Registration by analogy – Guidance for completing the check-list

(Version 26.05.2015)

Registration by analogy is a basic registration approach where a limited comparison is made between a pesticide product submitted for authorization in a resource-limited country and similar products in one or more reference countries. The registration authority may decide to register a pesticide which has already been authorized for use in a reference country, if it judges that its efficacy and risk are also likely to be acceptable in its own country.

This document provides guidance for completion of the check-list used to compare the registration of a pesticide product in the reference country with the application for registration in the local situation.

If more than one reference country is considered, the check-list should be filled out for each one of them.

1. Country

Name of the country in which the application for registration is done, and name of the reference country.

Reference countries can be selected for various reasons, such as: i) similar agronomic conditions or pesticide use practices; ii) environmental and ecological similarities; iii) reliable pesticide evaluation procedures; iv) same countries of origin of the imported pesticides; v) good working contacts with the registration authority

One or more reference countries will often be chosen because several of the above reasons are met.

APPLICANT/REGISTRANT

2. Name and address of applicant/registrant

An identical name (and address) of the applicant may support the claim that the pesticide product is identical or similar.

3. Name of manufacturer

Name of the manufacturer of the active ingredient and, if different, also the manufacturer of the commercial product.

An identical name of the manufacturer may support the claim that the pesticide product is identical or similar. However, even for the same manufacturer, the pesticide active ingredient and/or product may have been produced in different locations/factories. As a result, the pesticide product may not be identical.

4. Registration status in reference country

Note if the pesticide is registered with or without any restrictions, and what possible restrictions are. Of particular interest are any restrictions on the use in the reference country which may be difficult to implement in the local situation.

PESTICIDE PRODUCT

5. Product name

Complete product name, including formulation type and concentration indication, when available. E.g.: Killtox forte 40 SC

6. Active ingredient common name

In principle, pure active ingredients (PAI) with the same common name are identical. However, for the production of commercial products, technical grade active ingredients (TGAI) are used, which can contain various manufacturing impurities, some of which may be toxic. Thus, TGAIs with the same common name, but produced by different manufacturing processes or locations, are not necessarily identical.

Some active ingredients consist of a combination of isomers, some of which are more active than others. For such compounds to be identical, the isomer ratios in the active ingredient should also be identical.

7. Formulation type

Similar formulation types can be expected to result in similar efficacy and risks (but see points 9 & 10, below). Standardized coding of different formulation types is provided by CropLife International.

For registration by analogy, the following formulation types are considered similar:

- For residues: i) formulation types which are diluted in water prior to application including EC, WP, WG, SC, SL. Experience demonstrates that these formulations lead to similar residues.
- For occupational and bystander risks: i) all solid formulations to be applied as a spray; ii) all liquid formulations to be applied as a spray; iii.) formulations applied as granules
- For environmental risk assessment: i) all formulations applied as sprays; ii) formulations applied as granules; iii) formulations for seed treatments

8. Active ingredient concentration

For a pesticide product to be considered similar, the active ingredient content should not exceed the following variation:

Declared active ingredient content (in g/kg or g/L)	**Acceptable variation**
up to 25	± 15% of the declared content for homogeneous formulations (EC, SC, SL, etc.), *or* ± 25% for heterogeneous formulations (GR, WG, etc.)
above 25 up to 100	± 10% of the declared content
above 100 up to 250	± 6% of the declared content
above 250 up to 500	± 5% of the declared content
above 500	± 25 g/kg or g/L
Source: Manual on the development and use of FAO and WHO specifications for pesticides (2010)	

9. Declaration by applicant on equivalence of products

The applicant may provide a declaration to the registration authority that the product is identical or equivalent to the one in the reference country.

If the applicant is identical to the registrant in the reference country, and the products are indeed identical or equivalent, the applicant is in a position to provide such a declaration. It should include details about the manufacturing source of both products. If these sources are different, the specifications of both products, preferably those published by the FAO/WHO Joint Meeting on Pesticide Specifications, should be supplied to show equivalence.

If the applicant is not identical to the registrant in the reference country, the applicant will generally not have access to the manufacturing details of the product in the reference country. However, if both products have been evaluated by the FAO/WHO Joint Meeting on Pesticide Specifications, the applicant can use these specifications to show equivalence.

Otherwise, it will normally not be possible for an applicant to provide a justified declaration that his product is equivalent to one registered in the reference country. In such a case, the applicant should provide the information listed under points 10 – 12.

10. Active ingredient manufacturing source

The applicant should provide the manufacturing source (name and address) of the TGAI and product. The registration authority may contact the registrar in the reference country to check whether these sources are the same. If the manufacturing source is the same, this fact may support similarity of the pesticide product with the one registered in the reference country (provided that formulation type and active ingredient concentration are the same).

