for safety of the treated crop. This document does not, however, cover trials for other purposes, for example succeeding crops or taint.

In complex cases not sufficiently addressed in this Standard the applicant may wish to discuss the number of trials that may be necessary with the registration authority when planning a programme of work with a plant protection product.

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EPPO Standard PP 1/181 *Conduct and reporting of efficacy evaluation trials including good experimental practice* states that, in general, the number of trials in a trial series depends on consideration of factors including the following:

- the overall importance of the crop and pest
- the severity of damage caused
- cultivar effects
- the impact of soil and climatic factors
- prior knowledge of the active substance or product in related uses
- the general consistency of trial results.

These are all important criteria and, with other factors, are discussed below.

Number of trials for direct efficacy (effectiveness)

The number of trials is determined primarily by the importance of the crop and the pest (major or minor), and the possibility of extrapolation between crops and pests. A major pest is one that would normally be expected to occur each year at levels that cause significant economic damage in the absence of treatment to a large proportion of the crop area. A minor pest is one that does not occur routinely: its incidence would normally be localized, and significant damage on high proportion of the crop would not normally be expected.

Full number of trials

The full number of trials is needed, particularly for plant protection products or active substances which not have been on the market in the EPPO region in which authorization is sought, or for intended uses for which no extrapolation of any aspect of efficacy from other uses is possible.

There should be a high degree of confidence in the efficacy of a plant protection product when it is used against a major pest on a major crop. As a general guide, a total of 10 trials (Table 1) with results that are fully supportive of the direct efficacy (effectiveness) of the product should be sufficient to demonstrate efficacy against a major target pest species. Where authorization is sought across a range of diverse conditions, such as across an authorization zone (EPPO Standard PP 1/278 *Principles of zonal data production and evaluation*), then the number of trials conducted may need to increase. These trials should be done across the range of climatic and environmental conditions likely to be encountered, and over at least 2 years. They should be done against challenging pest attacks or in situations where challenging attacks are anticipated.

Table 1. Basic number of direct efficacy trials in an area of similar conditions required (for further explanation, see bullet points in the section 'Reduced number of trials')

	Fully supportive results required
Major pest on major crop	10 (range 6–15)
Minor uses	3 (range 2–6)
Major pest; protected conditions	6 (range 4–8)

Fully supportive results are those where the pest has occurred in sufficient numbers to be considered a challenging attack, and where the results show the product gave effective control or reduction of damage compared with the untreated plots and comparable with a reference treatment. Results that are less than fully supportive, for example where pest attack is low, may provide useful information. However, further trials may be necessary to add to the number of fully supportive results.

Similarly, if the results indicate the performance to be variable or of limited effectiveness, or if climatic or other variation across the region is high, then additional trials may be necessary to clarify the levels of performance. Such additional trials should investigate the particular conditions where the effectiveness of the product is impaired, with a view to providing specific information on the label. In any event, some explanation of the results, or of the specific trials where impaired effectiveness occurred, would normally be expected.

Reduced number of trials

In some situations there may be the opportunity to reduce the number of trials done, and a case may be made for this as follows.

- Where there is a large amount of supporting evidence from use of the product, or of similar products with the same active substance, on closely related pests or against the same pests on different crops, the number of trials necessary will be determined by the amount of supporting evidence and the similarity of the pests and crops sought. Expert judgement is required when considering reductions in the number of trials on this basis. In making extrapolations between crops or pests, it is important to explain and justify the reasoning for the extrapolation. Extrapolations from more challenging control situations to ones that pose a lower challenge to the active substance are more readily justifiable than extrapolations from less challenging to more challenging situations. More challenging situations would include, for foliar treatments, dense crops where good spray cover is difficult and, for herbicides, non-competitive crops. Less challenging situations might include thin crops where good cover is expected or, for herbicides, competitive crops where weed control is enhanced due to the competitive nature of the crop.
- Where the target pest or crop is of minor importance, once direct efficacy (effectiveness) against a major pest has been demonstrated, and where the additional pest is of minor importance or use on a minor crop is to be recommended on the label, a reduced number of trials may be accepted. As a guide for a minor pest, three trials are

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typically advisable within an area with comparable conditions demonstrating effectiveness (Table 1). The precise number will depend on the depth of knowledge of the product and the similarity of the crop and pest situation, and expert judgement will be required when considering the data submitted. See also EPPO Standard PP 1/224 *Principles of efficacy evaluation for minor uses*.

