3. RESPONSES TO SPECIFIC CONCERNS RAISED BY THE CODEX COMMITTEE ON PESTICIDE RESIDUES (CCPR)

The Meeting noted that the information supplied on some of the concern forms submitted by CCPR Members was inadequate to permit JMPR to clearly identify the critical issues underlying the concerns. Consequently, the Meeting had great difficulty in determining the issues involved, raising the possibility that the response provided by the Meeting might not actually address the true concern. The Meeting requested that any future concerns submitted to JMPR should be accompanied by comprehensive and transparent supporting information. If such information is not provided, the Meeting might be forced to conclude that it is not able to provide a meaningful response.

3.1 BIFENTHRIN (178)

Background

At the Forty-second Session of the Codex Committee on Pesticide Residues (CCPR), concern was raised by the European Union, France and CropLife International regarding the acute reference dose (ARfD) for bifenthrin established by the Joint FAO/WHO Meeting on Pesticide Residues (JMPR) in 2009. A concern form was submitted to the JMPR Secretariat by Kenya on 15 September 2010.

Comments by JMPR

The concern form was submitted long after the deadline established by CCPR and only a few days before the start of the JMPR meeting. Nevertheless, JMPR considered the concern and the points raised. However, the information provided in the concern form was very limited, and the short time available did not allow a thorough consideration of the concerns raised. The Meeting therefore decided to defer consideration of this item to the next meeting.

3.2 CYPERMETHRIN (118)

Background

On the request of Forty-second Session of the CCPR (ALINORM 10/33/24, para 43-44), the EU submitted a concern form to the present Meeting. The concern form stated that using the CXL MRLs on plant and animal commodities as inputs in the EFSA PRIMo rev. 2A, a chronic dietary intake concern was identified with up to 176 % of the ADI (NL child) as well as acute intake concerns with regards to the following crops: citrus (Oranges: 479% ARfD-VF = 5; Grapefruit: 446% ARfD-VF = 5; Mandarins: 209% ARfD-VF = 5; Lemons: 127% ARfD-VF=5), scarole (broad- leaf endive) (153% ARfD-VF=5)-covered by leafy vegetables, apples (126% ARfD-VF = 5), pears (114% ARfD-VF = 5)-covered by pome fruits, apricots (123% ARfD-VF = 5), plums (133% ARfD-VF = 5), peaches (217% ARfD-VF = 5)-covered by stone fruits, cauliflower (165% ARfD-VF = 5) and broccoli (104% ARfD-VF = 5)-covered by brassica vegetables.

The EU requested revocation of these Codex MRLs.

Evaluation of cypermethrin(s) by the JMPR and CCPR

Cypermethrin, alpha-cypermethrin and zeta-cypermethrin (pyrethroid compounds), are non-systemic broad spectrum insecticides acting by ingestion and contact. Cypermethrin was first evaluated by the 1979 JMPR and a number of times subsequently. It was reviewed for toxicology by the 2006 JMPR within the periodic review programme of the CCPR; the review included alpha-cypermethrin and zeta-cypermethrin, which had not previously been considered by the JMPR. A group ADI of 0–

0.02 mg/kg bw and a group ARfD of 0.04 mg/kg bw was established for cypermethrins (including alpha- and zeta-cypermethrin). The periodic review for residues was scheduled for 2008. Three manufacturers submitted residue data to JMPR on cypermethrins (including alpha and zeta cypermethrin) for consideration by the 2008 JMPR. The 2008 Meeting agreed that metabolism studies, environmental fate studies, methods of analysis and freezer storage stability studies of the cypermethrins were mutually supportive and should be considered together. Separate monographs were prepared for each of the three compounds, but they were considered together in a single appraisal. Definition of the residue (for plants and animals; for compliance with the MRL and for estimation of dietary intake)*: cypermethrin (sum of isomers).* The residue is fat soluble. The 2008 Meeting estimated a large number of maximum residue levels. In 2009, an additional evaluation was performed on the use of cypermethrin as grain protectant.

The Forty-first Session of CCPR in 2009 decided to advance the draft MRLs for all commodities (as proposed by 2009 JMPR) except asparagus for adoption at Step 5/8, noting the EU and Norway reservations on the MRLs for cauliflower; scarole (broad-leaf); apple (covered by pome fruits) and peach (covered by stone fruits) because of their acute intake concerns (ALINORM 09/32/24, para 90–94). Later in 2009, the CAC adopted all draft MRLs at step 5/8 as CXLs.

