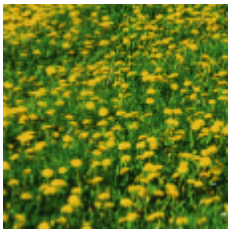

ECPA position on comparative assessment and substitution under Regulation 1107/2009 including a proposal for performing comparative assessment

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1. Summary

Regulation (EC) No 1107/2009 introduces the process of comparative assessment and substitution for plant protection products.

This position paper presents the European Crop Protection Association's recommendations on how to implement this process.

The first stage of the comparative assessment process is to determine which active substances are 'candidates for substitution'. Although this was supposed to be done by 14 December 2013, the list proposed by the Commission was voted in the meeting of the Standing Committee on Plants, Animals, Food and Feed on 27 January 2015[1].

While several criteria identifying substances as candidates for substitution are defined in the Regulation, others require definition or clarification. Based on criteria that are already defined in Annex II point 4, the list of candidates for substitution is expected to be extensive, representing about 20% of the approved active substances[2]. For future active substances applications, ECPA recommends that this number is not further increased by ensuring that the as yet undefined criteria (such as 'significantly lower ADI, AOEL or ARfD' and 'significant proportion of inactive isomer') are carefully defined and that scientifically robust principles are applied in the assessment of PBT (persistent, bioaccumulative and toxic) properties. It is essential that good judgement is applied to the evaluation of 'remaining concerns linked to critical effects'.

ECPA welcome the Commission communication on the nature of the list in the form of a question & answers document. In addition ECPA recommends that the Member State regulators and industry proactively communicate to prevent misinterpretation and misuse of the list of candidates for substitution. It is important to emphasise that all compounds listed as candidates for substitution will have received EU approval and therefore have passed all the stringent criteria and have been shown to have safe uses.

The second stage of the process requires that all Member State authorities compare the risks and the benefits of plant protection products containing candidates for substitution with those of alternative plant protection solutions (chemical or non-chemical). ECPA particularly recommends that an alternative should not be considered of lower risk than the candidate product unless a lower risk profile has been established for both human and environmental health. If alternatives exist for the uses considered, which are demonstrated to be of lower risk to humans and the environment, the candidate product should be substituted with the alternative only when substitution is not expected to have any unacceptable consequences. Only products which have been used in practice for a period of five years to ensure that sufficient experience has been acquired shall be considered for possible replacement.

This process has the potential to be complex and resource-demanding. ECPA therefore proposes a stepwise approach that evaluates substitution conditions[3] in a methodical and organised manner. The proposed process allows for the termination of the assessment as soon as it can be demonstrated that substitution is not possible due to failure of one of the

[1] Commission press release MEMO/15/3743, 27 January 2015: http://ec.europa.eu/food/plant/pesticides/approval_active_substances/docs/qaa_candidates_substitution_en.pdf

[2] Commission Questions and Answers on Candidates for Substitution, Rev. 1, January 2015, page 5: http://ec.europa.eu/food/plant/pesticides/approval_active_substances/docs/qaa_candidates_substitution_en.pdf

[3] Evaluation areas include efficacy, chemical diversity and potential for resistance development, safety for humans and the environment, practical and economic consequences of a possible substitution and impact on minor uses.

substitution criteria. Taking a stepwise approach should reduce complexity and limit the resource demand. The principles of this approach are described in this position paper while details are provided in a separate guidance document (ECPA document No 21246).

Comparative assessment should be properly documented by evaluators, with lists of uses that can or cannot be substituted and the rationale for the decision; applicants should be given the opportunity to comment on the assessment. ECPA recommends that a process be developed which allows substituted uses to be quickly re-authorised when conditions leading to the substitution have changed. Non-chemical methods should be factually evaluated for their safety to human health and the environment and their overall suitability (including financial impact) to crop protection. This should be done with a view to creating a 'positive list' of non-chemical solutions.

