Organisation de Coopération et de Développement Économiques
Organisation for Economic Co-operation and Development

22-May-2018

English - Or. English

ENVIRONMENT DIRECTORATE
JOINT MEETING OF THE CHEMICALS COMMITTEE AND
THE WORKING PARTY ON CHEMICALS, PESTICIDES AND BIOTECHNOLOGY

Cancels & replaces the same document of 16 May 2018

GUIDANCE DOCUMENT ON RESIDUES IN ROTATIONAL CROPS

Series on Pesticides
No. 97
Series on Testing & Assessment
No. 279

JT03432166

ENV/JM/MONO(2018)9
Unclassified
English - Or. English

OECD Environment, Health and Safety Publications

Series on Pesticides

No. 97

and

Series on Testing and Assessment

No. 279

Guidance Document on Residues in Rotational Crops

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Paris 2018

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or contact:

OECD Environment Directorate,
Environment, Health and Safety Division
2 rue André-Pascal
75775 Paris Cedex 16
France

Fax: (33-1) 44 30 61 80

E-mail: ehscont@oecd.org

FOREWORD

In 2007, OECD issued two Test Guidelines concerning the uptake of pesticides by rotational crops: *Metabolism in rotational crops* (TG 502) (1), and, *Residues in rotational crops, limited field studies* (TG 504) (2).

At the 2011 meeting of the OECD Registration Steering Group (RSG) (Ottawa, Canada), members discussed the possible need for guidance on Maximum Residue Level (MRL) setting for residues in rotational crops and requested a survey of national governments. In response, a survey was conducted in the first half of 2012 and the results were discussed at a meeting of the OECD Residue Chemistry Expert Group (RCEG) in November 2012 (Queenstown, New Zealand).

At the meeting, members concluded that the two Test Guidelines on rotational crops were not explicit with regard to some rotational residue issues. These issues included: i) determination of the annual high application rate; ii) use of proportionality with application rate; iii) accumulation testing over multiple years of use; iv) misinterpretation of environmental fate data vs. residue chemistry data requirements; v) crops grown under protection; vi) rotational crop testing on permanent and semi-permanent crops; vii) choice of crops for field rotation studies and possibilities of extrapolation; and viii) MRL setting.

The RCEG further concluded that rather than modify the TGs 502 (1) and 504 (2) to address these issues, the RCEG would develop a new Guidance Document. The present Guidance Document has been developed by the RCEG Writing Group associated with the effort.

After commenting among the WGP and the Working Group of National Co-ordinators of the Test Guidelines Programme (WNT), the Guidance Document was approved by the WGP and WNT in March 2018.

This document is being published under the responsibility of the Joint Meeting of the Chemicals Committee and the Working Party on Chemicals, Pesticides and Biotechnology, which has agreed that it be declassified and made available to the public.

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INTRODUCTION

1. Rotational crops are any field crops which may be produced after the harvest of a pesticide-treated primary crop (or in some cases replanting of crops after failure of the pesticide-treated primary crop). Limited field studies for residues in rotational crops [see OECD Test Guideline 504 (2)] are generally conducted if the results of a metabolism in rotational crop study [see OECD Test Guideline 502 (1)] indicate that significant accumulation of residues occurs through uptake from soil into food or feed commodities. Guidance on when to conduct the field study and what components of the residue, if any, require analysis may be found in the *OECD Guidance Document on Overview of Residue Chemistry Studies* (3) and the *OECD Guidance Document on Definition of the Residue* (4).

2. Recently, in several OECD countries, some *ad-hoc* requirements for additional crop testing have emerged to cover both primary residues and residues arising after crop rotation when accumulation of soil residues has been anticipated, to avoid impediments to international trade. Such requirements include: 1) rotational crop testing on non-annual [permanent and semi-permanent crops (e.g. orchards, vines)] and 2) crop/rotational crop accumulation testing over multiple years. Therefore, common approaches for when and how to determine - and then how to handle - inadvertent residues will support work sharing and joint reviews between OECD countries.

3. This document provides additional detailed guidance on rotational crop residue studies conducted according to OECD TG 504 (Residues in Rotational Crops) (2) with expanded flexibility in crop commodities to be tested, and approaches to mitigate additional testing. The following scope is addressed within this document:

- Derivation of application rates for rotational crop studies.
- Estimation of concentration levels for active ingredients and their metabolites in soil in terms of an assessment of rotational crop studies. Guidance on interpretation of the study results.
- Advice on the data requirements and procedures for MRL setting based on rotational crops and the possible use of label restrictions.
- Use of the proportionality concept in rotational crop assessments.
- Clarification of the relevant situations under which rotational crop studies are needed to cover protected crop situations.

4. A tiered approach is introduced which ensures that consumers are not exposed to unacceptable residue levels and supports OECD countries in their efforts to harmonise MRLs for inadvertent residues in rotational crops. The scope of this effort is limited to food and feed crops. Local situations related to uses such as ornamentals shall be handled on a case-by-case basis as these crops can be rotated back to food crops in a few years.

5. The primary goal of this document is to provide guidance on MRL setting for rotational crops. The alternative practice of label restriction on use, when appropriate, is also discussed.

EXISTING OECD ROTATIONAL CROP GUIDELINES

6. This guidance document does not make any changes to the basic requirements in the existing Test Guidelines 502 and 504 (1, 2). The guidance document does include a list of clarified definitions in Annex I.

Rotational Crop Metabolism Study

7. OECD Test Guideline 502 (Metabolism in Rotational Crops) (1) describes model studies which determine the potential for uptake of residues from the soil following treatment with a radiolabelled active ingredient and the magnitude and nature of the residues in three representative crop groups. The rotational crop metabolism study is not required for active ingredients which are intended to be used only on permanent or semi-permanent crops. However, if additional uses on annual crops are anticipated in the future, the metabolism study should be considered upfront.

Limited Field Rotational Crop Studies

8. OECD Test Guideline 504 (Residues in Rotational Crops - Limited Field Studies) (2) provides a basic structure for selecting representative crops and study design to determine the magnitude of residues in following crops under realistic field conditions. The Test Guideline does not encompass complex residue definitions, guidance for evaluation of metabolites, connection to other endpoint evaluations such as in environmental fate studies, or options for variation or addition of representative crops which would aid in the evaluation of the outcome of the limited field trials and adequate design for additional testing if necessary. It also does not provide guidance on how to handle residues in rotational crops on a regulatory level in the case that they are not covered by existing MRLs based on direct uses.

MOTIVATION FOR ADDITIONAL GUIDANCE

9. Various regional shifts in interpretation of the Limited Field Studies Test Guideline, which have resulted in varying national requirements for what has been considered a model study, has proven there is a need to provide guidance on design, interpretation, and further refinement in rotational crop field studies with a tiered approach in order to: 1) clarify the options for dealing with the active ingredient and metabolites, and 2) standardise the MRL setting process for rotational crops in order to facilitate work sharing across regions in OECD joint reviews and harmonised MRL setting for inadvertent residues in rotational crops. This would help to reduce the number of case-by-case assessments.

OECD survey

10. Differences across countries in rotational crop testing practices and data evaluation were investigated by means of an OECD survey which was circulated to regulatory organisations within OECD countries in order to compile current practices, concerns, triggers for conducting rotational crop studies, study design, data evaluation, and risk management actions (e.g. MRL setting, restrictions).

The survey results are summarised in Annex II with responses, including *ad hoc* national requirements, from government representatives from Australia, Canada, France, Germany, Ireland, Japan, New Zealand, the UK and the USA.

Conclusions from the survey

11. Differences and similarities across OECD countries became obvious. The Metabolism in Rotational Crops study (OECD TG 502) (1), commonly known as confined crop rotation, is considered a global study with limited differences in design based on target countries/regions of registration submissions. The Limited Field Rotational Crops study (OECD TG 504) (2) is conducted with variations in the crops used within the suggested crop groups based on the region of testing. They are routinely only conducted in Europe and two NAFTA countries: USA and Canada. Studies additional to the confined crop rotation and limited field trial studies are required on a case-by-case basis. Test concentrations are calculated differently in the regions of testing and soil sampling is supported only in some regions. Consistent guidance is needed about when to set label restrictions and when/how it is best to set MRLs.

TIERED APPROACH FOR INVESTIGATING RESIDUES IN ROTATIONAL CROPS

12. To meet time and resource constraints for regulatory submission, while at the same time generating adequate information for evaluation and regulation of residues in rotational crops, a tiered approach is proposed as follows:

Tier 1: Confined study (according to OECD TG 502) (1)
Tier 2: Limited field studies (according to OECD TG 504) (2) if triggered by Tier 1
Tier 3: Field studies for MRL determination (according to OECD TG 504, but expanded to a broader set of crops) if triggered by Tier 2 and/or required to provide data for MRL setting (along with acceptable Tier 1 and 2 data)
Post-Registration/Authorisation Activities:
Higher tier studies which may include post-registration testing or monitoring

13. With regard to Tiers 1 and 2, this approach is in agreement with current data requirements and OECD Test Guidelines 502 and 504 (1) (2). No precise requirements currently exist for Tier 3 or post-registration/authorisation activities in these guidelines although the tiered approach had been described previously in the *OECD Guidance Document on Overview of Residue Chemistry Studies* (as revised in 2009) (3).

14. Post-Registration/Authorization Activities are typically undertaken during or after the registration review process. However, some regulatory systems may require completion of Post-Registration/Authorization Activities before submission for registration of uses in rotational systems, for example, in Australia. These activities may occur after the first registration in a non-rotational system, either as small scale trials or in commercial systems under strictly controlled time-limited use approvals (see Annex III Boscalid example, Case 1). Post-Registration/Authorization Activities studies are intended for specific situations with case-by-case study design, to remove label restrictions or to address other concerns not covered in Tiers 1-3.

15. Normally, only when quantifiable residues occur in edible (≥0.01 mg/kg) or feed-relevant (≥0.05 mg/kg) plant parts, it is necessary to proceed to the next Tier and/or have label restrictions and/or consider these residues in MRL setting.

APPLICATION TO BARE SOIL VS APPLICATION TO PRIMARY CROPS

16. It is recommended to rely on bare soil application rather than on application to crops in all tiers of rotational crop testing, because the envisaged soil concentrations can be more easily achieved.

CONSIDERATIONS IN DERIVING THE APPROPRIATE APPLICATION RATE FOR ROTATIONAL CROP STUDIES

17. The EU requires a simulation of multi-year use by modifying the application rate in the rotational crop field studies to account for the soil plateau levels based upon environmental fate (e-fate) modelling. Plateau background residue levels in soil may need to be considered for field rotational crop studies (i.e. Tier 2 and 3) if field DT_{50} data are available and indicate a potential for soil accumulation higher than the usually accepted variation of 25% to the application rate. Thus, the application rate for the field rotational crop studies should then be the maximum seasonal rate plus the application rate corresponding to residual residues in the soil from long term use of the product.

18. The US EPA prefers that the maximum seasonal rate for a primary rotatable crop should be applied to the soil for Tier 1, Tier 2, and Tier 3 level rotational crop studies. However, the US EPA will accept rotational crop studies conducted according to the EU multi-year plateau requirement and will scale residues as necessary.

Deriving whether a plateau level in soil needs to be considered for design of field rotational crop studies

19. Guidance on how to derive appropriate soil DT_{50} values for a variety of kinetics scenarios can be obtained from the e-fate area [see references (6) to (11)].

20. Primary crops and corresponding rotational/succeeding crops may be grown in many crop regions under different soil and climate conditions leading to a distribution of soil half-life values (in e-fate studies) for a pesticide and its metabolites.

21. For the approach discussed in paragraph 17, field rotational crop studies should be conducted using an applied dose of substance that takes into account the potentially-accumulated residues from previous use as envisaged by the use to be registered. The accumulated residues can be calculated using data on persistence in soil available to the applicant at the time of design of the field rotational crop study. A field-determined soil dissipation DT_{50} value or DT_{90}, if available, is preferable to the corresponding laboratory soil DT_{50} value and should be used in the calculation of soil accumulation and plateau soil concentrations. A DT_{90} value should be used if this is the better description of decline of the residues in soil. However, if definitive field DT_{50} or DT_{90} values are not available at the time of initiation of field rotational crop studies (Tier 2 and higher), a geo-mean laboratory soil DT_{50} value should be used as an input parameter.

22. The method of deriving plateau soil residues available for uptake by rotational crops may be overly conservative since elements, as described below, are included as input worst-case parameters:

- a single maximum seasonal application rate for all rotated primary crops (highest application rate of most critical use pattern even if the maximum rate may not apply to all labelled primary crops),

- application of the same pesticide each year to the same crop site,

- minimum primary crop interception rate,

- availability of all pesticide residues applied in previous years in the rotational crop root zone, and

- complete bioavailability of aged soil residues.

