REPORT OF PESTICIDES PEER REVIEW TC 128

Bensulfuron methyl – AIR IV

Rapporteur Member State: IT

3. Residues

Date: 31 January 2024

List of participants:

Status	**Name of institution/attendee**
EFSA statutory staff member	EFSA
National Experts nominated by MS Austria	Austrian Agency for Health and Food Safety (AGES) - AT
National Experts nominated by MS Germany	Federal Environment Agency (UBA) - DE
National Experts nominated by MS France	Agence nationale de sécurité sanitaire de l'alimentation, de l'environnement et du travail (ANSES) - FR
National Experts nominated by RMS Italy	International Centre for Pesticides and Health Risk Prevention (ICPS) - IT
National Experts nominated by MS Netherlands	Board for the Authorisation of Plant Protection Products and Biocides (Ctgb) – NL

In accordance with EFSA's Policy on Independence[1] and the Decision of the Executive Director on Competing Interest Management[2,] EFSA screened the Annual Declarations of Interest filled out by the participants invited to the present meeting. No Conflicts of Interest related to the issues discussed in this meeting have been identified during the screening process, and no interests were declared orally by the members at the beginning of this meeting.

[1] http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/policy_independence.pdf

[2] http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/competing_interest_management_17.pdf

Discussion points/Outcome

3. Residues

Please note that information part of this report may have been masked by EFSA in accordance with Article 63 of Regulation (EC) No 1107/2009 as well as EFSA's Practical Arrangements concerning confidentiality in accordance with Articles 7 and 16 of Regulation (EC) No 1107/2009, or EFSA's Practical Arrangements concerning transparency and confidentiality as a consequence of confidentiality requests submitted by the applicant on application dossiers for pesticides active substances or Maximum Residue Levels, respectively. Please note that information disclosed in this report is without prejudice to pre-existing intellectual property rights and data exclusivity clauses set out in Union law, and particularly in Article 62 of Regulation (EC) No 1107/2009.

Minutes might be revised due to pending data gaps at the time of the meeting and /or eventual need for further follow up consultation after the meeting. If needed, the final agreement will be made available in the meeting report published at the end of the peer review process.

Subject	Conclusions Pesticide Peer Review Meeting
Experts' consultation 3.1 Experts to consider all available storage stability studies with wheat and rice and conclude on the maximum time for which stability can be considered for parent and metabolites. For open point regarding the validity of the storage stability studies with rice see open points in 3(6) and 3(7). For data requirement see also 3(24). See also comments 3(14), 3(15) and 3(54).	Based on the available information, a freezer storage stability of 11 months for bensulfuron-methyl in cereal grains was considered demonstrated. **Open point:** RMS to reevaluate the residue trials in cereal crops in terms of compliance with the supported storage stability period for bensulfuron-methyl in cereal grain of 11 months and assess the impact of potential deviations on the reported residue levels for bensulfuron-methyl and on the consumer risk assessment The experts noted that the available residue trials in rice that cover only the SEU zone are insufficient to address the use requested in Hungary (NEU). **Data gap:** Residue trials in rice in the NEU zone in order to support the GAP requested for Hungary.
Experts' consultation 3.2 Experts to discuss the shortcomings of the available metabolism studies on rice and wheat in terms of dosing (rice), extractability (wheat) and	The GAP with foliar application to cereals (rice, barley, wheat) can be supported by the acceptable wheat metabolism study based on comparability of the application scenarios in the GAPs and the extrapolation rules according to current guidance. The GAP in rice with pre-sowing application needs further clarification (see data gap). Bensulfuron-methyl by default is proposed as **enforcement residue definition** for foliar applications in cereal crops.

Subject	Conclusions Pesticide Peer Review Meeting
identification (rice and wheat) and conclude whether these studies fully elucidate the metabolic path of bensulfuron-methyl in these crops taking also into account the proposed application for rice as presowing and foliar. Experts should also discuss whether the studies can be used to derive residue definitions in the light of the shortcomings (e.g. not addressing the quantitative aspects due to underdosing). If this is the case, the experts should conclude on the RD taking into account the toxicological profile of the metabolites found. See also 2(71), 3(4), 3(28), 3(29), 3(32), 3(33), 3(44)-3(46), 3(48), 3(49), 3(57), 3(62), 3(66) and 3(72).	Whether this definition is appropriate to extend to the pre-sowing scenario is pending a data gap (see below). Bensulfuron-methyl by default is set as the **risk assessment residue definition** for cereal grain. For **cereal straw**, bensulfuron- methyl could be sufficient, provided that the metabolites found in straw do not lead to a significant intake by livestock which is still to be confirmed (open point). Specifically, metabolite IN-F78184 could be a driver of the dietary burden based on observations in straw in field trials. Therefore, the risk assessment residue definition for cereal straw is **provisional**. Residue definitions were only proposed for cereal crops because the uses of bensulfuron-methyl are limited to this crop category. **Data gap:** A scientifically based justification, considering the specific agricultural conditions of the GAP in rice with pre-sowing application, the environmental fate data applicable to saturated and/or flooded soil and the available data on metabolism in cereals, to address the expected metabolic pattern in rice with regard to the GAP with pre-sowing application. **Open point** RMS to verify the input values for the dietary burden calculation in the RAR and conduct an updated dietary burden calculation for the sum of bensulfuron-methyl and metabolites IN-F78184, IN-F7880 and IN-N5297 as a conservative approach. The RMS should reconsider the provisional residue definition for risk assessment for cereal straw in the light of the assessment outcome of this open point and of the additional open point on IN-F78184 (see open point in 3.3.) with regard to the need to include metabolites and provide a respective proposal.
Experts' consultation 3.3 Experts to discuss the available metabolism studies with poultry and ruminants and conclude on their validity. Based on these studies, experts should discuss the	According to livestock burden assessment presented by the RMS in the RAR, livestock studies are not triggered for the representative uses in the renewal review. However, an open point to update the dietary burden estimates according to the agreements of the meeting was identified (see 3.2). The poultry study was not considered acceptable and **residue definitions for poultry commodities could not be proposed.** The goat study was only conducted with one ring

Subject	Conclusions Pesticide Peer Review Meeting
information on the toxicity of the identified metabolites (especially IN-F7880, IN-N8989, IN-B6895 and IN-N5297) and the updated dietary burden and, if feasible, set animal residue definitions. See also 2(71) and 3(47) For plant residue definition see 3(31).	label (phenyl-label), which is insufficient because cleavage of the parent molecule is observed. Based on the available metabolism data in goats, O-desmethyl bensulfuron-methyl (IN-F7880) was proposed as **residue definition for enforcement for ruminant commodities**. This metabolite is not label specific. IN-F7880 should be included into the **provisional residue definition for risk assessment for ruminant commodities**, based on its significant occurrence in milk and liver. A final conclusion on the residue definitions for animal commodities in general is pending on the updated dietary burden estimates, potential additional uses, the availability of a ruminant study with pyrimidyl-label and, if necessary, poultry metabolism data. **Open point:** RMS to verify if IN-F78184 was analysed for in the ruminant metabolism study (IN-F78184 standard used?) and whether there was indication from the rat ADME study that IN-F78184 is a mammalian metabolite.
Experts' consultation 3.4 Experts to discuss the results of the three rotational crop metabolism studies and, if from the available data feasible, conclude whether and which residues can be expected in rotated crops. Experts to discuss whether on this basis rotational crop field trials should be requested.	Only very low and not further identified residues were demonstrated in rotational root crops, leafy crops and oilseed seeds. Bensulfuron-methyl as default residue definition for enforcement and risk assessment was confirmed for grains of rotational cereal crops, and this definition is in line with the residue definitions for grains of primary cereal crops. For cereal straw from a rotational crop, a decision whether or not to consider metabolite IN-N5297 in addition to bensulfuron-methyl is pending confirmation that the rotational crop study was appropriately dosed in terms of the PEC (data gap in section Environmental Fate & Behaviour). If the available rotational crop study turned out as underdosed and residues $\geq$0.05 mg/kg of IN-N5297 in straw could be expected, further action in line with current guidance will be triggered.

REPORT OF PESTICIDES PEER REVIEW TC 128

Bixlozone – NAS 1107 Rapporteur Member State: NL

3. Residues

Date: 31 January 2024

List of participants:

Status	**Name of institution/attendee**
EFSA statutory staff member	EFSA
National Experts nominated by MS Austria	Austrian Agency for Health and Food Safety (AGES) - AT
National Experts nominated by MS Germany	Federal Environment Agency (UBA) - DE
National Experts nominated by MS France	Agence nationale de sécurité sanitaire de l'alimentation, de l'environnement et du travail (ANSES) - FR
National Experts nominated by MS Italy	International Centre for Pesticides and Health Risk Prevention (ICPS) - IT
National Experts nominated by RMS Netherlands	Board for the Authorisation of Plant Protection Products and Biocides (Ctgb) – NL

In accordance with EFSA's Policy on Independence[1] and the Decision of the Executive Director on Competing Interest Management[2,] EFSA screened the Annual Declarations of Interest filled out by the participants invited to the present meeting. No Conflicts of Interest related to the issues discussed in this meeting have been identified during the screening process, and no interests were declared orally by the members at the beginning of this meeting.

[1] http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/policy_independence.pdf
[2] http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/competing_interest_management_17.pdf

Discussion points/Outcome

3. Residues

Please note that information part of this report may have been masked by EFSA in accordance with Article 63 of Regulation (EC) No 1107/2009 as well as EFSA's Practical Arrangements concerning confidentiality in accordance with Articles 7 and 16 of Regulation (EC) No 1107/2009, or EFSA's Practical Arrangements concerning transparency and confidentiality as a consequence of confidentiality requests submitted by the applicant on application dossiers for pesticides active substances or Maximum Residue Levels, respectively. Please note that information disclosed in this report is without prejudice to pre-existing intellectual property rights and data exclusivity clauses set out in Union law, and particularly in Article 62 of Regulation (EC) No 1107/2009.

Minutes might be revised due to pending data gaps at the time of the meeting and /or eventual need for further follow up consultation after the meeting. If needed, the final agreement will be made available in the meeting report published at the end of the peer review process.

Subject	Conclusions Pesticide Peer Review Meeting
Experts' consultation 3.1 1 - RDs in **primary crops**: Based on the metabolism studies provided in different crops, experts to discuss residue definitions for risk assessment and enforcement in plants, considering - the magnitude of the relevant metabolites analysed in the residue trials for which the proportionality approach may have to be applied, - available storage stability data on all the metabolites that were analysed in the trials - residue levels only available as "sum of free and conjugated" - the toxicological relevance of pertinent metabolites. - additional sources of metabolites e.g. from other a.s. (see 3(41)) or natural occurrence	Acceptable metabolism studies with primary and rotational crops were submitted showing a complete degradation of the parent molecule to several metabolites exhibiting a complex pattern in the various crops. The relevance and toxicological information of the metabolites were considered for setting the residue definition. Argumentation was brought forward that the metabolites 2,2-dimethyl-3-hydroxy-propionic acid (M118/1) and its downstream product dimethylmalonic acid (M132/1) are naturally occurring and therefore should not be included in the residue definitions. A **data gap** is set to obtain additional evidence other than from field trials on the natural occurrence of 2,2-dimethyl-3-hydroxy-propionic acid (M118/1) and its downstream product Dimethylmalonic acid (M132/1) in plants. Based on the available data the presence of Bixlozone-dimethylmalonamide (M289/2) in rotated crops cannot be excluded and therefore a **data gap** (for mammalian toxicology) is set to address the genotoxicity and general toxicity to decide on its relevance for the risk assessment residue definition It was noted that one additional rotational crop residue field trial in SEU is missing, and it understood that such a trial is in process (**data gap**). On the basis of the metabolism studies and residue trials for the representative uses the following RD are proposed: **Residue definition for enforcement** as "bixlozone by default" for all primary and rotated crops. **Risk assessment residue definition** is "bixlozone, free and conjugated" for all crops for pre-and postemergence.

Subject	Conclusions Pesticide Peer Review Meeting
Note: For the 2,2-dimethyl-3-hydroxy-propionic acid (M118/1), it is still requested to be demonstrated that it really does occur naturally in plants. (see 3(103)) 2- RDs in **rotational crops**: Experts to discuss residue definitions for risk assessment and enforcement in rotational crops, considering - the submission of additional rotational crop field trials, - the storage stability data on all metabolites analysed in the field trials, - the appropriate dosage of residue trials and metabolism study related to the calculated PECs, as well as the toxicological relevance of pertinent metabolites.,	**Risk assessment residue definition only for cereal feed items (forage, hay and straw)** as "bixlozone, free and conjugated and 5`-OH-bixlozone, free and conjugated". The RA RD is provisional and the expression is subject to information on the toxicity of the metabolite 5`-OH-bixlozone (M289/3). **Risk assessment residue definition for rotated crops (only leafy crop) is "Bixlozone, free and conjugates and Bixlozone-dimethylmalonamide, free and conjugates".** The RA RD is provisional and the expression is subject to the information on the toxicity of Bixlozone-dimethylmalonamide (M289/2). **Risk assessment residue definition for rotated crops (except leafy crop) is "Bixlozone free and conjugates".** Recommendations for future uses: **2,4-dichlorbenzoic acid (M190/1):** For future GAPs on oilseed rape with more critical conditions the magnitude of this metabolite should be investigated. **5`-OH-bixlozone (M289/3)**: For future GAPs on cereals with more critical conditions the magnitude of this metabolite should be investigated in cereal straw and its genotoxic potential should be addressed. **Bixlozone-dimethylmalonamide (M289/2):** For future GAPs in primary root and tuber, in leafy crops and in rice and depending on its toxicological profile the metabolite might be reconsidered for inclusion in the plant risk assessment residue definition. **Open point**: RMS to calculate the dietary burden for 5`-OH-bixlozone (M289/3) to demonstrate that exposure is below the trigger and transfer to animal commodities can be excluded for the representative uses. In case the trigger values will be exceeded either from cereal straw from representative uses (grown as primary and rotated crop) and/or with further uses, information on toxicological profile of 5`-OH-bixlozone (M289/3) is needed.  **Open point**: RMS to check and clarify the reporting of storage stability data for 5- and `5-OH-bixlozone.

Subject	Conclusions Pesticide Peer Review Meeting
	Open point: RMS to check the plausibility of the formation of ´5-OH-bixlozone in plant matrices as artefact of the analytical method.
Experts' consultation 3.2 RDs in **livestock**: Experts to discuss the appropriateness of the livestock metabolism studies conducted with bixlozone, considering the residue situation in feed items of primary and rotational crops, and whether robust residue definitions can be derived for the commodities of animal origin.	Bixlozone is recovered in feed items of primary and rotational crops and therefore animal studies with parent are considered relevant. The feed metabolite´5-OH-bixlozone is not found in animal matrices and therefore the fate of this metabolites in animals is not addressed. Depending on the outcome of the final dietary burden calculation (see data gap in 3.1) and in case that future uses will trigger animal studies it will be necessary to address the fate of `5-OH-bixlozone in animals. **The residue definition for enforcement** for all animal matrices is proposed as "5-OH-bixlozone, free and conjugated". The inclusion of conjugates, which are major in muscle and liver of poultry should ensure that residues in these matrices would not be underestimated. It is left to risk managers to decide on the inclusion of the conjugated forms of 5-OH-bixlozone into the residue definition for enforcement. The meeting was not able to set confidently a **risk assessment residue definition for animals** that would address potential future uses. Instead, it was suggested to set the **risk assessment residue definition** for animals on a provisional basis as "5-OH-bixlozone, free and conjugated expressed as bixlozone". Based on evidence from future uses the RA RD might be revised to take into account additional relevant metabolites. The occurrence of M118/1 and M132/ claimed to occur naturally should be further investigated also in animal tissues (e.g. 30%TRR in ruminant muscle) (**data gap**).
Experts` consultation 3.3 Pending the toxicological profiles of metabolites analysed in the residue trials, experts to discuss if conditions are met to apply the proportionality approach for the residue trials that systematically deviate from the application rate in the GAP	Residue field trials with oilseed rape deviated from the critical GAP parameters application rate (within 25% tolerance) and growth stage. Given the long period between dosing and harvest, the residue data set is deemed to be acceptable with respect the application on the earlier BBCH stage. A sufficient number of valid and GAP compliant residue field trials with cereals and with maize is available.

Subject	Conclusions Pesticide Peer Review Meeting
See also Experts' consultation 3(42).	

REPORT OF PESTICIDES PEER REVIEW TC 122

Ethiprole – MRL Art.10 Rapporteur Member State: NL

3. Residues

Date: 24 November 2023

List of participants:

Status	**Name of institution/attendee**
EFSA statutory staff member	EFSA
National Experts nominated by MS DE	German Federal Institute for Risk Assessment-DE
National Experts nominated by MS EL	Benaki Phytopathological Institute - EL
National Experts nominated by MS FR	ANSES- FR
National Experts nominated by MS HR	HAPIH- HR
National Experts nominated by RMS NL	CTGB -NL

In accordance with EFSA's Policy on Independence[1] and the Decision of the Executive Director on Competing Interest Management[2,] EFSA screened the Annual Declarations of Interest filled out by the participants invited to the present meeting. No Conflicts of Interest related to the issues discussed in this meeting have been identified during the screening process, and no interests were declared orally by the members at the beginning of this meeting.

[1] http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/policy_independence.pdf
[2] http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/competing_interest_management_17.pdf

Discussion points/Outcome

3. Residues

Please note that information part of this report may have been masked by EFSA in accordance with Article 63 of Regulation (EC) No 1107/2009 as well as EFSA's Practical Arrangements concerning confidentiality in accordance with Articles 7 and 16 of Regulation (EC) No 1107/2009, or EFSA's Practical Arrangements concerning transparency and confidentiality as a consequence of confidentiality requests submitted by the applicant on application dossiers for pesticides active substances or Maximum Residue Levels, respectively. Please note that information disclosed in this report is without prejudice to pre-existing intellectual property rights and data exclusivity clauses set out in Union law, and particularly in Article 62 of Regulation (EC) No 1107/2009.

Minutes might be revised due to pending data gaps at the time of the meeting and /or eventual need for further follow up consultation after the meeting. If needed, the final agreement will be made available in the meeting report published at the end of the peer review process.

Subject	Conclusions Pesticide Peer Review Meeting
Experts' consultation 3.1 Experts to conclude on the residue definitions for monitoring and risk assessment in cereals (applicable to rice grain and straw).	A minor uncertainty was noted in the rice metabolism study investigating foliar application regarding the growth stage at the time of the application of the active substance. This uncertainty might have an impact on the quantitative results of the study. From a qualitative point of view, no impact is expected on the study results. The study is therefore reliable to derive RDs in rice (and in cereals). In order to ensure proper consumer protection, the meeting decided to include in the residue definition for the risk assessment ethiprole-amide, a metabolite which is formed in rice upon soil treatment. **Conclusion** As for the **enforcement** it is concluded that the residue definition in cereals is defined as "ethiprole". As for the **risk assessment** it is concluded that the residue definition in cereals is defined as the "sum of ethiprole, ethiprole-sulfone RPA097973) and ethiprole-amide (RPA112916), expressed as ethiprole". **Open point:** EMS to update the evaluation report accordingly. The EMS is also requested to report information on the growth stage at applications in the rice metabolism study performed with foliar applications.
Experts' consultation 3.2	The available metabolism study on pepper was considered valid to conclude on the metabolism of ethiprole in fruit crops. For the metabolism study in cotton seed a low identification of total

Subject	Conclusions Pesticide Peer Review Meeting
Experts to conclude on whether the residue definitions proposed for cereals can also be proposed for all plant commodities.	radioactive residues in seed was noted as a shortcoming, however, not affecting the overall conclusion on the validity of the study. The study on cotton is considered representative for the pulses/oilseeds crop group. The EMS is requested to update the Evaluation report to clarify the figures on extraction rate and characterisations in cotton matrices. **Conclusion** General residue definition for all plant commodities for the foliar treatment was agreed as follows: - **enforcement** residue definition: "ethiprole" - **risk assessment** residue definition: "sum of ethiprole, ethiprole-sulfone RPA097973) and ethiprole-amide (RPA112916), expressed as ethiprole" **Open point:** EMS to update the evaluation report accordingly. The EMS is also requested to update the evaluation report to clarify the figures on extraction rate and characterisations in cotton matrices.
Experts' consultation 3.3 Experts to conclude on nature of residue in processed commodities and to propose a residue definition for processed commodities.	According to available hydrolysis studies slight degradation of ethiprole to ethiprole-amide and ethiprole-sulfone to ethiprole-sulfone-amide under sterilisation conditions is observed. The degradation was considered insignificant and therefore both compounds -ethiprole and ethiprole-sulfone- are concluded to be stable under standard hydrolysis studies. **Conclusion** It is concluded that residue definitions for risk assessment and enforcement in processed commodities is defined as follows: - **enforcement** residue definition: "ethiprole" - **risk assessment** residue definition: "sum of ethiprole, ethiprole-sulfone RPA097973) and ethiprole-amide (RPA112916), expressed as ethiprole" **Open point:** EMS to update the evaluation report accordingly.

REPORT OF PESTICIDES PEER REVIEW TC 122

Acetochlor – MRL Art.10 Rapporteur Member State: NL

3. Residues

Date: 24 November 2023

List of participants:

Status	**Name of institution/attendee**
EFSA statutory staff member	EFSA
National Experts nominated by MS DE	German Federal Institute for Risk Assessment-DE
National Experts nominated by MS EL	Benaki Phytopathological Institute - EL
National Experts nominated by MS FR	ANSES- FR
National Experts nominated by MS HR	HAPIH- HR
National Experts nominated by RMS NL	CTGB -NL

In accordance with EFSA's Policy on Independence[1] and the Decision of the Executive Director on Competing Interest Management[2,] EFSA screened the Annual Declarations of Interest filled out by the participants invited to the present meeting. No Conflicts of Interest related to the issues discussed in this meeting have been identified during the screening process, and no interests were declared orally by the members at the beginning of this meeting.

[1] http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/policy_independence.pdf
[2] http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/competing_interest_management_17.pdf

Discussion points/Outcome

3. Residues

Please note that information part of this report may have been masked by EFSA in accordance with Article 63 of Regulation (EC) No 1107/2009 as well as EFSA's Practical Arrangements concerning confidentiality in accordance with Articles 7 and 16 of Regulation (EC) No 1107/2009, or EFSA's Practical Arrangements concerning transparency and confidentiality as a consequence of confidentiality requests submitted by the applicant on application dossiers for pesticides active substances or Maximum Residue Levels, respectively. Please note that information disclosed in this report is without prejudice to pre-existing intellectual property rights and data exclusivity clauses set out in Union law, and particularly in Article 62 of Regulation (EC) No 1107/2009.

Minutes might be revised due to pending data gaps at the time of the meeting and /or eventual need for further follow up consultation after the meeting. If needed, the final agreement will be made available in the meeting report published at the end of the peer review process.

Subject	Conclusions Pesticide Peer Review Meeting
Experts' consultation 3.1 Experts to conclude based on the available information from soybean metabolism studies, the residue definitions for enforcement and risk assessment in soybean seed. Additional considerations - to propose the residue definitions in pulses/oilseed group	Acetochlor is not a good marker for enforcement and is not sufficient for risk assessment. In soyabean, major part of the TRR is hydrolysed to "HEMA moiety metabolites" and "EMA moiety metabolites". Validated enforcement method for a common moiety RD is available. Residue trial data are available for a common moiety RD. However, HEMA moiety and EMA moiety metabolites are not specific to acetochlor. **Conclusion** The proposed RD for risk assessment in pulses/oilseeds is: „sum of compounds hydrolysable with base to 2-ethyl-6-methylaniline (EMA) and 2-(1-hydroxyethyl)-6-methylaniline (HEMA), expressed in terms of acetochlor". The same RD is proposed for enforcement, noting that it is not acetochlor specific.
Experts's consultation 3.2. Experts to decide whether the residue definitions proposed for soybean could be extended to cereals/grass crop group. Particular attention to be paid to:	In cereals, similar results compared to P/O were found. However, the metabolite N-oxamic acid was found in maize forage and in rotational crops. For cereals, a RD RA including metabolite N-oxamic acid was already derived in the EU peer review. There are no new data for cereals. **Conclusion** RD enforcement for cereals: the same conclusion as for P/O was reached.

Subject	Conclusions Pesticide Peer Review Meeting
- the capabilities of analytical methods to enforce the residue for enforcement - the residue definitions proposed by the EU pesticides peer review and the residue definitions set for soybean by the JMPR and the U.S.EPA.	For RD risk assessment (no change proposed compared to previous conclusion): "all compounds forming EMA and HEMA on hydrolysis plus N-oxamic acid, expressed as acetochlor" (not impact on the import tolerance is expected).
Experts' consultation 3.3. To discuss a need to set the risk assessment and enforcement residue definitions in animal commodities despite the fact the livestock exposure from the intake of soybean will not result in significant residues in animal commodities.	Total residues (TRR) are expected to be below the LOQ in livestock commodities based on TRR results of the metabolism studies scaled to the EU dietary burden. A RD for livestock commodities is not needed in the framework of the present application. **Conclusion** RD for livestock commodities was not proposed. The RD derived by JMPR („Sum of compounds hydrolysable with base to 2-ethyl-6-methylaniline (EMA) and 2-(1-hydroxyethyl)-6-methylaniline (HEMA), expressed in terms of acetochlor") could be considered by risk managers for better enforcment of imported food commodities of animal origin (to be mentioned in the conclusion and recommendation of the reasioned opinion). In case of future import tolerances (or CXLs assessment) for food commodities of animal origin or for plant commodities affecting the EU livestock dietary burden, the livestock RDs for enforcement and risk assessment would need to be assessed.

REPORT OF PESTICIDES PEER REVIEW TC 122

Chlorotoluron – AIR III

Rapporteur Member State: BG

3. Residues

Date: 24 November 2023

List of participants:

Status	**Name of institution/attendee**
EFSA statutory staff member	EFSA
National Experts nominated by RMS BG	Risk assessment center on food chain -BG
National Experts nominated by MS DE	German Federal Institute for Risk Assessment-DE
National Experts nominated by MS FR	ANSES- FR
National Expertsnominated by MS HR	HAPIC- HR

In accordance with EFSA's Policy on Independence[1] and the Decision of the Executive Director on Competing Interest Management[2,] EFSA screened the Annual Declarations of Interest filled out by the participants invited to the present meeting. No Conflicts of Interest related to the issues discussed in this meeting have been identified during the screening process, and no interests were declared orally by the members at the beginning of this meeting.

[1] http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/policy_independence.pdf

[2] http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/competing_interest_management_17.pdf

Discussion points/Outcome

3. Residues

Please note that information part of this report may have been masked by EFSA in accordance with Article 63 of Regulation (EC) No 1107/2009 as well as EFSA's Practical Arrangements concerning confidentiality in accordance with Articles 7 and 16 of Regulation (EC) No 1107/2009, or EFSA's Practical Arrangements concerning transparency and confidentiality as a consequence of confidentiality requests submitted by the applicant on application dossiers for pesticides active substances or Maximum Residue Levels, respectively. Please note that information disclosed in this report is without prejudice to pre-existing intellectual property rights and data exclusivity clauses set out in Union law, and particularly in Article 62 of Regulation (EC) No 1107/2009.

Minutes might be revised due to pending data gaps at the time of the meeting and /or eventual need for further follow up consultation after the meeting. If needed, the final agreement will be made available in the meeting report published at the end of the peer review process.

Subject	Conclusions Pesticide Peer Review Meeting
Experts' consultation 3.1 The experts to discuss the compliance of the submitted poultry and ruminants' metabolism studies with the current data requirement and the proposed residue definitions for monitoring and risk assessment. The toxicological profile of the metabolites that are quantitatively relevant in animal matrices will also be discussed under experts' consultation 2(193) in the Mam Tox section.	The metabolism studies for poultry and ruminants are reliable and relevant for the assessment of the representative use. Cysteine conjugates of metabolite didesmethyl chlorotoluron and desmethyl chlorotoluron occurred in poultry liver in significant amounts but are not covered by toxicological data. In ruminants, a major metabolite N-Formyl chlorotoluron benzoic acid in milk (30%TRR), also present in other ruminant commodities, has a significant dietary exposure potential but genotoxicity data is not available. **Data gap:** Applicant to address the hydrolysis of at least the cysteine conjugate of didesmethyl chlorotoluron under physiological conditions of the human gut, or if not readily hydrolysed, the toxicological relevance of this compound. **Data gap:** Data to address the genotoxic potential of metabolite N-Formyl chlorotoluron benzoic acid should be provided to conclude on its relevance for the risk assessment. **Open point:** RMS to crosscheck in the livestock metabolism studies whether or not there was hydrolysis applied in the work up procedure of the samples that permits conclusions on whether or not conjugated residues (other than with cysteine) were present. The residue definitions for **poultry and ruminant** are as follows and were based on the metabolism data in both species: **Residue definition for risk assessment:** Sum of chlorotoluron and its metabolites chlorotoluron benzoic acid, chlorotoluron benzyl alcohol, desmethyl chlorotoluron,

Subject	Conclusions Pesticide Peer Review Meeting
	desmethyl chlorotoluron benzoic acid, desmethyl chlorotoluron benzyl alcohol, didesmethyl chlorotoluron, didesmethyl chlorotoluron benzoic acid and didesmethyl chlorotoluron benzyl alcohol, expressed as chlorotoluron. The residue definition is pending the verification on conjugated residues (see open point) and pending the data gaps to address the genotoxicity of N-Formyl chlorotoluron benzoic acid and the hydrolysis/toxicological relevance of the cysteine conjugate of didesmethyl chlorotoluron. **Residue definition for enforcement:** Chlorotoluron is not a good marker for monitoring as readily metabolised in the animals and hardly found in animal commodities. Therefore, options are proposed to risk managers: - All poultry and ruminant commodities: Sum of desmethyl chlorotoluron benzoic acid and didesmethyl chlorotoluron, expressed as chlorotoluron. - All poultry and ruminant commodities except milk: didesmethyl chlorotoluron, expressed as chlorotoluron, and, milk: desmethyl chlorotoluron benzoic acid, expressed as chlorotoluron; other metabolites would also qualify as marker compound in milk It is acknowledged that e.g. the availability of analytical standards will play a role for a final decision. **Open point:** RMS to conduct a reassessment of the actual exposure levels for poultry and ruminants, i.e. provide an updated dietary burden calculation taking into account the agreed residue definition for risk assessment and the recently submitted (more critical) residue trials in cereals and reassess the N rate of the poultry and ruminant metabolism studies accordingly.
Experts' consultation 3.2 The experts to discuss the compliance of the submitted metabolism studies in/on primary and rotational crops with the current data requirement and the proposed residue definitions for monitoring and risk assessment. The toxicological profile of the metabolites that are	The cereal and oilseed metabolism studies are reliable and the cereals study is relevant to address the data requirement for the representative GAP in cereals. Chlorotoluron and 8 metabolites were present in straw and grain in comparable amounts and the same TRVs apply to chlorotoluron and these metabolites. The metabolism study in rotational crops had shortcomings, leading to data gaps. **Data gap:** It should be clarified whether or not in the rotational crop study there was any mixing of the soil after application or at planting and it should be demonstrated that concentrations of chlortoluron and metabolites in the root zone of the crops in this

Subject	Conclusions Pesticide Peer Review Meeting
quantitatively relevant in plant matrices will also be discussed under experts' consultation 2(193) in the Mam Tox section.	study was sufficient to reflect the agricultural practice of ploughing the soil. **Data gap:** Storage stability data of the chlorotoluron metabolites for several plant commodities stored longer than 6 months are necessary. It is noted that the final report of a storage stability study was submitted by the applicant to the RMS just before the meeting but not within the period designated to the submission of additional data. The study is not available to EFSA and MS and is not eligible to be taken into account. The very recent submission by the applicant to the RMS contained also new residue trials. According to the RMS, these new trials lead to more critical endpoints for the consumer risk assessment and should therefore be taken into account. **Open point**: RMS to assess the residue trials submitted after the period for submitting additional information in the updated assessment report as they lead to more critical risk assessment endpoints. The following residue definitions were based on the available data (NOR and MOR) are different from the residue definitions in place (proposed by Art.12 MRL review) as new and more specific residue data have become available for the peer review. **Residue definition for risk assessment** Sum of chlorotoluron and its metabolites chlorotoluron benzoic acid, chlorotoluron benzyl alcohol, desmethyl chlorotoluron, desmethyl chlorotoluron benzoic acid, desmethyl chlorotoluron benzyl alcohol, didesmethyl chlorotoluron, didesmethyl chlorotoluron benzoic acid and didesmethyl chlorotoluron benzyl alcohol (all free and conjugated), expressed as chlorotoluron. The definition is applicable to foliar uses in cereal crops and can be extended to oilseed crops as needed. Applicability to rotational crops depends on the filling of the data gaps (see above). **Residue definition for enforcement** Cereal grain: Chlorotoluron benzyl alcohol, expressed as chlorotoluron

Subject	Conclusions Pesticide Peer Review Meeting
	Chlorotoluron benzyl alcohol is the most suitable marker for residues of chlorotoluron in grain. The current residue definition chlorotoluron alone is not suitable to enforce residues of chlorotoluron in cereal grain as in none of the cGAP residue trials was chlorotoluron ever detected in grain. Residue trials for commodities other than cereal crops are not available and therefore its suitability as marker for other food commodities was not assessed. As an option, the same residue definition as for risk assessment (using a common moiety method if feasible and sufficiently specific) could be considered by risk managers for enforcement purposes, although it is acknowledged that this is a very complex definition that could be difficult to implement in practice for the laboratories.

REPORT OF PESTICIDE PEER REVIEW TC 116

CLOVE OIL – Amendment of approval conditions Rapporteur Member State: MT

3. Residues

Date: 12 September 2023

List of participants:

Status	**Name of institution/attendee**
EFSA statutory staff member	EFSA
National Experts nominated by MS France (2)	Agence nationale de sécurité sanitaire de l'alimentation, de l'environnement et du travail (ANSES) - FR
National Experts nominated by MS Germany (1)	German Federal Institute for Risk Assessment (BfR) – DE
National Experts nominated by RMS Malta (1)	Benaki Phytopathological Institute – EL representing ML
National Experts nominated by MS Netherlands (2)	Board for the Authorisation of Plant Protection Products and Biocides (Ctgb) - NL
Observer (1)	Malta Competition and Consumer Affairs Authority (MCCAA)- ML

In accordance with EFSA's Policy on Independence[1] and the Decision of the Executive Director on Competing Interest Management[2,] EFSA screened the Annual Declarations of Interest filled out by the participants invited to the present meeting. No Conflicts of Interest related to the issues discussed in this meeting have been identified during the screening process, and no interests were declared orally by the members at the beginning of this meeting.

[1] http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/policy_independence.pdf
[2] http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/competing_interest_management_17.pdf

Discussion points/Outcome

3. Residues

Please note that information part of this report may have been masked by EFSA in accordance with Article 63 of Regulation (EC) No 1107/2009 as well as EFSA's Practical Arrangements concerning confidentiality in accordance with Articles 7 and 16 of Regulation (EC) No 1107/2009, or EFSA's Practical Arrangements concerning transparency and confidentiality as a consequence of confidentiality requests submitted by the applicant on application dossiers for pesticides active substances or Maximum Residue Levels, respectively. Please note that information disclosed in this report is without prejudice to pre-existing intellectual property rights and data exclusivity clauses set out in Union law, and particularly in Article 62 of Regulation (EC) No 1107/2009.

Minutes might be revised due to pending data gaps at the time of the meeting and /or eventual need for further follow up consultation after the meeting. If needed, the final agreement will be made available in the meeting report published at the end of the peer review process.

Subject	Conclusions Pesticide Peer Review Meeting
Experts' consultation 3.1 MSs experts to discuss the need for metabolism and feeding studies in livestock and fish considering the data provided by the applicant after data requirements 3(4) and 3(12).	The meeting agreed that the representative uses on cucumber and tomato do not lead to dietary exposure to livestock and therefore the discussion point is closed. No further action needed.
Experts' consultation 3.2 MSs to discuss if new metabolism data provided by the applicant after data requirement 3(4) are adequate and sufficient to support the GAP for the uses of clove oil as nematicide. MSs to discuss if the new residue trials provided by the applicant after data requirement 3(12) are adequate and sufficient to support the GAP for the uses of clove oil as nematicide. MSs to agree on reliability of metabolism and residue field trials data considering the stability of residues in	Metabolism data are only available for post-harvest treatment but not for the new intended use on soil. The meeting agreed not request a new metabolism study with clove oil or eugenol applied to soil. Instead, several data gaps are set: **Data gap**: Evidence on the fate and the potential metabolic pathway of clove oil should be provided by retrieving and combining information/data from all available sources (e.g., environmental fate studies, metabolism from post-harvest and other metabolism studies) for the major constituent, eugenol. **Data gap**: As regards the remaining 20% of unknown constituents of clove oil efforts should be made to evaluate their potential presence in the metabolic pathway of eugenol. Considering the representative uses conditions for application rate and depending on their potential amount available for uptake by plants information on their toxicological profile might be needed. **Data gap**: The dietary exposure to eugenol and/or clove oil from its natural presence in the diet should be estimated and compared with the exposure resulting from the intended uses.

Subject	Conclusions Pesticide Peer Review Meeting
stored samples (data requirement in 3(2) MSs to agree on the residue definitions applicable to the use of clove oil as nematicide on basis of available and new data provided by the applicant.	It was noted that the number of available residue field trials for the supported uses is not sufficient. **Data gap** for four residue field trials for the representative uses with tomato and cucumber according to the cGAP (see post meeting note) and analysing for eugenol and methyl-eugenol (including analysis of the test material as requested under GLP). The number of four trials is only applicable in case the residues are below LOQ, otherwise a full data set of eight residue field trials is needed. As methyl-eugenol is a known genotoxic substance the LOQ of 0.01 mg/kg for this substance is not sufficiently low. Therefore, the requested residue field trials should employ an analytical method with a considerably lower LOQ for methyl-eugenol. **Data gap:** storage stability data for eugenol and methyl-eugenol in high water commodities covering the storage periods in the existing and requested residue field trials are required. **Open point**: RMS to improve the reporting of the efficacy trials in the RAR and identify deviations from applicable test guidelines and the potential impact on the reliability of results. Furthermore, the reason why eugenol residues were found in untreated plots in efficacy trials should be clarified and results of the analysis of the soil samples of the treated plots should be included in the RAR. The **risk assessment residue definition** should include eugenol and methyl-eugenol based on occurrence and toxicological concern, respectively. Considering the presented information, the residue definition for plants is not finalised. Whether a **residue definition for enforcement** is needed will depend on outcome of the requested residue field trials and the decision of inclusion in Annex IV (see 3.3.) **Post meeting Note:** After the meeting, EFSA confirmed that the initial GAP table for the representative uses for nematicide as submitted by the applicant in the document D1 will be used as a basis of the risk assessment for the amendment of conditions of approval on clove oil. According to document D1 in the dossier, 8 applications with an application rate of up to 50.7 Kg /ha are proposed and this is the critical GAP applicable to the data gaps and the one that is considered in the assessment. The MS experts also considered that the crops supported by the applicant only concerned tomatoes and cucumber that are fruiting vegetables at the experts' meeting TC 116 (September 2023). It is noted that the GAP table as provided by the applicant cannot be changed during the peer review process, as stated in the EFSA Administrative Guidance (2019) – section 3.2.

Subject	Conclusions Pesticide Peer Review Meeting
Experts' consultation 3.3 MSs to assess if conditions to maintain the listing of clove oil in Annex IV to Commission Regulation (EC) No 839/2008 are still fulfilled when uses as soil nematicide will be approved, considering the data to be provided under data requirements in 3(2), 3(4), 3(12), 3(24) and 3(29). Natural occurrence of eugenol and / or other components of the residue of clove oil may be considered in this context only if data is provided by applicant to establish robust estimations of natural occurring levels.	The decision on inclusion of an active substance in Annex IV is a risk management decision. Regarding the 5 criteria, the meeting noted the following: Criterion I: basic substance. Not fulfilled. Criterion II: listed in Annex I of Regulation (EC) No 396/2005. Not fulfilled. Criterion III: no hazardous properties. Not fulfilled as the known genotoxic substance, methyl-eugenol, is present in clove oil. Criterion IV: natural exposure higher via diet then via intended use: not sufficient data available (see data gap under 3.2) Criterion V: no consumer exposure. Not fulfilled.
Open point	Open point: RMS to update the RAR and LoEP in line with the agreements of the meeting incl. a re-evaluation of the residue field trials considering the GAP from D1.

REPORT OF PESTICIDE PEER REVIEW TC 116

1-METHYLCYCLOPROPENE- Amend of approval conditions Rapporteur Member State: NL

3. Residues

Date: 12 September 2023

List of participants:

Status	**Name of institution/attendee**
EFSA statutory staff member	EFSA
National Experts nominated by MS France (2)	Agence nationale de sécurité sanitaire de l'alimentation, de l'environnement et du travail (ANSES) - FR
National Experts nominated by MS Germany (1)	German Federal Institute for Risk Assessment (BfR) – DE
National Experts nominated by MS Malta (1)	Benaki Phytopathological Institute – EL representing ML
National Experts nominated by MS Netherlands (2)	Board for the Authorisation of Plant Protection Products and Biocides (Ctgb) - NL
Observer (1)	Malta Competition and Consumer Affairs Authority (MCCAA)- ML

In accordance with EFSA's Policy on Independence[1] and the Decision of the Executive Director on Competing Interest Management[2,] EFSA screened the Annual Declarations of Interest filled out by the participants invited to the present meeting. No Conflicts of Interest related to the issues discussed in this meeting have been identified during the screening process, and no interests were declared orally by the members at the beginning of this meeting.