2. Introduction

Regulation (EC) No 1107/2009 concerning the placing of plant protection products (PPPs) on the market (the 'Regulation') entered into force on 14 December 2009. It repealed Directive 91/414/EEC on 14 June 2011 and has applied from that date. The Regulation implements the system of comparative assessment and substitution, which did not exist in the Directive. The Regulation requires that Member States shall not authorise uses of plant protection products containing active substances approved as candidates for substitution when alternatives exist. The alternatives (chemical or non-chemical), should provide a similar level of control of the target organism and must be of lower risk to man and the environment. Substitutions should not have unacceptable consequences.

This position paper presents the recommendations of the European Crop Protection Association (ECPA) for implementing the comparative assessment and substitution provisions [4].

It is important to note that the review program conducted under Directive 91/414 (article 8.2) has led to a significant number of active substances being phased out[5]. Regulation 1107/2009 also introduces hazard-based criteria that will phase out additional substances. The current context, in which the number of compounds available to provide crop protection solutions is decreasing, has been taken into account in this document and practical measures are proposed to limit further reduction through comparative assessment and substitution[6].

3. Summary of comparative assessment and substitution main provisions

The regulation provides that an active substance shall be identified as a 'candidate for substitution' according to Article 24 if:

- It meets all approval criteria set in article 4 and Annex II points 2 and 3, and
- It meets one or more of the criteria set in Annex II point 4

Approval of candidates for substitution cannot exceed 7 years and is renewable. Although this was supposed to be done by 14 December 2013, the list proposed by the Commission was voted in the meeting of the Standing Committee on Plants, Animals, Food and Feed on 27 January 2015.

When evaluating an application for the authorisation of a plant protection product containing a candidate for substitution, Member State authorities shall determine, according to Article 50 and Annex IV (comparative assessment), whether:

[4] Unless otherwise specified, articles and points mentioned in this document refer to Regulation 1107/2009.

[5] About 70% of substances available in the early 1990's were not supported and/or not included in Annex I of Directive 91/414/EEC

[6] A lack of products already exists for some crop/pest combinations

- Alternative plant protection solutions exist (chemical or non-chemical),
- The use of alternatives presents a significantly lower risk than the use of the candidate product under evaluation.
- Denying or revoking the authorisation of the candidate product in favour of the alternatives does not present unacceptable consequences.

Authorities shall not authorise or shall revoke PPP uses for which all above conditions are met (substitution). Comparative assessment covers efficacy, resistance, human health, environmental safety, economic and practical consequences of a possible substitution and its consequences on minor uses. Comparative assessment can be waived for up to five years where it is necessary to gather experience on the possible impact of any substitution. Substitution must be effective within three years of the decision.

4. Identification of candidates for substitution

Annex II point 4 provides criteria to identify an active substance as a candidate for substitution. Further definition or clarification of several of these criteria is required. Under those criteria (whether already defined or yet to be defined) it is estimated that about 20% of the approved active substances will be identified as candidates for substitution. This number is significant, as will the number of PPPs and uses reviewed under comparative assessment. Consequently the workload for authorities and applicants will be considerable.

ECPA makes the following recommendations relative to these criteria:

- ADI, ARfD or AOEL values should be considered as '*significantly lower than those of the majority of the approved active substances within groups of substances/use categories*' if they are lower than 0.05X the median value of ADI, ARfD or AOEL values in the active substance functional group[7,8].
- When determining whether an active substance '*meets two of the criteria to be considered as PBT substance*', ECPA's recommendations included in position paper No 19428 should be followed. In particular (excerpts):
    - The properties of the active substance should be evaluated, not those of its degradation products.
    - The two criteria should be met in the same environmental compartment (e.g. aquatic).
    - A holistic evaluation of all available information should be made, endpoints should not be selected arbitrarily.
    - Geometric mean values should be considered to decide on persistence.
    - Whether depuration occurs after exposure should be taken into account when deciding on bioaccumulation (in addition to the bioaccumulation endpoint).
- Critical effects should be defined as effects that i) are severe by nature **and** ii) drive risk assessments (human health or environmental safety). Other effects that occur at higher exposure levels should not be considered, irrespective of their nature and severity, as they

[7] Multiple approaches can be considered in this complex area. ECPA believes its proposal meets all of the following objectives: compliance with the regulation requirements, scientific robustness, predictability and avoiding an unnecessarily high number of substances concerned.