These highly conservative assumptions, used in conjunction with appropriate DT50 or DT90 values, provide the robust basis for calculating application rates for Tiers 2 and 3 field rotational crop studies.

23. Crop rotation in succeeding years is highly recommended on pesticide labels for best management practices and resistance management. Therefore, additional refinement based on the actual use pattern of the pesticide is acceptable on a case-by-case basis for the calculation of plateau soil concentration if the pesticide is intended to be registered on a broad variety of non-permanent crops with significantly different application rates and application timings resulting in different crop interceptions. This approach is still conservative since, generally, crop rotation and application of pesticides with different chemistries in consecutive years are requested on pesticide labels to address resistance management.

24. The extent of accumulation of a substance can be expressed by the accumulation factor (f_{acc}), which is defined as the ratio between the plateau soil concentration and the concentration on day 0 immediately after the application (peak concentration timing for the active ingredient). The following example is given for calculating accumulation, assuming a 1st order kinetic decline. In practice, non-first order decline is often observed. Advice on calculation of accumulation should be sought from the e-fate area. If first order decline is observed, this factor may be calculated using the following equation:

$$f_{acc} = \frac{e^{-k\Delta t}}{1 - e^{-k\Delta t}} \qquad (1)$$

Where:
k = degradation rate in soil derived from the half-life according to $\ln 2/DT_{50}$.
Δt = application interval (usually 365 days – annual; 730 days – biennial; 1095 days – triennial, etc.)

For example, for 1st order kinetic degradation the accumulation factor for an active ingredient with a field DT_{90} of 498 days (DT_{50} of 150 days) following consecutive annual applications is 0.23. This translates to 23% of the maximum seasonal rate, and is within the 25% variation allowed for application rates for field crop residue studies. Therefore, DT_{90} values >500 days (DT_{50} values >150 days) may be considered as triggers for including plateau background residue level concentrations in field rotational crop studies. This is done by adding the plateau to the maximum seasonal application rate.

25. The portion (fraction) of the accumulated residues available for uptake by rotational crops may be affected by the binding characteristics of the pesticide and its metabolites.

26. It is up to the regulator to re-calculate predicted residues in soil by introducing further e-fate data which became available after the study was conducted or by excluding data from the crop failure situation, if appropriate (e.g. if the active ingredient is applied late in the season). However, if PBIs are proposed on the label and DT_{50} values for the parent substance and its relevant metabolites are less than 50% of the respective label PBIs, consideration of a plateau level might not be needed.

DERIVING THE APPLICATION RATE FOR PLATEAU PLUS MAXIMUM SEASONAL RATE

27. A compilation of recent case studies has been distilled into the following calculation method to be used for active ingredients or soil metabolites which follow first-order dissipation rates in soil. The method is not applicable for relevant soil residues involving more than one compound, because the individual compounds might reach their maximum levels after different time periods. The plateau background residue level $A_{plateau}$ (expressed as g or kg ai/ha) may be calculated as follows:

$$A_{plateau} = A_0 f_{soil} f_{acc} \quad (2)$$

Where:
$A_{plateau}$ = Application rate corresponding to residual residues in the soil from long term use of the product (g ai/ha)
A_0 = Total seasonal application rate to target crop (g ai/ha)
f_{soil} = Fraction of the seasonal application rate reaching the soil after crop interception
f_{acc} = Accumulation factor

The interception rates for different crops during foliar applications have been experimentally determined (FOCUS Surface water, 2015) (12). The fraction reaching the soil (f_{soil}) equals "1 minus interception rate." Crop interception is only valid for applications made directly onto a primary crop and may be used to calculate the effective application rate to the soil if an application to a primary crop occurs at leaf development growth stage or later. Zero interception should be assumed for pesticide applications made directly onto bare soil (for example pre-emergence herbicide applications) and at leaf emergence stage. As rotational residue studies are intended to have relevance to all potential future uses of an active ingredient in any rotational system crop interception is generally considered to be zero.

28. An additional seasonal maximum application rate should be added to the plateau background residue level in soil to address soil residues available after failure of the treated primary crop and immediate replanting of rotational crops. The immediate replanting of a rotational crop following crop failure effectively represents a different interval between 1) application to the primary crop that preceded the rotational crop and 2) planting of the rotational crop, as compared to that reflected by usual seasonal use and the associated plateau residue levels. As a conservative assumption, plant/crop interception is not considered for the seasonal application occurring in the year of crop failure and planting of the rotational crop. This assumption accounts for potential crop failure followed by incorporation of the crop residues (including both the amount reaching the crop and the amount reaching the soil during treatment) prior to planting the rotational crop. Occurrence of ploughing is usually used by e-fate experts as a parameter for the predicted environmental concentration in soil

(PEC_{soil}) calculation. However, this parameter has no influence in the determination of the $A_{plateau}$ and A_{total} according to the presented methods. Based on these assumptions, the total soil residues (A_{total}) available for uptake after multiple years of application and crop failure after application to target crop may be calculated as follows:

$$A_{total} = A_0 + A_{plateau} = A_0(1 + f_{soil} f_{acc}) \quad (3)$$

29. The principal design of rotational crop studies involving application to bare soil and subsequent sowing/planting is identical to a pre-emergence soil treatment in a supervised field trial. For this kind of trial design (referring to all 3 tiers), the proportionality concept as outlined in the Guidance Document on Crop Field Trials (5) is applicable, allowing scaling of residues found in rotational crop plant samples within the described limitations (see below and Annex III ametoctradin example, Case 2) in cases where new information is available or application rates have changed post study conduct. The respective scaling factors are calculated according to the following formula:

$$F_P = \frac{C_{Peak\ soil}}{C_{RC}} \quad (4)$$

Where:
F_P = Proportionality (or scaling) factor
$C_{Peak\ Soil}$ = Predicted peak soil concentration for the active ingredient or its metabolites expressed on a kg ai/ha basis
C_{RC} = Applied amount of active ingredient or metabolite soil concentration in rotational crop study on a kg ai/ha basis

The resulting proportionality (or scaling) factor should be used according to the following guidance:

- to check whether the rate of the available rotational crop studies is appropriate when considering the scaling factor deduced and whether the scaling factor calculated is within the acceptable range limits for the application of the proportionality concept (see OECD Crop Field Trial Guidance Document (5) for further guidance);

- results from rotational crop metabolism studies (Tier 1) can be scaled downwards and, in some cases, can be up-scaled when there are no concerns over metabolite identification;

- to apply the scaling factor to levels of residues derived from studies on the magnitude of residues in rotational crops, in consideration of consumer risk assessment and residue levels input for MRL calculation purposes, arising from the GAP uses of the pesticide products (see Sections on **MRL setting based on residues in rotational crops** and **MRL setting vs label restrictions for rotational crops** for further guidance).

CONSIDERATION OF METABOLITES

30. For rotational crops, typically the main components found in food and feed commodities of primary crops, and soil metabolites, are potentially relevant. All metabolites exceeding 10% Total

Radioactive Residue (TRR), or 0.01 mg/kg (ppm) in crop commodities from the confined rotational study, may be considered for inclusion in residue definitions, especially risk assessment definitions (for further details, see Guidance Document on the Definition of Residue) (4). If residue definitions involve one or more metabolites, it is much more complicated to select the appropriate application rate for the field rotational crop study.

31. As is the case for the parent substance, individual degradation rates for each relevant metabolite can normally be obtained from e-fate studies. Depending on the decline of the parent, specific amounts of metabolites are formed and may add up with increasing time. However, the metabolites formed in soil are themselves subject to degradation, resulting in a peak concentration after a specific interval dependent on the field DT_{50} values of both parent and metabolite(s).

32. For metabolites having a potential for accumulation over multiple years, the long-term metabolite residues in soil available for uptake by rotational crops must be taken into account, based on the predicted plateau concentrations in the e-fate section. Specific consideration is needed concerning the point in time at which a relevant metabolite reaches its maximum concentration. Information on the DT_{50}/DT_{90} values of metabolites can be obtained from ^{14}C e-fate soil studies and terrestrial field dissipation studies OECD (2016) guidance (9). If sufficient soil cores (samples) over time have been taken, metabolite DT_{50}/DT_{90} values might also be obtained from rotational crop studies where such sampling is carried out additionally to the usual plant sampling described in OECD Test Guideline 504 (2).

33. Metabolites that are common to more than one active ingredient have limitations for consideration in rotational crop studies because of contamination in control samples and the difficulty of calculating adequate soil concentrations.

34. When (i) the metabolite concentration in soil is known and (ii) reaches its peak within the PBI investigated in the rotational crop study with the parent, the study information can also be used to conclude on metabolite residue levels in rotational crops.

35. Without knowledge of the metabolite concentration in soil, the kinetic behaviour may be modelled based on e-fate data, if available. If the metabolite reaches its maximum after a longer time period than investigated in the rotational crop study, this maximum metabolite concentration is not *per se* covered by the study. In such a situation scaling of metabolite residues in plant samples as described under paragraph 29 is recommended.

36. If the plateau level of the metabolite and its formation rate is known, but scaling is not possible, other options are:

- Application of a mixture of parent and metabolite in the rotational crop study at levels representing the individual maximum amounts found in soil, though these normally do not occur at the same point in time. This requires that the metabolite can be prepared in large enough amounts to conduct the testing.

- Application of exaggerated rates of the active ingredient in order to obtain sufficient concentrations of the metabolite at the level of its calculated maximum.

- Application of the metabolite at its plateau level in a separate study given that the metabolite can be prepared in large enough amounts to conduct the testing.

37. If parent and metabolite are both relevant for MRL setting and/or dietary risk assessment and if scaling of metabolite concentrations is not possible, separate studies might be needed to derive realistic concentrations for both compounds.

SELECTION OF ROTATIONAL CROPS TO BE TESTED

Tier 1 and Tier 2 Rotational Crop Studies

38. The OECD Test guideline 502 (1) gives guidance on the number and selection of crops to be tested for Tier 1 level rotational crop studies (confined studies).

Table 1 Selection of crops for Tier 1 studies

Crop group	Required by TG 502	Example crops
Root and tuber vegetables	Yes	carrots, radishes, sugar beets
Small grain (cereals)	Yes	wheat, barley, oats, rye
Leafy vegetables	Yes	spinach, lettuce
Oilseeds	No	Soybeans (surrogate for leafy crops in TG 502), oilseed rape

39. The OECD Test guideline 504 (2) gives guidance on the number and selection of crops to be tested for Tier 2 level studies. In Tier 2 the focus should be on those crops/crop groups with significant residues (≥0.01 mg/kg) in Tier 1 at appropriate application rates (i.e. after scaling, if necessary). It might be useful to replace one of the crop groups from the Tier 1 study, especially if it did not show significant residues, by a different and not yet tested crop group (e.g. by oilseeds or brassica vegetables) in the Tier 2 study.

Table 2 Selection of crops for Tier 2 studies

Crop group	Required by TG 504	Example crops	Further crops proposed as substitutes
Root and tuber vegetables	Yes	carrots, radishes, sugar beets	
Small grain (cereals)	Yes	barley, wheat	Maize
Leafy vegetables*	Yes	lettuce, spinach	
Brassica vegetables*	No		cabbage, kale
Oilseeds	No		soybeans, oilseed rape
Fruits, fruiting vegetables	No		Annual strawberries

*Extrapolation options are elaborated in Table 3 for possible alignment of Tier 2 and Tier 3

Tier 3 Rotational Crop Studies

40. If in Tier 1 or 2 studies residues in rotational crops were <0.01 mg/kg at PBIs ≥ 30 days and at appropriate application rates (i.e. after scaling, if necessary), no label restrictions and no MRLs are needed and Tier 3 studies are unnecessary. If in Tier 2 studies residues in rotational crops reach significant levels (≥0.01 mg/kg), a Tier 3 assessment is necessary based on an "extended RC field study data package" to decide on appropriate risk mitigation measures and/or to set MRLs. Studies should be conducted with application to bare soil.

