CODEX ALIMENTARIUS COMMISSION E

Food and Agriculture Organization of the United Nations

World Health Organization

Viale delle Terme di Caracalla, 00153 Rome, Italy - Tel: (+39) 06 57051 - Fax: (+39) 06 5705 4593 - E-mail: codex@fao.org - www.codexalimentarius.org

Agenda Item 8b **CX/RVDF 15/22/9**

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JOINT FAO/WHO FOOD STANDARDS PROGRAMME

CODEX COMMITTEE ON RESIDUES OF VETERINARY DRUGS IN FOODS

Twenty-second Session

San José, Costa Rica, 27 April – 1 May 2015

ALTERNATIVE APPROACH TO MOVE COMPOUNDS FROM THE DATABASE ON COUNTRIES' NEED FOR MRLS TO THE JECFA PRIORITY LIST

(Report of the EWG on Countries' Needs for MRLs)

(Argentina, Australia, Brazil, Canada, Chile, Costa Rica, Dominican Republic, European Union, France, India, Italy, Jamaica, Lebanon, Mexico, New Zealand, Panama, Peru, Republic of Korea, Singapore, Thailand, United States of America, Uruguay, Asociation Latinoamericana de Avicultura, and IFAH)

Background

1. The work on a database of Countries' Needs for MRLs began in 2009 following the 18th Session of the Codex Committee on Residues of Veterinary Drugs in Foods (CCRVDF) in Natal, Brazil. The vision for the database was to collect requests and information from countries in need of MRLs for specific veterinary drugs. The purpose was to create a list could help find sufficient data to permit an evaluation by JECFA.

2. At the 21st Session of the CCRVDF in Minneapolis, Minnesota, USA, an alternative approach for the database was proposed. The approach starts with the identification of the needs for treatment of animal diseases, identification of drugs to treat these disease and identification of known health and/or trade problems associated with them (step 1). The following steps consist of the identification of the data gaps (step 2) and of alternative approaches to fill these data gaps to allow assessment by JECFA (step 3). The Committee requested FAO and WHO's advice for step 1 and established an electronic working group for steps 2 and 3. The Committee noted that this was a long-term activity and that it would be necessary that FAO and WHO complete their work to allow the electronic working group to start the subsequent steps. The Committee agreed to:

> *(ii) Establish an electronic working group, co-chaired by the United States of America and Costa Rica, and working in English and Spanish, to:*
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> - *Identify data availability and gaps for the veterinary drugs identified, taking the information in the database into account; and*
> - *Explore alternative ways to fill data gaps, and prioritize veterinary drugs for evaluation by JECFA.*

3. In addition to the FAO and WHO advice and the electronic Working Group, the Committee agreed to circulate the existing Database on Countries' Needs for MRLs as a circular letter to allow the existing requested veterinary drugs to be updated.

Proceedings of the electronic Working Group

4. The co-chairs of the electronic Working Group worked with FAO and WHO and developed questions for an electronic questionnaire to be sent to contact points in countries. The FAO and WHO agreed to begin with a pilot survey to determine if this approach would be effective in obtaining the needed information. If the pilot survey provides sufficient and useful information, it can be expanded to a global survey. The short questionnaire included the following questions:

i. Which veterinary drugs are used in your country for food producing animals?

ii. For which food producing species and for what purpose are these drugs recommended and/or used?

iii. Are the conditions of use (route of administration, dose, duration, frequency of use) for these drugs available?
Note: Information about the conditions of use, particularly as they may change around the world, are

important to allow an evaluation of the drug by the Joint Expert Committee on Food Additives (JECFA).

iv. What are the key animal disease that may impact food producing animals in your country or (sub)region?

v. What is the extent of use of these veterinary drugs in food animals, can you rank the drugs according to use from most to least used?

vi. What veterinary drugs are produced in the country?

5. While the FAO and WHO pilot survey was in progress, the electronic working group focused on the second part of the charge from the Committee, to explore alternative ways to fill data gaps.

6. The electronic Working Group worked through email in English and Spanish. The electronic working group focused discussion on several questions:

A. Could critical information on the pharmacokinetics of the veterinary drugs in that additional species and one or more of the previously evaluated species allow the JECFA to evaluate this additional species? Would a pharmacokinetic study provide this critical information?

B. Are there other approaches to developing that information? Could a systematic review of all available residue, metabolism, and pharmacokinetic information for this veterinary drug across multiple animal species equally resolve the critical information gap?

C. Are there other approaches that might help us provide JECFA with the critical information they need to perform the necessary scientific assessments?

D. Are there organizations that might be able to provide the funds to develop this critical information through contracts or grants? Are there national, regional – or private – organizations within your region that you might identify as a potential source?

7. Comments on the above questions were received from Chile, Costa Rica, Jamaica, Mexico, Panamá, Perú, Uruguay, and the United States of America.

8. The Database on Countries' Needs for MRLs was circulated as CL 2014/09-RVDF. In response to the circular letter, comments were received from Algeria, Chile, and Costa Rica. Additional comments were also received from El Salvador. The Database was updated based on these comments (CX/RVDF 15/22/10)..

9. The Database on Countries' Needs for MRLs currently contains 91 veterinary drugs from 18 countries.

Discussion

Question A. Could critical information on the pharmacokinetics of the veterinary drugs in that additional species and one or more of the previously evaluated species allow the JECFA to evaluate this additional species? Would a pharmacokinetic study provide this critical information?

