

# codex alimentarius commission E



FOOD AND AGRICULTURE  
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Agenda Item 9

CX/RVDF 09/18/9 Part 1  
January 2009

**JOINT FAO/WHO FOOD STANDARDS PROGRAMME**  
**CODEX COMMITTEE ON RESIDUES OF VETERINARY DRUGS IN FOODS**  
**Eighteenth Session**

*Natal, Brazil, 11-15 May 2009*

**DISCUSSION PAPER ON CURRENT PRACTICES AND NEEDS FOR FURTHER WORK BY THE  
COMMITTEE**

**(Report of the electronic Working Group on Risk Management Topics and Options)**

*(Discussion paper by France, with the assistance of Australia, Argentina, Canada, European Community,  
Germany, Islamic Republic of Iran, Japan, Sweden, United Kingdom, United States of America,  
JECFA Secretariat, IDF and IFAH)*

Governments and international organizations wishing to submit comments on the discussion paper are invited to do so **no later than 10 April 2009** as follows: U.S. Codex Office, Food safety and Inspection Service, US Department of Agriculture, Room 4861, South Building, 14<sup>th</sup> Independence Avenue, S.W., Washington DC 20250, USA (Telefax: +1 202 720 3157 ; or *preferably* E-mail: [uscodex@usda.gov](mailto:uscodex@usda.gov), with a copy to the Secretary, Codex Alimentarius Commission, Joint FAO/WHO Food Standards Programme, Viale delle Terme di Caracalla, 00153 Rome, Italy (Telefax: +39.06.5705.4593; E-mail: [Codex@fao.org](mailto:Codex@fao.org), *preferably*).

**Background:**

1. When finalizing its document on Risk Management Methodologies, including Risk Assessment Policies, during its 16<sup>th</sup> session, the Codex Committee on Residues of Veterinary Drugs in Foods acknowledged that there was a need for further discussion related to risk management options including risk assessment policy (ALINORM 06/29/31 – para. 112-114). The 16<sup>th</sup> session of the Committee also agreed to establish an electronic Working Group, led by France, to prepare a Discussion Paper to identify risk management topics and options to be considered at its next session. At the last (17<sup>th</sup>) session of the Committee (Breckenridge, Colorado, USA – 3-7 September 2007), an in-session working group was convened to review the Discussion Paper [CX/RVDF 07/17/13] and the written comments submitted, to prioritize the recommendations in the document and to consider ways to advance the work further.

2. At the last (17<sup>th</sup>) session of the Committee, the Committee established an electronic working group, under the leadership of the delegation of France, to draft a discussion paper on risk management topics and options for the CCRVDF, based on the agreement at this meeting and further background material and comments provided in response to section C-3 of the Codex Circular Letter CL 2007/37-RVDF<sup>1</sup>, requesting members and observer organizations to provide detailed information on their current practices and suggestions for the scope of further work by the Committee for each of the topics that should be taken up immediately for consideration (ALINORM 08/31/26 – para 132 & 134-136).

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<sup>1</sup> Comments submitted in response to CL 2007/37-RVDF are compiled in sections 1 & 2 of CX/RVDF 09/18/9 Part 2.

3. The Committee agreed that a discussion paper be prepared that would:
  - (i) review the information provided in response to the Circular Letter (see paragraph 132);
  - (ii) assess whether it would provide sufficient ground for further work by the Committee and, where appropriate, would prepare a project document describing possible new work for consideration by the Committee or recommend delaying further action;
  - (iii) address possible changes in the status of the proposals listed in document CX/RVDF 07/17/13 and make appropriate recommendations to the Committee for further consideration and action; and
  - (iv) collate new proposals with relevant background information and appropriate recommendations to the Committee.
4. The Committee noted that active participation of the members of the electronic Working Group was required, especially in identifying the risk management issues and their rationale, in order to produce a useful document for consideration of the Committee.

5. The French delegation is grateful to acknowledge the inputs received from Australia, Argentina, Canada, European Community, Germany, Islamic Republic of Iran, Japan, Sweden, United Kingdom, United States of America, JECFA Secretariat, International Dairy Federation (IDF) and International Federation of Animal Health (IFAH)<sup>2</sup>, as they all have been of great importance for putting together this discussion paper.