[8] For example the ADI of insecticide 'A' shall be considered as 'significantly lower' if it is at least 20 times smaller than the median value of ADIs of all approved insecticides. Human safety reference values of substances whose function is not insecticide, fungicide or herbicide will be compared with the corresponding median value of all approved active substances; the 0.05X rule will apply. Substances with multiple functions (e.g. insecticide and nematicide) will be compared with active substances of the main functional group (insecticide in this case). Active substances for which it was not appropriate to establish an ARfD will be excluded from the ARfD comparison.

are not critical to the determination of use conditions that are safe for operators, consumers and non-target species.

- '*High potential of risk to ground water*' is mentioned as an example of a candidate for substitution trigger. ECPA believes that risk to ground water in the context of Annex II point 4 should only be considered as demonstrated if substantiated by monitoring data showing a consistent pattern of contamination[9].
- 'Very large buffer zones' are mentioned as examples of 'very restrictive measures' which characterise an active substance as a candidate for substitution. The availability and practicality of measures preventing off-site contamination should be taken into account (e.g. drift reduction nozzles and buffer strips). Where such measures can be implemented, very large buffer zones are not necessary and should not be considered in the context of Annex II point 4.
- Active substances '*containing a significant proportion of non-active isomers*' are to be listed as candidates for substitution according to Annex II point 4. Since the toxicity of inactive isomers is taken into account in risk assessments conducted with the technical active substance and its preparations, ECPA considers that this provision bears little relation to safety and should only apply to situations where a significantly purer isomer has been developed and approved. ECPA proposes the following definitions:
  - 'Significant' proportion: >25% of the technical active substance
  - A biologically active isomer is one that shows >10%[10] of the biological activity of the most active isomer against any of the target weeds, pests or diseases, or an isomer that can be demonstrated to be contributing to target control at commercially relevant rates.

5. List of candidates for substitution according to Article 80.7

On 27 January 2015 the Standing Committee on Plants, Animals, Food and Feed adopted the Commission proposal for a list of active substances included in Annex I of Directive 91/414/EEC which meet the candidate for substitution criteria.

Publication of that list will initiate comparative assessment for applications submitted as of 1 August 2015 -, and, where appropriate, substitution for all PPPs containing these substances and their uses. The list is likely to be vulnerable to misinterpretation, miscommunication and exploitation on the basis of unfounded claims. ECPA recommends that:

- The Commission should prevent any attempts to conduct comparative assessment and substitution of uses before the application date.
- Member State regulators proactively communicate, as the Commission did, on a regular basis about the list in order to minimise the potential for misinterpretation. In particular, it should be repeated that substances identified as candidates for substitution pass all approval criteria, including all safety criteria, and that safe use conditions have been established.
- European and national crop protection associations and member companies engage in active communication and prevent/address misuse of the list by stakeholders.

[9] An active substance can only be approved if the risk to ground water is assessed to be low. This is often evaluated on the basis of modelling results. Therefore a risk to ground water according to Annex II point 4 can only be considered as high if confirmed by monitoring data. This would represent a situation where modelling was not predictive enough of real use conditions and should concern a very limited number of cases.

