

CODEX ALIMENTARIUS COMMISSION



Food and Agriculture
Organization of the
United Nations



World Health
Organization

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Agenda Item 6.2

CX/RVDF 21/25/7

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JOINT FAO/WHO FOOD STANDARDS PROGRAMME CODEx COMMITTEE ON RESIDUES OF VETERINARY DRUGS IN FOODS

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PROPOSED DRAFT MRLS FOR ZILPATEROL HYDROCHLORIDE (cattle fat, kidney, liver, muscle) (Held at Step 4)

(Prepared by the Codex Secretariat in collaboration with the
Chairperson of the Codex Committee on Residues of Veterinary Drugs in Foods)

BACKGROUND

1. CCRVDF24 (2018) agreed to retain the proposed draft MRLs for zilpaterol hydrochloride (cattle fat, kidney, liver, muscle) as proposed by JECFA81 and confirmed by JECFA85 at Step 4 for further consideration at CCRVDF25. Therefore, no further comments have been requested on these MRLs.
 2. This document provides consolidated information of the outcomes of the JECFA81 and JECFA85 evaluations as well as the discussions at CCRVDF, CAC and CCEXEC on this compound to facilitate discussion at CCRVDF25. In addition, the document also includes information on the ongoing discussion in CCEXEC on how to facilitate a common interpretation and consistent application of the *Statement of Principles concerning the Role of Science in the Codex Decision-Making Process and the extent to which Other Factors are taken into account* as may be relevant to the consideration of MRLs for veterinary drugs by CCRVDF, and in particular these MRLs at CCRVDF25.
 3. The document is divided in four parts as follows:
 - Part I: Extracts from CCRVDF reports relevant to the discussion on MRLs for zilpaterol hydrochloride
 - Part II: Extracts from CAC reports relevant to the discussion on MRLs for zilpaterol hydrochloride
 - Part III: Extracts from CCEXEC reports relevant to the discussion on MRLs for zilpaterol hydrochloride and the establishment on consensus-based food safety standards (Statement of Principles)
 - Part IV: Extracts from JECFA reports relevant to the risk assessment of zilpaterol hydrochloride and the proposed MRLs for zilpaterol hydrochloride.
 - Part V: Acronyms used in this document
- For a chronological order of discussion please follow the discussion at CCRVDF20, CCEXEC67, CAC35, CCRVDF22, CCRVDF23, CCRVDF24, CCEXEC75, CAC41 and CCEXEC77.
4. Codex members and observers are invited to consult this document in preparing for the consideration of MRLs for zilpaterol hydrochloride at CCRVDF25 to have an informed discussion on this matter.
 5. The following sections of the Procedural Manual¹ may be relevant for the consideration of this matter and should not be considered an exhausted list:
 - *Risk Analysis Principles applied by CCRVDF*
 - *Statement of Principles concerning the Role of Science in the Codex Decision-Making Process and the extent to which Other Factors are taken into account*
 - *Measures to facilitate Consensus*
 - *Guidelines to Chairpersons of Codex Committees and Ad Hoc Intergovernmental Task Forces*
 6. It is noted that matters concerned to the request for the establishment of MRLs for zilpaterol in edible offal are not addressed in this document (see Agenda Item 8).

¹ The Procedural Manual is available on the Codex website at:
<http://www.fao.org/fao-who-codexalimentarius/publications/en/>
<http://www.fao.org/publications/card/en/c/CA2329EN>

**SUMMARY OF THE DISCUSSION ON
MRLs FOR ZILPATEROL HYDROCHLORIDE IN CCRVDF²**

CCRVDF20³ (2012) EXTRACTED**PRIORITY LIST OF VETERINARY DRUGS FOR EVALUATION OR RE-EVALUATION BY JECFA (Agenda Item 9a)⁴**

100. Australia, as Chairperson of the PWG that met immediately prior to the Session, introduced the report of the WG, as presented in CRD3.
101. CCRVDF noted that the WG had considered all the requests received in reply to CL 2010/50-RVDF and:
- recommended to include in the priority list for evaluation by JECFA:
 - gentian violet;
 - lasolacid; and
 - phenylpyrazole
 - identified some gaps in the request of Chile for the inclusion in the Priority List of the following compounds as no information was provided on data availability and the exact nature of the request:
 - flumequine,
 - emamectin benzoate and
 - oxolinic acid
 - could not achieve consensus as to the inclusion of zilpaterol hydrochloride, which met the criteria for inclusion in the *Priority List of Veterinary Drugs for Evaluation or Re-evaluation by JECFA* ("Priority List"), but for which there was no agreement as to its inclusion in the Priority List.
102. The Delegation further recalled that, as result of the discussion under Agenda Item 6 (proposed MRLs for veterinary drugs), CCRVDF had agreed to add three other veterinary drugs to the Priority List, namely:
- apramycin;
 - monepantel; and
 - derquantel (see Agenda Item 6b)
103. The WG had also recommended:
- to forward the Priority List to CAC35 for approval;
 - to solicit Members to submit all the requested information, when proposing veterinary drugs for inclusion in the Priority List; and
 - to establish a PWG, to meet immediately prior to its next Session, to consider proposals for inclusion in the Priority List.
104. CCRVDF discussed the recommendations of the WG as follows:
- Zilpaterol hydrochloride**
110. CCRVDF discussed this matter and could not reach consensus and, therefore, decided to request advice and direction from CAC regarding the appropriate steps to take regarding making a decision whether or not to include a veterinary drug in the Priority List, noting the following points that were raised during the discussion:
- A proposed veterinary drug, zilpaterol, had met the criteria for inclusion in the Priority List for JECFA evaluation;
 - CCRVDF was sharply divided and could not reach consensus on a decision on whether or not to include the veterinary drug (zilpaterol) in the Priority List for JECFA evaluation;
 - Several delegations strongly objected to the inclusion of zilpaterol in the Priority List. They mentioned the following:

² All CCRVDF working documents including CRDs, information documents and reports of their sessions are available from the CCRVDF website at: <http://www.fao.org/fao-who-codexalimentarius/committees/committee/en/?committee=CCRVDF>
<http://www.fao.org/fao-who-codexalimentarius/committees/committee/related-meetings/en/?committee=CCRVDF>
All CLs relevant to CCRVDF are available from the Codex website and also from the CCRVDF website as follows:
<http://www.fao.org/fao-who-codexalimentarius/resources/circular-letters/en/>
<http://www.fao.org/fao-who-codexalimentarius/committees/committee/related-circular-letters/en/?committee=CCRVDF>

³ REP20/RVDF, paras. 100 – 120, Appendix IX, Part B

⁴ CL 2010/50-RVDF; CX/RVDF 12/20/11 (Canada, Chile and Costa Rica); CX/RVDF 12/20/11-Add.1 (Kenya and USA); CRD3 (Report of the PWG/Priorities); CRD23 (Republic of Korea)

- the substance was similar to another beta-agonist: ractopamine, for which the draft MRLs have been kept at Step 8 for several years in the absence of consensus for their adoption;
- CCEXEC66 identified the critical funding situation for scientific advice for food safety and nutrition;
- the shortfall of FAO and WHO budget for scientific advice would negatively affect the Codex work.

