TECHNICAL WORKSHOP ON RISK ASSESSMENT OF THE PLANT PROTECTION PRODUCTS

TOPIC 2 : EXPOSURE AND RISK ASSESSMENT

Chair: Anja Friel, EFSA

Co-chair: Claudia Grosskopf, Germany

Report writer: Chloé De Lentdecker, EFSA

EUROPEAN FOOD SAFETY AUTHORITY

ITEM 1: MAPPING THE CURRENT PRACTICES OF THE MEMBER STATES

1.1. What are the current practices to assess PPPs.

For the majority of the Member States, the assessment of the co-formulants is usually based on hazard:

- SDS, classification are checked, especially CMR status – If CMR category 1 (some countries do not accept CMR category 2 neither) the assessment stopped. If the co-formulant is classified, its concentration in the PPP is verified whether it would trigger the classification of the PPP. In few case, genotoxicity studies on the PPP have been required from the APPL in order to conclude on the genotoxicity classification of the PPP.
- If no hazard identified i.e. no classification, no exposure assessment would be needed.

It is noted that the full composition of the PPP is asked to the applicant, who does not have always the information mostly in case when a co-formulant is a mixture. Therefore, the supplier should provide the requested information. The phys-chem properties and concentration of the co-formulant are requested as well if not available in the dossier.

It has been raised the lack of exposure data to perform a risk assessment while it is acknowledged by some MSs that the hazard based approach may not be sufficient.
When data are available from REACh dossier to set a reference value, then a risk assessment for the co-formulant may be performed. The question whether the information from REACh dossier could be used as it is or whether an assessment should be performed has been discussed.
To conclude, a toxicological risk assessment is not systematically performed for the co-formulants.

The biocide approach was also mentioned as an option to investigate, based on the 'substance of concern (SoC)' approach.

Regarding ecotox section, data on the PPP are provided for some endpoints as it is a data requirement. PPP toxicity is compared to active substance (a.s.) toxicity. In case the PPP is more toxic (> factor of 3) then a specific risk assessment with the PPP is performed.

In the area of residues there are no data, i.e. no decline or residue studies available with co-formulants.

ITEM 1: MAPPING THE CURRENT PRACTICES OF THE MEMBER STATES

1.2. Existing scientific information including monitoring data regarding exposure of humans and the environment.

In general, literature may be a source of data on exposure. Monitoring data have also been mentioned by the MSs. However, uncertainties are associated with the identification of co-formulants or sometimes only the a.s. is traceable. Furthermore, it may be difficult to identify the source of exposure for the co-formulant of interest.

For non-dietary exposure, the exposure and risk assessment would be based on the concentration of the co-formulant in the PPP.
The potential concerned linked to toxicokinetic interaction has been raised by a MS, when prediction of the combined exposure/risk would not be sufficient to anticipate them, while for the majority of the cases the concentration addition approach would be conservative. Therefore, data e.g. QSAR data, should be provided.

For dietary exposure, the question about the amount of the co-formulant still present on the food has been raised and is difficult to extrapolate from the concentration in the PPP.
It has been mentioned an ongoing work in one MS, to get real data for some co-formulants. The project is still at an early stage.
Some MSs indicated that field data on the co-formulant may be retrieved from the literature or may be requested in theory with the PPP in some cases e.g. based on the type of the formulation.

ITEM 1: MAPPING THE CURRENT PRACTICES OF THE MEMBER STATES

The phys-chem properties of the co-formulant may help to understand how the co-formulant is transformed. However, the specific environmental conditions (e.g. light, heat…) should be known to better anticipate the stability for instance, of the co-formulant.

For environment exposure of individual co-formulants, it would depend on the scenario and it is essential to know which parameters to be indicated in the model to get a reliable output. It was reported that simplistic exposure assessments for the PPP may be performed however such assessments were not able to provide information on the long-term exposure from the co-formulants.
ECHA may be a source for data (in case of high tonnage).
There are uncertainties for ecotox risk assessment, if no reliable data are coming from modelling data.
It was also mentioned that some function of co-formulants e.g. wetting agent, may be of potential concern for certain non-target organisms due to a physical effect.

Finally, poisoning data for at least acute toxicity or data related to accidental exposure for environment have been discussed as a potential source of data. It is acknowledged that many uncertainties are associated to this information as declarative information, but still may be considered as an indicator.
Wildlife poisoning investigations are likely only to focus on active substances but in the case an incident is linked to the use of a PPP it could be considered as to whether the incident was a result of the active substance or the product.