[10] Proposal of 10% based on the Alonso-Prados 2002 paper

6. Specific issues and recommendations relative to comparative assessment and substitution

Workload, timelines and complexity - ECPA recognises that comparative assessment will represent a substantial additional workload for Member State regulators, considering (not exhaustive):

- The likely high number of candidates for substitution estimated around 20% of approved active substances, and consequently the many PPPs containing them.
- The need for review at least every seven years[11] (but in practice more often[12])
- The specific complexity of reviewing PPPs with multiple active substances[13]
- Changes in the assumptions on which the substitution was made as products and uses are withdrawn.
- The diversity of use patterns and agronomic conditions to be evaluated.
- The 120-day timeline allowed to grant an authorisation following receipt of the registration report from the zonal rapporteur Member State. The potential complexity of comparative assessment and substitution makes meeting these timelines even more challenging.

With a view to avoid unnecessary workload, ECPA welcome the adoption of the guidance document SANCO/11507/2013 rev.2 e on comparative assessment and substitution that integrates a stepwise approach allowing evaluators to conduct harmonised assessments.

Reauthorisation of a substituted use – Changes in the conclusions that led to substitution are likely to occur over time as a result of evolving agricultural practice, pest pressure, resistance, or as a result of the timing of the EU approval which then triggers the substitution process. ECPA recommends that the Commission develops, and Member States implement, a process for the rapid reauthorisation of substituted uses when this is necessary to address the consequences of such changes. The reauthorisation process should, where applicable, take into account the previous authorisation of substituted uses. When such a re-introduction is necessary, the authorities should request an application from the previous authorisation holder. Should the re-introduction concern more than one Member State, the evaluation should be made by the original zonal rapporteur Member State. Otherwise, it should be made by the Member State concerned. Unless there have been significant changes to the previous conditions of use, the evaluation and reauthorisation decision (and notification to the other Member States if appropriate) should be completed within 60 days.

Non-chemical methods – There is no reason to consider that non-chemical methods are in principle safer than chemical methods, even though this is inferred in the Regulation. ECPA recommends that the ability to protect plants, the safety to human and environmental health and overall suitability of non-chemical methods should be assessed factually and documented as for chemical solutions, (although metrics may differ) and that improved safety is not assumed. Failing this, the replacement by non-chemical methods will result in poor quality substitution decisions and unforeseen problems, for example when the article 50.2 derogation is invoked.

[11] Article 24.1 of Regulation 1107/2009 states that candidates for substitution are approved for a maximum of 7 years. Article 32.1 provides that the validity of an authorisation shall not be set later than 1 year after the active substance approval expiry date

[12] Article 50.4

[13] Particularly when PPPs are evaluated for re-authorisation following the renewal of active substances (Article 43)

Given the emphasis placed on non-chemical control methods in the Regulation, ECPA invites the Commission to sponsor workshops during which non-chemical methods would be identified and discussed on the basis of their effectiveness, safety and overall suitability for crop protection (including their financial impact). Alternatively the Commission could contract out that evaluation.

Mutual recognition – While the authorisation of all PPPs is applied for and evaluated through the 'zonal system'[14], the mutual recognition of authorisations involving candidates for substitution is optional[15]. ECPA recommends that, when deciding on applications for mutual recognition of PPPs subject to comparative assessment, Member State authorities do not place their growers at competitive disadvantage by denying them access to tools available in neighbouring countries.

Sufficient experience – When experience needs to be gained for a substitution solution (chemical or not), that solution should be widely available (and if appropriate fully approved) and in use for at least five years.

Other legislation - Known or expected regulatory developments under other legislation such as the water framework Directive[16] or the Directive on the sustainable use of pesticides[17] should be taken into account when considering a substitution.