In their view, initiating a Codex process for developing MRLs for another similar type of beta-agonist would be a waste of resources of both JEFCA and CCRVDF as it was clear that there would be no consensus for their advancement. Under these circumstances, the inclusion of zilpaterol in the Priority List would not comply with the fundamental prerequisite for any new Codex work, i.e., the prospect of completing the work within a reasonable period of time; they urged CCRVDF to concentrate its efforts on several important issues on its agenda where consensus was achievable and, therefore, significant progress was possible;

- These delegations highlighted both their views regarding animal welfare and consumers concerns and it was also mentioned that JECFA could provide advice directly to Member countries;
- Another delegation wanted resolution of questions surrounding ractopamine residues before putting zilpaterol on the Priority List and urged the development of MRLs for offal tissues should CAC decide to put zilpaterol on the Priority List;
- Several other delegations strongly supported the inclusion of zilpaterol in the Priority List, noting that the protection of the health of consumers was the primary objective of Codex, and that, according to FAO, the number of undernourished people in the world remained unacceptably high and world food production had to increase substantially.

These delegations highlighted the importance of the development of safe technologies that aim to provide food at affordable prices. The starting point to take any decision about the safety of a veterinary drug intended to be used for food producing animals was to have its risk assessment done, and zilpaterol had met all the procedural criteria established by CCRVDF to be included in the Priority List. There was no point in delaying this inclusion while CCRVDF and many Codex members waited for a final decision about other standards held at Step 8 at CAC, since it was not science that held these standards from adoption.

Noting that zilpaterol had its use already approved in several countries around the world, the request for the scientific evaluation of this compound by JECFA should not be blocked at this Committee;

- A delegation noted that, if another JECFA meeting were held, the evaluation of zilpaterol could be accommodated;
- An Observer noted that there was no indication of animal welfare issues related to zilpaterol;
- The delegations supporting addition of the veterinary drug in the Priority List contended that the basis for support or opposition should be science-based and, as such, JECFA should be requested to evaluate submitted data and provide a scientific risk assessment to CCRVDF in order for the Committee to discuss risk management recommendations; and
- Several delegations added the importance of having a risk assessment by JECFA to guide national authorities risk management mitigations in the absence of Codex adopted standards.

111. CCRVDF further noted that:

- the Procedural Manual addresses the procedures to be followed in the section entitled "*Risk Analysis Principles applied by CCRVDF*";
 - in particular, Section 3.1 "*Preliminary Risk Management Activities*" (paragraphs 12 through 18).
- Specifically,
 - paragraph 16 states: "*CCRVDF considers the preliminary risk profile and makes a decision on whether or not to include the veterinary drug in the priority list.*";
 - paragraph 17 states: "*CCRVDF considers these recommendations {the recommendations of the Priorities Working Group} before agreeing on the priority list, taking into account pending issues such as temporary ADIs and/or MRLs.*"
- the Procedural Manual was silent on the criteria that should be used by CCRVDF in making this decision other than to consider the preliminary risk profile.

112. Therefore, CCRVDF requested guidance from CAC on the factors that should be considered in making this decision.

113. In addition, CCRVDF requested guidance from CAC as to whether the concerns noted above should be considered before or after the risk assessment evaluation by JECFA. Currently, CCRVDF begins its work on developing risk management measures regarding MRLs after the completion of the JECFA risk assessment and the recommendations for MRLs were circulated for comment at Step 3.
114. CCRVDF noted that the guidance sought from CAC might have impact on other Codex committees' work and, as such, requested advice and direction with a broader view to the varied work of CAC.

Conclusion

117. CCRVDF agreed to forward the Priority List of Veterinary Drugs for Evaluation or Re-evaluation by JECFA to CAC35, as attached in Appendix IX (Part A).
118. With regard to zilpaterol (Appendix IX, Part B), in the absence of consensus, CCRVDF requested CAC to provide guidance, as requested above, and in doing so, to either adopt the new work by including the veterinary drug zilpaterol hydrochloride in the Priority List for JECFA evaluation or to exclude the veterinary drug, zilpaterol hydrochloride, from the Priority List for JECFA evaluation.
119. CCRVDF also agreed to establish a PWG, chaired by Australia, open to all Members and Observers and working in English, French and Spanish, which would meet immediately before its next Session, to consider the replies to the CL requesting comments and information on the Priority List of Veterinary Drugs for Evaluation or Re-evaluation by JECFA.
120. The JECFA Secretariat highlighted again that financial resources to hold a JECFA meeting to address the requests from the Committee were not secured; hence it was not clear that a meeting could actually be scheduled, especially in time for the next Session of CCRVDF.

CCRVDF21 (2013)

CCRVDF held no discussion on zilpaterol.

CCRVDF22⁵ (2015) EXTRACTED

MATTERS FROM FAO AND WHO INCLUDING JECFA (Agenda Item 4)⁶

27. The JECFA Secretariat introduced the report and noted that some of the matters would be addressed when discussing the relevant agenda items.

Zilpaterol hydrochloride

41. An ADI was established by JECFA78 but data were insufficient to recommend MRLs. Further clarification has been provided on data needs to the sponsor and additional data have been received by the JECFA Secretariat which will be considered at JECFA81 with a view to completing the evaluation.

PRIORITY LIST OF VETERINARY DRUGS FOR EVALUATION OR RE-EVALUATION BY JECFA (Agenda Item 8a)⁷

105. CCRVDF considered the recommendations of the in-session WG as follows:

Priority List of Veterinary Drugs from Evaluation or Re-Evaluation by JECFA

106. CCRVDF agreed to the Priority List and made the following comments and amendments:
107. CCRVDF agreed to:
- Retain in the Priority List those compounds for which data availability was not yet confirmed, e.g. ampicillin, because this information was useful for the JECFA Secretariat when planning future JECFA meetings; it was understood that if data availability were not confirmed at CCRVDF23, these compounds would be removed from the Priority List;
 - Amend the request for MRLs for amoxicillin for "flat fish" as opposed to "finfish" and to explore the possibility to extrapolate the MRLs to other finfish;
 - Include the request to consider potential zilpaterol hydrochloride residues in animal lungs and other edible offal.

⁵ REP15/RVDF, paras. 41, 105-107, 112 and Appendix VIII

⁶ CX/RVDF 15/22/4; CRD4 (El Salvador); CRD5 (India); CRD6 (Peru); CRD7 (Gambia); CRD9 (AU); CRD10 (Kenya); CRD11 (Brazil); CRD16 (Egypt); CRD17 (Nigeria); CRD19 (Indonesia); CRD20 (Ecuador); CRD22 (Philippines); CRD26 (China); CRD27 (Canada)

⁷ CL 2014/3-RVDF; CX/RVDF 15/22/8 / CRD25 (Algeria, Chile, Costa Rica, Norway, Republic of Korea and USA); CRD6 (Peru); CRD9 (AU); CRD10 (Kenya); CRD14 (Argentina); CRD17 (Nigeria); CRD19 (Indonesia); CRD20 (Ecuador); CRD28 (Republic of Korea); CRD31 (Report of the in-session WG on Priorities)

Conclusion

112. CCRVDF agreed to forward the Priority List of Veterinary Drugs for Evaluation or Re-evaluation by JECFA to CAC38 for approval (Appendix VIII).

CCRVDF23⁸ (2016) EXTRACTED**MATTERS FROM FAO AND WHO INCLUDING JECFA (Agenda Item 3)⁹**

9. The Representatives of FAO and WHO introduced the paper and noted that some of the matters would be addressed when discussing the relevant items.

