codex alimentarius commission

FOOD AND AGRICULTURE ORGANIZATION OF THE UNITED NATIONS

WORLD HEALTH ORGANIZATION

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Agenda Item 5 **CX/RVDF 03/4**
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JOINT FAO/WHO FOOD STANDARDS PROGRAMME

CODEX COMMITTEE ON RESIDUES OF VETERINARY DRUGS IN FOODS
Fourteenth Session
Arlington, Virginia, 4 - 7 March 2003

CONSIDERATION OF DRAFT MAXIMUM RESIDUES LIMITS FOR VETERINARY DRUGS

Comments submitted in response to CL 2001/49-RVDF, Part B; CL 2001/49-RVDF, Part C; CL 2002/32-RVDF and CL-2002/34 RVDF, Part A

1) COMMENTS SUBMITTED IN RESPONSE TO CL 2001/49-RVDF, PART B - DRAFT MAXIMUM RESIDUE LIMITS AT STEP 5 (ALINORM 03/31, APPENDIX V)

(Comments from Czech Republic, the United States and the European Community)

Czech Republic

Thank you for submission of the materials of Codex Committee (Alinorm 03/31). As regards the Proposed Draft Maximum Residue Limits for clenbuterol, deltamethrin, dicyclanil, melengestrol acetate and trichlorfon we agree with submitted proposal.

We also got acquainted with report on WHO activities related to antimicrobial resistance and we would appreciate if we were able to participate in the planned training course in Poland for laboratories of Central Europe. So if it is possible send us some more information please.

United States

The United States (U.S.) would like to offer the following comment on CL 2001/49-RVDF, Part B: *Matters for Adoption by the 50th Session of the Executive Committee of the Codex Alimentarius Commission at Step 5,* respectfully:

Draft Maximum Residue Limits at Step 5 (ALINORM 03/31, Appendix V)

The U.S. supports the adoption of all permanent MRLs now at step 5. The U.S. notes that the temporary MRLs for melengestrol acetate in cattle liver and fat were finalized by the 58th JECFA. The United States supports adoption of these MRLs. The U.S. also supports the adoption of the temporary MRL for trichlorfon (metrifonate) at step 5. The U.S. notes that trichlorfon is scheduled for re-evaluation by JECFA at its 60th meeting in February 2003. Commitments have been made to provide JECFA with the data needed to re-evaluate the toxicity of trichlorfon.

European Community

The European Community would like to make the following comments :

The MRLs proposed for clenbuterol for tissues at step 5 are higher than those established in the European Union (0.2 µg/kg compared to 0.1 µg/kg for muscle, 0.6 µg/kg compared to 0.5 µg/kg for liver and kidney). The total residues would amount to 101 % of the ADI using the values proposed by JECFA.

For the substances trichlorfon (metrifonate) and flumequine certain data will be submitted to JECFA by the European Agency for the Evaluation of Medicinal Products (EMEA).

Editorial comment :

In Annex V metrifonate is spelt incorrectly.

2) COMMENTS SUBMITTED IN RESPONSE TO CL 2001/49-RVDF, PART C (I) - DRAFT MAXIMUM RESIDUE LIMITS RETURNED TO STEP 6 (ALINORM 03/31, APPENDIX IV)

(No comments)

3) COMMENTS SUBMITTED IN RESPONSE TO CL 2002/32-RVDF - REQUEST FOR COMMENTS AT STEP 6 ON DRAFT STANDARDS AND RELATED TEXTS OF THE CCRVDF

(Comments from Canada Costa Rica, the United States and the European Community)

Canada

Clenbuterol

Canada would support the advancement of the draft MRLs for clenbuterol to Step 8 but only with the inclusion of the warning footnote.

Deltamethrin

Canada suggests the return of this MRL to Step 5 pending the re-evaluation of the toxicity data by JECFA.

Dicyclanil (Synonyms : CLIK, A-9568 B, CGA 183893)

Canada supports the advancement of this MRL to Step 8.

Trichlorfon (Metrifonate)

Canada suggests holding the MRL at Step 6 pending the re-evaluation of the toxicity data by JECFA.

Costa Rica

Clenbuterol (cattle tissues)

There have been some cases of human clenbuterol intoxication in Mexico. Therefore, more attention should be focuses on this compound in terms of proper use, its correct use, and the potential consequences of incorrect use should be clearly established.

United States

Clenbuterol (cattle tissues)

The U.S. supports the decision of the 13th CCRVDF and supports the advancement of these MRLs.

Deltamethrin

Deltamethrin is on the agenda for evaluation by the 60th JECFA in February, 2003. The U.S. will formulate its position following review of the JECFA evaluation.

Dicyclanil

Dicyclanil is on the agenda for evaluation by the 60th JECFA in February, 2003. The U.S. will formulate its position following review of the JECFA evaluation.

Melengesterol acetate

The United States does not support advancement of these MRLs. New information is available on the

structure and biological activity of melengesterol metabolites that occur in edible tissues. The United States supports a re-evaluation of the MRLs for melengesterol acetate by JECFA, taking into consideration this new information, which will be available for evaluation by JECFA in 2004.

Trichlorfon (Metrifonate)

Trichlorfon is on the agenda for evaluation by the 60th JECFA in February, 2003. The U.S. will formulate its position following review of the JECFA evaluation.