[1] http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/policy_independence.pdf
[2] http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/competing_interest_management_17.pdf

Discussion points/Outcome

3. Residues

Please note that information part of this report may have been masked by EFSA in accordance with Article 63 of Regulation (EC) No 1107/2009 as well as EFSA's Practical Arrangements concerning confidentiality in accordance with Articles 7 and 16 of Regulation (EC) No 1107/2009, or EFSA's Practical Arrangements concerning transparency and confidentiality as a consequence of confidentiality requests submitted by the applicant on application dossiers for pesticides active substances or Maximum Residue Levels, respectively. Please note that information disclosed in this report is without prejudice to pre-existing intellectual property rights and data exclusivity clauses set out in Union law, and particularly in Article 62 of Regulation (EC) No 1107/2009.

Minutes might be revised due to pending data gaps at the time of the meeting and /or eventual need for further follow up consultation after the meeting. If needed, the final agreement will be made available in the meeting report published at the end of the peer review process.

Subject	Conclusions Pesticide Peer Review Meeting
Experts' consultation 3.1 Experts to discuss the shortcomings of the metabolism studies on apple, tomato and maize, i.e. missing identification attempts of residues above 0.01 mg/kg in apple/tomato leaves, tomato stems and maize forage and kernels. The impact of the volatility of 1-MCP together with the storage times of up to 2.5 months in the apple metabolism study on the total residues should be discussed. Furthermore, experts should consider the limited information on the total TRR in leaves and apples during the study period (results only for PHI 3 available). In the light of the available information, experts should conclude on the validity of the plant metabolism studies and the possibility to confidently depict the metabolic fate in plants.	Although a metabolic pathway in fruit for 1-MCP could not be derived from the available studies with apple and tomato, with regard to the cGAP for the representative uses, the studies are considered acceptable to demonstrate the residue situation in fruit. It was demonstrated by metabolism studies and residue trials that residues in fruit are extremely low (below the limit of detection). Consequently, a default residue definition can be set for fruit. The acceptability of the maize study cannot be concluded and it is disregarded in this context of reviewing the amendment of approval conditions. Data were sufficient to demonstrate that specific storage stability data are not required to demonstrate that residues were not lost during sample storage (2.5 months) in the metabolism studies and residue trials with pome fruit (up to 35 days) due to volatility issues.

Subject	Conclusions Pesticide Peer Review Meeting
Experts' consultation 3.2 On the basis of the outcome of the expert consultation on the validity of the metabolism studies with apple, tomato and maize, experts should discuss and agree on a residue definition for plants. It should be also addressed whether the residue definition can be extended or should be restricted to the crop group of fruits and fruiting vegetables.	A default residue definition for risk assessment and enforcement in fruit as 1-MCP is proposed, and is considered applicable to pre-and post-harvest uses on fruit. Refer to experts' consultation 3.1 for the rationale.
Experts' consultation 3.3 Experts to discuss whether decline residue field trials for the use on apples should be provided based on residues below LOQ in the current residue field trials, considering the volatility of 1-MCP and considering that no information is available on the residue situation before the cGAP PHI of 3 days from the metabolism study with apple.	Decline field trials are not necessary as the available evidence from the spiking experiment and the apple metabolism study samples (3 and 7 days after treatment the residues are the same) is considered sufficient.

REPORT OF PESTICIDE PEER REVIEW TC 112

DELTAMETHRIN – AIR III. Rapporteur Member State: AT

3. Residues

Date: 28 June 2023

List of participants:

Status	Name of institution/attendee
EFSA statutory staff member	EFSA
National Expert nominated by RMS Austria	Austrian Agency for Health and Food Safety (AGES)- AT
National Expert nominated by MS France	Agence nationale de sécurité sanitaire de l'alimentation, de l'environnement et du travail (ANSES) - FR
National Expert nominated by MS Germany	German Federal Institute for Risk Assessment- BE
National Expert nominated by MS Lithuania	State Plant Service under the Ministry of Agriculture- LT
National Expert nominated by MS Poland	Merit mark polska- PL
National Expert nominated by MS Netherlands	Board for the Authorisation of Plant Protection Products and Biocides (Ctgb)- NL

In accordance with EFSA's Policy on Independence[1] and the Decision of the Executive Director on Competing Interest Management[2,] EFSA screened the Annual Declarations of Interest filled out by the participants invited to the present meeting. No Conflicts of Interest related to the issues discussed in this meeting have been identified during the screening process, and no interests were declared orally by the members at the beginning of this meeting.

[1] http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/policy_independence.pdf
[2] http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/competing_interest_management_17.pdf

Discussion points/Outcome

3. Residues

Please note that information part of this report may have been masked by EFSA in accordance with Article 63 of Regulation (EC) No 1107/2009 as well as EFSA's Practical Arrangements concerning confidentiality in accordance with Articles 7 and 16 of Regulation (EC) No 1107/2009, or EFSA's Practical Arrangements concerning transparency and confidentiality as a consequence of confidentiality requests submitted by the applicant on application dossiers for pesticides active substances or Maximum Residue Levels, respectively. Please note that information disclosed in this report is without prejudice to pre-existing intellectual property rights and data exclusivity clauses set out in Union law, and particularly in Article 62 of Regulation (EC) No 1107/2009.

Minutes might be revised due to pending data gaps at the time of the meeting and /or eventual need for further follow up consultation after the meeting. If needed, the final agreement will be made available in the meeting report published at the end of the peer review process.

Subject	Conclusions Pesticide Peer Review Meeting
Experts' consultation 3.1 Experts to discuss the validity of the storage stability studies presented in the RAR in accordance with the current recommendations and supporting the representative uses. Experts to decide whether the data on storage stability is valid to extrapolate to the different crop categories.	From the different studies available, the studies on lettuce and cabbage were concluded as not reliable. Based on the studies considered acceptable, freezer storage stability periods for deltamethrin (cis and trans) for individual categories or specific commodities therein were agreed for: High oil content commodities: 36 months Citrus fruit: 25 months Fruiting vegetables/cucurbits: 24 months The use of data on maize forage that had shortcomings to confirm freezer stability for forage/fodder crops was not unanimously supported. Cereal grains: 36 months Extrapolation to the entire category of high starch commodities was not unanimously supported. Moreover, extrapolation across all five categories is not possible as one category is not addressed by data. **Open point:** The validity of the residue trials supporting the representative uses to be reassessed in the light of the agreed storage stability and the cGAP conditions.

Subject	Conclusions Pesticide Peer Review Meeting
Experts' consultation 3.2 Experts to decide based on the available information whether the available studies are sufficiently validated in accordance with the current recommendations to elucidate the metabolic pathway of deltamethrin in the primary crops.	It was agreed that valid metabolism studies are available in apple (F), lettuce (L), maize (C/G) and cotton (P/O). Overall, it was considered that the available metabolism data are sufficient to address the metabolic pattern of deltamethrin in primary crops and that an additional study in root/tuber crops is not needed. The qualitative metabolic pattern across crops categories can be considered comparable while quantities of metabolites may vary across different crops. As for the metabolite 3-phenoxy benzaldehyde cyanohydrin (3-PBC), a data gap for further tox data is proposed because conjugated 3-PBC was a major metabolite in lettuce. Further, investigation of levels in the field might be necessary. **Data gap:** Further data to address the toxicity of 3-phenoxy benzaldehyde cyanohydrin, i.e. at least sufficient data to conclude on genotoxicity should be provided. Before proceeding to data generation on general toxicity, occurrence of 3-PBC in residue trial samples should be investigated.
Experts' consultation 3.3 Experts to discuss if upon the requested detailed assessment of the livestock metabolism studies, these studies are acceptable in accordance with the current guidance documents and if the information available is considered sufficient to derive RDs for monitoring and risk assessment for animal commodities. Additionally, experts to consider the need for metabolism studies on trans and alpha deltamethrin for defining the metabolic pattern in	The poultry metabolism study is not considered reliable and a residue definition for poultry could not be derived. For ruminants, the following residue definition is proposed: **For enforcement:** Cis-deltamethrin **For risk assessment:** <u>Residue definition 1:</u> Sum of deltamethrin (sum of cis and trans isomers) and BR2CA (sum of cis and trans isomers) free and conjugated, expressed as deltamethrin; <u>Residue definition 2:</u> common pyrethroid metabolite 3-phenoxybenzoic acid PBA (M39), using the specific TRV Pending reassessment of the dietary burden, a **data gap** is proposed to address metabolism of deltamethrin in poultry in order to derive reliable residue definitions for poultry commodities and to assess if the metabolic pattern in ruminant and poultry is comparable.

Subject	Conclusions Pesticide Peer Review Meeting
livestock since a possible transfer it is foreseen from feed items (paper M-628340-01-1 highlighted by the applicant Bayer for addressing the livestock exposure to alpha and trans-deltamethrin (identified in feed items) will be considered).	
Experts' consultation 3.4 Experts to decide based on the available information on plant metabolism studies, the residue definitions for enforcement and risk assessment in primary crops and rotational crops. Particular attention should be paid to the toxicity of the identified isomers and metabolites in the different studies and the capability of the analytical methods. It must be noted that there is not information on the isomers formation in the supervised residue trials (only for one of the representative uses the three isomers were determined) and the information in the metabolism studies is unclear.	Based on the plant metabolism studies available and the information received from the meeting on toxicology on the metabolites of deltamethrin, the **residue definition for enforcement** of residues in plants is proposed as cis-deltamethrin. The **residue definition for risk assessment in plants** is concluded as follows: For the categories pulses/oilseeds, cereal/grass crops, fruit, and root crops: deltamethrin (sum of cis-and trans isomers) For leafy crops, provisionally: Sum of cis-and trans deltamethrin and BR2CA (free and conjugated), expressed as deltamethrin, pending investigation of the actual residue concentrations in leafy crops in residue trials; and 3-PBC (free and conjugated), pending further investigation of its toxicological properties and residue concentrations in field trials in leafy crops **Beyond the representative uses for renewal the following residue definition for risk assessment should apply for pyrethroid a.s. forming common metabolites:** For all crop categories a common definition for all pyrethroid pesticides should apply: Sum of PBA, PBA(OH) (including their conjugates) and PBAld, using the specific health-based guidance values derived for these compounds https://www.efsa.europa.eu/en/efsajournal/pub/7582 **Data gap:** the toxicity of m-phenoxybenzylaldehyde should be addressed

Subject	Conclusions Pesticide Peer Review Meeting
	Data gap: Residue field trials with leafy crops (i.e., lettuce and cauliflower) analysing for cis- and trans-isomers of dibromo carboxylic acid (becisthemic acid)
Experts' consultation 3.5 Experts to agree on the residue definition for processed commodities based on the available standard hydrolysis study and the toxicological properties of the degradation products.	Based on the studies available simulating standard food processing conditions and the information received from the meeting on toxicology on the metabolites of deltamethrin, for **processed commodities** the following residue definitions are proposed: **Residue definition for risk assessment:** Residue definition 1: Deltamethrin (sum of cis-and trans isomer) and Br2CA, expressed as deltamethrin Residue definition 2: PBAld, common metabolite to several pyrethroid compounds **Residue definition for enforcement:** Cis-deltamethrin

REPORT OF PESTICIDE PEER REVIEW TC 108

BUPROFEZIN – AIR IV

Rapporteur Member State: IT

3. Residues

Date: 31 May 2023

List of participants:

Status	**Name of institution/attendee**
EFSA statutory staff member	EFSA
National Expert nominated by MS France	Agence nationale de sécurité sanitaire de l'alimentation, de l'environnement et du travail (ANSES) (FR)
National Expert nominated by MS Germany	German Federal Institute for Risk Assessment
National Expert nominated by MS Netherlands	Board for the Authorisation of Plant Protection Products and Biocides (Ctgb) (NL)
National Expert nominated by RMS Italy (2)	International center for pesticides and health risk prevention (ICPS)

In accordance with EFSA's Policy on Independence[1] and the Decision of the Executive Director on Competing Interest Management[2,] EFSA screened the Annual Declarations of Interest filled out by the participants invited to the present meeting. No Conflicts of Interest related to the issues discussed in this meeting have been identified during the screening process, and no interests were declared orally by the members at the beginning of this meeting.

[1] http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/policy_independence.pdf

[2] http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/competing_interest_management_17.pdf

Discussion points/Outcome

3. Residues

Please note that information part of this report may have been masked by EFSA in accordance with Article 63 of Regulation (EC) No 1107/2009 as well as EFSA's Practical Arrangements concerning confidentiality in accordance with Articles 7 and 16 of Regulation (EC) No 1107/2009, or EFSA's Practical Arrangements concerning transparency and confidentiality as a consequence of confidentiality requests submitted by the applicant on application dossiers for pesticides active substances or Maximum Residue Levels, respectively. Please note that information disclosed in this report is without prejudice to pre-existing intellectual property rights and data exclusivity clauses set out in Union law, and particularly in Article 62 of Regulation (EC) No 1107/2009.

Minutes might be revised due to pending data gaps at the time of the meeting and /or eventual need for further follow up consultation after the meeting. If needed, the final agreement will be made available in the meeting report published at the end of the peer review process.

Subject	Conclusions Pesticide Peer Review Meeting
Experts' consultation 3.1 MSs experts to discuss and agree, if possible, RDs for honey.	Provided the proposed use on ornamentals grown in greenhouse is considered relevant for honeybee foraging, altogether the overall information presented is not sufficient to allow for setting a risk assessment residue definition for honey. There should be only one residue definition for honey which should include also relevant processing metabolites, therefore it is recommended to include in addition to the provisional RD for honey (based on primary crops definition – pending future review) at least aniline. As long as buprofezin is present in honey (which could be subject to processing) the formation of aniline cannot be excluded. Moreover, in the previous peer-review a data gap was set to address the toxicity of BF-4, BF-9, BF-12 and BF-25, but this is still not addressed and remains relevant (outstanding data gap). From the residue trials it seems that buprofezin is a good marker in honey and if necessary, could be proposed for the residue definition for enforcement. **Data gap**: applicant to address the occurrence of BF-25 in processed honey. The meeting confirmed the **data gap** identified by the RMS on storage stability data for all analytes which were investigated in the study with honey. **Open point**: RMS to address the potential formation of aniline in processed honey and its hazard properties in an updated RAR.

REPORT OF PESTICIDE PEER REVIEW TC 108

PYRETHRINS – AIR IV Rapporteur Member State: IT

3. Residues

Date: 31 May 2023

List of participants:

Status	Name of institution/attendee
EFSA statutory staff member	EFSA
National Expert nominated by MS France	Agence nationale de sécurité sanitaire de l'alimentation, de l'environnement et du travail (ANSES) (FR)
National Expert nominated by MS Germany	German Federal Institute for Risk Assessment
National Expert nominated by MS Netherlands	Board for the Authorisation of Plant Protection Products and Biocides (Ctgb) (NL)
National Expert nominated by RMS Italy (2)	International center for pesticides and health risk prevention (ICPS)

In accordance with EFSA's Policy on Independence[1] and the Decision of the Executive Director on Competing Interest Management[2,] EFSA screened the Annual Declarations of Interest filled out by the participants invited to the present meeting. No Conflicts of Interest related to the issues discussed in this meeting have been identified during the screening process, and no interests were declared orally by the members at the beginning of this meeting.

[1] http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/policy_independence.pdf
[2] http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/competing_interest_management_17.pdf

Discussion points/Outcome

3. Residues

Please note that information part of this report may have been masked by EFSA in accordance with Article 63 of Regulation (EC) No 1107/2009 as well as EFSA's Practical Arrangements concerning confidentiality in accordance with Articles 7 and 16 of Regulation (EC) No 1107/2009, or EFSA's Practical Arrangements concerning transparency and confidentiality as a consequence of confidentiality requests submitted by the applicant on application dossiers for pesticides active substances or Maximum Residue Levels, respectively. Please note that information disclosed in this report is without prejudice to pre-existing intellectual property rights and data exclusivity clauses set out in Union law, and particularly in Article 62 of Regulation (EC) No 1107/2009.

Minutes might be revised due to pending data gaps at the time of the meeting and /or eventual need for further follow up consultation after the meeting. If needed, the final agreement will be made available in the meeting report published at the end of the peer review process.

Subject	Conclusions Pesticide Peer Review Meeting
Experts' consultation 3.1 MSs experts to discuss the reliability and results of the available metabolism studies with respect: -Stability of the residues in these studies (OP3(17), OP3(29)) -Major metabolites and residue definitions relevant to the representative uses. Including discussion of the potential inclusion of metabolites pyrethrolone, pyrethric acid, based on their occurrence and toxicological characterization. -Uncertainty in relation to the stereoisomerism of the different metabolites (see OP 3(18) and 3(23)). -Whether further metabolism data may be needed. Among other further data may be needed:	The available metabolism studies with primary crops performed with pyrethrin 1 had shortcomings, i.e., no information on the fate of the other compounds of the active substance, i.e., pyrethrin 2, cinerin 1 and 2 and jasmolin 1 and 2 and only one of the four studies investigated the fate of the cyclopentenone-moiety. On this basis the **residue definition for risk assessment (RA RD)** for fruit upon foliar application is provisionally set as pyrethrins and pyrethrolone. The final residue definition will depend on the outcome of the residue field trials, the clarification with regard to the identity of the 5 signals in tomato extracts found in the TLC, the metabolism study with pyrethrin 2 and the toxicological profile of pyrethrolone. Potential candidates for the RA RD are also cyclopropyl-methyl hydroxylated chrysanthemic acid and dihydroxylated chrysanthemic acid after confirmation of their occurrence in residue field trials It is not clear from the tomato metabolism studies whether parent will be a good marker and depending on the data to be provided the residue definition for enforcement might be rediscussed/ extended to other crop categories For the moment being, the current **residue definition for enforcement for fruit crops** is proposed by default as pyrethrins.

Subject	Conclusions Pesticide Peer Review Meeting
1) To investigate the metabolism of pyrethrin II (pyrethrin 2, cinerin 2 and jasmolin 2), since pyrethric acid cannot be formed from pyrethrin 1 used in all the radiolabelled metabolism available. 2) To confirm the presence of pyrethrone as major metabolite and to identify conjugate metabolites. -In case RD for the representative uses is agreed, whether this residue definition can be extended for all crop groups (potential restriction in relation to application rate proposed by RMS). -If residue definition is agreed, to discuss if residue trials available are adequate and sufficient. Conversion factor for RD monitoring to RD risk assessment to be determined if possible. -Any other issue in relation of the metabolism data and residue definitions in plant matrices raised by the MSs comments.	**Data gap**: new metabolism studies with crops covering the representative uses performed with pyrethrin 2 with the cyclopropane- moiety labelled. The study should include as standards pyrethric acid and its hydroxylated forms and address the question whether conjugates occur. **Data gap**: further information from the recent tomato metabolism study with cyclopentenone-label should be provided to explain the different results obtained by HPLC and TLC analysis including information on the identity of the compounds TLC M1 to M5 as well as information on storage stability of the extracts. **Data gap**: evidence on the stability of pyrethrin in stored tomato specimen (processed or extracts) to sufficiently conclude on the reliability of the former tomato metabolism study (report number P0193018; MRID# 43554302) or to provide a new guideline metabolism study with a crop that covers the representative use and dosed sufficiently high to allow for identification of metabolites to investigate the fate of pyrethrin 1 labelled at the cyclopropane-moiety. **Data gap**: evidence on the storage conditions (temperature) and whether samples (whole or homogenised) or their extracts were stored for the indicated times (12 months for lettuce (Report P0193016; MRID# 43554303), 3 months for potato (Report P0193017 MRID# 43554301) and 12 months for tomato (report P0193018; MRID# 43554302)). **Data gap:** residue field trials performed according to the cGAP in both, greenhouse and outdoor, covering the representative uses and analysing for possible photolysis products (e.g. (E)-isomer see CA 7.2.1.2/1, report nr. P1192006) and pyrethrolone, cyclopropyl-methyl hydroxylated chrysanthemic acid, dihydroxylated chrysanthemic acid with a validated analytical method and covered by storage stability data. The analysis should also include potential conjugated forms. **Data gap:** investigation of the toxicological properties (both genotoxicity and general toxicity) of pyrethrolone, cyclopropyl-methyl hydroxylated chrysanthemic acid and dihydroxylated chrysanthemic acid. It should be noted that this data gap is provisional pending the additional requested data on residue trials and metabolism studies.

Subject	Conclusions Pesticide Peer Review Meeting
Experts' consultation 3.2 MS experts to discuss if the waiver for processing data proposed by the applicants is still acceptable taking into account any change in the RDs.	Since the residue definition is provisional due to data gaps, the need for processing data will need to be reassessed.
Experts' consultation 3.3 Experts to assess whether a revision of the consumer risk assessment is needed considering the agreed RD after the peer review.	Due to several data gaps on metabolism studies, residue trials, toxicological data the residue definition cannot be finalised and hence the consumer risk assessment cannot be performed.

REPORT OF PESTICIDE PEER REVIEW TC 103

PICLORAM – AIR III

Rapporteur Member State: PL

3. Residues

Date: 28 April 2023

List of participants:

Status	**Name of institution/attendee**
EFSA statutory staff member	EFSA
National Expert nominated by MS Austria	Austrian Agency for Health and Food Safety (AGES) (AT)
National Expert nominated by MS France (3)	Agence nationale de sécurité sanitaire de l'alimentation, de l'environnement et du travail (ANSES) (FR)
National Expert nominated by MS Greece (2)	Benaki phytopathological institute
National Expert nominated by MS Germany	German Federal Institute for Risk Assessment
National Expert nominated by MS Netherlands	Board for the Authorisation of Plant Protection Products and Biocides (Ctgb) (NL)
National Expert nominated by RMS Poland	National Institute of Public Health NIH - National Research Institute

In accordance with EFSA's Policy on Independence[1] and the Decision of the Executive Director on Competing Interest Management[2], EFSA screened the Annual Declarations of Interest filled out by the participants invited to the present meeting. No Conflicts of Interest related to the issues discussed in this meeting have been identified during the screening process, and no interests were declared orally by the members at the beginning of this meeting.

[1] http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/policy_independence.pdf

[2] http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/competing_interest_management_17.pdf

Discussion points/Outcome

3. Residues

Please note that information part of this report may have been masked by EFSA in accordance with Article 63 of Regulation (EC) No 1107/2009 as well as EFSA's Practical Arrangements concerning confidentiality in accordance with Articles 7 and 16 of Regulation (EC) No 1107/2009, or EFSA's Practical Arrangements concerning transparency and confidentiality as a consequence of confidentiality requests submitted by the applicant on application dossiers for pesticides active substances or Maximum Residue Levels, respectively. Please note that information disclosed in this report is without prejudice to pre-existing intellectual property rights and data exclusivity clauses set out in Union law, and particularly in Article 62 of Regulation (EC) No 1107/2009.

Minutes might be revised due to pending data gaps at the time of the meeting and /or eventual need for further follow up consultation after the meeting. If needed, the final agreement will be made available in the meeting report published at the end of the peer review process.

Subject	Conclusions Pesticide Peer Review Meeting
Experts' consultation 3.1 Experts to discuss the animal frozen storage stability data obtained in the context of the livestock feeding study, consider the data from the metabolism study and conclude whether storage stability can be established for picloram.	Taking into account the available data, residues of picloram can be considered stable for at least two months in milk, cream, muscle, liver, kidney, and fat when stored under frozen conditions. The analysis of the samples in the feeding study was conducted within that time frame. For poultry, freezer storage stability data are not available nor triggered. **Open point:** RMS to report in the updated RAR the procedural (freshly spiked) and stored recoveries according to Annex 2 of OECD TG 506 for study no.130022 and also add the storage stability data for kidney that are currently missing from the RAR
Experts' consultation 3.2 Experts to discuss the metabolism studies with wheat and oilseed with special emphasis 1) on the fact that they were not performed according to	Based on the metabolism studies in cereals and oilseeds, for the crop categories **pulses/oilseeds and cereals** the **residue definition for risk assessment** is • **Picloram, free and conjugated expressed as picloram** For **monitoring**, the existing residue definition is picloram only. The experts noted that because - according to the new study in oilseeds, the residues in seeds were largely present as conjugated picloram

Subject	Conclusions Pesticide Peer Review Meeting
agricultural practice, i.e. screenhouse and the possible impact on the metabolism, 2) the impact of the deviation of the application at critical growth stage 3) whether the characterisation attempts in oil seeds can be regarded as sufficient, 4) the possibility of [redacted] being an impurity rather than a metabolite and 5) the overall elucidation of the residues and conclude on their validity.	- in cereals a clear distribution of free and conjugated residues was not made, however the analytical report suggests that residues were mostly present as conjugates - that all residue trials in oilseeds were conducted with analysis of the sum of free and conjugated picloram, - and that a validated enforcement method analysing picloram, free and conjugated is available, it would be appropriate to propose a residue definition for monitoring as • **Picloram, free and conjugated expressed as picloram** As only studies in two crop categories as available, a global residue definition cannot be proposed in this review.
Experts' consultation 3.3 Experts to discuss finding of the ruminant and poultry metabolism study with respect to the amount and possible nature of unknowns and conclude on the validity of the two studies. On the basis of the findings and conclusion experts to propose residue definition for risk assessment and monitoring.	The metabolism studies in ruminants and poultry (new study) are acceptable and the unknown metabolites or metabolite fractions did not have to be further investigated due to very low individual levels. Based on the findings in these two metabolism studies, the animal residue definition for **risk assessment** should be • **Picloram, free and conjugated expressed as picloram** For **monitoring**, the residue definition should be the same as for risk assessment • **Picloram, free and conjugated expressed as picloram** **Open point for EFSA:** To review and confirm the analytical method for monitoring is capable to measure the conjugated picloram in animal commodities.
Experts' consultation 3.4 Experts to take note of the outcome of the consultation on the rate of degradation in soil for 4-	Based on the data available, it is proposed to set the same residue definition for **risk assessment** as for primary crops (see 3.2) • **Picloram, free and conjugated expressed as picloram**

Subject	Conclusions Pesticide Peer Review Meeting
amino-2,3,5,-trichloro-pyridine (also called ATCP or PYR) and discuss whether this metabolite is covered by the presented RC metabolism studies. Experts to consider also whether the PECsoil of picloram is covered by the application rate and conclude on the validity of the two metabolism studies in rotational crops and whether the metabolism can be considered equal to primary crops.	For **monitoring** it is proposed to apply the same residue definition as for the residue definition for primary crops (see 3.2) • **Picloram, free and conjugated expressed as picloram** Justification: The analytical method in the metabolism study did not clearly distinguish free and conjugated picloram, also in the field trials, free and conjugated picloram were extracted and analysed together. Based on observations in primary crops it is expected that residues will largly occur as conjugates. **Data gap:** Additional residue trials in rotational crops (Tier 3 studies) for the PBI 30 days according to OECD guidance to facilitate the assessment of whether specific MRLs have to be derived for rotational crops Justification: Residues in all rotational crops were observed at the 1st plant back interval (PBI 30 days) based on the available trials, and therefore, according to the OECD guidance, further investigations in additional crop groups are triggered.

REPORT OF PESTICIDE PEER REVIEW TC 103

PENOXSULAM – AIR IV

Rapporteur Member State: IT

3. Residues

Date: 28 April 2023

List of participants:

Status	**Name of institution/attendee**
EFSA statutory staff member	EFSA
National Expert nominated by MS Austria	Austrian Agency for Health and Food Safety (AGES) (AT)
National Expert nominated by MS France (3)	Agence nationale de sécurité sanitaire de l'alimentation, de l'environnement et du travail (ANSES) (FR)
National Expert nominated by MS Greece (2)	Benaki phytopathological institute
National Expert nominated by MS Germany	German Federal Institute for Risk Assessment
National Expert nominated by MS Netherlands	Board for the Authorisation of Plant Protection Products and Biocides (Ctgb) (NL)
National Expert nominated by RMS Italy	International center for pesticides and health risk prevention (ICPS)

In accordance with EFSA's Policy on Independence[1] and the Decision of the Executive Director on Competing Interest Management[2,] EFSA screened the Annual Declarations of Interest filled out by the participants invited to the present meeting. No Conflicts of Interest related to the issues discussed in this meeting have been identified during the screening process, and no interests were declared orally by the members at the beginning of this meeting.

[1] http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/policy_independence.pdf

[2] http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/competing_interest_management_17.pdf

Discussion points/Outcome

3. Residues

Please note that information part of this report may have been masked by EFSA in accordance with Article 63 of Regulation (EC) No 1107/2009 as well as EFSA's Practical Arrangements concerning confidentiality in accordance with Articles 7 and 16 of Regulation (EC) No 1107/2009, or EFSA's Practical Arrangements concerning transparency and confidentiality as a consequence of confidentiality requests submitted by the applicant on application dossiers for pesticides active substances or Maximum Residue Levels, respectively. Please note that information disclosed in this report is without prejudice to pre-existing intellectual property rights and data exclusivity clauses set out in Union law, and particularly in Article 62 of Regulation (EC) No 1107/2009.

Minutes might be revised due to pending data gaps at the time of the meeting and /or eventual need for further follow up consultation after the meeting. If needed, the final agreement will be made available in the meeting report published at the end of the peer review process.

Subject	Conclusions Pesticide Peer Review Meeting
Expert consultation 3.1 In the view of the requested additional information on the formulation type used in the studies and whether is similar or not to the one proposed for the representative GAP, expert's to discuss: 1. whether the available data in metabolism studies are sufficient to support the representative uses and to propose residue definitions in plant (primary and rotational). 2. Considering the results from the rotational metabolism studies and pending the additional tox data on the relevant metabolites expert's to discuss if further field rotational crop studies would be needed.	Plant metabolism studies in primary and rotational crops were sufficient to elucidate the metabolism of penoxsulam which was found to be similar in all three primary crop groups. It was noted that the kind of formulation might have an impact only on the quantitative aspects of the metabolism studies. For rotational crop metabolism studies it was not clear whether the application rate would cover the PECacc and therefore it could not be concluded whether to include BSTCA in the risk assessment. Plant **residue definition** for **risk assessment** and for **monitoring**: penoxsulam for all primary crops The **residue definition** for **rotational crops** as penoxsulam is provisional pending the open point and data gap. It is noted that in case BSTCA would be included in the residue definition, data on general toxicology are needed. **Open point**: RMS clarify whether the application rate used in the rotational crop metabolism study covers the max PECacc for BSTCA. **data gap pending the outcome of the open point**: rotational crop field trials (2 per zone) performed with an application rate covering the PECacc and analysing for penoxulam and BSTCA with validated analytical methods and covered by storage stability data are needed.

REPORT OF PESTICIDE PEER REVIEW TC 103

Paraffin oil CAS 8042-47-5 – AIR IV

Rapporteur Member State: EL

3. Residues

Date: 28 April 2023

List of participants:

Status	**Name of institution/attendee**
EFSA statutory staff member	EFSA
National Expert nominated by MS Austria	Austrian Agency for Health and Food Safety (AGES) (AT)
National Expert nominated by MS France (3)	Agence nationale de sécurité sanitaire de l'alimentation, de l'environnement et du travail (ANSES) (FR)
National Expert nominated by RMS Greece (2)	Benaki phytopathological institute
National Expert nominated by MS Germany	German Federal Institute for Risk Assessment
National Expert nominated by MS Netherlands	Board for the Authorisation of Plant Protection Products and Biocides (Ctgb) (NL)
National Expert nominated by MS Poland	National Institute of Public Health NIH - National Research Institute

In accordance with EFSA's Policy on Independence[1] and the Decision of the Executive Director on Competing Interest Management[2,] EFSA screened the Annual Declarations of Interest filled out by the participants invited to the present meeting. No Conflicts of Interest related to the issues discussed in this meeting have been identified during the screening process, and no interests were declared orally by the members at the beginning of this meeting.

[1] http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/policy_independence.pdf

[2] http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/competing_interest_management_17.pdf

Discussion points/Outcome

3. Residues

Please note that information part of this report may have been masked by EFSA in accordance with Article 63 of Regulation (EC) No 1107/2009 as well as EFSA's Practical Arrangements concerning confidentiality in accordance with Articles 7 and 16 of Regulation (EC) No 1107/2009, or EFSA's Practical Arrangements concerning transparency and confidentiality as a consequence of confidentiality requests submitted by the applicant on application dossiers for pesticides active substances or Maximum Residue Levels, respectively. Please note that information disclosed in this report is without prejudice to pre-existing intellectual property rights and data exclusivity clauses set out in Union law, and particularly in Article 62 of Regulation (EC) No 1107/2009.

Minutes might be revised due to pending data gaps at the time of the meeting and /or eventual need for further follow up consultation after the meeting. If needed, the final agreement will be made available in the meeting report published at the end of the peer review process.

Subject	Conclusions Pesticide Peer Review Meeting
Experts' consultation 3.1 MSs experts to discuss if the exception for consumers exposure data, requested by the applicants, is appropriate in this case taking into consideration the outcome of the toxicological peer review and information provided by the applicants against data requirements in 3(28) and 3(29). MSs to discuss if paraffin oil should remain in Annex IV of Reg. (EC) No 396/2005	The meeting agreed that the use of residue unit doses (RUD), usually employed in the risk assessment for birds and mammals, is not appropriate for consumer risk assessment. Furthermore, neither information on the proposed specification nor actual concentration data for [redacted] in paraffin oil are available. In the absence of such data and eventually data on background levels of [redacted] from other sources, a reliable exposure calculation is not feasible. **Data gap:** A residue estimation is requested for the impurity [redacted] using the approach based on application rate and yield rate. **Data gap (for section 1)**: Data on the actual concentration of [redacted] measured in the technical paraffin oil materials using a validated analytical method are needed to justify the assumptions made for the consumers exposure calculation, alternatively maximum theoretical [redacted] levels based on the pharmacopoeia method would need to be robustly justified. The following open points for the RMS were identified: **Open point:** RMS to update the RAR (Vol 1, Vol 3 B.7 and LoEP) to reflect the decision of the expert consultation. **Open point:** RMS to assess the applicability of the criteria for Annex IV to paraffin oil and to report the outcome in the RAR.

REPORT OF PESTICIDE PEER REVIEW TC 96

FENPROPIDIN – AIR III

Rapporteur Member State: CZ

3. Residues

Date: 26 January 2023

List of participants:

Institute	**Member States Country code**
Austrian Agency for Health and Food Safety (AGES)	AT
National Institute of Public Health	CZ
Federal Institute for Risk Assessment	DE
Benaki Phytopathological Institute	EL
National Institute for Agricultural and food research and technology (INIA)	ES
Agence nationale de sécurité sanitaire de l'alimentation, de l'environnement et du travail (ANSES)	FR
Board for the Authorisation of Plant Protection Products and Biocides (Ctgb)	NL

In accordance with EFSA's Policy on Independence[1] and the Decision of the Executive Director on Competing Interest Management[2,] EFSA screened the Annual Declarations of Interest filled out by the participants invited to the present meeting. No Conflicts of Interest related to the issues discussed in this meeting have been identified during the screening process, and no interests were declared orally by the members at the beginning of this meeting.

[1] http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/policy_independence.pdf

[2] http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/competing_interest_management_17.pdf

Discussion points/Outcome

3. Residues

Please note that information part of this report may have been masked by EFSA in accordance with Article 63 of Regulation (EC) No 1107/2009 as well as EFSA's Practical Arrangements concerning confidentiality in accordance with Articles 7 and 16 of Regulation (EC) No 1107/2009, or EFSA's Practical Arrangements concerning transparency and confidentiality as a consequence of confidentiality requests submitted by the applicant on application dossiers for pesticides active substances or Maximum Residue Levels, respectively. Please note that information disclosed in this report is without prejudice to pre-existing intellectual property rights and data exclusivity clauses set out in Union law, and particularly in Article 62 of Regulation (EC) No 1107/2009.

Minutes might be revised due to pending data gaps at the time of the meeting and /or eventual need for further follow up consultation after the meeting. If needed, the final agreement will be made available in the meeting report published at the end of the peer review process.

Subject	Conclusions Pesticide Peer Review Meeting
Experts' consultation 3.1 MS's experts to discuss if the stability of residues in plant and animal matrices has been sufficiently demonstrated by the available studies.	Based on the available information and considering the requirements in OECD test guideline 506, the following was agreed: Each of the 5 plant commodity categories (high water, high oil, high starch, high protein, high acid content) is represented by the commodities tested, and stability of fenpropidin was demonstrated over 24 months of frozen storage in these commodities. Therefore, the data allow for extrapolation across all plant commodity categories. For the sake of transparency, the reporting of storage stability data in the RAR has still to be improved. **Open point:** RMS to complement the reporting of all storage stability studies in plant commodities in the RAR by additional information in line with the OECD test guideline 506, such as crop tested and the individual stored recoveries for each sampling interval. For animal commodities, except eggs, the available information is insufficient to conclude on freezer storage stability for parent fenpropidin. Stability of fenpropidin, CGA289268 and CGA289267 over 4.5 months in eggs was demonstrated. Although the test conducted in the remit of the ruminant feeding study did not follow the OECD test guideline 506, the data may be acceptable to prove stability of the metabolites CGA289267 (24 months) and CGA289268 (30 months) in muscle, liver, kidney, fat and milk. For the sake of transparency, the reporting of storage stability data in animal commodities in the RAR has still to be improved.

Subject	Conclusions Pesticide Peer Review Meeting
	Open point: RMS to complement the reporting of storage stability tests in ruminant commodities in the RAR by additional information in line with the OECD test guideline 506 (Annex 2), such as the individual stored recoveries for each sampling interval, the value of day zero and the procedural recoveries for every storage interval, or clearly indicate if such information is not available **Data gap:** A freezer storage stability study to address the storage stability of parent fenpropidin in the specimens analysed in the feeding studies in ruminant and poultry (except eggs) over the relevant periods of sample storage in the feeding studies New freezer stability study in animal commodities, ref. 2020; VV-86836 is already available according to the applicant.
Experts' consultation 3.2 MSs experts to discuss the reliability of available metabolism studies in plants supporting the representative GAPs in cereals and the reliability of metabolism studies submitted to support other crops. MSs experts to discuss if the available information on the potential transformation or selective degradation of the stereoisomers of fenpropidin and its metabolites in plants is sufficient and how to consider the eventual related uncertainty. MSs experts to discuss the residue definitions for plant matrices on the light of available plant metabolism and field residue trial studies.	The experts agreed that the studies in spring wheat and sugar beet are reliable and can be used to elucidate the nature of residues in food and feed items for the categories cereal/grass crops and root crops, although some clarifications are still needed in the reporting of the study summaries in the RAR. Studies in grape and banana - not strictly necessary for assessment of the representative uses - are still scientifically relevant in the context of EU MRL assessments and for setting a global plant residue definition. Due to shortcomings in reporting these studies, further information is necessary, and a global plant residue definition for risk assessment is not set as outcome of this review, but the best marker for monitoring could still be identified. The plant residue definition for monitoring is proposed as sum of fenpropidin and its salts expressed as fenpropidin, and this definition is currently in place and confirmed by this review. For risk assessment, the residue definition for cereal grains and roots should be the sum of fenpropidin and its salts expressed as fenpropidin, while for feed items other than grains and roots, additional clarification is required to address the relevance of the metabolites CGA289263, CGA289268, and acyl glycoside dihydroxy CGA289267 for consumer risk assessment. The finalisation of residue definition for risk assessment is therefore pending for feed items. The following point for actions and data gaps were identified: <u>For the representative uses:</u> **Open point:**

Subject	Conclusions Pesticide Peer Review Meeting
	With regard to the 1994 metabolism study in spring wheat, further information should be extracted from the study report and included in the RAR: - on the correct identity of I13, and if applicable, the composition, number of compounds and individual levels of these compounds summarised under code I13; - on the identification attempts for the fraction of the unextracted radioactivity in grain that could not be attributed to starch but was still significant as a residue **Open point:** RMS to include the dietary burden calculations for metabolites CGA289263, CGA289268, and acyl glycoside dihydroxy CGA289267 in the RAR, based on the cereal metabolism studies **Data gap:** With regard to feed items, further information on the fate of metabolites CGA289263, CGA289268, and acyl glycoside dihydroxy CGA289267 in livestock, and/or toxicological information, at least on the genotoxic potential of these compounds is requested to enable further assessment if these metabolites could be potentially of concern if transferred through feed into animals <u>Overall scientific evidence /global residue definition:</u> **Open point:** With regard to all available plant metabolism studies, further information should be extracted from the study reports and included in the RAR regarding the metabolites identified and their codes for each of the studies, as inconsistencies were observed between Vol. 1 and the study summaries in Vol. 3, and this way several metabolites could not be unambiguously assigned a structure and assessed for their importance for the residue definition for risk assessment
Experts' consultation 3.3 MSs experts to discuss the residue definitions for animal matrices on the light of available metabolism and feeding studies.	The experts considered the available metabolism studies in hen and goat as acceptable despite some shortcomings. Following the best-marker concept, the residue definition for monitoring for all animal commodities is proposed as metabolite CGA289267 (2-methyl-2-[4-(2-methyl-3- piperidin-1-yl-propyl)-phenyl]propionic acid), and its salt, expressed as fenpropidin. The residue definition for poultry commodities for risk assessment was agreed as sum of fenpropidin and CGA289267, expressed as fenpropidin.