ITEM 2: ESTABLISH THE CRITERIA FOR CASES WHEN RISK ASSESSMENTS OF CO-FORMULANT/PPPS IS (NOT) NEEDED

2.1 What are the cases when risk assessment is not needed

2.1.1 Proposals for initial criteria to build a list of co-formulants categorised as no concern. What are the next steps needed to further develop such a list.

Possible solutions proposed	Proposed follow-up actions
• Risk assessment not needed if, e.g. - No/low hazard - Cut off criteria for unacceptable co-formulants e.g., classification CMR cat. 1 - No exposure for specific area (e.g., ornamental uses for dietary exposure) - Low exposure based on GAP (threshold to be defined) - Existing RMM ensure safety of the PPP on case-by-case approach? i.e., safety sentences - Regulated in other EU frameworks case by case e.g., feed/food additives	• Build a positive list of co-formulants of no concern (part of the bigger database on co-formulants) -> Creation of a Working Group (WG) or need for outsourcing the work for doing so. • Creation of a WG relevant to work on all the possible solutions. -> This could be part of a **Guidance Document (GD)** to be drafted. • Outsourcing of some tasks may be an option.

ITEM 2: ESTABLISH THE CRITERIA FOR CASES WHEN RISK ASSESSMENTS OF CO-FORMULANT/PPPS IS (NOT) NEEDED

2.2 Under which circumstances is the risk assessment of the co-formulant/PPP needed?

Possible solutions proposed	Proposed follow-up actions
• When there is a potential concern not only from classification but e.g., derived no effect level (DNEL) available identified during the hazard assessment of the co-formulant • When there is exposure • Critical function of co-formulants could be identified, e.g. wetting agents, emulsifier, preservatives (biocides) – may be relevant for ecotox aspects as NTO could be close to target pest. • PPP more toxic than the a.s. based on hazard (e.g., metabolic biomarkers, classification, adversity of the effects) -> need for data on PPP and find a way how to obtain those data -> need to investigate which co-formulant is triggering the toxicity • Potential for toxicokinetic interaction (test the PPP or produce toxicokinetic data as 'longer term' proposal) • Follow the current biocide and pesticide approach i.e. looking at the classified component and triggering the classification of the PPP • Use phys-chem properties e.g., LogPow, stability/persistence to be combined with exposure potential (e.g. availability of the co-formulant) to understand whether there is a need or not to perform a risk assessment • Environmental exposure: tool exists but some adjustments are needed/confidence on the parameters -> e.g. use uncertainty factors, identification of threshold…	• Proposal of drafting a flowchart/stepwise approach • Decision tree may also be proposed -> it could be included in the GD previously mentioned, that may be relevant for APPL and MSs. • Prioritising the need for risk assessments for co-formulants e.g., depending on specific criteria such as their function. • Preparation of e.g., an opinion regarding the toxicodynamic/kinetic aspects • Collection of the MS exposure assessment (methodology) already performed and available i.e. work sharing -> a call for assessment could be needed afterwards. • Consider requesting data for properties of the co-formulant/PPP (e.g. stability/persistence) to understand the potential for (long-term) exposure and to perform a fit for purpose exposure assessment -> creation of a WG for working on that

ITEM 3: SPECIFIC EXPOSURE AND RISK ASSESSMENT METHODOLOGY AND CONSIDERATIONS FOR PPP

Data on exposure

3.1 What data are needed to estimate the dietary exposure to co-formulants and/or PPP.

ITEM 3: SPECIFIC EXPOSURE AND RISK ASSESSMENT METHODOLOGY AND CONSIDERATIONS FOR PPP

Possible solutions proposed	Proposed follow-up actions
• Nature of residues: - Grouping of co-formulants by structure and phys-chem properties, predict degradation behaviour of group of similar compounds and group of compounds of similar degradation behaviour (e.g., literature search as a first step; chemistry; transformation models; limited experiments on model crops for instance; fate in soil info) • Magnitude: - Calculate a maximum application rate that is unlikely to lead to measurable residues (trigger) - Theoretical worst-case calculation to 'pass' the screening RA i.e., using application rate, assuming no degradation for instance… several factors may be hypothesised. - Look at approach similar to RUD -> need data. - For RUD approach: define protection goal for consumers in view of uncertainty of this approach - Analysis of MS data, US EPA data, Swiss data… - Targeted tests for most critical case GAPs close to harvest; post-harvest on representative categories -> extrapolation and envelope approach - Derived DT50 for all co-formulants that are not persistent and compare to default DT50 of the a.s. to estimate residues (as for NDE).	• Creation of a WG • Data collection i.e. literature search to narrow the focus • Stepwise approach: hazard, identification of co-formulant of potential concern -> exposure assessment • EFSA: Survey/call for data on exposure -> Drafting of a GD

