

# CODEX ALIMENTARIUS COMMISSION



Food and Agriculture  
Organization of the  
United Nations



World Health  
Organization

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Agenda Item 5(a)

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**ORIGINAL LANGUAGE**

## JOINT FAO/WHO FOOD STANDARDS PROGRAMME CODEX COMMITTEE ON PESTICIDE RESIDUES

51<sup>st</sup> Session

Macao SAR, P.R. China, 8-13 April 2019

### COMMENTS ON REPORT ON ITEMS OF GENERAL CONSIDERATION BY THE 2018 JMPR

(Submitted by the European Union, Germany and Kenya)

#### 2.1 Toxicological profiling of compounds and less-than-lifetime dietary exposure assessment

##### European Union

##### *European Union Competence European Union Vote*

In general, the initiative to critically review the currently used concepts for toxicological profiling and dietary exposure assessment is fully supported by the EU, considering that the approaches for chronic and acute exposure assessments have been developed more than 20 years ago and have been improved during that period. The EU also very much welcomes the JMPR recommendation that the applicability of the considerations reported under item 2.1 should be further discussed with JECFA.

Although in the meantime substantial progress has been made in the field of toxicology and with regard to availability and quality of food consumption data, development of a new methodology for less-than-lifetime exposure seems premature at this stage. First a clear definition of protection goals for consumers is needed and the existing exposure assessments revisited as to their capacity to fulfil these protection goals.

Before a new methodology is developed, a critical review of the availability of toxicological data is considered necessary. Furthermore, a dialogue with risk managers is necessary to define the regulatory questions that should be addressed with the new exposure methodology. In particular, the following aspects should be clearly defined:

- Which period is considered as “less-than-lifetime”?
- Which are the age groups (and the period) that are considered relevant?
- Definition of protection goals.
- Impact on MRL setting.

##### Toxicological considerations

For the derivation of a short term health-based guidance value (corresponding to a “dietary” Acceptable Operator Exposure Level – AOEL- in the EU peer review of pesticidal active substances), similar qualitative considerations are given to those described in the 2018 JMPR report. Considering the decision-tree (page 7 of the JMPR report), the proposed factor of 3 is currently not taken into account when comparing developmental toxicity and systemic toxicity, however, it is noted that, according to the recent EFSA opinion on pesticides in foods for infants and young children (EFSA, 2018<sup>1</sup>), pending on the completeness of the dossier (whether the active substance was sufficiently investigated, for instance through an extended one-generation reproductive toxicity study), an additional uncertainty factor of 3 may be considered in deriving the toxicological reference values to protect infant and young children >16 weeks of age and additional considerations have to be made for infant <16 weeks of age. This approach is not specific for less-than-lifetime exposures but would be relevant to derive any health-based guidance value.

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<sup>1</sup> EFSA Panel on Plant Protection Products and their Residues (PPR), Ockleford C, Adriaanse P, Hougaard Bennekou S, Berny P, Brock T, Duquesne S, Grilli S, Hernandez-Jerez AF, Klein M, Kuhl T, Laskowski R, Machera K, Pelkonen O, Pieper S, Smith R, Stemmer M, Sundh I, Teodorovic I, Tiktak A, Topping CJ, Gundert-Remy U, Kersting M, Waalkens-Berendsen I, Chiusolo A, Court Marques D, Dujardin B, Kass GEN, Mohimont L, Nougad \_ ere A, Reich H and Wolterink G, 2018. Scientific opinion on pesticides in foods for infants and young children. EFSA Journal 2018;16(6):5286, 75 pp. <https://doi.org/10.2903/j.efsa.2018.5286>

### Dietary exposure considerations

The methodologies to estimate the chronic and acute exposure have been developed in the late 1990ies , making best use of food consumption data available at that time. It is acknowledged that the International Estimate Daily Intake – IEDI and the International Estimated Short-Term Intake – IESTI methodologies are not sufficiently addressing the fact that within a certain developmental phase (e.g. infancy/childhood/pregnancy) exposure to pesticide residues may exceed repeatedly the exposure calculated according to the IEDI. The frequency of these events, the extent of the exposure above the IEDI and the possible consumer risk related to these exposure peaks is not captured by the currently used risk assessment methodologies.