Subject	Conclusions Pesticide Peer Review Meeting
	For ruminant commodities, the residue definition for risk assessment should contain fenpropidin, CGA 298267, SYN515213, SYN515213 sulphate ester, CGA 298268 sulphate ester. Whether expression of all residues as fenpropidin is appropriate, is pending information on the toxicity of the metabolites SYN515213, SYN515213 sulphate ester, CGA 298268 sulphate ester. Although the compounds included do not differ from those considered in previous reviews (peer review and MRL review), the residue definition for risk assessment in ruminant is provisional, pending its appropriate expression for consumer risk assessment. **Open point** The efforts to identify metabolite IA5b in poultry liver in the hen metabolism study should be further described in the RAR, as well as the tentative structure, and as appropriate, reasons why the identity of this metabolite could not be confirmed **Data gaps proposed for section on mammalian toxicology:** The toxicology should be addressed for metabolites SYN515213, SYN515213 sulphate ester, CGA 298268 as to whether the TRVs of fenpropidin can be applied or separate TRVs would be more appropriate A genotox assessment for SYN 515216 and SYN 515215 sulfate ester conjugate is requested
Experts' consultation 3.4 MSs experts to discuss the reliability of available field studies once the missing information is updated in the RAR. MSs to decide if enough reliable trials are available to support the representative GAPS	Independency of some of the available residue field trials in cereals was questioned by the experts, and a reassessment of the trials should be made by the RMS to establish the number of reliable and independent trials. **Open Point:** RMS to assess independency of the cereal residue trials in view of concerns raised over the same geographical locations and timing used in some of the trials **Data gap:** Pending the finalisation of the residue definition for risk assessment in primary crop feed items, additional residue trials might become necessary with analysis of parent and metabolites CGA289263, CGA289268, and acyl glycoside dihydroxy CGA289267 in cereal feed items, supported by a validated analytical method and, where appropriate, data demonstrating integrity of all residues during storage See expert consultation point 3.2

Subject	Conclusions Pesticide Peer Review Meeting
Experts' consultation 3.5 MSs experts to discuss if livestock feeding studies available are satisfactory and sufficient taking into account updated information and dietary burdens. MSs experts to discuss if the feeding studies are satisfactory with respect to the investigation of the levels of residues of metabolite CGA289268 or if further studies are needed. MSs experts to discuss if the available information on the potential transformation or selective degradation of the stereoisomers of fenpropidin and its metabolites in animals is sufficient and how to consider the eventual related uncertainty. MSs experts to discuss the adequacy of the MRL calculations in animal matrices.	The poultry study is considered guideline compliant and acceptable, confirming the presence of residues of fenpropidin and CGA289267 above LOQ for the dosing levels studied in line with the residue definitions set for poultry. For ruminants, also residues of fenpropidin and CGA289267 were found, and CGA 298268 at the highest dose, while it needs to be confirmed whether a major metabolite CGA 298268 sulphate ester conjugate was also determined in this study together with CGA 298268. SYN 515213 and SYN515213 sulphate ester conjugate were not determined and should be estimated to complete the consumer risk assessment in order to not request a new vertebrate study. Note: Storage stability data for fenpropidin to validate the levels in animal matrices other than eggs are still pending (see 3.1.). Information on isomers was also not available. **Open point:** Information if the conditions in the analytical method used in the ruminant feeding study would have been able to extract, cleave and determine the CGA 298268 sulphate ester conjugate as CGA298268 **Open point:** An estimation of residue levels of SYN 515213 and SYN515213 sulphate ester conjugate in animal commodities, as these compounds as a sum constitute the highest fractions of the total residues in the ruminant metabolism study (19.1% TRR in liver, 29.3% in kidney, 40.7% in muscle, 27.6% in fat, 25.5% in milk) but where not determined in the feeding study **Data gap:** The potential preferential degradation of isomers should be addressed, and the impact of the absence of this information for the consumer risk assessment
Experts' consultation 3.6 MSs experts to discuss the nature and magnitude of residues in rotational crops taking into account the new studies to be submitted by the applicant.	Based on the information from the confined studies and residue trials in rotational crops, the same monitoring residue definition as for primary crops should apply: Sum of fenpropidin and its salts expressed as fenpropidin. This is confirming the residue definition for monitoring currently in place. For the time being, it was agreed that the following residue definition for risk assessment is applicable for rotational crops: Sum of fenpropidin and its salts expressed as fenpropidin. The proposed residue definition is pending the proof of stability data for the metabolites CGA289263, CGA289267, CGA289268

Subject	Conclusions Pesticide Peer Review Meeting
	analysed in the tier 2 rotational crop field trials, as to ensure there was not decline in samples <LOQ during storage. **Open point:** RMS to clarify why further PBIs were not investigated, and verify and transparently report the identity of Fenpropidin-3-hydroxylic and Fenpropidin-4-hyroxylic compounds from the 2008 confined rotational crop study in the RAR **Data gap:** As only an interim study with 2 PBIs was available on the magnitude of residues, the finalised study report investigating all 3 PBIs is requested **Data gap:** A freezer storage stability study with metabolites CGA289263, CGA289267, CGA289268 in relevant commodities to demonstrate integrity of residues during freezer storage <u>For risk management consideration:</u> Residues of fenpropidin in succeeding crops cannot be excluded. If MRLs should be set for rotational crops, additional residue trials (tier 3) are necessary to establish robust residue levels to derive such MRLs.
Overall additional Open point	Open point for RMS to update the RAR according to the agreements of the expert consultation.

REPORT OF PESTICIDE PEER REVIEW TC 96

BIPHENYL-2-OL (2-PHENYLPHENOL)- AIR IV Rapporteur Member State: ES

3. Residues

Date: 26 January 2023

List of participants:

Institute	**Member States Country code**
Austrian Agency for Health and Food Safety (AGES)	AT
National Institute of Public Health	CZ
Federal Institute for Risk Assessment	DE
Benaki Phytopathological Institute	EL
National Institute for Agricultural and food research and technology (INIA)	ES
Agence nationale de sécurité sanitaire de l'alimentation, de l'environnement et du travail (ANSES)	FR
Board for the Authorisation of Plant Protection Products and Biocides (Ctgb)	NL

In accordance with EFSA's Policy on Independence[1] and the Decision of the Executive Director on Competing Interest Management[2,] EFSA screened the Annual Declarations of Interest filled out by the participants invited to the present meeting. No Conflicts of Interest related to the issues discussed in this meeting have been identified during the screening process, and no interests were declared orally by the members at the beginning of this meeting.

[1] http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/policy_independence.pdf
[2] http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/competing_interest_management_17.pdf

Discussion points/Outcome

3. Residues

Please note that information part of this report may have been masked by EFSA in accordance with Article 63 of Regulation (EC) No 1107/2009 as well as EFSA's Practical Arrangements concerning confidentiality in accordance with Articles 7 and 16 of Regulation (EC) No 1107/2009, or EFSA's Practical Arrangements concerning transparency and confidentiality as a consequence of confidentiality requests submitted by the applicant on application dossiers for pesticides active substances or Maximum Residue Levels, respectively. Please note that information disclosed in this report is without prejudice to pre-existing intellectual property rights and data exclusivity clauses set out in Union law, and particularly in Article 62 of Regulation (EC) No 1107/2009.

Minutes might be revised due to pending data gaps at the time of the meeting and /or eventual need for further follow up consultation after the meeting. If needed, the final agreement will be made available in the meeting report published at the end of the peer review process.

Subject	Conclusions Pesticide Peer Review Meeting
Expert consultation 3.1 Experts to discuss the metabolism studies with pears and oranges with respect to deviations from guidelines and conclude whether they are suitable to elucidate the metabolism of 2-phenylphenol (biphenyl-2-ol, OPP) in these crops in view of the identified metabolites and whether a common metabolic pathway can be depicted for fruit crops following post-harvest treatment by dipping. Experts should also discuss whether the studies which were conducted with the sodium salt of OPP can be acceptable to depict the metabolism of OPP in these crops.	The use of the 2-phenylphenol (biphenyl-2-ol, OPP) sodium salt instead of OPP in the metabolism studies was found acceptable since the salt will dissociate into the main compounds and do not impact the metabolism. The extraction procedure and the storage time of the specimen were discussed in the view of potential impact on the results. Both studies available were found reliable and fully acceptable to support the representative GAP. **Open point**: RMS to check the magnitude of residues in citrus trials for compliance of phenylhydroquinone (PHQ) with storage stability data (see also experts' consultation point 3.3)
Experts' consultation 3.2	Based on the available overdosed study conducted in goat and showing high rate of radioactivity excretion (more than 90% of the total radioactive residues (TRR)) and a low absorption level,

Subject	Conclusions Pesticide Peer Review Meeting
Experts to discuss upon presentation of the detailed reporting whether the results of the ruminant metabolism study permit to derive animal residue definitions (RDs). If so, experts should conclude on RDs. Experts should also discuss whether the metabolism of ruminants and rats could be considered as similar.	the residues were not identified and hence the metabolic pattern was not elucidated. On this basis the experts proposed the **residue definitions for monitoring and risk assessment** as "biphenyl-2-ol (2-phenylphenol), by default". They are limited to ruminants.
Experts' consultation 3.3 Experts to discuss whether it is possible and if feasible to propose plant residue definitions on the basis of the existing two metabolism studies with orange and pears. Experts should consider also the outcome of the toxicological properties of the metabolites. For the validity of the studies, see also expert consultation point 3.1.	Based on the data from the metabolism studies (see experts' consultation 3.1) and considering the results from supervised residue and processing trials the **residue definitions for monitoring and risk assessment** were agreed as**:** "Sum of biphenyl-2-ol (2-phenylphenol) and its conjugates expressed as biphenyl-2-ol (2-phenylphenol)." The residue definitions are limited to post-harvest treatment on fruits and fruiting vegetables. **Data gap** (for mammalian toxicology) to address the genotoxicity profile of phenylhydroquinone (PHQ). See also the open point from expert consultation 3.1.
Overall additional Open point	**Open point** for RMS to update the RAR according to the agreements of the expert consultation.

REPORT OF PESTICIDE PEER REVIEW TC 83

GLYPHOSATE – AIR V

Rapporteur Member State: Assessment Group on Glyphosate (AGG) consisting of FR, HU, NL, SE

3. Residues

Date: 2 December 2022

List of participants:

Institute	**Member States Country code**
Austrian Agency for Health and Food Safety (AGES)	AT
Federal Institute for Risk Assessment (BfR)	DE
Agence nationale de sécurité sanitaire de l'alimentation, de l'environnement et du travail (ANSES)	FR
National Food Chain Safety Office (NEBIH)	HU
Department of Agriculture, Food & Marine (DAFM) Ireland	IE
Board for the authorisation of plant protection products and biocides (Ctgb)	NL
Swedish Food Agency	SE
External experts (2)	EFSA

In accordance with EFSA's Policy on Independence[1] and the Decision of the Executive Director on Competing Interest Management[2,] EFSA screened the Annual Declarations of Interest filled out by the participants invited to the present meeting. No Conflicts of Interest related to the issues discussed in this meeting have been identified during the screening process, and no interests were declared orally by the members at the beginning of this meeting.

[1] http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/policy_independence.pdf
[2] http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/competing_interest_management_17.pdf

Discussion points/Outcome

3. Residues

Please note that information part of this report may have been masked by EFSA in accordance with Article 63 of Regulation (EC) No 1107/2009 as well as EFSA's Practical Arrangements concerning confidentiality in accordance with Articles 7 and 16 of Regulation (EC) No 1107/2009, or EFSA's Practical Arrangements concerning transparency and confidentiality as a consequence of confidentiality requests submitted by the applicant on application dossiers for pesticides active substances or Maximum Residue Levels, respectively. Please note that information disclosed in this report is without prejudice to pre-existing intellectual property rights and data exclusivity clauses set out in Union law, and particularly in Article 62 of Regulation (EC) No 1107/2009.
Minutes might be revised due to pending data gaps at the time of the meeting and /or eventual need for further follow up consultation after the meeting. If needed, the final agreement will be made available in the meeting report published at the end of the peer review process.

Subject	Conclusions Pesticide Peer Review Meeting
Experts' consultation 3.1 Experts to discuss the validity and the results of the storage stability studies in plant matrices and to conclude on the maximal storage time for which acceptable frozen storage stability has been demonstrated for all compounds included in the agreed plant residue definitions for monitoring and risk assessment. Special emphasis should be given to the following points: -Acceptable storage stability of glyphosate, AMPA and other compounds in the different plant matrices, - the use of mixed spiking solution of glyphosate, N-acetyl-glyphosate and AMPA	Based on the available information and considering the OECD test guideline 506, the following frozen storage stability periods were agreed: For **glyphosate**: High water content commodities: 24 months High protein content commodities: 18 months Oilseeds: 12 months - no extrapolation proposed across the category of high oil content commodities High starch content commodities: 24 months Citrus fruit: 24 months – no extrapolation proposed across the category of high acid content commodities Straw and stover: 12 months, or longer for individual matrices An overall extrapolation was confirmed for the frozen storage stability of glyphosate of at least 12 months for all commodities, including processed commodities. Individual commodities or categories are covered by longer storage stability periods. For **AMPA**: High water content commodities**:** at least 6 months across the commodities in this category due to decline observed in stored clover samples, while for several individual commodities in this category longer storage periods are supported by the data.

Subject	Conclusions Pesticide Peer Review Meeting
in several storage stability studies, -the representativeness of sample preparation in the storage stability studies for the metabolism studies and the field residue trials, -the suitability of the analytical methods including extraction efficiency used.	High protein content commodities: 12 months (based on a study submitted after the public consultation) Oilseeds: 12 months – no extrapolation proposed across the category of high oil content commodities High starch content commodities: 12 months Citrus fruit: 24 months – no extrapolation proposed across the category of high acid content commodities In "other commodities", sample storage stability was matrix dependent. An overall extrapolation was confirmed for the storage stability of AMPA of at least 6 months for all commodities, including processed commodities. Individual commodities or categories are covered by longer storage stability periods. The conclusions reached on the frozen storage stability on AMPA and glyphosate do not trigger a reassessment of the rotational crop residue trials, while they did for primary crops trials. The processing trials should also be reviewed in that context. **Open point:** RMS to assess the residue trials in primary crops and the processing trials in the light of the conclusions reached in the meeting on the storage stability of AMPA and glyphosate in frozen samples.
Experts' consultation 3.2 Experts to discuss the results and validity of the storage stability studies in animal matrices (study 1 and 2/3) and conclude on the maximal storage time for which stability has been demonstrated especially for AMPA in fat matrices (poultry, pig and ruminant) and glyphosate in milk. Special	Based on the available storage stability and analytical methods data, considering also the sample preparation, study 1 was agreed as fully acceptable, and study 3 with the limitation to milk only. Study 2 is not acceptable. Satisfactory frozen sample storage stability was demonstrated as agreed by the meeting as follows: **For AMPA:** Pig fat: 15 months Cow fat: 24 months Chicken fat: 25 months

Subject	Conclusions Pesticide Peer Review Meeting
emphasis should be given to the representativeness of sample preparation in the storage stability studies for the metabolism and feeding studies and the suitability/validity of the analytical methods used.	**For glyphosate:** Milk: 22 months Data on other commodities and analytes were not requested to be further discussed, and for them the assessment in the RAR is considered agreed.
Experts' consultation 3.3 Experts to discuss the potential impact of the use of trimesium salt in glyphosate plant studies (metabolisation, uptake through leaves and from soil, magnitude of residues) and the representativeness of such studies to inform on the uptake and metabolism of glyphosate acid and isopropylamine salt (representative technical and formulation). In case these studies are not considered fully representative, MSs to discuss if additional studies performed with the representative active substance and formulation need to be provided.	Metabolism studies in plants conducted with glyphosate trimesium can be used to support the assessment of the metabolism of glyphosate in plants. Studies conducted with the trimesium, diammonium and isopropylamine salt formulations showed that no differences - neither in the rate nor the amount absorbed – were observed when compared. The plant species is much more decisive for the absorbed and translocated amount than the salt present in the formulation used.
Experts' consultation 3.4 MSs experts: -to discuss if sufficient and reliable metabolism studies	*In the remit of this report the term 'conventional crop' refers to a traditionally bred variety that dies when treated with glyphosate, and 'glyphosate tolerant crop' to a crop variety, that maintains agronomic yield when treated with glyphosate; currently this is achieved by genetic modification.*

Subject	Conclusions Pesticide Peer Review Meeting
are available to support all the representative uses. -to propose a residue definition for risk assessment and monitoring for the representative uses, considering also potential residues in rotational crops to the representative uses. -to decide if the information available allows to extend the residue definitions proposed to other crop groups and if general residue definitions (RD) can be proposed (including monitoring RD to enforce MRLs in imported crops).	The experts agreed that the data selected as reliable were sufficient to use to elucidate the metabolic pathway and the nature of residues in plants to cover all crop categories. Based on the evidence submitted in the metabolism studies with conventional and glyphosate tolerant crops, separate **residue definitions for risk assessment** were set: 1) Conventional crops: Sum of glyphosate, AMPA, expressed as glyphosate. 2) Glyphosate tolerant crops: Sum of glyphosate, AMPA, N-acetyl glyphosate and N-acetyl AMPA, expressed as glyphosate. Glyphosate tolerant crops are currently not grown in the EU; however, imports of such crops are possible. For **monitoring**, two options were proposed for risk management consideration. Both options address crops with glyphosate tolerant modifications that were identified as being on the market in 2019 and consider specific metabolites that prevail in the crops. **Option 1 - According to Codex (FAO-WHO, 2019)[3]:** 1) For soya bean, oilseed rape (OSR), maize (including sweet corn): Sum of glyphosate and N-acetyl glyphosate, expressed as glyphosate 2) All other crops: Glyphosate only **Option 2- According to the proposal in the EFSA MRL Art.12 Reasoned Opinion of 2019[4]**, including also the metabolite AMPA: 1) For soya bean, OSR, cotton, maize (including sweet corn), sugar beet: Sum of glyphosate, AMPA and N-acetyl glyphosate, expressed as glyphosate 2) All other crops: Glyphosate only **Open point:**

[3] FAO and WHO. 2019. *Pesticide residues in food 2019 – Extra Joint FAO/WHO Meeting on Pesticide Residues Evaluation Part I: Residues*. Rome. https://www.fao.org/publications/card/en/c/CA6010EN/
[4] EFSA (European Food Safety Authority), 2019. Review of the existing maximum residue levels for glyphosate according to Article 12 of Regulation (EC) No 396/2005 – revised version to take into account omitted data. EFSA Journal 2019;17(10):5862 doi:10.2903/j.efsa.2019.5862

Subject	Conclusions Pesticide Peer Review Meeting
	RMS to cross-check the publications Eaton et al., 2022 (doi: 10.1016/j.ecoenv.2022.113300) and the therein referenced article Grandcoin, et al., 2017 (doi.org/10.1016/j.waters.2017.03.055), and other relevant literature sources given there in the context of assessing the evidence of other sources of AMPA from phosphonate detergents passing through sewage treatment and the practice of sewage sludge used as agricultural fertilizer.
Experts' consultation 3.5 Experts to discuss the validity of all animal metabolism studies with special emphasis on the tested materials (suitability of mixtures and equivalence of trimesium glyphosate), the overall extraction rate and the characterisation/identification. Special attention should be given to the characterisation/identification in milk and shortcomings of the studies. Experts should conclude on the suitability of the studies to elucidate the metabolism in animals. On the basis of the valid studies experts to discuss and agree on the animal residue definition for risk assessment and monitoring.	It was agreed that qualitatively the glyphosate trimesium data could be relied on to derive residue definitions. The experts agreed that the available data were sufficient to elucidate the metabolic pathway and the nature of residues present in animal commodities. The following residue definitions were agreed: **Residue definition for risk assessment in animal commodities:** **Considering the representative uses only**: sum of glyphosate and AMPA, expressed as glyphosate. In the context of **future MRL-setting procedures**: sum of glyphosate, AMPA, N-acetyl glyphosate and N-acetyl AMPA, expressed as glyphosate. **Residue definition for monitoring of animal commodities:** **Considering also future MRL-setting procedure**: sum of glyphosate and N-acetyl glyphosate, expressed as glyphosate.
Experts' consultation 3.6	The "risk envelope approach"[5] is not applicable in the context of the risk assessment of the active substance. The experts discussed and

[5] Guidance document SANCO/11244/2011 rev. 5 of 14 March 2011 on the preparation and submission of dossiers for plant protection products according to the "risk envelope approach".

Subject	Conclusions Pesticide Peer Review Meeting
Experts to discuss whether the reported residue trials can be considered as acceptable to support the representative uses despite the deviations noted for these trials compared to the Good Agricultural Practices (GAPs) regarding the number of applications, the pre-harvest interval (PHI) values at harvest, and the deficiencies identified as regards the lack of storage stability data on metabolites and validation data of the analytical methods. The results of the available metabolism studies in primary and rotational crops should also be considered as a support to this discussion as regards the potential soil uptake, translocation and accumulation of the residues throughout the plants following glyphosate application. Based on the overall discussion and agreement reached under this point, the applicability of the "risk envelope approach" to adequately address the magnitude of residues for all crops and crop groups according to the	agreed the approach for the assessment of the residue trials data set on the basis of the technical guideline SANTE/2019/12752[6]. It was agreed that the data indicated that residues were in the category between the limit of detection (LOD) and the limit of quantification (LOQ). The experts identified some situation where wider extrapolation between crops might be accepted based on whether the GAP have crops present at the time of application or not. Except for these situations, overall the outcome resulted in the following open points and data gap: **Data gap:** A sufficient number of residue trials for table olives in Northern EU (NEU). Note: Data gap identified in the RAR and confirmed by the meeting. **Open point:** RMS to update the RAR with the assessment of residue trials for olives picked from the ground. **Open point:** RMS to clarify the method used in the residue trials in olives with regard to the extraction solvent used, because there is a mismatch for the extraction solvent reported in RAR Vol.3 B.5 and B.7, and therefore it may not be the same method. **Open point:** RMS to assess the available trials with pre-sowing / pre-planting, pre-emergence uses a) taking into account the decision on storage stability data for the different commodities and categories b) identify where additional trials would be necessary for the different crops and zones requested in the GAP table, when assessed in line with the technical guidelines SANTE/2019/12752.

[6] Technical guidelines on data requirements for setting maximum residue levels, comparability of residue trials and extrapolation of residue data on products from plant and animal origin (Repealing and replacing the existing Guidance Document SANCO 7525/VI/95 Rev. 10.3).

Subject	Conclusions Pesticide Peer Review Meeting
representative uses, as proposed by the RMS, should be further discussed.	It is noted that all MS experts including the RMS disagreed with step b) of this open point and only EFSA considered step b) in this open point necessary. **Open point:** RMS to assess the available trials with inter-row uses a) taking into account the decision on storage stability data for the different commodities and categories b) identify where additional trials would be necessary for the different crops and zones requested in the GAP table, when assessed in line with the technical guidelines SANTE/2019/12752. It is noted that the RMS and the majority of MS experts disagreed with step b) of this open point while there was a minority opinion of EFSA and one MS expert considering step b) in this open point necessary.
Experts' consultation 3.7 Experts to discuss the relevance of all presented feeding studies (poultry, ruminant and swine) with respect to the administered substance(s) and in relation to the agreed animal residue definition and conclude on the validity of these feeding studies. Special emphasis should be given to the analytical methods used and the updated dietary burden calculation.	**Feeding studies** - **with N-acetyl glyphosate:** The studies are scientifically acceptable but were not used for the risk assessment because the metabolite is not formed in conventional crops that are assessed by the renewal review. - **with glyphosate-trimesium:** The study in poultry was not acceptable. The ruminant study was acceptable with the limitation to the milk commodity but should only be used if it is demonstrated that absorption, distribution and residue quantities in the study with the trimesium salt do not differ compared to glyphosate ion. - **with glyphosate : AMPA mixture (9:1):** The study is acceptable to assess the representative uses. Future use of the study would depend on the contribution of glyphosate and AMPA calculated in the animal diet consequent to the uses being assessed in the future. A minor update is requested for the dietary burden calculation and a change of the conclusions reached on residue levels is not expected. **Open point:**

Subject	Conclusions Pesticide Peer Review Meeting
	Dietary burden calculation should be repeated not including primary crop residue levels for cereal commodities. **Open point:** RMS to assess the data in the poultry feeding study 3 in terms of the duration of frozen sample storage for eggs to confirm that the sample storage time was less than 14 months. Residues in animal commodities with regard to the representative uses were assessed to be below the LOQ of the analytical method, pending confirmation that the data for eggs are reliable (see sample storage duration clarification task in the open point above).
Experts' consultation 3.8 Experts to discuss whether the nature of residues at the standard hydrolysis conditions for processing has been sufficiently investigated according to the data requirements for all compounds (glyphosate, AMPA, N-acetyl AMPA and N-acetyl glyphosate) that may potentially be included in the monitoring and risk assessment residue definitions for plants in view of the deviations/deficiencies identified in Study 1 CA 6.5.1/001 and in Study 3 CA 6.5.1/003.	Based on the available 3 studies (assessed as acceptable following justification provided by the applicants), the stability of the 4 compounds (glyphosate, AMPA, N-acetyl glyphosate and N-acetyl AMPA) included in the different residue definitions for monitoring and risk assessment under the standard hydrolysis conditions had been demonstrated.
Experts' consultation 3.9 Experts to discuss if the available information (metabolism studies and field	The experts agreed that the data selected as reliable were sufficient to use to elucidate the metabolic pathway and the nature of residues in rotational crops. Based on the evidence submitted in the metabolism studies with conventional crops, the following

Subject	Conclusions Pesticide Peer Review Meeting
residue trials) is sufficient to characterise the nature and magnitude of the residues expected in rotational crops from the representative uses and if any additional component needs to be added to the residue definitions in plants (risk assessment and monitoring) to inform the potential residues in rotational crops.	**Residue definition for risk assessment in rotational crops were derived for** all conventional rotational crops: Sum of glyphosate and AMPA, expressed as glyphosate. For glyphosate tolerant rotational crops, additional data would have to be submitted to address the potential relevance of additional metabolites (e.g. N-acetyl glyphosate and N-acetyl AMPA), should glyphosate tolerant crops be authorised in the EU in the future. **Residue definition for monitoring in rotational crops is proposed as:** Glyphosate by default. With regard to the studies on the magnitude of residues in rotational crops, data gaps were identified as the data package is still to be completed in view of the data requirements. **Data gap:** The ongoing two trials in rotational crops should be completed. **Data gap:** Two additional trial sites should be investigated for rotational crops. In order to increase the variety of crops tested it is suggested that the applicants test different crops to those already investigated.
Experts' consultation 3.10 Experts to discuss the residue definition in honey and bee products and the MRL derived for honey and bee products for the representative uses from the field trials available and information from the scientific literature.	The residue definitions derived for plant commodities (see expert consultation point 3.4) should also be applicable to honey in line with the guidance SANCO 11956/2016 rev. 9[7]. To establish MRLs in honey, the available four supervised trials (analysing glyphosate and AMPA) in Phacelia fields should be used in line with the guidance SANCO 11956/2016 rev. 9.

[7] Technical guidelines Sante/11956/2016 rev. 9 from 14 September 2018- Technical guidelines for determining the magnitude of pesticide residues in honey and setting Maximum Residue Levels in honey.

Subject	Conclusions Pesticide Peer Review Meeting
New experts' consultation point 3.11 proposed by EFSA for completeness of discussion (October 2022): Experts to consider some potentially relevant newly available publications arisen after the public consultation/reporting table stage. EFSA identified a number of publications that might be considered potentially relevant and therefore it was agreed to share these selected studies with MSs to allow a peer review and further consideration in the expert meetings. In particular, MS experts are asked to share their views whether these potentially relevant articles might be considered more critical or may alter the weight of evidence in the current assessment and to determine if any eventual follow up would be needed.	Formally, in line with the legislation, there is no legal obligation to consider newly available data submitted outside of the dedicated public and targeted consultations or after the deadline of the window for providing the additional information within the clock stop period, unless they constitute adverse data (cf Article 56 of Regulation (EC) No 1107/2009 regarding information on potentially harmful or unacceptable effects). For this reason, although a systematic review of the literature has not been carried out by EFSA or RMS, EFSA has identified newly available papers on glyphosate even outside of the legal requirements and collected a list of studies as a result. The experts agreed that none of the publications identified in the area of Residues were relevant for the assessment of the renewal of glyphosate.
	Based on the discussions and conclusions in the meeting, a general follow-up action for the RMS was identified as necessary: **Open point**: RMS to systematically update Vol.1, Vol.3 of the RAR and the list of endpoints in line with the agreements of the peer review experts' meeting. **Open point**:

Subject	Conclusions Pesticide Peer Review Meeting
	RMS to provide a screening assessment for the existing MRLs for glyphosate in the light of the conclusions of the peer review experts' meetings in residues and in mammalian toxicology, considering changes in terms of residue definitions and the toxicology of glyphosate and its metabolites.

REPORT OF PESTICIDE PEER REVIEW TC 76

(3E) 3-DECEN-2-ONE – NAS Rapporteur Member State: NL

3. Residues

Date: 05 May 2022

List of participants:

Institute	**Member States Country code**
Federal Institute for Risk Assessment (BfR)	DE
Agence nationale de sécurité sanitaire de l'alimentation, de l'environnement et du travail (ANSES)	FR
Board for the Authorisation of Plant Protection Products and Biocides (Ctgb)	NL

In accordance with EFSA's Policy on Independence[1] and the Decision of the Executive Director on Competing Interest Management[2,] EFSA screened the Annual Declarations of Interest filled out by the participants invited to the present meeting. No Conflicts of Interest related to the issues discussed in this meeting have been identified during the screening process, and no interests were declared orally by the members at the beginning of this meeting.

[1] http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/policy_independence.pdf
[2] http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/competing_interest_management_17.pdf

Discussion points/Outcome

3. Residues

Please note that information part of this report may have been masked by EFSA in accordance with Article 63 of Regulation (EC) No 1107/2009 as well as EFSA's Practical Arrangements concerning confidentiality in accordance with Articles 7 and 16 of Regulation (EC) No 1107/2009, or EFSA's Practical Arrangements concerning transparency and confidentiality as a consequence of confidentiality requests submitted by the applicant on application dossiers for pesticides active substances or Maximum Residue Levels, respectively. Please note that information disclosed in this report is without prejudice to pre-existing intellectual property rights and data exclusivity clauses set out in Union law, and particularly in Article 62 of Regulation (EC) No 1107/2009.
Minutes might be revised due to pending data gaps at the time of the meeting and /or eventual need for further follow up consultation after the meeting. If needed, the final agreement will be made available in the meeting report published at the end of the peer review process.

Subject	Conclusions Pesticide Peer Review Meeting
Experts' consultation 3.1 MSs experts to discuss if it has been demonstrated that residues are stable in available residue trials (considering information in the original ones and the new trials submitted)	Although standard storage stability studies were not provided, the meeting concluded that both the precautionary measures and the conditions of extraction and analysis, that characterized the experimental design in the trials, prevent the degradation of the residues through volatilization. The results of the residue trials can be considered as acceptable.
Experts' consultation 3.2 Experts to discuss the results of the metabolism study and the residue definition in tuber (both for risk assessment and monitoring) considering the result of the toxicological assessment on the relevance of the metabolites identified.	The meeting discussed the acceptability of the metabolism study considering the several shortcomings/deviations from the guidelines that were identified in this recent study (2020), i.e. deviation compared to the representative uses (total dose rate of application and number of applications: 1 instead of 4 applications), lack of characterization/identification of the total residues in the different fractions of the treated potatoes (rinse, peel and pulp). The meeting concluded that this metabolism study cannot be considered as fully guideline-compliant, and it is recommended that the applicant provides further analytical efforts to identify the unknowns that were found in significant concentrations in the different potato fractions. A **data gap** is set for the applicant to undertake all the analytical attempts to characterize and identify the unknown radioactive residues

Subject	Conclusions Pesticide Peer Review Meeting
	in whole potatoes fractions (rinse, peel, pulp) in order to comply with the current data requirements. **Open point**: RMS to report the detailed results of the analysis of the potato rinse fraction (extraction steps and metabolites characterization and identification and their respective occurrence in *„% TRR*" and *„mg/kg*") in a revised RAR. RMS also to present a consolidated table including the different steps of extractabilities, rinse fraction and rate of characterization and identification in whole potato and expressed as a percentage of the total radioactive residues in whole potato tuber in line with the OHT OECD tables. Special care should be taken to ensure that TRR refers actually to the total residue in the tuber and not in the fraction or part analysed. The RAR should be revised accordingly. The experts agreed on the following RDs: -**For monitoring**: „3-Decen-2-one" as the parent compound was considered as a valid marker of the total residues from the metabolism study and the GAP-compliant residue trials. -**For risk assessment**: Sum of 3-decen-2-one, 2-decanone and 2-decanol (free and conjugated) and 3-decen-2-ol (free and conjugated), expressed as 3-decen-2-one – **Provisional** The RD for risk assessment should be considered as provisional and will be revisited pending upon the outcome of the requested data and the toxicological properties of 3-decen-2-ol (free and conjugated) (see data gaps). The proposed residue definitions are restricted to root crops following treatment in storage. **Data gap for section 2**: The genotoxicity potential and general toxicity of the metabolite 3-decen-2-ol (free and conjugated) should be addressed.
Experts' consultation 3.3 MSs experts to discuss the need for metabolism on livestock to be provided taking	Based on the current dietary burden calculation (see DAR), the trigger value of 0.004 mg/kg bw per day is exceeded and a potential carry-over of the relevant residues to products of animal origin is therefore expected.

Subject	Conclusions Pesticide Peer Review Meeting
into account the results of the new metabolism in plants.	Although the metabolism pattern in livestock is very likely similar to the one observed in the rat, these studies should be provided to further elaborate for the quantification of the metabolites in animal matrices and determine whether a significant carry-over to products of animal origin could occur. **Data gap**: The experts agreed that poultry and ruminants metabolism studies are triggered and should be provided to quantify the identified metabolites. **Data gap**: The dietary burden calculation should be revised according to the agreed RDs for potatoes (see EC 3.2.), the submission of the requested residue trials (see EC 3.4.) and the toxicity of the metabolite 3-decen-2-ol (free and conjugated). Residue definitions for monitoring and risk assessment for products of animal origin cannot currently be proposed.
Experts' consultation 3.4 MSs experts to discuss if available reliable field trials are sufficient or further data would need to be generated, taking into account new metabolism study and new field residue trials provided.	5 independent residue trials compliant with the representative use were made available in the DAR. It was concluded that the precautionary measures and the conditions of extraction and analysis, that characterized the experimental design in these trials, prevented the degradation of the residues through volatilization. However, since the analytical method did not include a hydrolysis step to analyse the conjugates that are included in the provisional RA RD, the meeting agreed to request sufficient residue trials in compliance with the RDs for monitoring and risk assessment (provisional) (See EC 3.2). According to the new data requirements, 8 trials are normally required to support the post-harvest use. A **data gap** is therefore set for a complete dataset of GAP-compliant residue trials analysing for all compounds in compliance with the residue definitions for monitoring and risk assessment, once the residue definition for risk assessment is finalised (see EC 3.2), and considering specifically the precautionary measures to avoid volatilization and storage stability issues.
Experts' consultation 3.5	Background levels of the parent and metabolites (2-decanone and 2-decanol) are reported for several plant commodities (fruit and vegetables, etc...), in yogurt (as a flavouring agent or via feed items treatment), however, this information is associated to several

Subject	Conclusions Pesticide Peer Review Meeting
MSs experts to discuss if, with available information in the dossier, it is possible to conclude on the relative levels of residues in potatoes, due to the use of 3-decen-2-one as post-harvest treatment, with respect to those that are naturally present in crops.	uncertainties (sources of the occurrence) and no data were retrieved for potatoes. Based on the data reported in the RAR, a comprehensive consumer dietary risk assessment considering other sources of occurrence of 3-decen-2-one and metabolites cannot currently be conducted.
Experts' consultation 3.6 MSs experts to discuss if, based on available data in the dossier and following SANCO/11188/2013, the inclusion of 3(E)-3-decen-2-one in Annex IV of Regulation (EC) N°396/2005 can be proposed.	The 5 different criteria for potential Annex IV inclusion are not met for 3-decen-2-one. It is also noted that for the crops other than potatoes and having regard to the background levels, the setting of a default LOQ value as MRL might not be appropriate.

REPORT OF PESTICIDE PEER REVIEW TC 66

CYMOXANIL – AIR IV

Rapporteur Member State: LT

3. Residues

Date: 26 November 2021

List of participants:

Institute	**Member States Country code**
Federal Institute for Risk Assessment (BfR)	DE
Agence nationale de sécurité sanitaire de l'alimentation, de l'environnement et du travail (ANSES)	FR
State Plant Service under the Ministry of Agriculture	LT
Board for the Authorisation of Plant Protection Products and Biocides (Ctgb)	NL
Hearing expert	IE

In accordance with EFSA's Policy on Independence[1] and the Decision of the Executive Director on Competing Interest Management[2,] EFSA screened the Annual Declarations of Interest filled out by the participants invited to the present meeting. No Conflicts of Interest related to the issues discussed in this meeting have been identified during the screening process, and no interests were declared orally by the members at the beginning of this meeting.

[1] http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/policy_independence.pdf
[2] http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/competing_interest_management_17.pdf

Discussion points/Outcome

3. Residues

Please note that information part of this report may have been masked by EFSA in accordance with Article 63 of Regulation (EC) No 1107/2009 as well as EFSA's Practical Arrangements concerning confidentiality in accordance with Articles 7 and 16 of Regulation (EC) No 1107/2009, or EFSA's Practical Arrangements concerning transparency and confidentiality as a consequence of confidentiality requests submitted by the applicant on application dossiers for pesticides active substances or Maximum Residue Levels, respectively. Please note that information disclosed in this report is without prejudice to pre-existing intellectual property rights and data exclusivity clauses set out in Union law, and particularly in Article 62 of Regulation (EC) No 1107/2009.
Minutes might be revised due to pending data gaps at the time of the meeting and /or eventual need for further follow up consultation after the meeting. If needed, the final agreement will be made available in the meeting report published at the end of the peer review process.

Subject	Conclusions Pesticide Peer Review Meeting
Experts' consultation 3.1 Experts to discuss whether the old plant metabolism study with grapes can be considered as valid despite several shortcomings (no GLP, guideline, no info on storage conditions and growth stage at time of application, lack of details on the calculation of the radioactivity) or as supplementary study only. Experts to discuss the influence of the deviation from agricultural practise on the quantitative results in the recent study where grapes were placed indoor after the last treatment especially in view of the	3.1a There are no contradictory results between the old metabolism study and the more recent study with grapes although it is acknowledged that limited identification was observed in the old study. 3.1b Based on the data that were presented, it is not possible to conclude on the identity of the major metabolite M10 and further investigation should be undertaken to fully elucidate the structure of this metabolite as it occurs at high proportions and concentrations in grapes. 3.1c The experts were of the opinion that although the specific design to perform the metabolism study on grapes enhanced higher residue levels, this deviation is not expected to significantly impact the metabolic pattern of cymoxanil in grapes. 3.1a As a stand-alone study, the old study cannot be considered as acceptable in view of the identified shortcomings; overall, and considering both metabolism studies, the meeting concluded that a reliable metabolic pattern in grapes can be depicted. 3.1b

Subject	Conclusions Pesticide Peer Review Meeting
argument that this deviation might have caused the difference in water-extractable surface residues with respect to the first study. Experts should discuss whether the argumentation/data is sufficiently sound to conclude identity of M10 as being IN-U3204. Finally, experts should conclude whether the data allow to confidently conclude on the metabolism in grapes with the aim to set residue definitions.	**Data gap**: a complete elucidation of the structure of the metabolite M10 occurring at high proportions and concentrations in the most recent metabolism study with grapes is required. **Data gap for mam Tox section**: Once the structure of M10 (observed in the newer metabolism study with grapes) is fully elucidated, the general toxicity (incl. genotoxicity) of this compound should be further addressed. 3.1c It is agreed to consider the more recent metabolism study on grapes as representative of all growing conditions for fruit crops.
Experts' consultation 3.2 Experts to discuss the plant residue definitions for monitoring and risk assessment taking into account information on - the toxicological properties of the identified metabolites and - the identity of M10 (occurring in grapes) - possible influence of photolysis on the qualitative and quantitative formation of metabolites.	**3.2a:** See Mam tox background information **3.2b:** see 3.1b under EC.1 **3.2c:** The IN-R3273, IN-JX915 and IN-T4226 resulting from the photolytic degradation of cymoxanil, were analysed in all plant metabolism groups (grapes, tomato, lettuce and potato) but were only detected in the most recent grape metabolism study. Similar proportions of parent and the photolytic degradation compounds (IN-R3273, IN-JX915 and IN-T4226) were observed in the new metabolism study on grapes only. Nevertheless, since the presence of these compounds at quantifiable levels in grapes cannot be excluded in absence of GAP compliant residue trials on grapes analysing these compounds, the genotoxicity potential of IN-R3273, IN-JX915 and IN-T4226 should be addressed. **3.2d** **Residue definition for monitoring:**

Subject	Conclusions Pesticide Peer Review Meeting
Experts to discuss whether the existing general RD is appropriate considering the results of the new metabolism study with grapes and conclude on plant residue definitions both for monitoring and risk.	Parent cymoxanil was recovered in all crops (grapes, tomatoes, lettuce) except in potato tubers where cymoxanil was shown to be completely degraded into glycine and sugars. **Residue definition for risk assessment:** **IN-W3595** and **IN-KP533** occurred at much higher concentrations compared to the parent mainly in lettuces (18% TRR; 0.19 mg eq./kg and 2.8% TRR; 0.31 mg eq./kg, resp.) but also in mature grapes (grapes metabolism study) (7% TRR; 0.999 mg eq./kg and 16.6% TRR; 2.181 mg eq./kg, resp.). Their toxicity was concluded to be covered by the toxicity of the parent compound. **„AS999/glycine-related"** (tentatively identified as analysed in only one TLC system and the structure was not confirmed by a second analytical method) is recovered in significant proportions in lettuces only (11.4% TRR; 0.119 mg eq./kg). AS999 is covered by the toxicity of the parent compound. The experts were in favour to derive a general risk assessment residue definition (RA RD) for all crop groups including besides parent compound both metabolites **IN-W3595** and **IN-KP533** with the argumentation that these compounds are recovered in significant amounts in lettuces but also in some samples of grapes. This proposal will therefore cover the authorized uses on leafy and P/O crop groups (see Art.12 MRL review - EFSA Journal 2015;13(12):4355). Once the structure of metabolite „AS999/glycine-related" is confirmed or elucidated, its inclusion in the RD for RA specifically for leafy crops will need to be further considered based on requested GAP compliant residue trials analysing for the residues of this compound in the leafy crops under consideration. **3.2c Data gap for Mam Tox section**: The genotoxic potential of the metabolites IN-R3273, IN-JX915 and IN-T4226 resulting from the photolytic degradation of cymoxanil, should be addressed. **3.2d**

Subject	Conclusions Pesticide Peer Review Meeting
	Residue definition for monitoring: Cymoxanil only (for all categories of crops following foliar treatment). **Residue definition for risk assessment:** „Sum of cymoxanil, IN-W3595, IN-KP533, expressed as cymoxanil" – extended to all crops following foliar application – Provisional considering all the identified data gaps. **Data gap** The structure of the „AS999/glycine-related" metabolite observed in the lettuce metabolism needs to be fully elucidated.
Experts' consultation 3.3 Experts to discuss whether residue definitions for ruminants can be proposed on the basis of the presented metabolism study and if possible, to set animal RD for RA and monitoring.	Since cymoxanil is expected to be degraded extensively in rumen fluid and transfer to ruminant matrices and milk is not expected, the impact of the shortcoming regarding the length of storage of the samples can be considered as negligible and the metabolism study is valid. The parent compound is not detected and cannot therefore be considered as a valid residue marker of the total residues. Residue definitions for ruminant matrices are not proposed and are not required for the representative uses.
Experts' consultation 3.4 Experts to discuss whether the residue trials in greenhouse with tomato applying with less critical application rates in the first 3 applications and more critical in the last 2 applications should be considered for the risk assessment. Consideration	In the case where the residue trials were characterized by the 3 first applications that were underdosed followed by two applications either underdosed or overdosed (within the 25% tolerance limit), it is assumed that the final residues will be driven by the last 2 applications because of the non-persistence of cymoxanil. Ten trials (with 2 last treatments overdosed within 25%) and 2 trials (with 2 last treatments underdosed within 25%) were considered as acceptable. **Data gap:**

Subject	Conclusions Pesticide Peer Review Meeting
on the influence of photolysis on the quantitative results might be necessary.	To comply with the agreed general plant residue definition for risk assessment, a complete set of residue field trials in accordance with the indoor GAP on tomatoes is requested. **Data gap:** For all the other representative uses on potato, tomato (outdoor) and grapes, complete set of residue field trials compliant with the GAPs and analyzing all the compounds included in the RA RD should be provided. These trials should be conducted using validated analytical methods and supported by acceptable storage stability data.