41. However, if in Tier 1 and 2 certain groups of rotational crops have already been shown to bear negligible residues (typically <0.01 mg/kg) when an adequate application rate is used, these crops would not need to be tested again in Tier 3. The trials should be conducted as closely as possible to

common crop rotation practice on major indicator crops from different groups; i.e. the rotational crops tested should be typical for the uses (target primary crop/rotational crop combinations) to be evaluated. These trials should be conducted on bare soil at locations distributed over main production areas for the targeted uses. Depending upon the scope of uses submitted for the active ingredient, data sharing across regions should allow for meeting this data requirement; see OECD Crop Field Trial Guidance Document (5) for further guidance. It is important to keep in mind that this comprehensive strategy would only apply to a situation where study design (application rate, PBIs) is similar and all relevant substances were included in analysis. Before using rotational crop studies conducted outside the respective regulatory region, the applicant may consult with the responsible regulatory authorities.

42. Morphological differences are less important in rotational crops than when considering direct treatment. However, adequate coverage across crop groups is needed to account for metabolic and rhizosphere effects. From each of the six "super" crop groups listed in Table 3, at least one crop from each subgroup should be selected, and the selection should take into account any information obtained from Tier 1 and/or Tier 2 studies to ensure conservative, representative results from a rotational crop residue perspective. Overall, for each relevant PBI, the testing of at least 12 crops from 6 groups at 4 or 8 different geographic locations each (maximum of 60 individual trials) is required to meet the "super" crop group default approach. Most crops require only 4 trials, while cereals and oilseeds require 8 trials each. This is due to the importance of these crops in agriculture worldwide. Concerning the geographical distribution of trials and the use of trials from different regions such as US/Canada, Australia and the EU, it is referred to the recommendations in the Guidance Document on Crop Field Trials. Some trials might be waived depending on results of Tier 1 and Tier 2 studies or if pre-emergence field studies with primary crops provide enough information on the expected residue levels in the rotational crop situation. In addition, the magnitude and profile of residues following primary treatment in comparison to residues taken up from the soil need to be considered to decide on representative crops for Tier 3 studies. The design of Tier 3 studies should address the conclusions drawn from Tier 1+2 studies concerning the most critical PBI to be investigated, especially for complex residue situations including relevant metabolites.

Table 3 Selection of crops for Tier 3 (extended field) studies

"Super" crop group (each consisting of one or more crop groups) [1]	**Crops proposed for Tier 3 field studies for one or more subgroups (labelled 1, 2, 3), respectively** [2]	**Number of Trials** [3]	**Possible Extrapolation**
Root and tuber	1. Carrots or radishes or sugar beets (*) or other beets	4	Subterranean parts: Extrapolation to root and tuber vegetables, potatoes, roots of sugar plants, of herbal infusions and of spices Aerial parts: root crop based forage crops (**)
	2. Potatoes (optional) [4]	4	No Extrapolation
Bulb and stem vegetables	1. Leek or celery	4	Extrapolation to bulb vegetables and stem vegetables
Cereals	1. Wheat or barley (small grains: wheat, barley, triticale, oats and rye*)	8	Grains: Extrapolation to all cereal grains Forage: Extrapolation to sugar cane, pastures (**); forage crops derived from cereals (**) or sugar cane tops (**) Straw: extrapolation to straw and fodder of all cereals (**)
	2. Maize (maize and all other cereals; sugar cane*)	8	
Leafy vegetables and Brassicas	1. Lettuce or spinach (leafy vegetables except leafy brassicas, flowers and leaves of herbal infusions and of spices *)	4	Extrapolation to all other leafy and brassica vegetables, flowers and leaves of herbal infusions and of spices, brassica forage crops (**)
	2. Head cabbage or kale (head brassicas, leafy brassicas, brassica forage crops *)	4	
	3. Broccoli or cauliflower (flower head brassicas)	4	
Oilseeds and pulses	1. Oilseed rape or soybeans (oilseeds, immature soybeans, dry soybeans *)	8	Green immature pods with seeds: extrapolation to legume vegetables (green beans/peas with pods) *** Green immature seeds: Extrapolation to legume vegetables (green beans/peas without pods) *** Mature dry seeds: Extrapolation to all oilseeds and pulses (dry seeds) Forage: Extrapolation to forage of the legume vegetables and oilseeds group (**) Fodder: Extrapolation to fodder of the pulses and oilseeds group
	2. Dried beans or dried peas [legume vegetables (except immature soybeans), pulses (except dry soybeans)]	4	
Fruits and fruiting vegetables	1. Strawberry	4	Extrapolation to all other fruits planted as field crops, to fruiting vegetables and to fruits, seeds and berries of herbal infusions and of spices
	2. Cucumber (fruiting vegetables, small variety: fruiting vegetables, fruits	4	

"Super" crop group (each consisting of one or more crop groups) [1]	**Crops proposed for Tier 3 field studies for one or more subgroups (labelled 1, 2, 3), respectively** [2]	**Number of Trials** [3]	**Possible Extrapolation**
	& seeds & berries of herbal infusions and of spices)		
Total		**60**	

[1] The super crop group strategy assumes that residues are similar within the group (e.g., for fruits and fruiting vegetables, residues from strawberry and cucumber are similar). If residues within a group are not similar (by Kruskal-Wallis Test), then additional data may be necessary.

[2] If harmonised global MRLs are being sought for rotational crops, then distribute trials globally, as appropriate, to accommodate the predominant growing areas of the crop.

[3] Number of acceptable trials across Tiers 2 and 3.

[4] Residues in rotational potatoes are likely to be lower than those in smaller, shorter-season root crops such as radish, carrot, or beet. Potato is included primarily for refinement of dietary risk assessment due to the relatively high consumption of potato in relation to other root crops.

* Two trials on one or more of these crops may already be available from Tier 2 studies

** Highest residue is taken for livestock dietary burden calculations. MRLs are set in some countries for forage crops. MRLs are more generally set for fodders like straw and hay.

*** MRLs for legume vegetables can be extrapolated from crop subgroup 2 alone since crop subgroup 1 will not always result in data for immature seeds or immature pods with seeds (e.g. when only oilseed rape is available, immature seeds and pods are not typically analyzed).

Post-Registration/Authorization Activities to Address Rotational Crop Issues

43. Post-Registration/Authorization Activities for rotational crops are required on a case-by-case basis only. It is recommended to consult with authorities on specifics of the study design.

44. Circumstances under which Post-Registration/Authorization Activities might be required:

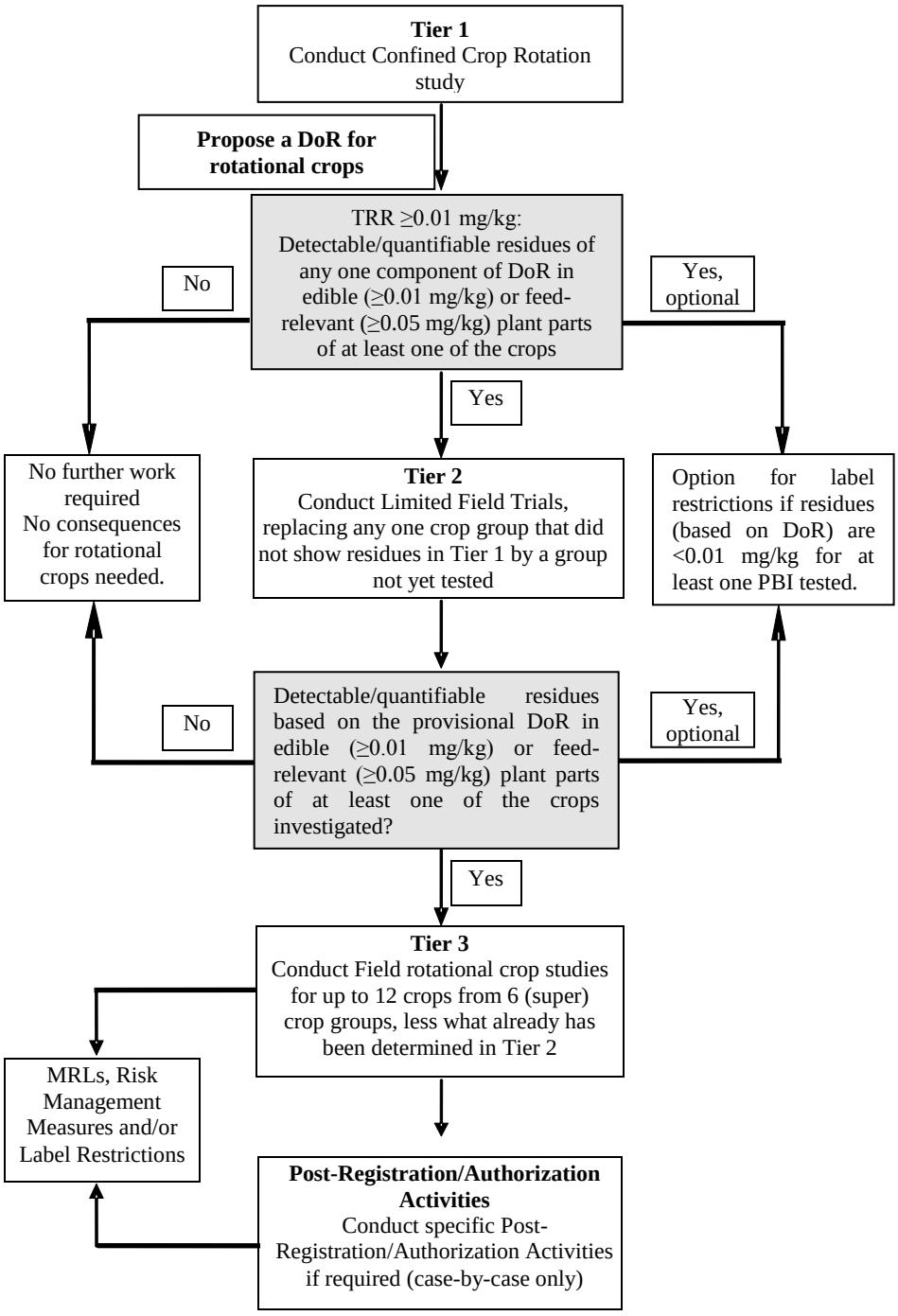
- to confirm that residues do not exceed predicted values (e.g. if the soil plateau level has been calculated to be higher than the application rate was in Tier 2 and 3 studies and scaling is not possible/appropriate)
- for compounds where the DT90 is not reached within one year after application to bare soil
- for compounds where accumulation studies are ongoing at time of registration
- to clarify metabolite issues in the case of complex residue definitions
- to confirm/mitigate label restrictions
- to monitor residues identified from registration review as a requirement for conditional registration

An example of post registration activity can be found in Annex III (Case 1 - Boscalid Example).

Decision trees to support setting up a rotational crop testing programme

The general decision tree based on the tiered approach is depicted in Figure 1.

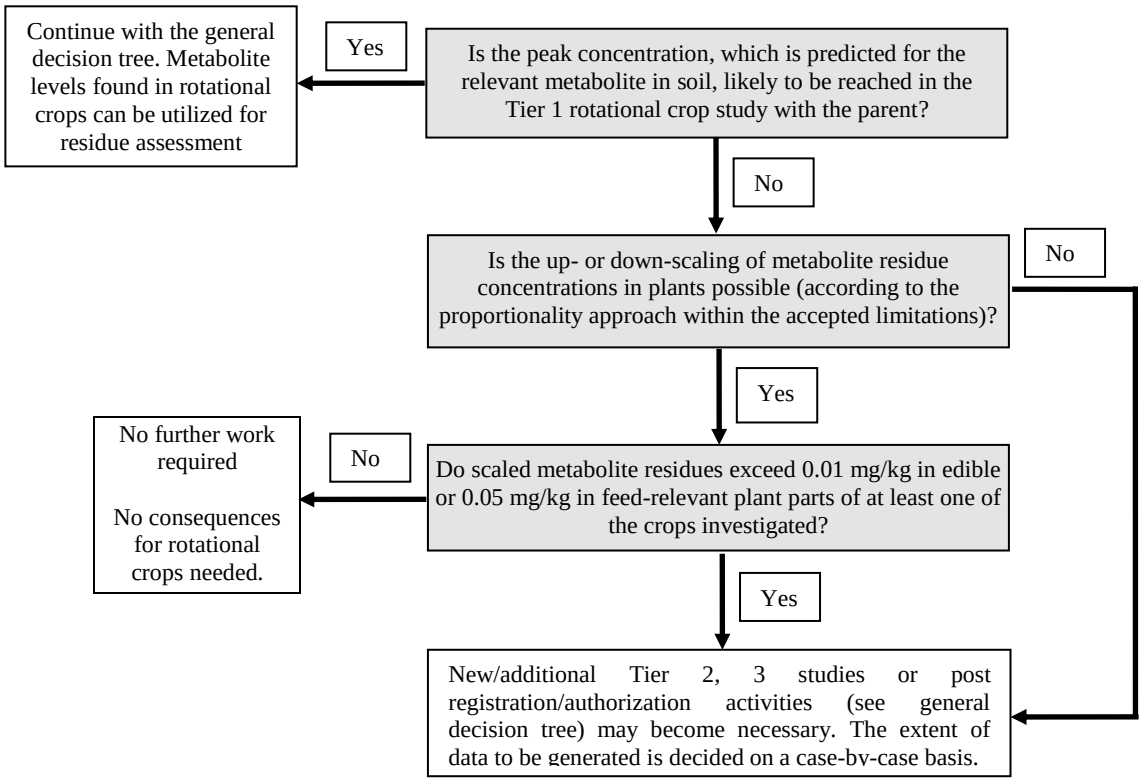
Figure 1. General Decision Tree



DoR = definition of residue

45. In situations where peak concentrations predicted for relevant metabolite(s) in soil are not reached in the Tier 1 study conducted with the parent molecule, a separate decision process may be triggered when metabolites found in rotational crops are considered relevant for enforcement and/or risk assessment. The decision tree for this situation is depicted in Figure 2.

