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European and Mediterranean Plant Protection Organization
Organisation Européenne et Méditerranéenne pour la Protection des Plantes PP 1/271 (2)

Efficacy evaluation of plant protection products
Evaluation biologique des produits phytosanitaires

PP 1/271 (2) Guidance on comparative assessment

Specific scope

This Standard provides guidance for comparative assessment (CA) to determine whether the substitution of a plant protection product (PPP) is appropriate in view of agronomic considerations. However, this Standard does not address comparative safety from the human and environmental perspective. It covers comparison with chemical and non-chemical pest control alternatives. The Standard provides a scheme to support decision-making. 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 (to harmonize requirements with the DG SANCO 11507/2013)[1].

Introduction

In authorizing the use of 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 may be considered. In the European Union, comparative assessment is required for authorization of PPPs, which contain an active substance that has been identified as a candidate for substitution (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 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;
- Assessing comparability regarding all aspects of efficacy and crop safety;
- Assessing risk of resistance developing;
- Assessing practical or economic disadvantages, including assessing impact on minor uses.

The decision support scheme follows a tiered approach which means that the process of CA may be stopped at any stage and it may not be necessary to continue through the whole scheme.

In undertaking a CA, information is required by the registration authority in order to be able to answer the questions in the scheme. The required information will normally already be available to the national authority through the previous authorization processes.

Information regarding the alternative may already be available to the registration authority when it concerns an alternative PPP although its use for such purposes will have to be considered in view of confidentiality of data. For non-chemical alternatives such information may not be readily available or may not exist. If that is the case, and when expert judgment would not be sufficient to fill the information gap and such information cannot be obtained from other sources, the CA may not be meaningfully performed, and in this event should be stopped. Substitution of the candidate for that use is (provisionally) not possible. The Regulation (EC) 1107/2009 foresees also that the candidate product can be authorized once for a period not exceeding five years without going through the CA process if this is necessary to acquire experience by using this product in practice first.

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

[1]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.

re-assessment 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 stopped and the candidate product remains available.

Initiation of comparative assessment

According to Regulation 1107/2009 the European Commission will establish a list of active substances[2] approved as candidates for substitution. A comparative assessment shall be performed when evaluating an application for authorization for a PPP containing an active substance approved as a candidate for substitution. 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;
- An application for a new PPP is received.

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. 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*.

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, 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 followed: Firstly, a use of the candidate against 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 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 can be stopped and further uses of the candidate product can be assessed following the same sequence.

Conduct of comparative assessment process

At the initiation of the CA process it may appear that specific issues related to the candidate product may result in retention of its authorization, for some or all of the uses of the product. As experience is gained of the stepwise CA process, it will be possible to assess the relevant steps earlier in the CA process to reduce or avoid the workload imposed by other steps. For example, if after having conducted step one to identify an alternative, it is considered that the alternative poses significant practical disadvantages, and then step 15 may be directly undertaken. If this consideration is confirmed, CA may be stopped. This may assist in streamlining the process and any decision and the steps undertaken should be appropriately recorded.

Assessing comparability regarding efficacy

1. Do alternatives (chemical or non-chemical) exist for controlling the target organism (or regulating plant growth) in the target crops of the candidate product (see Note a)?		
If yes,	a list of the alternatives should be made	Go to 2
If no,		Stop CA

(continued)

[2]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 plant protection products on the market and establishing a list of candidates for substitution.

2. Is the effectiveness of the alternative(s) comparable (see Note b) with the candidate product for that use?
   If yes, Go to 3
   If considerably less effective Stop CA
3. Is the crop safety (including effects on the target crops, adjacent crops, succeeding crops, plant parts used for propagation, taint or transformation processes) of the alternative comparable with the candidate product for that use?
   If yes, Go to 4
   If unacceptably lower, Stop CA
4. Will substitution of the candidate product by the alternative lead to pest problems for which there are no acceptable mitigation possibilities? (see Note c)
   If yes, Stop CA
   If no, Go to 5
5. Will substitution of the candidate product by the alternative lead to disruption of established IPM systems, prohibit establishment of new IPM systems, or for example have a negative impact on organisms beneficial to crop protection for which there are no acceptable mitigation possibilities
   If yes, Stop CA
   If no, Go to 6