10. Pharmacokinetic studies could provide partial information in most cases, but additional data would still be required. Extrapolating from species to species requires a higher level of risk and would require additional safety factors be applied. Pharmacokinetic studies may aid in extrapolating MRLs between similar species such as between ruminants, or extrapolating similar drugs in the same species. One country also noted that JECFA requires an approved use for any requested species and MRLs. Any extrapolation between species would still have to have an approved label from a country (dose, duration of dosing, withdrawal time, and formulation information). Questions were raised suggesting further discussion of the current requirement for an approved use in the species for which an MRL is sought may be warranted.

Question B. Are there other approaches to developing that information? Could a systematic review of all available residue, metabolism, and pharmacokinetic information for this veterinary drug across multiple animal species equally resolve the critical information gap?

11. A systematic review which focuses on gathering all available evidence to address the research questions gives a structured collection of all available evidence and evaluation of the information with a clear understanding of the confidence in that information and any known biases. If a systematic review is used, the literature included should be peer reviewed and of good quality. A systematic review could be used as a starting point but additional data would probably still be required. Meta-analysis can also help synthesize the results from multiple studies. Relying solely on literature does have some risks as publication bias may reduce the number of studies available with negative or contradictory results. One must consider similarity of research in animals and species considered in studies included in systematic reviews.

12. Data from regulatory agencies which conduct their own scientific assessments to establish MRLs may be available. JECFA could validate the studies and results used in the assessments performed by other government agencies.

Question C. Are there other approaches that might help us provide JECFA with the critical information they need to perform the necessary scientific assessments?

13. Once the data gaps are identified, we could negotiate with the pharmaceutical industry, universities or research organizations to see if they would fill the gaps with their own resources or with resources offered by interested governments. Government agencies may be able to provide the data that was used for registration in their countries with the legal permission of the pharmaceutical company. This is resource intensive. One country offered to provide information related to the analysis of veterinary drug residues in foods from animal origin as part of their National Residue Monitoring Program. Some of their data includes additional species such as goats, alpacas, llamas, and guinea pigs.

Question D. Are there organizations that might be able to provide the funds to develop this critical information through contracts or grants? Are there national, regional – or private – organizations within your region that you might identify as a potential source?

14. This depends on the type of information that is needed. Some international organizations such as FAO, WHO, IICA, or government agencies were identified and several countries identified potential funding sources in their countries for research. There are concerns as to whether funding would be available from many of these sources, whether the studies that could be conducted would be considered valid for a JECFA evaluation, and whether the veterinary drugs would be considered important to the specific regions where funding may be available. However individual sources of funding could not be further developed until priority veterinary drugs, and their corresponding data needs, could be identified.

Considering the results of the FAO/WHO pilot survey in light of the Database on Countries' Needs for MRLs (Co-Chairs discussion)

15. Before embarking on a global survey FAO/WHO suggested to first carry out a **pilot survey** in a limited number of countries to verify whether the proposed approach was effective in obtaining the needed information. The FAO and WHO successfully implemented a pilot survey for Latin America (Brazil, Argentina, Costa Rica, Paraguay), South Asia (Bangladesh, Bhutan, India, Nepal, Sri Lanka), Europe (Albania) Nigeria, Vietnam and one NGO. Additional information was made available through collaboration with OIE for India, Nigeria/Bangladesh, Panama, and Senegal.

The approach taken in the pilot survey was the following:

- A short questionnaire was sent to identified contact points (FAO and WHO regional/country officers as well as various stakeholders in each country) to ensure that more detailed and accurate information was collected, it was encouraged also a direct engagements/ consultations with different stakeholders in the country. This was primarily done by the FAO and WHO regional/country officers that facilitated this process.

16 The results of the pilot survey were shared with the electronic Working Group co-chairs, and due to time limitations were discussed by the electronic Working group co-chairs and the FAO and WHO secretariats.

17. The co-chairs found that preliminary examination of the results of the pilot survey complimented and extended the information available through the database on countries' needs.

18. The pilot survey uniquely provides information on disease issues across species and regions, suggesting the potential for pooling resources to address common needs and leverage data across a broader network of constituents.

19. Widespread information provided through the survey on national/regional good practices of veterinary drugs suggests the opportunity to make much more information related to the conditions of use available to the JECFA across a wide scope of national and climatic regions. Such information can inform the JECFA residue evaluation and MRL recommendation.

20. More than 40 veterinary drugs were identified in the Database on Countries' Needs for MRLs that were not included in the results of the pilot survey; this finding underscores the importance of implementing a larger global survey through FAO and WHO.

Recommendations

21. The electronic Working Group recommends that the Committee continue to develop and maintain the Database of Countries' Needs for MRLs through a circular letter.

22. The electronic Working Group identified potential approaches by which data-gaps may be addressed to inform JECFA evaluation of veterinary drugs with the goal of recommending MRLs to CCRVDF for residues in food.

23. The co-chairs of the electronic Working Group recommend that CCRVDF support the implementation of the full global survey with the goal of reporting the results to the 23rd CCRVDF. Recognizing that any comprehensive survey is resource intensive, it is recommended that the Committee discuss with the FAO and WHO secretariats the best way to implement the comprehensive global survey.

24. The co-chairs further recommend that the 23rd CCRVDF then establish an electronic Working Group to consider the results of the FAO and WHO survey, to identify priority veterinary drugs, and to identify data gaps for a successful JECFA evaluation of the priority veterinary drugs that could be filled as well as recommend approaches to obtain the needed data.