MRLs FOR IVERMECTIN (CATTLE FAT, KIDNEY, LIVER, MUSCLE), TEFLUBENZURON (SALMON FILLET, MUSCLE) AND ZILPATEROL HYDROCHLORIDE (CATTLE FAT, KIDNEY, LIVER, MUSCLE) AT STEP 4 (Agenda Item 6.2)¹⁰**Zilpaterol hydrochloride**

67. The JECFA Secretariat informed CCRVDF that JECFA81 had reaffirmed the ADI of 0-0.04 µg/kg bw and established an ARfD of 0.04 µg/kg bw based on a LOAEL of 0.76 µg/kg bw for acute pharmacological effects observed in a single-dose human study, with application of an uncertainty factor of 20, comprising a default uncertainty factor of 10 for human individual variability and an additional uncertainty factor of 2 to account for use of a LOAEL for a slight effect instead of a NOAEL. The GEADE is 1.9 µg/day for the general population, which represents approximately 80% of the ARfD, and 0.57 µg/day for children, which represents approximately 94% of the ARfD. Based on this data JECFA was able to recommend MRLs for cattle kidney, liver and muscle.

Discussion

68. The Chairperson informed CCRVDF of the discussion between JECFA and the pharmaceutical sponsor on some limitations of the data previously submitted to JECFA81 (as noted in the JECFA report) and the offer of the sponsor to provide additional data to JECFA. In view of this, the Chairperson proposed to hold the MRLs at Step 4 so that JECFA could evaluate the additional data and thus provide the best risk assessment possible of the compound.
69. Delegations generally supported or did not object to the proposal to hold the MRLs at Step 4.
70. While generally supporting or not objecting to holding the MRLs at Step 4, the following comments were put forward by individual delegations:
- concern that non-compliance with GVP might expose populations at risk; the use of growth promoters is not allowed in a number of countries;
 - it would be preferable to advance the MRLs to Step 5; the use of veterinary drugs should be restricted to therapeutic purpose; the use of growth promoters may lead to animal welfare concerns;
 - literature references indicate an increase loss of cattle due to the use of zilpaterol and a potential risk of additional exposure through grazing in pasture contaminated by excreta (urine and faeces) of treated animals and possibly ground water and drinking water.
71. The EU, supported by some delegations and one observer, stated that they were opposed to the advancement of zilpaterol in the Step procedure and to the establishment of Codex MRLs for zilpaterol. The EU stated they did not believe that our resources were wisely spent on the assessment of growth promoters. It is a general policy in the EU to prohibit the administration of beta-agonists to healthy animals solely for the purpose of growth promotion.
72. The Representative of FAO thanked the members and observers for the discussion and the issues raised and encouraged all participants to forward all relevant information and data so that they could be considered by JECFA at its next meeting.
73. Members were encouraged to forward their concerns to JECFA using the concern form¹¹.

Conclusion

74. CCRVDF agreed to hold the MRLs for zilpaterol hydrochloride at Step 4 for consideration at its next Session in light of the JECFA evaluation of the additional studies (Appendix V).

⁸ REP17/RVDF, paras. 67 – 74, Appendix V

⁹ CX/RVDF 16/23/3; CRD4 (Senegal); CRD5 (AU); CRD9 (HealthForAnimals); CRD10 (Nigeria); CRD15 (India); CRD21 (Trinidad and Tobago)

¹⁰ CX/RVDF 16/23/6; CX/RVDF 16/23/6-Add.1 (Brazil, Cuba, Philippines, HealthForAnimals); CX/RVDF 16/23/6-Add.2 (EU, Nigeria, Senegal, AU); CRD12 (Mali); CRD14 (Indonesia); CRD15 (India); CRD16 (Argentina); CRD17 (Ecuador); CRD18 (Republic of Korea); CRD19 (Panama)

¹¹ Risk Analysis Principles applied by CCRVDF (Procedural Manual)

CCRVD24¹² (2018) EXTRACTED**MATTERS FROM FAO AND WHO INCLUDING JECFA (Agenda Item 3)¹³****Other matters**

16. CCRVDF noted that other matters of interest raised in the document would be considered under the relevant agenda items.

MRLs FOR ZILPATEROL HYDROCHLORIDE (CATTLE, KIDNEY, LIVER, MUSCLE) (At Step 4) (Agenda Item 6.1)¹⁴

40. The JECFA Secretariat, introducing the item, confirmed the previous JECFA risk assessment and affirmed the proposed draft MRLs as contained in REP17/RVDF-Appendix V. Additional data provided by the sponsor following JECFA81 and evaluated at JECFA85 were discussed in CX/RVDF 18/24/3 (Agenda Item 3).
41. CCRVDF expressed strong support for the robust scientific evaluation carried out by JECFA. CCRVDF further emphasized that there were no public health or scientific concerns regarding the proposed draft MRLs.
42. Delegations opposed to advancing the proposed draft MRLs in the Step procedure expressed opposition based on concerns that:
- veterinary drugs should not be used for non-therapeutic purposes in food-producing animals;
 - such compounds did not belong to sustainable livestock production because of concerns for animal health and welfare;
 - by adopting MRLs for this compound Codex would be sending a signal that the use of zilpaterol was acceptable; and
 - that some member states did not authorize the use of zilpaterol in their countries and therefore could not support the MRLs.
43. Two delegations expressed concern that zilpaterol poses a health risk to humans, but no data were provided nor was a concern form prepared.
44. Delegations in favor of progressing the proposed draft MRLs for zilpaterol to Step 5 or 5/8 in the Step Procedure noted that:
- the work of CCRVDF was based on the scientific principles and procedures outlined in the *Risk Analysis Principles applied by CCRVDF* (Procedural Manual);
 - the arguments raised by those opposed (i.e. animal health and welfare) were outside the purview of CCRVDF and beyond the Codex mandate and neither national, regional nor political factors have any bearing on the deliberations of CCRVDF in this matter;
 - the Codex definition for a veterinary drug was not limited to veterinary drugs for therapeutic uses¹⁵;
 - with all issues relating to science and procedure fully addressed it was now appropriate to advance the work as JECFA evaluations had concluded that with Good Veterinary Practice (GVP) there was no risk to human health from the compound at these levels;
 - many countries who had not authorized use of zilpaterol, supported the advancement of the MRLs since they were supported by the science and that the MRLs would help to monitor imports of food from animal origin. Countries, in particular developing countries rely on Codex standards, as some lacked the capacity to undertake their own risk assessments and to establish their own MRLs;
 - any delay in adopting standards that had received scientific support discourages participation in Codex (especially from developing countries) both in terms of the preparation/submission of data and attendance at Codex meetings, discourages sponsors from submitting data; and discourages experts from giving their time and expertise for JECFA assessments; and
 - CCRVDF, in not advancing this work, risked compromising the role of Codex and weakening the multilateral system.

¹² REP18/RVDF, paras. 40-55, 117-120, Appendix III

¹³ CX/RVDF 18/24/3; CRD4 (Kenya); CRD7 (AU); CRD10 (Nigeria); CRD25 (Mali)

¹⁴ REP17/RVDF-App.V; CRD4 (Kenya); CRD5 (Egypt); CRD7 (AU); CRD9 (Panama); CRD10 (Nigeria); CRD11 (Ghana); CRD13 (Argentina); CRD16 (Philippines); CRD17 (HealthForAnimals); CRD18 (Cameroon); CRD20 (Uganda); CRD21 (Nicaragua); CRD22 (Indonesia); CRD23 (Russian Federation); CRD24 (Costa Rica); CRD25 (Mali); CRD28 (HealthForAnimals); CRD29 (Thailand); CRD31 (El Salvador); CRD32 (Ecuador)

¹⁵ *Veterinary Drug* means any substance applied or administered to any food producing animal, such as meat or milk producing animals, poultry, fish or bees, whether used for therapeutic, prophylactic or diagnostic purposes or for modification of physiological functions or behavior (Procedural Manual, Section I)