7. Process and conditions for comparative assessment and substitution

Annex IV of Regulation 1107/2009 includes a number of criteria and conditions to be used as the basis for a substitution decision. These are summarised in Diagram 1 below. ECPA welcome the adoption of the guidance document SANCO/11507/2013 rev.2. Under this guidance document, ECPA support an implementation following the principles below (see also ECPA document No 21246)

Stepwise approach: in order to conserve evaluators' resources, a stepwise approach is recommended. The process allows for the termination of the comparative assessment as soon one of the substitution conditions is not fulfilled. Criterion 1 (in the diagram) determines whether alternative plant protection solutions exist (chemical or non-chemical), for which sufficient experience has been gained. If they do, comparative assessment continues through the other criteria, otherwise it stops. It is recommended that comparative assessment should not be carried out with alternatives containing the same candidate for substitution.

Criteria 2-6 look at individual substitution criteria provided in Annex IV of the Regulation (diagram 1)[18]. Annex IV requires all criteria to be met in order for substitution to be applied. If at least one is not met, substitution is not applicable. Criteria 2-6 allow for the termination of the comparative assessment process as soon as the assessment shows the failure of one criterion. In the detailed ECPA guidance, the order is not prescriptive and comparative assessment can be continued anywhere from criteria 2-6. However, when it is not immediately possible to clearly identify a criterion that will fail the conditions of substitution, ECPA recommends that the sequence laid out in Diagram 1 below be adopted. This sequence is

[14] Articles 33-37

[15] Article 41.2(b)

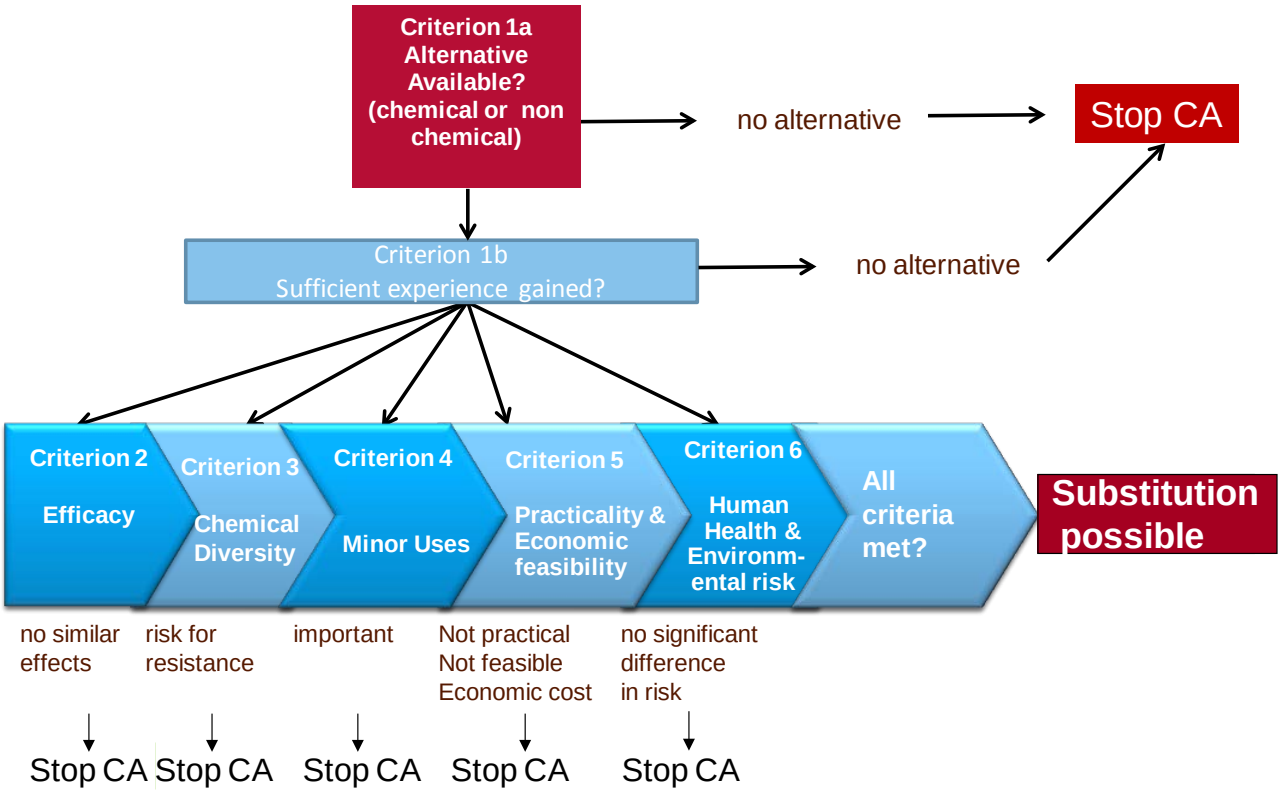
[16] For example any significant restriction of use resulting from river basin management

