European Union comments for the

CODEX COMMITTEE ON PESTICIDE RESIDUES
44th Session

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Agenda Item 6 a)

Draft and Proposed Draft Maximum Residue Limits for Pesticides in Foods and Feeds at Steps 7 and 4

European Union Competence.

European Union Vote.

The European Union (EU) would like to submit the following comments:

**General comment:** The EU does not accept those MRLs that are derived by applying the proportionality approach for crops which are considered as major crops in the EU. Therefore, the EU opposes the advancement of these MRLs.

**Dichlorvos (025):**

The EU makes a reservation for the ADI and ARfD recommended by JMPR because of a methodological disagreement about the use of human studies.

At EU level, only tentative toxicological reference values have been derived for dichlorvos, as the toxicological data package was considered insufficient to address the genotoxic and carcinogenic potential of dichlorvos.

**Acephate (095) / methamidophos (100):**

The EU makes a reservation for the MRL for rice recommended by JMPR because of a methodological disagreement about the use of human studies for deriving the ADI and ARfD. The addition of the rice MRL to the other EU MRLs would lead to exceedence of the ADI.

It is noted that the toxicological reference values derived at EU level for acephate are significantly lower (ADI 0.0025 mg/kg bw/d, ARfD 0.005 mg/kg bw) than the values derived by JMPR (ADI 0.03 mg/kg bw/d, ARfD 0.1 mg/kg bw). Although these values are not formally adopted, they are to be used for EU risk assessments. JMPR derived the toxicological reference values from human studies. This approach is not acceptable in the EU.

Also for methamidophos lower toxicological reference values have been established at EU level (ADI 0.001 mg/kg bw/d, ARfD 0.003 mg/kg bw) compared with the JMPR values (ADI 0.004 mg/kg bw/d, ARfD 0.01 mg/kg bw). The agreed EU values are to be used for the consumer risk assessment at EU level and for the calculation of the toxicological equivalence factor.

In the long-term intake calculation based on the EU ADI values for acephate and methamidophos, the CXL proposal for rice was identified as a minor contributor to the overall chronic intake. However, before the proposed CXL for rice is taken over in the EU legislation, the existing EU MRLs for
acephate and methamidophos need to be subject to a comprehensive MRL review to ensure that the European population will not be exposed to residues which might cause a chronic health risk.

**Cypermethrin (118):**

The EU agrees with the proposed MRLs although for tea a lower CXL of 10 mg/kg would be sufficient. Before the proposed CXL for asparagus and tea are taken over in the EU legislation, the existing EU MRLs for cypermethrin need to be subject to a comprehensive MRL review which will be undertaken in the near future to ensure that the European population will not be exposed to residues which might cause a chronic health risk.

**Diflubenzuron (130):**

In the EU the evaluation of diflubenzuron is ongoing. It is very likely that the outcome of the evaluation is that certain metabolites will be classified as carcinogenic and/or genotoxic. Because of this general reservation, the EU proposes to move the draft MRLs not beyond step 7. The EU will submit a concern form within a month after CCPR 44.

In addition to the general reservation, the EU has specific reservations for the proposals for peaches, plums and peppers. The proposed CXL for peanuts seems too high and a lower CXL of 0.08 mg/kg is proposed.

At EU level certain metabolites and/or degradation products formed in processed products and in livestock or which were taken up via soil were considered as being of toxicological relevance (2,6-diflubenzonic acid (for mushrooms only), 4-chlorophenylurea, 4-chloraniline and 4-chloracetanilide) and were therefore included in the provisional residue definitions. For the EU peer review the final toxicological evaluation of 4-chlorophenylurea (CPU) and 4-chloraniline (PCA) is still pending. PCA is currently considered as a genotoxic carcinogen. PCA has a legal classification as Carcinogen Cat 2 (R45 May cause cancer) according to Directive 67/548/EEC (Annex I, Adaptation to the Technical Progress 24). For the metabolite 4-chlorophenylurea, an assessment of its toxicological relevance was provided but data not were sufficient to derive reference values or to conclude that the reference values of the parent are also applicable.

In the framework of the pesticide and biocide evaluation, metabolism studies in pigs, goat and hens have been provided. From these studies it cannot be excluded that PCA is formed. Thus, the formation of PCA in humans cannot be excluded.

The JMPR residue definition was derived on studies on maize, soybean, cabbage, apple, orange, mushroom, beans, lima beans, rice, wheat and cotton (different modes of application of the radio labelled active substance). However, studies assessing the nature of residues in processed commodities were not assessed by JMPR. The degradation of parent into DFBA and CPU/PCA is expected and should therefore be taken into account in the risk assessment.

