

CODEX ALIMENTARIUS COMMISSION



Food and Agriculture
Organization of the
United Nations



World Health
Organization

E

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

Agenda Item 2

CX/EXEC 21/81/2 Add.1
September 2021

JOINT FAO/WHO FOOD STANDARDS PROGRAMME EXECUTIVE COMMITTEE OF THE CODEX ALIMENTARIUS COMMISSION Eighty-first Session

CRITICAL REVIEW - PART II (CCRVDF25)

Note: For general information about the critical review and the critical review for CCGP32, CCSCH5, CCCF14, CCMAS41 and CCFICS25, see CX/EXEC 21/81/2.

Structure

1. General information on the Committee and Session
2. Overall comments (Secretariat / Chairperson)
3. Status of work items (Overview)
4. Specific comments on individual work items (Secretariat / Chairperson)

1. General

Committee	Codex Committee on Residues of Veterinary Drugs in Food (CCRVDF)		
Host	United States of America	Chairperson	Dr Kevin Greenlees
Session reported on	CCRVDF25	12 - 20 July 2021	
Next Session	CCRVDF26	2023 (TBC)	
Report	REP21/RVDF		

2. Overall comments

Secretariat's comments:

Due to the COVID-19 pandemic, the session had been postponed twice from the originally scheduled dates in 2020. CCRVDF25 was successfully conducted as a virtual session and had high participation, both in number of delegations and number of participants. The session was overall productive and generally work is on time. However, the Committee was unable to reach consensus on a major item that has been on the agenda of CCRVDF since 2012 (MRLs for zilpaterol hydrochloride) despite many attempts and various approaches to facilitate consensus including addressing the issue in a pre-session webinar. CCEXEC recommendation and CAC decision is sought on how to resolve the deadlock.

Cooperation between CCRVDF and CCPR has proven important and fruitful and is further encouraged. CCEXEC advice on a mechanism for cooperation between CCPR and CCRVDF on establishment of harmonized MRLs for dual use compounds is sought.

Chairperson's comments:

CCRVD25 was the first all-virtual meeting for this Committee. The virtual venue had mixed impact; participation by the international community was at an all-time high offering increased transparency and global contribution. The virtual venue facilitated a briefing by Dr. Park of the Republic of Korea, Chair of TFAMR providing CCRVD25 with an update on the task force's progress. The presentation by Dr. Park was particularly relevant for the later plenary discussion on the draft MRLs for Halquinol discussed below. The decreased time available, and the limited time window to allow global participation, impacted the opportunity for plenary discussion. Technical difficulties on day one was resolved in subsequent days and participants of CCRVD25 were extraordinarily helpful in working to meet our time constraints. That said, those constraints still impacted the meeting.

The Committee has developed and maintains a database that identifies veterinary drugs that Members feel need standards, those Members supporting such standards, and other relevant information to assist the global community in leveraging data. The Committee launched and evaluated a pilot for simultaneous review of a veterinary drug by competent national authorities and JECFA, to reduce the time needed for development of a Codex Standard. An approach for extrapolation has been adopted to leverage JECFA risk assessments, and Codex standards for those species and tissues less common in international trade. CCRVD25 reached out to CCPR to parallel the similar efforts between JECFA and JMPR to leverage the available data for compounds with dual use as a veterinary drug and pesticide. Together these efforts reflect an intentional strategy to facilitate the development of MRLs for residues of veterinary drugs found in the international food trade. All of this reflects intense effort by CCRVD25 members – in some cases particularly with the assistance of some observer organizations – and a flexible, problem solving approach to risk management. The Committee was also able to advance MRLs for flumethrin, diflubenzuron, halquinol, and ivermectin. The Committee was not, however, able to reach consensus to either advance or retain the proposed MRLs for zilpaterol and this is discussed at length in item 8 with the Zilpaterol HCL MRLs discussion, and item 13 for issues impacting CCRVD25's ability to efficiently perform its work.

3. Status of work items

Topic	Job No	Target year	Recommendation of the Committee
For decision by the Commission			
1. MRL for flumethrin in honey			Adoption at Step 8
2. MRLs for diflubenzuron (salmon - muscle plus skin in natural proportion)		2021	Adoption at Step 5/8
3. MRLs for halquinol (swine - muscle, skin plus fat, liver and kidney)		2021	Adoption at Step 5/8
4. MRLs for ivermectin (sheep, pigs, and goats - fat, kidney, liver and muscle)		2021	Adoption at Step 5
5. Amendment to the <i>Glossary of Terms and Definitions (Residues of Veterinary Drugs in Foods)</i> (CXA 5-1993): Definition of edible offal		2021	Adoption
6. Priority list of veterinary drugs for evaluation or re-evaluation by JECFA			Approval
7. Amendment to the Procedural Manual, Risk Analysis principles applied by CCRVD25: Approach for the extrapolation of MRLs for veterinary drugs to one or more species			Adoption