45. The Observer from OIE stated that the WTO/SPS Agreement recognized animal health and animal welfare were within the purview of OIE. The Observer further noted that OIE has established standards for animal health and welfare and are actively working to update them.
46. An Observer supported the view that zilpaterol did not belong in animal husbandry. They further noted that healthy animals are important for the production of healthy food and expressed concern that potential synergistic effects with other drugs and toxins had never been evaluated and that consumers would not be aware of its presence in their food.
47. Another observer, speaking on behalf of the sponsor of the compound, noted OIE is the legally recognized global organization for animal health and welfare and that zilpaterol was the most scientifically studied veterinary drug for its potential impact on animal welfare. In their view independent researchers have concluded there are no adverse animal welfare impacts. In addition to the JECFA risk assessment, more than 65 studies since 2006 of cattle fed zilpaterol have concluded that zilpaterol is safe and effective. They noted that nearly 50% of beef produced in the world comes from countries that have approved zilpaterol, and that CCRVDF needed to establish global standards for countries to monitor imports of veterinary drugs in food. The observer requested delegates to support advancement to Step 5.
48. The Codex Secretary noted that CCRVDF appeared unable to achieve consensus for reasons beyond the mandate of the Committee and the mandate of Codex itself. He further noted that no voice had been heard from members rejecting the scientific basis of this work and that there was agreement on the appropriateness of the level of protection established by the JECFA evaluation. However, other considerations expressed by delegations remained preventing the advancement of the proposed draft MRLs. With reference to *“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”* in the Procedural Manual (Appendix, General Decisions), the Codex Secretary noted (paragraph 4):
- When the situation arises that members of Codex agree on the necessary level of protection of public health but hold differing views about other considerations, members may abstain from acceptance of the relevant standard without necessarily preventing the decision by Codex.*
49. The Chairperson proposed that delegations not in support of the proposed draft MRLs could abstain from acceptance as outlined in the Procedural Manual; however, those delegations who did not support advancing the proposed draft MRLs did not accept the proposal.
50. The Chairperson, noting that CCRVDF was divided as a committee, not due to concerns regarding science, but for other factors, stated that CCRVDF was not in consensus. He proposed to close the debate for the current session of CCRVDF and not to advance the proposed MRLs. He further noted that CCRVDF did achieve consensus on support for the JECFA evaluation of zilpaterol and the safety of the proposed MRLs, but that CCRVDF was unable to reach consensus on advancing the work in the Step Procedure for other reasons.
51. The Observer from HealthforAnimals expressed their strong concern about the failure to follow agreed Codex procedures that would have a discouraging effect on future sponsors to put forward compounds through the agreed Codex procedures and those who would suffer most would be developing countries who need these standards most. This failure should be discussed at CAC.

Conclusion

52. CCRVDF was unable to reach consensus and therefore did not advance the proposed draft MRL for zilpaterol in the Step Procedure at this session and the draft MRL for zilpaterol was retained at Step 4 (Appendix III).
53. New Zealand expressed its objection to the Chairperson’s decision not to advance the proposed MRLs for zilpaterol for the following reasons:
- CCRVDF had previously acknowledged that the compound had met those criteria for prioritization of the assessment as recommended by CCRVDF and endorsed by CAC;
 - There was explicit consensus within CCRVDF concerning JECFA’s conclusion that any residues that may be present associated with GVP in the use of this compound did not constitute a risk to consumers;
 - Furthermore, no other legitimate factors consistent with the Procedural Manual had been raised by members.
 - Accordingly, the decision not to advance the MRLs is not consistent with both the Procedural Manual and the rules or procedures adopted by CCRVDF.
 - The decision to not progress MRLs important for trade, especially for developing economies, solely based on philosophical objections outside the mandate of CCRVDF by several countries was unacceptable.
 - New Zealand opposes the application of *ad hoc* criteria in this case that were in contravention to the decisions explicitly taken by CAC.

54. Argentina, Australia, Bolivia, Brazil, Burkina Faso, Colombia, Costa Rica, Cote D'Ivoire, Dominican Republic, Ecuador, El Salvador, Ghana, Guatemala, Honduras, Japan, Kenya, Mali, Mexico, Nicaragua, Nigeria, Panama, Peru, South Africa, Tanzania, Togo, United States of America and Zimbabwe, also requested that their reservations to the decision not to advance the MRLs for the same reasons as stated by New Zealand.

Other matters in relation to the conclusion

55. The Codex Secretary noted that the decision of CCRVDF would send a strong message to CCEXEC and CAC to take action and discuss this issue. He expressed concern that CCRVDF was prevented from acting on this standard due to factors beyond science and expressed the hope that discussions could take place in the appropriate bodies to avoid potential damage to Codex in the future.

OTHER BUSINESS AND FUTURE WORK (Agenda Item 13)

The accomplishments of the current session and the issues and concerns that impact the ability of CCRVDF to efficiently perform its work

117. The Chairperson reviewed the work completed at the current session and congratulated CCRVDF on its accomplishments. He noted, however, despite the great progress made during this session that CCRVDF had struggled to address the lack of data to allow JECFA to conduct a risk assessment upon which to base MRL recommendations. He also pointed out the long-standing difficulty of CCRVDF, to reach agreement as an international community, on whether Codex standards should even be established for certain classes of veterinary drugs due to differences in deeply held values rather than differences in the interpretation of science. He stressed the importance of finding solutions to these problems and noted that there would not be a CCRVDF meeting in a few years' time otherwise.
118. In response to the remarks of the Chairperson, the following views were expressed:
- optimism that CCRVDF still had an important role to play in setting Codex standards for residues of veterinary drugs in food.
 - concern over the newly agreed principles for extrapolation of MRLs and related risks regarding the role of science in establishing MRLs and highlighted the need for a science-based approach in the EWG; and
 - the need to respect the rules of Codex and not have work delayed by factors not related to science.
119. The JECFA Secretariat expressed its thanks to CCRVDF for the clarity in the discussions, in particular regarding zilpaterol, by keeping any possible scientific concerns clearly and distinctly separate from other concerns. This clarity had certainly not been easy to achieve, yet, the JECFA Secretariat believed that it was a critical component in making progress towards a possible consensus.

