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THE PROBABILISTIC APPROACH TO ACUTE DIETARY EXPOSURE ANALYSIS AND ITS APPLICABILITY AT THE INTERNATIONAL LEVEL

(Transmitted by the United States of America)

Introduction

1. Risk assessment for acute dietary exposure poses a special problem not only for Codex (CCPR) but also for national regulatory agencies. From a food safety perspective, national regulatory agencies need to address the issue of acute dietary risk in an open and transparent way, in order to ensure the protection of their consumers and the maintenance of consumer confidence. At the same time, the national regulatory authorities need to ensure that risk management decisions are based on the best estimate of acute dietary exposure. Continuing work on the development of dietary exposure methodology for both chronic and acute exposure should be encouraged.

2. The 33rd CCPR considered the need to reflect on issues related to acute exposure assessment, especially the policy to be followed by CCPR when the acute dietary exposure exceeds the acute RfD, in order to facilitate the selection of appropriate risk management options. Also the feasibility of developing probabilistic methodology at international level should be explored.

3. The Delegations of the United States and the Netherlands, in view of their advanced experience in the development of acute dietary exposure assessment, agreed to develop a discussion paper for consideration by the next session of the Committee. The Delegation of Australia and the observers of CI and GCPF agreed to assist in the preparation of that paper.

4. In order to provide guidance to the Committee in this area, a separate document on the probabilistic approach to acute dietary exposure analysis and its applicability at the international level is attached to this paper. The desirability and feasibility to adopt a similar approach in the context of Codex is further discussed below. Also the policy options for the CCPR when the acute dietary exposure assessment exceeds the acute RfD are discussed below.

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Risk management in the CCPR in relation to acute dietary risk assessment

5. The 32nd CCPR, recognizing the urgent need for internationally agreed methodology on acute dietary risk analysis, agreed to endorse at an interim basis the acute risk assessment methodology as refined by the 1999 JMPR and to implement the acute risk assessment to the extent possible when elaborating Codex MRLs. The JMPR was requested a.o. to continue to refine the methodology on acute dietary risk assessment. Comments were sought from Governments on the JMPR methodology and information was asked on national acute dietary risk assessment methodologies and on consumption and other relevant data to expand the existing WHO data bases relating to acute intake assessment (large portion consumption data from persons/groups with specified ages and body weights, median weight of commodity units, edible percentage of the commodity, data reflecting the variability of residues in individual commodity units). No specific decision was recorded regarding the risk management in relation to acute intake concerns; document CX/PR 00/3 which was discussed by the 32nd CCPR mentions that when the IESTI (calculated for the most susceptible group, children age 6 and under) exceeds the acute RfD the MRL will not be advanced beyond step 7, and ALINORM 01/24 records that the EC and CI stated that MRLs should not be advanced beyond step 7 unless there was clear evidence that no acute intake concerns existed. CX/PR 00/3 mentions that when further refinement of the IESTI will not result in a dietary exposure below the acute RfD, a risk management decision is to be taken. CX/PR 00/3 further discusses a number of situations relating to the risk assessment of proposed MRLs and suggests the implementation of risk management decisions relating to those situations. The main difficulty in the various situations which are discussed is the question how to proceed when there is uncertainty regarding the international acute risk assessment. In a number of these situations it is suggested that the CCPR will proceed case by case. However, when the most refined estimates indicate that the acute reference dose might be exceeded, the subject MRLs will not be advanced beyond Step 7.

6. In the area of acute risk assessment refinement, the 2001 JMPR decided to convene a working group of experts to consider various aspects of the acute RfD-setting process (2001 Report, 2.1).

7. In order to make progress with this difficult issue it may be useful to recall that risk assessment relating to acute risks will always be an approximation of a kind of worst case but can not completely exclude the possibility that even higher consumption figures and even higher residues exist, so that the existence of higher exposures can not be excluded. Risk management regarding this issue should therefore not aim at asking the ultimate possible exposure level, but should aim at asking risk assessors at which level(s) of the possible exposure distribution it can be concluded that no acute intake concerns exist. It can be assumed that this question has aspects related to consumption data (how reliable are consumption figures at the upper end of the distribution), to toxicology (do acute intake concerns continue to exist when the acute RfD, which incorporates a safety factor, is calculated to be exceeded, even if only on a rare occasion by a minute number of consumers), to statistical aspects and considerations of scientific validity. As far as this question has a risk management side, it may be up to the risk managers to decide which (small) percentage of the population may be allowed to have a chance to exceed the acute RfD.