#### **Process:**

6. The discussion paper lists all the proposals received from Codex members and Observers and provides some background on each of them and an assessment of their relevance to the mandate of the Committee.
7. The electronic Working Group has considered each item thoroughly with the prospect of drafting a recommendation for endorsement by the Committee in plenary. The recommendations will be recorded in the report of the meeting for future reference and application when relevant issues arise. The electronic Working Group has also recorded all the topics under its consideration, but on which no recommendation has been finalized yet, in order to seek guidance on whether discussion on any of these items should be discontinued. However, only topics that fall within the terms of reference of the CCRVDF and are not considered in other fora, have been given serious consideration by the electronic Working Group.
8. The Committee may wish to challenge or endorse the assessment suggested by this electronic Working Group; it will select some items from this list with regard to their importance and the time available for discussion and prioritize them, when establishing its own agenda.

#### **Items identified for immediate consideration:**

9. The 17<sup>th</sup> session of the Committee agreed that the four topics should be taken up immediately for consideration (see ALINORM 08/31/26 – para. 130).
10. One observer suggested that the Committee consider methods for calculating the MRLs in conjunction with a full utilization of the ADI and develop procedures for calculating MRLs that are protective of human health but also recognize a more realistic consumption of edible tissues, eggs and milk.

#### A.- Use of the Estimated Daily Intake (EDI) concept

11. The 17<sup>th</sup> session of the Committee agreed that *“the work should focus on two issues: i) the means to improve communication between JECFA and CCRVDF on changes in risk assessment methodology, in advance of their implementation; and ii) the impact on the risk management process of the changes, introduced by the 66<sup>th</sup> JECFA in its method for the evaluation of residues of veterinary drug in foods.”*

12. The 66<sup>th</sup> JECFA identified the EDI as one of a number of issues that are being addressed as part of the Joint FAO/WHO Project to Update and Consolidate Principles and Methods for the Risk Assessment of

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<sup>2</sup> Comments received in response to the circulation of the draft document are compiled in section 3 of CX/RVDF 09/18/9 Part 2.

Chemicals in Food (<http://www.who.int/ipcs/food/principles/en/>). An international workshop, held in Bilthoven (The Netherlands) in November 2005 ([ftp://ftp.fao.org/ag/agn/jecfa/bilthoven\\_2005.pdf](ftp://ftp.fao.org/ag/agn/jecfa/bilthoven_2005.pdf)), agreed that the principles and methods for the estimation of exposure for chemicals used as veterinary drugs and pesticides should be harmonized to the extent possible and recommended that “*JECFA should consider using the median value of the distribution of residue concentrations from which the MRL is derived for the calculation of conservative estimates of long-term (chronic) intakes*” (recommendation n° 14).

13. JECFA at its 70<sup>th</sup> meeting confirmed the utility of the EDI. However, it acknowledged that the use of the EDI is currently applicable only to the evaluation of chronic toxicity of, and chronic exposure to, residues as reflected by the ADI. It also stated that the EDI should not be applied when there is concern for acute toxicity or acute exposure. For this purpose, appropriate tools and approaches will need to be developed.

14. The final Expert consultation on the FAO/WHO joint Project to Update and Consolidate Principles and Methods for the Risk Assessment of Chemicals in Food, held in Seoul, Republic of Korea 11-14 November 2008, supported the same conclusions and noted that additional work is required to address acute exposure for comparison with an acute reference dose (ARfD).

15. The electronic working group has provided an opportunity to receive a number of comments from members regarding this new approach. The main comments have emphasized the following issues:

- (i) The EDI approach is only valid for chronic toxicity /exposure;
- (ii) Further work should be performed on acute toxicity/exposure;
- (iii) The EDI approach may require a considerable amount of data and may be not applicable in all cases.
- (iv) Is the EDI approach conservative enough?