The Forty-second Session of CCPR invited the EU to submit a concern form clearly outlining their acute intake concerns. (ALINORM 10/33/24, para 43–44).

Comments by JMPR

The Meeting noted that for the long-term intake, it is unrealistic to assume that person will for his whole lifetime consume commodities with on all of them the pesticide present at the level of the CXL. Using the STMRs in the IEDI calculation revealed no exceedance of the ADI.

In addition the Meeting noted that also for the short-term dietary intake calculations the CXL values were used, not the HR values for the edible portion. For example, the intake of the residue from citrus fruits is largely overestimated when the calculation is based on the residue in whole fruit. In addition, a variability factor of 5 was used where JMPR employs a variability factor of 3.

Based on the above, the present Meeting confirmed that the short-term dietary intake of cypermethrin(s) from its use on citrus, scarole, apples, pears, apricots, plums, peaches, cauliflower and broccoli, as based on the results presented by the 2009 Meeting, is unlikely to present a public health concern.

3.3 FLUOPICOLIDE (235)

Background

At the Forty-second Session of the CCPR, the Delegation of Switzerland raised concerns regarding the acute reference dose (ARfD) for fluopicolide that had been established by the Joint FAO/WHO Meeting on Pesticide Residues (JMPR) in 2009. The JMPR was requested to reconsider the derivation of the ARfD for fluopicolide.

Evaluation of fluopicolide by the JMPR

Fluopicolide was reviewed for the first time by the JMPR in 2009 at the request of the CCPR. The JMPR established an ARfD for fluopicolide of 0.6 mg/kg body weight (bw) for women of child-bearing age on the basis of a no-observed-adverse-effect level (NOAEL) of 60 mg/kg bw per day to which a safety factor of 100 was applied. This NOAEL was identified based on a marginally increased incidence of skeletal defects of the vertebrae and sternebrae, which might be attributable to a single exposure to fluopicolide at 700 mg/kg bw per day in a study of developmental toxicity in rats.

The Meeting concluded that the establishment of an ARfD for the general population was not necessary for fluopicolide on the basis of its low acute toxicity, the lack of evidence for any acute neurotoxicity and the absence of any other toxicologically relevant effect that might be attributable to a single dose.

Concern submitted by Switzerland

The JMPR was requested to reconsider the rabbit developmental studies as an alternative basis for the derivation of the ARfD for fluopicolide:

> In the rabbit range-finding (4 animals per group) and the definitive developmental toxicity study (23 animals per group), 60 mg/kg bw per day, the level of the rat maternal and fetal NOAEL, proved to be lethal for 3/23 dams within three weeks of treatment and for 3/4 dams at 100 mg/kg bw per day (and 4/4 dams at higher doses). Additionally, 15/23 dams aborted at 60 mg/kg bw per day, one dam at the next lower dose level of 20 mg/kg bw per day, and none at 5 mg/kg bw per day and in the control group, respectively. The high incidence of abortions at 60 mg/kg bw per day are treatment-related and the abortion seen in one dam at a dose level only three fold lower should not be ignored as this might also be treatment related. Mortality and abortions could be seen as either an acute effect or as the final severe manifestation of not yet evident effects accumulating in the study period before.
>
> In view of the severe effects at 60 mg/kg bw per day, possibly being an acute effect or a final manifestation of sub-clinical effects accumulating in the study period before, the identification of the relevant NOAEL as the basis for an ARfD should be reconsidered as well as the relevance of these effects for the general population.

Switzerland proposed the use of 20 mg/kg bw per day as the basis for an ARfD with application of a safety factor of 200.