For monitoring	
8. MRLs for zilpaterol hydrochloride (cattle fat, kidney, liver, muscle)	CCEXEC is requested to provide a recommendation on the way forward in the framework of the critical review and to inform a CAC decision on the path forward for the MRLs in the Codex step process
For information	
9. Discussion paper on the principles and approach for parallel review of a new veterinary drug by JECFA and national regulatory agencies.	To keep as a reference for CCRVDF to identify new compounds for which MRLs could be developed in parallel between JECFA and national regulatory agencies as part of the process of the priority list of veterinary drugs for evaluation/re-evaluation by JECFA
10. Database on countries' needs for maximum residue limits for veterinary drugs in foods.	To be issued as an information document at every session of CCRVDF to support comments/consideration on the priority list of veterinary drugs for evaluation/re-evaluation by JECFA
11. Mitigation of trade impacts associated with the use of environmental inhibitors in agriculture	For information/consideration in the future as needed
12. Joint FAO/WHO expert meeting on carry-over in feed and transfer from feed to food of unavoidable and unintended residues of approved veterinary drugs.	Update
13. Issues and concerns that impact the ability of CCRVDF to efficiently perform its work	Ongoing. Not discussed at this Session due to lack of time.

4. Specific comments

1. Maximum residue limit for flumethrin in honey, paragraph 39, Appendix II.
<p>Status:</p> <p>CAC41 (2018) had adopted the MRL “is unnecessary” for flumethrin in honey at Step 5. This is considered a risk management decision considering the amount of residue of flumethrin that could be expected, which was very low or undetectable and represented a very low risk to human health.</p> <p>CCRVDF25 agreed to advance the MRL as “unnecessary” for flumethrin in honey to CAC44 (2021) for adoption at Step 8.</p>
<p>Chairperson’s comments:</p> <p>There was broad support by CCRVDF for advancement of the flumethrin MRL to CAC44.</p>
2. Maximum residue limits for diflubenzuron (salmon - muscle plus skin in natural proportion), paragraph 43, Appendix II.
<p>Status:</p> <p>The MRL proposal arose from JECFA88 (2019) evaluation and was forwarded to CCRVDF for consideration at Step 4 following circulation for comments at Step 3.</p> <p>There was consensus in CCRVDF25 supporting advancement of this MRL.</p> <p>CCRVDF25 agreed to forward the MRLs for diflubenzuron (salmon - muscle plus skin in natural proportion) to CAC44 (2021) for adoption at Step 5/8.</p>

<p>Chairperson's comments:</p> <p>None.</p>
<p>3. Maximum residue limits for halquinol (swine - muscle, skin plus fat, liver and kidney), paragraph 50, Appendix II.</p>
<p>Status:</p> <p>The MRL proposals arose from JECFA88 (2019) evaluation and was forwarded to CCRVDF for consideration at Step 4 following circulation for comments at Step 3.</p> <p>Delegations generally supported the advancement of the MRLs underlining that the proposed MRLs meet all the procedural and the scientific requirements required for advancement to final adoption by CAC and is in line with conclusions and recommendations of JECFA88 (2019). However, several Members expressed their reservation on the establishment of MRLs for halquinol since the compound was indicated for treatment of diarrhea and for growth promotion in some countries and the latter use was of concern.</p> <p>CCRVDF agreed to forward MRLs for halquinol (swine - muscle, skin plus fat, liver and kidney) to CAC44 (2021) for adoption at Step 5/8.</p>
<p>Chairperson's comments:</p> <p>Halquinol is an antimicrobial veterinary drug with particular applicability to the treatment of bacterial enteritis in swine. It is not a medically important antimicrobial for use in human medicine. The veterinary drug is registered for use by some members, and residues of the drug may be anticipated in food in international trade. JECFA88 (2019) evaluated halquinol, and established health guidance values for the human diet (ADI) and recommended MRLs. During the CCRVDF25 plenary discussion, concern was raised by some members because there are registered uses for halquinol as a production tool (growth promotion) in some countries and those members expressed concern that such uses were inappropriate for an antimicrobial veterinary drug and inconsistent with practices to limit the spread of antimicrobial resistance.</p> <p>It is notable, given the discussion that followed for zilpaterol (Agenda Item 6.2) where the same members took the opposite position, that the EU, Norway, Switzerland and Egypt expressed reservations for the advancement of MRLs for halquinol because of concern for its production uses, but did not object to advancing the MRLs. Similarly, the United Kingdom expressed concern for production uses of halquinol, noting that such uses were counter to domestic legislation, without objecting to advancement of the standard. These positions were entirely consistent with paragraph 4 of the Statements of Principle.</p>
<p>4. Maximum residue limits for ivermectin (sheep, pigs and goats – fat, kidney, liver and muscle), paragraph 59, Appendix II.</p>
<p>Status:</p> <p>The MRL proposals arose from JECFA88 (2019) evaluation and was forwarded to CCRVDF for consideration at Step 4 following circulation for comments at Step 3.</p> <p>Delegations generally favored the advancement of the MRLs in the Step Procedure. However, there were split in views as to advance the MRLs for final adoption at Step 5/8, or for adoption at Step 5.</p> <p>CCRVDF agreed to forward the proposed MRLs for ivermectin (sheep, goats, pigs – fat, kidney, liver, and muscle) to CAC44 (2021) for adoption at Step 5.</p>
<p>Chairperson's comments:</p> <p>Ivermectin is an antiparasitic veterinary drug for which Codex standards have been established a number of food producing animals. In response to a request from CCRVDF24 (2018), JECFA 88 (2019) proposed MRLs for fat, kidney, liver and muscle for sheep, pigs, and goats, and CCRVDF25 discussed these MRLs at Step 4. The EU provided a concern form on the basis that the proposed MRLs used a small fraction of the available Acceptable Daily Intake (ADI), were considerably lower than the MRLs established in the EU, and based on longer withdrawal periods; consequently there was concern that animal products containing residues resulting from registered uses following Good Veterinary Practices (GVP) in the EU may exceed the proposed MRLs, while still being safe for the human consumer. No data were provided to support the</p>