16. JECFA clarified that the EDI approach was only valid for chronic/toxicity/exposure and that further work needed to be done about acute toxicity/exposure. Furthermore, JECFA confirmed that when data was not adequate to estimate an EDI, JECFA would apply other conservative approaches to ensure that ADI was not exceeded

17. **Recommendation:** Focusing on the two areas identified by the Committee at its last session (17<sup>th</sup>), the Committee may wish to:

- (i) clarify whether the EDI approach is acceptable or is still source of concerns;
- (ii) if some concerns remain, request additional clarification from JECFA on the objectives, the scope of application and the implementation of the EDI approach, taking into account current limitations.
- (iii) suggest that JECFA co-ordinates a workshop with other regulatory bodies and concerned parties to discuss in detail the current and proposed systems and agree in discussion with these regulators how to implement the new system and assess its impact on the MRLs currently in use, if this is the agreed way forward.

18. Notwithstanding the fact that the 66<sup>th</sup> JECFA presented both TMDI and EDI calculations for transparency in its report to the Codex and that the use of the EDI has been discussed in a number of venues, outside of the JECFA sessions, several members have identified a failure in the consultative process between risk managers and risk assessors on this issue: JECFA has been repeatedly criticized for adopting and immediately using a fundamentally new MRL and intake calculation concept without any participation of regional scientific committees and authorities.

19. The JECFA secretariat has pointed out during the 17<sup>th</sup> session of the Committee that the EDI approach was developed based on request of CCRVDF to develop a more realistic exposure assessment and to base risk assessments on such realistic scenarios (consistent with the current Risk assessment policy for CCRVDF<sup>3</sup>). Moreover, scientific principles and method developed and used in risk assessment are inde-

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<sup>3</sup> Codex Procedural Manual, 17<sup>th</sup> edition. p. 147), and in particular point e) referring to that fact that risk assessment should be based on realistic exposure scenarios.

pendently developed by international experts in the relevant fields and are not subject to approval by risk management bodies.

20. The Committee may wish to express its view on the extent to which the provision in para. 33 of the *Risk analysis principles applied by the Codex Committee on residues of veterinary drug in food*<sup>4</sup> have been effectively implemented.

21. **Recommendation:** The Committee may wish to discuss with JECFA how to develop new approaches in collaboration with, and ensure a more effective consultation process with concerned parties before new scientific approaches are implemented by JECFA, consistent with the provisions in the *Risk analysis principles applied by the Codex Committee on residues of veterinary drug in food*.

#### B.- Utilization of full ADI

22. A member recalled that the general approach for the development of a maximum residue limit (MRL) has been refined over the years; the current definition of a MRLVD, in the 17<sup>th</sup> edition of the Codex Alimentarius Commission Procedural Manual (p.43) embodies the outcome.

23. It further noted that only the first part of the definition<sup>5</sup>, if followed, would allow use of the full ADI in establishing the MRL. However, the rest of the definition implied that MRLs recommended to Codex by the JECFA were typically further refined (reduced) by the consideration of good practices in the use of veterinary medicine, by other relevant public health risks, by food technological aspects and by the availability of practical analytical methods; and that many of these refining criteria were not directly related to food safety.

24. Some Members, having submitted written comments, reported that they utilized an approach of using full ADI for individual tissues (e.g. calculation “based on the standard 500g meat” in Canada) to establish MRLs and supported the use of full ADI for Codex MRLs.

25. However, a member noted that this approach would also require acceptance of the concept that on any given day only one edible tissue is likely consumed (muscle, liver, kidney, or skin/fat) and that the individual MRLs should not be combined. Another noted that in case of dual use substances (veterinary/pesticide use), the full usage of the ADI for one usage would automatically preclude setting MRLs for the other.

26. Other members were not in favour of this approach and support MRLs being developed that were relevant to appropriate use (i.e. Good Practice in the use of Veterinary Drugs [GPVD] rather than being theoretically calculated from the ADI). MRLs should be set at concentrations that could monitor GPVD. Some allowances have to be made of possible extra-label use of veterinary drugs and possible uses in minor species, exposure to drug residues from non-animal foodstuff, e.g., foods of plant origin, being contaminated with drugs from excreta released into the environment, not using the full ADI providing an extra safety margin to cope with situations of this kind.

27. **Recommendation:** The Committee may wish to request the opinion of the JECFA on this issue and postpone consideration of this issue at this time until it has reviewed JECFA’s response on this topic. It may also wish to take note that the resolution of outstanding issues may involve revising the current definition of the MRL for veterinary drugs in the future.

