Efficacy Guideline 101

UK Efficacy Guidance for the Preparation of a Biological Assessment Dossier (BAD)

Contents

Foreword

Efficacy guideline 101 was written to provide guidance on writing Biological Assessment Dossiers (BAD) and was based on an original EU document published in 1995 (Document 7600/VI/95 rev. 6). It was used to support submissions under Directive 91/414/EEC. When the directive was replaced by EU Regulation 1107/2009, no updated BAD guidance was provided to reflect the zonal process (although a document is under development in the EU). Applicants do have the guidance provided in the draft Registration Report on making concise summaries from the underlying BAD.

CRD will develop specific, updated UK guidance, on writing a BAD (reflecting for example the summarising of regional data packages to support a UK authorisation). However, in the meantime, the principles provided in this guideline remain valid and provides useful information. The guideline has been updated to reflect the current Efficacy product data requirements.

Documentation required

The biological assessment dossier (BAD) should follow the format set out below. In addition to this dossier, all individual test and study reports have to be available to the Authorities. It is suggested that these are listed in Appendix I to the Biological Assessment Dossier. Detailed guidance for reporting individual tests and studies, as provided in EPPO Standard PP 1/181, should be followed.

Applicants should provide a concise summary of the BAD in a draft Registration Report (Section 3).

Format of the biological assessment dossier

1 TITLE, REFERENCE, DATE, AUTHOR

The title should mention the name of the plant protection product and the use for which it is intended. The author should mention the name of the applying company and the person responsible for the biological assessment dossier.

2 LIST OF CONTENTS

The List of Contents should list the title of each section and its page number in the Biological Assessment Dossier, so that it can act as a check list to ensure that all the relevant points have been explained and justified.

3 INTRODUCTION

This is a vital part of the Biological Assessment Dossier. If sufficient information is provided, this will make the evaluation much easier and therefore more rapid.

i) A complete description of the plant protection product (including active substance(s) and its concentration, content of formulants, formulation type, chemical group(s), mode of action, biological properties) must be available.

ii) Background information on the plant protection product (e.g. any previous relevant use of the plant protection product or use of the active substance(s) in other products (whose efficacy data the applicant owns or has access to); any authorisation of the product/active substance in countries other than the one where authorisation is being sought).

iii) Background information on the harmful target organism(s) against which activity is claimed; this should include a justification that the organism is actually harmful. In cases where the proposed use concerns an effect other than the control of, or the protection against an organism, a justification has to be provided that the intended use is beneficial together with any other details that are relevant to support the specific use of the product.

iv) Where earlier formulations of the product or other products containing the same active substance(s) are cited as supporting evidence, all relevant formulation details must be given and the relevance of this evidence to the current formulation must be fully justified.

v) A draft of the proposed label has to be provided.

4 PRELIMINARY TESTS (6.1)

Results of preliminary tests must be submitted where requested by the Competent Authority. Results of preliminary tests and early screening studies can provide useful information on, for example, dose justification and evidence of safety to potential succeeding crops or adjacent crops. It is likely to be more appropriate to report the results of any preliminary tests in the individual sections to which they are relevant. However, their use should be referenced in Section 4 and they should be identified as preliminary tests results when they are reported.

5 TESTING EFFECTIVENESS (6.2)

5.1 Materials and Methods

Trials test methodology must be described in full detail, so that it is immediately clear to the Competent Authority how the results were obtained.

A suggested format is as follows:

5.1.1 Testing facility or organisation

The testing facility(ies)/organisation(s) which performed the test must be identified and it must be clearly stated whether the trials are performed by an official or officially recognised testing facility or organisation (see For trials conducted in the UK the ‘Official Recognition’ certificate numbers (ORETO) must be provided where appropriate (see https://www.hse.gov.uk/pesticides/pesticides-registration/efficacy-guides/official-recognition-introd.htm). For trials conducted in other countries a copy of the certificate of recognition of each testing facility/organisation, current at the times the trials were conducted, has to be included. Where trials were performed outside the EU or before relevant GEP was introduced in the country must be clearly stated.

