codex alimentarius commission

FOOD AND AGRICULTURE ORGANIZATION OF THE UNITED NATIONS

WORLD HEALTH ORGANIZATION

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Agenda Item 4 **CX/RVDF 06/16/3**
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JOINT FAO/WHO FOOD STANDARDS PROGRAMME

CODEX COMMITTEE ON RESIDUES OF VETERINARY DRUGS IN FOODS

Sixteenth Session

Cancun, Quintana Roo, Mexico, 8 -12 May 2006

INFORMATION ON MATTERS OF INTEREST ARISING FROM FAO/WHO

1. This document highlights ongoing activities in FAO and WHO related to a number of recommendations arising from the 66th meeting of the JECFA in terms of development of risk assessment principles. Please note, that this paper only highlights some aspects not covered under specific agenda items. Several important general considerations of the 66th JECFA meeting will be covered separately under the relevant agenda items.

2. Furthermore, information is provided on the publishing of output from JECFA, in particular the new FAO JECFA monographs series for MRL Monographs.

3. Information on FAO/WHO activities in the area of provision of scientific advice to Codex and Member countries, as well as other activities which are of interest for CCRVDF are provided.

Expression of the ADI and derivation of the MRL (Practices on rounding of ADI)

4. At its 66th meeting, JECFA considered the request of the CCRVDF to comment on certain practices suggested at its 15th session on rounding when establishing ADIs and recommending MRLs for veterinary drug residues.

5. The Committee considered the expression of the ADI at its thirty-sixth meeting in 1990. The Committee decided to express the ADI numerically to only one significant figure. If an ADI is calculated from a NOEL that has more than one significant figure, the ADI would therefore be rounded to one significant figure, consistent with accepted rounding procedures.

6. In the past, JECFA has applied its rounding practice to the derivation of ADIs for 25 veterinary drugs, resulting in 14 ADIs have been rounded down and 11 ADIs have been rounded up. Most of the veterinary drugs that have been reviewed by JECFA resulted in a calculated ADI of one significant figure without rounding. The Committee noted that the recommendation from the CCRVDF suggests a misunderstanding of the relationship between the ADI and the derivation of the MRL. The MRL and the ADI are separate outputs of the risk assessment process and serve different purposes.

7. The ADI is derived from the NOEL/LOEL from the appropriate toxicological studies, using a safety factor. Given that there are assumptions and uncertainties in deriving the ADI, such as the use of safety factors, the use of a range of doses in toxicological studies and normal biological variation, it is more meaningful to express the ADI to only one significant figure to avoid any inference of inappropriate precision.

8. The MRL recommendation procedure is an iterative process. The MRL is not derived directly from the ADI. If the ADI is based on toxicological end-points, all residues of toxicological relevance are considered, if the ADI is based on microbiological end-points, all residues of microbiological relevance are considered. The MRL recommendation procedure also takes into account the conditions of use (e.g. use of the veterinary

9. drug according to good practice in the use of veterinary drugs GPVD) and the residues that result from such use (e.g. residue depletion studies). It also considers results of radiolabeled residue studies, the bioavailability of bound residues, the identification of target tissues and a marker residue, the availability of practical analytical methods, estimated exposure resulting from recommended MRLs and consideration of extension of the MRLs to tissues, eggs and milk of other species.

10. The initial consideration in recommending an MRL is whether it is sufficiently protective of human health. If the use of the veterinary drug yields an estimated intake of veterinary drug residues consistent with the ADI, the recommended MRLs may then be adjusted accordingly when taking into account the other factors noted above. As a general principle, the Committee will not normally recommend an MRL that results in residue levels that lead to an estimated dietary intake exceeding the ADI based on toxicological or microbiological considerations.

11. The Committee confirmed that the rounding practices used in expressing the ADI are scientifically and mathematically sound. In addition, since the ADI is not directly used in the derivation of the MRL, the JECFA rounding practice has no direct consequence on the MRL.

Estimation of chronic dietary intake of residues

12. The Committee considered the recommendation on the estimation of dietary intake of residues from the joint FAO/RIVM/WHO workshop 200) workshop (Updating the Principles and Methods of Risk Assessment: Maximum Residue Levels (MRLs) for Pesticides and Veterinary Drugs) held in Bilthoven in November 2005 ftp://ftp.fao.org/ag/agn/jecfa/bilthoven_2005.pdf .