Before a new methodology is developed, it would be appropriate to perform an analysis of the exposure with regard to seasonal variations, variations for different subgroups of the population, to identify the relevant parameters and to develop a model that will address these aspects in the best way. The outcome of the project on the probabilistic modelling for the IESTI equations (see point 2.10) will be a useful source of information to identify the variabilities of exposure across individuals and should be used to underpin the model development for less-than-lifetime exposure.

#### **Germany**

As pointed out by JMPR, this is an issue of alignment between exposure and hazard characterization, deserving broader discussion.

#### **Kenya**

**Comment:** Kenya supports the outcome of the meeting that the decision-tree is a useful approach to considering the toxicological profiling of compounds and less-than-lifetime exposure. Further work by the WHO Secretariat of JECFA and JMPR is still being undertaken; therefore the acceptability of this approach will depend on the outcome of this work.

## **2.2 Need for sponsors to submit all requested data**

### **European Union**

*European Union Competence  
European Union Vote*

The EU supports the reminder of JMPR that all data and studies have to be submitted to JMPR within the agreed deadlines. In the interest of efficiency, JMPR should not waste time in assessing incomplete dossiers submitted by sponsors.

#### **Germany**

Data call-in deadlines should be considered as binding by sponsors for all of their studies and its submission in due times in order to allow experts for thorough meeting preparation.

From the reported problems it seems that some further improvement in priority setting for active substance assessment is necessary.

#### **Kenya**

**Comment:** Kenya supports the recommendation of 2016 JMPR on binary data on animal toxicity studies; on providing expanded guidance for these topics for EHC240.

## **2.3 Hazard characterization in the 21st century: assessing data generated using new mechanism based approaches for JMPR evaluations**

### **European Union**

*European Union Competence  
European Union Vote*

The EU supports the JMPR offer to evaluate data generated using new technologies as they become available in parallel with the results of traditional toxicity testing and encourages sponsors to submit such data. In the EU Regulation (EC) No 283/2013, describing the EU data requirements, it is recommended to undertake tests on vertebrate animals only when no other validated methods are available, and it is also noted that alternative methods to be considered shall include in vitro methods and in silico methods. The list of test methods and guidance documents relevant to the implementation of this Regulation has been published and should be regularly updated.

**Germany**

It is evident, that all relevant data on the toxicology of an active substance should be submitted and assessed. However, this requires prior evaluation of relevance, which is frequently confused with reliability. A clear definition of relevance criteria may facilitate selection and submission of data generated using new or alternative methodology.

**Kenya**

**Comment:** Kenya agrees to the fact that use of crop grouping is very important in supporting the establishment and harmonization of missing MRLs for minor crops. The approach of excluding some commodities from the crop group without due consideration of legitimate factors such as missing MRLs because it can impede trade especially in minor crops is a serious concern. We urge the CCPR to explore mechanisms to ensure that this does not set precedence on earlier agreed areas of harmonization.

**2.4 Update on the revision of principles and methods for risk assessment of chemicals in food (EHC 240).****European Union***European Union Competence  
European Union Vote*

An EFSA update on the use of the BenchMark Dose – BMD approach in risk assessment has been published in January 2017<sup>22</sup>, and concludes that the BMD approach is applicable to all chemicals in food for the establishment of health-based guidance values or to calculate margins of exposure. Its practical implementation in the EU peer review of pesticides still needs further development and harmonisation.

EFSA has also overarching Working Groups (WG on BMD and genotoxicity, both WGs dealing with specific questions from the EFSA panels, including from the pesticides Unit on request.

**Germany**

Germany actively supports the WHO activities regarding BMD methodology and has nominated an expert to participate in the meeting announced in 2.4.

**Kenya**

**Comment:** Kenya notes that only one compound was evaluated, there is need for more work using other compounds and crop combinations to evaluate the usefulness of this model. The model should be robust and all inclusive to cover various compounds and crop combinations.

**2.5 Microbiological effects****European Union***European Union Competence  
European Union Vote*

The EU would like to encourage the JMPR to also look at effects of pesticides, in particular fungicides on intestinal microbiomes.

