Questions and Answers on Candidates for Substitution

Rev. 1, January 2015

Background

The European Commission is required by Regulation (EC) No 1107/2009 ('the Regulation') to establish a list of substances identified as "candidates for substitution" (CfS). The list identifies active substances with certain properties. For plant protection products (PPPs) containing these active substances, Member States will be required to evaluate if they can be replaced (substituted) by other PPPs.

To prepare such a list, the Commission requested a consultant to prepare a report[1] on the implementation of the criteria set by the Regulation. The report does not contain any official listing, but presents different options drawn from possible interpretations of the criteria. Member States and stakeholders were consulted on the approach taken and on the input values taken to determine if an active substance qualifies to be a CfS.

Although according to Article 80(7) of the Regulation the list should have been established by 14 December 2013, this list has now been presented for a vote in the meeting of the Standing Committee on Plants, Animals, Food and Feed (PAFF Committee) of 27 January 2015. The *Guidance Document on Comparative Assessment and Substitution of Plant Protection Products in accordance with Regulation (EC) No 1107/2009* (SANCO 11507/2013 rev. 12, October 2014) was already noted in an earlier meeting of the Committee.

These answers in the present document represent the position of the Commission services but may not necessarily represent the opinion of the Commission. This document does not constitute any formal commitment on behalf of the Commission. Only the European Court of Justice can give an authoritative interpretation of EU law.

What is a CfS?

A CfS is an active substance used in a PPP that:

- is approved under the Regulation,
- and meets one or more of the criteria provided in Annex II point 4 of the Regulation (see appendix I to this document).

The majority of active substances approved under the Regulation was initially approved under its predecessor, Directive 91/414/EEC, and is deemed to be approved under the Regulation. The list that now has been voted contains the active substances approved by January 2013 that qualify as CfS. Following its adoption by the Commission, this list will be published as a Commission Regulation in the Official Journal.

[1] Final report: "Ad-hoc study to support the initial establishment of the list of candidates for substitution as required in Article 80(7) of Regulation (EC) No 1107/2009" (09.07.2013).

Are they safe?

Yes. They are approved active substances. The listing of active substances as CfS does not question the safety of the products; they have gone through the strict EU evaluation and have passed all safety requirements of Directive 91/414/EEC or Regulation (EC) No 1107/2009. PPPs containing them can only be authorised (or renewed or extended) if they too pass all such criteria.

Are they prohibited substances?

Clearly no, see above. PPPs containing CfS will remain on the EU market. Substitution may lead in the future to some authorisations for products containing CfS to be rejected.

Can they be considered as substances of high concern?

Active substances of high concern cannot be approved under Regulation (EC) No 1107/2009. For every active substance to be included in a PPP it should be demonstrated that they are not expected to have any harmful effect on human or animal health or any unacceptable effects on the environment.

When introducing the concept of 'candidates for substitution' in the Regulation, a category of substances with certain properties was created with the aim to replace them by PPP which require less risk mitigation or by non-chemical control or prevention methods.

On what basis do active substances qualify as a CfS?

The analysis has been conducted by comparing the agreed and peer reviewed chemistry, toxicology, environmental fate and ecotoxicology endpoints, against the relevant seven conditions specified in Annex II, point 4 of the Regulation.

The agreed and peer reviewed endpoints are specified in the following relevant documents:

- Latest version of the review report for approval of each active substance;
- Conclusions of the European Food Safety Authority (EFSA) on the relevant active substances (EFSA Conclusions); and,
- Where necessary, in the Draft Assessment Reports (DARs) and addenda and peer review reports provided by the Rapporteur Member State;

Only evaluated and peer reviewed data have been used and full traceability is guaranteed.

How are the criteria provided in Annex II, point 4 of the Regulation applied?

The 'seven conditions' as specified in Annex II, point 4 of the Regulation are based on the intrinsic hazardous properties of the active substance. The conditions refer not only to quantitative, but also to qualitative criteria. In the latter case several options have been

explored[2]. A detailed overview of the final approach taken for each of the seven conditions is provided in appendix II to this document.

What will happen to active substances approved after January 2013?

The current list (which received a favorable vote in the PAFF Committee on 27 January 2015) will be updated within the next months with the substances approved between January 2013 and early 2015 that meet the criteria for CfS. In the future, active substances applied for and approved fully under the Regulation (and not under the transitional measures) and that meet the CfS criteria will be listed in a separate Annex of Regulation (EU) No 540/2011 (the list of approved active substances) as foreseen in Article 24 of the Regulation.

What happens to CfS once identified?