Assessing comparability regarding the risk of developing resistance

6. Does the target pest have a high or medium inherent resistance risk (see Note d)?
   Yes, Go to 7
   No, Go to 10
7. Is there a product within the same Mode of Action (MoA) group authorized for use against the target pest?
   Yes, Go to 10
   No, Go to 8
8. Are there products with other MoA authorized for use against the target pest?
   Yes, Go to 9
   No, Stop CA
9. Does the candidate exhibit negative cross-resistance (see Note e) in the target pest(s)?
   Yes, Stop CA
   No, Go to 10
10. Given the available alternatives (chemical and non-chemical), is the candidate an important component (see Note f) of the resistance management strategy for the target pest and for other pests in the crop not themselves subject to the comparative assessment?
    Yes, Stop CA
    No, Go to 11

Assessing practical or economical disadvantages, and effects on minor uses

11. Are there significant practical or other disadvantages (see Note g) resulting from the use of the alternative if the candidate is no longer available?
    If no, Go to 12
    If yes, Stop CA
12. Is the candidate product authorized for minor uses (on-label or off-label)?
    If yes, Go to 13
    If no, Go to 14
13. Is substitution of the candidate product on a major crop anticipated to lead to unsustainable control (see Note h) of pests on a minor crop?
    If no, Go to 14
    If yes, Stop CA
14. Is gaining pest control with the alternative(s) considerably more expensive (see Note i) than the use of the candidate?
    If no, Go to 15
    If yes, Stop CA
15. Are there any wider consequences for maintaining effective crop protection, including the security of future pest control that might influence the decision of making a substitution (see Note j)?
    If no, Substitution possible
    If yes, Stop CA

(continued)

Comparability of risks for health and environment

Although this Standard does not address comparative safety from the human and environmental perspective, in order to complete the CA process, an assessment of the health and environmental aspects of the candidate and any chemical and/or non-chemical alternatives should be made by the appropriate experts.

Final conclusion of the CA

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.

Explanatory notes

Note a

CA is continued for those uses where an alternative is available. Substitution is not possible for those uses where there are no alternatives.

Note b

In comparing two PPPs it is generally likely that both PPPs 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.

Note c

The candidate product may have a broader spectrum of activity compared with the alternative and substitution may lead to pest problems which are not explicitly covered by the authorization.

Note d

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

Note e

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

Note f

Based on expert judgment it is recommended that in a low resistance risk situation a sustainable resistance management strategy includes at least two modes of action. However, in case 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 modes of action are recommended. In case 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). Current resistance situation should be considered when evaluating the required number of mode of actions.

In considering the effect of substitution for a resistance management strategy other factors of inherent risks (e.g. target site resistance versus metabolic resistance, cross resistance) or agronomic risks should be taken into consideration (see EPPO Standard PP 1/213).

Note g

Practical or other disadvantages including for example 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. The windows of application of other methods may differ considerably from the application of the candidate and limit the feasibility of the alternative.

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

Note h

Unsustainable control (i.e. the inability to ensure effective control without adverse practical or economic effects on crop production, or unacceptable resistance risk to the targets controlled) of pests in minor use should be clearly substantiated, describing the importance of the production associated with the minor use and the absence of effective alternatives for the candidate or the lack of adequate chemical diversity of products available for minor use. Analysis of the efficacy of pest control and assessment of resistance risks may be extrapolated from data on relevant major uses. The information required should come from experts, which may include the product approval holder in case of on-label use of the candidate, or from the benefiting organizations in case of off-label use of the candidate.

It is necessary also to consider whether the sole use of a candidate product for one (or more) minor uses only, may (because of the subsequently reduced market size) lead to the termination of the supply of the candidate product by companies in the short as well as longer term. A consideration of whether one of the major uses of the product should be maintained to secure the supply of the product is needed. In such cases the benefits of sustaining the minor crop production should be balanced to the draw-backs of a larger scale use.

Note i

The EU regulation 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 j

For example:

- 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.

In addition to considering what is currently authorized, consideration should be given to actives which may be at risk of losing authorization, based on current knowledge.

Reference

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.