[17] For example, any restrictions in national action plans or the suitability of a particular product to integrated pest management programs

[18] The detailed guidance has been taken from EPPO guidance No 11-16700 on comparative assessment and adapted to fit the ECPA stepwise approach in the following areas: efficacy, resistance, practical and economic consequences and effects on minor uses.

more likely to conserve evaluators time than any other assessment sequence in situations where conditions for substitution will not (all) be met.

Diagram 1: Stepwise approach for Comparative Assessment



Applicant's involvement: conducting risk assessments is a Member State obligation. However, because of the possible adverse consequences of an inaccurate substitution decision, ECPA highly recommends that the applicant is consulted during the process. This can be done either by requesting that the applicant provides evidence as to why substitution would not be appropriate for certain PPPs/uses (e.g. through a risk/benefits analysis) or by commenting on the authorities draft rationale for any intended substitution.

Chemical alternatives: these should be widely available and have been fully approved and/or used for at least 5 years.

Non-chemical alternatives: ideally, these would be selected from an existing positive list of non-chemical alternatives (see section 6 above). If such a list does not exist, the non-chemical alternative should be widely available in the Member State and should have been available for at least 5 years. It should be recognised as a viable alternative by the Member State authorities.

Risk assessment methods: in order to improve the accuracy of substitution decisions, it is important that candidate PPPs and alternatives be compared using the same scientific approaches. For example, when TERs are compared, they should have been calculated using the same modelling methods and equivalent tiers.

Risk comparison: it is not possible to rank (by order of protection importance) the different components of the human risk assessment (consumer, operator, workers, bystanders and

residents) or non-target species evaluated in ecological risk assessments. It is equally inappropriate to assign greater priority to human protection over environmental protection (and vice and versa). Therefore an alternative use can only be considered to have a lower risk than the use of a candidate product if it has been demonstrated that it shows lower risk for both human health and the environment.

Documenting comparative assessment: evaluators should include in their assessment report a table listing all uses of the candidate for substitution and indicate for each use whether or not substitution is possible.

If substitution is possible the table should also detail the reasoning for the decision. This table should be made available to the applicant(s)/authorisation holder(s) for comments prior to the substitution decision(s). ECPA welcome the inclusion as appendix to the guidance document SANCO/11507/2013 rev.2, of a template for information to support comparative assessment.

8. Conclusion

The review program conducted under Directive 91/414/EEC has resulted in a significant reduction in the number of approved active substances.

Regulation 1107/2009 replaced the Directive on 14 June 2011. It has introduced a system of comparative assessment and substitution for plant protection products containing active substances approved as ‘candidates for substitution’ which involves a comparison of risks and benefits. These new provisions have the potential to further reduce the number of authorised products/solutions available for crop protection.

In order to prevent unwarranted and damaging substitutions and further deterioration in the competitiveness of European agriculture, ECPA recommends that this system is implemented with pragmatism, rigor and along robust scientific principles. Particular care should be applied when identifying candidates for substitution and determining conditions under which substitution is applicable (or not).

Disclaimer

This document does not substitute for a thorough reading of Regulation 1107/2009. The European Crop Protection Association, its representatives and its members cannot on the basis of this document be held accountable for failing to comply with the Regulation.