**Peaches and plums:** The CXL proposal for peaches and plums is based on 3 trials on plums and 5 trials on peaches. At EU level the merging of data from plums and peaches is not acceptable. The number of trials on plums and peaches is not robust enough to derive individual MRL proposals for these crops. Thus, 3 additional trials in peaches or apricots and 5 additional trials in plums would be required.

**Peppers:** The CXL proposal for peppers is based on 6 trials. The number of trials is not sufficient to derive a robust MRL.

For **peanuts** nine residue trials were provided. Using the OECD calculator a CXL proposal of 0.08 mg/kg is derived. The JMPR proposal of 0.15 mg/kg seems therefore too high.
The potential formation of metabolites/degradation products during processing should be assessed by JMPR. In particular formation of DFBA and CPU/PCA and consumer exposure to these substances need to be considered.

**Tolylfluanid (162)**

All current CXLs can be revoked as these are based on EU uses which have been withdrawn in 2010.

**Hexythiazox (176):**

The EU makes a reservation on all MRLs for commodities that are consumed after processing (tea, hops and several commodities for which there are existing CXLs) until the toxicological profile of metabolite PT-1-3 is elucidated and the behaviour of metabolites during processing is investigated.

In the EU this substance is being evaluated and preliminary information shows that metabolite PT-1-3 has a higher acute toxicity than the parent compound. Additional toxicological information may elucidate the toxicological profile of the metabolite. Based on the outcome of the evaluation the EU may request the JMPR to review the toxicology of this substance. Since this metabolite is included in the residue definition derived by JMPR, the EU would have expected JMPR to perform a hazard characterisation for this metabolite

**Strawberry: The EU opposes the advancement of this MRL.** The MRL proposal was derived by applying the proportionality approach which is not acceptable for major crops (strawberries is a seasonal crop and is major in short/medium term consumption).

Tea: The EU received information from India about a GAP with a PHI of 5 days, while in the JMPR report a 0-day PHI is mentioned. The EU would like to be clarified what the correct GAP is.

**Bifenthrin (178, step 7)**

The EU proposes to withdraw the MRL proposal at step 4 for strawberry now. JMPR confirms that it is not safe and that there are no alternative GAPs.

**Etofenprox (184):**

The EU requests that the metabolite α-CO be included in the residue definition for plants because of its toxicological profile and its high occurrence in the residue trials, before the MRLs are moved to the next step.

In all metabolism studies except in rice the metabolite α-CO was below 10% of the TRR. However, since this metabolite was found in residue trials in higher concentrations than expected from metabolism studies, it should be included in the residue definition for plant commodities.

**Grapes:** The EU opposes the advancement of the MRL. The MRL was derived by applying the proportionality approach. This approach is not acceptable for major crops.

**Tebuconazole (189):**

The EU requests that conjugates of tebuconazole and hydroxy-tebuconazole be included in the residue definition for animal commodities, before the MRLs are moved to the next step, since these conjugates occur in significant concentrations and since the hydrolysis of these conjugates in the human intestinal tract cannot be excluded. It should be clarified whether these metabolites were considered in the livestock feeding studies considered by JMPR.
Because of acute intake concerns the EU opposes the advancement of draft CXLs on table grapes (1004%, VF 5), peaches (198%; includes nectarines at EU level), apples (163%), pears (152%), peppers (130%), cherries (126%) and apricots (103%) and therefore, the EU has submitted a concern form (as attached).

**Pyraclostrobin (210):**

The EU objects to the extrapolation from orange to the whole group of citrus because of the difference in GAP and proposes to fix an MRL of 2 mg/kg for orange only and 1.5 mg/kg for the other citrus crops. This applies also to the extrapolation in the oilseeds (except peanuts) because of the different GAP for cotton seed for which an MRL of 0.2 mg/kg is more appropriate. For papaya the residue trials would justify a lower MRL of 0.07 mg/kg. The draft MRL for tree nuts should apply to all tree nuts except pistachios.

It is noted that pyraclostrobin was considered to be **fat soluble** when it was assessed by JMPR in 2004 whereas in document CX/PR 12/44/5 it is classified as not fat soluble. This needs to be corrected.