REPORT OF PESTICIDE PEER REVIEW TC 66

ISOFLUCYPRAM – NAS 1107/2009 Rapporteur Member State: FR

3. Residues

Date: 26 November 2021

List of participants:

Institute	**Member States Country code**
Federal Institute for Risk Assessment (BfR)	DE
French agency for food, environmental and occupational health safety (Anses)	FR
The State Plant Service - Ministry of Agriculture	LT
Board for the Authorisation of Plant Protection Products and Biocides (Ctgb)	NL
Hearing expert	IE

In accordance with EFSA's Policy on Independence[1] and the Decision of the Executive Director on Competing Interest Management[2], EFSA screened the Annual Declarations of Interest filled out by the participants invited to the present meeting. No Conflicts of Interest related to the issues discussed in this meeting have been identified during the screening process, and no interests were declared orally by the members at the beginning of this meeting.

[1] http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/policy_independence.pdf
[2] http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/competing_interest_management_17.pdf

Discussion points/Outcome

3. Residues

Please note that information part of this report may have been masked by EFSA in accordance with Article 63 of Regulation (EC) No 1107/2009 as well as EFSA's Practical Arrangements concerning confidentiality in accordance with Articles 7 and 16 of Regulation (EC) No 1107/2009, or EFSA's Practical Arrangements concerning transparency and confidentiality as a consequence of confidentiality requests submitted by the applicant on application dossiers for pesticides active substances or Maximum Residue Levels, respectively. Please note that information disclosed in this report is without prejudice to pre-existing intellectual property rights and data exclusivity clauses set out in Union law, and particularly in Article 62 of Regulation (EC) No 1107/2009.
Minutes might be revised due to pending data gaps at the time of the meeting and /or eventual need for further follow up consultation after the meeting. If needed, the final agreement will be made available in the meeting report published at the end of the peer review process.

Subject	Conclusions Pesticide Peer Review Meeting
Expert's consultation 3.1 - Based on the additional data provided by the applicant on the magnitude if residues (i.e M01, M06), experts to discuss the relevant compounds for the residue definitions in primary plant. - Whether a general residue definition covering all the crops group could be derived based on the available metabolism studies. - Whether the inclusion of the metabolites M01 and M06 in the risk assessment residue definition in plant, trigger additional livestock metabolism studies should be also discussed in the expert meeting.	After considering the different metabolism studies available and residue trials available on cereals the MSs experts agreed that parent is a good marker for monitoring that can be applied to all crop groups after foliar application. However, due to the different pattern observed on the distribution of metabolites and metabolic pathways in the metabolism studies in the different crops, the residue definition for risk assessment can only be established for cereals following foliar application at this stage. Using worst case conversion factors derived from barley residue trials and applicable also for wheat in the dietary burden calculation was not fully justified. Since the metabolites M01 and M06 are identified as major metabolites in most of the animal matrices in the isoflucypyram dosed metabolism studies, no additional metabolism studies dosed with M01 and M06 are needed. **Plant matrices residue definitions** -Residue definition for monitoring (all plant groups after foliar application): Isoflucypyram

Subject	Conclusions Pesticide Peer Review Meeting
- Based on the overall available data (metabolism and feeding studies) and in the view of further expected data on M01 and M06, experts to discuss the most appropriate residue definitions for livestock. - Whether the results for M02 in milk in feeding studies are reliable considering the procedural recoveries (60%-150%) of the analytical method.	-Residue definition for Risk Assessment (cereals after foliar application only): Sum of isoflucypyram, M01 and its conjugates, M06 and conjugates, expressed as isoflucypyram. **Animal matrices residue definitions** -Residue definition for monitoring: Isoflucypyram - Residue definition for Risk Assessment Isoflucypyram, M01 (and its conjugates), M02 (and its conjugates) and M011 expressed as isoflucypyram. Despite deviations, the method for M2 in milk was considered fit for purpose for the feeding study. **Open points** - Open point: the RMS to check the impact of a dietary burden calculation based on actual wheat residue trials and to amend volume 1 of the RAR accordingly - Open point: incorporate in RAR the consumer exposure calculation for M50 considering the residues reported in ruminant kidney from the metabolism study to support further consumer risk assessment when genotoxicity end points become available. **Data gap** -A data gap was identified to address potential genotoxicity of animal metabolite M50 Reconsideration of inclusion of M50 in the residue definition for risk assessment is pending this genotoxicity assessment.
Experts' consultation 3.2 Experts to discuss: - the relevant compounds for the rotational crops	With available data, pending assessment of genotoxicity of metabolites M66 and M67, no relevant residues in rotational crops are expected to result from the representative uses and, as a pragmatic approach, the same residues definitions as agreed for primary crops will be applicable to rotational crops. This conclusion cannot be extended by default to other GAPs resulting in higher plateau

Subject	Conclusions Pesticide Peer Review Meeting
considering also the inputs from the toxicological evaluation and to finally conclude on the most appropriate residue definitions. - Whether the metabolic pattern is similar as in primary crops and whether additional studies (field trials in succeeded crops) are triggered.	concentrations, for which the occurrence of the identified metabolites in rotational crops will need to be reassessed and therefore the residue definitions will need to be reconsidered. **Residue definitions for monitoring and risk assessment in Rotational crops** -Pending the data gap below, same residue definitions as agreed for primary crops will be applicable to rotational crops succeeding the representative uses. This residue definition cannot be extended by default to other GAPs resulting in higher plateau concentrations, for which the occurrence of the identified metabolites in rotational crops will need to be reassessed and therefore the residue definitions will need to be reconsidered **Data gaps** -Data gap for genotoxicity data and assessment of rotational crop metabolites M66 and M67 is confirmed.

REPORT OF PESTICIDE PEER REVIEW TC 62

FENPYROXIMATE– AIR IV

Rapporteur Member State: AT

3. Residues

Date: 20-21 September 2021

List of participants:

Institute	**Member States Country code**
Austrian Agency for Health and Food Safety (AGES)	AT
Federal Institute for Risk Assessment (BfR)	DE
Agence nationale de sécurité sanitaire de l'alimentation, de l'environnement et du travail (ANSES)	FR
Board for the Authorisation of Plant Protection Products and Biocides (Ctgb)	NL

In accordance with EFSA's Policy on Independence[1] and the Decision of the Executive Director on Competing Interest Management[2], EFSA screened the Annual Declarations of Interest filled out by the participants invited to the present meeting. No Conflicts of Interest related to the issues discussed in this meeting have been identified during the screening process, and no interests were declared orally by the members at the beginning of this meeting.

[1] http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/policy_independence.pdf
[2] http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/competing_interest_management_17.pdf

Discussion points/Outcome

3. Residues

Please note that information part of this report may have been masked by EFSA in accordance with Article 63 of Regulation (EC) No 1107/2009 as well as EFSA's Practical Arrangements concerning confidentiality in accordance with Articles 7 and 16 of Regulation (EC) No 1107/2009, or EFSA's Practical Arrangements concerning transparency and confidentiality as a consequence of confidentiality requests submitted by the applicant on application dossiers for pesticides active substances or Maximum Residue Levels, respectively. Please note that information disclosed in this report is without prejudice to pre-existing intellectual property rights and data exclusivity clauses set out in Union law, and particularly in Article 62 of Regulation (EC) No 1107/2009.
Minutes might be revised due to pending data gaps at the time of the meeting and /or eventual need for further follow up consultation after the meeting. If needed, the final agreement will be made available in the meeting report published at the end of the peer review process.

Subject	Conclusions Pesticide Peer Review Meeting
Experts' consultation 3.1 MSs experts to discuss the residue definitions for risk assessment and monitoring in plants. In particular, if the conversion factor of 1 to be applied to the monitored residues of fenpyroximate is adequate taking into account that the residue definition for risk assessment also includes the metabolite M1 (Z isomer of fenpyroximate). Analytical methods used to determine the residues and the relative toxicological profile of the M1 (isomer Z) with respect to parent should be adequately considered for this discussion. In addition, experts should consider the need to add metabolite M12 in the residue definition for risk assessment. Also the characterization of unk metabolites 1,2 and 3	Considering the identification attempts made and the relative amounts of 3 unknown metabolites in the study in Swiss chard (2014), the majority of experts considered the study acceptable to address metabolism in the leafy crop category. Thus, acceptable metabolism studies with foliar application are available for 3 different crop categories. As for the occurrence of metabolite M12 in fruit crops at low absolute levels, M12 is not a candidate for the RD while a conclusion of its non-relevance for the consumer risk assessment is pending confirmation of absence of aneugenicity / clastogenicity. (M12 is grouped together with M3, a major livestock metabolite and formed during processing). Fenpyroximate (E-isomer) is the major residue in all plant matrices. The submitted enforcement method is capable of measuring separately fenpyroximate and its Z- isomer (M-1). It was considered sufficient to limit the proposed RD-Mon to fenpyroximate since for most commodity / GAP combinations subject to this review, residue trials show levels of Z-isomer (M-1) <LOQ in the majority of trials. The conversion factors need to be set crop specific. **General residue definitions for foliar application of fenpyroximate to plants:** **RD-RA:** Sum of fenpyroximate (E-isomer) and its Z-isomer (M1) expressed as fenpyroximate. TRV of fenpyroximate can be applied also to its Z-isomer (M1). **RD-Mon:** Fenpyroximate (E-isomer), confirming the RD currently in place.

Subject	Conclusions Pesticide Peer Review Meeting
found in Swiss Chart at levels above 0.01 mg/kg need to be considered by the experts.	The median **conversion factor** is close to 1 for most of the crops assessed in this review except citrus (ranging 1.1 up to 1.27). **Open point:** RMS to calculate the median conversion factors from the residue trials for all the crops in this review.
Experts' consultation 3.2 MSs experts to discuss the residue definition on processed commodities taking into consideration the toxicological relevance of metabolite M3.	Processing trials in strawberry, apple, grapes, hops, beans demonstrated that the formation of M-3 under industrial processing conditions is minor compared to the observed high proportions formed in the hydrolysis study. The majority of experts agreed that based on occurrence information in processing trials, M-3 is not a candidate for the RD processing. However, a conclusion of non-relevance of M-3 for the consumer risk assessment can only be made, when its toxicological potential is fully addressed. **Residue definitions for plant processed commodities:** **RD-RA:** Sum of fenpyroximate (E-isomer) and its Z-isomer (M-1) expressed as fenpyroximate. TRV of fenpyroximate can be applied also to its Z-isomer (M-1). **Note:** There was unanimous agreement that a final assessment of whether M-3 could pose a risk to consumers is only possible once the toxicology of M-3 is fully addressed, even if based on residue data M-3 occurrence is low compared to parent. EFSA is therefore of the opinion that the RD-RA processed commodities should be **provisional** as the pending relevance assessment for metabolite M-3 does not allow to finalised the consumer risk assessment. However, a unanimous agreement with the experts on the provisional status of the RD-RA processing could not be reached. **RD-Mon:** Fenpyroximate (E-isomer), confirming the RD currently in place. **Data gap in the tox section:** The toxicological potential of M-3 to be addressed (aneugenicity data and conclusions on general toxicity pending)
Experts' consultation 3.3 MSs' experts to discuss the residue definition for animal matrices. In particular:	Considering occurrence/levels of parent and metabolites and their isomers in ruminant metabolism and feeding studies, only some compounds were considered potentially relevant for inclusion into the RDs for monitoring and RA, while sufficient tox data were not available for the metabolites to conclude.

Subject	Conclusions Pesticide Peer Review Meeting
– Inclusion of Z isomer of M3. Since the Z isomer of the parent is part of the residues in the raw commodities it seems natural that the Z isomer of metabolite M3 would be also produced. It needs to be checked if Z isomer of the parent was also in the feed used. – Inclusion of metabolite Fen-OH – Since only metabolite M3 is proposed for monitoring, it needs to be considered if residues of parent are adequately collected by the analytical method or a conversion factor needs to be established. – To discuss whether an adequate analytical method for M3 is available.	The Z-isomer of M-3 does not seem to be formed in ruminants and can therefore be disregarded. The available enforcement method can analyse parent and M-3 separately. **RD-Mon** (marker principle): Ruminant muscle, fat and milk: - Fenpyroximate Ruminant liver and kidney: - M-3 Once the toxicological assessment of M-3 is finalised, it could be of merit to consider if setting a common definition for all ruminant matrices including parent and M-3 could be appropriate and feasible (RM consideration required). Note: The RD-Mon proposed corresponds to the RD-Mon currently legally in place, but deviates from the proposal in the Art. 12 MRL review (M-3, expressed as fenpyroximate). **RD-RA (provisional):** - Fenpyroximate - Fen-OH - M-3 pending the conclusions on tox properties/TRVs for metabolites M-3, Fen-OH and information addressing the internal transesterification potential of Fen-OH and the toxicology of its transesterification products. **Data gap:** Applicant to submit additional data to address the publicly reported internal transesterification potential of Fen-OH and the toxicological relevance of possible internal transesterification products, including assessment of the paper from public literature Motoba et al., 2000.

GENERAL REPORT OF PESTICIDE PEER REVIEW TELECONFERENCE 52

Peer Review Programme under Regulation (EC) No 1107/2009

Subject:

3 May 2021(h 13:30-18:00 GMT+2, Rome)

- Implementation of isomer guidance Q&A

4 May 2021(h 9:00-17:00 GMT+2, Rome)

- Residues and MRLs on rotational crops (EFSA draft technical report)

5 May 2021(h 9:00-13:00 GMT+2, Rome)

- Assessment of residues in honey. Update and Q&A
- Guidance on extraction efficiency

Declarations of interest

In accordance with EFSA's Policy on Declarations of Interests EFSA screened the available Annual Declarations of interest (ADoI) filled in by the nominated experts. In addition, at the beginning of the teleconference the experts were invited to declare orally (Oral Declaration of Interest (ODoI)) any interests which might be considered prejudicial to his/her independence in relation to the items on the agenda. No interests were declared.

In accordance with the ED Decision on Competing Interest Management, Observers are not required to submit DoIs. However, at the beginning of the teleconference the observers were reminded that they have confidentiality obligations.

Date: 3 - 5 May 2021

Venue: Teleconference

Attendance SANTE, EFSA and MS Experts: AT, BE, BG, DE, DK, ES, FI, FR, EL, HR, IE, IT, LT, NL, PL, SE, SI

General comments including comments concerning study requirements and evaluation of studies in the section **Residues** are listed below. The comments received were discussed in the respective section.

Date	Supplier	Content	File Name
30/4/2021	BE	Comments : Rotational crops	BE_Comments on the Technical Report_2021-04-30.doc
30/4/2021	DE	Comments : Rotational	Comments on the Technical

		crops	Report_BfR_rev1.doc Functions
30/4/2021	FR	Comments : Rotational crops	Comments on the Technical Report_FR.doc
30/4/2021	HR	Comments : Rotational crops	Comments on the Technical Report_HR.doc

General documents tabled at the teleconference:

Date	**Supplier**	**Content**	**File Name**
22/04/2021	EFSA	Presentation: Technical guideline on extraction efficiency	Discussions on extraction efficiency_general EM_May21.ppt
23/4/2021	EFSA	Presentation: Assessment of residues in honey	Peer review meeting_EFSA_May 2021_honey.pptx
25/4/2021	EFSA	Presentation: Isomer GD introduction	Guidance Isomers introduction. Expert Consultation Residues 4 May 2021.pptx
29/4/2021	EFSA	Presentation: Industry FAQ on isomers	Industry FAQ questions.ppt
23/4/2021	EFSA	Presentation: Isomers GD implementation	EFSA GD for stereoisomers_implementation_My_2021.pptx
3/5/2021	Italy	Overview table	Isomerism by classes ICPS2021 (003).xlsx
22/4/2021	EFSA	Presentation: Implementation of the OECD Guidance Document on Residues in Rotational Crops	Rotational_crops_introduction.ppt
20/4/2021	EFSA	Presentation: Criteria triggering investigation of residues in rotational crops "tier 0"	Criteria triggering investigation of residues in rotational crops (tier 0).ppt
26/4/2021	EFSA	Presentation: Implementing the applicable guidance documents on the nature of residues in rotational crops (Tier 1 studies on RCs)	Tier 1 studies on rotational crops.pptx
26/4/2021	EFSA	Presentation: MRL setting to account for residues in rotational crops	MRL setting for RC.pptx
25/4/2021	EFSA	Calculation tool	Rotational crops calculators.xlsx

29/4/2021	NL	Case study	Case study_NL_ assessment_residues_in_potato_P C.docx
Post meeting note: A background document provided by BE for the discussion on honey has accidently not been shared in the meeting documents folder prior to the meeting but is now available.			
04/03/2021	BE	Position paper: Implementation of requirements on residues in honey in particular originating from non-target crops	Pesticides Peer Review TC 52_2021-05_residues honey non-target crops_BE.docx

Appendix
Presentations

General discussion

1. Guidance on risk assessment of pesticide a.s. and transformation products that have stereoisomers – Q&A

The following presentations were given by EFSA to the participants:

- Guidance on the risk assessment of PPP a.s. and their transformation products that have stereoisomers
- Industry FAQ on isomers
- Considerations on the implementation of the EFSA guidance document on stereoisomers in the context of MRL applications (Art. 6 to 10 of Regulation (EC) No 396/2005) and MRL reviews (Art. 12)

EFSA provided a summary presentation on the isomer guidance (https://www.efsa.europa.eu/en/efsajournal/pub/5804; implementation date 1 Aug 2021, see https://ec.europa.eu/food/sites/food/files/plant/docs/pesticides_ppp_app-proc_guide_horiz_stereoisomers.pdf). At a workshop with EFSA last year, former ECPA (now CropLife Europe) has submitted questions that were also shared with attendees together with the answers provided by EFSA.

EFSA presented also the procedural aspects for future Art.12 and Art.10 applications, respectively, with regards to the new isomer's guidance, specifically the different cases that can occur during the process and what would be the implications. The flowchart should always be considered when dealing with MRL review and applications as by implementation date, and EFSA can be consulted in case of further questions.

Exchange of views among participants and further clarification by EFSA were provided.

2. EFSA draft technical report Residues and MRLs on rotational crops

The following presentations were given by EFSA to the participants:

- Implementation of the OECD Guidance Document on Residues in Rotational Crops
- Criteria triggering investigation of residues in rotational crops (Tier 0)
- Implementing the applicable guidance documents on the nature of residues in rotational crops (Tier 1 studies on RCs)
- MRL setting to account for residues in rotational crops

Prior to the meeting, MS experts provided comments to the draft Technical Report. Some of these comments were discussed during the meeting, others of more editorial nature were not discussed. All comments received will be considered by EFSA in the further update of the Technical Report. An additional week to provide further comments was offered to MS experts after the meeting report was submitted.

EFSA provided a **presentation on the legal background** and existing guidance documents, the implementation of the guidance documents in regulatory practice and an overview of the assessment of the nature and magnitude of the residues in rotational crops (Tiered approach).

Tier 0: The conditions when metabolism studies in rotational crops (RC) are required were presented. The specific case of import tolerance applications was also discussed.

Tier 1: The proposal by EFSA to consider the effective application rates (Aeff), representing active substance effectively reaching the soil after plant interception, as the basis of the identification of the critical GAP with respect to rotational crops was presented.
A calculator has been prepared by EFSA (as beta version) to derive the effective application rate (Aeff) for the GAPs under assessment. Some participants stressed that the interception rate is not

appropriate for the last year of application since crop failure is a scenario to be considered according to Reg. VO 283/2013, point 6.6.1.

EFSA invited MS experts to express their views on a number of questions related to Tier 0 and Tier 1, which were further discussed in the meeting.

Tier 2: Limited RC field trials (OECD TGL 504)

EFSA presented how the provisions in OECD GD 2018 with respect to the number of limited trials to be performed as Tier 2 need to be interpreted in the EU context and consulted MSs experts in relation to different options to interpret the OECD guidance. Among those:

-number of limited field trials on RCs required,
-independency of the limited residue trials on RCs,
-residue levels from mature and immature crops,
-extrapolation of results of leafy matrices from all crop groups as representative for leafy crops

Tier 3: Risk mitigation and MRL setting

The following topics were discussed:

-Risk mitigation measures vs. MRL setting (step 5)

EFSA presented the issues on the option to consider risk mitigation measures versus the alternative of MRL setting for rotational crops. Several MSs stressed that a harmonisation of risk mitigation measures throughout the EU MSs would be beneficial and that risk mitigation cannot be left just to the applicant proposals. Currently risk mitigation measures applied are mainly limited to PBIs and maximum dose rate of application. It was agreed that further discussion is needed involving risk managers.

- Derivation of the input values for exposure calculations

Different options of approaches used in the past were presented and discussed. The need to agree on a harmonized approach was emphasized.

- Derivation of MRLs for rotational crops

With respect to MRL setting, different options of approaches used in the past were presented and discussed. The need to agree on a harmonized approach was emphasized.

The participants presented their views and asked further clarifications to EFSA.

EFSA invited MS experts to express their views on a number of questions related to Tier 2 and Tier 3.

New fate and behaviour modelling tools (PERSAM)

EFSA presented new modelling tools from the environmental fate and behaviour section for assessment of the soil compartment. These are ready and expected to be noted at EU level soon. However, effective implementation in the assessment presented in the dossiers will take another 2-3 years. The methodology proposed in the technical report to consider fate information data on the assessment of residues in rotational crops will need to be updated to take on board the new paradigm implemented in the fate models (PERSAM).

The participants presented their views and asked further clarifications to EFSA.

Further discussions with risk managers will take place in the PAFF Residues in June 2021 and the technical report will be amended accordingly, for further consultation by MS prior to its finalisation and publication.

3. Assessment of residues in honey - Update and Q&A

The following presentation was given by EFSA to the participants:

- Assessment of residues in honey – case studies, monitoring data and future work

EFSA provided a summary presentation on the Technical Guidelines on pesticide residues in honey (implementation date 1 Jan 2020, see https://ec.europa.eu/food/sites/food/files/plant/docs/pesticides_mrl_guidelines_honey.pdf), case studies, monitoring data (EU annual report on pesticide residues) and future work on the area as initiation of the discussion.

Discussion Pesticides Peer Review Meeting	
Question	**Response / Feedback**
What's the approach of other MSs when data on residues in honey are not provided for PPP? The guidelines are not clear on whether the data must be submitted for PPP applications.	EFSA – if the applications are under the New data requirements, studies on residues in honey need to be provided for PPP.
Should residues in honey only be investigated from uses on non-target plants when it concerns a herbicide? Since other categories of active substances are not aimed at non-target plants, and as such the proportion of non-target plants that is being encountered with the active is very small compared to the target crop. This is of course in particular relevant for non-melliferous crops (e.g. cereals).	It was mentioned that applicants want to waive residue studies on honey for applications on non-melliferous crops. BE – suggests using AR x Drift Deposition factor to estimate the residues in nectar and pollen from adjacent crops, as indicated in the Bee GD (ecotoxicology). It is noted that this has never been discussed under the current guidelines, but this approach may be used. **Post meeting note:** A more detailed explanation of the approach by BE has accidently not been tabled for the meeting. EFSA considers this proposal valid but notes that the Bee GD is currently under review and the approach to consider which type of drift deposition values are applied will need to be reconsidered accordingly. Further to that EFSA proposes discussion of the topic in the OECD working group on Pesticide Residues in Honey. AT – Non-target plants are not considered for residues in honey in Austria. It is stated that it was internationally agreed (post-Annex I group) not to consider non-target plants for residues in honey. FR – In the OECD working group on Pesticide Residues in Honey, the question on non-target plants is still under discussion and needs to be clarified. In France the approach used in Austria is not followed. On this topic, reference is made to the example of spirotetramat[1].

[1] "In order to determine the fraction of the active substance reaching the soil and therefore the flowering weeds after application of spirotetramat on fruit orchards, the applicant applied a formula using interception and wash-off input values as outlined in the EFSA guidance documents for predicting environmental concentrations of active substances of plant protection products and transformation products of these active substances in soil (EFSA, 2014a, 2017b)." (EFSA, 2021)

	BE – The reference to the 'international agreement' (not to consider residues on non-target plants for the time being) should be clarified. Discussion in conferences and WG PAI is not enough. This should be confirmed at SCoPAFF level; now it is mentioned in the EC Guidelines. Residues in honey from non-target plants cannot be ignored. SANTE – The issue on the reference to 'international agreement' raised by AT is noted in view of further discussion in future PAFF meeting.
In case of a herbicide, it will easily be necessary to move the colonies to remote locations (out of the tunnel) due to decay of the plants. Isn't it expected that this will lead to possible dilution of the residues in the honey?	FR – There is an ongoing discussion suggesting that the syrup test could be a solution for assessing residues of herbicides in honey. Unfortunately, there's not yet a wide experience on these studies. Some experiments are ongoing and once the results will be available, they may indicate whether syrup tests are fit for purpose.
Criteria to select the cGAP for residues in honey?	EFSA – It is noted that in the EC guidelines it is indicated that the most critical GAP or scenario should be used to assess residues in honey. FR – As bees forage on different crops, it would be useful to perform the assessment on residues in honey from a worst-case scenario using the highest AR from the a.s. cGAP and Phacelia as a surrogate. The results will then cover the application of the a.s. in all other crops. This approach may lead to a high MRL, but it will still be representative of a cGAP. For the specificity, it is recommended to have tunnel trials, so it is sure bees forage on the treated crop. DE – would not be enthusiastic about this approach. DE also mentioned a study on sunflower where they found only very low pollen amounts of the target crop in honey, although the hives were directly located at the treated field. Reference of the study and further information was shared by DE (Moreno S., Galvez O. (2019): Study on the residue behaviour of Pyradostrobin (BAS 500 F) on flower heads from sunflower, pollen and honey from beehives after treatment with BAS 500 06 F on sunflower crop under field conditions in Italy and Spain, season 2018).
How to establish if an a.s. is systemic? It is noted that a footnote is included in the EC guidelines.	EFSA – It is noted that a footnote is included in the EC guidelines stating that "If metabolism studies in crops (studies conducted according to OECD guideline 501) clearly establish that neither the parent nor toxicologically-relevant metabolites are present in a non-treated part of the plant when the active substance is applied according to critical GAPs, then it can be considered that the active substance is not systemic. Indications can also be found in the rotational crop studies."

	It must be noted that data from metabolism studies on different parts of the plants are not always present. FR - It must be noted that the uptake of rotational crops from roots may differ from the uptake from the leaf when an a.s. is applied via foliar applications.
What is the approach used for cereals, considering that buckwheat is included in the list of crops with melliferous capacity, while other cereals are not? This question is referring to an MRL application.	EFSA – if the GAP is for all cereals (thus covering buckwheat which is listed in Appendix II as a melliferous crop), then residues in honey should be considered according to the criteria set in the EC Guidelines. It was noted that without the specifics of the application it was not possible to advise further on this issue. LT – one of the criteria included in the Guidelines: "Residues in honey can occur when a substance with systemic properties is applied prior to the flowering stage (before BBCH 60), including treatment of seeds, of a crop which is foraged by bees".
Can proportionality be applied for residues in honey?	FR – FR would apply proportionality.
Have any of the MSs experiences on setting risk mitigation measures to restrict residues in honey?	The majority of experts commented they do not have experience on that. HR added the use of SPe 8 sentences for protection of bees. LT – "If applicant do not provide residue data on honey and the application is during flowering, we put mitigation measures in the label." LT provided an oral clarification/amendment: applications on PPPs are rejected if data on residues in honey are not provided for the following cases: - If the PPP is applied during flowering - if the PPP is applied before flowering in the case the a.s. is systemic. It was added that, for emergency authorisation they do not ask for data on residues in honey.
Do residues in honey need to be addressed in Mutual recognition applications? (based on assessment from other MS prior to implementation of Honey guidance)	BE – "date of submission in reference MS is decisive to establish which GD should be applied". FR – "We would not require data if the initial assessment was made before the date of application of the guideline". FI – "We have same experiences with the mutual recognition applications, where the Review Report is often from before 2020 and often miss data for residues in honey. It is our understanding that with mutual applications, mainly only data concerning local conditions could be requested, such as environmental data."
For pre-emergence applications it is not clear whether we need to consider residues in honey from adjacent crops. There are no further details on that in the EC guidelines. If a data gap is identified, risk managers should take into consideration that honey only represents a low contribution in the diet.	This topic was not further discussed.

4. Guideline on extraction efficiency

The following presentation was given by EFSA to the participants:

- Application of technical guideline on extraction efficiency: sharing of Authorities' views

EFSA introduced the topic indicating that the scope of this discussion was to share its view on how to apply the SANTE extraction efficiency guideline (see https://ec.europa.eu/food/sites/food/files/plant/docs/pesticides_mrl_guidelines_wrkdoc_2017-10632.pdf) and to exchange views on how to demonstrate that the extraction efficiency requirements are met.
EFSA noted that the assessment of extraction efficiency is not new as it was already a requirement under the old and new data requirements. What is new in the extraction efficiency technical guideline is when and how to assess extraction efficiency. It was noted that extraction efficiency cannot be established during method validation with fortified samples and should be assessed with samples bearing incurred residues. This guideline applies to both pre- and post-registration methods. The extraction efficiency should be evaluated for all matrix groups for which residue analytical methods are required and for all analytes included in the residue definition for monitoring for post-registration methods and all analytes included in the residue definition for risk assessment for pre-registration methods. Ideally the evaluation is done from samples with radiolabelled pesticides used for metabolism studies. However, as the sample material with radiolabelled incurred residue is typically available for approval of active substances only, the evaluation of the extraction efficiency for additional matrices or for different solvents could be performed in cross-validation experiments with samples containing incurred residues (residue trials samples or monitoring samples).
Concerning the applicability of this guideline, EFSA indicated that the guideline is applicable for:

- new active substance approval and renewal of active substances (EU level) submitted after 22 November 2019
- new product authorisations and renewal of product authorisations (relevant at MS level)
- applications for new MRLs under Art. 6 of Reg. (EC) No 396/2005 (EU level) made after 22 November 2019
- MRL reviews and specific MRL assessments under respectively Art. 12 and Art. 43 of Reg. (EC) No 396/2005 (EU level) where the data requirements for the latest approval or renewal should be considered, so proof of extraction efficiency in line with this document will only be required if it was required for the latest approval or renewal.

According to the guideline it is required that the applicant addresses the extraction efficiency of the methods used to generate residue trials and for the enforcement method. The information provided by the applicant should be evaluated by the RMS/EMS and reported in the DAR/RAR/ER submitted to EFSA. It was highlighted that if the information on extraction efficiency is not reported in DAR/RAR/ER for applications submitted after 22 November 2019, EFSA will request clarifications considering the requirements of the extraction efficiency Guideline.

Discussion Pesticides Peer Review Meeting

It was questioned by a MS if this trigger date refers to the date of application or date of submission of the dossier. EFSA will double check and provide this information after clarifying it with the Commission.
Post-meeting note: Regarding the applicability from 22 November 2019, Commission clarified the following as the reference dates in the different processes:
- for MRLs applications pre-Transparency Regulation (submissions before 27.03.2021), the reference date is the submission date of the application form while for post-Transparency Regulation (submissions after 27.03.2021) is the date of submission of the IUCLID dossier;
- for MRLs review the reference date is the date of the launch of the data collection;
- for approval or renewal of active substances the reference date is the date of submission of the dossier.

A MS questioned what will happen in the process of renewal when the applicant has not submitted any data on the extraction efficiency. They understand this will not be a reason to invalidate the residue trials. So, if no data on extraction efficiency are reported, could the residue data be considered validated or should new residue trials be asked?
EFSA indicated that while the Guideline is now applicable there is not much experience in applying it yet and it could be a case by case decision on how to deal with the validity of residue trials when the extraction efficiency is not provided. In any case, it would be up to the applicant to make a case why the residues trials should be regarded as valid and to the RMS/EMS to have a view if the argumentations are acceptable. EFSA further indicated that if the information on extraction efficiency is not reported in the DAR/RAR/ER submitted after the triggering date for the applicability of the Guideline, EFSA will require further clarifications. Then if the lack of information on extraction efficiency is affecting the validity of the residue trials and it should be considered as a data gap it will depend on the validity of the arguments the applicant could put forward. Moreover, in case of a data gap, EFSA's view would be to set this data gap for the analytical method and not for the residue trials. So, in first instance, the request could be to clarify the extraction efficiency of the analytical method and only if this is not proved and the analytical method considered not suitable, then the residue trials should not be considered valid. It should be also noted that the Guideline does not say that new data have to be generated but that the extraction efficiency could be demonstrated by existing data (e.g. by means of cross-validation studies).

Another MS indicated it would be strange that if the extraction efficiency is not addressed it will not have an impact on the validity of the residue trials. This is part of the validation of a method to confirm the reliability of the residue trials values. This means we have a data gap to address the extraction efficiency of the method used for trials to support the existing or new MRLs. A different MS indicated if the extraction efficiency could be seen as a confirmatory data requirement, meaning that the residue trials could be valid pending the extraction efficiency is proved. This approach could be used particularly in renewal where there is very large data package. The applicability of this data requirement and possible confirmatory data/data gaps in the different processes should be better reflected and clarified in the different processes (Art.10, Art.12, peer-review).
EFSA indicated that in Art.10 it is difficult to reject trials based on the extraction efficiency not proved. Reasoned opinions with pending conclusions are not looked on favourably by the risk managers. So, the approach could be to ask for clarifications or stop the clock if the issue is not addressed or fully justified. Further clarifications with the Commission could also be sought.
Post-meeting note: Commission recommended further discussion on the impact of the lack of proven extraction efficiency on the validity of residue trials at the PAFF Residues meeting in June 2021, and also further discussion with the experts in the EURLs is envisaged.

The experts then discussed the cases when the metabolism group is not matching the analytical method category. A MS expressed the wish to harmonise the two tables with the different categories as in the metabolism study the categories are quite large while in the analytical method the categories are more specific. Another MS suggested that the applicant should make the case why they think extraction efficiency would be applicable. This could depend on the properties of the compound and the nature of the matrix. In case where this is not possible, it may be considered acceptable if extraction efficiency is shown for the other matrix types for which identical/similar extraction procedure is used. Additionally, references could be made to known internationally recognized analytical methods in which identical/similar extraction procedure are used for the same compound as these methodologies are often used in monitoring labs, which are subjected to proficiency/ring testing with incurred residues. However, this should be evaluated with care and on a case by case basis. Another MS questioned the use of PTs (proficiency testing) for cross-validation purposes as although in some PTs the distributed sample material bears incurred residues, the material is not radiolabelled. Another MS suggested consulting EURLs for data on PTs.

The next point addressed was related on ownership of data and access to full study report on metabolism, EFSA questioned how the extraction efficiency could be proved without the access to

the full study report. One MS indicated the possibility to build a database with the available data to facilitate the work and give information without the need of the complete study report. EFSA and some MSs questioned whether the database could be effectively built in view of intellectual property protection. Another MS indicated that if data is available to the MS (but not for the new applicant), in their opinion this information can still be used to assess the extraction procedure followed. The fact that access to the full metabolism study is not available for the new applicant does not mean that the extraction efficiency is not shown if the same extraction procedure is used for the same compound in the same matrix group. This interpretation was supported by other MSs.

Finally, it was discussed how to deal with matrices difficult to analyse, e.g. hops. A MS raised this question as it concerns quite often minor crops such as caraway, which is an important crop for this MS. They indicated that for these difficult-to-analyse matrices such as spices very often no extraction efficiency data or samples with radiolabelled incurred residues are available. Then they proposed to consider on a case by case basis data from another similar group like e.g. oilseeds in the case of caraway. In general, EFSA would be supportive of this approach on difficult-to-analyse matrices. It was noted that the extraction efficiency Guideline for difficult-to-analyse matrices states that in principle an evaluation of the extraction efficiency would be desired as well, depending on availability of radiolabelled sample material or samples with incurred residues. There was agreement that such situations should be analysed case by case and a justification needs to be provided and included in the evaluation report.

A MS presented a possibility for proceeding when extraction efficiency of residue analytical methods for further uses not belonging to the matrix groups covered by the metabolism studies is not addressed. Provided that available metabolism studies cover at least three crop categories and that the metabolic pathway is identical in these groups, an indirect evaluation was proposed based on the extraction of samples containing incurred residues>LOQ: 1) with the solvent systems of the metabolism studies and 2) with the solvent systems commonly used in residue analytical methods for the matrix group in question not covered by the metabolism study. For the cross-validation, at least 3 extractions per solvent system should be performed and the extraction efficiency could be considered as sufficient if the residue analytical method extracts at least 70% of the amount extracted by the most efficient solvent system used in the metabolism studies. No other MSs commented on this approach. It was clarified that this should not be seen as an alternative always applied by default.

It was concluded that more practical examples would be desirable to see how to apply the extraction efficiency guideline in future. Further discussions and reflections would be needed also to address the initial question when the applicant has not submitted any data on the extraction efficiency and how clarifications and/or data gaps could be set in order to finalize the assessment performed in the different processes.

Appendix

4 May 2021

Guidance on the risk assessment of PPP a.s. and their transformation products that have stereoisomers

J. Oriol Magrans

Pesticide Residues Unit
Regulated Products Dept.
EFSA

Trusted science for safe food

efsa
European Food Safety Authority

EC Mandate, adoption and implementation

- In October 2016, the European Commission sent a request to EFSA to produce an **EFSA guidance** to address the **risk assessments for active substances of PPP that have isomers and for its transformation products** that may have isomers.

- The **Terms of Reference** had been previously agreed at the **EFSA Pesticide Steering Network** (PSN) meeting with the EU Member State risk managers.

- The **Guidance document** was adopted by EFSA on **22 July 2019** and was **noted** in the PAFF legislation on **3/4 December 2020** with an implementation date of **1 August 2021.**

What are stereoisomers?

Definitions

- **Isomers** are substances that share the same molecular formula.

  E.g. ethanol CH_3CH_2OH and ether CH_3OCH_3 both have the molecular formula C_2H_6O

- **Stereoisomers** are substances that share the same molecular formula, connectivity and bond multiplicity, and differ in the spatial arrangement of two or more atoms.

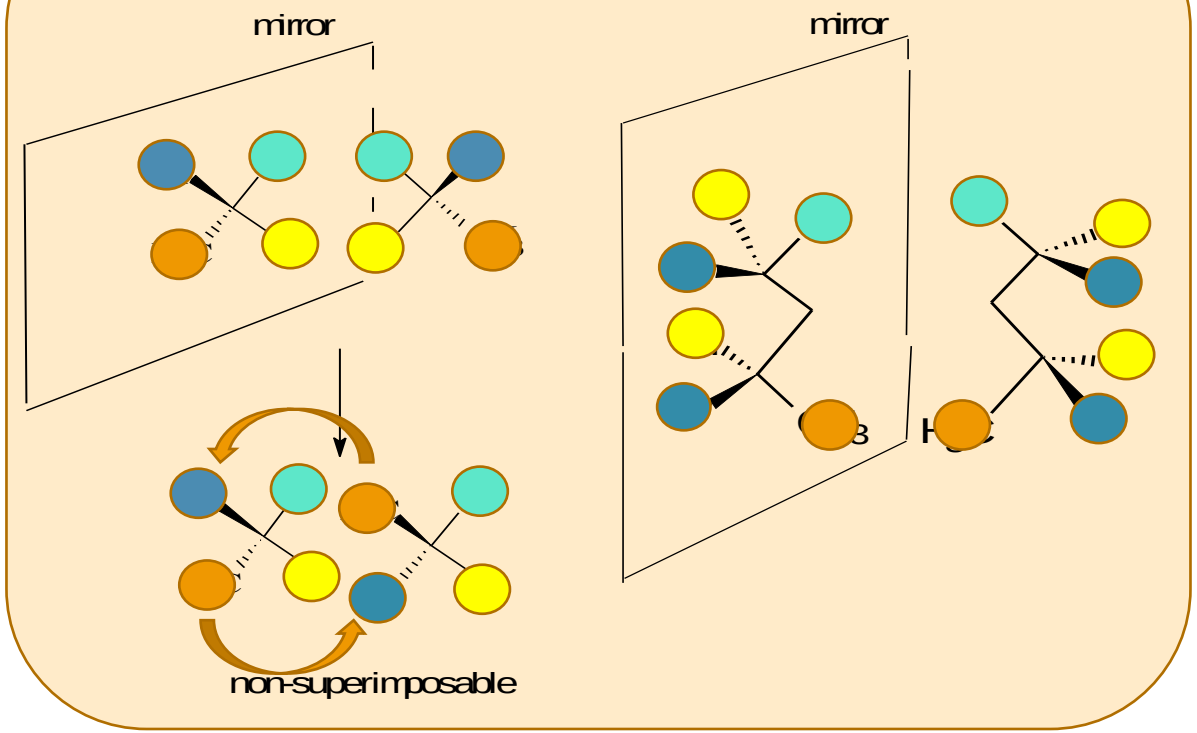
- **Enantiomers** are pairs of stereoisomers constituted by molecules consisting on the two non-superimposable mirror images of otherwise identically connected molecular structures.