5.1.2 Sites

Location of trial sites should be provided, e.g. in tabular form. It is recommended to present the major elements of the trial sites in tabular form. A proposed example is attached in Table 1; other important relevant factors may be added to this format (e.g. soil type for certain herbicide trials). However, full details on each trial site have to be reported in the individual trial reports.

For studies conducted outside the UK, a full justification of the relevance of non-UK data must be made. The extent of the information required will depend on the similarity of the two countries. Applicants should refer to the EPPO guidance on climate (PP 1/241 'Guidance on comparable climates'), and EPPO 1/278 'Principles of zonal data production and evaluation'.

Experimental details

Full experimental details must be provided in the individual trial reports (according to guidance given in Appendix 1 of EPPO guideline PP 1/181 'Conduct and reporting of efficacy evaluation trials including GEP).

These individual trial reports or trial series reports have to be available however, where relevant, it will be necessary to repeat certain details in the tables summarising the individual trials' results as described in 0 below.

Information on all the reference products used in the trials should be given in Appendix 4 and should include the name of the products, the active substance(s), its concentration (e.g. g/l), application rate (e.g. l/ha) and formulation type. A justification that the reference product has been used under the authorised conditions of use has to be submitted.

It must be clearly stated whether the trials have been carried out in accordance with specific EPPO guidelines, where available, or with National guidelines satisfying at least the requirements of the corresponding EPPO guideline. If no test guideline is available or where deviations from the methods prescribed or other methods were used, applicants should include a justification of the scientific validity of the method used. It must be clearly stated whether the design, analysis and reporting of trials is in accordance with EPPO guidelines PP 1/152 and PP 1/181. Deviations from EPPO guidelines must be fully explained and justified.

Where a statistical analysis has to be performed information should be given on the method used.

5.2 Summary and evaluation of individual trials results

All results should be reported in a systematic form, together with a detailed and critical assessment of the data.

It is recommended to present the major elements of the results in tabular form (a proposed example is attached in Table 2). It is often useful to sub-divide this section according to target pest e.g.

i) Wheat powdery mildew (*Erisyphe graminis* f.sp. *tritici*)

ii) Septoria tritici

iii) Barley powdery mildew (*Erisyphe graminis* f.sp. *hordei*)

iv) Barley leaf blotch (*Rhynchosporium secalis*)

It is recommended to explain/justify the label claims in the order that they appear on the label. Each use for which application for authorisation is made should be reproduced exactly as it is on the draft label, followed by tables of trials results and an explanation of how the trials results, references or extrapolations support the text. It may be necessary to annotate the draft label

(included as Appendix 2 to the biological assessment dossier) to indicate where to find the sections in the biological assessment dossier to support the individual label claims.

It is essential that all relevant data from all trials in a series, regardless of obtained level of control, are presented and that individual values are reported correctly. Where trials have been excluded this must be clearly stated together with a justification for their exclusion (e.g. trial errors). Presentation of only a 'typical' sample of results is not acceptable. Care must be taken that results are presented from all reports referenced in 'List of reports/references'.

Summaries of results must include tables of individual results.

The exact details required in these tables of individual trials results vary widely according to the particular use involved. Care should be taken to ensure that any particular piece of information, which is important to the interpretation of results, is included in the table. Explanation must be given for individual control values, which differ appreciably from the majority. In such cases, comparison to a treatment with a reference product can be particularly important in assessing whether other environmental factors have influenced performance.

Similarly, results can be presented in many different ways depending on the particular use involved. Actual values (numbers of weeds/pests or percentage plants/plant parts affected by a disease) may be presented. Alternatively, the preferred method is for results to be given as a percentage of control relative to the untreated control. In this latter case, it is essential to give the actual level of infection/infestation on the untreated control.

Each result must carry a reference to the report from which it was obtained.

Relevant results of statistical analyses should also be presented. These may include: least significant differences and letter suffixes to denote significant differences between treatment means.