8. Residue levels in food as well as the food intake levels can be visualized as frequency distributions. One should realize that in such distributions, most levels are near the middle of the distribution and fewer levels are at the extremes. In other words, levels in the middle of the distribution have a higher chance of occurring than levels at the extremes. In the deterministic approach, both the residue level and the food intake level used are selected to represent the worst-case, i.e. they are taken from the extreme (less-likely-to-occur) region of the distribution. The residue intake value thus calculated reflects a *possible* exposure, but it is not known how *probable* this exposure is to occur. Probabilistic assessments are in fact repeated deterministic assessments. They yield a range of *possible* values for the residue intake. In addition, they yield information on the *probability* at which these residue intakes will occur. This information on the probability of the exceedance of the acute RfD is the major advantage of the probabilistic approach as it will aid risk management decisions.

9. In the point estimation method which is presently performed by the JMPR it is not exactly known how large this percentage of possible exceedances is, because the figures used are the 97.5th percentile of the food-intake distribution for "eaters only" from a consumption database regarding the product in question and the highest residue from a residue database (generally multiplied by a standard variability factor). In the few countries working with probabilistic distributions, usually the 99.9% level of the calculated exposure distribution is used as a cut-off level, because higher levels would contain too high uncertainties to be used with any

confidence. This implies that risk managers may accept that 0.1% of the population (which is still a not insignificant amount of people) can theoretically be exposed to higher levels than the acute RfD without giving raise to health concerns.

10. Because of the further possibilities of using risk reducing factors at the national level (such as monitoring data, % use level of the pesticide in question), it is logical that this national probabilistic approach may often lead to a more easy acceptance of some pesticide uses, seen in relation to decision making on the basis of the point estimation method.

11. In the Annex to this paper (issued separately), the probabilistic risk assessment methodology as performed in the USA is discussed in detail. It can be concluded from this Annex that although probabilistic risk assessment is a valuable method to come to more realistic risk assessments, it is not easy to implement this method on an international basis, especially because of the lack of adequate consumption data which reflect the distribution of the consumption for individual consumers. It is advisable to recommend the collection of data which will make it possible to perform such type of assessments in the future also on an international basis. It seems possible to obtain the necessary data to be able to make Monte Carlo type of exposure assessments for several regions in the world in the near future. The possibilities of using this methodology in the JMPR on the basis of national or regional individual consumption patterns should be explored further. In the meantime, it should be recognized that this will not be possible for most of the regions of the world for a long time and therefore it seems advisable to reflect on risk management in the CCPR which deals with the problem that decisions regarding acutely toxic substances have to be taken in situations where the international guidance which can be given is only or mostly in the form of a worst case assessment. Further development of the point estimate method therefore is also of great importance.

12. Bearing in mind that the IESTI as calculated by the JMPR may be a substantial overestimation of the actual risk involved, it may be useful in the case of an IESTI calculation which exceeds the acute RfD (case 15b from CX/PR 00/3) to proceed with a tiered approach in the JMPR, involving using probabilistic assessment as far as this is possible in the international context. This implies in the next tier the calculation of the distribution of intakes in a Monte Carlo approach, using the same residue data set as is available to the JMPR, together with adequate consumption data from countries or regions with a relevant intake of the critical commodity in question. The exposures calculated in this way could help the CCPR in making appropriate decisions. It will always be necessary to state the limitations in this approach, but it should be recognized that the IESTI as such also is an even more limited worst case approach.

13. Considering that there is a need of further guidance in a number of cases in which there is insufficient guidance from the JMPR (cases 15 c-e from CX/PR 00/3) it could be an option for the CCPR to request the assistance of countries and organisations which are in a position to perform adequate probabilistic or deterministic risk assessments and which have information that is lacking in the international context, in order to help with the provisional decision making process. Before such information is used, it will be necessary to be clearly informed about the exact parameters used for the presentation of the results and to make sure that these are adequate for international decision making (bearing in mind the parameters mentioned in paragraph 18).

