

# codex alimentarius commission



FOOD AND AGRICULTURE  
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**Agenda Item 5(c)**

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## **JOINT FAO/WHO FOOD STANDARDS PROGRAMME**

### **CODEX COMMITTEE ON PESTICIDE RESIDUES**

**Thirty-third Session**

**The Hague, The Netherlands, 2-7 April 2001**

#### **RISK ANALYSIS PRINCIPLES AND METHODOLOGIES SO FAR APPLIED IN THE WORK OF THE CODEX COMMITTEE ON PESTICIDE RESIDUES**

**Prepared by the Chairman**

#### **INTRODUCTION**

1. The Joint FAO/WHO Conference on Food Standards, Chemicals in Food and Food Trade (1991) anticipated the results of the Uruguay Round and asked the Codex Alimentarius to review its procedures to establish Codex standards. The review focussed in particular on the application of risk analysis principles in relation to food safety. These principles had been considered in the course of a number of FAO/WHO Expert Consultations on respectively risk analysis, risk management and risk communication and are now further elaborated by Codex. Definitions on risk analysis and statements of principle relating to the role of food safety risk assessment have been published in the Procedural Manual of the Codex Alimentarius. Some of these principles are not only directed to the Codex Alimentarius but are also of relevance to FAO/WHO Expert bodies like the Joint Meeting on Pesticide Residues (JMPR).
2. The 23rd Session of the Codex Alimentarius Commission (ALINORM 99/37, paras 47-58) considered the principles of risk analysis. The Meeting recommended amongst others that relevant Codex Committees should inform the Commission on progress made in the implementation of risk analysis principles and methodologies in their work and that they also should consider the acute aspects of dietary exposure to chemicals.
3. The 32nd Session of the Codex Committee on Pesticide Residues (CCPR) agreed that the Chairperson, in collaboration with the Codex Secretariat, would prepare a brief paper on risk analysis principles and methodologies so far applied or used in the work of the Committee. It would enable the Committee to report these matters to the 24th Session of the Codex Alimentarius Commission in 2001 (ALINORM 01/24, paras 6-8).

#### **A BRIEF OVERVIEW**

##### ***Chronic Dietary Intake***

3. The CCPR is entrusted with the elaboration of Maximum Residue Limits (MRLs) of pesticide residues in food and feed. Time and again the question has been raised at the CCPR of whether acceptance of Codex MRLs could result in a situation in which the Acceptable Daily Intake (ADI) of a

pesticide would be exceeded. A definitive answer to this question can only be obtained by means of dietary intake studies. In cases where such studies are not feasible - at the international level relevant dietary intake studies are rarely available - or where the pesticide has not long been in use, it is necessary to predict the pesticide residue intake on the basis of available data. Consequently, a best possible estimate of the dietary intake has become part of the MRL setting process.

4. In 1989 the WHO published Guidelines for Predicting Dietary Intake of Pesticide Residues<sup>1</sup>. These Guidelines were developed by an FAO/WHO Consultation held in 1987 in collaboration with the CCPR and are mainly related to the estimation of the chronic dietary intake. The Guidelines follow a tier approach, ranging from a worst-case estimate of the dietary intake (TMDI = Theoretical Maximum Daily Intake) to a more realistic estimate (EDI = Estimated Daily Intake), which can only be performed at the national level. The input for the estimate of the dietary intake is the MRL which is further refined, when going through the tiers, by applying correction factors, for example for the edible portion of the commodity or for changes in the residue level on storage, processing and cooking. For the purpose of predicting pesticide residue intake at the international level, the average food consumption data given in de FAO Food Balance Sheets for five regional diets are used. For intake estimations at the national level national food consumption data are applicable. Finally the estimate of the (chronic) dietary intake then can be compared with the ADI of the pesticide.

5. Since the early 1990s both the CCPR and the JMPR have successfully used these Guidelines. Despite its success, already soon certain disadvantages in the estimation of the dietary intake estimates became apparent at Meetings of the CCPR. Refinement of the intake estimate beyond the TMDI requires data that are not always available at the international level. The CCPR could not reach consensus on how to proceed in cases where the TMDI exceeded the ADI and no further refinement of the intake estimate was possible at the international level. Some Governments wished to make decisions regarding MRLs on TMDI estimates whereas other Governments were of the opinion that this was overly conservative as the TMDI is a gross overestimate of the intake. They stressed the need also to take into consideration national intake estimates.