A full explanation must be given as to how the data are considered to support the proposed label claims, including parameters, such as dose/ dilution, spray volume, timing of application, growth stage of harmful organisms and crops, need for repeat treatments, number of treatments, interval between treatments. Included in this explanation is the need to justify the dose for which authorisation is being sought.

An explanation should also be given of the environmental factors that might influence the performance of the plant protection product.

All recommendations and claims reported on the draft label and not supported by data must be explained. This may involve extrapolation of data from one crop to another (e.g. control of powdery mildew from winter wheat to spring wheat). In the case of warnings/restrictions (e.g. weather conditions), which are not supported by data, extrapolation may be appropriate from already authorised products containing at least one of the active substances. In these instances, it should be stated clearly that no specific trials data exist and that extrapolation has been used. Where appropriate, labels of other already authorised products cited may be included in Appendix 3 of the biological assessment dossier and full explanation made as to how they support the proposed label statements.

Similarly, justification must be given for all instructions which are not supported by data but which are considered to constitute accepted Good Plant Protection Practice.

5.3 Minimum Effective Dose

This is also considered under 6.2. An appropriate summary of data must be included for those key targets where data are available from doses lower than label

recommendations. Ideally this should be separate to the summary of data described above, particularly if data are available from several trials, rather than simply referencing several tables. EPPO guideline PP 1/225 ‘Minimum effective dose’ provides more details on addressing this requirement and generation of data.

6 INFORMATION ON THE OCCURRENCE OR POSSIBLE OCCURRENCE OF THE DEVELOPMENT OF RESISTANCE (6.3)

Details information should be reported to allow the risk of the development of resistance to be evaluated. The EPPO Guideline ‘Resistance risk analysis’ PP 1/213 provides further guidance, along with UK Efficacy guideline 606 ‘Resistance risk analysis and use of resistance management strategies’.

Where a management strategy is proposed, justification must be included for the proposals made. There are also additional UK guidance documents on resistance restrictions and label warnings for individual product groups. Applicants should also refer to relevant UK-Resistance Action Groups (UK-RAGs, hosted on the Agricultural Horticultural Development Board (AHDB) website; and relevant industry Resistance Action Committee (RAC) sites. Please note, UK labels should include the Mode of Action group.

6.1 Materials and methods

Follow principles detailed in 0.

6.2 Summary and evaluation of individual experimental results

Follow principles detailed in 0.

7 ADVERSE EFFECTS ON TREATED CROPS (6.4)

7.1 Phytotoxicity to target plants (including different cultivars) or to target plant products (6.4.1)

Assessments of phytotoxicity often form part of designated crop safety trials and/or efficacy trials, which also include assessments of quality (section **Error! Reference s ource not found.**) and yield (section 0).

7.1.1 Materials and Methods

Follow principles detailed in 0.

Full experimental details must be provided in the individual trial reports (according to guidance given in EPPO guideline PP 1/135 ‘Phytotoxicity assessments’).

It is essential that all symptoms and the extent of damage are described accurately. Assessments may need to be repeated at regular intervals throughout the period of the experiment or until symptoms disappear. In the absence of any observable effects, it should be clearly stated that this was the case.

Where necessary the trials should be followed until harvest (see section 0).

7.1.2 Summary and evaluation of individual trials results

Follow principles detailed in 0.

All results should be reported in a systematic form. If appropriate, results may be presented in tabular form. It is recommended to present the major elements of the results in tabular form. It is often useful to sub-divide this section according to crop, e.g.

i) Winter wheat

ii) Spring wheat

iii) Winter barley

iv) Spring barley

In addition, where any adverse effects have been observed, these should be discussed and it may be necessary to propose appropriate limitations of uses, for example, use of the product could be restricted to certain crop growth stages or to certain defined weather conditions.

7.2 Effects on the yield of treated plants or plant products (Annex 6.4.2)

Measurement of yield should be submitted, depending on the type of product, from efficacy or crop safety trials, which also include assessments of phytotoxicity (section 0) and quality (section 6.4.**Error! Reference source not found.**).

Where no measurements of yield were performed, the justification for not providing these data should be provided in this section.

7.2.1 Materials and Methods

Follow principles detailed in 0.