Conclusion

120. CCRVDF noted the comments made.

**SUMMARY OF THE DISCUSSION ON
MRLs FOR ZILPATEROL HYDROCHLORIDE IN CAC¹⁶**

CAC35¹⁷ (2012) EXTRACTED

MATTERS REFERRED TO CAC BY CODEX COMMITTEES AND TASK FORCES (Agenda Item 9)¹⁸

B. Matters referred by Codex committees and task forces

CCRVDF: Zilpaterol hydrochloride

169. The Chairperson introduced the matter arising from CCRVDF20 and explained that the Committee could not reach consensus on the inclusion of zilpaterol in the Priority List of Veterinary Drugs for Evaluation or Re-evaluation by JECFA (“Priority List”) and had sought the Commission’s guidance regarding the factors that should be considered in making a decision on whether or not to include a veterinary drug in the Priority List. CCRVDF had further requested guidance as to whether the concerns of countries not in favour of the inclusion should be considered before or after the risk assessment evaluation by JECFA. CCRVDF had finally requested CAC to either adopt the new work by including the veterinary drug zilpaterol hydrochloride in the Priority List for JECFA evaluation or to exclude the veterinary drug, zilpaterol hydrochloride, from the Priority List for JECFA evaluation.
170. The Chairperson further recalled that CCRVDF20 had forwarded a Priority List to the Commission for approval as new work, as contained in Appendix IX, Part A of its report, and that zilpaterol had been included in Part B of the same Appendix, pending the outcome of CAC’s discussion.
171. Delegations who objected to the inclusion of zilpaterol in the Priority List mentioned that the compound was similar to another beta-agonist, ractopamine, for which draft MRLs had been kept at Step 8 for several years in the absence of consensus and that this issue needed to be considered taking into account other pending issues as provided for in the Procedural Manual¹⁹ before proceeding with another similar compound in the Priority List.
- They were of the view that the inclusion of zilpaterol in the Priority List did not meet one of the *Criteria for the Establishment of Work Priorities*, as outlined in the Procedural Manual²⁰, to complete work in a reasonable period of time.
 - They further expressed the view that the inclusion of zilpaterol in the Priority List could waste JECFA resources because of the difficulties to find a consensus. In view of its limited resources, requests to JECFA needed to be prioritised to allow JECFA to focus on compounds, for which Codex could complete work within a reasonable time. It was further noted that Member countries could address their requests directly to JECFA²¹.
 - They further noted the importance for Codex to strive for consensus-based decisions to ensure its credibility as the pre-eminent authority in the field of food safety and food quality. A delegation suggested to also include consideration of offal in the evaluation of JECFA, in case zilpaterol is added to the Priority List.
172. Delegations that supported the inclusion of zilpaterol in the Priority List highlighted that the compound was approved for use in several countries and met the CCRVDF criteria for inclusion and “other legitimate factors” should not be taken into account in taking the decision.
- They pointed out that the evaluation of zilpaterol could help to re-assure consumers on the safety of its use in animal food production.
 - They were of the opinion that there was no need to change the CCRVDF procedure for the inclusion of veterinary drugs in the Priority List and that it was not appropriate to pre-empt the outcome Codex discussions on the JECFA assessment of zilpaterol, by preventing its evaluation.
 - They stressed that risk management decisions should be taken only after the risk assessment had been carried out.

¹⁶ All CAC working documents including CRDs, information documents and reports of their sessions are available from the CAC website at: <http://www.fao.org/fao-who-codexalimentarius/committees/cac/meetings/en/>

¹⁷ REP12/CAC, paras. 169 – 178, Appendix VI

¹⁸ CX/CAC 12/35/10; CX/CAC 12/35/10-Add.1; CX/CAC 12/35/10-Add.2; CRD11 (IFAH); CRD21 (EU); CRD 24 (Dominican Republic)

¹⁹ Procedural Manual: Risk Analysis Principles applied by CCRVDF (para. 17)

²⁰ Procedural Manual: page 43 (Codex Secretariat Note: The page was corrected to reflect the 27th Edition of the Procedural Manual)

²¹ Procedural Manual: Risk Analysis Principles applied by CCRVDF (para. 6)

173. On the issue of the status of the criteria of paragraph 13 of the *Risk Analysis Principles applied by CCRVDF*, the Representative of the Legal Counsel of FAO, speaking on behalf of the legal offices of both FAO and WHO, noted that compliance with the criteria could not, normally, trigger an automatic decision for inclusion in the Priority List and that members of Codex would normally retain a degree of discretion on inclusion of a veterinary drug in the Priority List.
174. The Representative indicated that there was a clear need for predictable procedures in Codex and noted that a consistent practice in CCRVDF had been established over the years. It was, therefore, reasonable for Codex members to expect that when a compound met the criteria for inclusion in the list, inclusion would follow. On that basis, the legal offices considered that a veterinary drug should be included in the Priority List for JECFA evaluation if it meets the criteria of paragraph 13 of the *Risk Analysis Principles applied by CCRVDF*. He further recalled that acceptance of new work required approval by CAC irrespective of inclusion of drugs in the priority list by CCRVDF. If changes to the criteria or procedures were needed, the appropriate channels of Codex could be followed, for example through CCGP.
175. A Delegation also questioned how precedence could be established when to their knowledge CCRVDF had never experienced similar situation i.e. “no consensus on the substances in the Priority List”.
176. The Chairperson noted the views expressed by the Representative of the Legal Counsel and the discussion above. He concluded that the Procedural Manual provided sufficient guidance for the inclusion of zilpaterol in the Priority List and that several countries depended on JECFA evaluations to assess veterinary drugs. The Chairperson further noted that the Representative of the Legal Counsel had stated that once the criteria listed in paragraph 13 of the *Risk Analysis Principles applied by CCRVDF* were met, inclusion of the veterinary drug the Priority List would follow.

Conclusion

177. The Chairperson concluded that, based on the above legal opinion, zilpaterol should be included in the Priority List for JECFA evaluation, that no further guidance was required for CCRVDF, that risk management decisions should follow the risk assessment and that CAC approved the Priority List with the addition of zilpaterol hydrochloride. On this basis, CCRVDF would initiate work based on the recommendations of the JECFA evaluation.
178. China, Croatia, Egypt, EU, Norway and Switzerland expressed their reservation to this decision.

CAC41²² (2018) EXTRACTED

REPORT BY THE CHAIRPERSON ON THE 74th and 75th SESSIONS OF CCEXEC (Agenda item 2)²³

5. Pursuant to Rule V, paragraph 7, of the CAC Rules of Procedure, the Chairperson drew the attention of the Commission to the reports of CCEXEC74 and CCEXEC75, observing that CAC would consider their recommendations under the relevant agenda items.

CCEXEC74 (2017)

6. CAC took note of the discussions and conclusions contained in the report of CCEXEC74.

CCEXEC75 (2018)

7. CAC took note of the discussions and conclusions contained in the report of CCEXEC75.

MRLs for zilpaterol hydrochloride (cattle fat, kidney, liver, muscle)

8. CAC noted the discussion and conclusions²⁴ of CCEXEC75 regarding its Critical Review of the consideration by CCRVDF24 of proposed draft MRLs for zilpaterol hydrochloride (cattle fat, kidney, liver, muscle).
9. Members, in expressing their views:
- (i) reiterated the importance of science as the cornerstone of Codex, stressing that it was fundamental to Codex’s credibility and role as reference under the WTO framework;
 - (ii) noted that to block the development of Codex texts on grounds extraneous to scientific advice and the Codex mandate prevented the many countries lacking the capacity to develop their own standards from fully benefiting from undisputed FAO/WHO risk assessment and monitoring foods for residues;
 - (iii) recalled that, procedurally, Members were free to make reservations or not to apply a Codex text;

²² REP18/CAC, paras. 5-12

²³ REP18/EXEC1; REP18/EXEC2(Rev.1); CRD12 (Brazil, Bolivia, Chile, Costa Rica, Colombia, El Salvador, Ecuador, Guatemala, Honduras, Jamaica, Mexico, Nicaragua, Panama, Paraguay, Peru, Dominican Republic, Trinidad and Tobago, Philippines)

²⁴ REP18/EXEC2 Rev.1, paras. 30-40

- (iv) stressed the need to ensure adherence to the Procedural Manual at all times and stated that CAC should issue guidance to the chairpersons of subsidiary bodies in this regard;
 - (v) stressed that careful consideration should be given to the weighting of factors beyond science in Codex decision-making procedures, as already provided for in the Procedural Manual, subject to certain agreed criteria contained in the Procedural Manual;
 - (vi) noted that existing procedures were already clear and should be followed;
 - (vii) noted that CAC and its subsidiary bodies should only consider factors other than science that were within the mandate of Codex as articulated in the Procedural Manual;
 - (viii) underscored that consensus was a core value of Codex;
 - (ix) noted that, in accordance with the Procedural Manual, it was legitimate for Codex as risk manager to take into consideration factors beyond risk assessment;
 - (x) recalled the joint FAO/WHO legal opinion, contained in paragraphs 31 and 32 of the report of CCEXEC75, that CCRVDF24 had breached no Codex rules;
 - (xi) noted the statement within the joint FAO/WHO legal opinion that recent developments had altered the original nature and status of Codex standards;
 - (xii) proposed a review of 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* (Statements of principle), as described in the final paragraph of the legal opinion; and
 - (xiii) noted that, in the light of the joint FAO/WHO legal opinion and repeal of the acceptance procedure, the Codex Secretariat should prepare a report on the history and implications of paragraph 4 of the Statements of principle.
10. Different views were also expressed regarding the correct forum, whether CCEXEC, CCGP or both, for further debate on this matter.
11. Observers expressed several views, including that there were scientific reasons to hold back the standard, Codex needed to update its procedures to avoid being left behind, better address sustainable and culturally appropriate foods and innovative products, ensure scientific credibility, avoid perceived conflicts of interest, favour independently funded science and use consistent terminology. Consistency across committees based on sound science and clear procedures was key to the credibility of Codex.