Conclusions and recommendations

14. It is concluded that probabilistic exposure assessment is already practiced in various countries and, as such, is a methodology which can lead to a better general assessment of the exposure than point estimates and can lead to better decision making regarding residues of acutely toxic pesticides. This methodology therefore deserves to be promoted to be utilised more broadly, both nationally and also on an international basis. It is acknowledged however that it is a difficult methodology regarding the necessary data (especially consumption data for individual consumers of all ages) to perform this type of assessment, and it will take many years to reach a situation where this can be applied to all regions of the world in an international assessment. Therefore the CCPR has to face the fact that for many years the international acute exposure assessment will be mainly in the form of point estimates. Even when probabilistic methodology is widely introduced, it seems wise to maintain point estimates as a check of worst case exposures. Therefore every effort also has to be made to improve this point estimate methodology.

15. It is recommended that the JMPR should consider adopting a tiered approach for the acute risk assessment. In those cases where the acute RfD is exceeded, a Monte Carlo simulation should be performed,

using the same assumptions and data sets that were used in the point estimate, combined with adequate national or regional consumption data sets, in order to provide the CCPR with information regarding the probability aspects of high exposures.

16. It is recommended that probabilistic risk assessment methodologies be developed nationally and also that the requirements are gathered to be able to make regional international risk assessments based on Monte Carlo methodology as soon as reasonably possible. When various regional databases are available to make this type of assessment, it may be possible to use statistical techniques and knowledge about consumption patterns to introduce some form of probabilistic assessment also in cases where only average consumption figures are available, so that probabilistic approaches could be used more widely. Adequate consumption data sets should be made available to the JMPR in order to be used in international probabilistic exposure assessments.

17. Before deciding to apply probabilistic modeling at the international level, there would need to be a clear international consensus on the assumptions underlying the probabilistic approach. The most important of these is that the probabilistic approach is looking at the distribution of residues and the distribution of consumption and that some percentage of the population under consideration will be at risk. Different distributions result from the assumptions utilized.

18. Before implementing the use of international probabilistic assessments in an international context, it is important to realize that a probabilistic risk assessment (for instance using a Monte Carlo simulation) can be performed in many ways. Several decisions have to be made before starting the simulation. These decisions also have to be made when performing a deterministic risk assessment, and most of them already have been made in the international meetings leading to the current JMPR approach. In the same way, it is important that there is international consensus on the assumptions underlying the probabilistic approach. It is recommended that before using this approach at the international level, or using national contributions in an international context, these assumptions are discussed and agreed by CCPR on the basis of proposals for the methodology to be used by the JMPR. It is recommended that the following activities take place and issues and discussions be considered and further developed.

- Conduct inventory of available consumption and monitoring data
- Develop electronic library/database of available monitoring data
- Discussion and agreement on certain standard methodological protocols with respect to a number of policy issues. For example:
 - Consider consumption data from “eaters only” or “eaters and non-eaters” together?
 - Incorporate residue data from supervised residue trials or monitoring data (or both)? And under what circumstances?
 - How are percent crop treated used in the analysis, if at all?
 - How, and under what circumstances, is a variability factor incorporated, if at all, to allow for the fact that composite samples may not reflect residues in individual samples? Is there merit to a consideration of the extent of blending which occurs in determining whether such variability factor needs to be included?
- How are processing factors considered and incorporated?
- How are non-detected residues incorporated (1/2 LOD or LOQ vs. full LOD or LOQ? or something else?)?
- Are adjustments made to account for seasonal consumption patterns or for consumption which occurs only or predominantly at certain times of the year?

19. The risk assessment methodology also needs to be looked at in the wider context of finite resources for JMPR, the expert body that underpins the work of CCPR. It is apparent to many that the work of CCPR and its relevance as an international standard setting body is being affected by the lack of resources available to the technical committee. There is a danger that the adoption of a resource intensive methodology such as probabilistic modeling for acute dietary intake assessment could adversely impact on resources available to JMPR and its ability to service the needs of CCPR. Who will pay for the proposed developments and if it is

FAO/WHO will this be taken out of the finite resources available for JMPR? Will any additional resources allocated for probabilistic modeling and the development of the necessary databases mean there is less money for addressing current resource problems with JMPR?

20. Additional considerations include the resources and the ability of national governments to participate in the generation of data for probabilistic modeling, should the Committee agree to adopt this methodology. Considerable time will be taken before enough data/information is available for valid use at the international level.