Figure 2. Decision Tree for complex residue definitions including relevant metabolites when predicted soil concentrations are not reached in the Tier 1 study conducted with the parent molecule



46. If the metabolite is part of an enforcement residue definition for food and feed of plant origin (including metabolites in common with other active ingredients), a dataset sufficient for MRL setting is required (usually Tier 3) unless appropriate label restrictions are introduced instead.

47. In case of common metabolites, in principle the simultaneous occurrence from various sources should be the basis for an assessment, unless clear limitations exist (e.g. label restrictions or limitations on combined pesticidal use due to resistance management reasons). It also needs to be considered whether or not one of the sources dominates the uptake of residues by rotational crops. When such a driving source is identified and the other combined sources contribute less than 25% to the final residue concentration in the rotational crops, the sole consideration of the most sensitive source can be justified for MRL setting and dietary risk assessment. An example from the 2014 Joint Meeting on Pesticide Residues (JMPR) on the common metabolite 2,6-dichlorobenzamide in brassica vegetables, which may arise in primary treated and rotational crops after application of the active ingredients dichlobenil and fluopicolide, is presented as Case 3 in Annex III of this document.

48. As an amendment of the decision trees depicted in figures 1 and 2: metabolites not exceeding 0.01 mg/kg, but being part of a dietary risk assessment residue definition, may require particular consideration in the following situations:

- the scaled residues in the confined rotational crop study result in an exceedance of the common toxicological endpoints such as Acceptable Daily Intake/Acute Reference Dose (ADI/ARfD) and/or

- metabolite concentrations when added to the parent residues alter the dietary intake or livestock dietary burden significantly (>25% parent equivalents) and/or

- the metabolite has different toxicological endpoints than the parent (separate ADI/ARfD values).

If case study results are needed for dietary intake assessments, higher tier rotational crop studies should be based on a conservative residue scenario, i.e. they should focus on crops with a high sensitivity in the intake assessment. For metabolites only relevant for dietary intake assessment, and not exceeding 0.01 mg/kg, moving to the next higher Tier is required when an impact to the consumer risk (including carry-over into animal products) as described above cannot be excluded.

SOIL SAMPLING IN ROTATIONAL CROP STUDIES

49. Several guidelines and guidance documents are available from the e-fate area aiming at the determination of residue levels and degradation rates of active ingredients and their metabolites in soil [see references (6) to (11)].

50. According to test guidelines OECD TG 502 and 504 (1) (2), soil sampling in rotational crop studies is not mandatory. Data needed to derive the appropriate application rate and to identify relevant soil metabolites can be obtained from the e-fate area. Normally a tiered approach is applied which starts with laboratory studies, followed by field dissipation and soil accumulation studies, depending on the degradation rate. From this set of e-fate studies, DT_{50} values are determined as well as plateau concentrations and DT_{90} values, if required. Applicants and risk assessors are encouraged to make use of data generated in the radiolabelled soil metabolism studies so that appropriate metabolites are monitored and evaluated from the initiation of the rotational crop tiered process.

51. Terrestrial field dissipation studies would provide a more robust set of data than soil residue data from a rotational crop study; however, they may not be sufficient for deriving parameters in a multi-component dissipation model. Caution should be taken because:

- Some field studies do not have an active rhizosphere. While that would probably not affect which metabolites are formed, it could have a significant influence on the kinetics of formation/degradation.

- There is a high degree of variability in pathway kinetics from one site to the next and due to the very large number of variables, it is difficult to determine which data are representative of any particular site.

- There are many compounds whose metabolic pathways do not follow first-order kinetics, so that assumption may lead to significant errors in predicted residue levels.

If necessary, mixed kinetic models for parent and metabolites should be applied.

52. Voluntary soil sampling in rotational crop studies adds valuable information for the interpretation of rotational crop studies. Soil data generated within the rotational crop study are not meant to replace the soil degradation data collected in the e-fate area, which is a more comprehensive set of studies for predicting concentrations in soil, but they can help to:

- validate the residue pattern observed in rotated plants;
- provide soil residue concentrations available for uptake via the roots precisely for the substrate in which the rotational crops investigated were planted;
- provide tailored soil concentrations for specific plant-back intervals;
- clarify which levels of metabolites were actually present for each crop rotation (e.g. to clarify if the peak/plateau concentration has been reached or to calculate the kinetics for parent/metabolite after certain plant-back intervals being targeted in the rotational crop study) if enough data are not available from the e-fate studies;
- apply the proportionality approach to rotational crop metabolites to provide meaningful results by using soil degradation data from the same study.

53. Although not required by the test guidelines, analysis of treated soil is recommended at the selected plant-back intervals in field rotational crop studies to provide actual soil residue data as a basis for study interpretation and scaling of results. The general sampling of soil at each plant-back interval, after ploughing and before planting of rotational crops, is suggested for each site. For the soil sampling, the root zone (20 cm depth without segmentation) provides sufficient information for the assessment of potential residues in rotational crops. Sampling recommendations are further specified as follows:

- Sampling is only requested for limited field (Tier 2) studies. Plot sizes would need to be increased to allow for obtaining a representative soil sample (5 cores per composite sample, taken per plant-back interval/site in a random manner across a treated area as would be done to obtain a representative crop commodity sample). Separate samples per rotational crop planted are not necessary unless the application timing or method is not consistent across all crops per interval tested;
- Data from Tier 1 studies and e-fate endpoints should help to guide optimum sampling timing. As a default, sampling may be at the beginning of each PBI tested, after any ploughing of plant material and before planting;
- Analysis of parent plus rotational plant and soil metabolites in soil samples would provide the most useful information;
- Results may only be relevant for comparison within a test site, not across test sites, since soil type and test site variability would add uncertainty.

54. For the identification of relevant metabolites in rotational crops special attention should be paid to the circumstance that the potential of the metabolite to be taken up via the roots is not necessarily linked to high soil concentrations found in e-fate soil studies. Minor metabolites found in soil may show a high rate of uptake, resulting in major concentrations in the plants. Therefore, both the occurrence in the soil and the concentration in plant samples obtained from confined rotational crop studies need to be considered.

INTERPRETATION OF RESULTS OF FIELD ROTATIONAL CROP STUDIES

55. It is necessary to confirm that the Tier 2 and 3 studies (may also be applicable to Post-Registration/Authorization Activities) comply with requirements and reporting elements outlined in Test Guideline 504 - Residues in Rotational Crops. Several general points to consider when interpreting data from rotational crop studies are described there. The impact of residues following direct treatment has always to be considered in comparison to an additional uptake from the soil (rotational crop situation).

56. It is necessary to confirm that the actual application rate administered is equivalent to the maximum required rate.

57. When common metabolites arising from different pesticides or other sources are found in treated or control plots, the pesticide use history needs to be considered for an interpretation of the findings.

EVALUATION OF RESIDUES IN ROTATIONAL CROPS UNDER PROTECTED CONDITIONS

58. Residues in rotational crops grown under protected conditions do not need to be considered in the following cases:

- soil free production methods ("hors-sol", e.g. rockwool with hydroponic irrigation),
- permanent crops (e.g. berry bushes),
- exchange of soil after each cultivation cycle included in the label (potential residues in compost or spent growing media is outside the scope of this document),
- cultivation in plant pots (e.g. nursery plants),
- ornamentals, on a case-by-case basis, as these crops can be rotated back to food crops in relatively few years.

59. In other situations, potential residues in rotational crops may differ significantly between field and protected environments. While natural conditions mostly allow the cultivation and harvest of one primary crop and the sowing/planting of one succeeding crop per year, a higher number of crop cycles with shorter PBIs is possible in protected conditions. Specific higher tier studies might be required to cover this situation.

60. In glasshouse the cultivation of up to three crops per year is common, normally involving fast growing early and late crops (e.g. lettuce species) and a main crop in the middle of the year (e.g. fruiting or legume vegetables). Unless restricted by respective labels, the calculation of the annual amount of active ingredient to be applied should be based on three crop cycles per year. Concerning the microbial degradation of residues in soil, no significant differences have to be expected between field and glasshouse allowing the use of field studies to address residues in rotational crops grown under protected conditions. However, if soil photolysis plays an important role in the degradation of an

active ingredient or its metabolites, the extrapolation of data generated for field conditions to indoor environments has to be considered on a case-by-case basis.

61. Other protection structures include, for example, low tunnels or plastic shelters. These mobile structures are typically used in the field (i.e. on grown soil) to accelerate plant growth, especially early in the growing season. After harvest or under favourable weather conditions, these tunnels may be removed leaving normal field conditions for a succeeding crop. Concerning the evaluation of residues, such structures can be assumed to provide similar environmental conditions as the normal field. However, due to the accelerated growth of the primary crop, the interval between application and planting/sowing of the succeeding crop may be much shorter than usual, requiring a PBI of approximately 30 days or less to be tested.

MRL SETTING BASED ON RESIDUES IN ROTATIONAL CROPS

62. The default course of action following the Tier 1 trigger for additional field rotational crop testing is to conduct Tier 2 limited field trials. Based on the results of the Tier 2 limited field trials, a decision needs to be made on progressing to Tier 3 trials. This decision will normally be made by the applicant pre-submission, but may be made in consultation with regulatory agencies. Tier 3 testing is generally considered necessary when results from Tier 2 testing indicate that residue components within the residue definition are expected to be ≥0.01 mg/kg in rotational crops and/or residues accumulate in soil. MRL setting based on Tier 2 data is possible per crop type (see Table 3), when at least the required number of trials per crop type are available to set MRLs. It should be noted that, normally at the Tier 2 stage, data are not sufficient to derive adequate MRLs for all crops and that any MRL setting by extrapolation for crops not tested at this stage is associated with large uncertainties.

63. When Tier 3 testing is deemed necessary, then the recommendation is to use the "super crop group" extrapolation approach to determine MRLs for all rotational crops as indicated in Table 3.

64. There is always the option to design a complex testing protocol at the Tier 2 level to generate adequate data for MRL setting. Depending on the magnitude of the residues obtained [consistently ≥0.01 mg/kg for commodities for human consumption or ≥0.05 mg/kg for commodities for livestock consumption (or lower when animal transfer data indicate that this will result in residues of consequence in animal commodities)] and the number of tests available per crop type, use of or ability to scale to the appropriate application rate, and the consistency of calculated MRLs among subgroup commodities within a super crop group, MRLs may be set in lieu of Tier 3 testing. Options for generating data to set rotational crop MRLs are provided below, considering the super crop groups described in Table 3.

65. In the case where, after Tier 2 study completion, some acceptable data for MRL setting have been generated, but it is deemed necessary that more field data are needed for setting MRLs for rotational crops, these data should be generated as a subset of the Tier 3 super crop group approach. In principle, each super crop group has to be covered by at least four or eight tests per crop subgroup (see Table 3). They should be conducted using the correct inputs and one of the proposed commodities for this subgroup.

66. Field rotational crop studies (Tier 2 as well as Tier 3) that have been conducted at or scaled to the appropriate application rate (maximum seasonal application rate for USA and Canada, normally plateau background residue level plus the maximum seasonal application rate for EU purposes) are selected. Residues in edible and feed-relevant plant parts of rotational crops planted at a PBI of ca 1 month are normally selected from the studies. This interval mimicking crop failure and immediate

replanting normally represents the worst case with respect to rotational crop residue levels. There might, however, be situations where it is appropriate to select the residue data from a longer PBI instead (e.g., when residues are higher and/or the residue of concern has changed or when label restrictions dictating a longer PBI are in place).