Comments by the JMPR

After consideration of the concerns from Switzerland and after reviewing the conclusions of the 2009 JMPR, which included a reassessment of the original report from the rabbit range-finding study and the main developmental study in rabbits, the present Meeting highlighted the following points:

- In the rabbit range-finding study (four animals per group), dosing was on days 6–28 of gestation. All rabbits from the 100, 250, 500 and 1000 mg/kg bw per day dose groups were found dead, killed while in a moribund condition or killed after abortion from day 13 to day 23 of the study. The dose of 100 mg/kg bw per day was lethal after at least 10 days of dosing for four of four dams (days 16, 20, 22, 22). Nonspecific symptoms, including impaired motility and consciousness, respiratory sounds, decreased defecation and hay consumption, hyperactivity, hypoactivity and discoloured urine, were observed from day 13 to day 23 of the study. At 50 mg/kg bw per day, one of four dams showed decreased defecation and discoloured tray and aborted on day 29. Therefore, it was killed on day 29. The other animals at this dose did not show any clinical signs. The dose of 50 mg/kg bw per day was considered to be a suitable high dose for the main study.
- In the main study, dosing was on days 6–28 of gestation (0, 5, 20 and 60 mg/kg bw per day). At 60 mg/kg bw per day, 15 of 23 dams aborted from days 22 to 29; 1 dam at the next lower dose level of 20 mg/kg bw per day was killed after premature delivery on day 28.
- The high incidence of abortions at 60 mg/kg bw per day was treatment related, and the abortion seen in one dam at a dose level only 3-fold lower might also be treatment related. However, mortality and abortions cannot be seen as an acute effect. The affected animals showed decreased defecation, reduced hay consumption, hypoactivity, bristling coat, pultaceous faeces and discoloured urine between days 22 and 29. This is considered as a manifestation of subchronic effects. The mean food consumption in the 60 mg/kg bw per day group, expressed as a percentage of food consumption per unit body weight before treatment,

was statistically significantly decreased between days 23–26 and days 26–29 and not immediately after treatment began on day 6 of gestation. This decrease was only slight in the first week but prominent thereafter. With an obvious delay, the body weights in the 60 mg/kg bw per day group were also lower between days 26 and 29. No teratogenic effects were observed in the fetuses.

- Because the severe effects at 60 mg/kg bw per day occurred in the latter part of the treatment period, they are considered a manifestation of the subchronic effects of the prior dosing period. The NOAEL for these findings is not a relevant basis for an ARfD.

In conclusion, the JMPR does not agree with the proposal to use the effects observed in the developmental study in the rabbit at 20 mg/kg bw per day as the basis for an ARfD. The Meeting reaffirmed the ARfD for fluopicolide of 0.6 mg/kg bw for women of child-bearing age based on a NOAEL of 60 mg/kg bw per day and a safety factor of 100.

3.4 PARAQUAT (057)

Background

On the request of the Forty-second Session of the CCPR (ALINORM 10/33/24, para 33–34), the EU submitted a concern form to the present Meeting. The concern form stated that using EU endpoints (ARfD 0.005 mg/kg bw/day) and risk assessment methodologies (PRIMo rev2) for children, dried beans are 150% and potatoes are 154% of the ARfD, using HR values of 0.41 mg/kg (39 trials) and 0.05 mg/kg (25 trials) for pulses and root and tuber vegetables, respectively. It was acknowledged that a higher ARfD of 0.006 mg/kg bw/day is accepted by JMPR, but indicated that EU risk assessment methodologies using these endpoints still indicate 125% and 128% of the ARfD using the JMPR HR values.

Evaluation of paraquat by the JMPR and CCPR

Paraquat, a non-selective contact herbicide, is usually available as the dichloride salt or the bis(methylsulfate) salt but is determined as paraquat ion in analysis. It can be used for pre-plant and pre-emergence weed control, resulting in little or no residues in the harvested crop, but also for post-emergence weed control and as a harvest aid desiccant. When used for pre-plant and pre-emergence weed control, paraquat is not sprayed directly onto crops and is strongly adsorbed to soil.

Paraquat was first evaluated by the JMPR for toxicology and residues in 1970. The Meeting reviewed paraquat toxicologically within the Periodic Review Programme in 2003 and established an ADI of 0–0.005 mg/kg bw and an ARfD of 0.006 mg/kg bw as paraquat cation. The 2004 JMPR evaluated paraquat for residues under the Periodic Review Programme and concluded that the definition of residue for compliance with MRLs and for estimation of dietary intake was paraquat cation. Maximum residue levels were recommended for several fruits, several vegetables, maize, sorghum, cotton-seed, sunflower, hops, tea and animal commodities. In addition, the 2009 JMPR estimated a maximum residue level for rice.