concern; however data were promised to allow the JECFA to evaluate residues resulting from GVP according to registered use in the EU, and to consider re-evaluation of the proposed MRLs.

It is notable that data supporting residues following GVP were only provided by two members for the JECFA88 (2019) evaluation. This experience highlights the importance of members responding to the JECFA calls for data in a timely manner so that the data are available to inform the JECFA risk assessment rather than waiting until proposed MRLs are available for discussion in CCRVDF. CCRVDF's risk management practice is to establish MRL's according to the As Low As Reasonably Achievable (ALARA) principle, and no higher than necessary considering GVP. Considering the variety of climatic conditions, agricultural practices, breed differences, etc., it is reasonable to expect such residue data would vary on a global basis. It is important that members respond to JECFA calls for data to ensure that conditions in their country or region are taken into account during the risk assessment process.

Arguments were proposed that the MRLs should be advanced to CAC at Step 5/8 to provide a safe standard for ivermectin residues in sheep, pigs, and goats for international trade, and to adjust those MRLs if needed following the JECFA evaluation. However, consensus could not be reached on this approach and it was agreed to forward the MRLs to CAC44 at Step 5, recognizing that the MRLs might require adjustment based on the pending availability of data and JECFA review. This approach means that an MRL to protect consumers and ensure fair practices in international trade will not be available for at least another 2 years, while products containing the compound remain in international trade and in consumption by the public.

5. Amendment to the *Glossary of Terms and Definitions (Residues of Veterinary Drugs in Foods)* (CXA 5-1993): Definition of edible offal, paragraph 116(i), Appendix IV.

Status:

The proposed definition had been developed in cooperation between CCPR and CRVDF through the parallel work between the CCRVDF/EWG on edible offal and the CCPR/EWG on the revision of the *Classification of Food and Feed* (CXA 4-1989) for the purpose of harmonization of terms to facilitate the establishment of single MRLs for compounds with dual uses.

In order to better describe the situation where skin is considered as edible offal, CCRVDF agreed to amend the definition by indicating that edible offal comprises those parts of the animal considered fit for human consumption apart from the skeletal muscle, fat and attached skin and to incorporate this definition in the *Glossary of Terms and Definitions* (CXA 5- 1993).

CRVDF agreed to forward the definition of edible offal as amended by the Committee for inclusion in the *Glossary of Terms and Definitions* (CXA 5-1993) to CAC44 for adoption.

CCRVDF25 further recommended that CCPR adopt the same definition for consistency and facilitation of establishment of MRLs for compounds with dual purposes, and to re-establish the EWG, chaired by Kenya and co-chaired by New Zealand, to work in parallel with the CCPR/EWG-Classification on issues pertaining to harmonization of edible offals (see also CCPR Critical Review).

Chairperson's comments:

Kenya, as Chair of the Electronic Working Group (EWG), has provided extraordinary efforts in outreach to CCPR to discuss harmonization of the approach of the two committees to edible offal. The EWG has developed a list of widely consumed and frequently traded edible offal tissues to guide JECFA in the risk assessment of veterinary drugs for these tissues, developed and discussed with CCPR a definition for edible offal, and identified additional issues for further discussion between the two committees. CCRVDF25 agreed to forward a definition of edible offal for inclusion in the *Glossary of Terms and Definitions* (CXA 5-1993) to CAC44 for adoption and to reestablish the EWG, chaired by Kenya and co-chaired by New Zealand to work in parallel with the CCPR EWG on classification of additional issues of harmonization for edible offal.

6. Priority list of veterinary drugs requiring evaluation or re-evaluation by JECFA, paragraph 150 (i), Appendix VI (Parts I and V).

