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European and Mediterranean Plant Protection Organization
Organisation Européenne et Méditerranéenne pour la Protection des Plantes PP 1/271 (3)

Efficacy evaluation of plant protection products

PP 1/271 (3) Guidance on efficacy aspects of comparative assessment

Specific scope

Plant protection products (PPP) may be subject to a process of comparative assessment (CA) to determine whether substitution by alternative PPP**s** or other control methods is possible. Substitution should only be made if, among the other alternatives, there are no significant economic or practical disadvantages. This Standard provides guidance and a decision support scheme to determine whether the substitution of a PPP is appropriate in view of agronomic considerations. This includes practical and economic impacts of identified alternatives (both chemical and non-chemical), as well as resistance risk management. The Standard does not address comparative safety from the human and environmental perspective.[1] Expert judgment is required in answering the questions (which may include the need to seek specialist advice).

Specific approval and amendment

First approved in 2011-09.
Minor revision approved in 2015-09.[2]
Revision approved in 2019-09 following discussion in the EPPO Workshop on Comparative Assessment of Plant Protection Products (Lisbon, 2018-10-24/25)

1. Introduction

In authorizing the use of plant protection products (PPPs), aspects such as sustainable pest control and safe use are considered. In the authorization process, comparison with safer alternatives may be considered on the level of uses, and when a safer and effective alternative is available substitution of a use may be considered. In the EU, **c**omparative **a**ssessment (CA) is required for authorization of PPPs which contain an active substance that has been identified as a candidate for substitution (CfS) in Regulation (EC) 1107/2009 (Articles 24 and 50). This Standard provides specific and technical guidance with the objective of meeting the requirements of this EU Regulation. The principles of this Standard are also applicable to other EPPO members where CA may be carried out and where there is a consideration on the agronomic impact.

The Standard covers the following stages of CA:

- Initiation of CA
- Defining the uses of the candidate product
- Determining the alternatives to consider as substitute(s) for the uses of the candidate product
- Conduct of CA process
- Impact on minor uses (Stage A)
- Assessing risk of resistance developing (Stage B)
- Assessing efficacy of available alternatives (Stage C)
- Assessing practical and economic disadvantages (Stage D)
- Further advice where the CfS active substance is with a co-formulated mixture PPP.

The decision support scheme follows a tiered approach based on a series of questions grouped within four stages (A–D described above). The CA may come to an end on completion of an individual stage, as indicated. Therefore, it may not be necessary to continue through the whole scheme addressing all four stages. The order that the stages are considered may reflect individual national guidance and procedures outlining how CA will be conducted in their Member State.

In undertaking a CA, information is required by the registration authority to answer the questions in the scheme.

[1]For EU Member States, guidance is available covering human health and environmental aspects of CA: 'Draft Guidance document on Comparative Assessment and Substitution of Plant Protection Products in accordance with Regulation (EC) No 1107/2009 SANCO/11507/2013 rev.12, 10 October 2014'. SANCO 11507/2013 recommends a stepwise approach with the agronomic assessment conducted first, for which specific reference is made to using this EPPO Standard.

[2]To harmonize requirements with DG SANCO Guidance Document 11507/2013.

The required information will normally already be available to the national authority through the previous authorization processes, by reference to the current authorized uses and any accompanying authorized national labels.

Information regarding alternative PPPs may already be available to the registration authority, although its use for such purposes will have to be considered in view of confidentiality of data. For non-chemical alternatives, it is recognized that information on effectiveness, economics and practical issues may not be readily available and requires reference to a number of sources. Where expert judgment would not be sufficient to address significant information gaps, the CA may not be meaningfully performed and completed. In this event, substitution of the candidate for that use is (provisionally) not possible.

At the end of the CA process, the assessor should fully document the evaluations undertaken and the reason(s) for the outcome of the CA. To communicate the report of the assessment to the registration holder or applicant, or to make it available to other registration authorities and for possible reassessment in the future, it is important that all steps of the procedure are fully documented. It should be indicated how each decision was reached and on what information it was based. Any uncertainties regarding data or conclusion(s) should be noted. In the case that there is a high level of uncertainty regarding the alternative, the CA is completed at that point and the candidate product remains available.

2. Initiation of Comparative Assessment

A CA shall be performed when evaluating an application for authorization for a PPP containing an active substance approved as CfS. In the EU, according to Regulation 1107/2009 the European Commission has established a list of active substances[3] approved as CfS. Initiating a CA is considered when:

- a review is required of an existing registered PPP, i.e. at renewal of the PPP authorization
- an application for amendment of the registration of a PPP is received (e.g. requesting a new use), whereby assessment of alternatives may only be done for the requested new uses
- an application for a new PPP is received.

