

codex alimentarius commission



FOOD AND AGRICULTURE
ORGANIZATION
OF THE UNITED NATIONS

WORLD
HEALTH
ORGANIZATION



JOINT OFFICE: Viale delle Terme di Caracalla 00100 ROME Tel: 39 06 57051 www.codexalimentarius.net Email: codex@fao.org Facsimile: 39 06 5705 4593

Agenda Item 6(b)

CX/PR 01/8
March 2001

JOINT FAO/WHO FOOD STANDARDS PROGRAMME

CODEX COMMITTEE ON PESTICIDE RESIDUES

Thirty-third Session
The Hague, The Netherlands, 2-7 April 2001

APPROPRIATENESS OF THE CURRENT ADI AND MRL SETTING IN RELATION TO INFANTS AND CHILDREN

Prepared by the Netherlands

INTRODUCTION

1. The 32nd CCPR considered CX/PR 00/9, in which the feasibility of establishing specific MRLs for cereal-based infant foods and infant formulae was discussed, in relation to a request from the CCNFSDU (ALINORM 99/26, para 74). The CCPR concluded that the establishment of MRLs for these processed products was not feasible at this time, in relation to the complex methodology which would have to be developed, and to questions regarding the scientific basis for establishing Codex MRLs derived in such a way. It was noted that the EC had established a common limit of 0.01 mg/kg for all pesticides for ready-to-eat foods for infants and children as a temporary precautionary measure, pending further toxicological evaluations of the substances. The CCPR however could not reach consensus at this time on the establishment of a generic common limit (e.g. at the limit of determination) for these products. The option of two MRLs for a raw commodity, one for adults and another for infants and children, which was mentioned in CX/PR 00/9 as a subject for discussion, was not supported.
2. The Committee decided to request JMPR, in its evaluation of specific pesticides, to explicitly comment on the adequacy of the database for assessing risks for infants and children. Recognizing the need to consider the question of cumulative intake in cases of common mechanism of action of different pesticides, the CCPR agreed to ask JMPR to comment on the issue when information came available to JMPR.
3. The Committee agreed to invite governments by circular letter to provide information on:
 - National policies regarding the protection of infants and children; and
 - Which compounds were of particular concern; and the rationale, concern and actual problems experienced for each compound.

This information was intended to facilitate establishing a list of pesticides for which special consideration might be needed for the protection of infants and children. Another goal was to determine whether there was a need for an expert consultation, and if there was such a need, identifying specific objectives for consideration by a consultation.

Summary of comments from governments and international organisations

4. The questions indicated above were published in CL 2000/27 - PR, part 3 C. Comments were received from the USA, New Zealand, and from Consumers International. The comments are briefly reviewed here (complete submissions will be available at the meeting in CRD). Some views from the EC, which were not yet received officially, are also mentioned here.

5. The US indicates that it operates according to the Food Quality Protection Act (FQPA), in which it is stated that MRLs should be explicitly determined to provide a reasonable certainty of no harm for children. The FQPA directs evaluators to include an additional 10-fold safety factor (above normally used safety factors which account for intra- and inter-species variability) into risk assessments that compare hazards and exposures to children, unless there are sufficient data on which to conclude that this factor may be reduced. The US EPA has implemented this requirement in its procedures for establishing and reassessing food tolerances in relation to pesticide uses. In addition to the more stringent risk assessment procedures, the toxicological data requirements for some chemicals are increased, to specifically assess functional and structural neurological effects on young animals, for compounds which have been shown to produce neurological effects in adult animals. The EPA will in practice apply the 10-fold safety factor if it lacked complete reliable data to assess pre- or postnatal effects, or if there are indications of those effects. If data are sufficient to demonstrate no potential pre- or postnatal effects of concern, no additional safety factors will be applied. In intermediate cases, an additional safety factor between 3 and 10 would be applied.

A list of compounds which have been or are currently being evaluated by the US EPA, is supplied.

6. New Zealand states that its approach is that national toxicological evaluations leading to the establishment of ADIs are considered sufficient to identify and address any special toxicological effects relating to infants and children. MRLs are only progressed when NEDI calculations, including a specific estimate of dietary risk to children, indicate no dietary intake concerns to a.o. infants and children.