ITEM 3: SPECIFIC EXPOSURE AND RISK ASSESSMENT METHODOLOGY AND CONSIDERATIONS FOR PPP

Data on exposure

3.2 What data are needed to carry out the non-dietary risk assessment for co-formulants and/or the PPP.

Possible solutions proposed	Proposed follow-up actions
• Use data retained for the a.s. considering the concentration of the co-formulant in the PPP (e.g. ratio co-formulant/a.s. and DT50) • DFR default value, refinement needed based on PPP data (different depending on the zone) -> need for data from the APPL as a second tier.	• Creation of a WG • Data collection i.e. literature search to narrow the focus • Stepwise approach: hazard, identification of co-formulant of potential concern -> exposure assessment • EFSA: Call for data/models from e.g., CLE -> Drafting of a GD

ITEM 3: SPECIFIC EXPOSURE AND RISK ASSESSMENT METHODOLOGY AND CONSIDERATIONS FOR PPP

Data on exposure

3.3 What data are needed to estimate the fate and behaviour of the PPP and/or co-formulants in the different compartments?

ITEM 3: SPECIFIC EXPOSURE AND RISK ASSESSMENT METHODOLOGY AND CONSIDERATIONS FOR PPP

Possible solutions proposed	Proposed follow-up actions
Narrow down the co-formulants relevant for environmental assessment - Grouping of co-formulants by structure and phys-chem properties, predict degradation behaviour of group of similar compounds and group of compounds of similar degradation behaviour especially for long term exposure and GW (e.g. literature search as a first step; chemistry; transformation models; fate in soil info from REACH for instance) - New data to be generated by APPL i.e. complete data package for env (PEC needed for co-formulant too) - extrapolation to be applied in some cases - Further reflect on the protection goal for co-formulants in GW as not covered in the directive (only a.s.). - Calculate a maximum application rate/% in the PPP that is unlikely to lead to measurable residues in the environment (trigger) - Theoretical worst case calculation to pass screening RA i.e. using application rate, assuming no degradation for instance… several factors may be hypothesised. - Analysis of data of other sources (literature, regulatory) when available - Derived DT50 for all co-formulants that are not persistent and compare to default DT50 of the a.s. to estimate residues (as for NDE). - Use data used for the a.s. considering the concentration of the co-formulant in the PPP (e.g. ratio co-formulant/a.s. and DT50	• Creation of a WG, involving ECHA when relevant • Data collection i.e. literature search to narrow the focus on some co-formulant depending on the concentration used in PPPs • Stepwise approach: hazard data available, identification of co-formulant of potential concern -> exposure assessment • EFSA: Survey/call for data/models from e.g., CLE -> Drafting of a GD on the exposure assessment of the PPP and co-formulants and building of a database for co-formulants (as mentioned for item 1)

ITEM 3: SPECIFIC EXPOSURE AND RISK ASSESSMENT METHODOLOGY AND CONSIDERATIONS FOR PPP

Data on exposure

3.4 What models or tools exist to calculate or estimate exposure? Which exposure scenarios to be considered.

Background

Non-exhaustive available pesticide exposure models:

- EFSA calculator, 2022 : for operators, workers, residents and bystanders.
- EFSA Pesticide Residues Intake Model (PRIMo) : for consumers.
- FOCUS simulation models and FOCUS scenarios: concentrations of PPP in groundwater and surface water
- The US EPA Pesticide Handler Exposure Database (PHED): for workers
- CLE exposure assessment tools: OWB tool, SpERCs, LET: for workers and consumers and environment as well
- Pesticide Emission Assessment at Regional and Local scales (PEARL): pesticide behaviour in the soil-plant system

Possible solutions proposed	Proposed follow-up actions
• Same models as for a.s. , see above.	• Check if the models are applicable to co-formulants.

ITEM 3: SPECIFIC EXPOSURE AND RISK ASSESSMENT METHODOLOGY AND CONSIDERATIONS FOR PPP

Methods on risk assessment

3.5. Which methods to use for the risk assessment of the PPP/co-formulants.

Possible solutions proposed	Proposed follow-up actions
• Standard approach based on hazard versus exposure. • Look at the single component for assessing the whole PPP for humans, while for ecotox PPP data are available. • Additional considerations required in case of synergistic/additive effects	• May be covered by a WG • Stepwise approach to be further elaborated with the evolution of the knowledge

ITEM 3: SPECIFIC EXPOSURE AND RISK ASSESSMENT METHODOLOGY AND CONSIDERATIONS FOR PPP

Methods on risk assessment

3.6. In which cases can a combined assessment be performed.

Background

- Regulation (EC) 1107/2009 requires that 'interaction between the active substance, safeners, synergists and co-formulants shall be taken into account' in the evaluation and authorisation of Plant Protection Products (Article 29). Commission Regulation (EU) No. 284/2013, further requests 'any information on potentially unacceptable effects of the plant protection product on the environment, on plants and plant products shall be included as well as known and expected cumulative and synergistic effects'.