13. The most important outcome of this meeting was the recommendation regarding the estimation of long-term (chronic) dietary intakes of residues of veterinary drugs to be used by JECFA. Instead of using a one point estimate, it was recommended that the median residue concentrations be used instead, being a more realistic yet conservative estimate. Similar procedures are used by JMPR to estimate intake of pesticide residues from food. JECFA has in the past used a calculated figure of total residue of toxicological or microbiological concern, the “Theoretical Maximum Daily Intake” (TMDI) for comparison with the ADI. The new procedure uses the same formula as used previously for the calculation of the TMDI including factors such as the ratio of marker to total residue concentrations - with the only exception that the median concentration replaces the MRL as point estimate of the residue concentration in the formula.

14. The MRL and the median concentration are derived from the same time point of the depletion data of the marker residue. The MRL is a point on the curve describing the upper one-sided 95% confidence limit over the 95th percentile. The median is the corresponding point on the regression line for the same time point. Both figures are obtained from a statistical evaluation of the data

15. In developing this new calculation procedure, the present Committee concluded that the TMDI was no longer the most suitable estimate of chronic intake because the MRL was a single concentration representing the estimated upper limit of a high percentile of the distribution of marker residue present in a given tissue of the treated animals. The Committee concluded that it was not realistic to use an extreme value of the distribution in a scenario describing chronic intakes. In such a scenario all concentrations of the distribution of residues should be considered. The median concentration represents the best point estimate of a central tendency over a prolonged period of time, because the concentrations of residues in a given tissue consumed varies from day to day as reflected in the distribution. Therefore the Committee decided to use the median of the residue distribution to substitute for the MRL in the intake estimate. The new estimate of intake is called “Estimated Daily Intake”. In calculating the median from an array of results including values below the limit of quantification (LOQ) or below the limit of detection (LOD) half of the respective limit is used for the calculation of median concentrations of residues. In the considerations of the substances on the agenda of the 66th JECFA meeting, both TMDI and the Estimated Daily Intake were calculated. The comparison of the intake with the ADI was in all cases based on the new estimate.

Call for experts for JECFA rosters 2007 – 2011

16. FAO has issued a call for experts to serve on JECFA for the period of 2007 to 2011. Details on the scientific expertise required for the fields in which JECFA is mandated to perform risk assessment and the application procedure and process is available at http://www.fao.org/ag/agn/jecfa/experts_en.stm . WHO has an open call for experts and the information can be accessed through http://www.who.int/ipcs/food/jecfa/experts/en/index.html .

Provision of Scientific Advice

17. FAO and WHO have continued their efforts in the enhancement of the FAO/WHO work to provide scientific advice. Efforts have been concentrated in two main activities:

a) Further work on the framework for the provision of scientific advice which will include a compilation of all written procedures followed by FAO and WHO in relation to the provision of scientific advice. This document will be finalized during 2006.

b) A joint FAO/WHO technical meeting to explore new approaches to enhance participation of experts and the use of data from developing countries was organized in Belgrade, 12 – 15 December 2005. The report of the meeting is in preparation and will be available at http://www.fao.org/ag/agn/proscad/index_en.stm. The meeting was intended to provide a fully comprehensive plan to facilitate an increased presence of scientific experts and contribution of reliable data from developing countries to the FAO/WHO program on scientific advice.

18. The completion of the FAO/WHO review process on provision of scientific advice has been postponed to 2006 as it requires the support and involvement of member countries and requires additional resources to meet the expectations of the CAC and member countries.

Joint FAO/WHO/OIE Expert Consultation on Antimicrobial Use in Aquaculture and Antimicrobial Resistance,13-16 June 2006, Seoul, Korea

19. Considering that antimicrobial usage and resistance is a multifactorial problem the Executive Committee of the Codex Alimentarius Commission in its 53rd session, recommended that FAO, WHO and OIE should give consideration to convening a multidisciplinary expert consultation. All issues of antimicrobials in agriculture and veterinary use (including aquaculture) should be considered and the role played by antimicrobials as essential human and veterinary medicines should be taken into account.

20. Following this request from Codex a consultative process on non-human use of antimicrobials and antimicrobial resistance was initiated jointly by FAO, WHO, and OIE, with a first workshop on risk assessment organized in December 2003 in Geneva followed by a workshop on risk management options organized in Oslo in March 2004. These workshops did not address thoroughly the use of antimicrobials in aquaculture and the public health impact of such use. The present consultation is planned to fill this gap and complement this consultative process.

21. This joint FAO/WHO/OIE Consultation on Antimicrobial Usage in Aquaculture and Resistance will use the risk analysis framework, promoted by the three organizations for more than a decade following the recommendation of the Codex Alimentarius to analyse all pertinent and scientific information collected over the last years on antimicrobial use in aquaculture and its consequences for human public health, using the complementary expertise of WHO, FAO and OIE.

22. The overall objective of the consultation will be to discuss and to outline strategies and recommendations to minimize the risk related to antimicrobial use in aquaculture and its consequences for human public health, based on scientific assessment.