Ideally, and where practically possible, regulatory authorities may consider conducting CA of products containing the same active substance candidate for substitution at the same time. This would facilitate comparisons with all relevant alternative methods.

[3]The Commission regulation establishing a list of candidates for substitution was published on 11 March 2015. COMMISSION IMPLEMENTING REGULATION (EU) 2015/408 of 11 March 2015 on implementing Article 80(7) of Regulation (EC) No 1107/2009 of the European Parliament and of the Council concerning the placing of PPPs on the market and establishing a list of candidates for substitution.

In some cases, a Member State may have no experience or relevant information on the use of a product containing the CfS. In such circumstances, experience may be gained by use of the product under relevant practical conditions and the CA procedure may be postponed.

3. Defining the uses of the candidate product

The PPP for which CA is initiated is called the candidate product. The first step after initiation of CA is to define the use(s) of the candidate product. Definition of the use(s) could be presented in tabular form. This information should already be available to the registration authority.

In order to facilitate the exchange of information between registration authorities, it is recommended that this information is presented in accordance with EPPO Standards PP 1/240 *Harmonized basic information for databases on plant protection products* and PP 1/248 *Harmonized classification and coding of the uses of plant protection products*.

4. Determining the alternatives to consider as substitute(s) for the uses of the candidate product

When the use(s) of the candidate product have been specified, alternatives for these uses should be identified against which CA will be performed. Alternatives may be another (authorized) PPP, a non-chemical alternative, a measure to prevent the occurrence of the pest or a combination of two or more methods.

A non-chemical method (or methods), including a preventative method (e.g. a resistant variety), can only be considered as a potential alternative when it is a practical method which is already used by growers for the same target pest, or when the method has been assessed by research and shown to be suitable for use in the particular environmental and agronomic situation over a number of years. Such a method should be broadly applicable as some non-chemical methods may be restricted by soil type, rotational cycle, or season or local conditions.

When alternatives for the uses of the candidate product have been identified, the CA can start. As CA requires substantial information to be available or collected, it is recommended that the CA is carried out as follows: firstly a use of the candidate against a chemical (either preventative or curative) alternative for that same use may be assessed, following the decision support scheme.

Secondly, a use of the candidate against a non-chemical (either preventative or curative) alternative for that same use may be assessed, assisted by the decision support scheme.

Finally, a use of the candidate against a system including two or more alternative methods, including a programme of treatments, for that same use may be assessed, based on the questions of the decision support scheme.

As soon as a question results in the alternative not being a suitable substitution for the assessed use of the candidate, the CA process for that use is considered to be completed. Further uses of the candidate product can then be assessed following the same sequence.

5. Conduct of comparative assessment process

The CA scheme for efficacy described below is grouped into four main assessment stages for consideration:

- Stage A: Assessing effects on minor uses
- Stage B: Assessing comparability regarding the risk of developing resistance
- Stage C: Assessing efficacy and use within integrated pest management (IPM) of available alternatives
- Stage D: Assessing practical and economic disadvantages

For each stage, having appropriately addressed the questions, the indicated outcome will be either (a) the CA is concluded at that stage or (b) the CA should continue, by addressing the questions in the next relevant stage. The order in which each stage is considered by the national authority may reflect the individual national procedures for conducting CA. Experience gained has led to developing processes which prioritise key issues and facilitate completion of the CA at the most relevant point.

For example, consideration of minor uses is a common first step for many individual national regulatory authorities, with CA stopped if there are minor uses associated with the PPP containing the CfS. In such circumstances, Stage A is the logical place to start the CA and, if appropriate, it may be completed at this point without needing to consider other stages. If, however, resistance risk is the key concern, then Stage B is a more suitable starting point. Any decision and the steps undertaken should be appropriately recorded.

6. Comparative assessment decision scheme

The stages of the scheme are described below and may be addressed in any order. However, the questions within each stage should be answered in the order given:

- If the answer to a question indicates that CA can be concluded at that point, no further questions within that stage, or other stages, need to be addressed.
- If at the end of the stage it is indicated that CA should continue, then the next relevant stage should be selected.
- CA is continued for those uses where an alternative is available. Substitution is not possible for those uses where there are no alternatives.

If all stages have been completed without an indication that CA can be concluded, then substitution may be possible from an efficacy perspective. However, assessment of further aspects such as human health and the environment may also be necessary.