One needs to distinguish between:

- Active substances in the list of CfS based on Article 80(7), which received a favorable vote by the PAFF Committee on 27 January 2015and
- Active substances which will be identified as such according to Article 24 of the Regulation.

For active substances in the first group, their current expiry dates will not be affected. Comparative assessment has to be applied to applications for authorisation of PPPs containing those substances that are submitted after 1 August 2015. The current listing will not affect ongoing applications, but only new applications submitted after 1 August 2015.

For active substances in the second group, they will only be approved or renewed for a maximum period of 7 years (instead of 10 or 15 years for other active substances); that approval can be renewed as long as approval conditions are met. Comparative assessment has to be applied to applications for authorisation of PPPs containing those substances that are submitted after 1 August 2015. The current listing will not affect ongoing applications, but only new applications submitted after 1 August 2015.

What is a comparative assessment and a substitution?

Decisions to approve active substance as CfS do not include comparison with other active substances; comparative assessment is not applied at active substance and Community level.

1. Member State Authorities will subject PPPs containing CfS to comparative assessment, i.e. will compare them with adequate alternative solutions (chemical and non-chemical) which are already available to farmers. Where alternatives exist, evaluators will consider their relative safety for human and environmental health and the possible agronomic (e.g. development of resistance), economic and practical consequences of a substitution.

[2] For more details see final report: "Ad-hoc study to support the initial establishment of the list of candidates for substitution as required in Article 80(7) of Regulation (EC) No 1107/2009" (09.07.2013).

2. If i) ‘significantly safer’ alternatives exist and ii) the substitution is not expected to present unacceptable consequences, uses of the product will be ‘substituted’, i.e. denied or revoked.

The result can be different from Member State to Member State and from one use to another.

Comparative assessment areas and conditions under which substitution applies or does not are specified in Annex IV of the Regulation (see appendix III to this document).

The comparative assessment process is described in detail in the *Guidance Document on Comparative Assessment and Substitution of Plant Protection Products in accordance with Regulation (EC) No 1107/2009* (SANCO 11507/2013 rev. 12, October 2014) and will apply to applications for authorisation submitted after 1 August 2015.

When will the comparative assessment start?

After 1 August 2015, Member States Authorities are required to apply comparative assessment to new applications for authorisation, renewal or extension of use of a PPP containing a CfS. The publication of the CfS list does not have an impact on existing authorisations and does not trigger an immediate review of existing authorisations. These will be reviewed in the frame of the renewal program.

What will happen following the adoption of the list for CfS?

On 1 August 2015, the overall process of comparative assessment and, where appropriate, substitution (see above) will start for new applications.

However, it must be emphasized that:

- The active substances which meet the criteria for CfS remain approved active substances. They are still considered 'safe', i.e. a detailed evaluation concluded that they have no harmful effects on human and animal health and no unacceptable effect on the environment.

- Authorised products containing these active substances remain authorised and can be used safely, taking into account any risk mitigation measures, where appropriate.

When an active substance qualifies as a CfS, will it have an impact on Maximum Residue Limits (MRLs) and import tolerances?

In principle no. Listing as Candidate for Substitution does not in itself trigger revision of existing MRLs or import tolerances.

Once a Candidate for Substitution always a Candidate for Substitution?

No. As explained above the analysis has been done and will be done on agreed and peer reviewed endpoints. So every time new endpoints will be set after an assessment at EU level, for example at the time of the renewal of the approval of the active substance, it will be assessed if an active substance (again) meets one or more of the criteria provided in Annex II, point 4 of the Regulation.

What is the main criterion for active substances to qualify as a CfS?

It is estimated that about 20% of the approved active substances will be CfS. The majority were identified as CfS because they meet two of the three criteria to be considered as a PBT substance (persistent, bio accumulative, toxic). Among them, the most frequent combination was that of persistence in the environment with toxicity (P and T).

What is the impact for the pesticides sector?

The comparative assessment and substitution by Member States should contribute to the use of plant protection products that require less risk mitigation and of non-chemical control or prevention methods. Overall it contributes to a more sustainable use of pesticides as foreseen by Directive 2009/128/EC. In the longer term, comparative assessment and substitution provide an additional incentive for the pesticides industry to further innovate and develop active substances and PPPs with less hazardous properties.