6. In 1995 a FAO/WHO Consultation was held in York, United Kingdom, aiming at the revision of the aforementioned Guidelines<sup>2</sup>. An important recommendation from this Consultation was to replace the tier approach of the current Guidelines by a system that makes the best use of all available data at the same time resulting in the International Estimated Daily Intake (IEDI) or the National Estimated Daily Intake (NEDI). The TMDI was maintained as a quick screening tool for potential intake concerns. Moreover, the Consultation recommended the use of the Supervised Trial Median Residue (STMR) instead of the MRL as the input for the chronic dietary intake estimate. The STMR value is derived from the same data base on which the MRL is based. The Consultation felt that for chronic intake purposes the STMR is a more accurate figure than the MRL. As toxicological relevant metabolites not necessarily are included in the residue definitions for enforcement, it was also recommended to establish a separate residue definition for intake purposes where relevant.

7. Based on the recommendations of this Consultation the WHO revised the Guidelines for predicting dietary intake of pesticide residues that were published in 1997<sup>3</sup>. Already the 1996 JMPR

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<sup>1</sup> WHO (1989) Guidelines for predicting dietary intake of pesticide residues, prepared by the Joint UNEP/FAO/WHO Food Contamination Monitoring Programme in collaboration with the Codex Committee on Pesticide Residues. WHO, Geneva.

<sup>2</sup> WHO (1995) Recommendations for the revision of the guidelines for predicting dietary intake of pesticide residues. Report of an FAO/WHO Consultation, 2-6 May 1995, York, United Kingdom. WHO, Geneva.

<sup>3</sup> WHO (1997) Guidelines for predicting dietary intake of pesticide residues (revised), prepared by the Global Environment Monitoring System-Food Contamination Monitoring and Assessment Programme (GEMS/FOOD) in collaboration with the Codex Committee on Pesticide Residues. WHO, Geneva.

began to implement the recommendations of the York Consultation and estimated in that year for the first time STMR values. The JMPR continues to recommend MRLs but routinely establishes STMRs for new and periodic review compounds for dietary intake purposes. In cases the intake exceeds the ADI in one or more of the regional diets the JMPR, when recommending MRLs, flags this situation indicating the type of data which may be useful to further refine the dietary intake estimate. For the risk manager, like the CCPR, then the question remains how to proceed in such cases.

8. The 29th Session of the CCPR (1997) considered this question in detail. The Committee was of the opinion that a clear distinction should be made between international and national approaches. CCPR and JMPR, being international organizations, should base their recommendations solely on internationally available data, following international Guidelines and internationally established ADIs. When for a given pesticide the ADI is not exceeded in any of the five regional diets, the MRLs of that pesticide can be advanced to step 8 for adoption by the Commission, even when objected by a Government. The latter flags a situation of non-acceptance of MRLs by a given Government which ultimately may be also of relevance in view of the WTO SPS-Agreement. However, when the ADI is exceeded in one or more regional diets, then the MRLs will not advance to step 8 pending further refinement of the intake at the international level. If further refinement is not possible then the intake concerns become an issue for risk management. In practice it means withdrawal of MRLs (and CXLs) until the remaining MRLs and CXLs no longer give rise to intake concerns. The Meeting decided to work along these lines and to review the procedure within three years.

9. The CCPR was of the opinion that this approach was a reasonable compromise. It is not overly protective or underestimating the risks. On one hand it does not take into account the intake of special subgroups of the population, like infants and children, on the other hand it excludes factors that are usually used at the national level to refine an intake estimate, like monitoring data. A remaining point is the selection of MRLs to be withdrawn when the intake exceeds the ADI. In practice it is generally the data owner, supporting a compound, which will recommend deletion of certain uses that are no longer commercially of interest. However, Members of Codex may have different views based on agricultural considerations.

10. The 32nd Session of the CCPR (2000) started a review of the chronic intake procedure based on the revised Guidelines, focussing in particular on the management decisions to be taken when the intake exceeds the ADI. The Committee was of the opinion that the procedure worked quite well in recent meetings, but that there were still situations where the IEDI exceeds the ADI in one or more regional diets. As national intake calculations for the same compounds usually do not indicate intake concerns it seems that IEDI calculations overestimate the risk for consumers. It suggests, therefore, that there is a gap between what can be done at the international level and national level and that there is a need to improve the science of dietary intake estimates at the international level.