67. The selected residue data are attributed to the commodities associated with the six super crop groups as listed in Table 3. Each of these 6 groups (which encompass a total of 12 subgroups) needs to be covered in one way or another. This means that if no rotational crop field trials are available for a particular subgroup, possibilities for extrapolation from other groups or from primary crop pre-emergent application uses are explored on a case-by-case basis. If no further extrapolation is possible, then an MRL is not supported until further data are generated or a label restriction is recommended for all groups or commodities within a group not yet covered.

68. For MRL setting, each subgroup should be covered by the required minimum of acceptable, independent trials unless sufficient information is available from lower-tier rotational crop studies or pre-emergence primary crop studies. For super crop groups consisting of two or three subgroups, the residue populations of the subgroup common commodities (e.g. subterranean to subterranean, aerial to aerial) are compared (see the updated Crop Field Trial Guidance Document for details on criteria for dataset comparison) and combined if similar. The MRL proposal is then based on the combined data set for the whole super crop group. If the data sets within a crop group appear to be different, separate MRL proposals are calculated with the OECD calculator for each subgroup (see Annex III, Case 4).

69. If residues (≥0.05 mg/kg) are observed in feed commodities obtained from rotational crop studies, this requires specific consideration. Depending on the overall primary and rotational crop data set, these residues also have to be considered in dietary burden calculations and for MRL setting if applicable.

70. For all non-annual crops [semi-permanent and permanent crops (e.g. citrus, pome fruit, stone fruit, tree nuts, berries)], rotational crop residues normally do not have to be considered because these crops are not grown in rotation. Long-term active ingredient or metabolite concentrations in soil may also results in residues in permanent crops, when they are easily taken up via the roots (e.g. dichlobenil). In such cases and for times of land-use change, it may be appropriate to generate some data to assist in managing residues.

71. MRLs should be set at a level that covers the residues from application to the commodity as a primary crop and residues arising from rotational sources. An example on how MRLs could be derived based on rotational crop data is presented for chloridazon as Case 5 in Annex III of this document. Another example of pesticides registered in the USA with residues in rotational crops is provided for flutriafol in Case 4 of Annex III.

72. MRLs for crops that may be exposed to a primary application of an active ingredient and, in addition, to residues of the same active ingredient remaining from applications to the preceding crop, need special consideration. If the additional contribution by rotational crop residues is >25% of the residues arising after primary treatment, this contribution is considered significant and has to be considered in MRL setting. The MRL should then be established based on an adjusted residue data set: the highest residue value obtained in GAP-compliant or scaled field rotational crop studies are added to each residue value obtained in GAP-compliant crop field trials. The MRL, STMR and HR is calculated from these adjusted residue values. JMPR uses a similar approach to derive HR and STMR values in such situations.

MRL SETTING VS LABEL RESTRICTIONS FOR ROTATIONAL CROPS

73. This document provides a data generation and assessment framework for residues in rotational crops to allow establishment of MRLs as trading standards and to ensure dietary exposure to the active ingredient and its metabolites can be appropriately accounted for. In some instances, label restrictions may be considered as an alternative to establishing such MRLs.

74. Typical label restrictions include:

- Types of crops excluded from being planted directly in rotation.
- Plant-back intervals.
- Controls on the number of applications of the active ingredient per year.
- Controls on the maximum amount of the active ingredient applied per season or year.
- Controls on use of the active ingredient in consecutive years.

75. Label restrictions may be used to allow registration of products while additional higher tier studies are undertaken.

76. It is preferable that data generation focus on providing adequate information to establish MRLs for rotational crops, rather than on relying on country-specific label restrictions for mitigating residue levels. This will maximize the potential for data sharing and reduce the potential for trade barriers associated with differing national MRLs.

77. Reliance on label restrictions without MRL establishment may sometimes require generation of datasets addressing longer plant back intervals than those required for MRLs, as generally label restrictions would aim to produce non-detectable residues in rotational crops. This is particularly the case in countries that do not adopt a default low-level MRL (uniform limit).

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(11) EFSA, 2017: EFSA Guidance Document for predicting environmental concentrations of active substances of plant protection products and transformation products of these active substances in soil. Adopted: 29 August 2017 doi: 10.2903/j.efsa.2017.4982 (This guidance published on 19 October 2017 replaces the earlier version published on 28 April 2015*)

(12) FOCUS 2015: Generic guidance for FOCUS surface water Scenarios, Version 1.4, May 2015.

ANNEX I. DEFINITIONS

1. **Accumulation factor:** the ratio between the plateau soil concentration after multiple year applications of a pesticide and the soil concentration on day-zero right after the first application.
2. **Accumulation study:** a study conducted to define the accumulation of a pesticide in soil under field conditions following multiple year applications or accumulation of residues in rotational crops from uptake of soil residues following multiple year application to primary crops.
3. **Aged soil:** soil treated with a pesticide product for an extended time period (as opposed to freshly treated soil).
4. **Artificial substrates/growing media:** soilless media (e.g. water in hydroponics, bark, peat, rockwool, and perlite) typically used in greenhouses/glasshouses for growing crops.
5. **DT_{50}:** 50% dissipation time; the amount of time required for 50% of the initial pesticide concentration to dissipate.
6. **Field soil dissipation:** the transformation, transport (e.g. loss through volatilization or movement), and fate of pesticide residues in soil under representative actual field conditions.
7. **First-order kinetics:** method to describe the degradation of a pesticide with a rate-limiting step linearly dependent on the concentration of only one compound. Reference 9: A model that assumes that the rate of degradation/dissipation is proportional to the concentration of the reactant and remains constant during the reaction time period.
8. **Import tolerance:** Maximum residue limit set for pesticide residues in/on an imported crop commodity when the pesticide is not registered for domestic use on that commodity in the importing country or when the domestic MRL has been set at a lower level based on domestic GAP and a higher MRL is needed to import the traded commodity.
9. **Inadvertent residues:** Residues found in rotational crops following the uptake of residues remaining in soil following direct soil, foliar, or seed treatment application of a pesticide product to primary crops.
10. **Label restriction:** restrictions placed on a pesticide product label to mitigate a variety of issues such as maximum application rate allowed on a crop per crop season or year, re-entry interval (hours) after application, plant-back intervals for rotational crops, and feeding of treated crop commodities to livestock, and buffer zones. Label restrictions may also be put into place because of crop safety issues such as phytotoxicity, which may be totally unrelated to rotational crop concerns.
11. **Maximum seasonal application rate:** the total amount (e.g. g, kg, lb, oz) of a pesticide active ingredient per unit area (e.g. acre, hectare) allowed on a crop during a crop season on the pesticide product label.
12. **Maximum Residue Limit (MRL):** the upper legal or permissible levels of the concentration of pesticide residues expressed as mg/kg food/feed in or on food or feed based on good agricultural practices or in livestock commodities following consumption of pesticide treated feed.
13. **Negligible residues:** less than LOQ (typically <0.01 mg/kg).
14. **Permanent crops:** Crops that are harvested for several seasons or years and do not need to be replanted/replaced after each harvest (e.g. citrus, coffee, grapes, pome fruits, tree nuts).
15. **Persistence:** the length of time a chemical can exist in the environment before being transformed or degraded by natural processes.
16. **Plant-back interval (PBI):** The interval (days, months, years) between the final application of a pesticide product to a primary crop and the planting of a rotational crop.

17. **Primary crops:** Crops listed on pesticide product labels intended for protection against specific pests (insects, fungi, weeds, etc.) by direct treatment (soil, foliar, seed treatment, etc.) with the pesticide.
18. **Proportionality concept**: assumption of a proportional relationship between pesticide application rate and resulting residues on the harvested commodity, allowing proportional adjustment (or "scaling") of residues from field trials with higher or lower application rates.
19. **Protected/glasshouse/greenhouse uses:** label uses of a pesticide product on crops grown in protected/glasshouse/greenhouse.
20. **Residue definition:** definition of residue (DoR); pesticide residues (active ingredient and/or metabolites) that may be found in crop/livestock commodities following label/legal uses and considered to be relevant for data gathering, risk assessment, or enforcement of maximum residue limits.
21. **Rotational crops:** crops planted following the harvest or destruction of primary crops treated with a pesticide.
22. **Semi-permanent crops:** primary crops (e.g. alfalfa, asparagus, strawberry, sugarcane) that are replanted or replaced biennially or at longer intervals.
23. **Soil residue plateau level:** the steady state carry-over residue concentration in soil after multiple years of applications, measured prior to the next application.
24. **Super crop group:** expanded crop group for the selection of representative crops for Tier 3 testing and setting of MRLs.
25. **Triazole Derivative Metabolite (TDM):** Triazole-based metabolites (1,2,4-triazole, triazolylalanine, triazolylacetic acid, and triazole lactic acid) formed primarily from pesticides from the azole class of chemistry.

ANNEX II. SUMMARY OF RESULTS OF THE OECD SURVEY ON ROTATIONAL CROPS (FULL SURVEY TO BE AVAILABLE FROM OECD)

Table 4: Overview of survey results

Survey Question (shortened)	General Theme of Responses
QUESTION #1A-D: Are there pesticides registered in your country that have the potential to have carryover of residues into rotational crops? Are such pesticides approved for use for a range of crops? Are there any label restrictions that limit their use to certain cropping situations? During the course of the assessments for those pesticides, did you require (additional) data related to residues in rotational crops? Did you require any additional monitoring data for soil and/or crops after approval or registration was granted? What specific data were requested?	– Most countries did have such pesticides registered for a range of crops. – There is a selection of non-restricted use, label restrictions, MRL setting examples. – Most countries required the Confined Crop study and the limited field trials. Case-by-case additional field rotational and soil accumulation studies were also requested. – Monitoring data for soil and/or crops were rarely requested.
QUESTION#2 Does your country have a listing or common understanding of primary crops and the corresponding crops that are typically grown in rotation with them?	– Only the US has documentation on crops typically grown in rotation with primary crops. Further information may be available on a regional level in some countries.
QUESTION#3A-C What data are required to support a registration of a pesticide for use on permanent or semi-permanent crops? What additional data are required if a pesticide is initially registered for use on permanent or semi-permanent cropping situations and then is extended to other non-permanent cropping situations? Has your national/regional authority encountered issues with a) residues on permanent crop commodities one or more years after a pesticide use has been discontinued or b) on non-permanent crops planted subsequent to the destruction of a permanent or semi-permanent crop?	– For uses on permanent and semi-permanent crops supervised crop field trials and all kinds of core data are required, but no rotational crop studies. – If initial registrations on (semi-) permanent crops are extended to non-permanent crops, a full data package including rotational crop studies is required. – No uniform list of permanent and semi-permanent crops is currently available and should be provided. (Note: a non-exhaustive list of permanent and semi-permanent crops is provided in OECD 502 and 504) – A couple of issues with residues in permanent crops as described in a) or b) has been reported.
QUESTION #4: How does your national regulatory authority estimate the concentration of residues in soil available for uptake by a rotational crop? Is only the total annual	– Some countries rely on the maximum annual rate, while others use the plateau concentration.

Survey Question (shortened)	**General Theme of Responses**
treatment rate of the primary crop considered? Are plateau soil residues considered? Are rotational scenarios based on real agronomical practices over several years with different treated crops considered? Have you implemented label restrictions to cover such aspects?	– USA has rotational crop incorporated into accumulation studies. Need to consult with industry e-fate experts focused on European models and requirements.
QUESTION #5: How does your regulatory authority handle metabolites common to multiple active ingredients, such as TDMs (triazole derivative metabolites), which mainly occur in rotational crops? How are they considered in risk assessment and MRL setting?	– Most countries are not in favour of incorporating such metabolites into residue definitions for monitoring. – For TDMs separate MRLs might be set in future based on cumulative assessments.
QUESTION #6: Are rotational crop residues considered when a pesticide is registered for use in glasshouse/protected environments where plant back intervals can be very short?	– Some countries consider rotational crop residues as not relevant for greenhouse uses, others do, especially in view of cultivation on natural soil and short cropping intervals.
QUESTION #7: Are separate tolerances/MRLs established for rotational crops, or are the expected residues in the rotational crops covered by tolerances/MRLs established for specific primary crops or for crop groups?	– Most countries have only one type of MRL covering both residues from primary uses and residues remaining after crop rotation. The US has separate MRLs (inadvertent residues) set for rotational crops. – Consistent guidance is needed when and how to set MRLs for inadvertent residues in general terms.
QUESTION #8: In considering import tolerance/MRL situations, does your national regulatory authority also consider possible residues in rotational crops from the exporting country? Are import tolerances granted only for the specific primary crop commodities applied for per active ingredient or will potential residues in succeeding crops from the primary crop use also be taken into consideration (with extension of the import tolerances to those commodities)?	– Normally residues in rotational crops are not considered in the context of granting import tolerances.
QUESTION #9: If rotational crop tolerances/MRLs are established by your national regulatory authority, are they put in place for the purpose of compliance/enforcement, to facilitate international trade, or both?	– Usually for both purposes.
QUESTION #10: What types of information about rotational crops does your national regulatory authority include on registered labels?	– Types of crops are indicated, which may (or may not) be planted in rotation. – Further label restrictions refer to the max number of applications per year or prescribe min plant-back intervals. – Consistent guidance is needed when to set label restrictions and when better to set MRLs.