European Community

The European Community has to reiterate its reserve with regard to further advancement from Step 6 of the « Proposed Draft Maximum Residue Limits for Veterinary Drugs: Deltametrin, Dicyclanil, Melengestrol acetate and Trichlorfon (Metrifonate). The European Community has previously expressed concerns regarding these MRLs at the 13th session of CCRVDF regarding these substances. CCRVDF referred the substances Deltamethrin, Dicyclanil and Trichlorfon (metrifonate) back to JECFA for re-evaluation (paragraph 98 ALINORM 03/31). The European Community will also further reiterate its reserve regarding the advancement of the draft standard for Melengestrol acetate as part of the comments to CL 2002/34-RVDF.

The 13th session of CCRVDF agreed to add a footnote to the draft standard for Clenbuterol as follows: "Due to the potential for abuse of this drug, the MRLs are recommended only when associated with a nationally approved therapeutic use, such as for tocolysis or as an adjunct therapy in respiratory disease". The European Community is supportive this footnote.

4) COMMENTS SUBMITTED IN RESPONSE TO CL 2002/34-RVDF, PART A - REQUEST FOR COMMENTS ON RECOMMENDATIONS ON MAXIMUM RESIDUES LIMITS FOR VETERINARY DRUGS ARISING FROM THE 58TH MEETING OF THE JOINT FAO/WHO EXPERT COMMITTEE ON FOOD ADDITIVES

(Comments from the United States and the European Community)

United States

The United States is pleased to submit the response to CL 2002/34-RVDF, Part A (Recommendations on Maximum Residue Limits).

Ivermectin

The United States supports the final MRL for cattle milk recommended by the 58th JECFA and will support its final adoption at step 8.

The U.S. and JECFA ADI are identical and the TMDI does not exceed the ADI.

Cefuroxime

The United States does not support advancement of this MRL due to the temporary status of the ADI.

Chlortetracycline/Oxytetracycline/Tetracycline

The United States supports adoption of this MRL at Step 8.

Cypermethrin

The United States supports advancement of these MRLs.

Alpha-Cypermethrin

The United States supports advancement of these MRLs.

Dihydrostreptomycin/Streptomycin

The United States supports advancement of these MRLs.

Lincomycin

The United States supports adoption of the MRLs for cattle milk and tissues of pigs and chickens at step 8.

Melengesterol Acetate

The United States does not support advancement of these MRLs. New information is available on the structure and biological activity of melengesterol metabolites that occur in edible tissues. The United States supports a re-evaluation of the MRLs for melengesterol acetate by JECFA, taking into consideration this new information, which will be available for evaluation by JECFA in 2004.

European Community

The European Community would like to present the following comments to the recommendation on maximum residue limits for veterinary drugs arising from the 58th meeting of the Joint FAO/WHO Expert Committee on food additives. These comments relate to positions for draft MRLs for ivermectin for bovine milk (at step 5/8), cefuroxime (at step 3), oxytetracycline (at step 8), cypermethrin (at step 3), alphacypermethrin (at step 3), dihydrostreptomycin/streptomycin for milk (at step 3), lincomycin (at step 5/8) and melengestrol acetate (at step 5).

The maximum residue limits proposed for **dihydrostreptomycin/streptomycin** for cattle and sheep milk**, lincomycin** for pig and chicken tissues and **cypermethrin** for sheep provide for appropriate protection of consumer safety and are therefore acceptable.

The proposed maximum residue limits for the following substances can not be supported due reasons provided for each substance(1):

Ivermectin: No information is available on the ratio of marker to total residues in cows milk, which gives an unacceptable uncertainty to the estimation of the theoretical maximum daily intake. Furthermore, there is only limited information concerning residues in milk following different routes of administration and the information requested by the 54th JECFA meeting has not been provided. It is known that from published literature that ivermectin residues in milk are persistent and higher than the MRL proposed for a considerable period of time after administration.

Cefuroxime: The proposed draft MRL for milk do not take into consideration all microbiologically active residues and no reliable estimate can therefore be made of the relevant amount of residues in milk. The parent compound only represents a small part of the total residues with antimicrobial activity, although JECFA assumed, contrary to studies in the dossier (Fergusson and Batten, 1996), that cerfuroxime was the only microbiologically active residue. In addition, data on effects on starter cultures available to JECFA were not taken into account. The MRL proposed for milk has been shown to inhibit the acid production by commercial starter cultures. Finally, a clarification regarding the analytical method is required. It is stated in the JECFA report that the method had been validated according to existing criteria in the EU for drug registration, contrary to the evaluation in the EU, which had concluded that the same method was insufficiently validated.

Alphacypermethrin: Maximum residue limits for alphacypermetrin should be identical to those proposed for cypermethrin. Alphacypermethrin consists of the two most toxic isomers of cypermethrin and a lower ADI was consequently adopted for alphacypermethrin at the 47th meeting of JECFA. To employ different values for these two substances will lead to problems in residue surveillance and eventually in international trade.

Chlortetracycline/Oxytetracycline/Tetracycline: The maximum residue limits proposed for cattle, pigs, sheep, poultry, giant prawns and fish are not supported. The ADI adopted by JECFA is too high and not acceptable as it does not sufficiently take into consideration the uncertainties with the method employed to derive the ADI. A safety factor is necessary as the microbiological model study has not been validated and it is further assumed that no variation in the human population is possible as regards the selection of resistant Enterobacteriaceae strains for tetracyclines. The 4-epimer is also microbiologically active and it is considered necessary to include this substance in the marker residue.

Melengestrol acetate: Due to the non-availability of a dossier for this substance in the EU, no definite position can be taken on this substance. It is noted, however, that no analytical method for the monitoring of

residues is available and therefore further advancement of this substance is not supported. The substance was evaluated by JECFA partly for use as growth promotor, a use that is prohibited in the European Community.