#### C.- Starter cultures

28. The observer from IDF was of the opinion that, in establishing MRLs in milk that are used for international trade purposes, Codex did not need to consider the effect on starter cultures. MRLs should be based solely on concentrations that did not compromise the safety of consumers and technical processing issues for the specific dairy products that involved starter cultures, could be managed effectively by processing controls by dairy businesses. One member also supported this approach.

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<sup>4</sup> Codex Procedural Manual –17<sup>th</sup> edition p.139-144.

<sup>5</sup> “Codex maximum limit for residues of veterinary drugs (MRLVD) is the maximum concentration of residues resulting from the use of a veterinary drug (expressed in mg/kg or µg/kg on a fresh weight basis) that is recommended by the Codex Alimentarius Commission to be legally permitted or recognized as acceptable in or on a food”.

29. In the “*Discussion Paper on Risk Management Topics and Options for the CCRVDF*” (CX/RVDF 07/17/13), it was noted that some Codex members would support the consideration of food technological aspects in the establishment of an MRL because the approach was used at their national/regional levels.

30. Written comments submitted confirmed that, in the European community, assessment of effects on industrial starter cultures in milk is part of the normal MRL risk assessment for antibiotics (“*For milk, the MRLs should not exceed the concentration without effect on dairy starter cultures*”) and that there is an opportunity for lowering MRLs to take account of undesired effects on starter cultures. Australia also noted that, for regulators, this issue might form part of the assessment of a chemical product and, in this context, the Australian Pesticides and Veterinary Medicines Authority (APVMA) has developed a guideline in relation to dairy starter cultures (“*The APVMA takes into account the effects of antimicrobial residues on starter cultures when setting MRLs for antimicrobials in milk*”<sup>6</sup>).

Other members, while appreciating these differences in processes among countries, noted that Members were not excluded from elaborating on any established Codex MRL at their national/regional level.

31. Overall, irrespective of general issues raised by some Members in their written comments under this item, there is a general agreement to use, as a precedent, the approach applied at the 16<sup>th</sup> session of the Committee<sup>7</sup> in the case of pirlimycin, whenever the issue of starter cultures arises in the future. It will permit Codex Members to consider the full range of uses of animal products from treated animals and to adapt national/regional MRLs in order to address this technological aspect for trade of fresh liquid milk intended for processing using starter culture (provided the MRL proposed on safety grounds was not exceeded).

32. **Recommendation:** The Committee may wish to conclude on this topic by agreeing on a policy decision for the future, namely: “*When establishing a MRL for a veterinary drug, the residues of which JECFA has evaluated for their effect on starter cultures and has recommended a MRL for milk, on the basis of food safety consideration, the Committee shall append a risk management statement informing Codex Members that they may therefore adapt national/regional MRLs in order to address this technological aspect for trade of fresh liquid milk intended for processing using starter culture*”.

#### D.- Appending risk management recommendation(s) to MRLs

33. The 17<sup>th</sup> session of the Committee agreed that “*the work should consider whether additional recommendations on risk management could be provided by the Committee when it establishes MRLs.*”

34. Members, having submitted written comments, noted that the device has been used in the past, on several occasions<sup>8</sup>. It was noted that the Committee has acted on a case by case basis and that it had permitted the adoption of Codex MRLs which had been the subject of disagreement among Codex Members. Members were generally supportive of appending risk management recommendations to MRLs as a means of providing guidance on Good Veterinary Practice or food technological aspects. (Some members expressed the view that, as these factors are not directly related to human food safety, they should not be considered when setting MRLs).

35. However, on the other hand, some members supported the opinion expressed by JECFA that implementation of the established MRLs and withholding time for milk should be addressed under national/regional regulatory programmes. (for instance, in Canada, the withholding time in milk greater than 96 hours is not considered to be practical, therefore, the use of Doramectin products is not allowed in lactating dairy cow) It was also noted that appending such recommendations should not constrain national authorities on matters that are to be addressed by national authorities within each individual country.