If the manufacturing source and/or process is different, different impurities may be formed when producing the active ingredient (see point 11 below).

11. Impurities

If the manufacturing source and/or process is different, different impurities may be formed when producing the active ingredient. Either the type of the impurity or its concentration may affect the toxicity of the product.

The registration authority can check whether the FAO/WHO Specification for the technical grade active ingredient lists any toxic impurities. (See Specifications new procedure or Specifications old procedure). If toxic impurities are listed in the specification, any difference in manufacturing process may well result in difference in toxicity of the active ingredient. If no toxic impurities are listed, a difference in manufacturing process may still result in a difference in toxicity of the active ingredient, but its likelihood is less great.

12. Co-formulants triggering a hazard classification

In addition to the active ingredient, pesticides generally consist of various co-formulants, added to improve the performance of the product or reduce risks. These co-formulants may thus have considerable influence on the efficacy and risks of the formulated pesticide product. In principle, the type and concentrations of co-formulants should be similar in the pesticide submitted for registration and the one registered in a reference country. Very often, this will not be the case.

Equivalence of co-formulants can be checked by comparing the CAS numbers of the substances in the application dossier or the Safety Data Sheet of the product. The same CAS numbers indicate the same co-formulant; however, different CAS numbers do not necessarily means chemical non-equivalence of the co-formulants.

Alternatively, equivalence of co-formulants can be evaluated by comparing the hazard classification on the Safety Data Sheet: co-formulants with the same hazard classification can be considered equivalent with respect to hazard.

Changes in the contents of the same co-formulant in a pesticide product can be considered similar if they do not exceed the following variation:

Initial concentration range of the compound (in g/kg or g/L)	**Acceptable variation**
up to 5	± 100%
above 5 up to 10	± 50%
above 10 up to 25	± 30%
above 25 up to 100	± 20% of the declared content
above 100 up to 250	± 10% of the declared content
above 250	± 5% of the declared content
Source: European Commission – Guidance document on significant and non-significant changes of the chemical composition of authorized plant protection products (2012)	

13. Conclusion with respect to the pesticide product

Based on parameters 2 – 12, evaluate whether the pesticide product submitted for registration is identical, equivalent or sufficiently similar to allow comparison with the pesticide in the reference country.

If parameters 2, 3, 5, 6 & 7 are the same when compared to the reference country, the product submitted for registration can be considered identical to the reference country.

In other cases, the registration authority will need to make an expert assessment whether the differences between the products are so large that registration by analogy to the reference country is not justified anymore.

USE

14. Crop or use situation

If the crop or use situation is identical between the local situation and the reference country, registration by analogy is facilitated.

However, often (minor) differences between countries will occur. Evaluate whether the crop or use pattern in the reference country compares well enough with the proposed use in the country. The following aspects will generally have to be taken into account: efficacy, residues, occupational & bystander risk, environmental risk (various types). Unfortunately, similarity for one aspect (e.g. operator risk) does not necessarily indicate similarity for another (e.g. residues), so these will have to be assessed separately.

The Codex Alimentarius has defined commodity groupings within which residue data can be extrapolated (Codex classification of foods and animal feeds – click on CAC/MISC 4). As an approximation, the same commodity groups can be used for extrapolation of efficacy data. Thus, crops falling within the same commodity group would aid registration by analogy.

For occupational and bystander risks, a distinction is generally made between high crops and low crops, with the former posing a higher exposure risk than the latter.

For environmental risk assessment, similar crop structure at the moment of pesticide application tends to indicate similar risks for groundwater and surface water exposure. Spraying on flowering compared to non-flowering crops is a main indicator of pollinator exposure.

15. Pest

If the pest is identical between the local situation and the reference country, and occurs on the same crop, pesticide efficacy is likely to be similar, and registration by analogy is facilitated.

However, pests will often be (slightly) different; or pests may be the same, but attacking different crops. If it can be expected that the pests in the two situations show similar susceptibility to the pesticide, registration by analogy is facilitated. Presently, no global "pest groupings" exist that can be used for extrapolation of efficacy data. However, certain groups of pests, often of similar taxonomy, can be expected to have similar susceptibility to, at least chemical, pesticides (e.g. aphids, thrips, whiteflies, powdery mildews; but many other cases exist).

16. Dose rate

The dose rate, or application rate, of the pesticide expressed as g a.i./ha or g a.i /unit, directly influences efficacy and risks.

If dose rates in the reference country and the local situation are identical, registration by analogy is facilitated.

If dose rates are similar, then efficacy, residue levels and risks can be expected to be similar too. For the purpose of this guidance document, an increase or decrease of less than 25% of the (active ingredient) application rate – under otherwise identical conditions – will be considered similar.