Status:

CCRVDF25 decided to:

- include imidacloprid, ivermectin and nicarbazin on the priority list for approval by CAC
- remove fipronil from the priority list

- extrapolate MRLs for ivermectin in goats and sheep milk for approval by CAC
- retain amoxicillin, ethoxyquin and norfloxacin on the priority list; noting that data availability would be confirmed by the next session of CCRVDF
- note that ethion, flumethrin and fosfomycin will remain on the JECFA agenda to complete the evaluation pending additional data/information

CCRVDF25 agreed to forward the priority list of veterinary drugs as amended to CAC44 for approval as per compounds listed in the first and third bullet points.

Other matters:

Cooperation between CCPR and CCRVDF (see also edible offal)

CCRVDF25 agreed to request CCEXEC advice on a mechanism for cooperation between CCPR and CCRVDF on establishment of harmonized MRLs for compounds with dual uses.

Establishment of action levels for residues of approved veterinary drugs in non-intended edible tissues

See Expert Meeting on Carry-Over and decisions taken by CCRVDF25 in relation to the revision of the COP/AF and the establishment of Action Levels.

Chairperson's comments:

Recalling the discussion on carryover under Agenda Item 3.2, CCRVDF 25 agreed to establish an EWG, chaired by Australia, and co-chaired by Canada, to prepare a discussion paper on the possible requirements or criteria for developing tolerance levels or action levels for residues of veterinary drug in feed and in animal tissues as a result of the unavoidable carryover of residues in animal feed. The Committee further agreed to use nicarbazin as a case study.

Fipronil was removed from the Priority List as the sponsor decided to withdraw the compound. The rationale provided was that as fipronil was also being re-evaluated by JMPR, Brazil, the sponsoring member, would wait on that outcome.

However, conversations with industry suggest that the process in CCRVDF to advance MRLs is increasingly seen as unpredictable and often objections and concerns often not based on science or data. In addition, sponsors have questioned the value of submitting compounds that are subsequently subject to plenary objection and debate in CCRVDF based on arguments and factors that are not based on food safety and are outside of the mandate of Codex. Such perceptions pose a significant problem for the development of Codex standards to protect the human consumer.

7. Amendment to the Procedural Manual, Risk Analysis principles applied by CCRVDF: Approach for the extrapolation of MRLs for veterinary drugs to one or more species, paragraph 105(i,ii), Appendix III.

Status:

CCRVDF25 discussed the work done in the EWG on extrapolation of MRLs to one or more species including a pilot on extrapolation of MRLs identified in Part D of the priority list and the outcomes and recommendations in the discussion paper.

CCRVDF25 agreed to forward the approach for extrapolation as revised to CAC44 for adoption and inclusion as Annex C to the Risk Analysis Principles applied by CCRVDF.

CCRVDF25 also agreed to include a footnote in paragraph 30, 2nd bullet point of the principles, with the following text: "The approach for extrapolation of MRLs for veterinary drugs to one or more species is presented in Annex C to these principles" as a consequential amendment for adoption by CAC44.

CCRVDF25 further agreed to re-establish the EWG, chaired by the European Union and co-chaired by Costa Rica, and Uganda, to further discuss the extrapolated MRLs taking into account the comments received and prepare a revised proposal for consideration by CCRVDF26 as needed as well to prepare a suitable approach for extrapolation of MRLs for edible offal.

Chairperson's comments:

CCRVDF24 established an EWG, chaired by the EU, to develop a discussion paper on extrapolation of maximum residue limits in one or more species. Part of the charge to the group was to include a pilot on

extrapolation for MRLs identified in Part D of the CCRVDF priority list. The EWG completed its work and prepared a report prior to CCRVDF25. To encourage further discussion and to inform the anticipated CCRVDF25 plenary, an informal on-line discussion (open to all members) on the Codex Forum was held and consequently a revised proposal and report was prepared. Following a robust plenary discussion, the proposal contained in Conference Room Document 3 (CRD3) was revised and accepted. CCRVDF25 agreed to forward this approach to CAC44 for adoption and inclusion as Annex C to the Risk Analysis Principle applied by CCRVDF, with a footnote pointing to the actual approach in Annex C of the principles.

Due to the time constraints of a virtual meeting, the proposed extrapolated MRLs were not discussed, and the EWG was re-established, chaired by the EU and co-chaired by Costa Rica and Uganda. It is notable that Costa Rica offered to assist in providing Spanish translations, allowing the EWG to work in both English and Spanish. This is not the first time that a member has stepped up to assist the host country to allow EWGs to be conducted in more than one language and is a notable model for member participation within the committee.

The EWG was further charged to consider the extrapolation of MRLs for ivermectin in goat and sheep milk.

8. Maximum residue limits for zilpaterol hydrochloride (cattle fat, kidney, liver, muscle), paragraph 87, Appendix II.

Status:

The development of MRLs for zilpaterol has been discussed in CCRVDF since 2012 and been held at Step 4 by CCRVDF since 2016. To help the discussion at CCRVDF25, the outcomes of the JECFA78 (2013), JECFA81 (2015) and JECFA85 (2017), and the history of the discussions on zilpaterol in CCRVDF, CCEXEC and CAC had been summarized in CX/RVDF 21/25/7 including the ongoing discussions in CCEXEC and CAC on the implementation of the Statements of Principle and development of practical guidance for such implementation.