11. The Committee could not reach agreement on proposed alternatives. The Committee decided to maintain the agreed procedure on chronic dietary intake for the time being pending further consideration of the issue at its next Session. It further agreed that it was premature to request an expert consultation on the improvement of chronic dietary risk assessment and that it was necessary to proceed with caution.

### ***Acute Dietary Intake***

12. The CCPR has expressed several times, particularly since the 1990s, the need to pay specific attention to acute dietary intake assessment for those compounds that exert an acute toxicity. The Committee, however, also noted the lack of appropriate methodology both at the international and national level, to estimate the acute dietary intake of pesticide residues.

13. The Codex system has long experience using chronic toxicological endpoints (like the ADI) in assessing the risk of chronic exposure to chemicals but international guidance concerning acute toxicological endpoints, like the acute RfD (reference dose), was limited. Since 1993 the JMPR has developed procedures that led to the establishment of several acute RfDs for pesticides. JMPR has recognized the need to consider what specific data should be provided by data owners to provide a more secure basis for the estimation of acute RfDs. In response to the request of the 30th CCPR, the 1998 JMPR reviewed the principles of establishing acute RfDs and drafted a provisional guidance document on procedures for estimating an acute RfD. Currently, the JMPR routinely establishes acute RfDs where appropriate and indicates cases where an acute RfD is not necessary. The 2000 JMPR further considered guidance on establishing acute RfDs. Being aware of ongoing initiatives on this issue in other international organizations like OECD, JMPR has expressed the wish to harmonize its procedure to the extent possible.

14. Significant progress with acute dietary risk assessment has been made since 1997. In that year a Joint FAO/WHO Consultation held in Geneva (hereafter referred as "1997 Geneva Consultation") established a possible approach for acute dietary risk assessment and coined two new terms: the International and National Estimates of Short-term Intake, respectively the IESTI and the NESTI<sup>4</sup>. The procedure allows for estimating the short-term risk for relevant subgroups of the populations, like adults and children. The 1999 JMPR for the first time calculated the short-term dietary intake estimates following this approach for new and periodic review pesticides. The JMPR flags cases when the IESTI for a given commodity exceeds the acute RfD.

15. The acute dietary risk assessment of pesticide residues proves to be a very complicated matter. The estimate of the acute dietary intake requires substantial food consumption data (large portion consumption data of a given commodity related to specific age groupings, median weight of commodity units) that currently are only sparsely available. So far only a few countries have submitted these food consumption data to the WHO for development of international diets for IESTI estimates. The JMPR is aware of the deficiencies of the databases but endorsed the use of these data in calculating the IEST on an interim basis.

16. The 31st Session of the CCPR considered risk management options for acute dietary risk assessment of pesticide residues. The Committee agreed to a number of preliminary measures that would require further development. The aforementioned procedure was endorsed at an interim basis and the Committee decided to implement the acute risk assessment to the extent possible when elaborating Codex MRLs. Governments were once again urged to generate relevant consumption data and to submit these data to the WHO.

## CONCLUSIONS

17. Since the publication of the Guidelines for predicting dietary intake of pesticide residues much progress has been made in the implementation of risk analysis in the work of the CCPR and JMPR. In particular the application of the revised Guidelines has contributed to the assessment of chronic dietary risk. These revised Guidelines have also contributed significantly to facilitate the risk management decisions of the CCPR. In practice for most compounds no chronic intake concerns remained when applying these Guidelines. The current review of the chronic intake procedure nevertheless indicates that there is a need for further improvement of the science for chronic intake estimates at the international level. At the national level gradually more sophisticated methodology becomes available, like probabilistic approaches.

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<sup>4</sup> WHO (1997) Food Consumption and exposure assessment of chemicals. Report of a FAO/WHO Consultation, 10-14 February 1997, Geneva, Switzerland. WHO, Geneva.

18. Acute risk assessment is a more complicated issue. The JMPR has made considerable progress in establishing acute RfDs. However, JMPR has already indicated for several compounds that establishing of an acute RfD is necessary but is pending waiting a future review. In these cases CCPR is reluctant to advance MRLs on chronic dietary risk assessment only. For that reason the CCPR is considering acute toxicity as an additional criteria in establishing priorities for JMPR. Also in those cases where the JMPR has established an acute RfD the consumption database is so preliminary that solid decisions by CCPR are not easily to be reached. It is to be expected that for acute toxic compounds the process of MRL setting will cease, in particular for commodities that are consumed as single unit, as long as no estimates can be made of the acute dietary intake on a routine base, As in the case for chronic dietary risk assessment there is a need to improve the underpinning science.