**Germany**

The intestinal microbiome is a diverse microbial community which can hardly be standardized for testing. Any impact on intestinal homeostasis seen in such studies is therefore difficult to interpret and the resulting consequences appear rather unclear.

Although effects of fungicides on the human intestinal microbiome were mentioned in literature neither studies were provided by the sponsors nor publications found on the internet for five fungicides (fenpicoxamid, fluazinam, mandestrobin, pydiflumetofen and pyriofenone) assessed in JMPR 2018. This might be an indication that further research on this issue is necessary.

<sup>22</sup> EFSA Scientific Committee, Hardy A, Benford D, Halldorsson T, Jeger MJ, Knutsen KH, More S, Mortensen A, Naegeli H, Nøtø H, Ockleford C, Ricci A, Rychen G, Silano V, Solecki R, Turck D, Aerts M, Bodin L, Davis A, Edler L, Gundert-Remy U, Sand S, Slob W, Bottex B, Abrahamtes JC, Marques DC, Kass G and Schlatter JR, 2017. Update: Guidance on the use of the benchmark dose approach in risk assessment. EFSA Journal 2017;15(1):4658, 41 pp. doi:10.2903/j.efsa.2017.4658

**Kenya**

**Comment:** Kenya appreciates the new approach in evaluating intestinal microbiota given the emerging challenges with antimicrobial resistance which is a global challenge. Some pesticide residues in food may have antimicrobial properties and there is potential exposure of intestinal microbiota following ingestion of such residues in food.

**2.6 Transparency of JMPR procedures****European Union***European Union Competence  
European Union Vote*

The EU fully supports transparency of JMPR procedures. Also within the EU, transparency is a key requirement for risk assessment for pesticides. It is essential to describe the source of the data used, the validity of the studies, the results of studies and the assessment of the data leading to conclusions as well as the potential conflict of interest of assessors. Any initiative to increase transparency is supported.

**Germany**

The proposed approach is supported with a view to public mistrust and contemporary requirement for full transparency in all areas.

**Kenya**

**Comment:** Kenya welcomes the information on the processes followed by JMPR and encourages JMPR to continue to be transparent in their work. We would also seeks for clarification on the purpose and use of the “disclaimer”; and its impact on JMPR reports and monographs.

**2.7 Review of the large portion data used for the IESTI equation****European Union***European Union Competence  
European Union Vote*

The EU fully supports the update of food consumption data to be used in acute exposure assessment. The EU would like to offer support to collaborate with FAO/WHO in the preparation of the guidance how to calculate the large portions; in the EU a lot of experience has been gained on the compilation and aggregation of food consumption data provided by different data providers. This experience might be of value for FAO/WHO.

**Germany**

Given steadily changing consumption habits the data on large portions should be the most recent ones available. To this end, JMPR’s announced call for such data is welcomed. For reasons of comparability of data submissions it is also highly desirable to reach a common position on the number of consumers necessary to derive statistically robust percentiles.

**Kenya**

**Comment:** Kenya supports the use of large portion of data to be used for IESTI equation.

**2.8 Update of the IEDI and IESTI models used for the calculation of dietary exposure: commodity grouping according to the revised codex classification and new large portion data****European Union***European Union Competence  
European Union Vote*

The work done by RIVM (the Dutch National Institute for Public Health and the Environment) to develop and maintain the calculation spreadsheets for IEDI and IESTI calculations is highly appreciated, in particular the efforts made to integrate the large portion data (LP) used in the EU dietary risk assessment tool (EFSA, Pesticide Residue Intake Model - PRIMo revision 3). It should be noted that also at EU level new diets will be incorporated in future revisions of the EFSA PRIMo. Thus, to maintain a high level of consistency of the EU tool and the IEDI/IESTI models used by JMPR, the EU will keep FAO/WHO informed on progress made in the update of the EU diets.

**Germany**

No comment (only point for information on recent amendments).

## Kenya

**Comment:** Kenya welcomes the update on the database based on the newly adopted Codex Classification of Food and Feed for Vegetable Commodity Groups and Grasses of Cereal Grains, as well as consumption data for fish.