The evidence can be provided from the general phytotoxicity trials or often from effectiveness trials where the pest has failed to develop. It is essential that the yield data for crop safety purposes are obtained from trials which remain more or less weed/pest/disease free in order to avoid that yield response resulting from control measures mask any negative yield effects resulting from phytotoxicity.

7.2.2 Summary and evaluation of individual trials results

Follow principles detailed in 0.

All results should be reported in a systematic form. Relevant details of statistical analyses should also be presented. It is often useful to sub-divide this section according to crop, e.g.

i) Winter wheat

ii) Spring wheat

iii) Winter barley

iv) Spring barley

7.3 Effects on the Quality of plants or plant products (6.4.2)

Assessments of quality often form part of designated crop safety trials, which also include assessments of phytotoxicity (section 6) and yield: quantity (section 7.2). In this case, it may be more convenient to combine the Materials and methods and Summary and evaluation of individual trials results for these sections. If this approach is adopted, it is essential to identify clearly the specific data requirement that is being addressed.

7.3.1 Materials and Methods

Follow principles detailed in 0.

7.3.2 Summary and evaluation of individual trials results

Follow principles detailed in 0.

In addition, where any adverse effects have been observed, these should be discussed and it may be necessary to propose appropriate limitations of use, for example, use of the product could be restricted to crops not intended for processing. EPPO guideline PP 1/242 ‘Taint tests’ provides specific guidance on when and how to address taint for relevant uses’.

7.4 Effects on transformation processes (6.4.4)

7.4.1 Material and Methods

Follow principles detailed in 0.

7.4.2 Summary and evaluation of individual trails results

Follow principles detailed in 0.

EPPO guideline PP 1/243 ‘Effects of plant protection products on transformation processes’ provides specific guidance on when and how to address this point for relevance.

7.5 Impact on treated plants or plant products to be used for propagation (6.4.5)

7.5.1 Materials and Methods

Follow principles detailed in 0.

The EPPO guideline PP 1/135 ‘Phytotoxicity assessments’ includes specific guidance on the situations where data are required. Please not in the absence of relevant data, label restrictions may be added (for example, not to use against crops grown for seed.

7.5.2 Summary and evaluation of individual trials results

Follow principles detailed in 0.

In the event of any unacceptable adverse effects on plant parts intended for propagation, the applicant must propose appropriate limitations of use. For example, a warning could be given not to use on seed crops.

8 OBSERVATIONS ON UNDESIRABLE OR UNINTENDED SIDE-EFFECTS (6.5)

8.1 Impact on succeeding crops (6.5.1)

8.1.1 Materials and Methods

Follow principles detailed in 0.

In some instances, a case may be made for the safety to following crops based on evidence from fate and behaviour studies and results from crop screening studies of soil activity. The EPPO guideline PP 1/207 ‘Succeeding crops’ provides further guidance.

8.1.2 Summary and evaluation of individual trials results

Follow principles detailed in 0.

In the event of any unacceptable adverse effects on succeeding crops, the applicant must propose appropriate limitations of use. For example, a minimum interval between treatment and sowing/planting of a succeeding crop could be specified. If necessary the cultivation of susceptible crops and varieties should be excluded.

8.2 Impact on other plants, including adjacent crops (6.5.2)

8.2.1 Materials and Methods

Follow principles detailed in 0.

In most circumstances, a case for the safety to adjacent crops could be made on the basis of a demonstrated lack of known herbicidal effects or a lack of the possibility of vapour drift. Results from post-emergence screening studies may provide useful information to demonstrate safety to adjacent crops. The EPPO guideline PP 1/256 ‘Adjacent crops’ provides further guidance.

<u>Cleaning application machinery</u>

6.5.2 also mentions that sufficient data shall be reported to permit an evaluation of possible adverse effects of a treatment with the plant protection product on other plants, including adjacent crops. Further details are provided in PP 1/292 ‘Cleaning pesticide application equipment (PAE) – efficacy aspects’. Data should be summarised in following principles detailed in 5.2.