Conclusion

12. Reiterating the value of Codex as the preeminent international rules-based food standards-setting body, and underscoring its commitment to both science and consensus, CAC endorsed the approach proposed by CCEXEC75 in paragraphs 38-40 of its report, emphasized the value of holding regional coordination meetings to inform the process, and stressed that the reports prepared on the matter should be shared with the broader membership, not only CCEXEC. CAC:
- (i) highlighted the importance of science, the observance of Codex procedures and consensus in the Codex decision-making process;
 - (ii) endorsed the importance of the work proposed by CCEXEC75 to be considered at CCEXEC77;
 - (iii) requested that the Codex Secretariat make the reports to inform CCEXEC77's work available to all Members sufficiently in advance to enable regional coordinators to solicit views from their respective regions; and
 - (iv) took note of the comments made during the discussion and requested that the Codex Secretariat take them into account in preparing the reports on the matter for CCEXEC77.

**SUMMARY OF THE DISCUSSION ON
MRLs FOR ZILPATEROL HYDROCHLORIDE IN CCEXEC²⁵**

CCEXEC67²⁶ (2012) EXTRACTED

PROPOSALS FOR THE ELABORATION OF NEW STANDARDS AND RELATED TEXTS (Agenda Item 2b)²⁷

17. CCEXEC recalled the criteria established in the Procedural Manual for the critical review, considered the proposals for new work and made the following comments.

CCRVDF

MRLs for zilpaterol hydrochloride (cattle fat, kidney, liver, muscle)

21. CCEXEC noted different views expressed by some members on the proposal for inclusion of zilpaterol in the *Priority List of Veterinary Drugs for Evaluation or Re-evaluation by JECFA*. The Chairperson recalled that the mandate of CCEXEC was to consider proposals for new work forwarded by CCRVDF as included in Part A of the Priority List. He further recalled that in CCRVDF there had been no consensus on the inclusion of zilpaterol in the Priority List and that this matter had been referred to CAC by CCRVDF.
22. A Member expressed the view that, as there had been no consensus in CCRVDF to change current criteria for inclusion of substances in the Priority List, CCRVDF should have included zilpaterol in the Priority List in conformity with the established process, and therefore the question put forward to CAC was not appropriate.
23. In reply to some requests for clarification, the Codex Secretariat recalled that CCRVDF had requested guidance from CAC as there was no consensus on the inclusion of zilpaterol in the Priority List and that Appendix IX referred to zilpaterol with a note clarifying its status “*retention of this veterinary drug in the list will depend²⁸ on the outcome of the discussion at CAC35*”. The Chairperson noted that this question would be considered in CAC as requested by CCRVDF.
24. CCEXEC supported new work on all substances presented in Part A of Appendix IX of REP12/RVDF.

CCEXEC75²⁹ (2018) EXTRACTED

CRITICAL REVIEW (Agenda item 3)³⁰

CCRVDF

MRLs for zilpaterol hydrochloride (cattle fat, kidney, liver, muscle)

30. CCEXEC noted concerns regarding the decision of CCRVDF24 not to advance the proposed draft MRLs for zilpaterol hydrochloride despite consensus in that Committee on the validity of the JECFA assessment and underlying science. The relevance of considerations beyond the scope of the Codex mandate was questioned.
31. In response to a query whether relevant Codex procedures had been followed, a Representative of the FAO Legal Office presented the following joint FAO/WHO legal opinion:

“A question has arisen whether or not it was procedurally correct to hold a proposed standard at Step 4 of the *Procedures for the Elaboration of Codex Standards and Related Texts* in the absence of consensus to move the standard to Step 5. Such a decision was taken by CCRVDF at its last, 24th Session held in April of 2018.

“The matter attracted some controversy, as evidenced by a number of reservations that were included in the report of the Session. Such reservations questioned the holding of the draft standard at Step 4 under the circumstance that the members opposing the standard did not, in fact, challenge the scientific analysis, which confirmed that a certain MRL for zilpaterol would not present a risk to human health. Instead, the absence of consensus in CCRVDF up to that point was based on factors other than scientific factors, within the Codex Alimentarius mandate.

²⁵ All CCEXEC working documents including CRDs, information documents and reports of their sessions are available from the CAC website at: <http://www.fao.org/fao-who-codexalimentarius/committees/executive-committee/meetings/en/>

²⁶ REP12/EXEC2, paras. 17, 21-24

²⁷ CX/EXEC 12/67/3, CX/EXEC 12/67/3-Add.1

²⁸ REP12/RVDF, para. 118

²⁹ REP18/EXEC2-Rev.1, paras. 30-40

³⁰ CX/EXEC 18/75/2; CX/EXEC 18/75/2-Add.1; CRD2 (Brazil, Bolivia, Chile, Costa Rica, Colombia, El Salvador, Ecuador, Guatemala, Honduras, Jamaica, Mexico, Nicaragua, Panama, Paraguay, Peru, Dominican Republic, Trinidad and Tobago)

“As is often expressed, the two core values of CAC are science and consensus³¹, both of which find expression in the Procedural Manual. Standards are adopted on the basis of scientific risk assessments and voting is resorted to only once every efforts have been made to reach consensus.

“In such a framework, the Chairpersons of CAC and its subsidiary bodies must necessarily have sufficient operating margin to find ways to reach consensus. As recognized in the Guidelines to Chairpersons “[m]uch of the responsibility for facilitating the achievement of consensus would lie in the hands of the Chairpersons.” To this end, the Chairpersons are encouraged, inter alia, to ensure “that matters are not progressed from step to step until all relevant concerns are taken into account and adequate compromises worked out.”³² Such leeway should be available at all levels of the standard development process, until such time it is considered that all efforts have been made to reach consensus and voting could be resorted to as a last option.

“It is further noted that the Chairpersons of CAC and its subsidiary bodies perform their duties at all times under the authority of the body that they chair. In the case at hand, the Chairperson’s proposed way forward was accepted by CCRVDF, even if a number of reservations were recorded.

“In view of these circumstances, there is no reason to suggest that the decisions taken at CCRVDF breached any rule of Codex.”

32. The Representative of the Legal Office further stated:

“The above does not exclude that CAC further clarifies the role of science and the extent to which other factors are taken into account. In this context, it is important to note that the *Statement of Principles concerning the Role of Science in the Codex Decision-Making Process and the extent to which Other Factors are taken into account* make reference to the acceptance procedure as a mechanism to address the dilemmas that arise at times in connection with ‘other considerations’, while avoiding the blocking of the adoption of standards. The acceptance procedure, however, was abolished in 2005, largely due to the advent of the international trade agreements, which have altered the original nature and status of Codex standards. These developments would seem to warrant a review of the Statement of Principles to better clarify the extent to which “*other legitimate factors relevant for health protection and fair trade practices*”³³ may be taken into account in the adoption of Codex standards.

