

CODEX ALIMENTARIUS COMMISSION



Food and Agriculture
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World Health
Organization

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Comments submitted by Croplife International

Agenda Item 5(a)

Section 2 of the JMPR Report

DISCUSSION PAPER ON DEVELOPMENTS IN DIETARY EXPOSURE METHODOLOGY FOR PESTICIDES RESIDUES IN FOOD AND REQUIREMENTS FOR DATA ON THE IMPACT OF RESIDUES ON THE HUMAN INTESTINAL MICROBIOME

DEVELOPMENTS IN DIETARY EXPOSURE METHODOLOGY FOR PESTICIDES RESIDUES IN FOOD

BACKGROUND

1. As summarized in the 'General Considerations' chapter of the Report from the 2023 Joint Meeting on Pesticide Residues (JMPR), the JMPR continued its work on Global Estimate of Chronic Dietary Exposure (GECDE) based dietary exposure methodologies and concluded:
 - a) The JMPR should 'transition from the use of the IEDI to the use of GECDE-mean'
 - b) The JMPR should continue to investigate implementation and modification options for the GECDE-high for the assessment of dietary exposure to pesticide residues for chronic and shorter-than-lifetime assessments with the aim of a transition to adoption.
 - c) Further investigate the degree of conservatism in the GECDE (mean and high) and the IEDI.

COMMENT

2. Use of the GECDE-mean for chronic dietary exposure assessments

CropLife International supports the development of scientifically valid improvements to dietary exposure assessments. For chronic exposure, using data from individual food consumption surveys (the GECDE-mean methodology) is likely a more appropriate source of data than the food balance sheet approach (the current IEDI methodology).

3. CropLife International recognizes that whilst many countries do conduct individual food consumption surveys, there are many countries which do not, and this raises a question about the range of countries for which data are included in the GECDE-mean model; is it broad enough for a global JMPR assessment? There is also a question on quality and reliability of the food consumption surveys. Unfortunately, there does not appear to be a transparent working model or tool for the GECDE-mean approach in the public domain to help answer these questions.
4. CropLife International also recognizes that the chronic dietary exposures using the GECDE-mean approach are in almost every case higher than the existing IEDI methodology. The median increase in exposure was 5 times higher (range 1 – 63) using the GECDE-mean compared to using the IEDI (covering 22 active ingredients in the 2023 JMPR report). This is a significant increase in calculated exposure and the impact of using these increased exposures when setting Codex MRLs should be considered further.

5. CropLife International has not seen evidence demonstrating the current IEDI methodology does not protect consumer safety and therefore proposes the following activities should be undertaken before any changes are made.
 - a) A comprehensive impact assessment of using the GECDE-mean methodology should be conducted and made publicly available for all active ingredients where Codex MRLs exist.
 - b) To enable this impact assessment a working model, description of content and user manual for the GECDE-mean approach should be made publicly available; this will also help:
 - i. The JMPR, in order to be efficient and to maintain transparency in their work and outputs.
 - ii. Industry, in order to assess likely outcomes and makes decisions about what data to generate and what uses to support (or not) in JMPR submissions.
 - iii. Other stakeholders.
6. **Realistic residue levels** from food monitoring surveys should also be included in this impact assessment to quantify the actual dietary exposure levels compared to calculated exposure levels and to inform discussions on levels of consumer protection.
7. **Risk managers** at CCPR should be actively involved in decisions on changing dietary risk assessment models used by the JMPR and have the comprehensive impact assessments available to help inform the decisions.
8. If it is agreed by JMPR and CCPR to change the exposure models for chronic dietary risk assessment, **a clear future date for implementation** is needed and a process described for how and when the JMPR will re-evaluate all the existing Codex MRLs
9. Further work on the GECDE-high for the assessment of dietary exposure to pesticide residues for chronic and shorter-than-lifetime assessments

CropLife International questions the need for further time and resources to be dedicated to the continued investigation of the GECDE-high approach in dietary risk assessments. This should only be done if there are substantiated concerns about consumer risk when using existing approaches. CropLife International believes sufficient levels of conservatism are already built into these current approaches.