- **Diasteromers** are stereoisomers that are not enantiomers (have identically connected molecular structures but those do not correspond as mirror images of each other).

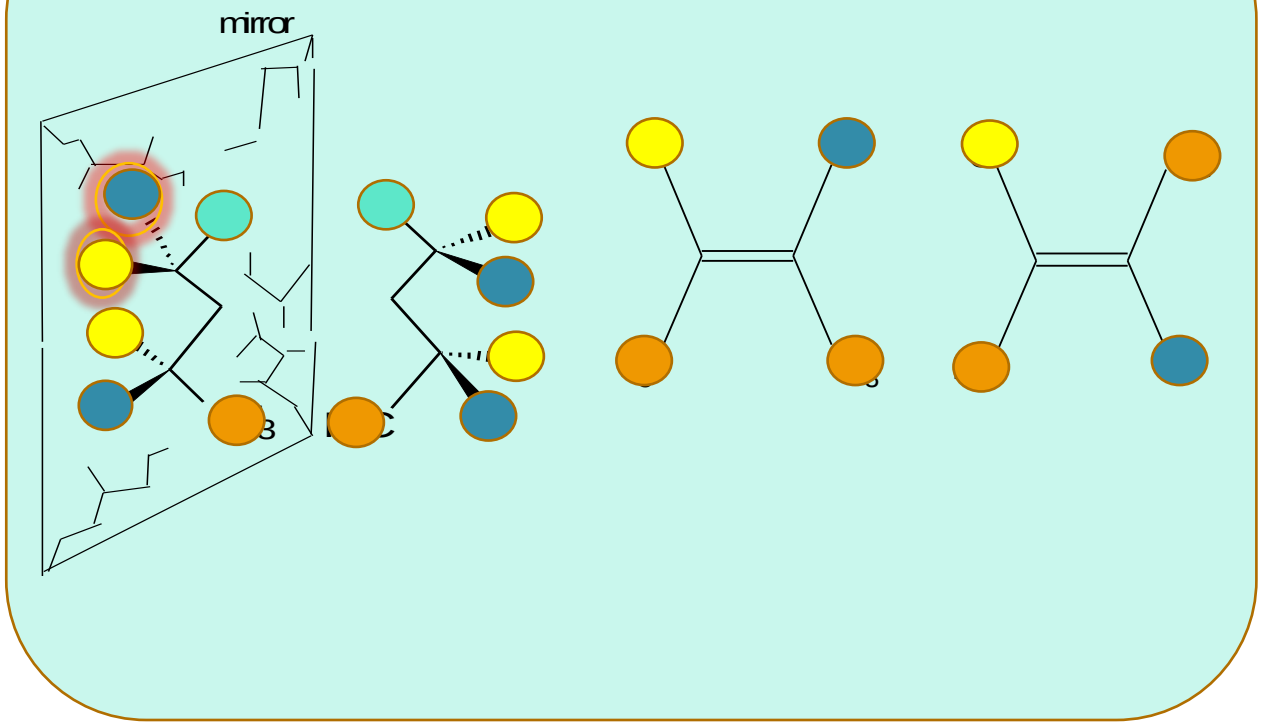
Examples

stereoisomers

enantiomers



diasteroisomers



PPP active substances containing isomers

An active substance is an ***active substance containing stereoisomers*** **when its three-dimensional chemical structure can give rise to stereoisomers** (by the exchange of two or more atoms).

The term **applies to**:

-active substances containing **several components consisting of stereoisomers**, or,

-active substances **consisting of a single component that has the potential of having stereoisomers** (which may eventually be present impurities or formed by the active substance transformation).

The **same criteria applies for** a transformation product considered as a **metabolite containing stereoisomers.**

IMPORTANT !!! Metabolites containing stereoisomers may be generated from substances that do not contain stereoisomers.

Examples I

Active substances containing **several components consisting of stereoisomers**

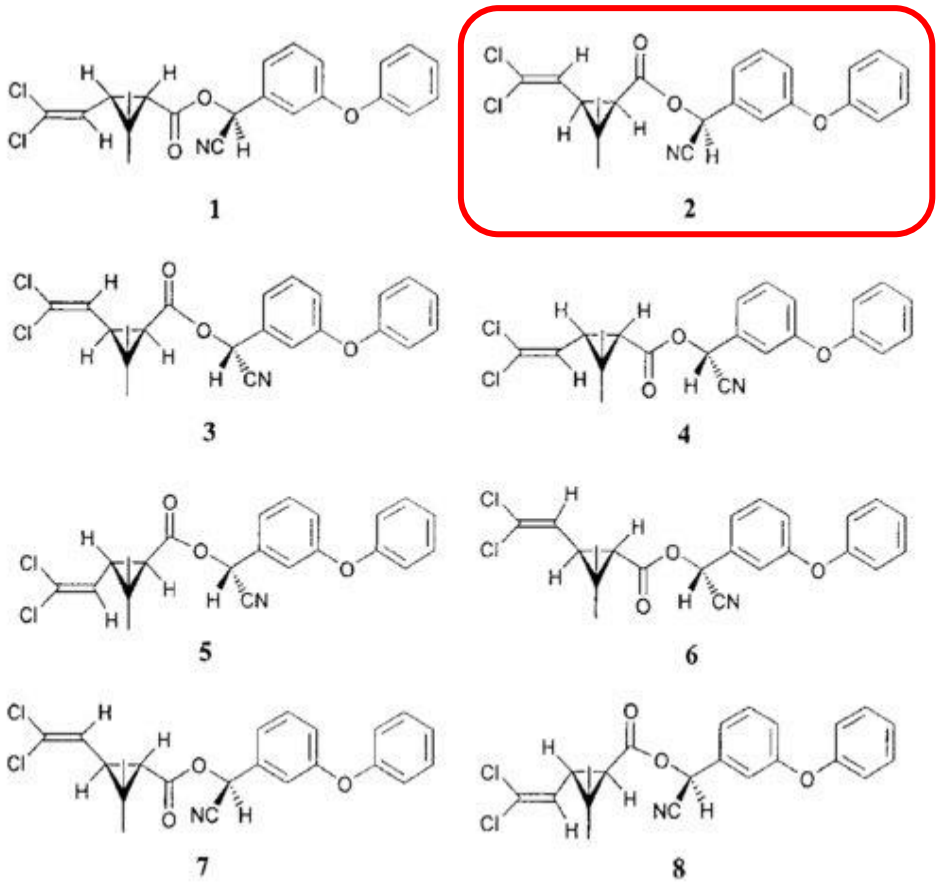
cypermethrin (8 isomers), **fenvalerate** (4 isomers), **dichlorprop** (2 isomers), **metalaxyl** (2 isomers), **diniconazole** (2 isomers), **metolachlor** (4 isomers, generated by a chiral carbon and the impeded rotation: atropisomers), (2 isomers), **acetochlor** (2 isomers, rotamers atropisomers), **alachlor** (2 isomers, rotamers atropisomers), **fenamiphos** (2 isomers), **fonofos** (2 isomers), **malathion** (2 isomers), **imazapyr** (2 isomers), **imazaquin** (2 isomers).

Active substances **consisting of a single component that has the potential of having stereoisomers.**

dichlorprop-P (R isomer of dichlorprop), **metalaxyl-M** (R isomer of metalaxyl), **diniconazole-M** (R isomer of diniconazole), **mecoprop-P** (R isomer of mecoprop).

Examples II

Striking complex situations… e.g. Cypermethrin related active substances.



Isomer 2 (**1S,cis, αR**) is the most biologically active. Isomers 3, 5 and 8 are between 30 and 100 times less active and isomers 1, 4, 6 and 7 between 100 and 10 000 times less active than 2.[1]

Alpha–Cypermethrin is the racemic mixture of **2** and **4** and it is the most biological active cypermethrin in the market.

Cypermethrin: mixture of the 8 isomers

Beta–Cypermethrin: isomers **2, 4, 6** and **8**

Zeta-cypermethrin: isomers **1, 2, 7** and **8**

Theta-cypermethrin: isomers **6** and **8**

1. Ackermann, P., Bourgeois, F., Drabek, J., **1980**. The optical isomers of a-cyano-3-phenoxybenzyl-3-(1,2-dibromo-2,2-dichloro-ethyl)-2,2-dimethylcyclopropanecarboxylate and their insecticidal activities. *Pestic. Sci.* **11**, 169–179.

General principle

Since they may show different chemical (diasteromers) and biological (all) properties, **stereoisomers** must be treated as **different chemical components** with respect to the **risk assessment**.

Issues the guidance intends to address

-On **how to address the data requirements** in the case of substances containing or generating stereoisomers.

-On **how to make the best use of available information** in situations when information on individual stereoisomers is not available or difficult to obtain.

-On **how to optimize the studies performed** and decide the best design for them to obtain the maximum information on stereoisomers properties.

General requirements

Regulation (EU) 283/213 requires

-to establish and provide a **detailed description** (specifications) of the active substance, which will include **isomeric composition** and perform tests required with material representative of such specifications

-to report the **relative biological activity of isomers**, both in terms of **toxicity and efficacy**

-to assess toxicological ecotoxicological **relevance of isomers present as impurities**

Further information on the as

Regulation (EU) 283/2013 requires that when the substance is a mixture of isomers, it should be clarified how this influences on the effects, based on the mode of action of the individual isomers.

Candidates for substitution

One of the conditions for considering a substance a candidate for substitution is that it contains a significant proportion of non-active isomers (Regulation (EU) 1107/2009 ANNEX II, point 4)

General strategies I

- **Chemical analysis** to separately quantify the stereoisomers during the course of the studies.

  To identify if conversion or preferential transformation of stereoisomers occurs

  To adequately relate the effects observed to the different stereoisomer composition.

- **Additional effect experiments** with materials containing purified stereoisomers or different proportions of stereoisomers from those in the a.s.

  To individualize the effect of each isomer

  To assess the effect of the actual mixture of isomers to which organisms will be exposed to.

General strategies II

- **Bridging studies** may allow to infer the general relative behavior and biological effects of different stereo isomers on basis of a limited amount of tests.

- **Use of data** generated for **different active substances** consisting on **different proportions of the same stereoisomers**.

Consideration of stereoisomerism

Stereoisomers may differ in their toxicological potency or profile, changes in the stereoisomeric composition need to be considered in the risk assessment. Eventual differences in the stereoisomeric composition of the toxicologically tested substance and the steroisomeric composition of the actual residue to which humans and animals may be exposed to need to be addressed.

Metabolism, distribution and expression of the residues

-Metabolism studies must elucidate preferential metabolism, distribution of stereoisomers and stereoisomer interconversion.

-If the a.s has enantiomers a "chiral" analytical method must be used.

-Metabolism legacy studies (not addressing stereoisomerism) can be used if enough information on stereoisomers behavior has been obtained in field trials and animal feeding studies.

efsa
European Food Safety Authority

Magnitude of residues, plant and animal trials.

-Stereoselective analytical methods may or not be needed depending on the results of the metabolism studies

-Nevertheless, the use of stereoselective methods in field trials and animal feeding studies is strongly recommended to increase the robustness of the metabolism data and to allow the use of legacy metabolism studies.

Residue definition

- Guidance does not add study requirements to those already established in the regulation but helps to clarify the information that needs to be collected in these studies.

- Application of the guidance helps to minimize the need to separately monitor stereoisomers, providing strategies to perform worst case risk assessment in situations where information on levels of separated stereoisomers is not available.

Residue monitoring

-Decision on the need of stereoselective monitoring is out of the scope of the guidance. Such decision may be considered by risk managers based on the relative toxicological properties of stereoisomers and the need to monitor them separately for adequate risk assessment and GAP enforcement.

Fate and behavior into the environment

Degradation in soil

-Stereoisomeric composition of the residue in soil needs to be investigated and changes with respect to a.s. stereoisomeric composition are considered a transformation.

-Degradation and / or formation of individual stereoisomers of the active substance or its metabolites should be characterized.

-Changes of stereoisomeric composition ≥ 10 % s.e are considered significant with respect to the environmental risk assessment.

On the ≥ 10 % s.e trigger

-Changes ≥ 10 % s.e in the residue with respect to the substance as manufactured are considered potentially significant.

-The trigger should not be considered a "hard trigger" but on a *case by case* basis and weight of evidence.

-Stereoisomeric excess is only defined for pairs of stereoisomers.

-Stereoisomeric excess changes may be matrices' dependent.

-The relative change between stereoisomers may depend of the initial proportion.

-Effect of analytical method errors need to be considered.

-Further information in Appendix A of the guidance.

Uncertainty factor

-If information is incomplete to determine the changes in stereoisomeric composition of the residue or their relative toxicological potency an uncertainty factor can be introduced in the risk assessment.

-The uncertainty factor is calculated with the worst-case assumption that the toxicity of the original mixture can be attributed to a single stereoisomer and that this isomer constitutes the totality of the residue.

-Less worst-case can be assumed if information on the relative toxicity or residue stereoisomeric composition is available.

-Further information on the calculation of the uncertainty factor can be found in Appendix B of the guidance.

Thanks for your attention

Stay connected

Subscribe to
www.efsa.europa.eu/en/news/newsletters
www.efsa.europa.eu/en/rss

Engage with careers
www.efsa.europa.eu/en/engage/careers

Follow us on Twitter
@efsa_eu
@plants_efsa
@methods_efsa

Industry FAQ on isomers

J. Oriol Magrans

4 May 2021

Trusted science for safe food

efsa
European Food Safety Authority

Analytical methods and uncertainty factors

- Is there a need to use UF when residues are <LoQ and or LoD ?

The UF should be applied on residues < LoQ in a first instance. This may be further refined when residues are consistently non detected (< LoD).

- Is there a requirement for chiral monitoring methods?

Depending on the residue definition, non-chiral and chiral monitoring methods may be needed by risk managers for the monitoring and enforcement needs (e.g. to distinguish two different active substances in the market).

- Should a chiral method be developed for each enantiomer of conjugates which are natural products (e.g. sugar conjugates) when the aglycon itself has no chiral center.

In special situations, such as active substances that are constituted by only natural products, the analytical methods should allow to separate only those components known or expected to occur naturally. This is also the case for metabolites consisting of conjugates of a synthetic active substance to natural products (e.g. sugar conjugates), where the synthetic component does not contain a stereogenic element.

Residues

- Do we need to consider for further isomer assessment food and feed items or are food items sufficient?

Feed items are considered for livestock.

- Could the analysis of the liver (central organ for metabolism) in animal metabolism studies with regard to the isomer ratio be sufficient or are the other matrices (e.g. muscle, kidney) still of interest?

If no different metabolites are found in other matrices (eg. milk and muscle) the isomer ratio in liver may be used as a surrogate for other matrices. If metabolites are specific to a given matrix the isomer ratio will need to be investigated in that matrix.

- The test material should in principle reflect the ratios of isomers in the terminal residue. A "representative" ratio should be considered for the material to be used in the test studies. How can this "representative" ratio be defined?

On the basis of the available data from metabolism studies and / or residue trials.

On the 10 % trigger

- 10% TRR is discussed but for example in Consumer Safety mg/kg is also a 'trigger value'. Concentration must be taken into account for technical feasibility?

10 % in the guidance refers to e.e or, more in general, s.e (stereoisomeric excess) and no change with respect to other percentile or absolute level trigger is proposed. See Appendix A of the guidance for further explanations.

- It is difficult to understand how the 10% se change trigger should be employed for molecules with >2 chiral centers.

For more complex mixtures of stereoisomers, it is recommended to use residue decline studies to investigate the fate of each individual stereoisomer in order to decide if the stereoisomers behave differently during metabolism and ageing of the residues (see Appendix A for further discussion and examples).

Considerations on the implementation of the EFSA guidance document on stereoisomers[1)] in the context of MRL applications (Art. 6 to 10 of Regulation (EC) No 396/2005) and MRL reviews (Art. 12)

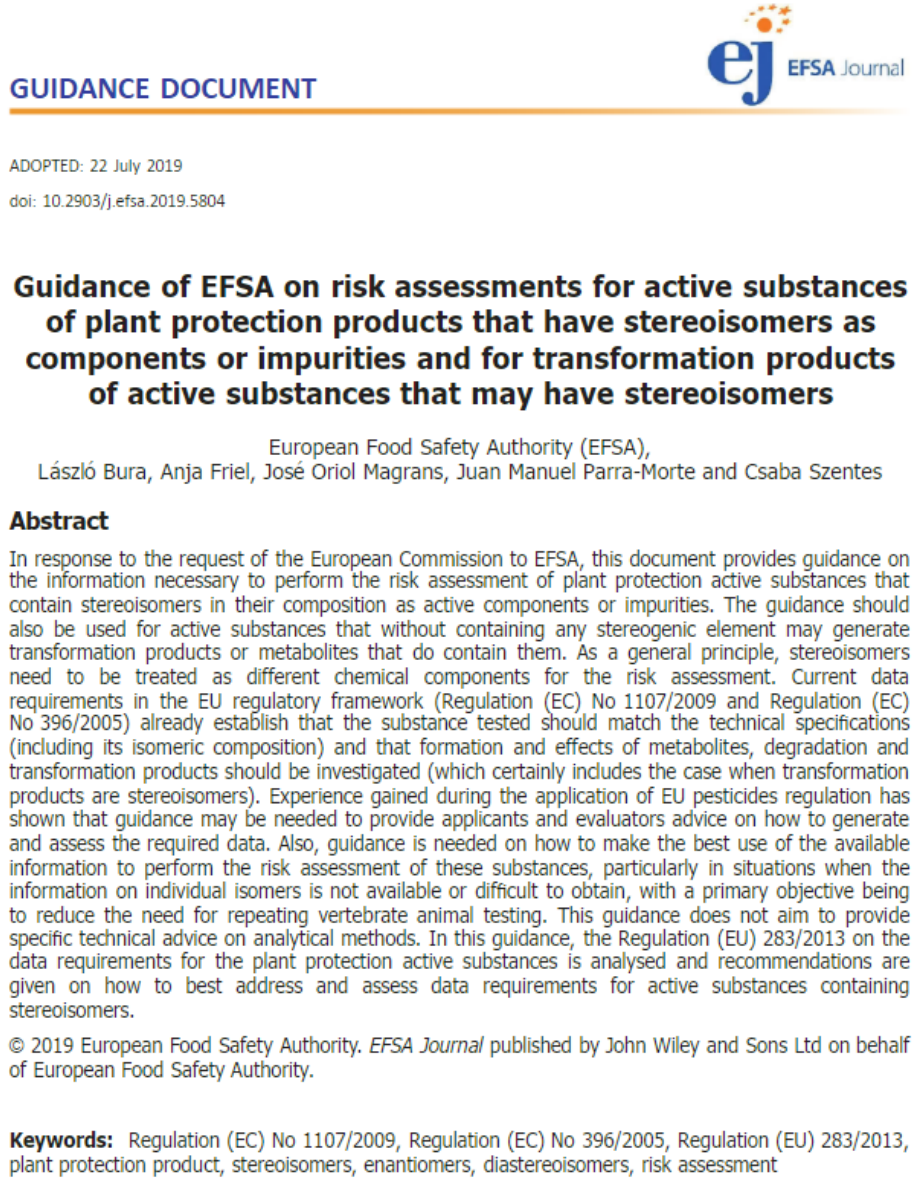
The guidance document on isomers provides specific options how to perform the dietary risk assessment for stereo isomers in food/feed resulting from the treatment with active substances:

- isomeric mixtures unchanged compared to a.s. applied or
- isomeric mixture different to a.s. applied.

Stereoisomers occurring in different amounts compared to a.s. applied should be considered as a specific type of metabolites that need to be assessed in view of consumer health risks. In contrast to other metabolites, the guidance document offers tools for their assessment, and options to avoid the generation of new studies.

The guidance document does not introduce new data requirements.

[1)] https://www.efsa.europa.eu/en/efsajournal/pub/5804



GUIDANCE DOCUMENT

EFSA Journal

ADOPTED: 22 July 2019

doi: 10.2903/j.efsa.2019.5804

Guidance of EFSA on risk assessments for active substances of plant protection products that have stereoisomers as components or impurities and for transformation products of active substances that may have stereoisomers

European Food Safety Authority (EFSA),
László Bura, Anja Friel, José Oriol Magrans, Juan Manuel Parra-Morte and Csaba Szentes

Abstract

In response to the request of the European Commission to EFSA, this document provides guidance on the information necessary to perform the risk assessment of plant protection active substances that contain stereoisomers in their composition as active components or impurities. The guidance should also be used for active substances that without containing any stereogenic element may generate transformation products or metabolites that do contain them. As a general principle, stereoisomers need to be treated as different chemical components for the risk assessment. Current data requirements in the EU regulatory framework (Regulation (EC) No 1107/2009 and Regulation (EC) No 396/2005) already establish that the substance tested should match the technical specifications (including its isomeric composition) and that formation and effects of metabolites, degradation and transformation products should be investigated (which certainly includes the case when transformation products are stereoisomers). Experience gained during the application of EU pesticides regulation has shown that guidance may be needed to provide applicants and evaluators advice on how to generate and assess the required data. Also, guidance is needed on how to make the best use of the available information to perform the risk assessment of these substances, particularly in situations when the information on individual isomers is not available or difficult to obtain, with a primary objective being to reduce the need for repeating vertebrate animal testing. This guidance does not aim to provide specific technical advice on analytical methods. In this guidance, the Regulation (EU) 283/2013 on the data requirements for the plant protection active substances is analysed and recommendations are given on how to best address and assess data requirements for active substances containing stereoisomers.

Keywords: Regulation (EC) No 1107/2009, Regulation (EC) No 396/2005, Regulation (EU) 283/2013, plant protection product, stereoisomers, enantiomers, diastereoisomers, risk assessment

Purpose of the following flowcharts

- The introduction of new guidance documents for pesticides has implications on the assessments performed by EFSA in the different workflows (i.e. approval or renewal of the approval of active substances under Regulation (EC) No 1107/2009, MRL reviews under Article 12 of Regulation (EC) No 396/2005 and MRL applications under Art. 6 to 10 of Regulation (EC) No 396/2005).
- For assessments of the **approval/renewal of active substances and for import tolerance applications for new active substances** not assessed previously in the EU, a comprehensive data set as specified in the legal data requirements is provided by the applicants and is assessed by EFSA/EMS/RMS. In these cases, the **assessment will follow the GD without the need for further considerations**.
- The assessment of **MRL applications** (active substances assessed previously in the EU) typically focusses on the specific data required to support the **intended uses only**, **taking over conclusions of the approval and the MRL review process**.
- **Existing uses which were assessed previously** and for which MRLs have been implemented in Regulation (EC) No 396/2005 undergo a comprehensive review in the framework of Article 12 of Regulation (EC) No 396/2005 **taking over conclusions of the approval**.
- **The following flowcharts describe the approach for assessment of stereoisomers in the context of MRL applications Art. 6 to 10** (except import tolerances for substances not assessed previously at EU level) and **Art. 12**:
  - Slides 3 to 5 provide explanations on the procedural aspects for Art. 12
  - Slides 6 to 8 outline the procedural aspects for Art. 6 to 10
  - Slides 9 to 11 visualise the scientific assessment as suggested in the EFSA Guidance document.
- **The general principle of the approach to be taken for MRL applications and MRL reviews is that the assessment of isomers** (either by providing data to address the hazard of the individual isomers or the exposure to the individual isomers) **should follow what has been done in previous assessments of the active substance in the peer review.**
- If the approval/renewal or the MRL review was performed without mentioning the isomer aspects, the assessment of isomers would not become an issue in a subsequent MRL assessment under Art. 6 to 10 of Regulation (EC) No 396/2005 and MRL reviews.

Procedural aspects for MRL review (Art 12) for isomers – Part 1

No data gaps related to isomers:
Hazard characterisation for individual isomers is available;
information on isomeric composition of residues for the existing uses are available

Assessment according to the principles of EFSA GD

No consumer risk identified

Derive MRL recommendations

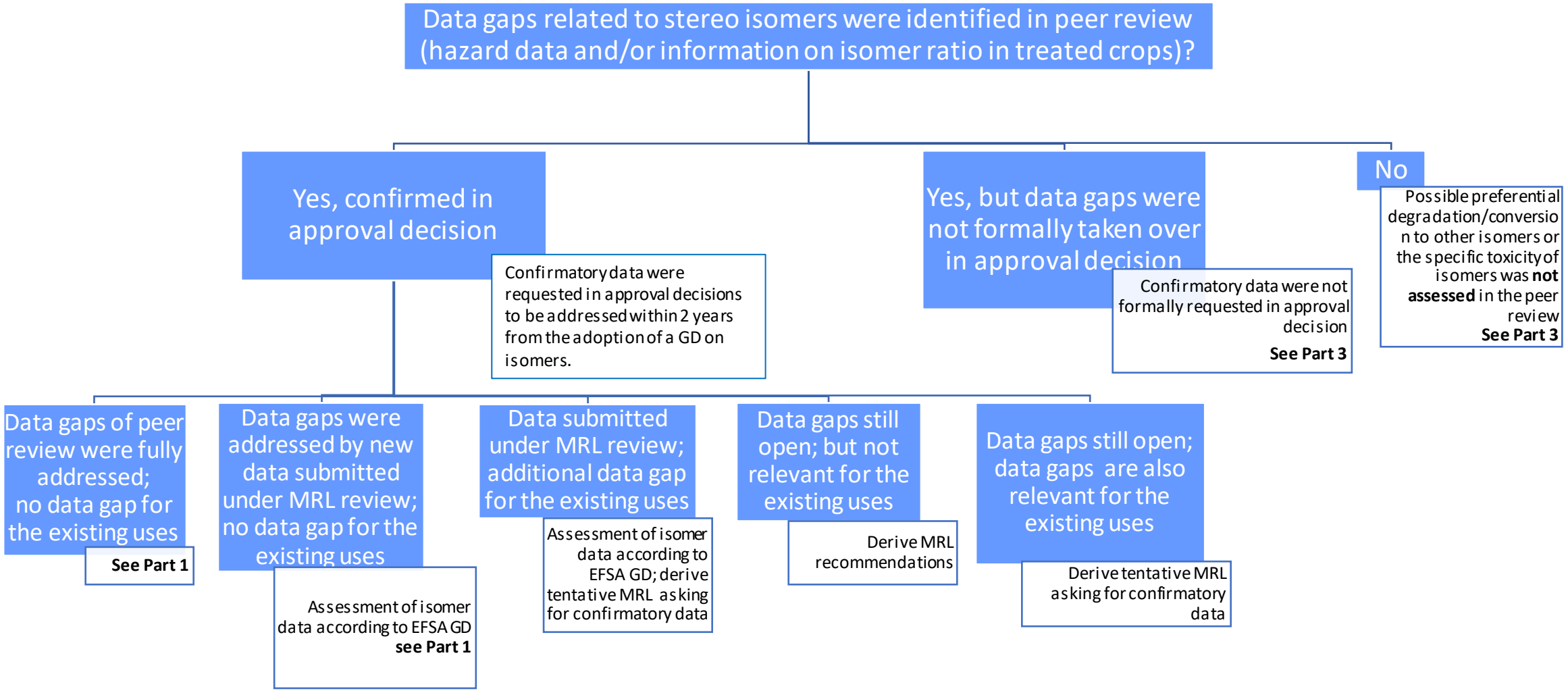
Acute risk identified for one or several existing uses

Propose a refinement identifying a fall-back MRL or proposing to lower the MRL to the LOQ

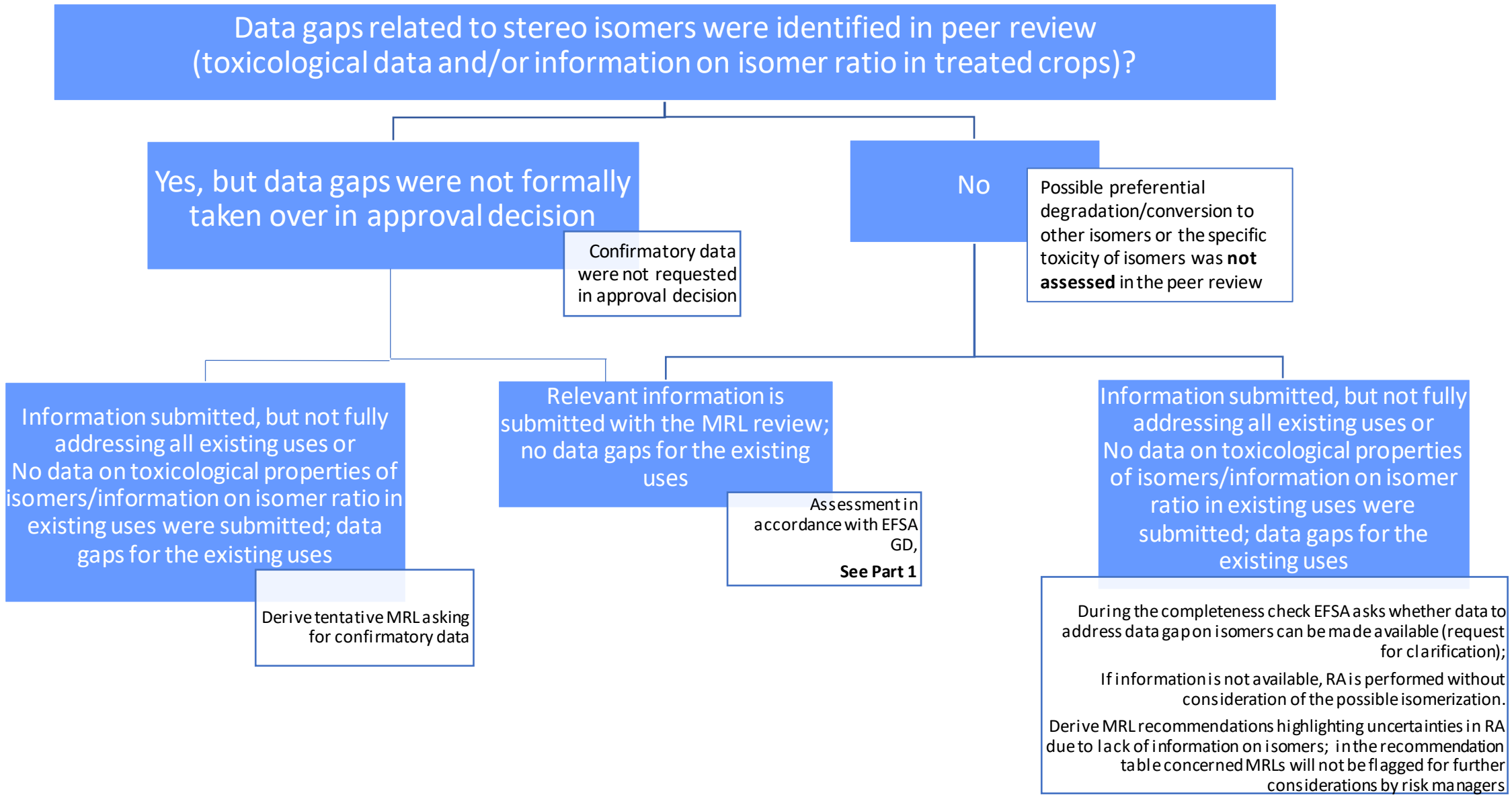
No acute risk for existing use, but chronic risk identified

Propose a possible refinement considering fall-back GAPs or proposing to lower the MRL to the LOQ

Procedural aspects for MRL reviews (Art 12) for isomers – Part 2



Procedural aspects for MRL applications (Art 12) for isomers – Part 3



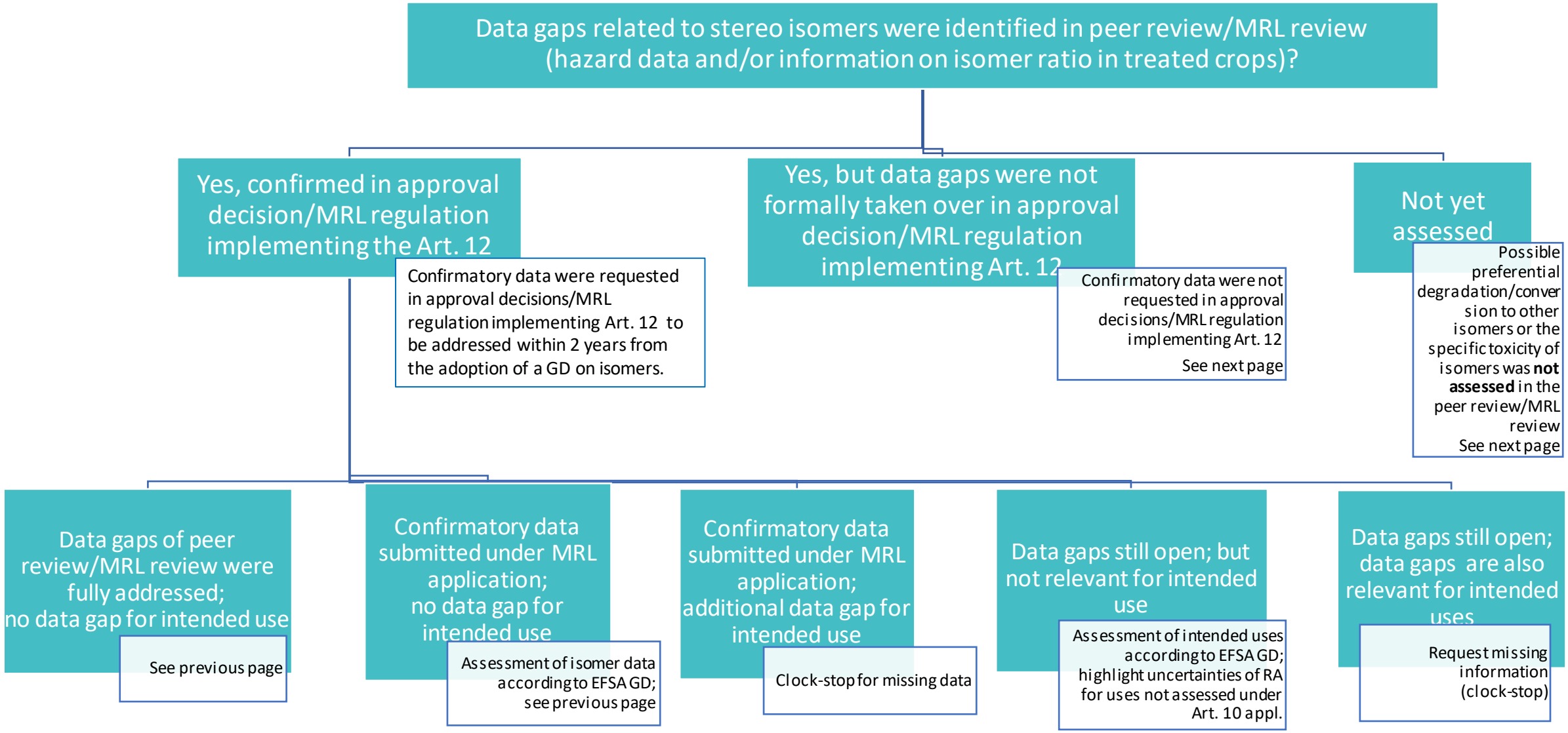
Procedural aspects for MRL applications (Art 10) for isomers – Part 1

No data gaps related to isomers:
Hazard characterisation for individual isomers is available (peer review, MRL review or previous Art. 10 applications); information on isomeric composition of residues for intended uses are available

Assessment according to the principles of EFSA GD

- No consumer risk identified
  - Derive MRL recommendations
- Acute risk identified for intended use
  - No modification of existing MRL recommended
- No acute risk for intended and existing use, but chronic risk identified for existing + intended use
  - Present the data for intended use for further risk management consideration
- No chronic risk for existing + intended uses, no acute risk for intended use, but acute risk for existing MRL(s)
  - MRL recommendation for intended use; Inform RM on concerns for existing MRL

Procedural aspects for MRL applications (Art 10) for isomers – Part 2



Procedural aspects for MRL applications (Art 10) for isomers – Part 3

Data gaps related to stereo isomers were identified in peer review/MRL review (toxicological data and/or information on isomer ratio in treated crops)?

Yes, but data gaps were not formally taken over in approval decision/MRL regulation implementing Art. 12

Confirmatory data were not requested in approval decision/MRL regulation implementing Art. 12

Relevant information is submitted with the MRL application; no data gaps for existing and intended use

Assessment in accordance with EFSA GD,

See slide 6

Relevant information submitted with MRL application, no data gap for intended use, but lack of information on isomer ratio for existing uses

No clock-stop, but contact EMS to ask whether data to address data gap on isomers can be made available (request for clarification);
If information for existing uses is not available, perform RA with current RD RA and TRV, highlighting uncertainties ;

additional RA scenario for intended uses in accordance with GD

No data on toxicological properties of isomers/information on isomer ratio in existing uses were submitted; data gap for intended and existing uses

No clock-stop, but contact EMS to ask whether data to address data gap on isomers can be made available (request for clarification);

RD RA If information for intended and existing uses is not available, perform RA is performed with current and TRV

Highlight uncertainties in RA due to lack of information on isomers

Not yet assessed

Possible preferential degradation/conversion to other isomers or the specific toxicity of isomers was **not assessed** in the peer review/MRL review

Scientific assessment – Part 1

Case 1: a.s. is a mixture of stereoisomers

1) Toxicological properties of individual constituent isomers are available?

- **Yes**
- **No** — See next page

2) Constituent isomers are of same toxicity

- **Yes** — Exposure assessment with Σ of isomers, TRV for mixture
- **No** — Derive relative potency factor (RPF) for isomers

3) Change of isomer ratio?

Based on metabolism studies, residue trials, processing studies, feeding studies

- **No change of isomer ratio (ee<10%)** — Exposure for individual isomers according to ratio of isomers in a.s., TRV for individual isomer, considering RPF
- **Change of isomer ratio (ee>10%)** — Exposure to individual isomers according to the actual isomer ratio, TRV for individual isomers, considering RPF
- **Not known** — Exposure with Σ of isomers, TRV for mixture/RPF

ee/se: absolute difference between the mole fractions of each stereoisomer;
se (%) =(|F_{A1}-F_{A2}| x 100)%
F_{A1}, F_{A2} : mole fraction of stereoisomer A1 and stereoisomers A2

Scientific assessment – Part 2

Case 1: a.s. is a mixture of stereoisomers

1) Toxicological properties of individual constituent isomers are available?

No

2) Change of isomer ratio ?