8.2.2 Summary and evaluation of individual trials results

Follow principles detailed in 0.

In the event of any unacceptable adverse effects on adjacent crops, the applicant must propose appropriate limitations of use. For example, a warning could be given not to

spray during weather conditions when spray/ vapour drift is likely to occur.

8.3 Impact on beneficial and other non-target organisms (6.5.3)

This information results from observations made in efficacy trials. All observations should be reported in a systematic form, together with a detailed and critical assessment of the data. It should be noted, however, that evidence of effects on non-target organisms *per se* will be evaluated as part of the ecotoxicology risk assessment. The conclusions of both assessments should therefore where relevant be compared.

Usually, any positive effects on other harmful organisms will result in a claim of activity against that harmful organism, which will be addressed in section 0. In this situation, the issue need not be addressed in section 0.

9 SUMMARY AND EVALUATION OF DATA PRESENTED (6.7)

The summary should comprise the applicant's overall assessment of the biological assessment dossier, and a reasoned statement of the conclusions which the applicant believes should be reached on the basis of the data and information provided; this should reflect:

- the weight of the evidence available - the extent, quality and consistency of the data;
- where relevant, the conditions or restrictions with respect to the inclusion of active substances in Annex I;
- the evaluative and decision making criteria specified in the Uniform Principles

A summary of all data and information should be provided. The benefits of the plant protection product should be stated, along with any adverse effects and measures necessary to avoid or minimise the adverse effects.

The conclusions (including, where relevant, justifications for not providing data) should be presented in accordance with the order proposed above and should reflect the evaluative and decision making criteria specified in Uniform principles. It is particularly important that the concluding element for each point and the concluding part of sections, highlight the parameters of relevance to decision making, and include the rationale relied on for the conclusions reached in the light of the weight of evidence provided by the data reported.

The relevance of the location of studies to the proposed geographic area of use should be justified.

A conclusion resulting from all the data presented reiterates the biological properties and conditions of use of the plant protection product for the use proposed (advantages of the product, known or probable negative effects and the necessary measures to obviate them or restrict them to a strict minimum).

The duration of the effects of the treatment should be reported in relation to the control of the target organism or to the effect on the plants or on plant products treated. When more than one application is recommended, the trials establishing the duration of the

effects of one application, the number of applications required, and the suitable intervals between applications should be indicated.

Proof should be provided to evidence that the dose, timing, number and mode of application recommended provide adequate results for control or protection or that they produce the required effect in all the proposed conditions of use.

Unless there is evidence that the action of the plant protection product is not likely to be significantly reduced by environmental factors such as temperature or rainfall, a survey of the effects of such factors on the action of the product should be reported, especially if such information on similar active substances is available.

When the specifications on the label include recommendations on the use of the plant protection product in a mixture with other plant protection products and/or adjuvants, an evaluation must be provided on the mixture.

10 APPENDICES TO THE BIOLOGICAL ASSESSMENT DOSSIER

Appendix 1: LIST OF REPORTS/REFERENCES

The reference list provided in the biological assessment dossier should give full titles and reference numbers of reports, full literature references of published papers and adequate identification of any other relevant documents. All references and reports have to be available to the Competent Authority.

Appendix 2: DRAFT LABEL

Must relate to claims for which authorisation is sought.

Appendix 3: LABELS OF ANY OTHER PRODUCTS CITED IN SUPPORT

Appendix 4: DETAILS ON REFERENCE PRODUCTS USED IN THE TRIALS

Table 1 : Example format for presenting information on site/application details (Summary form)

(bold text included as an example)

Title of table ①: e.g. Trials details on: Test product: Winter wheat: Control of powdery mildew (Erysiphe graminis)

Trials reference	Year	Country/Region	Testing organisation	Official recognition status of testing organisation ②	Test method	Experimental design ③/ Replicates ④	Plot size ⑤	Application Volume ⑥	Assessment sample size⑦	Type of trial ⑧	Remarks ⑨
PM 96/1	**1996**	**France/Rheims**	**ABC Trials 1, rue des Remarques PARIS 75016 Tel 33-11-12345678**	**Yes**	**CEB No. 2**	**Randomised complete block/4**	**20 m^2**	**200 l/ha**	**30 tillers per plot**	**F/N/R**	
PM 96/2	**1996**	**UK/York**	**Agro Trials 1, London Road CAMBRIDGE Tel 01223 123456**	**Yes**	**EPPO No. 26**	**Randomised complete block/4**	**20 m^2**	**200 l/ha**	**30 tillers per plot**	**F/N/R**	
etc.											

