Efficacy Guideline 106

General Principles on Conducting Efficacy Trials to Support UK Plant Protection Products (PPP)

Contents

Introduction

This guideline provides a general introduction to the principles of generating efficacy data, and use of European Plant Protection Organisation (EPPO) standards. This general introduction should be read in conjunction with EPPO standards and the specific UK guidance.

EPPO standards

Detailed specific advice on conduct and reporting of efficacy trials is provided in the standards for the evaluation of PPP produced by the European and Mediterranean Plant Protection Organisation (EPPO) (www.eppo.int). These are internationally recognised by HSE, OECD, and FAO and in the EU as the minimum standard for efficacy testing. The standards provide detailed trials methodology as well as how to address the relevant data requirements. As such they should be followed unless a sound justification can be given for not doing so.

Deviations from EPPO standards

There can be justified reasons to deviate from the EPPO standard methodology. For example, if a suitable standard treatment is not available, or if there are practical constraints on plot size, number of replicates. There should be a sound and scientific consideration of the impact of such deviation on the integrity of the trial and the information obtained from it. In the reporting of the trial a full explanation of, and justification for, the deviation should be provided.

In other situations, there may be justification for conducting the trial in a way that does not conform to the EPPO standard, but is at least to the minimum standard specified. There may be many reasons for such deviations. For example, novel modes of action of plant protection compounds may require a different approach to assessment methodology and to timing of assessments, as may scientific advances in the knowledge of the pest. The methodology that has been used, and the reasoning that it is appropriate for the trial should be fully explained.

Availability of specific pest/situation standards

While EPPO standards are available for a great many target pests and situations there may be some where there is currently no published methodology. Where no specific standard is available the following options should be considered towards determining suitable methodology.

1 Is there an EPPO standard for a similar situation or for the same or closely related pest on the same or similar crop?

2 Are there any UK national guidelines that are suitable for the relevant?3 Is there any other source of information that can be used to identify appropriate methodology.

In considering the appropriateness of any methodology available or proposed, it is important to consider the biology of the target and the mode of action of the test compound. Further information should also be obtained from PP 1/152, Design and analysis of efficacy evaluation trials.

Number of trials

The applicant should aim to provide data to support the claims made on the product label and to provide evidence of the suitability and crop safety of the product for the use envisaged. The number of trials required to achieve this depends on many factors such as:

- The extent of the knowledge already gained on the active substance or product
- The importance of the crop/animal/produce and the significance of the harmful organism
- Availability of testing possibilities e.g. rare occurrence of the harmful organism

Generally, a minimum of 10 appropriate field trials results demonstrating effectiveness and crop safety are required to support a UK authorisation of a PPP for major uses. For insecticides and fungicides some, or possibly all, data on crop safety may be obtained by appropriate assessment of effectiveness trials. A case may be made for fewer trials results to be accepted, for example where there is a large amount of supporting evidence or when there is a very high level of consistency in different trials. In all cases, for a new use the trials programme should be carried out over at least 2 years. In principle, additional major uses will also require 10 trials results, for both effectiveness and crop safety. But again a reasoned case may be made to reduce the number of trials, for example existing data on related crops or target(s).

For protected uses, generally a minimum of 6 appropriate results will be required, and because of the consistency in environmental conditions may be conducted over one year. A case supporting the consistency of conditions should be provided if conducting trials in a single season.

In addition, a reduced number of trials is permitted for PPP containing active substances classified as ‘low risk’.

For UK minor uses (minor target and/or minor crop), usually only 3 consistent trials results are required, provided data on a relevant major target/crops have already been considered, and a level of extrapolation may be permitted between different crops for a single target organism that affects more than one crop.

There is a range of more detailed available guidance on trials numbers and extrapolation possibilities. This includes EPPO standards PP 1/226 ‘Numbers of trials’; PP 1/296 ‘Principles of efficacy evaluation for low risk plant protection products’; PP 1/257 ‘Efficacy and crop safety extrapolations for minor uses’. (and associated minor use extrapolation tables: https://www.eppo.int/ACTIVITIES/plant_protection_products/extrapolation_tables

There are a number of specific UK guidelines which outline major and minor crops/targets, and the indicative number of appropriate supporting trials results. This includes cereals, maize, potato, oilseed rape and vegetable brassicas, and a working document list of major/minor targets on a range of other crops.

Location of field trials sites

The crops chosen for experiments may be specifically grown for experimental use or be part of crops grown for commercial purposes, but in all cases should be grown according to normal commercial practice. They should be in areas representative of those in which the crop and harmful organism normally occur. If there is a possibility that soil types may affect the action of a product, sites should be chosen which are representative of the range of soil types typically encountered. The experimental site should be uniform and crops should preferably not be under any stress other than that attributable to the problem to be treated (except where the effects of stress are being investigated). All other cultural operations apart from that being tested should be according to normal practice and should be recorded.