Appendix I

Regulation (EC) No 1107/2009 (Excerpts)
Annex II, Point 4 – Candidates for Substitution

An active substance shall be approved as a candidate for substitution pursuant to Article 24 where any of the following conditions are met:

- its ADI, ARfD or AOEL is significantly lower than those of the majority of the approved active substances within groups of substances/use categories,
- it meets two of the criteria to be considered as a PBT substance,
- there are reasons for concern linked to the nature of the critical effects (such as developmental neurotoxic or immunotoxic effects) which, in combination with the use/exposure patterns, amount to situations of use that could still cause concern, for example, high potential of risk to groundwater; even with very restrictive risk management measures (such as extensive personal protective equipment or very large buffer zones),
- it contains a significant proportion of non-active isomers,
- it is or is to be classified, in accordance with the provisions of Regulation (EC) No 1272/2008, as carcinogen category 1A or 1B, if the substance has not been excluded in accordance with the criteria laid down in point 3.6.3,
- it is or is to be classified, in accordance with the provisions of Regulation (EC) No 1272/2008, as toxic for reproduction category 1A or 1B if the substance has not been excluded in accordance with the criteria laid down in point 3.6.4,
- if, on the basis of the assessment of Community or internationally agreed test guidelines or other available data and information, reviewed by the Authority, it is considered to have endocrine disrupting properties that may cause adverse effects in humans if the substance has not been excluded in accordance with the criteria laid down in point 3.6.5.

Appendix II

The way the conditions listed in Annex II, Point 4 are applied

The way the conditions listed in Annex II paragraph 4 to Regulation (EC) No 1107/2009 are applied is described below:

Condition 1: Its ADI, ARfD or AOEL is significantly lower than those of the majority of the approved active substances within groups of substances/use categories

This condition may be defined in statistical terms (fractions of the median, multiples of the SD from the mean, and percentiles of a ranked data set) or toxicological terms (fixed absolute thresholds). The 5% percentile appears to be a good discriminator for identifying those active substances that differ significantly from the majority both in statistical as well as in toxicological terms. However, an absolute threshold is preferred compared to a dynamic threshold because it provides greater predictability. These threshold values will be revised on a regular basis.

In this case the following values have been set:

- Threshold for ADI of 0.001 mg/kg bw/d;
- Threshold for ARfD of 0.004 mg/kg bw and
- Threshold for AOEL of 0.001 mg/kg bw/d.

This condition requires considering ADI, ARfD and AOEL values "*within groups of substances/use categories*". The EU Pesticides Database provides an allocation of active substances to one or more out of 21 different use categories. On the basis of the given relevant information sources, this was considered to be the most clear and solid reference for the necessary grouping of substances. From a discriminative point of view a use category should contain a minimum of 5 substances.

Condition 2: It meets two of the criteria to be considered as a PBT substance

This criterion is made operational by the Commission Working Document on "Evidence needed to identify POP, PBT and vPvB properties for pesticides" (25.09.2012 – rev. 3)*"*. In addition it has been decided that soil persistence data measured under field circumstances will supersede data obtained from laboratory studies.

Condition 3: There are reasons for concern linked to the nature of the critical effects (such as developmental neurotoxic or immunotoxic effects) which, in combination with the use/exposure patterns, amount to situations of use that could still cause concern, for example, high potential of risk to groundwater; even with very restrictive risk management measures (such as extensive personal protective equipment or very large buffer zones)

The assessment whether an active substance falls under Condition 3 does not only require information about distinct inherent substance properties, but the integrated consideration of toxicological properties, use conditions and exposure situations is needed. No agreed data have been identified for the qualification of active substances fulfilling this criterion.

Condition 4: It contains a significant proportion of non-active isomers

Regarding Condition 4 three requirements must be fulfilled for the identification of a corresponding CFS:

(1) The active substance must be known to be a **mixture of isomers**;

(2) One or more of these isomers must be known to be **non-active** against the target organism; and

(3) The amount of this or these non-active isomer(s) must be assessed to make up a **significant proportion** of the total active substance.

Condition 4 is not applicable to approved active substances that are micro-organisms, but to chemicals only. As a second pre-requisite, Condition 4 implies that the chemicals of concern must be well defined in terms of their molecular structure. An assessment of Condition 4 is not applicable to substances that are complex mixtures of not fully known compounds with variable composition, such as oils, fats, plant extracts or blood meal for instance. As a consequence, all chemical substances that are not defined by a systematic chemical name according the IUPAC nomenclature of chemistry were out of the scope of all further considerations.
Racemic mixtures contain the active and the inactive isomer forms in equal amounts. Hence 50% of the approved active substance have no benefits but may pose known or unknown risks to human health and the environment. As this is the highest possible proportion, it has been considered as 'significant' in the light of this condition.