## 2.9 Recommendations for (sub) group maximum residue levels for fruiting vegetables, other than cucurbits revisited.

### European Union

#### *European Union Competence European Union Vote*

The EU appreciates the re-evaluation of the extrapolation approach for the fruiting vegetables group by JMPR. The use of normalised initial residue concentrations can give valuable indications whether the residue behaviour in different crops is comparable.

Subgroup of tomatoes: The EU notes the JMPR proposal to extrapolate residue data on tomatoes to the whole sub group. The EU would need to further examine this approach and has the following preliminary comments:

- extrapolation of residue data from tomatoes (any variety) to other crops belonging to the subgroup of tomatoes bears the risk that the Maximum Residue Level – MRL may not cover small varieties, such as cherry tomatoes or goji berries, which usually contain higher residues than varieties with bigger fruit size.
- for cape gooseberries the Codex MRLs – CXLs are applicable to the commodity after removal of the husk. Thus, for this crop the CXL proposal derived from tomatoes may be too high. Regarding consumer exposure, it is important that for the commodities with the highest consumption within the subgroup the risk assessment values (Highest Residue – HR and Supervised Trials Median Residue – STMR - values) are reliable.

Subgroup of peppers: The EU notes the JMPR proposal to extrapolate residue data on bell peppers and non-bell peppers to the whole sub group of peppers except okra, martynia and roselle. In the EU extrapolation from peppers to okra is currently acceptable. Based on the data presented in the JMPR report showing that pepper data are expected to underestimate the residues occurring in okra, the EU needs to further examine the proposed approach. As regards martynia and roselle, considering the low relevance of these commodities in the diet, a more pragmatic approach may be acceptable, allowing extrapolation from peppers. Also in chili peppers higher residues are expected compared to bell and non-bell peppers. A case-by-case decision may be necessary to decide whether the MRL for peppers can be applied to chili peppers.

Subgroup of eggplants: The EU notes the JMPR proposal to extrapolate from peppers to eggplants, rather than from tomatoes to eggplants (as is the current practice), as pepper is a better representative commodity for eggplants. JMPR further proposed to use the dataset for tomatoes instead of peppers wherever the dataset on tomatoes would lead to a higher MRL recommendation for eggplants. At EU level the extrapolation from tomatoes to eggplants is acceptable, but not the extrapolation from peppers to eggplants. The EU needs to further examine the proposed approach and would like to make the following initial comments: considering that the normalised initial residue concentrations in eggplants are higher than in tomatoes, trials in bell peppers may be more appropriate to derive the MRL for eggplants than residue trials in tomatoes. However, it needs to be born in mind that the growth stage of the crop at the time of treatment and the PHI are parameters that may influence the residues in the harvested product. The growth rate of eggplants is expected to be higher, leading to a higher dilution of residues compared to tomatoes or peppers. Thus, if the last application is close to harvest, the use of pepper data might be more appropriate, while in the case of earlier applications, depending on the residue decline of the pesticide, the tomato data might be also valid.

### Germany

Subgroup peppers: It is comprehensible from the explanations that the subgroup of peppers should not include okra, roselle or martynia. It remains unclear however, whether intended uses on these crops have to be supported by specific residue trials on these crops or may be extrapolated from other crops.

Subgroup eggplants: It would be desirable to get more detailed information on the trials underlying the new proposal for extrapolation from peppers.

## Kenya

**Comment:** Kenya supports the Recommendations for (sub) group maximum residue levels for fruiting vegetables, other than cucurbits revisited

## 2.10 Preliminary results for probabilistic modelling of acute dietary exposure to evaluate the IESTI equations

### European Union

#### *European Union Competence European Union Vote*

The outcome of the probabilistic modelling of acute dietary exposure only recently became available. The EU welcomes this important milestone in the project on reviewing the currently used IESTI equation, but will need more time to examine the results in more detail. Preliminary comments from the EUMS will be submitted under agenda item 4a in relation to document CX/PR 19/51/3 Add2.

### Germany

No comment (only info point).

### Kenya

**Comment:** Kenya anticipates the full report of the outcome of the probabilistic review in 2019. This will inform the review process for some of the parameters under review in the IESTI equation.