7. The European Community (EC) states that the ADI or ARfD must protect the most sensitive consumer group in the population, which may or may not be young children, and therefore should be based on the most critical endpoint. In 1999 the Commission adopted a temporary default MRL of 0.01 mg/kg, on precautionary basis, for individual pesticide residues in foods for infants and young children. Specific MRLs (higher or lower as appropriate) can be set at a later date when data is sufficient to do so. The EC is preparing draft legislation for highly toxic pesticides (ADIs less than or equal to 0.0005 mg/kg bw) whereby their use would not be permitted in the production of food destined specifically for infants and young children.

These comments are drawn from a preliminary issue of the views of the EC.

8. Consumers International (CI) mentions recently conducted large analyses of pesticide residues in foods by two CI member organisations, based on government monitoring data, in the US and in The Netherlands, respectively. The approach by the Consumers Union of US attributes a Toxicity Index (TI) to pesticide residues in food, based on the acute and chronic toxicity of the chemical, the frequency of the detection of the residue and the average residue level found in positive samples. The highest ranking pesticide residu-commodity combinations are mentioned in a list (Annex I, Table 2 of the CI-contribution).

9. The analysis of the Dutch data (performed by the Consumentenbond, using Dutch monitoring data from the Health inspectorate and with the help of the RIKILT Institute for the Monte Carlo calculation of the exposure) includes the use of Toxicity Equivalence Factors (TEFs) based on the ratio of comparable NOAELs for acetylcholinesterase inhibition for the calculation of cumulative exposure to all cholinesterase inhibiting compounds (organophosphorous pesticides). Chlorpyrifos was used as the index compound. Separate TEFs were calculated for chronic and acute exposure. This approach leads in Monte Carlo calculations to conclusions about cumulative risk for (parts of) the population and can also be used for indicating commodities which contributed most to the total cumulative intake, but cannot easily be translated to individual pesticides causing most of this risk. In the calculation all necessary and available factors, such as detailed individual food consumption figures, conversion factors to translate foods as eaten to primary commodities, processing factors for the residues in question, and residue levels as found in monitoring analyses, were used. In order to obtain indications about the residues in the food commodities that contributed mostly, specific analyses were performed in apple, grapes and spinach. The results regarding the pesticides involved are mentioned in Annex II of the CI-contribution.

10. CI recommends that Codex should seek consensus on an approach to take at the international level, while in the interim encouraging national governments to use some precautionary approach. More specifically, CI recommends that:

- A consensus list is developed of pesticides which are of particular concern to infants and children.
- An expert consultation is held to address risk assessment policy and risk management recommendations for protection of infants and children from pesticide residues. Proposed discussion items include:
 - Criteria regarding the adequacy of the (toxicological) data base
 - Situations where a default limit would be appropriate
 - Guidance on how to apply uncertainty factors
 - Other aspects relating to how JMPR/CCPR procedures should be modified to ensure a reasonable certainty of no harm to infants and children.
- As long as no further guidance is available, a default low common limit or additional safety factor is proposed to be applied to pesticides identified as to pose a particular concern for infants and children.
- After the proposed expert consultation has given guidance, CCPR should request JMPR to give priority review to those pesticides identified to pose a particular concern for infants and children.
- MRLs for pesticides with an effect on the nervous system should not be advanced in the Codex system when the database does not include a developmental neurotoxicity study and existing CXLs for OP-pesticides should be re-evaluated as a priority and deleted when no adequate database is available.
- CCPR should affirm that MRLs should be established at levels that protect infants and children.

Discussion and conclusions

11. The number of contributions was very limited, so conclusions can only be drawn with great care. The issues involved can be separated in various main items, namely toxicology (data base and endpoints like ADI and ARfD), pesticides which deserve priority for further evaluation in relation to risks for infants and children, intake assessment and risk management regarding MRLs and CXLs which are challenged.