Information that is available from Review Reports, EFSA Conclusions, and DARs & addenda, was searched for any relevant statement about active, inactive or non-active isomers, racemic mixture or any other explicit or implicit information about different activities of the isomers against target organisms.

Condition 5: It is or is to be classified, in accordance with the provisions of Regulation (EC) No 1272/2008, as carcinogen category 1A or 1B, if the substance has not been excluded in accordance with the criteria laid down in point 3.6.3 of Annex II of Regulation (EC) No 1107/2009

For those active substances for which classification has been agreed in the context of Regulation (EC) No 1272/2008[3] and a decision has been published, this should be used as the basis for conducting the comparison against the relevant criteria of Annex II, point 4 of Regulation (EC) No 1107/2009. 'Is to be classified' is interpreted as substances that are

[3] OJ L 353, 31.12.2008, p.1.

planned to be classified as C1A or C1B under Regulation (EC) No 1272/2008 based on the outcomes of an ECHA assessment/RAC opinion.

Condition 6: It is or is to be classified, in accordance with the provisions of Regulation (EC) No 1272/2008, as toxic for reproduction category 1A or 1B if the substance has not been excluded in accordance with the criteria laid down in point 3.6.4 of Regulation (EC) No 1107/2009

For those active substances for which classification has been agreed in the context of Regulation (EC) No 1272/2008 and a decision has been published, this should be used as the basis for conducting the comparison against the relevant criteria of Annex II, point 4 of Regulation (EC) No 1107/2009. 'Is to be classified' is interpreted as substances that are planned to be classified as R1A or R1B under Regulation (EC) No 1272/2008 based on the outcomes of an ECHA assessment/RAC opinion.

Condition 7: If, on the basis of the assessment of Community or internationally agreed test guidelines or other available data and information, reviewed by the Authority, it is considered to have endocrine disrupting properties that may cause adverse effects in humans if the substance has not been excluded in accordance with the criteria laid down in point 3.6.5 of Regulation (EC) No 1107/2009

Pending the adoption of specific scientific criteria for the determination of endocrine disrupting properties, the interim criteria set out in Annex II point 3.6.5 third and fourth paragraph are applied. For those active substances for which classification has been agreed in the context of Regulation (EC) No 1272/2008 and a decision has been published, this should be used as the basis for conducting the comparison against the relevant criteria of Annex II, point 4 of Regulation (EC) No 1107/2009. 'Is to be classified' is interpreted as substances that are planned to be classified as C2 and R2 under Regulation (EC) No 1272/2008 based on the outcomes of an ECHA assessment/RAC opinion.

Appendix III

Regulation (EC) No 1107/2009 - ANNEX IV - Comparative assessment pursuant to Article 50

1. Conditions for comparative assessment

Where refusal or withdrawal of an authorisation of a plant protection product in favour of an alternative plant protection product or a non-chemical control or prevention method is considered, referred to as 'substitution', the alternative must, in the light of scientific and technical knowledge, show significantly lower risk to health or the environment. An assessment of the alternative shall be performed to demonstrate whether it can be used with similar effect on the target organism and without significant economic and practical disadvantages to the user or not.

Further conditions for refusal or withdrawal of an authorisation are as follows:

(a) substitution shall be applied only where other methods or the chemical diversity of the active substances is sufficient to minimise the occurrence of resistance in the target organism;

(b) substitution shall be applied only to plant protection products where their use presents a significantly higher level of risk to human health or the environment; and

(c) substitution shall be applied only after allowing for the possibility, where necessary, of acquiring experience from use in practice, where not already available.

2. Significant difference in risk

A significant difference in risk shall be identified on a case-by-case basis by the competent authorities. The properties of the active substance and plant protection product, and the possibility of exposure of different population subgroups (professional or non-professional users, bystanders, workers, residents, specific vulnerable groups or consumers) directly or indirectly through food, feed, drinking water or the environment shall be taken into account. Other factors such as the stringency of imposed restrictions on use and prescribed personal protective equipment shall also be considered.

For the environment, if relevant, a factor of at least 10 for the toxicity/exposure ratio (TER) of different plant protection products is considered a significant difference in risk.

3. Significant practical or economic disadvantages

Significant practical or economic disadvantage to the user is defined as a major quantifiable impairment of working practices or business activity leading to inability to maintain sufficient control of the target organism. Such a major impairment might be, for example, where no technical facilities for the use of the alternative are available or economically feasible.

Where a comparative assessment indicates that restrictions on and/or prohibitions of use of a plant protection product could cause such disadvantage, then this shall be taken into account in the decision-making process. This situation shall be substantiated.

The comparative assessment shall take authorised minor uses into account.