- Where there is little variation in climatic conditions in the use of the product, for example in some protected situations or in storage premises (grain stores), a reduced number of trials may be sufficient to demonstrate effectiveness. As a guide, typically six effectiveness trials are required for a demonstration of effectiveness in protected situations (Table 1), and data from a single year may be sufficient. In specialized storage situations this number may be reduced further if there is relevant preliminary or laboratory data representative of the commercial use. The number of trials done against minor targets may also be reduced along the above lines. EPPO countries within the European Union are considered as one 'zone' for protected situations and post-harvest treatments. However, even in those situations where conditions are controlled, consideration still needs to be given to any potential variations in pest biology, light conditions, agronomy, growing practices, etc. Therefore, this should be reflected in the placement and number of trials.
- In exceptional circumstances, the number of trials required may be reduced when there are extreme difficulties associated with their conduct. Such difficulties may include: use against pests of sporadic occurrence or under special conditions (e.g. trials on quarantine pests); testing of pheromones (where very large plots are necessary) and use in large structures requiring whole-site fumigation.

Number of trials for crop safety

It is advisable to demonstrate that use of a plant protection product has no unacceptable adverse effects on the treated crop. Unacceptable effects include symptoms of phytotoxicity on the treated crop as well as effects on the quality and quantity of harvested produce. The nature of the activity of herbicides (and plant growth regulators) means that the potential for adverse effects (both visual and effects on yield) on treated crops is much greater than for insecticides and fungicides. It is for this reason that Regulation 1107/2009 (EC, 2009) requires that herbicides are tested for phytotoxicity at both the normal (N) and at twice the normal (2N) recommended dose in the absence of weeds. Because weeds compete with the crop, and because their presence may reduce the amount of herbicide reaching the crop, specific phytotoxicity testing in the absence of weeds is required for herbicides. For other plant protection products, absence of adverse effects can be demonstrated adequately in the normal efficacy trials. Nevertheless, if adverse effects, however transitory, are seen during testing at the normal dose with other plant protection products, then testing at twice the normal dose is required.

Crop safety trials should cover the range of proposed growth stages on the label, as well as any sensitive timings (e.g. flowering). For all crops, the absence of specific varietal sensitivity should be established. This can be done by trials over a range of cultivars, by testing a series of cultivars with limited or no replication or by a combination of both.

Herbicides and plant growth regulators

Specific crop safety trials in the absence of weeds, with a commercial reference product, are usually required over 2 years. Typically, at least eight trials per major crop are required in an area of similar conditions to cover the range of conditions of use, including soil types and weather conditions that are likely to be encountered. The number of trials may be reduced if there are clearly no adverse effects and the mode of action would support this, for example a graminicide being applied to a minor broad-leaved crop. As knowledge of the active substance and formulation is gained from use on a number of crops it may also be possible to reduce the number of specific crop safety trials on additional related crops.

Both N and 2N doses of the test product and the reference product should be used. Intermediate doses should also be investigated if serious adverse effects are seen. Effects on yield should be assessed in all trials.

Observations from direct efficacy (effectiveness) trials provide useful supporting information but are no substitute for specific crop safety trials.

Insecticides and fungicides

For insecticides and fungicides (and other products such as acaricides or molluscicides), observations for phytotoxic effects should be made in the direct efficacy (effectiveness) trials. However, for seed treatments special crop safety trials are needed (typically four). In addition, for active substances, or major uses where no information on effects on yield is available, or where a case for crop safety cannot be made, some assessment of effects on yield (or components of yield) should be made, preferably over 2 years, to demonstrate there are no unacceptable adverse effects. While these assessments should preferably be made on specific crop safety trials in the absence of the pest, this is not essential provided yield can be determined in the direct efficacy trials at low pest levels with similarly performing reference products. If any adverse phytotoxic effects occur at the N dose, then the effects of 2N doses should be investigated and specific crop safety trials should be conducted.

When sufficient knowledge of safety of the active substance and formulation is gained on several crops, adequate crop safety information for additional crops (including major crops) may be gained from visual observations made in the direct efficacy trials without the need for yield

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assessment. For example, where crop safety has previously been demonstrated for several crops, and no significant visual damage has been observed in direct efficacy trials across a broad range of conditions on new crops, then further evidence of crop safety (including yield assessments) would not usually be required.

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* **L309**, 1–50.