The delegations discussed at length the issue and the various arguments for and against the advancement of the MRLs for zilpaterol were presented extensively. The issue remained very polarized with two blocks unable to find agreement.

Despite many efforts, CCRVDF25 was unable to reach consensus of advancing the MRLs to either Step 5 or 5/8 nor to retain them at Step 4. CCEXEC81 is therefore requested to provide a recommendation on the way forward in the framework of the critical review and to inform a CAC decision on the path forward for the MRLs in the Codex step process.

Chairperson's comments:

Background

Zilpaterol HCl is a beta receptor agonist drug and used to improve cattle production in a number of member countries (affecting rate of weight gain, feed efficiency and carcass leanness). Zilpaterol was proposed for evaluation by JECFA at the 20th CCRVDF (2012) meeting. The Committee was extraordinarily divided over that proposal and unable to reach consensus. The CCRVDF23 Chair at the time, Steven Vaughn, brought the issue to the 35th Commission (2012), noting that the veterinary drug met all of the Committee's criteria for such an evaluation. The 35th Commission agreed, and the veterinary drug was forwarded to the 78th JECFA. Zilpaterol HCl has been evaluated by the 78th (2013), 81st (2015) and 85th (2017) JECFA; an ADI and Acute Reference Dose (ARfD) have been established and MRLs for muscle, liver, and kidney of cattle have been recommended by JECFA.

During CCRVDF24 (2018) the Chair Kevin Greenlees, noted consensus on the robustness of the JECFA risk assessment and the safety of the proposed zilpaterol MRLs however the committee was unable to reach consensus on advancing the MRLs for zilpaterol HCl in cattle for reasons inconsistent with Codex Procedural Manual Statements of Principle Concerning the Role of Science in the Codex Decision Making Process and the Extent to Which Other Factors Are Taken Into Account. While the Codex Secretariat discussed and explained paragraph 4 of the Statements of Principles, none of the members against advancing the zilpaterol standard were in agreement to abstain from acceptance of the standard without preventing it to continue through the Codex step process. The Chair requested guidance from CCEXEC75 (2018) and the 41st Commission (2018) on what to do when consensus was unable to be achieved due to arguments outside of the Codex mandate. CCEXEC75 took up the issue and agreed to continue discussion

at CCEXEC77 (2019), which would be facilitated by a report, prepared by the Codex Secretariat, the CAC Bureau and the legal counsels of FAO and WHO. CCEXEC77 discussed the issues and the report, History and Implications of The Fourth Paragraph of the Statements of Principle prepared by the Codex Secretariat. CCEXEC broadly affirmed the role of science in establishing Codex standards and established a sub-committee of the CCEXEC on the application of Statements of Principle Concerning the Role of Science. However, despite the intervening 3 years and the 5 CCEXEC meetings that have occurred during that period, the guidance requested from the CCEXEC remains unavailable to CCRVDF.

CCRVDF25 (2021)

In the three years intervening between CCRVDF24 and CCRVDF25 there has been no progress towards agreement within the committee on standards (MRLs) for zilpaterol HCl in cattle. Prior to CCRVDF25, I met with representatives from CCLAC, UK, USA, Japan, CCAFRICA, EU, and representatives from N. Africa and the Near East, some more than once. While my discussions covered the breath issues for the coming CCRVDF25 meeting, zilpaterol was always a key part of those conversations.

Taking advantage of our virtual platforms, with the support of the Codex Secretariat we held two webinars as a prelude to discussions in CCRVDF25, with zilpaterol HCl standards featuring prominently in the second webinar of the series. The Codex Secretariat prepared a comprehensive history and background of the zilpaterol discussions (CX/RVDF 21/25/7), using text taken en-bloc from the reports of CCRVDF, CCEXEC, CAC, and JECFA. This document presented an impartial fact-based the history and issues to CCRVDF25.

CCRVDF24 (2018) expressed a clear consensus that the JECFA risk assessment for zilpaterol HCl was robust and complete, and that the proposed MRLs posed no human health concerns. At CCRVDF25 (2021) the explicit question was asked by the Chairperson whether there were any new data/information that would call into question the safety of the proposed MRLs; no participants intervened in response to provide such information.

During CCRVDF25, there continued to be a broad consensus regarding the safety of the zilpaterol MRLs for muscle, liver and kidney of cattle expressed in the interventions from the Members during the discussion. Consensus does not necessarily mean unanimity, and during the extended discussions one Member, and one observer expressed strongly held concerns for the safety of residues of zilpaterol HCl in food. However, neither provided published nor unpublished studies or offered any data that could inform CCRVDF as risk managers, or JECFA as risk assessors, on these concerns.

