9 June 2023

CODEX COMMITTEE ON PESTICIDES RESIDUES

(Fifty-fourth Session)
Beijing, China
26 June – 01 July 2023

European Union comments on

AGENDA ITEM 5 (a)

Report on items of general consideration arising from the 2022 JMPR meeting

(Section 2 of the 2022 JMPR Report)

European Union Competence
European Union Vote

The EU would like to provide the following comments on section 2 of the 2022 JMPR Report:

2.1 Requirements for data on the impact of residues on the human intestinal microbiome

The European Union (EU) would like to thank JMPR for the efforts to take into account possible effects on the gut microbiome. The EU concurs with JMPR considerations on the potential relevance of chemicals (including pesticides and their residues) on human and animal intestinal microbiome and reckons that further developments are needed in this area to understand the importance of the microbiome in risk assessment and identify dedicated strategies and methodologies accordingly. Currently, the assessment of microbiome(s) is not part of the regulatory requirements for plant protection products and their residues in the EU and no internationally agreed guidelines are in place in the pesticide area. The EU is starting to build capacity on this subject and the European Food Safety Authority launched a thematic grant in March 2020 to collaborate with EU Member States to identify indications for future EU research agendas with a focus on specific needs from a risk assessment perspective. The EU is willing to contribute to the proposed microbiome expert working group to develop guidance for discussion and adoption by JMPR. Further information on the implementation (would the evaluation apply to only new compounds or also would it be included in periodic re-evaluations of old compounds) would be desirable.

2.2 Non-linear kinetics (KMD)

The EU welcomes the establishment of an electronic working group on the assessment and interpretation of non-linear dispositional kinetics. The EU agrees that more guidance on assessment and interpretation of non-linear dispositional kinetics would be desirable. The guidance should more generally deal with the interpretation of non-linearity in the dispositional kinetics of pesticides. At EU level, hazard classification is an important element to decide on the approval of an active substance. According to the European Chemicals

Agency (ECHA) the kinetically-derived maximum dose (KMD) approach is not appropriate to fulfil the legislative needs for classification and labelling; instead, the maximum tolerated dose (MTD approach; with inclusion of the non-liner kinetic only as a complementary information) would be the most appropriate methodology to derive selection of the high dose level for toxicological studies.

Further information on the electronic Working Group (eWG) and the progress of the activities would be desirable. The EU is willing to contribute to the critical revision of the announced guidance.

2.3 Interpretation and follow-up of positive results in in-vitro gene mutation assays

The EU welcomes JMPR clarifications on the interpretation and follow-up of positive results in in vitro gene mutation assays. The EU notes that the proposed testing strategies for follow up of positive results in in vitro gene mutation assays are not fully in line with the approaches followed in the EU:

- As a follow-up for positive *in vitro* gene mutations assays, the EU considers that routine testing for *in vivo* germ cell mutation is not necessary [1].
- As a follow-up for positive *in vitro* gene mutation results, the JMPR report states: '*However, for bacterial gene mutation caused by non-DNA reactive gene mutagens (for instance intercalating agents likely to be detected only by tester strains such as TA 1537 used in the Ames test) the in vivo alkaline comet assay is not appropriate[…]*'.
  The EU proposes to state that the *in vivo* alkaline Comet assay is not appropriate for substances that are not considered to induce single-strand breaks or double-strand breaks (SSBs or DSBs), either directly or via DNA repair intermediates, based on structural considerations and positive results in TA1537 and TA98.
- As regards clastogenicity and aneugenicity endpoints, the EU agrees with the JMPR proposal that in the case of a positive in vitro chromosomal aberration assay or in vitro micronucleus assay the recommended follow-up is the in vivo micronucleus assay. The EU suggests adding that evidence of target tissue exposure should be demonstrated in the in vivo micronucleus assay[1,2].

2.4 A risk-based decision tree approach for the safety evaluation of residues of pesticides, veterinary drugs, food additives and contaminants

The EU welcomes the discussion to develop an approach for giving advice to risk managers on substances which are found in food, but for which the data are insufficient to perform a full risk assessment.

Regarding the use of the threshold of toxicological concern (TTC) approach, the EU consider that it is a pragmatic, scientifically valid methodology to assess the safety of substances of unknown toxicity found in food and the environment. However, the TTC approach should not be used for substances for which EU food/feed legislation requires the submission of toxicity

[1] EFSA Scientific Committee, 2011, Scientific opinion on genotoxicity testing strategies applicable to food and feed safety assessment. https://doi.org/10.2903/j.efsa.2011.2379
[2] EFSA Scientific Committee, 2017, Clarification of some aspects related to genotoxicity assessment. https://doi.org/10.2903/j.efsa.2017.5113

data. Hence in the EU, the TTC approach is usually not applied for pesticides to waive toxicological studies defined in the legal data requirements[3].