Survey Question (shortened)	**General Theme of Responses**
QUESTION #11A-B: Are the existing OECD test guidelines (TG 502 and 504) adequate in terms of describing situations where pesticides are known to be very persistent in soils for periods greater than about 1 year, and where residues are known to be taken up by rotational crops? If not, how could those test guidelines be improved? The current OECD confined and limited rotational crop field trial studies are conducted on representative commodities of each of the following crop groupings: root and tuber vegetable, leafy vegetable, and cereal grain or oilseed. How are rotational crops not represented by these crop types handled? Should the current representative crop types tested be expanded? Are there particular factors that must be considered when determining which type of crop will be rotated?	– Soil analysis is recommended. – Clear definition of persistence is needed, as well as guidance on how to handle potentially long living compounds being used year after year (prolonging the study period vs. basing the study on plateau levels). – Guidance on the selection of crops and number of trials for field rotational crop studies and/or MRL setting is needed. – Guidance is required on how to account for metabolites. – Crop groups which are not covered by rotational crop studies are handled by extrapolation of available data. Expansion of current representative commodities is suggested.
Question #12: Are there additional aspects of rotational crops that should be considered for guideline/guidance development?	– All relevant issues mentioned above.

ANNEX III. EXAMPLES OF REGULATORY REQUIREMENTS TO SUPPORT ROTATIONAL CROP USES

Note: All cases were handled before the present guidance document was available.

Case 1: Boscalid

Estimation of boscalid residues in soil

Boscalid is used in a broad variety of crops at various annual application rates. For the estimation of the highest boscalid levels in soil relevant for the evaluation of residues in follow crops, it must be assumed that boscalid is applied for several consecutive years due to the broad use pattern. Under consideration of the annual application rates for non-permanent crops and the DT_{50} values obtained from aerobic soil degradation and field dissipation studies, a 1st order kinetic model can be used to estimate the boscalid plateau reached in soil. Annual application rates of boscalid on non-permanent crops are normally in the magnitude of 0.9 to 1.2 kg ai/ha per year (see GAP list in JMPR Evaluation 2006). The only uses involving higher application rates are reported from the US for bulb vegetables with 1.9 kg ai/ha per year (6 × 0.32 kg ai/ha) and various uses from Japan at the maximum rate of 4.5 kg ai/ha per year (up to 3 × 1.5 kg ai/ha). Concerning the rate of degradation, DT_{50} values were determined for up to 208 days in field dissipation studies. Under laboratory conditions most DT_{50} values were in the magnitude of 1 year (365 days), while in aged soil receiving several consecutive applications the DT_{50} values were determined at up to 746 days.
Under consideration of these input parameters, the plateau levels of boscalid equivalent to an application rate to bare soil after consecutive applications over several years can be estimated (1st order kinetics assumed):

Figure 3: Accumulation of boscalid in soil – DT_{50} = 208 days

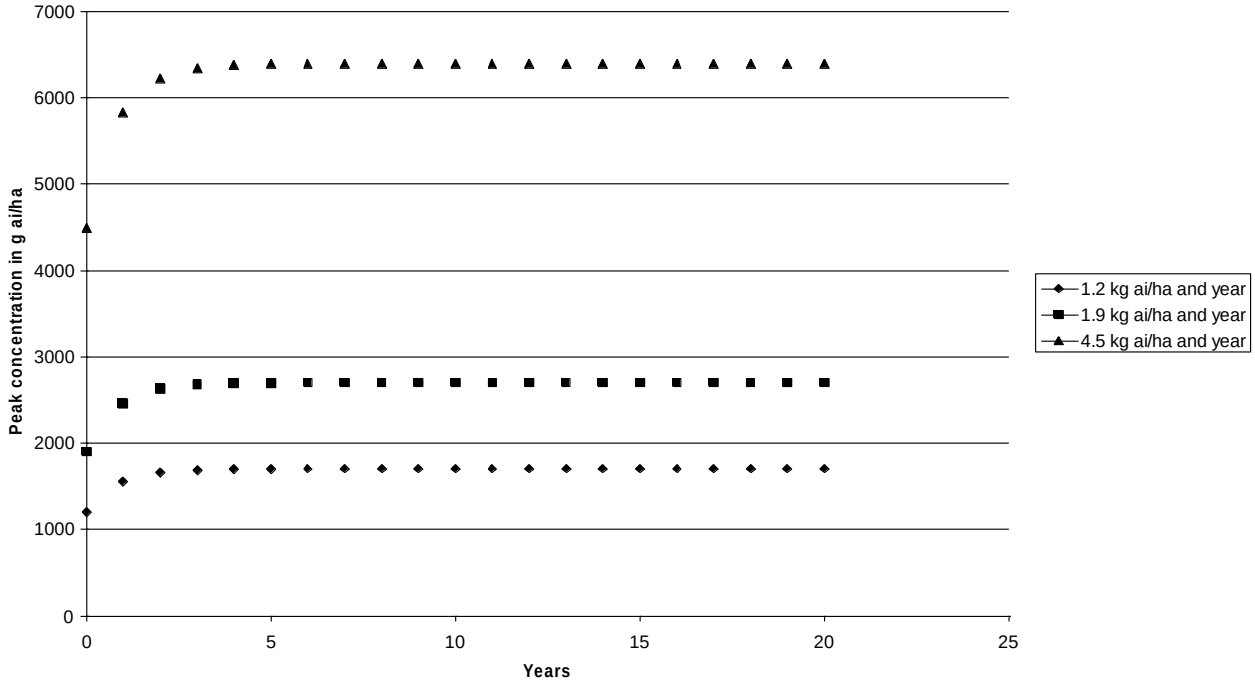


Figure 4: Accumulation of boscalid in soil – DT_{50} = 365 days

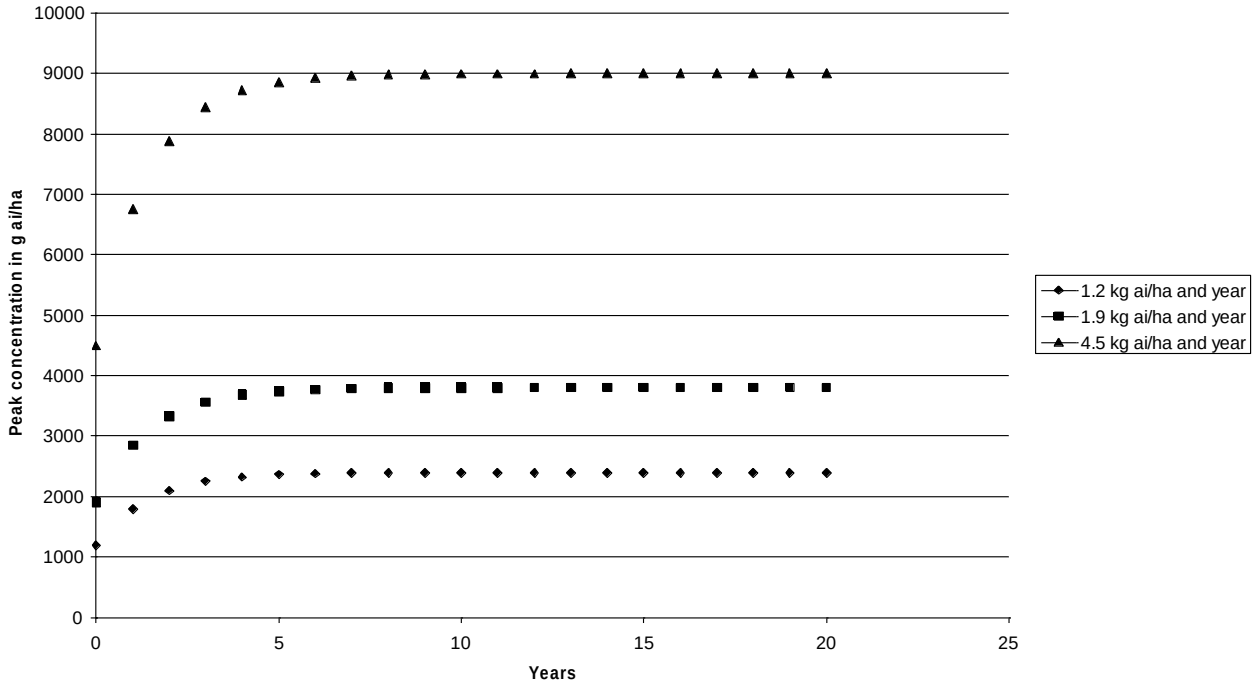
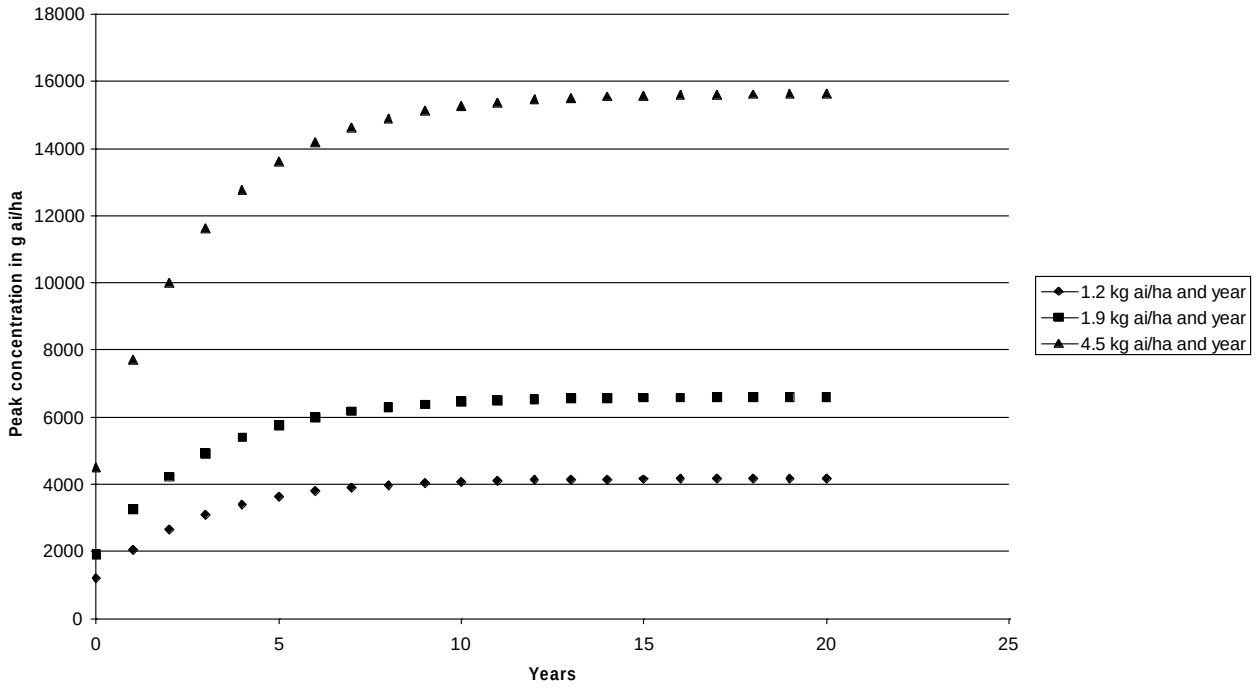


Figure 5: Accumulation of boscalid in soil – DT_{50} = 746 days



The results for the estimation are dependent on the DT_{50} values for boscalid in soil. For a DT_{50} value of 208 days estimated in field dissipation studies, the plateau is reached after five annual applications of boscalid. Plateau levels were equivalent to an application rate of 1.7 kg ai/ha to bare soil for a treatment using 1.2 kg ai/ha per year, 2.7 kg ai/ha for 1.9 kg ai/ha per year and 6.4 kg ai/ha for 4.5 kg ai/ha per year, respectively.