Some members expressed concern for the safety of edible tissues other than the muscle, liver, and kidney for which MRLs are proposed. Similarly, there was some concern expressed that dietary consumption patterns among some Members were not taken into account by the JECFA assessment. Some concerns were expressed for the potential for combined effects of multiple residues, including zilpaterol, in the diet. No published or unpublished studies were offered or provided to inform CCRVDF as risk managers or JECFA as risk assessors regarding these concerns.

Those Members in favor of advancing the MRLs for zilpaterol, either to step 5/8 or to step 5 pointed to the detailed explanations provided for this position in CCRVDF24 (2018) and provided considerable further detail during CCRVDF25. They presented interventions that included that the work of CCRVDF was based on scientific principles consistent with the risk analysis principles in Codex procedures, that CCRVDF24 recognized and supported the robust JECFA risk assessment and the safety of the proposed MRLs, that no new scientific information or data had been provided relevant to the safety of zilpaterol, and that many countries who had not registered zilpaterol for domestic use nonetheless supported development of international standards whether to facilitate international trade or to assist countries where national capacities were insufficient to perform their own risk assessments, and that in not advancing this work CCRVDF compromises the role of Codex.

Those Members against advancing the MRLs for zilpaterol HCl pointed to the detailed explanation of their concerns provided in CCRVDF24. These concerns were also well-articulated and included that veterinary drugs should not be used for non-therapeutic purposes in food producing animals, such compounds should not be used because of concern for animal welfare, adopting MRLs would signal acceptability of such use, and support for the MRLs could not be provided by some countries because zilpaterol is not authorized in that country.

Each of these arguments, while eminently appropriate for domestic regulation of veterinary medicinal products, fall outside of the Statement of Principles, and some, such as what is or is not an appropriate use of a veterinary drug, or issues of animal welfare related to the use of the veterinary drug, fall outside of Codex and within the authority of competent national authorities domestically, and OIE, internationally.

I am particularly concerned about the increasing stridency of arguments provided in this meeting that are based on a veterinary drug not being approved for use by a given Member as a basis for objecting to advancement of an international Codex standard for the safety of residues of that drug in food. In addition to falling outside of those bases identified in the Statements of Principle (not accepted on a worldwide basis, not reflecting safety to the human consumer, or impact on the international food trade) such arguments, if taken to their logical conclusion, would prevent progression of MRLs for most, if not all, veterinary drugs (and pesticides) as many countries especially developing countries do not establish MRLs until one is established by Codex. The independent JECFA risk assessment and Codex step process offers a solution when there are differing or divergent national MRLs and / or when products are in international trade but no MRL has been established as is the case for zilpaterol. By not establishing an MRL, Codex is failing to protect consumers as products are already in international trade with a recognized international standard

Those Members opposed to advancing the MRLs for zilpaterol HCl were asked by the Chairperson, the Codex Secretariat, and other Members in attendance to follow paragraph 4 of the Statements of Principle, and, if desired, record a reservation against the advancement of the standard while not opposing it. No Members opposing advancing the standard agreed to that approach.

CCRVDF has a specific problem with the development of standards (MRLs) for zilpaterol HCl in cattle (muscle, liver, and kidney). However, this problem reflects a larger concern for Codex as a whole and its inability to adopt standards for products already in international trade and that are required by developing countries to protect their population, when developed countries object based on issues outside of the Codex mandate, resulting in trade barriers and hindering the ability of countries who do want the product to protect consumers.

The Codex Procedural Manual clearly defines veterinary drugs, and maximum limits for veterinary drugs, such that there is no distinction between intended uses. Indeed, Codex has a history of developing standards for veterinary drug residues resulting from production uses, most notably for natural and artificial hormone products.

The consistent objection to advancing standards, when those objections are not based on safety to the consumer, international trade, and rely on factors such as whether or not the product is registered for use domestically, thrust at the heart of Codex principles and exceed the ability of any technical committee to address. As noted in my report to CCEXEC75 (2018), there is no question that all sides are bringing deeply held beliefs to the table. While not discussed in detail above, those supporting the advancement of the MRLs for zilpaterol emphasize the robustness of the science supporting the safety of the proposed standards, the importance of such Codex standards for safety of food in international trade, and the importance of adherence to sound science and to the procedures outlined in the Procedural Manual. They emphasize that the concerns against advancing the MRLs clearly fall outside of Codex procedures, and in doing so can adversely impact human public health and fair-trade practice, and that those expressing those concerns are unwilling to abstain from acceptance of the zilpaterol standard without preventing a decision by the Committee, threatens the future and relevance of Codex as a standard setting body.