REQUIREMENTS FOR DATA ON THE IMPACT OF RESIDUES ON THE HUMAN INTESTINAL MICROBIOME

BACKGROUND

10. At the 2022 JMPR it was recommended to convene a microbiome expert working group to consider requirements for data on the impact of pesticide residues on the human intestinal microbiome.
11. At CCPR54, during the discussion on General Considerations arising from the JMPR, it was noted that this was an important and evolving matter and the meeting welcomed the establishment of an expert Working Group to look into this.
12. In the 2023 JMPR report there is no mention of this matter in the chapter on General Considerations and very limited statements are made opposite the individual active ingredient reviews; these mostly state that no information was available and no experimental data were submitted.

COMMENT

13. CropLife International would like to request an update on this matter including:
 - a) The progress made in establishing the expert working group.
 - b) The achievements of the working group to date and likely timelines for outputs to be made public.

14. At the same time, CropLife International would like to restate and expand on some of its concerns that were raised during CCPR54.
- a) The science relating to, and the understanding of the human gut microbiome and its influence on human health are still evolving. The FAO Thinking about the future of food safety – A foresight report (<https://doi.org/10.4060/cb8667en>) identified many of the scientific challenges on this matter, such as the lack of consensus on definitions of a healthy microbiome and normal fluctuations in the microbial composition, the challenge of connecting microbiome disturbances with health effects and the need to define fit-for-purpose experimental models. Similar statements are made in other recent publications e.g. EFSA's roadmap for integration of gastro intestinal microbiomes into risk assessment ([EFSA \(2024\). Roadmap for the integration of gastro-intestinal \(GI\) tract microbiomes \(human and domestic animal\) in risk assessments under EFSA's remit](#)).
 - b) CropLife International proposes the WHO engages in collaborative activities with other related and respected organisations e.g. the FAO and EFSA to develop the necessary scientific understanding. Only when this has made progress, should there be discussions on the need for additional data requirements for pesticides; if a need for test methods and guidelines is identified, they should be developed via the OECD.
 - c) CropLife International also highlights that extensive mammalian toxicology data are available for all crop protection pesticides. The vast majority of these data are generated using oral dosing, including chronic oral toxicity studies in animals with intact gut microbiota. Therefore, meaningful apical adverse health outcomes mediated by the gut microbiota have been assessed and incorporated into the comprehensive human health safety evaluation.
 - d) At CCPR54 it was stated that the starting point of work for the microbiome working group should be the VICH Guideline 36 ([VICH \(2019\). Studies to evaluate the safety of residues of veterinary drugs in human food: general approach to establish a microbial ADI. VICH GL36 \(R2\)](#)), which is currently being used by JECFA in their scientific assessments. CropLife International has concerns with the assumption that this is an appropriate starting point for pesticides because:
 - i. The VICH Guideline 36 is not a standardized test method but describes a general approach, a range of possible ways of generating data, and how to derive microbiological endpoints from certain types of data.
 - ii. The VICH Guideline 36 states it is specifically intended for situations where “a drug intended for food producing animals has antimicrobial activity”. JECFA has only very recently decided to go beyond the stated intent of the VICH guideline and additionally apply it to non-microbial veterinary medicine products. This was first documented in the Report of the 94th Meeting of JECFA (2022) ([Evaluation of Certain Veterinary Drug Residues in Food – 94th Report on the Joint FAO/WHO Expert Committee on Food Additives](#)). This is therefore not a long-term established practice by JECFA for non-microbial products but rather, is a new approach and so far has only been applied to a very limited number of non-microbial chemical substances. JECFA outputs showed this to be for only two active ingredients in the 94th session of JECFA, 2022 and one additional active ingredient in the 98th session of JECFA, 2024 ([Summary and conclusions of 98th Meeting of the Joint FAO/WHO Expert Committee on Food Additives](#)).
 - iii. The above-mentioned limitations of the VICH Guideline 36, in association with the current state of scientific knowledge and the lack of consensus highlighted by the FAO, demonstrate this guideline is unlikely to be suitable to establish meaningful human health endpoints for use by JMPR when proposing Codex MRLs.