Assessing effects on minor uses (Stage A)	
A1. Is the candidate product authorized, or authorization requested, for minor uses?	
Yes	Go to A2
No	Go to next appropriate Stage (B, C or D)*
A2. Are minor uses sufficient to stop CA, according to the available national CA procedure?	
Yes No	Stop CA Go to A3
A3. Is the substitution of the candidate product on a major crop anticipated to have a significant impact (see Note A) on minor uses?	
Yes	Stop CA
No	Go to next appropriate Stage (B, C or D)*
*If all other stages have already been considered without an indication that the CA should be stopped, substitution may be possible.	
Explanatory note **Note A** Impacts on minor uses should be clearly substantiated, describing the commercial viability of the product if the major uses are lost. Argumentation based on it not being economically feasible to support only the remaining minor uses should be evidence based. This may include the product approval holder in the case of on-label use of the candidate or the benefiting organizations in the case of off-label use of the candidate.	

Assessing comparability regarding the risk of developing resistance (Stage B)	
B1. Does the target pest(s) have a high or medium inherent resistance risk (see Note B(i))?	
Yes	Go to B2
No	Go to B5
B2. Is there a product within the same mode of action (MoA) group authorized for use against the target pest(s)?	
Yes	Go to B5
No	Go to B3
B3. Are there products with another MoA authorized for use against the target pest(s)?	
Yes	Go to B4
No	Stop CA
B4. Does the candidate exhibit negative cross-resistance in the target pest(s) (see Note B(ii))?	
Yes	Stop CA
No	Go to B5

(continued)

B5. Given the available alternatives (chemical and non-chemical), is the candidate an important component (see Note B(iii)) of the resistance management strategy for the target pest and other pests in the crop not themselves subject to CA?	
Yes	Stop CA
No	Go to next appropriate stage (A, C or D)*
*If all other stages have already been considered without an indication that the CA should be stopped, substitution may be possible.	

Explanatory notes

Note B(i)

The risk of resistance can be analysed based on PP 1/213 Resistance risk analysis. In CA the impact on a risk management strategy in the situation that a PPP is subject to substitution is assessed.

Note B(ii)

See detailed guidance provided in EPPO Standard PP1/213, section 5.3.5.

Note B(iii)

Based on expert judgment it is recommended that in a low resistance risk situation a sustainable resistance management strategy includes at least two MoAs. However, in the case where there is evidence of a medium risk of resistance to one or more of these PPPs or a medium risk of resistance in the target organism, at least three MoA are recommended. In the case where there is evidence of a high risk of resistance to one or more of these PPPs or a high risk of resistance in the target organism, at least 4 modes of action are recommended (Rotteveel et al., 2011). The current resistance situation should be considered when evaluating the required number of mode of actions.

Assessing efficacy and use within IPM of available alternatives (Stage C)	
C1. Do alternatives (chemical or non-chemical) exist for controlling the target organism (or regulating plant growth) in the target crops of the candidate product for that use?	
If Yes, a list of alternatives should be made	Go to C2
No	Stop CA
C2. Is the effectiveness of the alternative(s) comparable (see Note C) with the candidate product for that use?	
Yes	Go to C3
If the alternative(s) is (are) unacceptably less effective	Stop CA
C3. Is the crop safety of the alternative comparable (e.g. comparing existing label crop safety warnings and restrictions on succeeding crops) with the candidate product for that use?	
Yes	Go to C4
If unacceptably lower	Stop CA
C4. Will substitution of the candidate product by the alternative lead to disruption of established IPM strategies, prohibit establishment of new IPM strategies or, for example, have a negative impact on beneficial organisms, for which there are no acceptable mitigation possibilities?	
Yes	Stop CA
No	Go to next appropriate Stage (A, B or D)*
*If all other stages have already been considered without an indication that the CA should be stopped, substitution may be possible.	

Explanatory notes

Note C

When comparing two PPPs, in some cases they will have the same mode of application and result in the same or similar controlling effect on the target. Differences in effectiveness, e.g. indicated by differences in level, consistency and longevity of control, and where relevant yield or quality, provide a good basis for comparison. Limitations in the use according to the label (e.g. number and timing of applications, buffer zones) of the alternative also need to be taken into account. This information may come from the authorized label claims, independent technical institutes and researchers.

Assessing practical and economic disadvantages (Stage D)	
D1. Are there significant practical or other disadvantages (see Note D (i)) resulting from the use of the alternative if the candidate is no longer available?	
No	Go to D2
Yes	Stop CA
D2. Is gaining pest control with alternative(s) considerably more expensive (see Note D(ii)) than the use of the candidate?	
No	Go to D2
Yes	Stop CA
D3. Are there any wider consequences for maintaining effective crop protection, including e.g. the security of future pest control, that might influence the decision of making a substitution and/or adverse impacts for non-crop uses (see Note D(iii))?	
Yes	Stop CA
No	Go to next appropriate Stage (A, B or C)*
*If all other stages have already been considered without an indication that the CA should be stopped, substitution may be possible.	