“Such a review could consider factors, including, but not limited to, the need for an efficient standard adoption process; the science-based nature of standard setting in Codex, the role of scientific risk assessment versus risk management; the role of voting in efficient standard setting and develop ideas as to how to overcome the stalemates that sometimes arise. CAC could be invited to refer such questions to an appropriate body for discussion and consideration, taking into account the terms of reference of the subsidiary committees of Codex.”

33. CCEXEC noted the legal opinion that in seeking consensus the CCRVDF Chairperson had acted within his authority.
34. Members expressed concern that the legal opinion had not been made available in advance, leaving little time for review and consideration.
35. The Codex Secretariat clarified that the legal opinion had been prepared in advance of the meeting in case the relevant question had been raised and had not been intended for prior distribution. Legal advice was commonly provided during Codex sessions as and when questions arose.
36. It was raised that it was important not to put other factors ahead of science. Members also recalled that: risk analysis comprised the three elements of risk assessment, management and communication; CAC and its committees were risk managers; and the consideration of other factors was an important element of risk management.
37. The Chairperson clarified that consideration of other factors was covered in the Procedural Manual and that science was also the basis for risk management, as part of the risk-analysis process.
38. In discussing the suggestions contained in the legal opinion on clarifying procedural considerations, it was proposed that:

³¹ See for example Rule XII(2) of the Rules of Procedure of CAC; Guidelines to Chairpersons Of Codex Committees and Ad Hoc Intergovernmental Task Forces, Procedural Manual, 27th edition, pp 107-111; Measures to Facilitate Consensus, Procedural Manual, 27th edition, p. 248
Codex Secretariat Note: For convenience the references to the Procedural Manual have been updated to reflect the 27th (latest) edition as opposed to the original reference to the 26th edition. The same applies to footnotes 32 and 33.

³² Guidelines to Chairpersons of Codex Committees and Ad Hoc Intergovernmental Task Forces, *ibid.*, p. 109, and p. 110 (letter e)

³³ 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; Procedural Manual, 27th edition, pp 245-246.

- i. Chairpersons be provided advice on applying the provisions of the Procedural Manual;
 - ii. the Codex Secretariat/Legal Counsels prepare a paper on the history and implications of paragraph 4 of the Statements of Principle;
 - iii. approaches to overcoming lack of consensus be given further consideration;
 - iv. a review be undertaken of the Statements of Principle Concerning the Role of Science, as described in the final paragraph of the legal opinion; and
 - v. discussion proceed on these issues in either CCGP or CCEXEC.
39. Taking into account the extensive discussion and agreement in CCEXEC on the follow-up, the Chairperson asked the Coordinators to work within their regions in order to avoid further extensive discussion at CAC41.

Conclusion

40. Acknowledging the importance of addressing the issues and challenges raised, CCEXEC agreed to continue discussion at CCEXEC77 on the matter facilitated by a report, to be prepared by the Codex Secretariat in conjunction with the CAC Bureau and the legal counsels of FAO and WHO, building on the comments made at the session.

CCEXEC77³⁴ (2019) EXTRACTED

HISTORY AND IMPLICATIONS OF THE FOURTH PARAGRAPH OF THE STATEMENTS OF PRINCIPLE (Agenda Item 6)³⁵

77. The Codex Secretariat introduced the document and highlighted the similarity of the situation that Codex had found itself in 1991 with that of 2018 when Members agreed on the JECFA evaluation of certain MRLs for veterinary drugs, but there was no consensus to adopt a Codex standard. He clarified that the Statements of Principle concerning the Role of Science had been developed following the 1991 situation to assist Codex with such cases; however, they did not seem to have helped in resolving such problems. Since then there had been seven similar situations that had led to voting, most recently in 2012 on ractopamine. In most cases the results were very close, showing how divided CAC was on the topic.
78. The Codex Secretary emphasized that during this period of almost 30 years, thousands of Codex standards and maximum limits had been adopted by consensus, even though finding consensus had sometimes been difficult. The Codex Secretary considered that the value and effectiveness of Codex should not be measured by the few problematic cases, but on its overall success and that the time dedicated to these few issues took time and attention away from other important topics.
79. The Codex Secretary outlined the different approaches (besides voting) that CAC had taken when difficult situations had arisen, all of which had advantages and disadvantages:
- reservations;
 - holding standards at Step 8;
 - building differences of application into the text to explain different situations in different countries/regions; and
 - declaring a topic as not amenable to standardization and discontinuing work.
80. The Codex Secretary noted that reservations had been a successful tool though it had never been explicitly mentioned in Codex reports where this was related to an application of Statement 4. An exception to this was the 24th Session of CCRVDF where this possibility had been proposed. The Secretary further explained that the document contained a textual analysis of Statement 4, illustrating how the statement could be interpreted.
81. The Codex Secretary clarified that the final two paragraphs in the document contained proposals for possible further steps:
- (i) to explore how a consistent application of the Statements of Principle concerning the Role of Science could help Codex setting standards that are needed by members and are based on science, while acknowledging different situations in different areas of the world; and/or
 - (ii) to follow up on the legal opinion transmitted to CCEXEC75, which suggests “*a review of the Statements of Principle to better clarify the extent to which ‘other legitimate factors relevant for health protection and fair trade practices’ may be taken into account in the adoption of Codex standards*”.
82. CCEXEC welcomed the thorough document prepared by the Codex Secretariat.

³⁴ REP19/EXEC2, paras. 77-87

³⁵ CX/EXEC 19/77/10

83. CCEXEC, in a first round of interventions, noted the following:

- Codex should be an impartial, science-based and rules-based, predictable standards setting body and everything needed for this is contained in the Procedural Manual including the Statement of Principles and the Criteria for the Consideration of Other Factors referred to in the Second Statement of Principle. The only guidance needed is to send clear instructions to apply them. The failures are not due to unclear rules, but to the fact that the rules have not been consistently applied.
- A cursory review, by one Member, of committee reports showed that over the last 10 years the issue of “other factors” had been raised 98 times in various Codex committees, and not just in CCRVDF. In the assessment of the Member, of these 98 instances, factors outside the mandate of Codex, and excluded by the criteria in the Procedural Manual, had been raised at least 24 times to delay or prevent adoption of standards. The Member concluded that on at least 74 occasions committees and chairpersons had followed the Statements and the criteria so more often than not Codex had been successful in following its principles.
- In order to find a solution there needs to be a mechanism for dialogue that should be open and inclusive so that the views of all parties are properly considered.
- The mandate of CCEXEC is to work for Codex as a whole, and not to repeat arguments and positions given at committee level. History shows the success of Codex as it has adopted thousands of standards, and where applicable based these on scientific advice provided by FAO and WHO scientific bodies. The periodic problems experienced in CCRVDF related to MRLs for growth promoters should not create polarization and division. Codex should rather find ways to work together. One possibility could be to explore how the Statements of Principle could be applied in order to move forward and find a good solution.
- We need to be careful not to undermine science and our scientific expert bodies. However, we need to keep the concerns of all in mind and since we know there is an issue, there is a need to look for a solution. It is difficult to say that one side is right and the other is wrong. An option could be to establish a small task force within CCRVDF to look at this.
- Codex is at a critical point in time and it is important not to undermine the work of the scientific expert bodies or waste limited resources. The delay in advancing standards is a real hindrance. Consumer health protection and not creating food trade obstacles should be the focus of Codex work. Since Codex standards are the basis of national regulations, and are particularly important for countries with limited resources it is difficult to justify participating in Codex if the work leads to a deadlock. Voting is a legitimate tool, and consensus is not the only option, we can also take decisions by majority. We need to be creative and innovative, but presently there is no need to revise Codex procedures.
- Members place a high value on the role of science. Even though blockages do not arise often, when they do, they cause problems. We should not continue discussing in the abstract but find a way forward to make the Statement of Principles work for Codex and apply them consistently across Codex committees.
- Codex should not draft yet another document on this topic, but rather communicate on the need to apply the established Statement of Principles, to prevent damage to the work and reputation of Codex. Codex standards allow Members to contribute to international food trade due to their science-based nature.
- It is time to think innovatively and identify what else we can do. More importantly, the Statement of Principles should not be reopened, but a small group or sub-committee could address this issue in a process that will feed into decision-making.
- The guidance in the Procedural Manual is sufficient and the important thing is to operationalise it. Codex has many other issues to discuss and should not lose time by reopening procedures but rather use what is already there.