Metabolism studies, residue trials, processing studies, feeding studies

No change of isomer ratio (ee<10%)

Exposure for Σ of isomers, TRV for mixture

Change of isomer ratio (ee>10%)

Exposure to Σ of isomers, TRV for mixture/UF

Not known

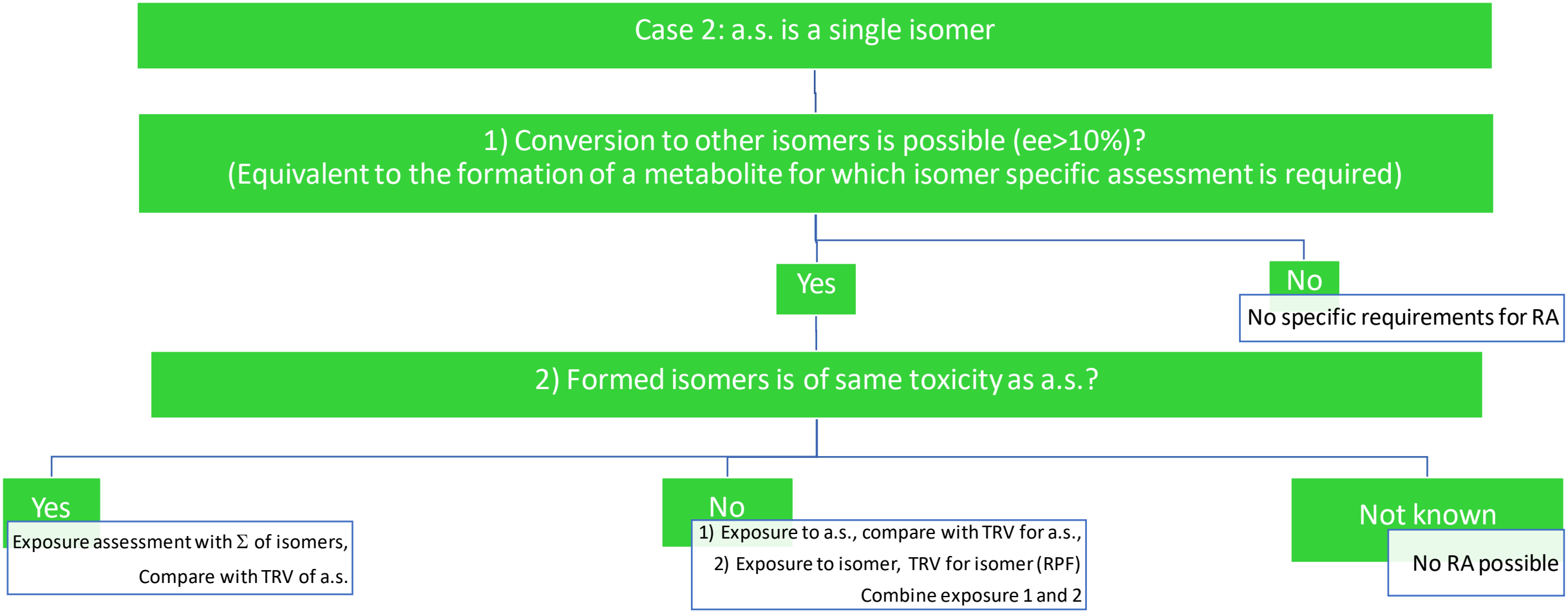
No RA possible

UF: uncertainty factor, calculated based on isomer ratio in a.s. used in toxicological studies

UF= 100/$isomer_{min}$

$Isomer_{min}$: minor isomer (% in a.s. mixture of isomers)

Scientific assessment – Part 3



Implementation of the OECD Guidance Document on Residues in Rotational Crops

Hermine Reich

Senior Scientific Officer

Trusted science for safe food

efsa
European Food Safety Authority

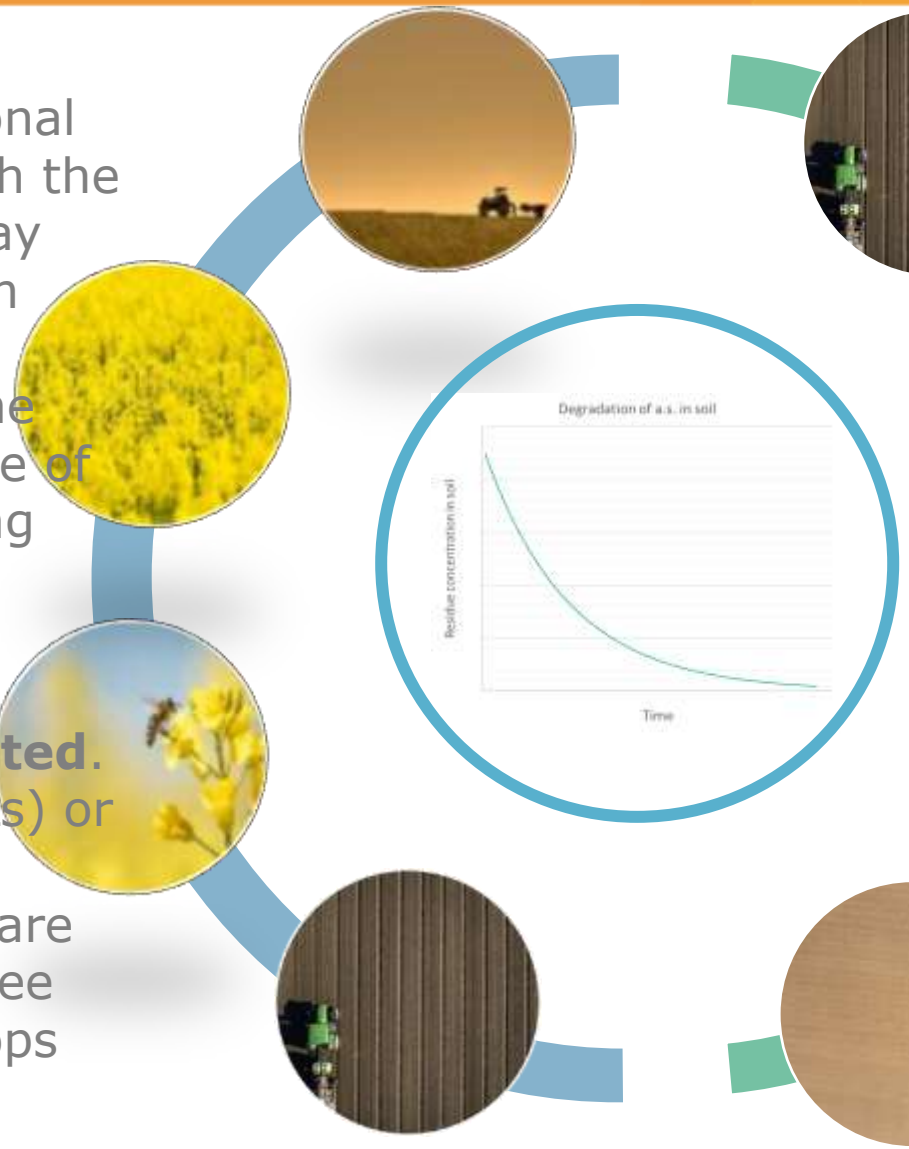
Outline

- Introduction: Why are residues in rotational crops relevant?
- Legal background and existing guidance documents
- Implementation of the guidance documents in regulatory practice
- Open questions that require further clarifications
- Conclusions, recommendations

Introduction

In succeeding/rotational crops not treated with the pesticide residues may occur via uptake from soil.
The assessment of the nature and magnitude of residues in succeeding crops is important

- to ensure that **consumers** are sufficiently **protected**.
- **Legal limits** (MRLs) or **restrictions for rotational crops** are defined to guarantee that rotational crops are **safe** and **compliant with MRLs**.



Treatment of primary crops with pesticides…

…can lead to residues in soil.

Depending on the properties of the active substance, the soil and other factors….

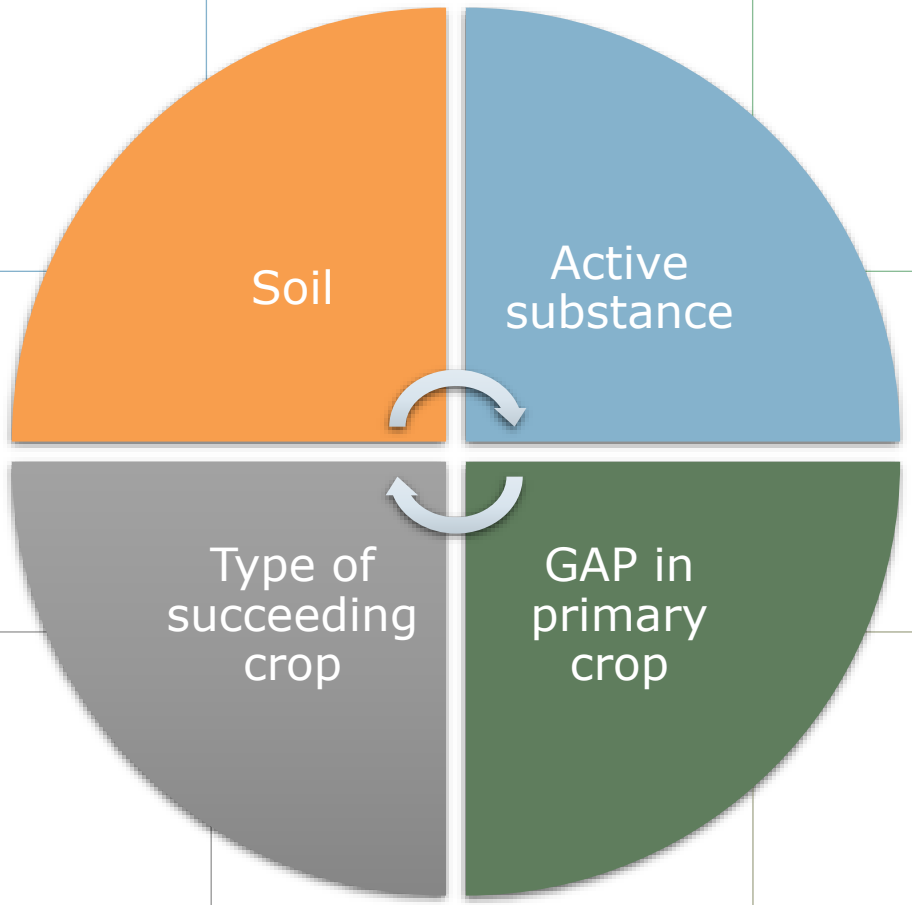
…these residues may still be present in the soil at harvest of the primary crop.

Introduction

Parameters relevant for assessment of rotational crops

- Soil type
- Temperature
- Humidity
- Metabolic activity

- Persistence/stability of a.s.
- Degradation kinetics
- Formation of soil metabolites
- Degradation rate of metabolites



- Type of crop
- Timing of planting

- Type of crop
- Application rate
- Number of treatments
- Crop development

Complex system, requiring interdisciplinary assessment approach with close collaboration of residue and soil experts

Legal basis: Regulation (EC) No 283/2013

General provisions on data requirements

para 1.1 of the Annex to Regulation (EC) No 283/2013
Information to be submitted, its generation and its presentation:

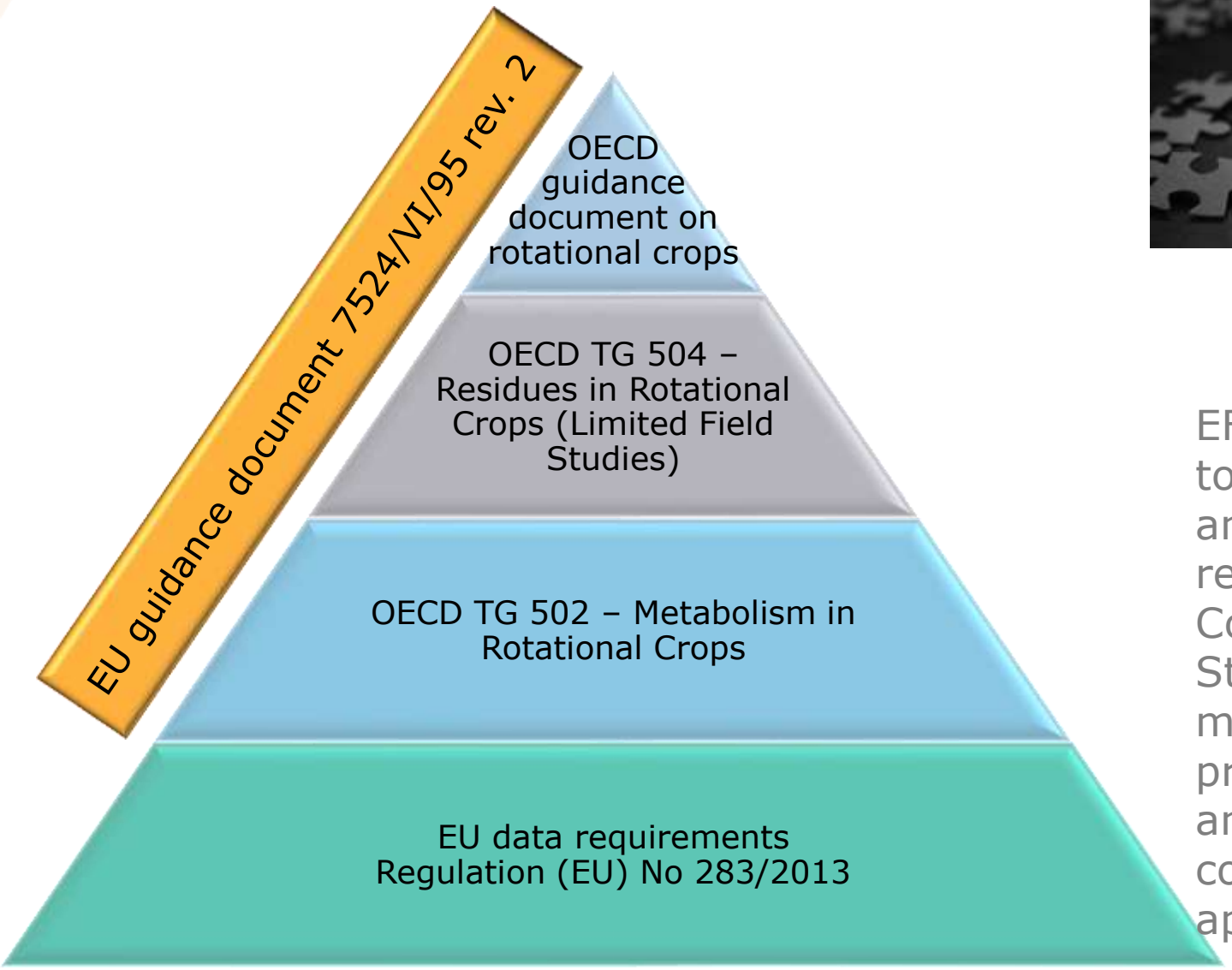
The **information** shall be sufficient to **evaluate foreseeable risks**, whether immediate or delayed, which the **active substance may entail for humans**, including vulnerable groups, animals and the environment. The dossier shall **contain** at least the information and results of the **studies** referred to **in this Annex**.

Legal basis: Regulation (EC) No 283/2013

Studies concerning residues in rotational crops shall be performed to allow the determination of

- the **nature** and extent of potential residue accumulation in rotational crops from soil uptake and
- the **magnitude of residues** in rotational crops under **realistic field conditions**.

How to perform the assessment?



Provisions of the different guidelines and guidance documents are not fully compatible, leave room for interpretations, do not define clear criteria for assessment (trigger values, thresholds).

EFSA started to prepare **technical report** to define how to implement the OECD TG and OECD guidance document in EU regulatory practice.

Consultation of Member State experts and risk managers essential to provide clear guidance and practical solutions compatible with the legal framework (a.s. approval, MRL applications, MRL reviews).

Tiered approach

‘Tier 0’

Pre-conditions for rotational crop assessment

Tier 1

OECD TG 502

- Confined studies with radiolabelled a.s. in three different crop groups

Tier 2

OECD 504

- Limited field studies if triggered by Tier 1

Tier 3

OECD

- Field studies for deriving MRLs if triggered by Tier 2

OECD guidance document on residues in rotational crops (2018)

Additional clarifications mainly on OECD TG 504;

Examples on current practices in different OECD countries;

Guidance on MRL setting for rotational crops and possibility to define label restrictions;

Recommendations not binding.

Assessment of rotational crops is not required, if

'Tier 0'

pesticide is used only in permanent or semi-permanent crops

uses do not lead to residues in soil

- e.g. post-harvest uses, cultivation in hydroponic systems or in artificial substrates, structural treatment

no uptake of a.s. and soil metabolites

- e.g. from metabolism studies in primary crops (root crops)

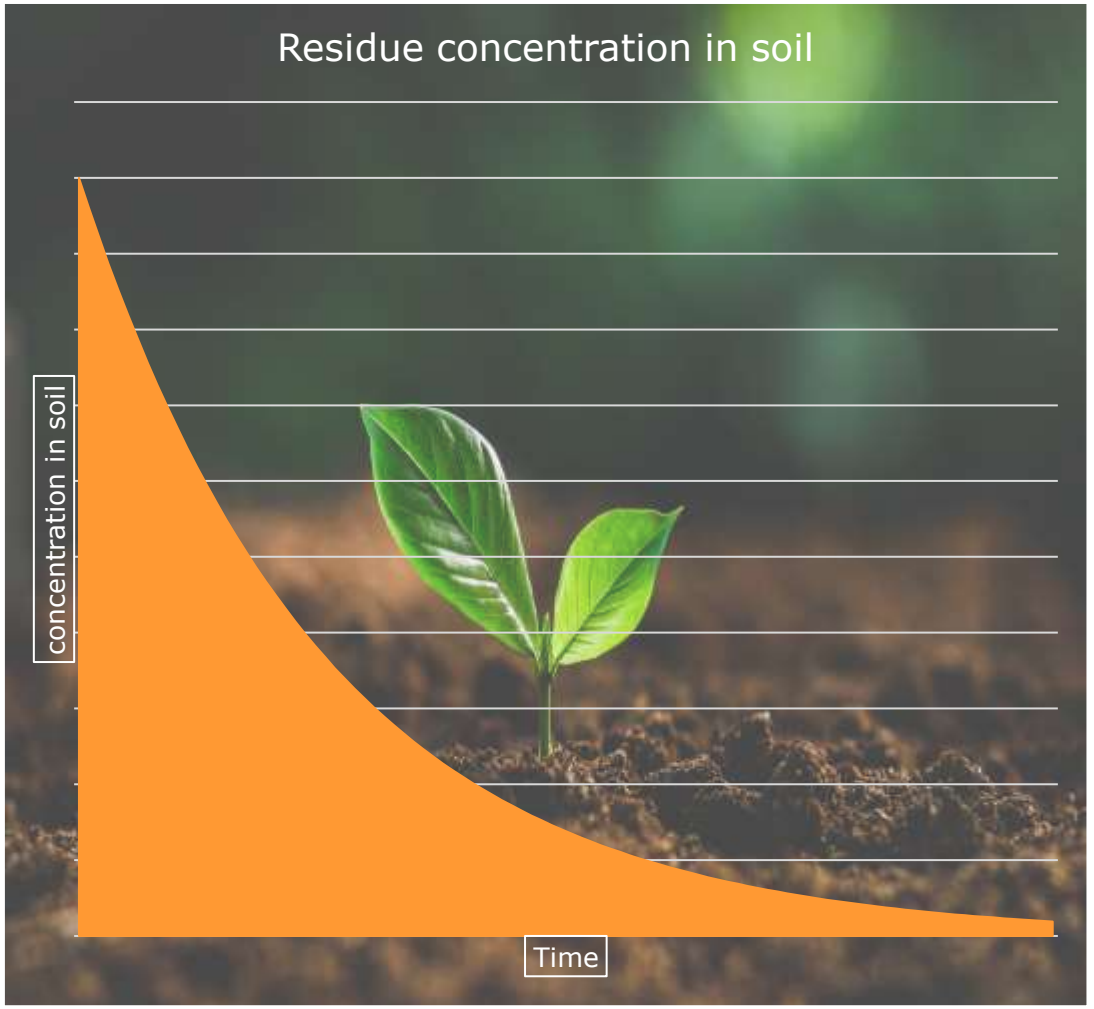
a.s. and metabolites are not stable/persistent in soil, significant concentrations of metabolites in soil do not occur

Practical implementation ‘Tier 0’

EU guidance document:
Trigger value which was interpreted as DT_{90} in soil for a.s. >100 d

OECD documents:
No trigger values defined

EFSA technical report:
- Definition of trigger values for a.s and relevant soil metabolites
- Guidance how to identify relevant end-points to decide whether Tier 1 studies are triggered
- Guidance for import tolerance applications
  - Under which conditions are data on rotational crops required?



Purpose of Tier 1 studies

Tier 1 studies should

- provide an estimate of the total terminal residues in the relevant portion of crops at harvest of rotational crops following treatment of the preceding crop as proposed;
- identify the major components of the total terminal residue;
- indicate the distribution of residues between relevant crop parts;
- quantify the major components of the residue;
- allow to decide on the necessity of field residue trials in rotational crops (limited field studies)
- provide information on the components to be analysed for in higher tier studies;

Practical implementation Tier 1

OECD TG 502 Metabolism in rotational crops

- Representative crops for the three crop groups
- Study design
  - Application rate for Tier 1 studies (max. seasonal application rate of a.s.)
  - Plant Back Intervals (PBIs) simulating
    - crop failure (7-30 d),
    - typical rotation after harvest of primary crop (60-270 d) and
    - crop rotated in the following year (270-360 d)
- Parts of the crops to be analysed
- Interpretation of results
  - Trigger values for residue concentration (mg eq/kg and % of TRR) that require characterisation/identification.

Root and tuber vegetable

Leafy vegetable

Cereals/small grain

Practical implementation Tier 1

EFSA technical report

- Further guidance on study design and practical examples on
  - application rate for a.s. and metabolites that accumulate in soil;
- Practical examples on how to consider crop interception
- Interpretation of results of Tier 1 studies
  - Scaling if studies were performed with higher dose rates than expected under realistic conditions
- Considerations on residue definitions for RC

Practical examples

Root and tuber vegetable

Leafy vegetable

Cereals/small grain

Purpose of Tier 2

Tier 2 studies should

- determine the amount of pesticide residues which may accumulate in rotational crops via soil uptake (semi-quantitative aspect);
- allow to decide whether Tier 3 studies are required;

Practical implementation Tier 2

OECD TG 504 Residues in rotational crops (Limited Field Studies)

- Study design and crops to be tested: very general, high level advice
- Analytical aspects: only general provisions

OECD Guidance document on residues in rotational crops (2018)

- Application rate for Tier 2 studies, considering the soil plateau concentration
- Considerations of metabolites mentioned, but no detailed provisions
- Examples for crops in which Tier 2 studies should be performed

Practical implementation Tier 2

EFSA technical report

- Further guidance on study design to be representative for predicted PEC soil
  - Option 1: separate testing of parent and metabolites,
  - Option 2: study with parent only (soil aging and analysis of residues in soil),
  - Practical examples to calculate the application rates for a.s. and metabolites that accumulate in soil
- Interpretation of results of tier 2 studies
  - Scaling if studies were performed with higher dose rates than expected under realistic conditions
  - Scaling for parent and metabolites for option 2

Purpose of Tier 3 studies

Tier 3 studies should

- provide data for MRL setting,
- provide information to estimate the impact of restrictions on residue levels in rotational crops.

Practical implementation Tier 3

No precise requirements defined in OECD TG 504

OECD Guidance document on residues in rotational crops (2018)

- Selection of crops for Tier 3 studies for the 'Super crop groups'
  - Number of trials required
  - Examples of possible extrapolations of results to other crops
- Proposes an approach to derive MRL proposals based on rotational crop studies and where relevant primary crop uses
- Considerations how to perform risk assessment
  - How to derive input values for risk assessment
- General considerations of MRL setting versus restrictions

Practical implementation Tier 3

EFSA technical report

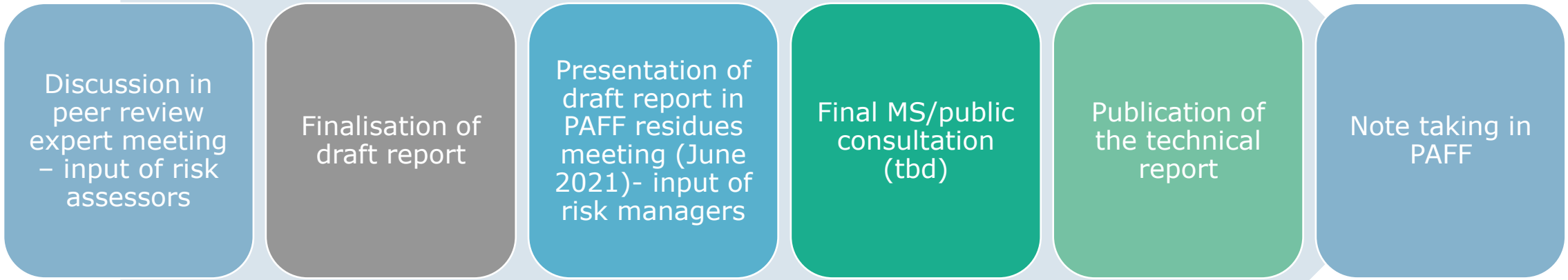
- Under which circumstances the setting of MRLs should be considered?
  - What are realistic worst case conditions (worst case PECsoil, plateau level reached after x years)?
  - Which are realistic plant back intervals (PBIs)?
- Number of trials required for European situation
- Practical advice how to perform risk assessment
  - Input values for risk assessment
  - How to combine risk assessment for primary crops and rotational crops
- Practical advice how to derive MRL proposals
- Further guidance on extrapolations of results to derive MRLs for crops in which no tier 3 studies are available.
- Which restrictions for rotational crops should be considered?

Conclusions, recommendations

Implementation of provisions of OECD TG and guidance is complex and requires collaboration of residue and fate experts.

Further guidance/practical advice is required.

EFSA started to work on a technical report to address the open issues for assessment of residues in rotational crops.



For future, relevant endpoints for assessment of residues in rotational crops should be reported explicitly in the List of Endpoints (LOEP).

Calculation tools for soil endpoints relevant for residue assessment.

Thanks for your attention!

Thanks to EFSA colleagues working on the technical guidance document and Member State experts who share their experience!

Thanks to Maja and Ilvie for illustrations.

Stay connected

Subscribe to

efsa.europa.eu/en/news/newsletters
efsa.europa.eu/en/rss

Receive job alerts

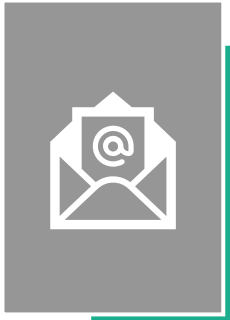
careers.efsa.europa.eu – job alerts

Follow us on Twitter

@efsa_eu
@plants_efsa
@methods_efsa
@animals_efsa

Follow us Linked in

Linkedin.com/company/efsa



Contact us

efsa.europa.eu/en/contact/askefsa

Criteria triggering investigation of residues in rotational crops "tier 0"

Rotational crops FOCAL point

PRES

4th May 2021

Trusted science for safe food

efsa
European Food Safety Authority

When residues in rotational crops need to be investigated?

Regulation (EC) No 283/2013

*Studies concerning residues in rotational crops shall be performed to allow the **determination of the nature and extent of potential residue accumulation in rotational crops from soil uptake and of the magnitude of residues in rotational crops under realistic field conditions**. Rotational crop studies shall not be required for uses of plant protection products in permanent crops (such as citrus and pome fruits crop group), semi-permanent crops (such as asparagus, pineapples) or fungi, where rotations on the same substrate are not part of the normal agricultural practices.*

*The **information** shall be **sufficient to evaluate foreseeable risks**, whether immediate or delayed, which the active substance may entail for humans, including vulnerable groups, animals and the environment and contain at least the information and results of the studies referred to in this Annex.*

Which soil metabolites need to be considered with respect to rotational crops? Significant soil metabolites

Metabolites that are reported in the LoEP (section "Environmental fate and behaviour; Residues requiring further assessment; Soil") need to be considered with respect to potential residues rotational crops and in the context of the Technical Report are classified as **significant soil metabolites**.

Example

Residues requiring further assessment

Environmental occurring residues requiring further assessment by other disciplines (toxicology and ecotoxicology) and or requiring consideration for groundwater exposure.

Soil:	Fluxapyroxad (BAS 700 F) and the metabolites M700F001 and M700F002
Surface water:	Fluxapyroxad (BAS 700 F) and the metabolites M700F001, M700F002 and M700F007
Sediment:	Fluxapyroxad (BAS 700 F)
Ground water:	Fluxapyroxad (BAS 700 F) and the metabolites M700F001 and M700F002
Air:	Fluxapyroxad (BAS 700 F)

When are rotational crop metabolism studies are necessary?

Metabolism (tier 1) studies are required if the following conditions are met:

- The PPP is **used in crops which are grown in rotation** with other crops (Section 2.2 and Appendix A) and

- the use of a **pesticide leads to residues in soil** (Section 2.3) and

- the **active substance and/or its soil metabolites are sufficiently stable/persistent in soil** to be present in relevant amounts at the time of planting the rotational/succeeding crops (Section 2.4) and

- the **active substance and/or its soil metabolites are taken up via roots by the rotational/succeeding crops** (Section 2.5).

Persistence criteria

Regulation (EC) No 283/2013

Metabolism studies in rotational crops shall be provided if the parent compound or soil metabolites are persistent in soil or significant concentrations of metabolites in soil occur.

"Old" data requirements (Regulation (EC) No 544/2011)

*Where data generated in accordance with point 7.1 of this Annex or point 9.1 of the Annex to Regulation (EU) No 545/2011 shows that significant residues (**>10% of the applied active substance as a total of unchanged active substance and its relevant metabolites or degradation products**) remain in soil or in plant materials, such as straw or organic material up to sowing or planting time of possible succeeding crops, and which could lead to residues above the limit of determination in succeeding crops, consideration shall be given to the residue situation.*

Persistence triggers

Two basic triggers are proposed

- The active substance or any of the significant soil metabolites show a $DT_{90} \geq 100$ d in soil, tier 1 studies need to be provided.

- In case the soil DT_{90} of the parent compound and the significant soil metabolites are individually below 100 days, but the sum of the soil DT_{90}s for the parent and the significant metabolites in any lineal degradation pathway exceeds 100 days , tier 1 studies are required.

The DT_{90}s to be considered in these triggers are those consistent with the end points selected as result of the fate and behaviour assessment to be used for the calculation of the PEC soil.

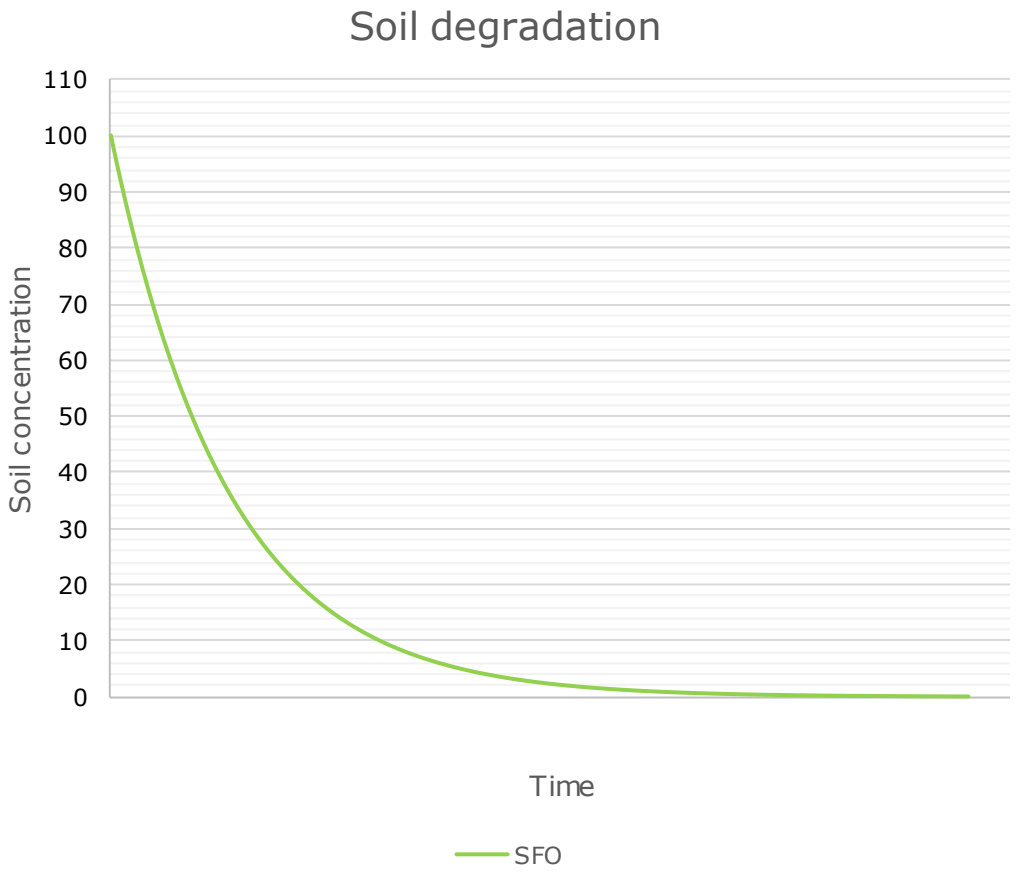
- **DT90 for a.s. and/or significant soil metabolites**

PEC soil (Regulation (EU) N° 284/2013, Annex Part A, points 9.1.3 / 9.3.1)

Parent	DT_{50} (d): *470* days
Method of calculation	Kinetics: *SFO*
	Field: *longest non-normalised field* DT_{50}
Application data	Crop: Leafy veg
	Depth of soil layer: *5cm*
	Soil bulk density: *1.5g/cm*^{3}
	% plant interception: 70
	Interval (d): *70*
	Application rate(s):
	Leafy Veg: 1 or 2 x *120* g a.s./ha (1 application per successive crop)

SFO Kinetics: DT90=DT50×3.32

(first order kinetics)



DT90 for a.s. and/or significant soil metabolites

PEC soil (Regulation (EU) N° 284/2013, Annex Part A, points 9.1.3 / 9.3.1)

Parent
Method of calculation

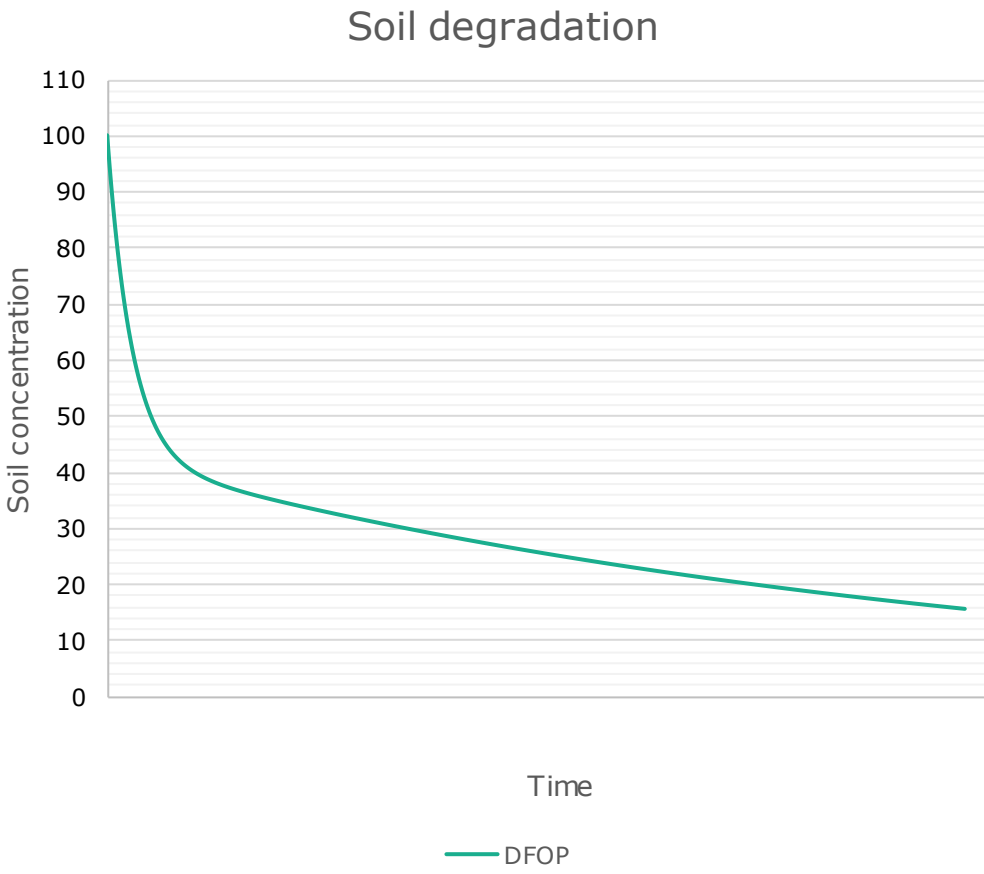
FOCUS standard PECsoil
DT_{50} (d): 348 days (k1=0.07037, k2=0.002, g=0.575)
Kinetics: DFOP
Field or Lab: representative worst-case from lab studies

Rate of degradation in soil (aerobic) laboratory studies active substance (Regulation (EU) N° 283/2013, Annex Part A, point 7.1.2.1.1 and Regulation (EU) N° 284/2013, Annex Part A, point 9.1.1.1)

Parent	Dark aerobic conditions						
Soil type	USDA Texture class	pH[a)]	t. °C / % MWHC	DT_{50} /DT_{90} (d)	DT_{50} (d) 20 °C pF2/10kPa[b)]	St. (χ^2)	Method of calculation
Yolo	Loam	7.2	20 / 50% MHC	34 / 791	348	1.27	DFOP (slow phase)
RefSol 03-G	Loam	6.2	20 / 50% MHC	12 / 249	129	1.83	DFOP (slow phase)
Site E1	Silt Loam	5.9	20 / 50% MHC	11 / 148	116	1.43	DFOP (slow phase)
Site I2	Loamy sand	7.4	20 / 50% MHC	2.5 / 30	8.9	7.08	FOMC (DT90/3.32)
pH dependence					No		

[a)] Measured in 1:1 soil:water ratio
[b)] Normalisation not necessary since soils were incubated at 20 °C and Walker equation coefficient of 1 (soils were at moisture level > pF2)

Non-SFO Kinetics: take highest DT90 from aerobic rate of degradation in soil



Plant uptake

If it can be clearly demonstrated that soil residues are not taken up by certain rotational crop groups, no further investigations are required for the relevant crop groups.

The use of simplified screening tests, such as hydroponic assays, may be only acceptable on a case-by-case basis. The studies must be representative of the relevant rotational crop groups and must allow extrapolation of the results from the assay to the soil situation. Currently, OECD is developing a Test Guideline to determine the uptake of chemicals by plant roots (OECD Project 3.15, OECD, 2019). The application of this test as a screening tool on the investigation of residues in rotational crops may deserve further consideration once it is adopted and published.

Waiving option

If all significant soil metabolites are identical with metabolites identified in primary crop as part of the residue definitions, Tier 1 studies can be omitted, and the assessment for rotational crops could directly start with of the assessment of the magnitude of residues in rotational crops (Tier 2 studies, limited filed trials).

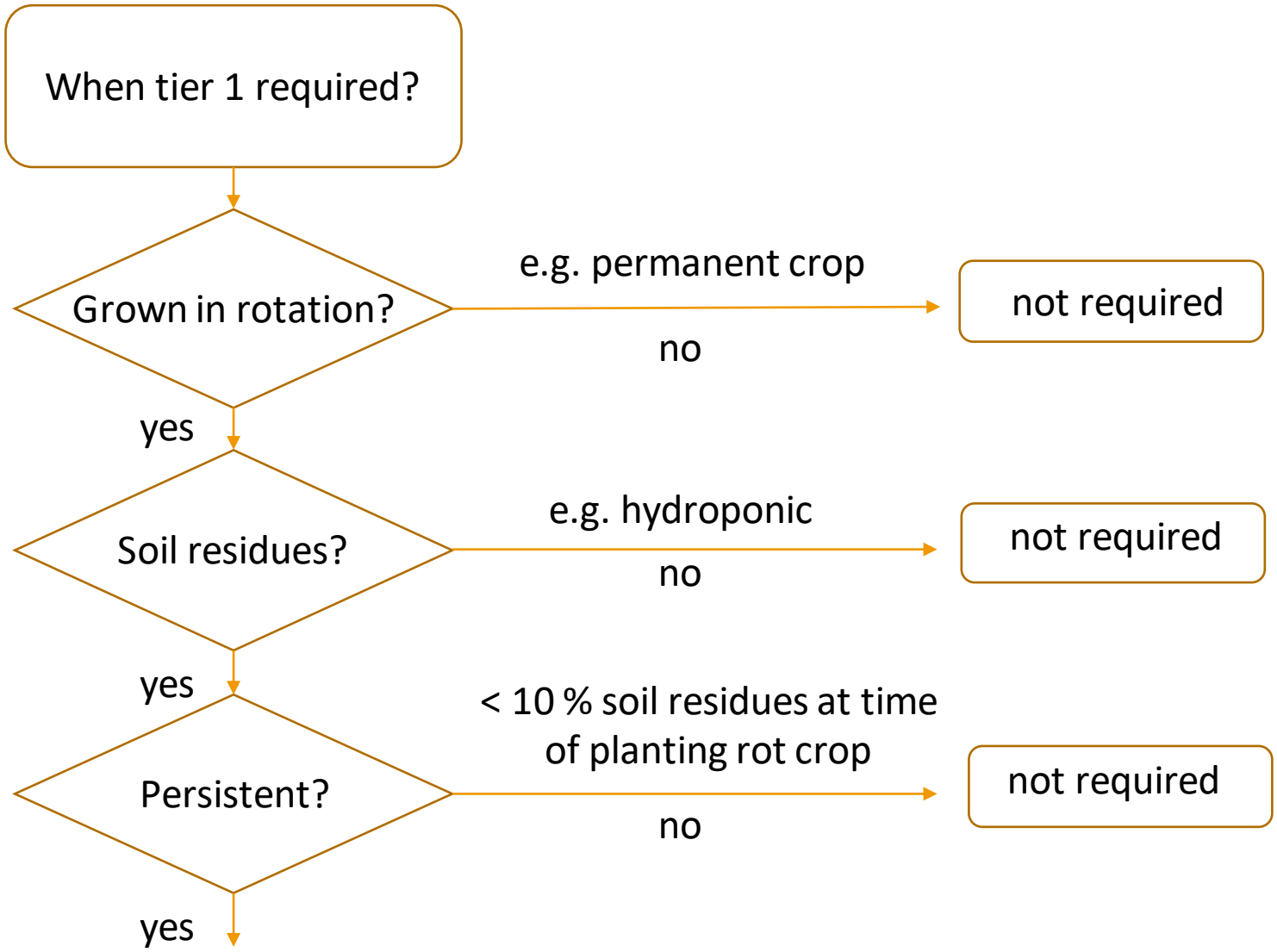
Case of import tolerance applications: is there need for studies on rotational crops?