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<sup>6</sup> <http://www.apvma.gov.au/guidelines/rgl30.shtml> (Assessment of the effect of antimicrobial substances on activity of dairy starter cultures – Assessment of the effect of antimicrobial substances on activity of dairy starter cultures – Residue Guideline No. 30 – August 2003); <http://www.apvma.gov.au/guidelines/rgl25.shtml> (Residues in milk – antimicrobials – Residue Guideline No. 25 – February 2000); <http://www.apvma.gov.au/guidelines/rgl22.shtml> (Residues in milk – parasiticides and drugs other than antimicrobials – Residue Guideline No. 22 – 6 February 2001).

<sup>7</sup> See ALINORM 06/29/31 para 60.

<sup>8</sup> The document CX/RVDF 07/17/12 (para. 9) collates relevant instances of risk management recommendations for national or regional authorities appended to MRLs adopted by the Codex Alimentarius Commission.

36. **Recommendation:** The Committee may wish to conclude on this topic by agreeing on a policy decision for the future, namely: *“The Committee will append risk management recommendations to MRLs, as footnotes, (i) on a case by case basis, where appropriate; (ii) in order to assist risk managers in formulating adequate risk management provisions; (iii) as a means of providing guidance on Good Veterinary Practice (possibly including, but not limited to, duration and frequency of administration, extra/off label use, restricting the marketing of certain veterinary drugs with respect to e.g. species, production group, route of administration, pharmaceutical form, withdrawal period ...) or food technological aspects.”*

**Items on which the Committee, at the 17<sup>th</sup> session, requested further clarification before its next session:**

#### E.- Use of Regional Consumption Factors

37. The Bilthoven Workshop re-confirmed use of the traditional standard food basket for animal derived commodities, in the absence of better alternatives based on empirical consumption factors (“the theoretical food basket approach leads, in combination with the MRL, to over conservative estimates of the long-term exposure to veterinary drugs of "average eaters" and highly conservative estimates for the "preferential eaters"). It also noted that “the current data provided by GEMS/Food to conduct short-term intake assessments lack the detailed information needed for optimal assessment”<sup>9</sup>.

38. The food basket approach has been retained by JECFA, as it represents a further conservative estimate to protect eaters of the specific foods in the population. This food basket was originally drawn up based on information gathered and agreed by CCRVDF.

39. One member also noted that MRLs were not routinely established for edible offals (other than liver and kidney) of cattle, goat and sheep, such as rumen, abomasums and brain.

40. Another member pointed out that daily residue exposure, as determined through either the traditional TMDI or the recently elaborated EDI approach, if calculated based upon cumulative consumption of edible tissues to the full market basket amount, would overestimate true dietary exposure. It proposed recommending MRLs using an exposure calculation that recognized a more realistic daily consumption of meats, respecting that eggs and milk are separate commodities: presuming that on any given day the consumer of a meal derived from muscle would not regularly also have a meal from kidney, and so forth, it could be appropriate to calculate daily cumulative exposure, based on only one meat plus milk plus eggs (where applicable) with MRLs assigned accordingly.

41. Among Members, having submitted written comments, there was recognition of the need for additional data before the use of regional consumption values in developing MRLs and evaluating dietary exposure to veterinary drug residues could be implemented. They also expressed their willingness to continue discussion on this topic.

42. **Recommendation:** The Committee may wish to request the opinion of the JECFA on the implementation of the “one meat, plus egg, plus milk” approach, outlined in para. 41 above and postpone consideration of this issue at this time until it has reviewed JECFA’s response on this topic.

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<sup>9</sup> Updating the Principles and Methods of Risk Assessment: MRLs for Pesticides and Veterinary Drugs. FAO, Rome, 2006. – [http://www.fao.org/ag/AGP/AGPP/Pesticid/JMPR/DOWNLOAD/bilthoven\\_2005.pdf](http://www.fao.org/ag/AGP/AGPP/Pesticid/JMPR/DOWNLOAD/bilthoven_2005.pdf)

## F.- Old Drug Policy

43. Two different issues were raised in the discussion paper CX/RVDF 07/17/13 under this heading and could be best dealt with separately: (a) veterinary drugs for which no ADI and MRL has been recommended by JECFA due to specific human health concerns<sup>10</sup>; (b) veterinary drugs routinely used by developing countries in their food animal production programmes<sup>11</sup>.