Explanatory notes

Note D(i)

Practical or other disadvantages include lack of labour availability for hand weeding, insufficient land available to permit sufficiently long rotations to enable pest, weed or disease management through crop rotation, versatility of alternatives, etc. For herbicides in particular, the lack of weed control can significantly adversely impact the following crop in the crop rotation. The windows of application (including pre-harvest intervals) of other methods may differ from the application of the candidate and limit the feasibility of the alternative.

(continued)

Consideration should be given to the need and acceptability of the use of additional PPPs or alternative measures to control additional pest problems.

Note D(ii)

The EU Regulation 1107/2009 defines significant economic disadvantage to the user as a major quantifiable impairment of business activity leading to an inability to control the target organism. A clear criterion should be established to decide whether it concerns a considerably more expensive pest control or not. For example, the alternative leads to a substantive increase in production costs to obtain the same yield value. It should be remembered that economic disadvantage with a non-chemical method may need to be considered over more than a single year. When, for example, fleeces are used as an alternative, their durability may be such that they can provide effective insect control for several years, and cultivation methods as alternatives may result in high seed return from the soil seed bank. Independent experts should be consulted where necessary.

Note D(iii)

Wider consequences include:

- dependence on a single product for a major use
- sustainable production of the crop concerned
- control possibilities for quarantine pests
- control possibilities for emerging pests
- need for diversity of products to minimize impacts on water quality and biodiversity
- impact on human health, for example mycotoxin levels in cereals, contamination of harvested produce with poisonous weeds, allergic reaction to Lepidoptera species such as Oak processionary moth
- impact on human safety, for example airfield management to avoid bird strikes, vegetation management in railway line verges

In addition to considering products that are currently authorized, consideration should be given to active substances which may be at risk of losing authorization, based on current knowledge.

7. Conducting an assessment where the candidate for substitution active substance is within a co-formulated mixture containing other active substances

Further advice is given below on how to consider the resistance and agronomic factors when a candidate for substitution is part of a co-formulated mixture containing other active substances. In particular, advice is given on the implications of resistance management and whether the assessment should be based on the uses of the PPP as a whole or differentiate the CfS active substance from that of other active substances present.

7.1. Resistance management

As described in Stage B, the first consideration is whether there is sufficient chemical diversity in terms of the number of alternative modes of action against the target pest. If there is not, then CA will be completed at that point.

If there is a sufficient number, then further consideration of the contribution of the CfS active substance in resistance management may be required. For example, it should be considered whether the CfS active substance is contributing to the overall resistance management strategy and lowering the risk of resistance development by the target by being combined in a mixture with other active substances.

Is the mixture of active substances in the PPP new and/or unique or are there other authorized PPPs which have a similar association involving active substances belonging to the same modes of action?

There may be other wider resistance considerations at a national level (occurrence, level, known cross-resistance) that may form part of the assessment on the implications for resistance if the CfS is removed.

The resistance considerations therefore should be considered at a product level, alongside maintaining sufficient diversity of modes of action.

7.2. Comparison of agronomic, economic and practical aspects

Because CA is conducted on the PPP, the focus of comparisons should generally be based on the effectiveness of the mixture. A primary consideration would be first to identify if there are similar authorized mixture PPPs (same/similar mode of action and spectrum of use) authorized for the same crop/pest and whether such alternatives are used in a similar position within the overall season treatment programme for that crop (e.g. another PPP based on a mixture involving a contact multisite active substance and a systemic active substance).

Where it is possible to distinguish the efficacy contribution of each active substance within the mixture containing the CfS, the comparisons will be between the CfS active target/use and other products authorized for the same target/use. Typically, this will be where each active substance has a very specific mode of action, is effective against distinct pest species and there is no overlap in activity.

8. Final conclusion of the comparative assessment

The assessor should establish a summary table listing all uses of the candidate product and indicating for which uses substitution is possible as part of the assessment report.

References

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 Directives 79/117/EEC and 91/414/EEC.

Rotteveel T, Jorgensen LN & Heimbach U (2011) Resistance management in Europe: a preliminary proposal for the determination of a minimum number of active substances necessary to manage resistance. *Bulletin OEPP/EPPO Bulletin* **41**, 432–438.