European Food Safety Authority

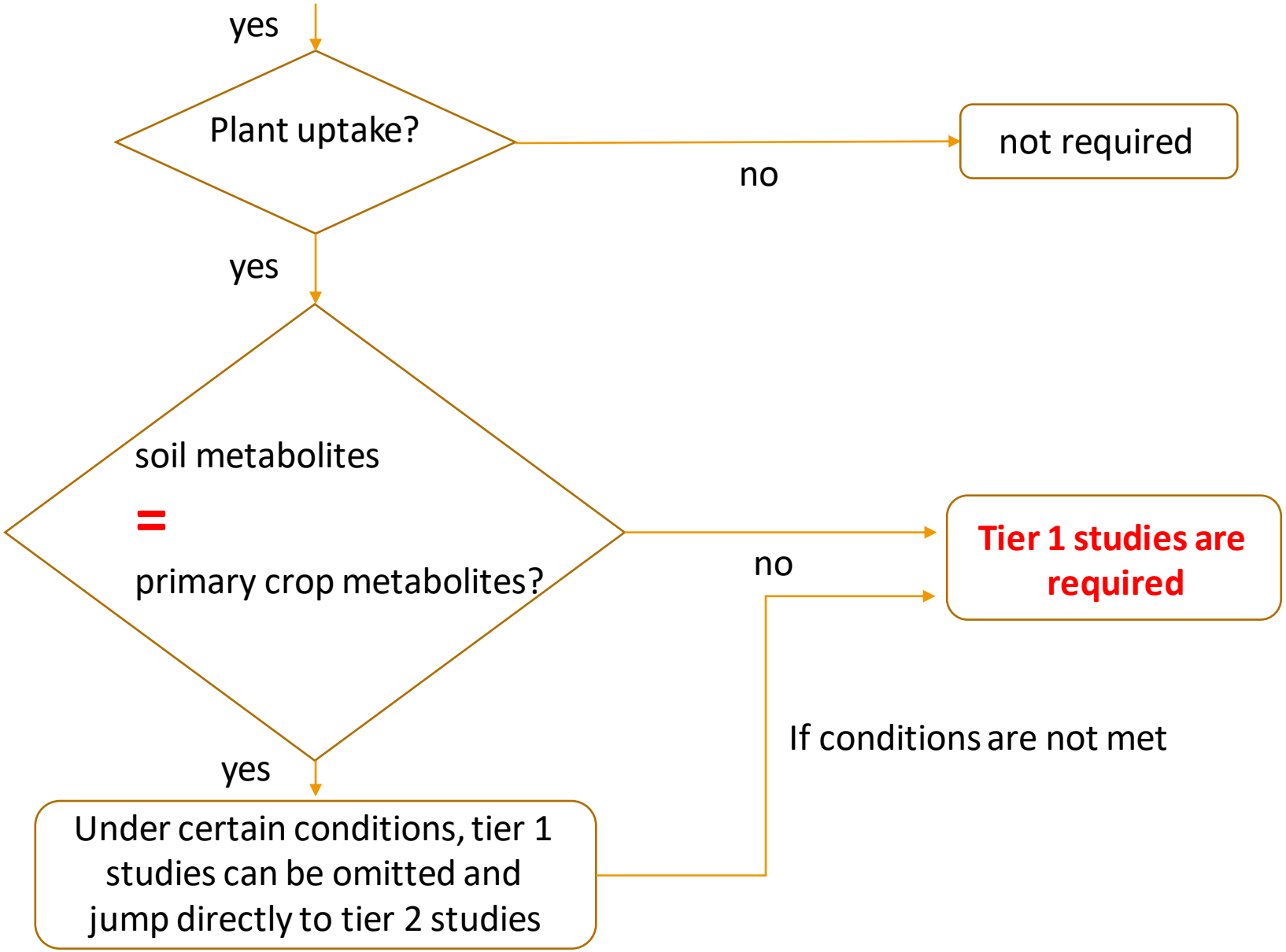
Studies on rotational crops in the framework of import tolerance applications are required when:

- **EU MRLs are established for metabolites occurring in rotational crops (e.g., for trifluoroacetic acid, TFA): Since imported products need to comply with the EU MRLs, data on the occurrence of soil metabolites in annual crops resulting from critical uses in the country of origin that are likely to lead to residues in rotational crops are required.**
- **Metabolites in rotational crops included in the EU residue definition for RA: need of tier 2 and, if triggered, tier 3 studies for crops under consideration. .**
- **Active substance not (yet) fully assessed in the EU for presence of residues in rotational crops: tier 1 studies and, if triggered, toxicological studies to characterize the toxicological profile of soil metabolites taken up by rotational crops and eventually higher tier studies might be required (to further discuss with risk managers).**

Flow chart for rotational crop metabolism studies



Flow chart for metabolism studies



End of “tier 0”

Implementing the applicable guidance documents on the nature of residues in rotational crops (Tier 1 studies on RCs)

Focal Point Group on Rotational crops

EFSA Pesticide Residues unit, 4 May 2021

Trusted science for safe food

efsa
European Food Safety Authority

Support the implementation of OECD TG 502

- **Provisions of the different guidelines and guidance documents are not fully compatible, leave room for interpretations, do not define clear criteria for assessment (trigger values, thresholds).**

- **OECD TG 502 on metabolism studies on rotational crops: absence of values triggering the need for such studies (tier 0), no info available on how to identify the critical GAP and maximum seasonal rate, $PEC_{(s)}$ for a.s. and metabolites not discussed, accumulation in soil not considered, protocol specific to the a.s. only (provision for application of relevant metabolites in soil not available).**

When are tier 1 studies required? Tier 0

- **Tier 1 studies are required if soil residues constituted by parent and significant metabolites after 100 d are higher than 10 % of applied amount on molar basis.**
- **A trigger based on the soil DT_{90} is proposed to assess this criterium:**

Total (a.s. plus metabolites) DT_{90} > 100 d

Tier 1 studies: general considerations

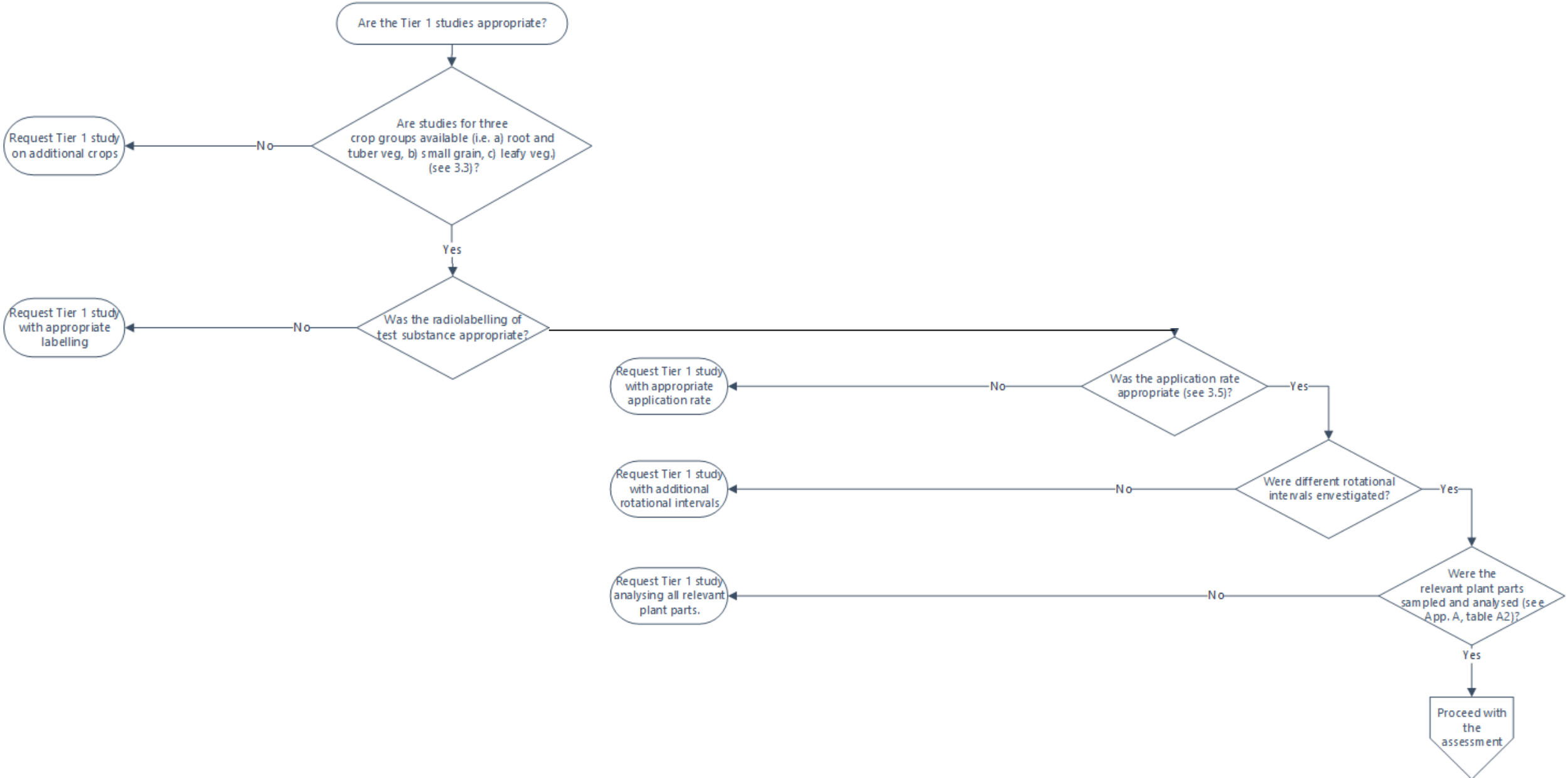
- **Purpose of metabolism studies on rotational crops:**

  Identify the major residues taken up by rotational crops, establish residue definitions for rotational crops and decide whether limited rotational crop field trials (tier 2 studies) should be performed. Tier 1 studies can also serve as a basis to decide on restrictions in crop rotation.

- **Tier 1 studies, need to be conservative:** In order to ensure that tier 1 studies are **representative for the critical situations** encountered in practice as regards the active substance and its metabolites in soil, they should be performed with soil concentrations representative for the most critical case, taking into account the **application rate in primary crops**, **plant interception**, **soil metabolism** and **possible accumulation** of a.s. and/or metabolites in soil.

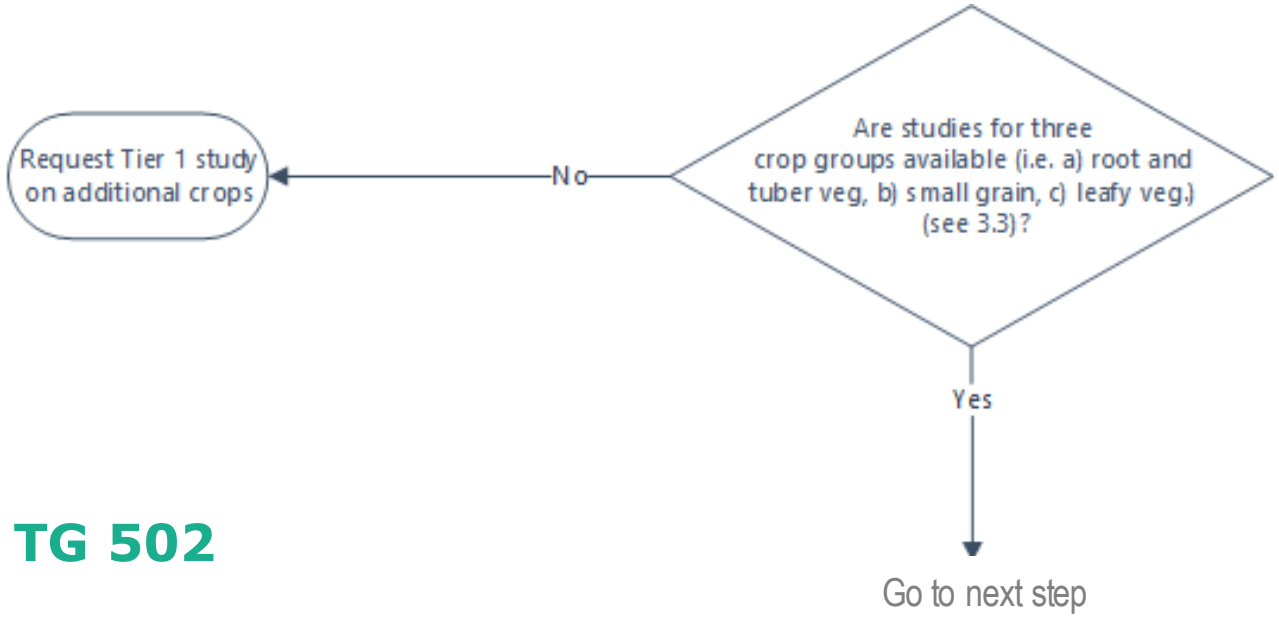
  If the studies are overdosed, results can be proportionally scaled-down**.**

Tier1 studies decision tree



Crops to be subjected to tier 1 studies

- **Three crop groups to be considered, covered by OECD TG 502**
- **Root and tuber vegetables,**
- **Small grain (cereals) and**
- **Leafy vegetables**



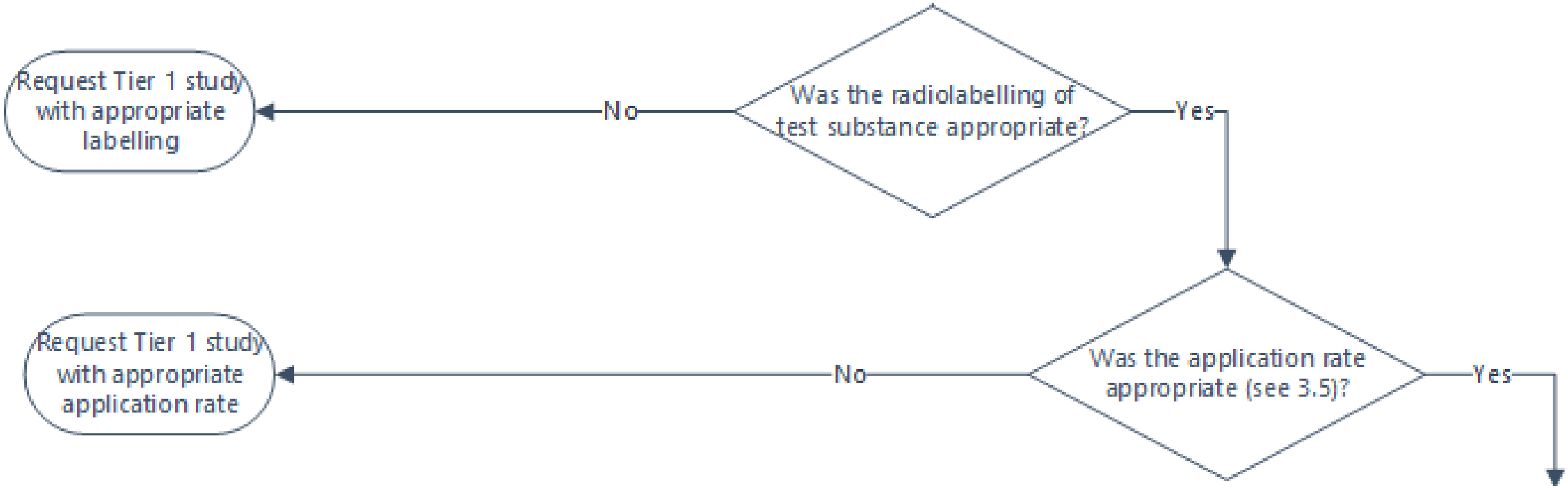
However,

- **Oilseeds are not discussed in OECD TG 502**

Tier 1 studies with oilseeds (oilseed rape or soybeans) may be requested if the three mandatory crop studies do not allow to derive a definitive conclusion on residue definitions for rotational crops (e.g. if the results in the three mandatory crop groups differ substantially or lipophilic substances are among the expected residues).

Radiolabelling of the test substance

- **For tier 1 studies the tested substances shall be appropriately radiolabeled (OECD TG 502)**



- **Is the application rate appropriate?**

How significant soil metabolites are investigated?

Following OECD 2018 Guidance document:

- **Soil metabolites can be investigated with separate studies where the metabolite is appropriately applied or dosed to the soil.**

- **Alternatively, rotational crop studies may be performed by dosing the soil with a mixture of active substance and the significant soil metabolites.**

- **Finally, studies where only the parent active substance is applied can also be used to investigate residues of soil metabolites in rotational crops if it is demonstrated by chemical analysis that those are formed in soil at sufficient amount in at least one of the plant back interval investigated.**

How the critical GAP is identified?

General principle:

- **The critical GAP is the one resulting in the highest soil residues at the time of planting the rotational crop. This GAP does not necessarily coincide with the most critical GAP in primary crops which is selected to derive MRLs.**

Main driving factors

- **Application rate and the number of applications.**
- **Timing of the application (crop development) and the crop interception**

Since it is difficult to determine the exact time of planting rotational crops and the residues at that time, it is assumed that a direct proportionality will be maintained between the applied substance and the amount remaining at the time of planting. Therefore, **it is proposed** that the effective application rates (A_{eff}) for each GAP under assessment can be calculated to identify **the critical GAP** which **would be the one with** the **highest A_{eff}**.

Calculation of the A_{eff}

- **A calculator is available to derive the effective application rate (A_{eff}) for the GAPs under assessment. The calculation of A_{eff} is based on agreed crop interception values per crop and growth stage used in the environmental assessments (Focus, 2001) and uses as input value the annual application rate of the GAP under assessment.**

- **The GAP resulting in the highest estimated A_{eff} (i.e. highest residues reaching the soil) would be the critical GAP and the estimated A_{eff} for this GAP will be used to derive the appropriate application rate to use in tier 1 studies.**

How to calculate the application rate (or soil dose) for rotational crop studies?

- **In metabolism studies on rotational crops the substance applies directly in soil.**

  OECD recommends 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 (OECD guidance, 2018).

- **The target concentration in soil to be attained in the study is the maximum concentration of the substance in soil (max $PEC_{(s)}$).**

  The conc. of the active substance in soil ($PEC_{(s)}$ in mg a.s./kg soil) over a 20 cm horizon can be calculated from the effective application rate (A_{eff}) of the active substance estimated for the critical GAP.

How to calculate the application rate (or soil dose) for rotational crop studies?

Active substances not accumulating in soil (DT90 < 365 days)

- **If the substance is applied directly to soil.**

  OECD recommends to rely on bare soil application rather than on application to crops in all tiers of rotational crop testing (OECD guidance, 2018). A_{eff} (g a.s / ha) determines the application rates in these studies.

- **If the study is done in container, with soil dosed, the target concentration in soil is the initial concentration of the a.s. in soil (initial $PEC_{(s)}$).**

  The initial $PEC_{(s)}$ over a 20 cm horizon can be calculated from the effective application rate (A_{eff}) of the active substance estimated for the critical GAP.

$$PEC_{(s)20cm}\ (mg\ a.s./Kg\ soil) = (A_{eff}\ (g\ a.s./ha) * 1000\ (mg\ a.s\ /\ g\ a.s)\ )/(100000\ (m^2/ha) * 0.2(m) * 1{,}5(Kg/\ dm^3)\ * 1000\ (dm^3/m^3))$$

How to calculate the application rate (or soil dose) for rotational crop studies?

Active substances accumulating in soil (DT90 > 365 days)

- **If the substance is applied directly to soil.**

  The "accumulated" application rate A_{acc} (g a.s / ha) determines the application rates in these studies. A_{acc} takes into account accumulation after multiple years of application of the a.s. on the crop. OECD provides a method to calculate A_{acc} (OECD guidance, 2018). Since the OECD method only works with substances degrading following first order kinetics, the Technical Report describes a procedure to derive the A_{acc} using the Peak accumulated $PEC_{(s)}$ calculated by fate and behavior which is not kinetic dependent.

- **If the study is done in a container, with soil dosed, the target concentration in soil is the one derived from the accumulated peak $PEC_{(s)\ 20\ cm}$**

  Peak accumulated $PEC_{(s)}$ over a 20 cm horizon must be used as target dosing concentration.

How to calculate the application rate (or soil dose) for rotational crop studies?

Application rate for metabolites tested in tier 1 studies

As a general principle, target concentration in soil in the study should correspond to the **maximum $PEC_{(s)}$** (if metabolite DT_{90} < 365 d) or **accumulated $PEC_{(s)}$** (if metabolite DT_{90} > 365 d) over the 20 cm soil horizon.

- **Case 1. GAP under assessment identical to one peer reviewed GAP**

  Available $PEC_{(s)}$ (converted to 20 cm horizon) can be directly used to dose the study or calculate the application rate of the metabolite.

- **Case 2. Critical GAP under assessment is not addressed in the peer review**

  Technical Report provides a method to linearly convert the available $PEC_{(s)}$ in the GAP of reference (form the peer review) to the GAP under assessment.

Estimate the $PEC_{(s)\ 20\ cm}$ for significant metabolites

In order to study significant metabolites in soil under tier 1:

- **If maximum $PEC_{(s)\ 20\ cm}$ (or accumulated $PEC_{(s)\ 20\ cm}$) of significant metabolite for 5cm soil horizon available in the peer review conclusions,** conc. of metabolite to apply in bare soil ($PEC_{(s)\ 20cm}$) estimated by converting the available $PEC_{(s)\ 5cm}$ in the excel calculator.
- **If PEC(s) (or accumulated $PEC_{(s)}$) of significant metabolite for 5cm soil horizon not available in the peer review (extension of use not previously considered),** conc. of metabolite to apply in bare soil ($PEC_{(s)\ 20cm}$) estimated
  (i) by converting the $PEC_{(s)\ 5cm}$ to $PEC_{(s)\ 20cm}$ in the excel calculator and
  (ii) multiplying the result by an adjustment factor (AF):

$$PEC_{(s)\ 20cm}\ [\text{GAP under assessment}] = PEC_{(s)\ 20cm}\ [\text{peer reviewed GAP}]^{*} \times AF$$

$$AF = A_{eff}\ \text{GAP under assessment} / A_{eff}\ \text{for representative GAP}$$

Scaling down from overdosed studies

It is recommended that tier 1 studies are performed with exaggerated rates compared with the application rate required to obtain the maximum concentration in soil based on the most critical identified GAP.

- **Results of tier 1 studies can be scaled down, using the proportionality approach.**

- **Underdosed tier 1 studies are not recommended but upscaling from underdosed tier 1 studies may be accepted if adequately demonstrated that metabolites occurring below LOQ have not been overlooked (e.g., based on information in fate in the environment data).**

How are N rate and scaling factors calculated for overdosed studies? (active substance)

- **In order to check if an available study has been adequately dosed or to derive the scaling factor, N rate can be calculated as follows:**

N (active substance) =

application rate in the study (g/ha) / A_{eff} (or the A_{acc}) for critical GAP (g/ha)

=

dose in the study (mg a.s / kg soil) / $PEC_{(s)\ 20\ cm}$ (initial or accumulated peak) for critical GAP (mg a.s / kg soil).

How are N rate and scaling factors calculated for overdosed studies? (metabolites)

For metabolites N rate can be calculated as follows:

- For metabolites the same formulas are applicable if the study design implies the direct application or dosing of the metabolite to soil.
- If soil metabolites are generated in the study dosed with the parent, then chemical analysis of the soil at the beginning of the test must be performed to demonstrate that the soil concentrations of the soil metabolites are within the desired range by calculating the N rate for the corresponding metabolites.

- **N (metabolite)** =

measured concentration of the metabolite in soil at planting / max $PEC_{(s)\ 20\ cm}$

(or Peak accumulated $PEC_{(s)\ 20cm}$, in case of metabolites with DT_{90} > 365 d)

How are N rate and scaling factors calculated for overdosed studies? Further consideration

Important considerations

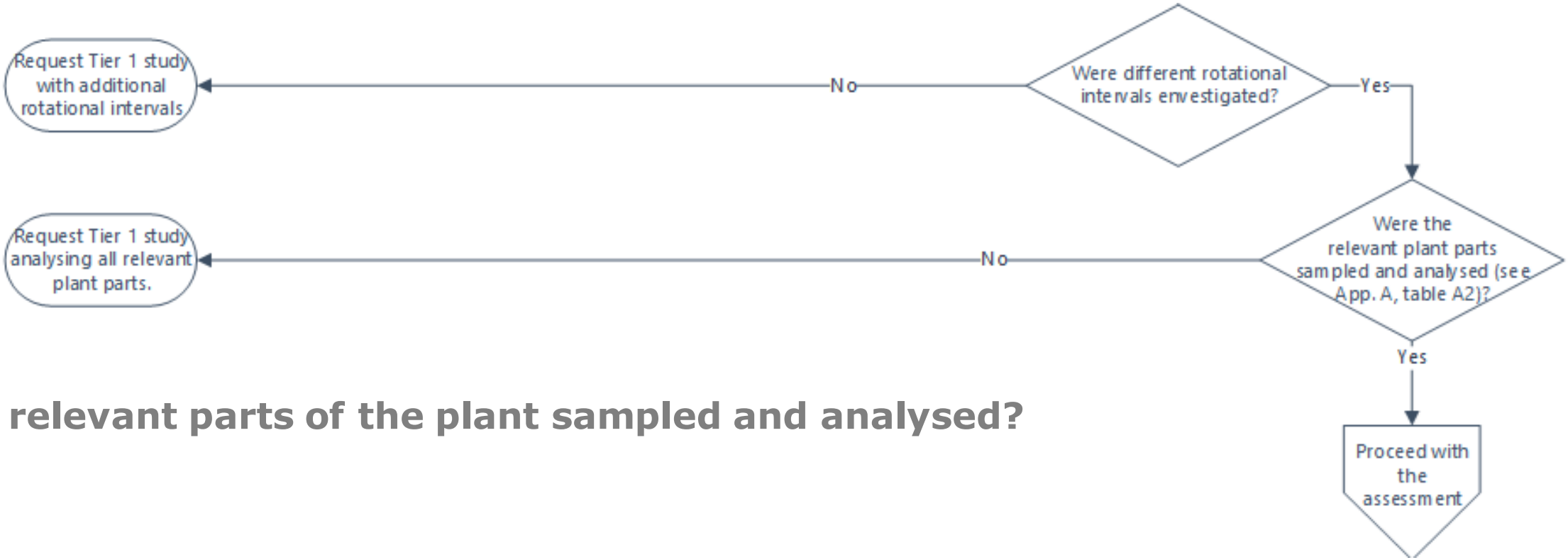
- Different N rates can be obtained for a study depending on if the nominal rates or soil analysis are considered.
- Scaling of the residues observed is justified when N significantly deviates from 1. Small deviations that can be justified on basis to the experimental variability do not trigger the need to scale observed plant residues. This is especially true for the case of metabolites.

- **Calculation of the scaling factor**

The scaling factors are the inverse of the N rate and are calculated as follows:

$$\textbf{Scaling factor} = 1/N$$

- **Were different rotational intervals investigated? (Covered by OECD TG 502)**



- **Are relevant parts of the plant sampled and analysed?**

Are relevant parts of the plant sampled and analysed?

Crop group Tier 1 representative crop	Matrix
Leafy crops Lettuce or Spinach or Soyabean[(b)] or Any other leafy crop (Table B2)	Immature leaves[(a)]
	Mature leaves
Root and tuber vegetables Beetroots or Carrots or Radishes or Sugar beets or Any other root and tuber vegetable crop (Table B2)	Roots
	Leaves
Barley or Oats or Rye or Wheat or Any other cereal crop (Table B2)	Grain
	Forage
	Hay
	Straw
Oilseeds Oilseed rape or Soyabean or Any other oilseed crop (Table B2)	Forage
	seeds

[(a)]harvested at crop stage representing approx 50% of the normal time period for the plant to reach full maturity

Interpretation of results from tier 1 studies

- For each substance (a.s./met), results to report per crop, PBI and part of plant analysed.
- **Results to be scaled to the nominal rate** if tier 1 studies over- or underdosed.
- Proceed with identification/characterization based on table by OECD TG 502
- Derive **residue definitions** for rotational crops (**open**, results from higher tier studies performed with more realistic conditions should also be considered).

Relative amount (%)	Concentration (mg/kg)	Required Action
< 10	< 0.01	No action if no toxicological concern
< 10	0.01 – 0.05	Characterize. Only attempt to confirm identity if straightforward, e.g., a reference compound is available or the identification is known from a previous study.
< 10	> 0.05	Characterisation/identification needs to be decided on a case- by-case basis taking into account how much has been identified.
> 10	< 0.01	Characterize. Only attempt to confirm identity if straightforward, e.g., a reference compound is available or the identification is known from a previous study.
> 10	0.01 – 0.05	Significant attempts to identify should be made especially if needed to establish a pathway, ultimately characterisation might be accepted.
> 10	> 0.05	Identify using all possible means.
> 10	> 0.05 unextracted radiolabel	Unextractable radiolabel – See paragraphs 42-46 and Figure 1.

OECD TG 502

When results from tier 1 studies trigger the need for tier 2 studies?

- **If TRR<0.01 mg/kg plant for a.s./metabolite (expressed as parent) at all plant parts and PBIs, no further assessment required**
- **If TRR≥0.01 mg/kg plant for a.s./metabolite (expressed as parent) at any plant matrix and PBI≥30 days (for discussion), studies on tier 2 are required.**

MRL setting to account for residues in rotational crops

4 May 2021

Trusted science for safe food

efsa
European Food Safety Authority

Outline

- Current practice for MRL setting in rotational crops
- Presentation of the main steps and related questions for the MRL setting for rotational crops
- Presentation and discussion on possible approaches

Current practice for MRL setting in rotational crops

- Peer review:
  - Based on critical representative use
  - In the past, usually specific group MRLs set for a crop group based on field studies

- MRL review:
  - Based on critical authorised GAP on primary crops, selected from all authorized uses in EU
  - MRL proposals based on residues from primary uses and rotational crop soil uptake considering the most critical GAP, but in most of the cases recommendation to implement risk mitigation measures

- Art 10:
  - Based on critical new use on primary crop
  - Upon request by the application, especially for rotational crops
  - For import tolerances - if requested by the applicant
  - Eventually proposals for risk mitigation measures (i.e., plant back intervals)

Main steps for MRL setting in rotational crops

Step 1. Selection of cGAP on primary crop

Step 2. Calculation of PECsoil for the cGAP

Step 3. Calculation of the *N-rate*

Steps 1 to 3 covered by Tier 0/1 ppt

Step 4. Selection of rotational crop residue data (PBI, mature/immature crop, extrapolation)

Step 5. Verify whether risk mitigations are possible and decide for which crops MRLs should be derived

Step 6. Derive the input values for exposure calculations (consumers and livestock)

Step 7. Derive MRLs

Pre-meeting note

For each step of the MRL setting covered by this ppt (4 to7), a list of questions/points for reflection has been identified (reported in red).

MSs experts are invited to look at the questions and bring their experiences and views for discussion at the meeting.

Step 4 Select the relevant results of the field trials – OECD, 2018

- ***When are the limited RC field trials required?***
  - From the metabolism studies, residues of the parent compound or relevant metabolites either from plant or soil metabolism are **≥0.01** mg/kg in food commodities and **≥0.05** mg/kg in feed commodities

- ***Purposes of these trials?***
  - To determine the magnitude of the pesticide residues which may accumulate in rotational crops via soil uptake considering the critical GAPs
  - To decide on the need for MRLs in rotational crops -->extended field trials (see also steps 6 and 7)
  - To establish crop rotations restrictions (if residues according to the DoR are <0.01 mg/kg for at least one PBI tested)

- ***Experimental design of the trials***
  - The trials conducted in **two different geographical regions** (major areas of cultivation) and over **two different test sites** within a region

Step 4 Select the relevant results of the field trials – OECD, 2018

- Application of the pesticide according to the critical GAP (**maximum seasonal application rate/appropriate application rates**), either to the primary crop or to bare soil
- Representative rotational crops: root crops, small grain (cereals), leafy vegetables
- *A*n additional representative crop group may also need to be included if a crop important to the rotation is not covered by these crop groups, e.g., soybean in the US
- These trials should focus on the crops/crop groups with **significant residues (≥0.01 mg/kg)** identified in the RC metabolism studies or to replace a crop group from the RC metabolism studies where no significant residues occur by another crop group (e.g., oilseeds, brassica vegetables)
- Standard plant back intervals: 7-30 d; 60-270d and 270-365 d (?)

- ***Sampling***
- RACs as food and feed items
- Crops harvested immature for consumption (young leaves of spinach/salad)

Step 4 Select the relevant results of the field trials – questions

Questions/points for reflections:

- ***Which is the number of independent RC limited field trials on crops representative of the relevant crop groups that should be required for NEU/SEU/Indoor?***

Example: flutolanil (PPR Meeting 09)(2NEU/2SEU)

- If sufficient number of limited field trials have been submitted for certain rotational crop groups, provided that an appropriate application rate has been used in these trials, in principle these crops should not be tested again for the extended field trials.

- ***Soyabean – P/O crop group can be considered relevant for EU?***

- Limited field trials on oilseeds are in principle not required according to the OECD TGL 504. Is it acceptable to consider this crop group in place of a representative crop group?

- ***How to select the residue levels based on the RC limited field trials?***

- Consider always the highest residues throughout the different parts of the crops and PBIs investigated?
- Consider results from mature or immature crops? (If the highest residue levels occur in immature crop parts, this may lead to an overestimation of the residue levels, e.g., immature to mature spinaches)

Step 4 Select the relevant results of the field trials – questions

- ***Which "extrapolation rules" can be applied?***
  - In absence of crops representative of leafy vegetables, can the upper leafy parts of the root crops be representative for leafy vegetables?
  - Vegetation period length of crops (from which crops mature leaves and from which immature (sugar beet leaves vs. lettuce))
  - Is there a need to develop a list with possible extrapolations for crops that are food and feed items? See proposals made under the assessment of Dimethomorph(PPR Meeting 191)

Step 5 Verify whether risk mitigations are possible – OECD, 2018

'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'*** (*para* 40 from OECD, 2018).

Possible risk mitigation measures (label restrictions) (*para* 74 from OECD, 2018):

- *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.*

Label restrictions may be used to allow registration of products while additional higher tier studies are undertaken (*para* 75 from OECD, 2018).

Step 5 Verify whether risk mitigations are possible - existing approach

Example: MRL review methoxyfenozide (EFSA, 2014).

The magnitude of the residues of methoxyfenozide was investigated in leafy vegetables (mustard), fruiting vegetables (tomatoes, cucumbers), root and tuber vegetables (potatoes, carrots, turnips, radish, sugar beet, green and bulb onions), pulses and oilseeds (beans, peas, soya beans) and cereals (wheat, sorghum, rice).

The results of the rotational crop field studies showed that it is not excluded that residues of methoxyfenozide occur at levels above the LOQ of the method (0.01 mg/kg), particularly in the edible matrices of leafy vegetables, root and tuber crops and in feed commodities (straw, forage, hay) when grown in rotation with treated crops according to the authorized European uses.

Furthermore, in view of the high persistence of the parent compound (DT90field> 1000 days), EFSA is of the opinion that additional field trials covering the maximum soil plateau concentration of methoxyfenozide are required in order to address the actual residue levels of methoxyfenozide in the rotated crops.

EFSA therefore concludes that Member States granting authorisations for methoxyfenozide should take the appropriate risk mitigation measures in order to avoid the presence of residues of methoxyfenozide in leafy vegetables, root and tuber vegetables and the feed commodities (cereals straw, forage and hay) used in rotation.

Step 5 Verify whether risk mitigations are possible - questions

Questions/points for reflections:

- Should risk mitigation measures considered as the first option to avoid 'unnecessary residues' to occur in not-treated crops also considering that they can be limited to the most critical uses only?
- Other risk mitigation/label restrictions possible?
- Risk mitigation not harmonised among MS, further guidance from risk management to be provided/expected (as done in ecotox)

Step 5 Decide for which crops MRLs should be derived – OECD, 2018

When MRL proposals should derived based on the available rotational field trials?

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 (OECD, 2018)

Step 5 Decide for which crops MRLs should be derived - questions

Questions:

- Do you agree with the approach proposed by the OECD GD?
- How to apply the 25% principle (comparing HR_{RC} to HR or MRL of primary crop?)
- At which PBI (30 days?; irrespective if residues at longer PBIs<LOQ)?

Other possible options to set combined MRLs in rotational crops:

- if calculated MRL for RC is lower than the EU MRL for primary crop = no need to consider rotational crop residues for MRL setting
- if significant uptake (residues>0.01/0.05 mg/kg according to the RD for enforcement) can be excluded at certain PBIs = no need to consider rotational crop residues for MRL setting

- Is it possible to take into account monitoring data to conclude on whether there is the need to raise the MRL (at least in the MRL review where all the existing uses are considered but relevant also for the renewal)?

Step 6 Derive input values for exposure calculations – OECD, 2018

OECD, 2018:

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 **(primary) crop field trials**.

The (MRL), **STMR** and **HR** is **calculated from** these **adjusted residue** values.

Step 6 Derive input values for exposure calculations – initial considerations

The goal is to **estimate** the residue levels (**residue distribution**) in a rotational crop, when residues may come from two **independent sources**.

1. Uptake from soil (**RC** uses)
    a. level of residues reaching the soil
    b. accumulation of the residues in soil (properties of the a.s./metabolites; climatic conditions, soil type)
    c. Uptake by the succeeding crops
2. Primary treatment of the succeeding crop, if relevant (**PC** uses)

Examples for risk assessment value derivation (1)

Option 1a: derive the RA from the PC and RC field trials, separate risk assessment, the acute and the chronic exposures are combined

Option 1b: HR rotational crops +HR primary crops; STMR rotational crops + STMR primary crops;

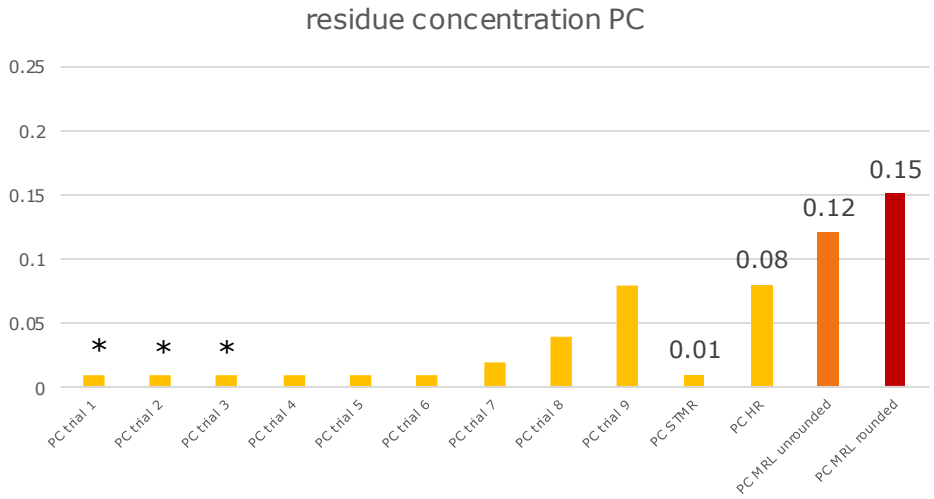
Option 2a: adjusted residue (each individual PC residue value + HR_{RC}).

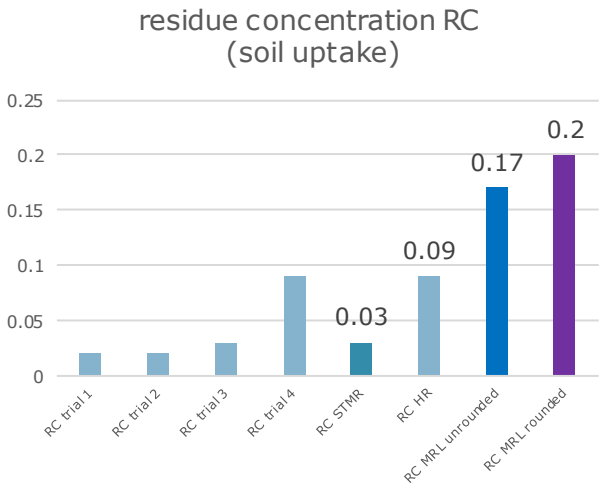
Option 2b: adjusted residue (each individual PC residue value + $STMR_{RC}$).

Option 3: HR/STMR derived for primary crop and rotational crops; select higher RA value.

Crop	Residues in trials		PC only		RC only		Option 1b		Option 2a		Option 2b	
	Primary crop residues	Rotational crop residues	STMR	HR	STMR	HR	STMR	HR	STMR	HR	STMR	HR
Broccoli	< 0.01; 0.02; 0.05; 0.14	0.02; 0.03; 0.03; 0.09;	0.4	0.14	0.03	0.09	0.07	0.23	0.19	0.23	0.07	0.17
Brussel sprouts	0.01; 4x 0.04; 2x 0.07; 0.14	0.02; 0.03; 0.03; 0.09	0.4	0.14	0.03	0.09	0.07	0.23	0.19	0.23	0.07	0.17
Head cabbage	3x < 0.01; 3x 0.01; 0.02; 0.04; 0.08	0.02; 0.03; 0.03; 0.09	0.01	0.8	0.03	0.09	0.04	0.17	0.1	0.17	0.04	0.11

Step 6 Derive input values for exposure calculations
Example: head cabbage



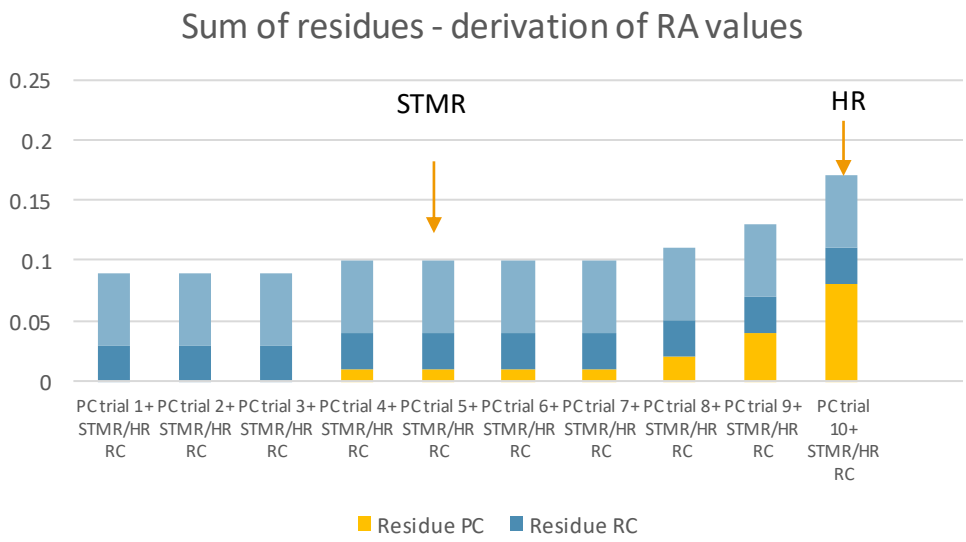


Option 1a:∑ separate risk assessment for PC + RC

Option 1b: ∑ STMR PC + STMR RC; ∑ HR RC+HR PC

Option 2a: ∑ each PC residue value + HR RC.
Option 2b: ∑ each PC residue value + STMR RC.