44. In para. 84 of the discussion paper CX/RVDF 07/17/13, it was suggested that the issues in para. 82 “*would be best discussed by the group considering how to deal with substances without ADI/MRLs.*”. The proposal for new work on “*Proposal for new work on the development of risk management recommendations/guidance for veterinary drugs for which no ADI and MRL has been recommended by JECFA due to specific human health concerns*” (ALINORM 08/31/31 – Appendix VIII), forwarded by the last session of the Committee to the 31<sup>st</sup> session of the Codex alimentarius Commission, was not agreed as new work and was referred back to this session of the Committee for review.

45. JECFA at its 40th meeting developed an approach for evaluating veterinary drugs with a long history of use that takes into account concerns about incomplete data packages and defines in principle minimum data requirements<sup>12</sup>. As for all other evaluations, a minimum of adequate data is required for JECFA to perform an evaluation.

46. **Recommendation:** The Committee may wish to discuss topic (a) further and to refer topic (b) to its electronic Working Group on Priorities, for further consideration.

## G.- Threshold of Toxicological Concern for Veterinary Drugs (CX/RVDF 07/17/13, para. 85)

47. While in agreement with the position expressed in para. 85-86 of discussion paper CX/RVDF 07/17/13, one Member noted that, although the Threshold of Concern (TTC) appeared to be a promising tool for establishing risk-based lower residue limits for substances that have no ADI/MRL (superior to the often used approach to use analytical performance limits as for instance detection/quantification limits), one major limitation of the approach was that, at present, no suitable TTCs for pharmacological, hormonal or microbiological effects were available, as such effects often played a considerable role in the risk assessment of veterinary drugs<sup>13</sup>. The Member concluded that the TTC concept was in need of further development and extension/validation before it could be used in the assessment of pharmacologically active substances.

48. The JECFA Secretariat noted that, with regards to the TTC concept and its application to veterinary drugs further work is necessary. It also pointed out that some compound specific data have to be available for the assessment, both in relation to chemical and toxicological data as well as for data on exposure.

49. Based on recommendations by the 66<sup>th</sup> JECFA and subsequently by the 17<sup>th</sup> session of the CCRVDF, JECFA at its 70<sup>th</sup> meeting has started discussion on the development of a decision-tree approach for the evaluation of veterinary drugs which includes application of the TTC concept. The development of this decision tree approach will take several years and close interaction between JECFA and CCRVDF is required.

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<sup>10</sup> See discussion paper CX/RVDF 07/17/13 – para. 82: “*An observer recalled that, several years ago, JECFA developed an old drug policy and used it to recommend MRLs for veterinary drugs that had a long history of use in both human medicine and veterinary medicine: These older drugs did not have safety data that meet current standards and these data were not collected on current good laboratory practices. The Observer suggested that, as many of the veterinary drugs without a Codex ADI/MRL could be classified as “old drugs”, CCRVDF should re-examine the utility of the old drug policy. It noted however that, as these old drugs had no patent protection, it was unlikely that a sponsor would undertake the expense to submit the appropriate data to JECFA/Codex.*”

<sup>11</sup> See discussion paper CX/RVDF 07/17/13 – para. 83: “*The observer also recalled as “extremely important” one of the recommendations by the Bangkok Conference, namely: “CCRVDF should amend its procedures in its ad hoc working group on priorities for selection of veterinary drugs for JECFA evaluation to facilitate development of MRLs for veterinary drugs routinely used by developing countries in their food animal production programmes and take other measure as appropriate.*”

<sup>12</sup> See the report of the 40th meeting [http://whqlibdoc.who.int/trs/WHO\\_TRS\\_832.pdf](http://whqlibdoc.who.int/trs/WHO_TRS_832.pdf).

<sup>13</sup> For instance, JECFA’s pharmacological ADI for dexamethasone was set as low as 0-0.000015 mg/kg bw or 0-0.015 µg/kg bw (or daily intake of 0.9 µg/person/day), much lower than most of the TTC values for toxicological endpoints established so far (except for the TTC for high potency genotoxins/carcinogens which was estimated with 0.15 µg/day).

50. **Recommendation:** The Committee may wish to discuss these specific issues further.