Note that an increase or decrease in the dose rate will have a different impact on efficacy on the one hand, and residues and risks on the other. An increase in dose rate in the local situation when compared to the reference country will tend to confirm the efficacy in the local situation, and encourage registration by analogy. However, the same increase in dose rate in the local situation will also increase residue levels and human health and environmental risks when compared to the reference country, which discourages registration by analogy.

17. Number of applications per growing season

Similarly to point 16, the frequency of application influences both efficacy and risks. If frequency of application in the reference country and the local situation are the same, registration by analogy is facilitated.

If the number of applications are similar, then efficacy, residue levels and risks can be expected to be similar too. For the purpose of this guidance document, an increase or decrease of less than 25% of the application frequency – under otherwise identical conditions – will be considered similar.

18. Withholding period

Withholding, such as pre-harvest intervals, pre-slaughter intervals, and re-entry intervals for livestock or humans may influence consumer and occupational risks.

If the withholding periods in the reference country and the local situation are the same, registration by analogy is facilitated.

If the withholding periods in the local situation are similar or longer, then residue levels and risks can be expected to be similar or less too. For the purpose of this guidance document, an increase or decrease of less than 25% in the withholding period – under otherwise identical conditions – will be considered similar.

Conclusion with respect to use

Based on parameters 14 – 18, evaluate whether the use of the pesticide product submitted for registration is identical or sufficiently similar to allow comparison with the pesticide in the reference country.

If parameters 14 – 18 are the same when compared to the reference country, the use of the pesticide can be considered identical to the reference country.

Alternatively, evaluate whether the efficacy of the pesticide can be expected to be similar, or better, in the local situation than in the reference country. In such a case, registration by analogy may be possible.

HUMAN HEALTH RISKS

19. Use restrictions

Note any use restrictions or risk reduction measures for the pesticide and its use which have been defined by the registration authority of the reference country. Assess whether these restrictions can and should be imposed, and will be effective, in the local situation.

20. Required/recommended PPE

Note any personal protective equipment and clothing that is required for use of the pesticide in the reference country. Assess whether this PPE can and should be imposed, and will be effective, in the local situation.

21. Level of training/experience of operators

Estimate the likely level of training and experience that operators will have when handling and applying the pesticide in the reference country. Assess whether operators in the local situation are likely to have similar levels of training and experience.

22. Conclusion with respect to human health risks

Evaluate if human health risks (occupational, bystander, consumer) as a result from the proposed use of the pesticide in the local situation will be similar or less than in the reference country. If this is the case, registration by analogy may be possible.

Take into account the pesticide product composition (which may have an effect on toxicity of the product), the use details of the pesticide, and the human health section (which may have an effect on exposure).

ENVIRONMENTAL RISKS

23. Use restrictions

Note any use restrictions or environmental risk reduction measures for the pesticide and its use which have been defined by the registration authority of the reference country. Assess whether these restrictions can and should be imposed, and will be effective, in the local situation.

24. Rainfall, temperature, soil

Climatic and soil conditions can have an impact on the persistence and mobility of the pesticide. Definite rules cannot be given but, indicatively, higher rainfall may increase leaching to groundwater and runoff/drainage to surface water; higher temperatures may increase the degradation of the pesticide in soil and water; and lower soil organic matter and/or a higher sand fraction (or lower clay fraction) in the soil may increase leaching to groundwater.

25. Sensitive ecosystems/organisms

Certain ecosystems and non-target organisms may be particularly sensitive to pesticides. If the pesticide is to be used in a sensitive ecosystem in the local situation, but this is not the case in the reference country, environmental risks may be greater. Some examples of sensitive ecosystems for pesticides are: pollinated crops (in particular for insecticides); irrigated agriculture (for all types of pesticides); organic agriculture or livestock breeding (for all types if pesticides); agro-ecosystems under biocontrol or integrated pest management (for all types if pesticides); agriculture in/close to protected areas and nature reserves (in particular for insecticides and herbicides); areas with surface waters or delta-estuary areas (for all types if pesticides).

26. Conclusion with respect to environmental risks

Evaluate if environmental risks as a result from the proposed use of the pesticide in the local situation will be similar or less than in the reference country. If this is the case, registration by analogy may be possible.

Take into account the pesticide product composition (which may have an effect on toxicity of the product), the use details of the pesticide, and the environmental section (which may have an effect on exposure and resulting adverse effects).

28 Overall conclusion

Evaluate whether registration by analogy is feasible and describe the main uncertainties. Judge whether the pesticide product can be registered for use in the local situation. Determine whether any risk mitigation measures or use restrictions are required.