Conclusion

In conclusion, zilpaterol HCl has registered use among a number of Codex Members. Food containing residues of zilpaterol HCl may be found in international trade. Data were provided and JECFA has completed a robust risk assessment, established health-based guidance values (ADI and ARfD) and proposed draft MRLs. There is a broad consensus by CCRVDF on the robustness and acceptability of the JECFA risk assessment. The European Food safety Agency (EFSA) reviewed the JECFA88's evaluation of zilpaterol assessed the available scientific literature. EFSA concluded that "In general, the approach followed by JECFA for setting MRLs for zilpaterol appears to be scientifically robust" and even though animal welfare is outside the purview of Codex it is important to note that EFSA decided that despite some reports of increased mortality, heart rate, and respiration rate in cattle "The observed effects in cattle could not be directly linked with the administration of zilpaterol at the recommended dose levels." (EFSA Journal 2016;14(9):4579).

Yet due to factors outside the Statements of Principle Concerning the Role of Science in the Codex Decision Making Process and the Extent to Which Other Factors Are Taken Into Account (reflecting the decisions of the 21st and 24th Commissions), CCRVDF is unable to reach agreement to advance the standards for this veterinary drug. Indeed, positions on both sides of the discussion have firmed to the point that the Committee cannot reach agreement to advance the standard to step 5/8 to recommend finalization by the Commission, to step 5 for that allows for further discussion by CCRVDF, or even to retain it at step 4. In addition to offering guidance on the particular question of standards for zilpaterol HCL in cattle, it is imperative that CCEXEC and the Commission use tools such as the report on paragraph 4 of the Statements of Principle, developed following CCEXEC75, and the implementing guidance on the implementation of the Statements of Principle anticipated by the subcommittee established by CCEXEC77 to address these issues that threaten Codex as a standard setting body.

9. Discussion paper on the principles and approach for parallel review of a new veterinary drug by JECFA and national regulatory agencies, paragraph 122, Appendix V.

Status:

The EWG had considered advantages and disadvantages of a parallel approach to compound evaluation based on experience at country level as well as inputs from JECFA. The paper outlined the key principles (transparency, confidentiality and independence) that should be followed when undertaking a parallel evaluation and a three-phased process for consideration by CCRVDF. It was noted that this process would shorten time for the establishment and adoption of MRLs from 6 - 9 years as opposed to the current situation of 9 – 12 years.

CCRVDF25 noted the significant advantages shown by the pilot especially with regard to the speed with which Codex MRLs could be developed and that the current prioritization criteria as set out in the Risk Analysis Principles applied by CCRVDF effectively already allowed for such a process.

CCRVDF25 agreed to encourage future compounds that might take advantage of this process and to keep the discussion paper on the principles and approach for parallel review of a new veterinary drug by JECFA and national regulatory agencies available as a reference for the Committee.

Chairperson's comments:

The report of the EWG, chaired by Canada, was discussed in detail during CCRVDF25, as was the experience of JECFA88 with the pilot in parallel review using selamectin. While selamectin is still undergoing review for registration by a member country, JECFA88 was able to successfully complete the toxicological evaluation for the establishment of an ADI and ARfD and provide comment on the information still required to allow a robust evaluation of residues for the recommendation of MRLs. CCRVDF25 noted that the approach has the potential to considerably shorten the development of standards for residues of veterinary drugs in food while noting the importance and impact of the GPVD developed for registration by the member country on the proposed MRLs. CCRVDF25 agreed that the current prioritization criteria for veterinary drugs allowed for this approach, to encourage future compounds to take advantage of the approach when appropriate, and to retain the discussion paper on the principles and approach for parallel review of a new veterinary drug by JECFA and national regulatory agencies as a reference for the committee.

10. Database on countries' needs for MRLs for veterinary drugs in foods, paragraphs 126-128.

Status:

CCRVDF25 concurred with the recommendations for the further steps on the use and maintenance of the database on countries' needs for MRLs for veterinary drugs in foods as presented to them.

CCRVDF noted that the United States of America as Host Country of CCRVDF and Costa Rica would continue to maintain and update the database on countries needs as necessary. CCRVDF agreed to recommend that the database on countries' needs for MRLs for veterinary drugs in foods be made available at every session of CCRVDF; and should be available to the Codex Secretariat to accompany the distribution of the Circular Letter requesting comments on the priority list of veterinary drugs for evaluation by JECFA.

CCRVDF further agreed to recommend encouraging Codex Members and observers to submit relevant data/information to allow the evaluation of those compound/commodity combinations identified as high

priority needs and as feasible starting points for establishment of relevant MRLs, as well as other compound/commodity combinations identified in the database on countries' needs for MRLs for veterinary drugs.

Chairperson's comments:

None.

11. Mitigation of trade impacts associated with the use of environmental inhibitors in agriculture, paragraph 151.

Status:

CCRVDF25 was briefly informed about the growing interest in agricultural products that inhibit the development and progression of adverse environmental factors such as greenhouse gases and that future evaluation of environmental inhibitors in agriculture might be needed and would be consistent with Goal 1 of the Codex Strategic Plan 2020-25 as more and more countries tried to address the impact of agricultural animals on climate change.

CCRVDF25 noted that the definition of veterinary drug did not exclude those veterinary drugs which are used solely for environmental purposes.

Chairperson's comments:

CCRVDF25 lacked the time in the all-virtual meeting for a robust discussion of this issue brought to its attention by one of the members.