Under the assumption of a DT_{50} value of 1 year (365 days) mainly found in aerobic soil metabolism and dissipation studies on soil treated for the first time plateau levels equivalent to an application rate to bare soil were estimated at 2.4 kg ai/ha for a treatment rate of 1.2 kg ai/ha per year, 3.8 kg ai/ha for 1.9 kg ai/ha per year and 9 kg/ha for 4.5 kg ai/ha per year.
The highest DT_{50} value for boscalid was found in aged soil under laboratory conditions with a half-live time of 746 days. The resulting plateau levels equivalent to application rates to bare soil were 4.1 kg ai/ha following treatment at 1.2 kg ai/ha per year, 6.6 kg ai/ha for 1.9 kg ai/ha per year and 15.6 kg ai/ha after treatment at 4.5 kg ai/ha per year. The Meeting noted that boscalid shows a reduced uptake into plants from soil (52.8% on average) when applied for several consecutive years. Since the plateau in soil is reached after 5 years at a minimum, the Meeting decided to apply an additional factor of 0.5 to the plateau concentration reflecting the reduced uptake of residues from aged soil. Field trials on succeeding crops were normally conducted using unaged soils resulting in higher residues potentially available for an uptake via the roots of the plants. The following table shows the derivation of the predicted plateau levels for boscalid residues in soil after the GAP application rates.

Table 5: Derivation of the predicted plateau levels for boscalid residues in soil

Application rate	Assumed DT_{50} value in days	Predicted plateau level equivalent to an application to bare soil	Adjusted plateau level equivalent to an application to bare soil available for uptake from aged soil (factor 0.5)
1.2 kg ai/ha and year	208	1.7 kg ai/ha	0.85 kg ai/ha
	365	2.4 kg ai/ha	1.2 kg ai/ha
	746	4.1 kg ai/ha	2.05 kg ai/ha
1.9 kg ai/ha and year	208	2.7 kg ai/ha	1.35 kg ai/ha
	365	3.8 kg ai/ha	1.9 kg ai/ha
	746	6.6 kg ai/ha	3.3 kg ai/ha
4.5 kg ai/ha and year	208	6.4 kg ai/ha	3.2 kg ai/ha
	365	9 kg ai/ha	4.5 kg ai/ha
	746	15.6 kg ai/ha	7.8 kg ai/ha

The JMPR noted that most of the GAPs globally reported involve an annual application rate of 1.2 kg ai/ha or less. Even under assumption of the most critical DT_{50} value of 746 days the level of boscalid available for an uptake into plants is at, or below, the dose range of the field trial data submitted for succeeding crops. Under the assumption of the DT_{50} value of 208 days or the DT_{50} value of 365 days, the next higher GAP from the US on bulb vegetables using 1.9 kg ai/ha still results in a plateau within the treatment range of the field studies on succeeding crops. The national GAPs involving up to 4.5 kg ai/ha per year may lead to a predicted plateau of at least 50% above the application rate of the field trial on succeeding crops submitted. The JMPR decided that the field trial data submitted on succeeding crops represents the maximum residues in soil available for an uptake via the roots for all GAPs submitted, except for GAPs using more than 1.9 kg ai/ha per year. These results are also confirmed by field accumulation studies over eleven years, leading to plateau residue levels equivalent to an application rate to bare soil between 2 and 3 kg ai/ha. For the estimation of boscalid residues in commodities obtained from follow crops, the results from the field trial data on succeeding crops may be taken into account without further adjustment.

In Australia, expansion of the registration of boscalid in rotational systems was originally withheld owing to concerns of potentially unacceptable residues occurring in animals grazing areas where previous crops had been treated with boscalid. This was particularly a concern for trade in animal commodities, as standards had not been established in some international markets and regulatory or existing industry systems were not able to manage the risks associated with residues in animal commodities arising from the

use of boscalid in rotational systems. Time limited approvals were allowed (APVMA Permits) and an "all other foods" MRL was established to allow use in rotational systems under strict controls while additional data was generated internationally and in Australia to allow refinement of the risk analysis. Those controls included a registrant/ manufacturer developed stewardship program to ensure that crops producing animal feeds were not grown in close rotation with treated crops. The additional data included: the previously discussed information on bioavailability of aged residues and an additional animal feeding study; finalised soil accumulation studies from the northern hemisphere; field rotational residues studies conducted in New Zealand where residues in pasture were determined following treatment of preceding horticultural crops; and residues data for forage of various crops grown after commercially treated horticultural crops in Australia. That data were considered along with the soil degradation data from the environment package and allowed refinement of the risk assessment. Registration in rotational crops was subsequently approved with removal of related restrictions on use other than labelled restrictions on maximum annual application rates. The inclusion of maximum annual application rate restrictions on labels is not common in Australia and provides regulatory challenges as the instructions must relate to the active ingredient and be practicable and enforceable across all products regardless of manufacturer.

Case 2: Ametoctradin (as an example for the use of proportionality for rotational crop MRL assessment)

Limited field rotational crop studies were available from Europe and the USA. In Europe (Germany, The Netherlands, Southern France and Italy), soil was treated once with ametoctradin at a rate of 960 g ai/ha. Wheat, carrots, cauliflower and lettuce were grown at plant back intervals (PBIs) of 30, 120 and 365 days. Residues of parent were not observed (LOQ of 0.01 mg/kg) in carrots, lettuce, wheat grain or wheat forage at any PBI. At one site, residues of parent were observed at 0.04 mg/kg in wheat straw, and at one site, residues of parent were observed in cauliflower inflorescence at 0.02 mg/kg, both following a PBI of 30 days. Residues of parent were not observed in wheat straw or cauliflower inflorescence at other sites or at other PBIs.
In the United States (Georgia and California), soil was treated with three applications of ametoctradin at a rate of 300 g ai/ha. Radish, lettuce and wheat, were grown at PBIs of 30, 60, 90 and 120 days. Residues of parent were not observed at either site at any PBI (LOQ of 0.01 mg/kg).

Residues of ametoctradin of potential rotational significance were identified in limited field rotational studies conducted in the EU. The application rate to bare soil in the field rotational studies was approximately 10× that of the annual application rate proposed for Australia, which was to consist of up to 4 individual applications (minimum of 7-day intervals with a maximum of 2 consecutive sprays). Applying the proportionality principle, residues in wheat straw and cauliflower grown 30 days after application would be expected to approximate 0.004 mg/kg and 0.002 mg/kg, respectively. It was considered that label restrictions were not needed for this use and were unlikely to be needed for similar use patterns in rotational situations. This assessment was conducted prior to the agreement on the rate range for applying the proportionality principle of 0.3× to 4× specified in the *Crop Field Trial Guidance Document* (5). Scaling to 0.3× (noting the 0.1× rate differential) would estimate residues of 0.012 mg/kg in wheat straw and 0.006 mg/kg in cauliflower. The initial consideration is considered to be robust as the proportionality relationship for soil treatments is reported to be strong (Ratio of rate versus residue of 0.88, CI of 0.78-0.98 in simulations of the US EPA as reported in the *Crop Field Trials Guidance Document* (5)).

Case 3: 2,6-dichlorobenzamide, arising in rotational crops from the application of dichlobenil and fluopicolide (JMPR Report 2014, Dichlobenil)

For dichlobenil the 2014 JMPR concluded that 2,6-dichlorobenzamide is the only relevant residue in plant matrices and proposed a corresponding residue definition (for MRL setting and dietary intake purposes in plant and animal commodities). However, the Meeting also recognized that 2,6-dichlorobenzamide may also be formed after application of fluopicolide and therefore the proposed maximum residue levels have to accommodate for both sources. As an example for the simultaneous consideration of common metabolites from different sources, the JMPR assessment for brassica vegetables is presented:

In the data set for head cabbage (with wrapper leaves) used by the 2009 Meeting for fluopicolide MRL estimation and dietary risk assessment, residues of 2,6-dichlorobenzamide were < 0.01 (6), and 0.02 mg/kg. Residues of 2,6-dichlorobenzamide in Brussels sprouts arising from use of fluopicolide were < 0.01 (8) mg/kg. In the USA data set for broccoli used by the 2009 Meeting for MRL estimation and dietary risk assessment for Flowerhead brassicas, residues were < 0.01 (6) mg/kg.

The Meeting noted that 2,6-dichlorobenzamide residues of < 0.01 (6), 0.02, and 0.04 mg/kg were found in head cabbage grown as a rotational crop.

The Meeting agreed to combine the head cabbage dataset for 2,6-dichlorobenzamide residues resulting from in-crop use of fluopicolide with the dataset for residues of 2,6-dichlorobenzamide in head cabbage resulting from use of fluopicolide in a preceding crop:
< 0.01 (12), 0.02 (2), and 0.04 mg/kg

Recognizing that residues of 2,6-dichlorobenzamide could occur in brassica vegetables other than cabbage grown in rotation with a crop treated with fluopicolide, the Meeting decided to estimate a group maximum residue level of 0.05 mg/kg, together with an STMR of 0.01 mg/kg and an HR of 0.04 mg/kg, based on the combined head cabbage dataset.

Case 4: Flutriafol (Example of a Pesticide Registered in the USA with Residues in Rotational Crops)

The petitioner initially requested application of flutriafol fungicide to soybean and apple and submitted confined and limited field rotational crop studies. Although the rotational crop data were found to be unacceptable (confined and field), these data combined with the soil metabolism data (long half-life) indicated that residues in rotational crops were likely. Despite the lack of acceptable rotational crop data, the Health Effects Division of US-EPA (HED) concluded that sufficient information was available to recommend for the petition provided the label was revised to restrict rotation to only soybean (D340513). Subsequent to this decision, the petitioner submitted an adequate confined rotational crop study and adequate field corn, sweet corn, and cotton field rotational crop studies (extensive field rotational crop trials [i.e. numbers/locations as required for a primary crop]; 180-day PBI). Based on these data, it was concluded that the label may be revised to indicate the following rotational crop restrictions (corn and cotton tolerances were established; D380493): treated fields may be rotated to a labelled crop at any time or may be rotated to cotton or corn (sweet, field, pop) 180 days after application; rotation to any other crop is prohibited.

The petitioner then requested registration for application to several permanent crops (stone fruit, grapes) and field corn, popcorn, sugar beet, and peanut (D388603 and D391039). Based on the proposed field corn, popcorn, and sugar beet application rates, HED concluded that the available rotational crop data were sufficient and the above rotational crop restrictions were applicable to these crops (with removal of the 180-day PBI for field corn and popcorn as these would now be primary crops). Since the field rotational crop data employed a rate 0.5x the peanut rate, HED concluded that only a labelled crop may be rotated following application of flutriafol to peanut. Residue values from rotational field trials with sweet corn (n=12) and cotton (n=12) were used as input to the OECD MRL calculator (Table 6; values for sweet corn kernel plus cob with husk removed and cotton seed were all <0.01 mg/kg).

Table 6. OECD MRL Calculator Entries to Determine Tolerances (MRLs) for inadvertent residues of Flutriafol in sweet corn and cotton commodities.

Compound	Flutriafol	Flutriafol	Flutriafol
Crop	Sweet Corn Forage	Sweet Corn Stover	Cotton Gin Byprod.
Region / Country	US	US	US
GAP	Rot. Crop: 0.228 lb ai/A	Rot. Crop: 0.228 lb ai/A	Rot. Crop: 0.228 lb ai/A
Total number of data (n)	12	12	12
Percentage of censored data	75%	50%	92%
Number of non-censored data	3	6	1
Lowest residue	0.010	0.010	0.010
Highest residue	0.030	0.035	0.028
Median residue	0.010	0.012	0.010
Mean	0.012	0.015	0.012
Standard deviation (SD)	0.006	0.008	0.005
Correction factor for censoring (CF)	0.500	0.667	0.389
Proposed MRL estimate			
- Highest residue	0.030	0.035	0.028
- Mean + 4 SD	0.035	0.045	0.032
- CF x 3 Mean	0.018	0.030	0.013
Unrounded MRL	0.035	0.045	0.032
Rounded MRL	**0.04**	**0.05**	**0.04**
	High uncertainty of MRL estimate due to high level of censoring.		High uncertainty of MRL estimate due to high level of censoring.