Option 3: higher RA value selected from PC or RC.



Step 6 Derive input values for exposure calculations – existing approaches

Approach		Pros/cons
Option I	**A)** HR/STMR primary HR/STMR rotational Separate consumers exposure calculations for primary and rotational crops and results summed up flupyradifurone (for consumers exposure) **B)** STMR primary + STMR rotational HR primary + HR rotational (boscalid/flupyradifurone (for DBC only)/fluopyram)	**Pros:** - less resource intensive/easy to update for GAP changes -> less subject to mistakes - more transparent: if concern identified, source is clearer -> easier & more targeted actions can be proposed (RMMs/or need for fall-back MRL) - Suitable for complex RD RA for rotational crops (only relevant for option IA) **Cons:** - deviates from OECD, 2018 - statistical analysis? - require summing up results 2 different exposure calculations (only relevant for option IA)
Option II	Individual residue values primary crop + HR rotational Use of OECD MRL calculator to derive the STMR and HR (dimethomorph, fluxapyroxad)	**Pros:** - OECD, 2018 compliant **Cons:** - statistically not sound, combines incompatible data sets (HR RC vs potentially large PC data set etc.) - resource intensive -> difficult to adapt for GAP changes - use of STMR adjusted with HR value for calculations based on median residue levels ("bulk" commodities, feed by-products) -> overestimates (acute/chronic) exposure
Option III	highest RA values between PC and RC datasets (chloridazon)	**Pros:** - easy to perform - easy to update **Cons.** - May it underestimate exposure? - deviates from OECD, 2018 core text <–> case 5: example how MRL setting done in the EU

Step 6 Derive input values for exposure calculations – Considerations

Questions:

- Practices/observation of the MSs?
- Experiences, if any, with deriving RA values? (acute/chronic concern identified, etc..)
- Preferences?

Step 7 Derive MRLs (1)

OECD, 2018:

- **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** (residue soil uptake) (OECD, 2018)
- 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 (OECD, 2018)
- **Combined MRL**: the **highest residue** (HR) value obtained in GAP-compliant or scaled field rotational crop studies are added to **each residue** value obtained in GAP-compliant primary crop field trials (OECD, 2018)

- the approach not legally binding
- not harmonized
- and what about **specific rotational crop MRL =** reflecting **only** the residue soil uptake in cases where **untreated crop** is grown in soils containing residues at soil plateau concentrations

Step 7 Derive MRLs (2)

The MRL shall be:

✓Realistic ⟶ to avoid overestimation

⟶ to consider sustainable use and management practices

✓Simple and practical to implement

✓Harmonised

✓Transparent ⟶ source of an MRL to easy to identify

Current combined MRLs:

not harmonised

not transparent

not practical

not flexible (for revisions)

⟶ improvements required

Step 7 Derive MRLs - existing approaches combined MRL

Combined MRL *residues in crop from primary use and the soil uptake		**Pros/cons**	**Comments**
Option I	**MRL primary + HR rotational** → sum rounded to nearest highest MRL class (boscalid/flupyradifurone)	**Pros:** -more transparent, less subject to mistakes -less resource intensive/easy to update for GAP changes -source of concern is more apparent -results lower MRL than Option II* **Cons:** -methodology new -extrapolations between PC and RC not always one to one -statistical analysis?	May residues be accounted for twice? *see case study by NL on fluopyram/flupyradifurone
Option II	**Individual values primary + HR rotational** Use of MRL calculator (dimethomorph, fluxapyroxad)	**Pros:** -OECD, 2018 compliant **Cons:** -not statistically sound method (addition of HR) -combines incompatible data sets (large/small,etc) -resource intensive - results in higher MRL than in Option I* - artificially high mean residue* - difficult to adapt for GAP changes - source of MRL may not be transparent - individual residue data for primary crops may not always be available (e.g. MRL based on CXL/IT)	*see case study by NL on fluopyram/flupyradifurone
Option III	**MRL rotational v.s. MRL primary** → max MRL (chloridazon) OECD MRL calculator	**Pros:** **-e**asy to perform -less resource intensive/easy to update **Cons.** -might not account for combined residues	Could this be followed in case applicant does not request a higher MRL for certain RC?

Step 7 Derive MRLs - existing approaches rotational crops specific MRL

Rotational crop specific MRL *in cases when crop is not treated as primary crop but grown in soils with background residue concentrations		**Comments**
Option I	Rounding of HR rotational crop to nearest MRL class (pydiflumetofen)	Widely used approach Easy to calculate Transparent/Easy to update
Option II	MRL calculation using OECD MRL calculator	Statistical methods for estimating residues in RC not applicable (JMPR) Normally small datasets available

Step 7 Derive MRLs - Considerations on rotational crops specific MRLs

Specific rotational crop MRL:

- normally based on a small residue data set

Use of OECD MRL calculation – not really applicable (*JMPR: "use of statistical methods for the estimation of MRL is not possible when considering potential carryover of residues in succeeding crops since the basis arising from the additional root uptake cannot be adequately calculated, using OECD MRL calculator"*)

- higher uncertainty due to low number of trials
- calculator not developed for that purpose

Q: Merging of SEU/NEU/indoor data to expand data set?

Proposed approach

HR in rotational crop selected from the critical PBI and rounded to nearest highest MRL class

Q: Critical PBI applicable to all crops (also those with long vegetation periods)?

Other arguments?

Step 7 Derive MRLs – Considerations on combined MRL

Combined MRL ! provided that the steps 1-6 leading to MRL setting are harmonised

Option I (MRL_{PC} + HR_{RC}): new methodology, other concerns?

Option II (each $_{PC}$ residue + HR_{RC}): use of OECD MRL calculator

Mean +4SD –more realistic?

3*Mean*CF – inflated?

Q: entry of values at the LOQ?

addition of HR increases mean value

Option III (MRL_{PC} vs. MRL_{RC}): use of OECD MRL calculator for RC MRL not supported

Q: Practices/observation of the MSs?

Q: Experiences, if any, with existing combined MRLs? (compliances, exceedances..)

Q: Perhaps a different option available/proposed? (e.g., HR primary crops + HR rotational crop, rounded to next highest MRL class; without using OECD MRL calculator/Individual values primary crops plus STMR rotational crop, using OECD MRL calculator)

Step 7 Derive MRLs – proposed approach

Proposed approach: MRL primary crop + HR rotational crop, rounded to next higher MRL class

25% (contribution) to be applied

Rounded/unrounded (?) MRL primary crop compared with HR rotational crop

HR derived for the enforcement residue definition

Separate consumer exposure calculations for primary crops/animal commodities

Separate exposure calculation for untreated crops that can take up soil residues

→ exposure combined (summed)

Examples for MRL calculation (1)

Option 1: MRL primary + RC HR -> rounded to next MRL class

Option 2: Each individual PC residue value + HR_{RC}) using the OECD MRL calculator; calculations performed with, or without * if residues values from primary treatment are <LOQ.

Option 3: MRL_{PC} vs. MRL_{RC}

a) Derived with OECD calculator

b) In brackets combined residue input value is considered with "*" in OECD calculator, if residues from primary treatment are <LOQ

	Residue		**MRL**				
Crop	**Primary crop residues**	**RC HR**	**PC only**[a]	**RC only**[a]	**Option 1**	**Option 2** (Input value censored (*))[a, b]	**Option 3**
Potato NEU	13x<0.01; 18x<0.02; 2x0.02; 0.04	0.02	0.04	0.03	0.06	**0.1** (0.06)	0.04
Potato SEU	7 x <0.05	0.02	0.05*	0.03	0.07	**0.2** (0.07)	0.05
Potato SEU+NEU	13x<0.01; 18 x< 0.02; 2x0.02; 0.04; 7 x<0.05	0.02	0.08	0.03	0.1	**0.15** (0.1)	0.08
Broccoli	< 0.01; 0.02; 0.05; 0.14	0.05	0.4	0.1	**0.5**	0.4	0.4
		0.09		0.2	**0.5**	**0.5** (0.4)	0.4
Brussel sprouts	0.01; 4x 0.04; 2x 0.07; 0.14	0.05	0.3	0.1	**0.4**	**0.4**	0.3
		0.09		0.2	0.4	**0.5**	0.3
Head cabbage	3x < 0.01; 3x 0.01; 0.02; 0.04; 0.08	0.05	0.15	0.1	0.2	**0.3** (0.2)	0.2
		0.09		0.2	0.3	**0.4** (0.3)	0.15

Examples for MRL calculation (2)

Option 1: MRL primary + RC HR -> rounded to next MRL class
Option 2: Each individual PC residue value + HR_{RC} using the OECD MRL calculator; calculations performed with, or without * if residues values from primary treatment are <LOQ.
a) Derived with OECD calculator
b) In brackets combined residue input value is considered with "*" in OECD calculator, if residues from primary treatment are <LOQ

	Residue			**MRL**		
Crop	**Primary crop residues**	**HR PC**	**HR RC**	**PC only**(a)	**Option 1**	**Option 2** (*) a, b
Potato	Broadcast application 6x <0.01; 0.016, 0.019	0.019	0.02	0.026	**0.046**	-
	Adjusted residue data set: 6x 0.03; 0.036, 0.039	0.039	0.02	-	-	**0.096** (0.05)
	In furrow at sowing <0.01, 2x 0.018, 2x 0.020, 0.024, 0.029, 0.032	0.032	0.02	0.059	**0.079**	-
	Adjusted residue data set 0.03, 2x 0.038, 2x 0.040, 0.044, 0.049, 0.052	0.052	0.02	-	-	**0.124** (0.11)

Thanks for your attention and contribution!

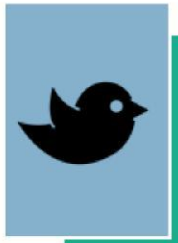
Stay connected

Subscribe to

efsa.europa.eu/en/news/newsletters
efsa.europa.eu/en/rss

Receive job alerts

careers.efsa.europa.eu – job alerts

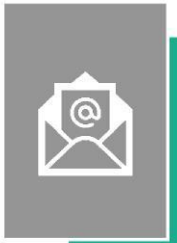


Follow us on Twitter

@efs a_eu
@plants_efsa
@methods_efsa
@animals_efsa

Follow us Linked in

Linkedin.com/company/efsa



Contact us

efsa.europa.eu/en/contact/askefsa

Application of technical guideline on extraction efficiency: sharing of Authorities' views

Luis Carrasco Cabrera, PhD

Scientific Officer, PRES unit

General experts' meeting

05 May 2021

efsa
European Food Safety Authority

Background and Scope of this session

- In preparation for PAI (post Annex I inclusion) meeting (March 2021), EFSA provided comments for discussion on the applicability of the technical guideline on extraction efficiency. PAI meeting suggested to discuss the at the General expert meeting EFSA-MSs.

- How to apply the "Technical guideline on evaluation of extraction efficiency (SANTE 2017/10632 Rev.3)": to exchange views on how to demonstrate that the extraction efficiency requirements are met.

- This session is intended as an exchange platform for experiences gained by MSs and relevant for assessments at EU level (not for product authorization). It is not intended to present the content of the technical guideline.

OUTLINE

- Studies and samples used for evaluation of extraction efficiency according to SANTE 2017/10632 Rev.3
- Application of SANTE 2017/10632 Rev.3
- EFSA considerations
- Questions on how to apply SANTE 2017/10632 Rev.3: Feedback from MSs (NL, IT, FI, SE, AT). Open to further discussions

GD on extraction efficiency: SANTE 2017/10632

- To assess suitability of extraction procedures applied in pesticide residue analytical methods was already required in e.g., SANCO/825/00.
- The new GD give advice on when and how to assess extraction efficiency (**new!**).
- Extraction efficiency **cannot be** established during method validation with **fortified samples.**
- Extraction efficiency should be assessed with samples bearing **incurred residue**.
- Extraction efficiency might (strongly) **depend on extraction solvent used**.
- It applies to both, **pre- and post-registration methods**, i.e., data generation and monitoring methods, for plants and animals.

Studies and samples used for evaluation / 1

- **Extraction efficiency** should be **evaluated** for **all matrix groups** (including matrices difficult to analyse, depending on availability of radiolabeled sample material or samples with incurred residues) or **animal** commodities for which **residue** analytical **methods** are **required**

- **All analytes** included in the **residue definition for monitoring** (relevant for post-registration methods)

- **All analytes** included in the **residue definition for risk assessment** (relevant for pre-registration methods)

- When analytes included in the residue definition differ for a certain matrix, the **extraction efficiency** should be **evaluated** for the corresponding **analyte/matrix combination**.

Studies and samples used for evaluation / 2

- Samples from **metabolism studies** with primary crops or rotational crops (depending on the predominance of the considered analyte(s)) and with animals (and **feeding studies**, where applicable) with radiolabeled pesticides.

- The sample material with radiolabeled incurred residue is typically available for approval of active substances, only. For the **evaluation of the extraction efficiency** for **additional matrices** or for **different solvents,** food samples containing incurred residues should be used (**cross-validation**).

- **Crop field trials** or from food monitoring can be used for **cross-validation studies** from non-radiolabeled samples

- For internationally standardized **multi-residue methods**, a huge amount of validation data was already published. Nevertheless, these data are normally not generated by using sample materials with known concentrations of incurred residues. Consequently, an **evaluation of the extraction efficiency** is also necessary for the **solvents and conditions used in multi-residue methods**.

Application of SANTE 2017/10632

Concerns the **data requirements (old – Reg. (EC) No 544/2011 and new – Reg. (EC) No 283/2013)** for:

- **New active substance approval** and **renewal** of active substances (EU level) submitted after 22 November 2019
- New product authorisations and renewal of product authorisations (MS level)
- Applications for **new MRLs** under Art. 6 of Reg. (EC) No 396/2005 (EU level) made after 22 November 2019
- **MRL reviews** and **specific MRL** assessments under respectively Art. 12 and Art. 43 of Reg. (EC) No 396/2005 (EU level): the data requirements for the latest approval or renewal should be considered, so proof of extraction efficiency in line with this document will only be required if it was required for the latest approval or renewal.

EFSA considerations

- According to the technical guideline, it is **required** that **applicant addresses extraction efficiency** of the methods used to generate residue trials and for enforcement methods. The **EMS/RMS** should **evaluate** information provided by the applicant on **extraction efficiency** in the ER/DAR/RAR submitted to EFSA.

- If the information on **extraction efficiency** is **not reported** in the ER (for MRL applications), DAR/RAR submitted after November 2019, **EFSA will require clarifications**. Data requirements will be set during the peer-review process.

Questions on how to apply the GD / 1

- When metabolism group does not match with the analytical method categories: e.g., the metabolism study was performed on citrus fruits and the new MRL application/representative uses under renewal are e.g., on avocado. Citrus and avocado fall in the same metabolism group (fruits), but not on the same analytical method categories (high acid vs high oil content), how then to prove extraction efficiency?

- *Feedback from NL, IT*

Questions on how to apply the GD / 2

- How the technical guideline can be implemented for new MRLs applications where the new MRL will be set based on extrapolation from another commodity belonging to a different analytical group? E.g., extrapolation from tree nuts to chestnuts.

- *Feedback from NL, IT*

Questions on how to apply the GD / 3

- How to deal with matrices difficult to analyze, e.g hops? According to the technical guideline, it is desirable that extraction efficiency is proven for the matrix difficult to analyze (depending on availability of radiolabeled sample material or samples with incurred residues), but how to do it if the radiolabeled material is not available for this crop? Would it be acceptable in that case that extraction efficiency will not be proved?

- *Feedback from FI, IT*

Questions on how to apply the GD / 4

- It can be foreseen that often the situation will be that the applicant of the metabolism studies was different to the one submitting a new MRL application. How to prove the extraction efficiency without the access to the full study report?

- *Feedback from NL, IT*

05/05/2020

Assessment of residues in honey – case studies, monitoring data and future work

TC 52 General peer review meeting

Giulia BELLISAI, Miguel SANTOS
PRES Unit

Trusted science for safe food

efsa
European Food Safety Authority

OUTLINE

- The EC guideline
- Case study 1: MRL for thiacloprid (Art 10)
- Case study 2: MRL for boscalid (Art 10)
- Case study 3: MRL for spirotetramat (Art 10)
- Case study 4: bixafen (Art 12)
- Case study 5: alpha-cypermethrin (Peer Review)
- Available monitoring data in EU
- EU annual report in pesticides residues
- Work under OECD guidance residues in honey
- Questions to the experts' group

The EC guideline

TECHNICAL GUIDELINES[1]

SANTE/11956/2016 rev. 9
14 September 2018

Technical guidelines for determining the magnitude of pesticide residues in honey and setting Maximum Residue Levels in honey

Implemented by 1 January 2020

[1] This document has been conceived as a guidance document of the Commission Services. It does not represent the official position of the Commission. It does not intend to produce legally binding effects. Only the European Court of Justice has jurisdiction to give preliminary rulings concerning the validity and interpretation of acts of the institutions of the EU pursuant to Article 267 of the Treaty.

- To fill the gap on type and conditions of the studies to be performed to address the new data requirements (Regulation (EC) 283/2013) as regards residues in pollen and bee products for human consumption.

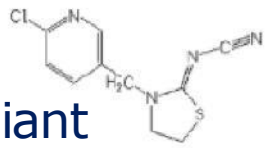
- Guideline includes test studies: syrup test, semi-field (tunnel tests) and field residue trials.

Case study 1: MRL in honey for thiacloprid (2016)

Therefore, EFSA proposes risk managers to decide which of the three different approaches listed in the table below should be considered for the setting of an MRL in honey.

Code[(a)]	Commodity	Existing EU MRL (mg/kg)	Proposed EU MRL (mg/kg)	Comment/Justification
Enforcement residue definition: Thiacloprid[(F)]				
104000	Honey and other apiculture products	0.05*	0.2	Field trials
			0.2	Monitoring data, FAO spice approach
			0.15	Monitoring data, FAO EMRL approach (99.5th or 99th percentile)

(a): Commodity code number according to Annex I of Regulation (EC) No 396/2005
(*): indicates that the MRL is set at the limit of analytical quantification (LOQ)
(F): fat soluble
EMRL: extraneous maximum residue limit



- Supervised residue trials from Germany compliant with the GAP for rapeseed (table 4; next slide)
- Monitoring data from 2013 (table 7, next slide)

Modicaon of the exisng maximum residue level for thiacloprid in honey

Appendix C – Thiacloprid residue levels observed in honey in the 2013 EU national monitoring programs.

Thiacloprid residues in honey (mg/kg) and Member state (MS)[(a)]							
MS	mg/kg	MS	mg/kg	MS	mg/kg	MS	mg/kg
AT	0.233	DE	0.043	DE	0.017	DE	0.005
AT	0.140	DE	0.040	DE	0.016	DE	0.005
AT	0.140	DE	0.039	DE	0.016	LV	0.005
AT	0.118	DE	0.039	DE	0.016	LV	0.004
AT	0.116	DE	0.037	DE	0.016	DE	0.003
AT	0.112	DE	0.036	DE	0.015	DE	0.003
DE	0.110	DE	0.033	DE	0.015	AT	0.002
AT	0.102	DE	0.032	DE	0.014	AT	1x <0.040
AT	0.097	DE	0.029	CZ	0.013	AT	8x <0.020
DE	0.094	DE	0.029	DE	0.012	AT	36x <0.010
DE	0.082	DE	0.028	DE	0.012	CY	10x <0.010
DE	0.080	AT	0.028	DE	0.012	BE	1x <0.010
DE	0.078	AT	0.025	DE	0.012	BG	1x <0.010
AT	0.073	DE	0.024	DE	0.011	CZ	2x <0.010
DE	0.073	DE	0.023	DE	0.011	DE	231x <0.010
DE	0.071	AT	0.022	DE	0.010	DE	38x <0.005
AT	0.070	DE	0.021	DE	0.010	EE	1x <0.005
DE	0.069	DE	0.021	DE	0.010	ES	6x <0.005
DE	0.068	BG	0.020	AT	0.010	EL	10x <0.005
DE	0.062	CZ	0.020	AT	0.009	HU	52x <0.005
DE	0.061	DE	0.020	DE	0.008	FR	21x <0.005
DE	0.059	DE	0.019	DE	0.008	FR	1x <0.001
DE	0.054	DE	0.019	DE	0.007	DE	3x <0.001
AT	0.052	DE	0.018	DE	0.007	HU	21x <0.001
AT	0.050	DE	0.018	DE	0.006	IE	12x <0.001
AT	0.050	DE	0.017	DE	0.006	IT	6x <0.001
DE	0.049	DE	0.017	DE	0.006	LV	3x <0.001
DE	0.049	AT	0.017	DE	0.006	PL	1x <0.001
DE	0.045	DE	0.017	DE	0.006	RO	3x <0.001

(a): Underlined values: thiacloprid residue level in organic honey

https://doi.org/10.2903/j.efsa.2016.4418

Case study 1: MRL in honey for thiacloprid (2016)

Table 4: Summary of the experimental designs and residue levels in honey (mg/kg)

Location	Treatment[a]					Hives installation	Honey harvest		Plot size (ha)	mean level (mg/kg)
	g/ha	BBCH stages		dates			date	DAT (day)		
	T1&2	T1	T1/2	T1	T1/2					
Burscheid	72		63-65		11/05/06	05/05/06	27/05/06	16	1.5	0.056
Martfeld	72		63-65		12/05/06	01/05/06	03/06/06	22	7	0.057
Lensahn	72		63-65		24/05/06	winter	18/06/06	25	100	<0.005
Lehrte	72		63-65		13/05/06	02/05/06	02/06/06	20	4	0.016
Burscheid	72	61	65	03/04/07	11/04/07	02/04/07	10/05/07	29	6	0.080
Lehrte	72	59	65	27/03/07	22/04/07	-	13/05/07	21	5.5	0.090
Martfeld	72	61	63	02/04/07	14/04/07	winter	13/05/07	29	2	0.038
Lehnsahn	72	57	61-63	13/04/07	30/04/07	01/05/07	25/05/07	25	30	0.087

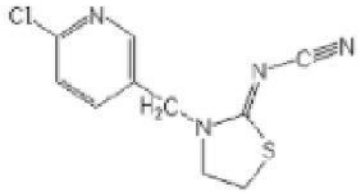
(a): T1: 1st Treatment T1/2: 1st or 2nd treatment

Based on these data and using the OECD MRL calculator (OECD, 2011), an MRL of 0.2 mg/kg is proposed for thiacloprid in honey (MRL_{OECD}: 0.18/0.2) with a median (STMR) and highest (HR) residue values of 0.06 and 0.08 mg/kg respectively. However, this MRL proposal is driven by various uncertainties:

- Relevant information on the experimental designs was missing and has not been provided (e.g. general overview of the experimental sites, information on the surrounding crops…),
- Pollen analyses have not performed, to confirm whether the sampled honey results effectively from the foraging on rapeseed,
- The 2006 experiments were conducted with a single application and not according to the critical GAP defined for rapeseed with a total of 2 treatments,
- The metabolism and detoxification pathways of thiacloprid in bees has not been investigated.

Table 7: MRL estimations for thiacloprid in honey

FAO approach for the setting of MRL in spices		
Number of samples ≥ LOQs	**94**	
Highest residue level	0.233 mg/kg	
Lowest residue level	0.002 mg/kg	
95th percentile	0.113 mg/kg	(Rank: 89.3)
Upper confidence interval	0.181 mg/kg	(Rank: 93.4)
MRL proposal (rounded)	**0.2 mg/kg**	
FAO approach for the setting of EMRLs		
Number of samples	**562**	
Highest residue level	**0.233 mg/kg**	
Lowest residue level	<0.001 mg/kg	
Median residue level (STMR)	**0.010 mg/kg**	
EMRL at 99.5th percentile	0.122 mg/kg	(Rank: 559.2
EMRL at 99th percentile	0.111 mg/kg	(Rank: 556.4)
MRL proposal (rounded)	**0.15 mg/kg**	
EMRL at 97.5th percentile	0.073 mg/kg	(Rank: 548.0)
EMRL at 95th percentile	0.045 mg/kg	(Rank: 533.9)



Monitoring data confirm the MRL from field studies!

Case study 2: MRL in honey for boscalid (2019)

- Honey technical guidelines published but not in force yet!

Code[a]	Commodity	Existing EU MRL (mg/kg)	Proposed EU MRL (mg/kg)	Comment/justification
Enforcement residue definition: Boscalid[F]				
01040000	Honey and other apiculture products[b]	0.05*	0.15	The available data are sufficient to derive an MRL proposal for honey. The MRL proposal is higher than the boscalid residues found in EU pesticide monitoring programmes (1,583 samples analysed between 2013 and 2017) Since boscalid is a fat-soluble compound, residues are expected to accumulate in lipophilic matrices, such as beeswax. Thus, the MRL proposal might not cover honey that contains honeycombs The proposed MRL for honey is unlikely to pose a risk for EU consumers

MRL: maximum residue level.
*: Indicates that the MRL is set at the limit of analytical quantification (LOQ).
(a): Commodity code number according to Annex I of Regulation (EC) No 396/2005.
(b): Currently, MRLs set for honey are not applicable to other apicultural products (Commission Regulation (EU) 2018/62).
(F): Fat soluble.

It must be noted that the investigation of possible risk to honey bees related to the use of boscalid in oilseed rape or in any other crop is outside the scope of this reasoned opinion. The risk to honey bees is currently under assessment in the framework of the peer-review process of the renewal of the first approval of boscalid. Additionally, national competent authorities at Member State level have to pay attention to the bee health and bee protection when granting authorisations for plant protection products.

B.1.2.2. Summary of residues in honey found in EU pesticide monitoring

	EU monitoring data submitted to EFSA under Art. 32 of Reg. 396/2005	
Total number of samples	1,583[a]	
Number of samples per year	2013	420
	2014	221
	2015	333
	2016	204
	2017	405
Number of samples with residues > LOQ (% of samples > LOQ)	27 (1.7%)	
Number of samples with residues > current MRL (0.05 mg/kg)	1[a]	
Mean[b]	0.0082 mg/kg	
Standard deviation[b]	0.0096 mg/kg	
Median[c]	0.01 mg/kg	
Maximum	0.082 mg/kg	
P90[c]	0.01 mg/kg	
P95[c]	0.02 mg/kg	
P97.5[c]	0.05 mg/kg	
P99[c]	0.05 mg/kg	

P: percentile; MRL: maximum residue level; LOQ: limit of quantification.
(a): Seven additional samples were reported where the LOQ of the analytical method was greater than the current MRL of 0.05 mg/kg; these samples were excluded for the statistical analysis.
(b): Upper bound approach: For samples with residues below or at the LOQ, the calculation was performed assuming the residues were equal to the numerical value of the LOQ.
(c): Percentiles calculated using Microsoft Excel.

https://doi.org/10.2903/j.efsa.2019.5897

Case study 2: MRL in honey for boscalid (2019)

Taking into account experiences gained in using the EU technical guidelines for the MRL setting in honey (European Commission, 2018), EFSA recommends that in a future revision of the EU guidance document further details should be elaborated particularly to consider the following aspects:

A. Design of residue trials representative for the uses under assessment:

- More guidance should be provided on the selection of the geographical location and distribution of residue trials with regard to the authorised uses across Europe. EFSA recommends that field residue trials for honey should be performed in the different European regulatory zones if Good Agricultural Practices (GAPs) are authorised or intended for crops attractive to bees in Northern and Southern Europe;
- Further guidance should be developed on the design of field residue trials in the crops under consideration or surrogate crops like oilseed rape or *phacelia* to ensure realistic results for honey reflecting the intended/authorised uses (e.g. dose rate, timing and frequency of the applications);
- Further information on the landscape composition of the field residue trials should be given (i.e. typology of vegetation in vicinity to the beehive that may contribute to or dilute the final residues in honey);
- EFSA recommends that pollen composition is always reported in the field residue trials in order to verify whether the bees forage in the treated crop or in other non-treated crops;

B. Information related to the nature of the residues in honey to which consumers might be exposed to:

- Further guidance should be given how to interpret available information from metabolism studies in primary crops and rotational crops (e.g. representative for oilseed and pulses/ fruits/leafy crops/root crops/cereals) in the different parts of the plants with regard to the nature of residues in honey.
- Further guidance should be given on how to decide whether an active substance and/or relevant metabolite(s) may pose systemic properties. According to the technical guidelines (European Commission 2018), in several scenarios of the decision-making scheme, the investigation of residues in honey is triggered by this characteristic and therefore further clarification is necessary with this regard;
- Information on the potential enzymatic processes occurring in the bee gut involved in the production of honey have an impact on the nature of the pesticide residues in honey. This information might elucidate if the processing by bees and in-hive processing might impact the nature of the residues to which final consumers might be exposed to;
- Further investigation on the behaviour of the residues in the honey bee combs would be desirable in particular for active substances and metabolites that might accumulate in beeswax in order to guarantee that the MRL proposal covers also honey with honey bee combs placed in the market or other apicultural products.

Few **RECOMMENDATIONS** based on how to apply the EC, 2018 and current knowledge:

- More guidelines/clarity on requirements for MRL in honey
- Recommendations on how to conduct the residue trials for determining magnitude of residues in honey
- Clarification on the decision tree and the "systemic properties" of a.s.
- Recommendations on which data should be clearly reported for giving robustness of the MRL
- Consideration of stability and processes inside the hive and/or in field that might alter the nature of residues in honey

Case study 3: MRL in honey for spirotetramat (2021)

- Honey technical guidelines in force

Honey

Surrogate crop: Phacelia tanacetifolia, 2 × 175 g a.s./ha, interval = 14 days, BBCH 50–65

The applicant provided four residue trials (two conducted in NEU and two in SEU) compliant with the use pattern that was estimated by the applicant to be the most critical with regard to spirotetramat residues in honey. The active substance was applied to *Phacelia tanacetifolia* as a surrogate crop under semi-field conditions (tunnel trials). The nature of the residues determined in honey is based on the major constituents of the residues detected in primary crops, rotational crops and processed crops.

- *Phacelia* considered a valid surrogate crop to estimate residues in honey;
- Tunnel test performed according to the most critical scenario.
- Tunnel test conducted in two geographical zones (NEU and SEU)
- Amount of honey sampled was 10-120 g, but this was considered a minor deficiency not affecting validity of trials

https://doi.org/10.2903/j.efsa.2021.6517

Case study 3: MRL in honey for spirotetramat (2021)

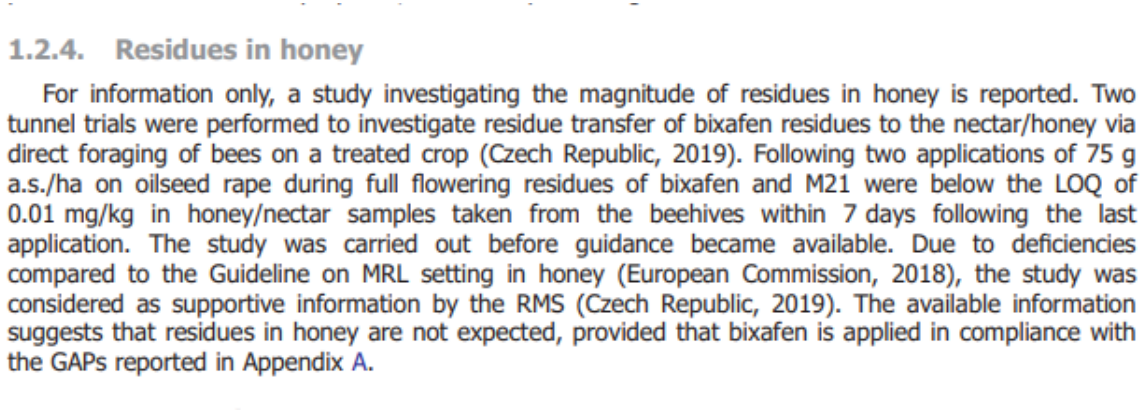
It must be also noted that the investigation of possible risk to bees related to the use of spirotetramat is outside the scope of this reasoned opinion. The evaluation of the risk to honeybees was evaluated in the framework of the peer review of the approval of spirotetramat at EU level. Additionally, national competent authorities at Member State level should pay attention to the bee health and bee protection when granting authorisations for plant protection products.

Few **RECOMMENDATIONS** based on how to apply the EC, 2018 and current knowledge:

- Risks to bees was outside the scope of the MRL application: bee health is in the remit of national competent authorities

Case study 4: bixafen MRL review (2020)

- Honey technical guidelines not yet in force



1.2.4. Residues in honey

For information only, a study investigating the magnitude of residues in honey is reported. Two tunnel trials were performed to investigate residue transfer of bixafen residues to the nectar/honey via direct foraging of bees on a treated crop (Czech Republic, 2019). Following two applications of 75 g a.s./ha on oilseed rape during full flowering residues of bixafen and M21 were below the LOQ of 0.01 mg/kg in honey/nectar samples taken from the beehives within 7 days following the last application. The study was carried out before guidance became available. Due to deficiencies compared to the Guideline on MRL setting in honey (European Commission, 2018), the study was considered as supportive information by the RMS (Czech Republic, 2019). The available information suggests that residues in honey are not expected, provided that bixafen is applied in compliance with the GAPs reported in Appendix A.

- Tunnel tests performed before guidance was available
- Deficiencies identified in the conduction of the tests compared with EC guideline
- Study considered as supportive only
- Residues not expected to occur in honey

https://doi.org/10.2903/j.efsa.2020.5998

Case study 5: alpha-cypermethrin peer review (2018)

- Honey technical guidelines not yet in force

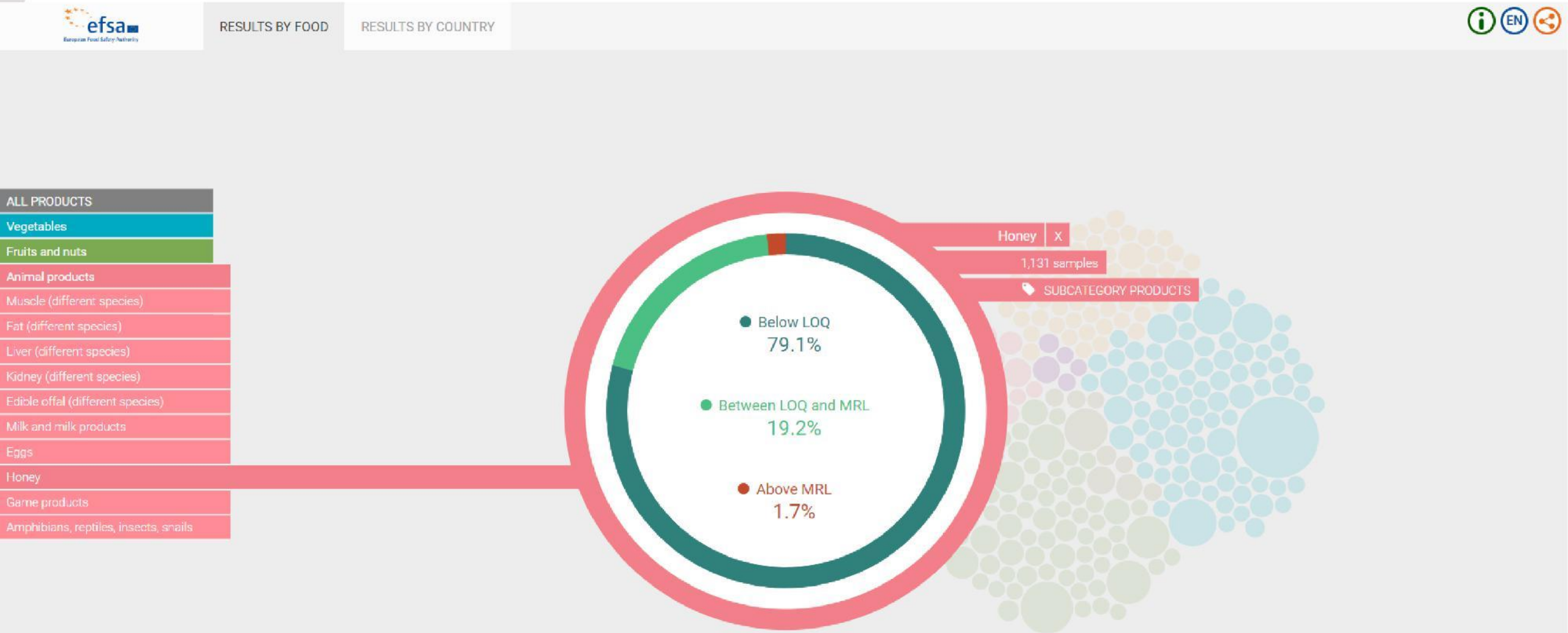
Field residue trials on *Phacelia* and on oilseed rape were submitted to analyse the residues of alpha-cypermethrin in flowers, pollen and nectar. In the residue trials on *Phacelia* (application at flowering), residues of alpha-cypermethrin were analysed in honey and were not detected (< 0.003 mg/kg) whilst in the residue trials on oilseed rape, residues of alpha-cypermethrin analysed in nectar and pollen showed a considerable decline after application, with residue levels ≤ 0.05 mg/kg in pollen and were not detected (< 0.003 mg/kg) in nectar. Considering that a low translocation of alpha-cypermethrin residues in the different plant parts was observed in the plant metabolism and taking into account the lipophilic properties of the active substance, further residue trials for the determination of residues of alpha-cypermethrin and its relevant metabolites in honey in regards to the other representative uses are not required to address the data requirement for the determination of residues in pollen and bee products for human consumption resulting from residues taken up by honeybees from crops at blossom.

- Field residue trials with *Phacelia* and OSR
- Residues not detected in the field trials
- Residues not expected to occur in honey based on low translocation from met studies and lipophilic properties of substance

https://doi.org/10.2903/j.efsa.2018.5403

EU Annual report in pesticides residues

efsa
European Food Safety Authority



https://www.efsa.europa.eu/it/interactive-pages/Pesticides-report-2016?do=food&lang=en

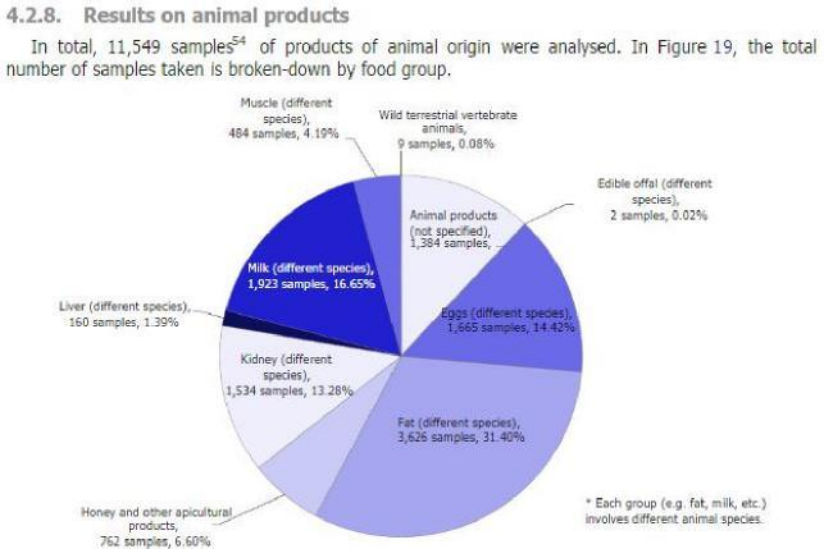
EU Annual report in pesticides residues 2018

European Food Safety Authority

- In 2018, 762 samples of honey and other apicultural products were analysed. In 601 samples (78.9%), no quantifiable residues were found.
- In 152 samples (19.9%), residues at or above the LOQ but below or at the MRL were identified.
- MRL exceedances were reported in 9 samples (1.2%), at least for one of the residues analysed.
- The pesticides uniquely reported in honey and other apicultural products above the LOQ were thiacloprid (106 samples), amitraz (25 samples), acetamiprid (24 samples) and dimoxystrobin (14 samples).
- MRLs were exceeded for the following substances: glyphosate (5 samples), acetamiprid (RD) (2 samples), boscalid (2 samples) and dimoxystrobin (RD) (2 samples).

RECOMMENDATIONS

Honey is a minor contributor to dietary exposure to pesticide residues. Therefore, EFSA recommends honey samples to be analysed by Member States under their national programmes, keeping the analytical scope as wide as possible. As a minimum, the following pesticides should be included: acetamiprid, amitraz, boscalid, dimoxystrobin, glyphosate and thiacloprid.



OECD WG residues in honey

- OECD drafting group on pesticides residue in honey;
- Includes representatives from regulatory national agencies, EFSA, DG SANTE, IND, and Academia;
- Starting point was the EC guideline;
- Work on the residue definition, list of melliferous crops, flowchart (decision tree) and MRL setting;
- Study design and test conditions still to be addressed in the WG.

Questions to the experts' group

- Should residues in honey only be investigated from uses on non-target plants when it concerns a herbicide? Since other categories of active substances are not aimed at non-target plants, and as such the proportion of non-target plants that is being encountered with the active is very small compared to the target crop. This is of course in particular relevant for non-melliferous crops (e.g. cereals).

- In case of a herbicide, it will easily be necessary to move the colonies to remote locations (out of the tunnel) due to decay of the plants. Isn't it expected that this will lead to possible dilution of the residues in the honey?

- How to establish if an a.s. is systemic?

- Criteria to select the cGAP for residues in honey?

Stay connected

Subscribe to

efsa.europa.eu/en/news/newsletters
efsa.europa.eu/en/rss

Receive job alerts

careers.efsa.europa.eu – job alerts

Follow us on Twitter

@efs a_eu
@plants_efsa
@methods_efsa
@animals_efsa

Follow us Linked in

Linkedin.com/company/efsa

Contact us

efsa.europa.eu/en/contact/askefsa