#### **Update on items to be taken up for consideration in the future:**

##### H.- Residues at injection sites

51. The 17<sup>th</sup> session of the Committee “also agreed that proposal (C-3) “Residues at injection sites” be taken up for consideration in the future taking account of the estimation of acute reference doses published by JMPR, the work on the same topic planned by JECFA and the consideration planned by VICH, when they become available.” (see ALINORM 08/31/26 – para. 131)

52. The 21<sup>st</sup> session of the VICH Steering Committee (Paris, July 8<sup>th</sup>-9<sup>th</sup> 2008) agreed to develop a “concept paper”, involving consideration of Residues at injection sites. At the time of this writing, the scope of the work to be undertaken by VICH is not known.

53. A member noted that it is a critical food-safety issue and suggested that this topic should be elevated in priority and included in the list of topics to be taken up immediately for consideration by the Committee.

54. **Recommendation:** The Committee may wish to consider the scope and schedule set by VICH for work on this issue, before deciding on the course to be followed.

##### I.- Harmonisation of withdrawal period’s calculation

55. The 17<sup>th</sup> session of the Committee “noted that information on methods for calculation of withdrawal period were included in the guidance available on the EMEA webpage; and that the VICH Expert Working Group (EWG) on Metabolism and Residue Kinetics was considering the issue around harmonisation of statistical methods for calculation of withdrawal period as one of its major topics and that draft guidelines would be discussed at the next meeting of the Working Group in October 2007 and the output would be reported at the 18th Session of the Committee, if available.” (see ALINORM 08/31/26 – para. 133)

56. It was noted that the objective of the VICH Expert Working Group (EWG) was to provide a global comparison of differences in statistical (and possibly non-statistical) withdrawal time calculation tools and model assumptions and of their impact on data requirements for residue studies in the different regions. If this exercise showed that the tools and assumptions can significantly affect residue study design and a study (accepted by authorities in one region could be rejected elsewhere), then it would consider harmonizing the statistical approaches.

57. As an interim result, the EWG noted that the greatest impact on current differences in withdrawal periods would probably not come from the statistical calculation tools. It was agreed however that additional examples would be needed to further assess the impact of non-harmonized statistical tools.

58. **Recommendation:** The Committee may wish to wait for the conclusion of the on-going work by VICH, before taking up this matter again.

#### **Review of the status of other items in Annex 1:**

59. No comments received.



**Annex 1****Status of the proposals reviewed at the 17<sup>th</sup> session of the Committee**

The in-session Working Group, held during the 17<sup>th</sup> session of the Committee, had classified the proposals listed in document CX/RVDF 07/17/13 into four main categories:

- **Topics that should be taken up immediately for consideration by the Committee:** (B-1) Use of the Estimated Daily Intake (EDI) concept; (C-1) Utilization of Full ADI; (E-2) Starter Cultures; and (E-7) Appending Risk Management Recommendation(s), to MRLs.

- **Topics that the Committee should address in the future:** (B-2) Expression of Risk Assessment Results in Terms of MRLs; (B-4) Scientific evaluation; (B-5) Recommendations from the Joint FAO/WHO Technical Workshop on Residues of Veterinary Drugs without ADI/MRL (Bangkok, 24-26 August 2004): CCRVDF should develop a risk assessment policy that would allow extrapolation of risk assessments from species to species; and (C-3) Residues at Injection Sites.

- **Topics for which no further work was required:** (A). Substances recognised of toxicological concern; (B-5) Recommendations from the Joint FAO/WHO Technical Workshop on Residues of Veterinary Drugs without ADI/MRL (Bangkok, 24-26 August 2004): Recommendation to undertake work on a threshold of toxicological approach for residues of veterinary drugs; (C-2) Rounding of the ADI; (C-4) Definition of Good Agriculture Practices; (D-1) Risk Management Options; (D-2) ALARA (As Low As Reasonably Achievable); (E-1) Withholding Time Calculations; (E-3) Data Protection; and (E-6) Threshold of Toxicological Concern for Veterinary Drugs (CX/RVDF 07/17/13, para.83).

- **Topics for which further clarification should be provided at the next session of the Committee:** (B- 3) Use of Regional Consumption Factors); (E-5) Old Drug Policy; and (E-6) Threshold of Toxicological Concern for Veterinary Drugs (CX/RVDF 07/17/13, para. 85).