**Citrus:** The proposed group MRL is based on 8 trials on oranges reflecting the Spanish GAP for oranges which was extrapolated to the whole group. According to the EU guidance document this extrapolation would not be acceptable, because the GAP on oranges is not identical with the GAPs for the other citrus crops and because the number of trials is not sufficient to support the extrapolation. Thus, for the Spanish GAP on oranges (4 x 0.225 kg a.s./ha; PHI 7 days) sufficient data would be available to derive the MRL value of 2 mg/kg for oranges. For other citrus, except oranges a MRL of 1.5 mg/kg would be derived from the combined dataset of oranges (13), grapefruit (6) and lemons (5) compliant with the GAP for citrus fruits (3 x 0.225 kg a.s./ha; PHI 0 days). This extrapolation would be in line with the extrapolation rules discussed last year in CCPR.

**Oil seed, except peanuts:** The proposed group MRL is based on the results of residue trials on sunflowers which were extrapolated to the whole group (except peanuts). For cotton seeds, this extrapolation is not acceptable since the GAP is not comparable. Sufficient data would be available to derive a lower MRL value of 0.2 mg/kg for cotton seeds.

**Papaya:** The residue trials justify a lower MRL of 0.07 mg/kg (7*<0.05 mg/kg, 0.06 mg/kg).

**Tree nuts:** It is noted that JMPR recommended maintaining the CXL of 1 mg/kg for pistachios (see JMPR report p. 220). Thus, an editorial change is required for the description of the commodity (tree nuts (except pistachios)).

**Spirotetramat (234):**

The EU proposes to set the MRL for edible offal (mammalian) at 0.7 mg/kg (based on the trial data) and to set the LOQ for milk at 0.005 mg/kg (based on validated methods).

**Edible offal (mammalian):** The highest residue resulting from the calculated maximum dietary burden is 0.55 mg/kg (cattle kidney). Thus, 0.7 mg/kg would be a sufficient CXL for edible offal (mammalian)

**Milk:** Validated analytical methods are available for an LOQ of 0.005 mg/kg. Since in the feeding studies at the expected dietary burden residues were below the LOQ of 0.005 mg/kg, the CXL should be set at this level.
**Clothianidin (238, step 7)**
The EU opposes advancement of the draft MRL of 0.2 mg/kg for the whole group of root and tuber vegetables, because the performed extrapolations were on crops with widely differing GAPs and application methods.

The EU agrees with the JMPR 2011 recommendation not to include the Z-isomers in the residue definitions for enforcement and risk assessment purposes for plant and animal commodities. This has no impact on the recommendations and risk assessment made by the 2010 JMPR.

The EU reservation regarding the advancement of the CXL proposal for root and tuber vegetables expressed in the 43rd CCPR is still valid for the following reason (EU position paper 43rd CCPR):

“Root and tuber vegetables (including sugar beet roots): GAPs were reported for carrots, potatoes, radishes and sugar beet (in addition, GAPs for clothianidin were reported for carrots, chicory roots, tuberous and corm vegetable and sugar beet, but they were less critical than the use of thiametoxam.)

The GAPs were not comparable: seed treatment for sugar beets, foliar application for the other crops, different application rate for carrots and radishes compared with potatoes “

The EU had no reservations to the advancement/adoptions of the other clothianidin draft MRLs that are now again presented to CCPR 44, i.e. for banana, dried grapes, edible offal (mammalian) (except liver), eggs, grapes, mammalian fats (except milk fats), meat (from mammals other than marine mammals), milks, pome fruits, poultry fats, poultry meat, rice, sorghum, sorghum straw and fodder (dry), stalk and stem vegetables (except artichoke and celery), sugar cane and sweet corn.

**Dicamba (240):**

The MRL for soybeans was derived by applying the proportionality approach. The EU does not accept this approach in the case of a herbicide use on a major crop and therefore opposes the advancement of this MRL.

Clarifications should be provided by JMPR whether the residue trials and the metabolism studies were performed on genetically modified soybeans (dicamba tolerant soybeans) or on conventional crops. The inclusion of the conjugates in the residue definitions for estimating the dietary intake and for enforcement (plants and animal commodities) should be considered.

**Etoxazole (241):**

The EU considers that a slightly lower MRL for pome fruit of 0.05 mg/kg would be sufficient.

**Acetamiprid (246):**

The residue definitions reported in the circular letter and in CX/PR 12/44/5 are not correct and conflicting with the residue definition reported in the JMPR report.¹

The EU makes a reservation for the MRL for spring onions and plums because the number of trials is not sufficient to derive a reliable CXL.

Using the EU methodology a potential acute consumer health risk is identified for scarole (leafy vegetables except spinach). The EU opposes the advancement of the MRL and will submit a concern form.

¹ (“Definition of the residue (for compliance with the MRL for plant commodities and for estimation of dietary intake for plant and animal commodities): acetamiprid.
Definition of the residue (for compliance with the MRL for animal commodities and for estimation of dietary intake for plant and animal commodities): sum of acetamiprid and N-desmethyl-acetamiprid, expressed as acetamiprid.”)