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15. In conclusion, CropLife International continues to:
- a) Support the need to further develop and understand the science of the human gut microbiome and its impact on human health.
 - b) Believe it is premature for the JMPR to follow its current practice of requesting specific data for individual pesticides on their effects on the human gut microbiome or to be unilaterally developing novel data requirements for pesticides.
 - c) Propose that following scientific advancements, if new data requirements for pesticides are deemed appropriate by CCPR, internationally agreed and validated test methods and guidelines should be developed via the OECD.

DISCUSSION PAPER ON ENHANCING OPERATIONAL PROCEDURES OF JMPR AND CCPR TO ELIMINATE THE BACKLOG OF EVALUATIONS AND MEET THE FUTURE DEMAND OF ESTABLISHING CODEX MAXIMUM RESIDUE LIMITS FOR PESTICIDES

BACKGROUND

1. A [discussion paper](#) summarizing the work of the Electronic Working group (eWG) Enhancement of work management of CCPR and JMPR is presented to the CCPR. The discussion paper emphasizes the enhancement of processes that involve the work of the Joint FAO/WHO Meeting on Pesticide Residues (JMPR) and continues the important work by the eWG reported and discussed at CCPR54 ([Enhancement of the operational procedures of CCPR and JMPR: Opportunities, Challenges, and Recommendations on Next Steps](#)).
2. CropLife International has been an active member of the Codex Enhancement eWG and has provided multiple documents to support its work, particularly focusing on identifying and implementing improvements in CCPR and JMPR processes and increasing available resources to the JMPR in order to assist resolving the multiyear backlog in assessment of new compounds and new uses, as well as periodic reviews. Previous CropLife International contributions to the eWG work are as follows: for [CAC44](#) and [CCPR52](#) in 2021; for [CCPR53](#), in 2022; and for [CCPR54: Agenda Item 13 Enhancement of the operational procedures of CCPR and JMPR](#), in 2023. In the latest of these documents, CropLife International highlighted a particularly worrying trend “concerns have been raised that the current CCPR/JMPR system is unable to keep up with global demand for the evaluation of new compounds, new uses, and periodic reviews. Increased demand for evaluation and increased work required to evaluate a dossier have been identified to be major challenges for resolving the current and future anticipated backlogs. CropLife International has estimated that to meet the future demand for new active compounds, new uses, and periodic reviews the output from the JMPR needs to increase by a factor of three”.
3. In addition to providing input to the work of the eWG on Codex Enhancement, CropLife International has held virtual workshops in [2022](#) and [2023](#) which were very well attended by Codex members, CCPR delegations, JMPR experts, Food and Agriculture Organization of the United Nations (FAO), World Health Organization (WHO) and CODEX, CCPR and JMPR Secretariats as well as observers attended, in total with over 150 non-industry participants. This shows that, Codex delegations and observers continue to recognize the value of the CCPR and JMPR especially given the global nature of food and feed supply chains and acknowledge the challenges Codex is facing. Codex members, CCPR delegations, JMPR experts, Food and Agriculture Organization of the United Nations (FAO), World Health Organization (WHO) and CODEX, CCPR and JMPR Secretariats attended, and in the 20223 workshops over 150 non-industry participants were noted). The results of the 2023 workshop are available [here](#).
4. CropLife International uses this Conference Room Document (CRD) as an additional opportunity to support the great work of the eWG, the JMPR, CCPR, Codex secretariat and Codex members and make further recommendations for the enhancement of Codex’ work, for the Codex members’ consideration and further discussion at the CCPR54.

RECOMMENDATIONS

5. To tackle the current challenges, improve existing systems and meet future demands, CropLife International proposes the Codex Enhancement eWG continue its work using the general recommendations in the eWG report: multiprong short- and longer-term work toward the identification and implementation of efforts in enhancement, particularly in the work of the JMPR:

Short term: CropLife International supports the eWG recommendation that CCPR endorses the continuation of the eWG to adopt the multiprong approach over the next three years (2024 – 2026) with a focus on:

- Convening an extraordinary meeting of JMPR to reduce the backlog of evaluations: CropLife International recommends that any initial extraordinary meeting of JMPR (potentially in 2025) focuses on the evaluation of new uses as done at previous extraordinary meetings of JMPR. If additional extraordinary meetings of JMPR are organized in the short-term, one to two new compounds or periodic reviews should be considered for these additional extraordinary meetings.