12. Joint FAO/WHO expert meeting on carry-over in feed and transfer from feed to food of unavoidable and unintended residues of approved veterinary drugs, paragraphs 27-28.

Status:

The Expert Meeting was convened at the request of CCRVDF22 (2016) to address the carry-over in feed and transfer from feed to food of unavoidable and unintended residues of approved veterinary drugs and its potential impact on food safety/trade. The Expert Meeting provided two key recommendations for consideration by CCRVDF, i.e. the partial revision of the COP/AF (CXC 54-2004) and the establishment of action levels for such unintended/unavoidable residues.

Code of Practice on Good Animal Feeding (CXC 54-2004)

CCRVDF25:

- considered that the provisions in the COP provided sufficient advice to Codex members to address this matter
- noted that the recommendations of the Expert Meeting, especially those related to strengthening countries capacities to implement the COP to avoid/contain cross-contamination of feed, complement/support the guidance provided in the COP to member countries.
- agreed that no further action from CCRVDF would be required on the *Code of Practice on Good Animal Feeding* at present.

Establishment of Action Levels

CCRVDF25 agreed:

- that the Committee might consider establishing such levels in the future as needed, on the understanding that good feeding practices have been followed in accordance with the *Code of Practice on Good Animal Feeding (CXC 54-2004)*.
- to develop criteria or requirements for the establishment of action levels for unintended or unavoidable carryover from feed to food of animal origin using nicarbazin as a pilot study based on the information provided by the Expert Meeting.

Chairperson's comments:

CCRVDF23 discussed the issue of unintentional carryover of veterinary drug residues in animal feed. Following plenary discussion, CCRVDF23 requested FAO and WHO to provide scientific advice and risk

management options. FAO and WHO hosted an expert meeting, Carryover in feed and transfer from feed to food of unavoidable and unintended residues of approved veterinary drugs, January 8-10, 2019.

The results of the expert meeting were provided in a March 25, 2021 Webinar, prior to CCRVDF25. The results of the expert meeting and the recommendations were presented by FAO during CCRVDF25 and discussed in plenary. CCRVDF25 concluded that the current *Code of Practice on Good Animal Feeding* (CXC 54-2004) provides sufficient guidance to Codex members and that the recent 2020 FAO/IFF manual, Good practices for the feed sector. Implementing the Codex Alimentarius Code of Practice on Good Animal Feeding (FAO Animal Production and Health/Manual24), offered practical advice on implementation of the code of practice and no further actions were needed. CCRVDF25 agreed that the Committee might consider establishing action levels for residues of veterinary drugs that are unintentionally carried over in feed if needed. In keeping with this conclusion, CCRVDF25 established an EWG to develop a discussion paper on possible requirements or criteria for such action levels (see the discussion for nicarbazin under Agenda Item 11).

13. Issues and concerns that impact the ability of CCRVDF to efficiently perform its work, paragraph 152.

Status:

CCRVDF25 under the adoption of the agenda had agreed to discuss this issue under “other business and future work”, but was not able to proceed with the discussion due to lack of time.

Chairperson’s comments:

CCRVDF is a highly functional expert committee encountering some serious problems with developing and forwarding standards for residues of veterinary drugs in foods to the CAC. Some of the problems derive from difficulties in obtaining the underlying data needed for a robust JECFA risk assessment, particularly for older veterinary drugs, or for veterinary drugs used for food animal species less common in the international food trade. CCRVDF has made a number of innovative efforts as a risk management body to address the problem. As reported in CCRVDF25, the Committee has developed and maintains a database that identifies veterinary drugs that members feel need standards, those members supporting such standards, and other relevant information to assist the global community in leveraging data. The Committee launched and evaluated a pilot for simultaneous review of a veterinary drug by competent national authorities and JECFA, to allow reduce the time needed for development of a Codex Standard. An approach for extrapolation has been adopted to leverage JECFA risk assessments, and Codex standards for those species and tissues less common in international trade. CCRVDF reached out to CCPR to parallel the similar efforts between JECFA and JMPR to leverage the available data for compounds with dual use as a veterinary drug and pesticide. Together these efforts reflect an intentional strategy to facilitate the development of MRLs for residues of veterinary drugs found in the international food trade. All of this reflects intense effort by CCRVDF members – in some cases particularly with the assistance of some observer organizations – and a flexible, problem solving approach to risk management. The second category of problems stem from efforts by some members (also supported by some observer organizations) to prevent the development of standards based on reasons that are outside of the Statements of Principle, where there is consensus on the robustness of the JECFA risk assessment and the safety of the proposed MRLs, but the reasons to object include, among others, a refusal to support development of standards for veterinary drugs intended to enhance animal food production and citation of lack of registration within their country as a basis for objection to development of the standard. This second category particularly threatens the core of Codex’s mission (protection of consumer health and facilitation of international trade) and threatens to undermine the functionality of CCRVDF as a Committee.