Possible solutions proposed	Proposed follow-up actions
• When reference values are set • Look at targeted organ/AOP (single component approach) for performing a combined assessment • When same residues of different co-formulants are retrieved in a PPP • Same concept applies to co-formulants as for a.s. • Investigate the frequency of use of co-formulants and prioritise the need for conducting a combined assessment	• May be covered by a WG • Tiered approach (maybe combined assessment not needed) • Look at ECHA data/REACh dossiers (CSR for instance) • Develop test methods to investigate the whole mixture • Sharing data i.e. all databases to list the most commonly used co-formulants at national level

ITEM 3: SPECIFIC EXPOSURE AND RISK ASSESSMENT METHODOLOGY AND CONSIDERATIONS FOR PPP

Methods on risk assessment

3.7. Use of uncertainty factors (in some cases) to compensate for possible synergistic effects.

- Sub-item not discussed as such but it was agreed that could be covered by a WG above-mentioned.

ITEM 3: SPECIFIC EXPOSURE AND RISK ASSESSMENT METHODOLOGY AND CONSIDERATIONS FOR PPP

Methods on risk assessment

3.8. Co-formulants with particular properties (e.g., CMR, PBT).

Possible solutions proposed	Proposed follow-up actions
• Same criteria as for the a.s. to be applied	• To be mentioned in a GD

ITEM 3: SPECIFIC EXPOSURE AND RISK ASSESSMENT METHODOLOGY AND CONSIDERATIONS FOR PPP

Methods on risk assessment

3.9. Additional data for PPP for derivation / confirmation of reference values

Possible solutions proposed	Proposed follow-up actions
• in silico tools (read across, QSAR etc.)? • in vitro studies (e.g., comparative studies for active substance(s) and whole mixture)? • in vivo studies (which kind of studies)?	• Stepwise approach to be defined • Covered by a WG • To be further considered

ITEM 4: ORGANISATIONAL ISSUES AND ADAPTATION

4.1. Harmonised approach for the completeness check of the dossier.

Possible solutions proposed	Proposed follow-up actions
• Creation of a completeness check list for harmonisation	• Creation of a completeness check list by a WG -> for time being, data collection, collaboration with ECHA to improve searchability of the information e.g., xml format. • At the next PSN certainly in Oct 2023, communication to Industry • Minimum level of data required may be added in a checklist to be requested to the APPL and ensuring harmonisation among MSs (e.g., work done in the northern zone, PAI…)

ITEM 4: ORGANISATIONAL ISSUES AND ADAPTATION

4.2. Adaption of existing templates to harmonise assessment and improve transparency e.g., DAR/RAR/CLH report and/or draft registration report format

Background

- EC Guidance document for applicants on preparing dossiers for the Approval of a chemical new active substance and for the renewal of Approval of a chemical active substance according to Regulation (EU) No 283/2013 and Regulation (EU) no 284/2013
- All guidances on a.s. and PPP: https://food.ec.europa.eu/plants/pesticides/approval-active-substances/guidelines-active-substances-and-plant-protection-products_en

- Sub-item not discussed as such (refer to topic 1 proposals), to be further discussed based on concrete needs.

ITEM 4: ORGANISATIONAL ISSUES AND ADAPTATION

4.3. Ways to ensure efficiency in the process.

- Sub-item not discussed as such, to be further discussed based on concrete needs.

STAY CONNECTED

SUBSCRIBE TO
efsa.europa.eu/en/news/newsletters
efsa.europa.eu/en/rss
Careers.efsa.europa.eu – job alerts

LISTEN TO OUR PODCAST
Science on the Menu –Spotify, Apple Podcast and YouTube

FOLLOW US ON TWITTER
@efsa_eu @methods_efsa
@plants_efsa @animals_efsa

FOLLOW US ON LINKEDIN
Linkedin.com/company/efsa

FOLLOW US ON INSTAGRAM
@one_healthenv_eu

CONTACT US
efsa.europa.eu/en/contact/askefsa

efsa
EUROPEAN FOOD SAFETY AUTHORITY