Regarding the toxicological database and the use of uncertainty factors

12. The contributions received point to the fact that at least one, possibly more specific additional studies have been required by the US EPA to evaluate the risk of chemicals for infants and children. The JMPR mentions this aspect in its 1999 Report, and mentions that results of these studies will be compared with results of conventional data packages. It seems necessary that an evaluation is performed of the necessity of requiring further studies for a satisfactory evaluation of a data base. Further precise comments are desirable from US EPA and JMPR on this matter. This subject might be an item for discussion in an expert consultation.

13. Related issues, which were addressed by US EPA and also brought forward as a discussion point by CI, such as the situations where a default limit would be appropriate and guidance on how to apply uncertainty factors, also deserve further attention from the JMPR and might also be raised in an expert consultation.

Regarding the toxicological endpoints

14. The contribution from the US makes clear that a different "ADI" for infants and children can be attributed to substances by applying an additional safety factor to the existing ADI (for the general population), at least in risk assessments. The question can be raised if it is intended here that the final evaluation of a satisfactory database will lead to a single ADI covering all population groups, or if the ADI will be allowed to diverge and be different for various population groups. It seems likely that consensus can be reached on the notion that from a risk management point of view ADIs, ARfDs or other toxicological recommended endpoints should be established in such a way that they include all relevant toxicological aspects and all population groups and age groups, and therefore should include the possible sensitivity of infants and children, and thus be valid also for this group. Although the JMPR did not mention this specifically in its 1999 Report when discussing the issue of the sensitivity of infants and children to pesticides, it is assumed that this has been and is also the case for JMPR evaluations. It might be useful to obtain a confirmation or other opinions regarding this issue. Because the issue is related to the previous item, it should also be covered when an expert consultation is planned.

15. Of course the principle of using a single ADI in risk analysis procedures does not mean that acknowledged differences in sensitivity among population groups should not be recorded, used in refined risk assessments and possible also used as argument in borderline risk management decisions. Further guidance might be useful on this issue, when more information is available.

Pesticides which deserve priority regarding evaluation of risks for infants and children

16. The US provided a list of pesticides which have been or are under evaluation for the risks for infants and children. Details about the phase of the evaluation and conclusions are not provided, but can be found on the EPA website.

17. CI provided a list of pesticides for which residues in a number of mentioned commodities are a reason for concern, in their view. This matter is discussed further under the item MRLs and CXLs.

18. The EU mentions concerns regarding pesticides with a very low ADI (equal to or lower than 0.0005 mg/kg bw).

19. The best way to move forward regarding the required list of pesticides which are of concern seems to be to start with the list provided by US EPA. The list can be shortened by scrutinising the details of the US evaluation of the substances and to leave out pesticides which did not need additional safety factors, also those which are still under evaluation, those with additional safety factors which even then do not have significantly lower US ADIs than the corresponding JMPR ADIs, and those that are not on the Codex pesticide list. The list can be extended by adding those pesticides that correspond to the definition of a very low ADI according to the EC. The next step can be to note the reasoning for

the US evaluations and to forward this annotated shortened list to the JMPR, for a first screening discussion and for priority scheduling for full JMPR evaluation at the earliest opportunity.

Risk management of pesticides about which concern has been expressed

20. CI proposes to apply a default low common limit or additional safety factor to pesticides identified as to pose a particular concern for infants and children, as long as no new review by the JMPR is available. No government views were received on this issue, except that the EC is preparing legislation regarding highly toxic pesticides (with a very low ADI), whereby their use would not be permitted in the production of food destined specifically for infants and young children. The matter might be discussed again by the CCPR after a first initial screening of the list as defined in paragraph 14 has been completed by the JMPR and it has become clear when further evaluations by JMPR can be performed. Further important information will be the conclusions of the JMPR regarding the adequacy of the database of recently evaluated pesticides regarding the assessment of risks for infants and children (as required by the 32nd CCPR) and the consequences of these conclusions for the toxicological endpoints. It is suggested that CCPR decisions await this information and initially are made on a case by case basis and that when necessary further views are asked on a general policy regarding this issue.