- Consulting with JMPR and stakeholders to identify specific projects that will improve its evaluation process: CropLife International suggests establishing an electronic submission and storage system for submissions to JMPR using existing tools built for electronic submission by the OECD Working Party on Pesticides. A harmonized approach has advantages for the expert evaluators and data sponsors alike.
- In addition to the above recommendations included in the eWG report to the CCPR, we continue to recommend that the eWG develop a framework for converting national/regional reviews into primary initial draft review documents for use by the JMPR expert panels.

Longer-term: CropLife International supports continuing the work of the eWG until 2028 to address more strategic issues, with a particular focus on JMPR Organizational Structure, Staffing and Resources, as indicated in [CX/PR 24/55/10](#).

- CropLife International continues to recommend consideration and implementation of our previously proposed pilot project to employ contracted staff (e.g., 4-6 part-time roles) for 3-5 years who provide support for the JMPR Expert Panels. As stated in CropLife International's [CCPR54 CRD](#), the primary role of this contracted staff would be the production of initial reviews of new active compounds, periodic reviews, or new uses in the JMPR format to initiate the review and consideration by the JMPR expert panels. In addition, the contracted staff would support the execution of the JMPR in-person meetings in September (e.g., providing drafting support for the experts in the making of changes in review documents under JMPR consideration), and otherwise generally support the WHO/FAO Secretariat in the operation of the JMPR expert panels. With this support, the independent experts of JMPR can review more new compounds, new uses and conduct periodic more reviews and hence reduce the backlog in evaluations. For convenience, the full original proposal for this pilot project, as presented to CCPR53, is included in Annex I of this document.
- Explore options for establishing a standard operating procedure for the use of Large Language Models (LLM such as ChatGPT), Reinforcement Learning from Human Feedback, and other Artificial Intelligence tools to develop a method for converting national/regional reviews into primary initial draft review documents for use by the JMPR expert panels. The LLM could be trained using existing JMPR reviews and recommendations along with national/regional reviews. Developing this standard operating procedure for the use of LLM may particularly create efficiencies for the review of new compounds and periodic reviews.

Annex I

From <https://CropLife International Codex Enhancement CCPR54.pdf>

DISCUSSION PAPER ON ENHANCING OPERATIONAL PROCEDURES OF JMPR AND CCPR TO ELIMINATE THE BACKLOG OF EVALUATIONS AND MEET THE FUTURE DEMAND OF ESTABLISHING CODEX MAXIMUM RESIDUE LIMITS FOR PESTICIDES, Item 13, Pages 4-5

1. Based on the discussions from the 2022 and 2023 CropLife International workshops, as well as considering the responses to the eWG Circular Letter, CropLife International would like to put forward the following recommendations to improve the functioning of JMPR/CCPR. Please note that CropLife International intends to discuss these recommendations with stakeholders that share our interest in enhancing CCPR/JMPR outside of the CCPR/JMPR process:
 - To improve JMPR resources and resourcing:
 - Establish a pilot project for 3-5 years to create 'permanent' staff to provide support for the JMPR Expert Panels. The primary role of this 'permanent' staff would be the production of initial reviews of new active compounds, periodic review or new uses in the JMPR format used to initiate review and consideration by the JMPR expert panels. In addition, the 'permanent' staff would support the execution of the JMPR in-person meetings in September (e.g., providing drafting support for the experts in the making of changes in review documents under JMPR consideration), and otherwise generally support the WHO/FAO Secretariat in the operation of the JMPR expert panels.
 - i. To fill these 'permanent' staff roles in this pilot project, secondments from existing institutions, or recently retired experts from governments could be considered. Consideration should also be given for retirees from the industry as their work would be limited to preparation of the initial review draft (i.e., not involved in the expert panel decisions).
 - ii. To support the pilot project of creating 'permanent' staff, establish a 'fee system' that would allow funding from industry resources to support new active compounds/new uses. Existing fee systems at a national/regional level should be leveraged to establish such 'fee system' at JMPR.
 - iii. Increase the number of experts particularly in regions underrepresented in current and past JMPR expert panels. In addition, it is crucial to identify and implement a process for training experts for JMPR work by leveraging ongoing capacity building efforts (e.g., establishment of Regional Excellence Center National at the University of Colombia in Bogotá).