The Thirty-seventh Session of CCPR in 2005 decided to advance all MRLs as proposed by the 2004 JMPR to Step 5. The Committee decided to consider for withdrawal at its next Session all existing CXLs (ALINORM 05/28/24, para 99–100).

The Thirty-eighth Session of CCPR in 2006 decided to revoke most existing CXLs as recommended by the 2004 JMPR (except the CXL for rice, because new data would become available). The Committee decided to advance all draft MRLs except those for animal forage to Step 8 (ALINORM 06/29/24, para 67-68). Later in 2006, the CAC adopted all draft MRLs at step 8 as CXLs.

The Forty-second Session of CCPR in 2010, when considering a new maximum residue level on rice, as proposed by the 2009 JMPR, noted the acute dietary intake concern of the EU for pulses and potatoes, and invited the EU to submit a concern form clearly outlining their concern (ALINORM 10/33/24, para 33–34).

Comments by JMPR

The Meeting noted that the current CXLs are generally in the range of 0.01(*) to 0.05 mg/kg, except for animal feed commodities and oil seeds. However, a CXL for pulses (VD 0070) of 0.5 mg/kg is in place. For Root and tuber vegetables (VR 0075; includes potatoes) the CXL is 0.05 mg/kg. Currently, all EU MRLs are set at the LOQ (either 0.02 mg/kg or 0.05 mg/kg).

The 2004 JMPR reported that the levels of residues arising from the use of paraquat as a harvest desiccant on legume vegetables and pulses were higher than those from pre-emergence or post-emergence application. The 2004 Meeting combined the results of trials on field peas and chick peas in Australia and on soya beans in Brazil and the USA in which paraquat was used as a desiccant harvest aid to estimate a group maximum residue level for pulses. The combined residue levels in seeds, in ranked order, were: < 0.01 (2), < 0.02, 0.02 (4), 0.03 (4), 0.04 (2), < 0.05 (2), 0.05 (2), 0.06, 0.07 (2), 0.08 (3), 0.09 (2), 0.10, 0.11 (2), 0.12, 0.13 (2), 0.15, 0.16 (2), 0.23, 0.25, 0.28 (3), 0.31 and 0.41 mg/kg.

The present Meeting noted that the EU dietary intake calculations for beans employed the IESTI equation case 1 (based on the HR value and no variability factor). The 2004 JMPR employed case 3, which is based on the STMR value (also with no variability factor). Case 3 is used where processed commodities are bulked or blended so that the STMR-P represents the likely highest residue level. The case 1 equation would only apply to pulse commodities when the estimates are based on post-harvest use of the pesticide. The Meeting noted that pre-harvest desiccant use can not be considered a post-harvest use. A post-harvest use is defined as a use where harvested commodities from different farms are combined and treated as one, resulting in a batch or lot containing the same residue and marketed to the same location. In a pre-harvest use crops from different farms that are treated differently can be combined, thereby averaging out a possible high residue coming from one of the farms.

The use patterns of paraquat on root and tuber vegetables as considered by the 2004 JMPR concerned pre-plant, pre-emergence treatments in Japan and the USA. Since paraquat binds strongly to soil, limited uptake by the roots and tubers is expected. This is in line with the residue levels in potato trials of pre and post-emergence application: < 0.01 (8) and 0.02 mg/kg. The Meeting noted that the combined results from trials on beetroot, sugar-beet, carrot, turnip and potato on which the 2004 JMPR recommendations were based were, in ranked order: < 0.01 (12), 0.02, < 0.03 (4), 0.03 (2) and < 0.05 (6) mg/kg. The HR for the group of Root and tuber vegetables (including potatoes) is therefore based on the highest LOQ of 0.05 mg/kg as reported for six trials on sugar-beet root. The actual HR for potatoes is probably lower, as the highest residue found in potato trials was 0.02 mg/kg. Furthermore, the dietary risk assessments are based on the consumption of raw potatoes. Processing information for potato, as reported by the 2004 JMPR, shows that most of the residue is in/on the peel (PF for peeled potato is 0.27). Furthermore, the EU dietary intake model employed a variability factor of 7 in the IESTI calculation, whereas the JMPR dietary intake model employs a variability factor of 3.

Based on the above, the present Meeting confirmed that the short-term dietary intake of paraquat from its use on pulses and potato, based on the results presented by the 2004 Meeting, is unlikely to present a public health concern.