Intake assessment in relation to infants and children

21. Several responses to the CL mention the different food intake by children, especially when calculated on the basis of their body weight, as compared to adults, but no specific suggestions are given. Although the acute intake assessment by WHO incorporates the intake by children up to 6 year old, there may be room for debate whether this sufficiently covers all age groups. The chronic intake assessment by WHO lacks a specific assessment of the intake of infants and children. The reasons for this are known (lack of sufficient international data), but it should not be ruled out that ways can be found to overcome this problem. Nationally, it is obviously becoming more common that the diet of children is used in chronic risk assessments. The possibilities of making progress also on the international level about this subject in general might benefit from an expert consultation.

Pesticide-commodity combinations which are of concern

22. Only CI specifically mentions a list of such combinations.

23. It seems appropriate to ask JMPR to check if this list indeed can be identified to be of concern in relation to acute intake and where applicable also chronic intake, using available information and methodology. Further refined evaluations can be performed when more specific methodology has been developed.

Risk management of pesticide-commodity combinations about which concern has been expressed

24. CI proposes not to advance MRLs for organophosphorous insecticides and other pesticides known to act on the nervous system, when the database does not include a developmental neurotoxicity study. Existing CXLs should be reevaluated as a priority and deleted where an adequate database is not available.

25. This option can be discussed when the outcome of the primary assessment by JMPR of the list mentioned in paragraph 17 is reported. Obviously also the conclusions mentioned in paragraph 15 have to be taken into account.

26. Suitable risk management and prioritization of further assessments, according to existing CCPR procedures, should be applied. When it has become clear that further risk management guidelines have to be developed, this will have to be considered on the basis of adequate information on the extent of the problem.

Cumulative risk assessment

27. In view of the previous conclusions of the 1998 JMPR about cumulative risk assessment of pesticides, it may be appropriate to ask the opinion of the JMPR on the scientific aspects of the cumulative risk assessment mentioned by CI.

Expert Consultation

28. Only CI proposes an expert consultation in response to CL 200/27 - PR, and mentions specific subjects for discussion. Although no government comments were brought forward on this issue, a number of possible subjects for an expert consultation were identified in this paper. It may be useful to make a distinction between toxicological aspects and intake assessment aspects; because of the rather different expertise necessary for these subjects these could be the subject of different expert consultations. Another reason for separate expert consultations is that also questions in relation to other topics might have to be dealt with by the same group of experts. It is suggested that this matter is discussed again in plenary. It may be wise to await the outcome of the JMPR evaluations proposed on the issues mentioned earlier in this paper, and also probably forthcoming further US experience about this matter, and to decide about the necessity and the agenda of an Expert Consultation next year, when this might mean that better results can be expected.

Recommendations

29. It is recommended that the subject of the possible extra vulnerability of infants and children to pesticides and the acknowledged possibility of higher exposure of infants and children to pesticide residues via food is considered both as an important general risk analysis issue and as a priority aspect in relation to specific decisions and recommendations of the CCPR and in relation to the work schedule of the JMPR. It is necessary that these aspects are also explicitly integrated in the procedures, the methodology, the evaluations and the recommendations of the CCPR and the JMPR.

30. In view of the lack of clarity which seems to exist regarding the applicability of ADIs and the safety of MRLs regarding infants and children it is recommended that it is clearly confirmed that ADIs and MRLs are intended to be valid and safe for all population groups, so also for infants and children, and that possible uncertainties or exceptions are clearly stated, so that appropriate risk management can be considered.

31. Although only limited response was received on CL 2000/27 - PR, it is recommended that the suggestions and information received regarding a list of pesticides of concern and regarding a list of pesticide-commodity combinations of concern are taken up for primary screening of this concern in the light of information available to the JMPR, and that priority is given to full evaluation by the JMPR at the first opportunity of those cases where concerns can not be alleviated.

32. CCPR is encouraged to take appropriate risk management action for those cases where serious concerns regarding the health aspects of infants and children may exist and can not be alleviated.

33. An Expert Consultation on issues of toxicology and intake assessment in relation to infants and children seems warranted and could be helpful in developing further guidance in how to deal with this important but difficult subject. Further information and debate about the optimal planning of this consultation, in relation to evaluations asked from JMPR and information which may be forthcoming from countries may be useful however.