The EU requests JMPR to include EU trials on orange (HR=0.83) and raise the proposed MRL to 1 mg/kg.

Emamectin benzoate (247):

It is noted that the residue definition reported in the CL and in CX/PR 12/44/5 is conflicting with the residue definition reported in the JMPR report (emamectin B1a benzoate). Regarding the EU residue definition for risk assessment (for plant commodities) evaluations are still ongoing whether the avermectin-like metabolites need to be included.

The EU considers that for aubergines a lower CXL of 0.01 mg/kg would be sufficient (based on trials on normal sized tomatoes and not from cherry tomatoes).

Flutriafol (248):

Grapes: The EU opposes the advancement of the MRL. The MRL was derived by applying the proportionality approach. This approach is not acceptable for major crops.

Isopyrazam (249):

The EU evaluation concluded on a lower ADI and ARfD compared to the JMPR assessment (EU ARfD is based on the maternal NOAEL of 20 mg/kg bw/day for reduced maternal body weight observed during the first days of dosing in the developmental toxicity study in rat; the EU ADI was derived from the same study, but the LOAEL was defined differently. Since no NOAEL was identified, a higher SF was applied). Thus, the ADI and the ARfD were set at EU level is 0.03 mg/kg bw/d and 0.2 mg/kg bw.

Regarding the residue definition for risk assessment derived by JMPR clarifications should be provided to explain if the CXCD459489 (hydroxyl-isopyrazam anti isomer) is included.

The EU proposes that the MRLs are not advanced until these issues are clarified.

Propylene oxide (250):

The JMPR database consists mainly of published papers, often with limited levels of detail and no statements of compliance with good laboratory practice. Pending the availability of the detailed evaluation including the confirmation of GLP compliance of the studies, the acceptability of the ADI and the ARfD cannot be concluded. EFSA shares the view of JMPR that for propylene chlorohydrin and propylene bromohydrin a full toxicological evaluation needs to be made. It is also noted that according to EU CLP (classification, labelling and packaging) Regulation (EC) No. 1272/2008 propylene oxide is classified for its mutagenic and carcinogenic properties:

- Muta. 1B H340: May cause genetic defects
- Carc. 1B H350: May cause cancer

The EU considers the very brief summary presented in the JMPR report does not permit an opinion regarding the proposed residue definitions. The submitted metabolism data for plants and animals might be insufficient for a sound conclusion. Data in rats alone are usually not considered sufficient to conclude on livestock metabolism.

Sulfoxaflor (252):

JMPR decided on a ADI value of 0.05 mg/kg bw/day based on liver effects in the female rat at a dose of 750 ppm in the 2 year rat study although the same non-neoplastic liver effects were seen at a lower dose (500 ppm) in the males, often with greater severity. The EU toxicological evaluation is still
ongoing. The EU proposed ADI is 0.04 mg/kg bw, based on a NOAEL of 4.24 mg/kg bw/day (100 ppm) in male rats in a 2 year carcinogenicity study and application of a safety factor of 100. The EU is of the opinion that a value of 0.25 mg/kg bw per day for the ARfD is more appropriate than rounding to 0.3 as done by JMPR. This is based on a NOAEL of 25 mg/kg/day derived from an acute neurotoxic study on rats and an application of a 100-fold safety factor. Therefore, the EU reserves its position on the toxicological endpoints.

CXL proposals were made as part of the CCPR Pilot project and are not based on official GAPs - (Pilot project in which JMPR conducted an independent and parallel review along with a joint review team from Australia, Canada and the USA and recommended MRLs before national governments or other regional registration authorities). It needs to be discussed whether the global dataset method is acceptable.

Regarding the dietary risk assessment, no acute intake concern was identified when the highest residue values for the crops for which a CXL is proposed were taken into consideration using the EFSA PRIMo Model (max. IESTI: 84.5% ARfD, scarole broad-leaf). However, when using the preliminary EU ARfD (0.25 mg/kg bw, vf 5) the exposure related to residues on scarole exceeds the ARfD (101.4% of the ARfD). The EU has also a reservation for extrapolation from six spinach trials to the whole leafy vegetable group (VL 0053) and insists on setting separate CXLs for the individual crops in this group. It is this leafy vegetable CXL that leads to the intake concern on the earlier mentioned scarole.

The EU opposes the advancement of the draft MRLs beyond step 4 until the completion of the global joint review and reconsiders these MRLs as soon as the reports from the Global Joint review Chemical were available.