Notes:
① Title of identity of product under test/crop/pest (common and scientific name)
② Indicate with a YES or NO if the trials organisation is official/officially recognised
③ Indicate the experimental design.
④ Indicate the number of replicates.
⑤ Indicate the net plot size.
⑥ Indicate application volume.
⑦ Indicate the assessment sample size.
⑧ Indicate the type of trial: F = field; G = glasshouse; N = natural infestation; A = artificial inoculation; M = mist irrigated; R = rainfall only.
⑨ Explanation of any deviations from official test methods.

Table 2: Example format for presenting efficacy data (summary form) -

(bold text included as an example)

Title of table ①: e.g. Test product: Winter wheat: Control of powdery mildew (Erysiphe graminis)

Treatments				Trial reference Country/Region Year of trial Cultivar Treatment (date and growth stage)	**PM 96/1** **France/Rheims** **1996** **Riband** **1 April** **GS 31**	**PM 96/2** **UK/York** **1996** **Brigadier** **14 April** **GS 31**	etc. ⑧	**Mean of results and range ⑨**
Products ②	Active substance(s) ③	Rate g. a.s./ha	Number/ Interval ⑤	Pest incidence/ severity at application Assessment ⑥, ⑦ Date/days after treatment Growth stage Plant part assessed Soil type (if relevant)	**5 % on leaf 2** **% disease** **29 April/28 DAT** **GS 37** **leaf 2** **-**	**5 % on leaf 2** **% disease** **12 May/28 DAT** **GS 37** **leaf 2** **-**		
untreated control **(% area affected)**	**-**	**-**	**-**		**(20)**	**(50)**		**(35) (20 - 50)**
Test product(s) ***"Testo"***	**novodin 100 g/l EC**	**100**	**1**		**90**	**80**		**85 (80 -90)**
Reference product(s) ***Horizon EW***	**tebuconazole 250g/l EW**	**250**	**1**		**90**	**70**		**80 (70 -90)**

Notes:
① Title of identity product under test/crop/pest (common and scientific name).
② Indicate the development code and/or the commercial name of each product tested and the control plot with the word 'control' or 'untreated control'.
③ If not already provided elsewhere, indicate the a.s. content and formulation type of each product.
④ Adjust the units if necessary (e.g. for seed treatments **kg/tonne**).
⑤ Indicate the total number of treatments and the interval between them (e.g. **5, 14**).
⑥ For pest assessment, indicate the units of assessment (e.g. **% leaf area affected**, **number of pests per leaf**).
For the (untreated) control plot, indicate in parentheses the actual incidence/severity in the (e.g. **(36%)).**
For the treatments, indicate the % control relative to the incidence/severity on the (untreated) control (e.g. **95%).**
Indicate the statistical significance per trial and treatment.
⑦ The design of table can be used to present results of phytototoxicty or other side-effects and yield.
For assessments of phytotoxicity etc., indicate clearly the damage recorded (e.g. **% chlorosis on leaf 2**).
For yield, indicate the units of measurement (e.g. **tonnes/ha**). For the (untreated) control plot, indicate in parentheses the actual yield e.g. (10.5 t/ha) and for the treatments, indicate yield relative to the (untreated) control (e.g. **125**).
⑧ Results of other trials in the same series may be presented in further columns.
⑨ The final column may be used to provide a mean and range of the results (e.g. **90 % (80-100)).**

Further information

For information about health and safety, or to report inconsistencies or inaccuracies in this guidance, visit www.hse.gov.uk/. You can view HSE guidance online and order priced publications from the website. HSE priced publications are also available from bookshops.

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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