Residues (mg/kg)		Residues (mg/kg)		Residues (mg/kg)	
0.010	*	0.010	*	0.010	*
0.010	*	0.010	*	0.010	*
0.010	*	0.010	*	0.010	*
0.010	*	0.010	*	0.010	*
0.010	*	0.010	*	0.010	*
0.010	*	0.010	*	0.010	*
0.010	*	0.013		0.010	*
0.010	*	0.015		0.010	*
0.010	*	0.019		0.010	*
0.012		0.020		0.010	*
0.015		0.020		0.010	*
0.030		0.035		0.028	

Case 5: Chloridazon (as an example for the use of the tiered approach and the setting of MRLs for rotational crops in the EU)

Chloridazon is applied pre- and early post- emergence in the EU in sugar and fodder beets, beet roots, chard (1x 2.6 kg ai/ha), onions (1x 2.6 kg ai/ha), shallots, garlic (1x 0.91 kg ai/ha), horseradish (1.3 kg ai/ha), leaves and sprouts of brassica, fresh herbs (1x 0.98 kg ai/ha) and spinach (1x 2.6 kg ai/ha). The substance and its main metabolite have a clear potential to be transferred to succeeding crops and the occurring residues need to be accounted for by appropriate risk mitigation measures or MRLs. EFSA published a Reasoned Opinion (EFSA Journal 2015;13(9):4226; doi:10.2903/j.efsa.2015.4226) on the review of existing MRLs for chloridazon according to Art. 12.1 of Reg. (EC) No 396/2005 and proposed MRLs which cover both primary and RC residues. As the enforcement residue definition EFSA proposed the sum of chloridazon and its metabolite B, expressed as chloridazon. EFSA's Reasoned Opinion and the underlying RC data for chloridazon are used to elaborate an example for the tiered RC risk assessment, the scaling of RC residue data and the mitigation of residue levels in rotational crops by MRL setting.

Appropriate application rate for RC studies

Normally it is recommended to derive the application rate from the plateau background residue level plus an additional seasonal application rate to address soil residues available after treated primary crop failure and immediate replanting of rotational crops.
As chloridazon uses in the EU are restricted to uses with a maximum application rate of 2.6 kg ai/ha only every third year on the same field (Dir 2008/41/EC of 31 March 2008), which is due to a groundwater and not a rotational crop issue, the minimum interval between two consecutive treatments is 3 years and it is sufficient to conduct RC studies with the maximum seasonal rate for a primary rotatable crop and plateau background residue levels do not need to be added in this case.

Application to bare soil

The application to bare soil in RC studies is considered appropriate as a worst case. Besides, the authorised GAPs for chloridazon in the EU are soil or early post-emergence applications. Interception of residues by the primary crop is negligible.

Tier 1: Confined RC study

The residue levels and the nature of the residues were investigated in a confined rotational crop study in three different succeeding crop groups following application of ca. 3.4 kg ^{14}C-chloridazon per hectare to bare soil:

- Small grain cereals: sorghum, wheat, oats
- root and tuber vegetables: sugar beet; turnip and radish
- leafy vegetables: chard

The investigations were performed under field and greenhouse conditions. The results indicated a clear potential for residues occurring in all investigated plant parts of succeeding crops at all investigated plant-back intervals (1 month, 3-4 months, 1 year). As in primary crops, the major constituents of the residue were the parent compound and the metabolite B (desphenyl-chloridazon), which is formed by microbial degradation in soil. In most cases metabolite B was present at a clearly higher level than chloridazon and was mainly present as free form.

Conclusion from Tier 1: Residues occur in edible or feed-relevant plant parts and there is a need to proceed to Tier 2.

Tier 2: Limited field RC studies

US studies
Six field rotational crop trials were run in the US with a tested rate of 8.52 kg ai/ha (6.73 + 1.79 kg ai/ha, interval 3 weeks, application to bare ground). After a plant-back interval of 360 days spring wheat was planted at two sites in North Dakota, leaf lettuce at two sites in California and potatoes at two sites in Michigan. Two replicates of each matrix from each site were analyzed for chloridazon and its desphenyl metabolite. Results were expressed in terms of total residues of chloridazon.
EFSA did not consider these trials due to the overdosing factor of 3.3 compared to the critical authorised GAPs in the EU. As detailed in paragraph 29 of the present GD, scaling of residues is considered appropriate in RC studies within the limitations described in the GD on Crop Field Trials. According to the revised version of this CFT GD the proportionality concept can be applied to data from field trials conducted within a rate range of between 0.3x and 4x the GAP rate and thus is applicable in this case.

Table 7: Overview of the residues data from the field RC study conducted in the US

Crop/ Matrix	Days application to harvest	Site	Residues of chloridazon+ metabolite B, expressed as chloridazon (mg/kg)	Scaled residues of chloridazon+ metabolite B, expressed as chloridazon (mg/kg)
Leafy vegetables				
Lettuce	409	Site 1	0.293; 0.299	0.089; 0.091
	434	Site 2	<0.10; <0.10	<0.03; <0.03
Root and tuber vegetables				
Potato	495	Site 1	<0.10; 0.111	<0.03; 0.034
	495	Site 2	<0.10; <0.10	<0.03; <0.03
Small grain cereals				
Wheat forage	384	Site 1	0.149; 0.184	0.045; 0.056
	386	Site 2	<0.10; 0.141	<0.03; 0.043
Wheat hay	424	Site 1	0.117; 0.140	0.035; 0.042
	424	Site 2	<0.10; <0.10	<0.03; <0.03
Wheat grain	468	Site 1	<0.10; <0.10	<0.03; <0.03
	468	Site 2	<0.10; <0.10	<0.03; <0.03
Wheat straw	468	Site 1	<0.10; <0.10	<0.03; <0.03
	468	Site 2	<0.10; <0.10	<0.03; <0.03

European studies
Two European field studies on the magnitude of residues in rotational crops were available, reflecting the current maximum application rate of 2.6 kg ai/ha, applied to bare soil. The first study was conducted in Germany, Denmark and the UK and focuses on the replant interval of 30 days while the second one was conducted in Germany, Italy, The Netherlands and Spain and covers the replant intervals of 120 and 365 days. Residues analyses were performed either for the enforcement residue definition "sum of chloridazon and its metabolite B, expressed as chloridazon" (PBI of 30 DAT) or for the risk assessment residue

definition "sum of chloridazon, its metabolite B, and their conjugates, expressed as chloridazon" (PBI of 120 and 365 DAT), but never for both simultaneously. Nevertheless, according to the confined rotational crops studies, the major constituents of the residue are the free parent compound and the free soil metabolite B. Therefore, it is assumed that residue data for plant-back intervals of 120 and 365 DAT do not overestimate the STMR and HR based on the enforcement residue definition and can be used to calculate MRLs. Representative crops for leafy vegetables (spinach, lettuce, and cauliflower), roots vegetables (carrots) and cereals (wheat) were planted/sown on aged soils. At harvest, crop samples were analysed for chloridazon and metabolite B in the first study, or for total residues corresponding to the risk assessment residue definition (sum of chloridazon, its metabolite B and their conjugates, expressed as chloridazon) in the second study. An overview of the results is reported in Table 8.

Table 8: Overview of the residue data from the European RC field trials

Data on	DAT (days)	Residue levels referring to chloridazon plus metabolite B, expressed as chloridazon[#] (mg/kg)
Leafy vegetables		
Spinach	30	0.14; 0.81; 0.92; 2.47
	120	0.17; 0.33; 0.37; 0.95
	365	0.10; 0.13; 0.20; 0.63
Lettuce	30	-
	120	0.07; 0.14; 0.18; 0.20
	365	0.05; 0.05; 0.14; 0.25
Brassica vegetables		
Cauliflower	30	4 x <0.1
	120	0.03; 0.03; 0.04; 0.04
	365	2 x <0.025; 0.03; 0.03
Root and tuber vegetables		
Carrots roots	30	4 x <0.1
	120	0.03; 0.03; 0.03; 0.05
	365	0.03; 0.03; 0.04; 0.04
Small grain cereals		
Wheat forage*	30	0.19; 0.71; 0.79; 1.38
	120	-
	365	-
Wheat grain	30	4 x <0.1
	120	-
	365	-
Wheat straw	30	0.08; 0.17; 0.45; 1.03
	120	-

Data on	DAT (days)	Residue levels referring to chloridazon plus metabolite B, expressed as chloridazon[#] (mg/kg)
	365	-

*sampled at BBCH 30-33 and BBCH 61-65, the higher value was selected
this residue definition applies to the 30day-PBI samples, while for the 120 day and 365 day-PBI samples additionally conjugates of both substances contribute to the reported residue (presumably negligible contribution, see text)

Conclusion from Tier 2:
Brassica vegetables were added as a further crop group. Residues occur in edible or feed-relevant plant parts, mainly in wheat straw, spinach and lettuce. There is a need to proceed to Tier 3 or take risk management actions (MRL setting, label restriction).

Tier 3 Extended Field Studies/Risk management actions

Tier 2 study results give a clear indication of a potential residue uptake in leafy crops and cereals straw, which is significant even with a PBI of 365 DAT. Therefore, it is not possible to propose a risk mitigation measure such as a certain plant back interval, which is sufficiently protective to avoid residues uptake in these crops.

The option of choice is to consider rotational crop residues in MRL setting for chloridazon. As outlined in paragraph 66, results obtained at a PBI of 30 days are considered most appropriate for MRL setting. This interval represents the worst case with respect to chloridazon residue levels and no further label restriction such as a minimum replanting interval will be required together with MRL setting. Since in the US studies the PBI of 30 days was not investigated, these studies were not considered further.

Additional field studies for crops not yet investigated in field rotational crop studies in Tier 2 were not provided. Available data for chloridazon are sorted by "super" crop groups and subgroups as proposed in Table 3 in the following table.

Table 9: Overview of available field RC studies for a PBI of 30 days

"Super" crop group	**Crops proposed for Tier 3 field studies**	**Number of available trials (PBI 30 days)**	**Remarks**
Root and tubers	1. carrots or radishes or beets	4	Note: Potato trials would not be required, as no dietary risk was seen for MRLs when extrapolated from carrots or sugar beets (primary crop use) to potatoes
	2. potatoes (optional)	--	
Bulb and stem vegetables	1. leek or celery	--	Note: according to the present Guidance Document 4 trials would have been required
Small grain cereals	1.wheat or barley	4	Note: according to the present Guidance Document 8 trials would have been required each for wheat or barley and for maize.
	2. maize	--	
Leafy vegetables, brassica vegetables	1. lettuce or spinach	4	Note: according to the present Guidance Document further 4 trials would have been required for head cabbage or kale.
	2. head cabbage or kale	--	
	3. broccoli or cauliflower	4	

"Super" crop group	**Crops proposed for Tier 3 field studies**	**Number of available trials (PBI 30 days)**	**Remarks**
Oilseeds, Pulses	1. oilseed rape or soybeans	--	Note: according to the present Guidance Document 8 trials on oilseed rape and 4 trials on pulses would have been required.
	2. dried beans or peas	--	
Fruits, Fruiting vegetables	1. strawberry	--	Note: according to the present Guidance Document 4 trial would have been required each on strawberry and cucumber.
	2. cucumber	--	

Conclusions by EFSA:

EFSA assessed the impact of proposing a minimum plant-back interval of 30 DAT (option 1), 120 DAT (option 2) or 365 DAT (option 3). If the uptake of residues from rotational crops exceeds the MRL derived from primary treatment, EFSA proposes to raise the MRL based on the rotational crops data. On the opposite, if the uptake of residues is inferior to the MRL derived from primary crop treatment, EFSA keeps the MRL proposal derived from the primary treatment. For all crops that may be grown in rotation but for which GAPs are not authorised, the need for an MRL proposal was estimated on the basis of the results of the rotational crops data.

As for food crops, residues remaining from previous treatments also have to be considered in feed crops when calculating the dietary burden. The decision if primary or rotational crop residues are considered to dominate the residues in the respective feed crops follows the same lines as for food crops. The level of residues in feed crops and the overall dietary burden is determined and compared to the results of livestock feeding studies. On this basis, MRL proposals for animal commodities are derived.

The following decisions were taken by the EU Commission, based on proposals by EFSA:

- Option 1 (30 day PBI) was selected.
- For root, tuber and bulb vegetables MRLs were based on primary crop residues except for those without authorized uses which were based on rotated carrot data.
- For brassica vegetables MRLs were based on rotated cauliflower data. For the super crop group leafy and brassica vegetables 4 data were available on spinach and 4 on cauliflower which clearly belong to two very different residue populations and therefore different MRL proposals were derived for the subgroups.
- For all leafy and stem vegetables as well as spices and herbal infusions obtained from aerial plant parts MRLs were based on rotated spinach data.
- For cereals MRLs were based on rotated wheat data.
- For fruits, fruiting vegetables, pulses and oilseeds no conclusion could be drawn and all MRLs were kept at LOQ level.
- A couple of MRLs was flagged as tentative because EFSA considered further 4 trials on rotated spinach necessary and identified some other data gaps.