The EU is in favour of a harmonized risk assessment approach and the elaboration of an applicable decision tree. The EU will welcome further specific information on certain details on the decision tree, such us the methodology to calculate the exposure or the subgroups of the population for which exposure estimations should be derived, and the definition of certain criteria like "meaningful margin of exposure", "low margin of exposure" or "acceptable margin of safety".

2.5 Unnecessary use of *in vivo* animal studies

The EU strongly supports the recommendations of JMPR to avoid unnecessary *in vivo* studies. It is highlighted that in the EU, the replacement, reduction and refinement of the use of animals for scientific studies supporting applications for pesticide approvals and MRL applications are a fundamental principle implemented in the pesticide legislation.

The EU considers that for new compounds, the respective endpoints should be addressed by appropriate *in vitro* studies. With regard to old substances that are subject to periodic re-evaluation, old *in vivo* studies can be used if their quality is still considered sufficient but should not be repeated.

The EU recommends to review the title as "*in vivo* studies".

2.6 Establishment of MRLs for pesticides for okra

The EU appreciates the comprehensive work done by JMPR to evaluate monitoring data and to analyse the normalised initial residue concentrations measured at day 0 in different fruiting vegetables in view of identification of options for setting MRLs in okra by extrapolation. The EU agrees with the conclusion of JMPR that monitoring data are not appropriate to find representative commodities for okra, since for monitoring data usually no information is available on the treatment history. Without information on the use patterns, a meaningful interpretation of these data is not feasible.

The available data on normalised residue trials do not provide sufficient evidence that the residue behaviour in other fruiting vegetables is comparable to okra. Hence, the data do not support option 1 and option 2 on the classification of okra in the Codex food classification; option 3: introduction of a specific sub-group 12D for okra (including martynia and roselle) seems to be the only viable option at the moment.

The EU acknowledges the difficulties in generating data for the minor crop of okra and it recommends to explore if normalised residue data at day 0 in other crops show comparable residue levels with okra.

2.7 Enhancing operational procedures of JMPR to reduce the backlog

The EU supports the discussion to identify opportunities for enhancing the operational procedures of the JMPR and CCPR to reduce the backlog of evaluations. EU experiences on streamlining the assessment processes might be helpful to identify steps of the process which could be improved.

[3] EFSA Scientific Committee, 2019, Guidance on the use of the Threshold of Toxicological Concern approach in food safety assessment. https://doi.org/10.2903/j.efsa.2019.5708

2.8. OECD Update to the Guidance on Residue Definitions

The EU encourages the active involvement of JMPR experts in OECD projects, as JMPR experts have a lot of experiences in assessments at international level and therefore they are expected to provide valuable input to the development of OECD documents.

2.9. Information on residues in rotational crops following use on paddy rice

For European rice cultivation, crop rotation is not completely excluded, but is expected to take place only after several years of cultivation of rice. For EU assessments, a new guidance document on rotational crop assessment is under preparation. In a draft version of this guidance document, rice is considered as semi-permanent crop. Hence, primary crop uses in rice would not trigger rotational crop studies. If rotational crop studies are required due to uses in other primary crops than rice, it is not recommended to conduct rotational crop studies (confined studies and higher tier studies) with rice (crop grown as rotational crop) to investigate the uptake from residues in soil. Instead, other cereal crops should be used as test crop for rotational crop studies, as rice is considered not a crop representative for other cereals.

2.10. Common pyrazole metabolites

The EU agrees with JMPR observation and consider that there is a need to harmonise the assessment of the common metabolite of pyrazole carboxamide fungicides exists. The active substances assessed by JMPR in 2022, belonging to the pyrazole class are the following: benzovindiflupyr (261), chlorantraniliprole (230), inpyrfluxam (329), isoflucypram (330) and tetraniliprole (324). However, for a number of additional active substances containing a pyrazole structure such us fenpyroximate (193), fipronil (202), pyraclostrobin (210), isopyrazam (249), fluxapyroxad (256), sedaxane (259), bixafen (262), cyantraniliprole (263), oxathiapiproline (291) and ethiprole (304) Codex MRLs are in place, and therefore, should be also considered. Harmonisation should also include the use of a unique code number for a metabolite in all the parts of a dossier.

Since this issue is not specific to pyrazole, a more general approach for assessing common metabolites should be elaborated. At EU level, for triazole derivative metabolites (TDMs) a risk assessment approach which comprises the different sources of triazole metabolites has been elaborated. A similar approach should be established for class of pyrazole pesticides.