There is no specific requirement to have UK only trials to support a UK product authorisation in most circumstances, and typically data may be generated from wide ranging European regional areas. What is important is to clearly explain and justify the relevance of the data to UK agronomic conditions. EPPO PP 1/278 'Principles of zonal data production and evaluation' provides a comprehensive overview of the relevant issues when generating and using regional data packages. EPPO have developed a specific area on zonal efficacy assessments, with accompanying examples. A number of the examples are relevant to UK crops/targets:

http://www.eppo.int/PPPRODUCTS/zonal_efficacy/zonal_efficacy.htm

Trials design

The design, analysis and reporting of trials should be in accordance with EPPO

Standards PP 1/152 'Design and analysis of efficacy evaluation trials' and PP 1/181 'Conduct and reporting of efficacy evaluation trials including good experimental practice', and where available specific EPPO standards applicable to the situation.

The design of the trial should, where relevant, permit a statistical evaluation. Usually a randomised block design is adequate. Each block should generally contain one plot treated with the PPP to be evaluated, one treated with a suitable reference product (positive control) and an untreated control. The plots should be randomly distributed within the block. Consider whether design and analysis as a trial series is appropriate rather than, or as well as, analysis of results from the individual trials . This may affect trial design as the use of larger numbers of trials gives a more statistically powerful test than greater numbers of replicates in each trial. See EPPO standard PP 1/152 for further information on the statistical analysis of efficacy data.

The design of the trials should not be made any more complicated than is required by the objectives of the test. Where it is necessary to introduce additional factors into the experiment in addition to the PPP under study at the recommended dose e.g. various times of application or other doses, this can be accomplished by splitting the main plots into sub-plots, provided that the size of the sub-plots are still sufficient to allow a

reliable evaluation.

Plot size

The most suitable plot size depends upon many factors, including the particular crop,

pest, disease or weed situation, the mobility of the target organism, the available equipment for application of the treatment and harvesting of the crop. Since guard rows/areas often have to be included, the overall plot size should be sufficiently large to allow the net plots on which periodic sampling and evaluation of the crop yield or harvest are carried out to be of adequate size. Guidance on the minimum net plot size is usually indicated in individual EPPO standards.

The number of replications required depends on plot size, number of treatments and uniformity of distribution of the target organism. The number of replications required is also related to the particular techniques employed. Further specific guidance is given in EPPO standards, but 4 replicates is normally the minimum number for field experiments. 3 replicates are usually acceptable for the evaluation of post-emergence weed control by herbicides, provided the yields are not intended to be measured.

Control and untreated areas

Untreated areas are normally an integral part of a trial. There should be at least one per replicate. If there are 10 or more experimental treatments there should be at least 2 untreated plots in each replicate, provided there are at least 4 replicates. Where there are only 3 replicates then 8 or more treatments would require at least 2 untreated plots. If maintaining the untreated plots at the same area as treated plots represents an unacceptable economic loss their size may be reduced, but not the number of untreated plots. Except in trials designed to test safety to the crop, these plots may be treated after they have been evaluated. Exceptionally the requirement for untreated control plots may be waived. Positive controls should be suitable authorised products, but in appropriate cases there may need to be (in addition or instead) a control not exposed to the harmful organism.

Target organism

As far as possible the target organism should be present, or be expected to occur, evenly distributed and at a level of agronomic importance. The organism must be identified and described by its full scientific name and EPPO code. Where relevant, subspecies, variety and pathotype, etc. should be stated. Stage of growth, density, frequency or level of infestation/infection and other factors having a bearing on the situation should be noted and, if necessary, be quantified before treatment in accordance with EPPO standards.

A naturally occurring infestation/infection is preferred. If artificial inoculation of a pathogen or introduction of a pest or weed is necessary, this should be recorded and the procedure described. Untreated and standard treated plots should be infested, inoculated or populated in the same manner as plots to be treated with the product under test. Consideration should be given to allowing a suitable period of time following inoculation for the infection or pest to become established before treatment. Additional useful information (especially on crop safety) may be obtained in appropriate cases from the inclusion of treated but uninoculated/ uninfested/ unpopulated plots.

Trials should include different stages of growth of the harmful species where relevant. Trials should also include different strains or races where these are likely to show different degrees of susceptibility. Evidence of effect in appropriate representative species, cultivars or breeds having resistance to the harmful organisms in question should be provided where such resistance is known or suspected.

Dose

The dose at which the product is likely to be recommended should be included in trials. In trials to test efficacy, doses above and below the recommended dose should, where appropriate, also be included. EPPO PP 1/225 'Minimum effective dose' gives more details on generating data to address dose justification.

In trials to determine safety to crops, the recommended dose, and for herbicides and plant growth regulators at least double the recommended dose, should be tested. For insecticides and fungicides inclusion of a higher than recommended dose is not a requirement for crop safety unless effects are seen at the recommended dose. Nevertheless, inclusion of a greater than recommended dose for such products may help to give greater confidence in the results obtained and should therefore be given due consideration.

Any adjuvants, where it is intended to make a positive recommendation on the label (e.g. increased effectiveness), should be mixed with the test product and tested in at least a proportion of the trials to support the specific label claims. It may be advisable to test the product and the adjuvants separately to detect any phytotoxic effect.

The test material should not be applied in mixture with other products, fertilisers, or other substances (other than adjuvants and diluents) except where the purpose is to obtain information on the performance of such mixtures, or where the inclusion of such products or substances would normally be considered as good agricultural practice. Where two or more products in tank mixture are being tested, the individual products should be tested in the same trial.

Application method and water volume

The method and conditions of application should be the same, or as similar as possible to that to be recommended for the product. The application pattern used in trials should be like that used in commercial practice, both in particle size and distribution and in deposition on the treated surfaces. For sprays the volume and diluent should be as recommended for commercial use except where these factors are being evaluated.

The water volumes that are to be recommended on the product label should be considered to be a pre-requisite for the protocols of trials to demonstrate the effectiveness and crop safety of a product. For situations where a dilution rather than a specific volume of water per hectare is to be recommended trials should reflect the recommendation. Where appropriate information on crop or canopy size should be provided, and should follow EPPO PP 1/239 'Dose expression for plant protection products', which requires assessment using 'leaf wall area' (LWA) in efficacy trials. However, all relevant parameters must be recorded to accurately express the dose in amount active substance/ha (ground) in the Good Agricultural Practice (GAP) table.

It is accepted for most arable and horticultural crops that the range of water volumes,

using standard hydraulic nozzles, is 200 - 400 litres/ha. Trials data using any water volume within this range are acceptable for such label recommendations. For all other label recommendations there is a need for trials data using the recommended water volumes or a reasoned case as to why trials data using a different volume are applicable. Where fully supportive efficacy data are not available or are insufficient to support water volumes lower than those used in trials it is possible for the applicant to request that reduced volumes are presented on-label as a 'Qualified recommendation'. In some situations this may also be addressed by providing a reasoned case.

Timing and treatments

The proposed timing should be tested. Inclusion of earlier and later timings, where appropriate, may provide additional useful information. Where repeated application is the norm the timing of the first application should be that expected to be recommended for the product being tested. Different frequencies of application may be compared. The optimum interval between applications may have to be established by experimentation.

Recording and assessment

Records of the weather before, at and after treatments should be kept and relevant data included in the reports of experiments. Rainfall, frost, air and soil temperatures, and air humidity are usually the most important factors influencing results. Other measurements e.g. wind speed and direction may be required in some circumstances. If experimental crops are not grown in their usual environment this should be stated (e.g. field crops in pots or under temporary or permanent shelter from the weather).

Variety of crop, stage and vigour of growth and all other relevant information should be recorded on the date of treatment. Crop growth stage should be defined either by using an accepted code (e.g. growth stage keys published by EPPO), or by a detailed description. A pre-treatment assessment is often also essential to determine the level of infestation/infection and stage of development of the harmful organism and/or stage of growth and condition of the crop. One or more post-treatment assessments should be made and these should be timed to elucidate the maximum of information on the behaviour of the product and its duration of effect, whilst also avoiding undue damage to the experimental area and needless expenditure (frequent inspection may be necessary to minimise the number of assessments). Assessment at different stages of growth of the target organism and/or of the crop may be required. Further specific guidance on assessment methodology is given in the specific EPPO standards.

Results should be assessed by counts or measurements wherever possible. Only when the use of such assessment methods is inappropriate should any other methods, such as scoring or grading be used. Any such method should be related to an absolute count or other measurement on the untreated or the standard treatment (or both). When scoring schemes are to be used, widely accepted scoring systems such as those in EPPO standards should be used in preference to others. Where appropriate data should be statistically analysed, and methods fully described.

Raw data need not be submitted but should be held by the applicant for reference in case of a need for clarification. Individual trials reports, alongside the Biological Assessment Dossier, and draft Registration Report (Section 3) should be provided (See EPPO standard PP1/152 for further information).

Further information

For information about health and safety, or to report inconsistencies or inaccuracies in this guidance, visit www.hse.gov.uk.

This guidance is issued by the Health and Safety Executive. Following the guidance is not compulsory, unless specifically stated, and you are free to take other action. But if you do follow the guidance you will normally be doing enough to comply with the law. Health and safety inspectors seek to secure compliance with the law and may refer to this guidance.

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Published by the Health and Safety Executive 01/2021