84. Following the emerging consensus on the usefulness to develop guidance to committees and chairpersons on how to operationalise the Statements of Principle while not reopening them, the Committee discussed the best way to develop such guidance and identified the following options:

- CCEXEC could give direct instructions to committees and chairpersons to apply the Statement of Principles;
- An EWG could be formed by CAC to allow this topic to be discussed in an open and inclusive forum where all interested parties could participate. The EWG could for example be co-chaired by USA and EU. An example of the important success of such a group is the work on Note 161 in CCFA;
- A sub-committee of CCEXEC could be established to develop draft guidance while consulting with Codex chairpersons and the membership;

- The chairpersons of technical committees could be consulted at the meeting of chairpersons to understand their views on what guidance would be helpful to them;
- The decision of whether to use a sub-committee of CCEXEC or an EWG under CAC, could be left to the Commission;
- The task could be given to CCGP as the forum for procedural questions.

85. A question arose on how the EU as one of the main interested parties in the debate could contribute to the work if it was undertaken by a CCEXEC sub-committee. The Representative of the Legal Counsel of WHO indicated that this could be done through the Coordinator for Europe.

86. The Chairperson taking into consideration the views expressed, proposed to create a sub-committee of the CCEXEC to further address the issue.

Conclusion

87. CCEXEC agreed to establish a sub-committee of CCEXEC on the application of Statement of Principles concerning the Role of Science with the Terms of Reference as contained in Appendix IV.

CCEXEC80³⁶ (2020) EXTRACTED

CCEXEC SUB-COMMITTEE ON THE APPLICATION OF THE STATEMENTS OF PRINCIPLE CONCERNING THE ROLE OF SCIENCE - UPDATE (Agenda item 4)³⁷

37. Following the introduction by the Chairperson of the sub-committee and the update by the Codex Secretary, CCEXEC noted the exceptional and unprecedented challenges that prevented the progress of this work, confirmed its ongoing importance, recalling also the strong interest of Codex Members in this work³⁸, and supported the extension of the mandate of the sub-committee until CCEXEC81 to facilitate completion of the work.

38. Members noted the approach to the development of the guidance presented by the Codex Secretary based on discussions held with Codex subsidiary body Chairpersons. In the absence of a draft guidance document, the following views were expressed by Members:

- The practical guidance should be a simple/concise text and/or in the form of a flow chart or decision tree and could be included in the Codex Chairperson's Handbook.
- The guidance should be concise, i.e. brief, but comprehensive.
- There was sufficient guidance in the PM and operationalization of the SoP should not be overcomplicated.
- Chairpersons needed to ensure that Codex work remained within its mandate and the Codex Chairperson's Handbook already provided an important resource.
- The guidance should reiterate that decisions in Codex need to be based on science and consistent with the criteria for consideration of other factors in the PM.
- Moving forward the work should adhere to the mandate provided to the Secretariat and the sub-committee by CCEXEC78.
- This work should not lead to any changes in the text on the Statement of Principles (SoP) in the PM.
- The guidance should include options available to Chairpersons in case of disagreements/difficulties finding consensus in the standards development process, and provide examples of their use in order to raise awareness of the available options and their utility, noting that these options were outlined in the paper on "History and implications of the fourth paragraph of the statements of principle"³⁹ presented to CCEXEC77.
- Different views were expressed on the matter of the use of footnotes in Codex standards and while some considered it relevant for the further development of the guidance, others were of the opinion that this was not relevant to the operationalization of the SoP.
- The suggested development of a registry of reservations caused some concern and that it could lead to misunderstanding as this could give more weight to reservations than currently afforded and thus undermine Codex standards.

³⁶ REP21/EXEC1, paras. 37-43

³⁷ CX/EXEC 21/80/4

³⁸ CX/EURO 19/31/CRD 9; REP19/CAC

³⁹ CX/EXEC 19/77/10

- Guidance on reservations should be provided as the PM currently does not cover criteria for reservations.
 - Countries have a good understanding of reservations and their use in Codex and other international organizations and this was not part of the charge to the sub-committee. this sentence seems to miss something
 - Reservations did not necessarily need to be a part of application of the SoP.
 - Reservations are commonly used in reports of committees and CAC together with their justification, and CCEXEC78 had already requested the Chairpersons of subsidiary bodies to include the technical basis of reservations in meeting reports so no further guidance was needed.
 - The terms used in the SoP were sufficiently clear and the Chairpersons of subsidiary bodies had indicated their comfort with the text, so no further clarification was needed.
 - The work of the sub-committee should not re-open discussions on or interpret the terms in the SoP.
 - The guidance should be relevant to Codex Members as well as the Chairpersons of Codex subsidiary bodies, in particular new Chairpersons, to enhance their understanding and facilitate Members' participation in Codex meetings, particularly with regard to the use of reservations and application of the SoP.
39. Noting the range of comments expressed, the Codex Secretary indicated that this provided the Codex Secretariat with a better sense of views within CCEXEC. These would be carefully considered in developing a first draft of the practical guidance.
40. In response to a request about providing information on this topic in the margins of CCGP32 (2021), the Secretary noted that this would not be possible since the draft guidance was yet to be developed. However, given the experience with virtual meetings, he suggested that the subcommittee could assess virtual options for engagement with the Codex membership once the guidance had been drafted.
41. Acknowledging the views not to overcomplicate the guidance, the Secretary noted however that understanding the SoP required an extensive knowledge of Codex, hence the guidance may need to bridge that knowledge gap for many Members.
42. The Chairperson of the sub-committee confirmed that in moving forward the mandate of the sub-committee remained the same and noted that CCEXEC had already agreed that there would be no changes to the PM.

Conclusion

43. CCEXEC agreed:
- i. to extend the mandate of the sub-committee to CCEXEC81;
 - ii. that, as mandated by CCEXEC78, the Codex Secretariat, in cooperation with FAO and WHO, will develop the first draft of the practical guidance for presentation to the sub-committee, taking into account the comments made at CCEXEC80; and
 - iii. that the sub-committee should consider how to ensure the engagement of the wider Codex membership in the development of the guidance.

ADDITIONAL INFORMATION**1. SUMMARY ON JECFA EVALUATIONS ON ZILPATEROL HYDROCHLORIDE⁴⁰****JECFA78⁴¹ (2013) EXTRACTED**

1. JECFA78 was convened in Geneva, Switzerland, from 5 to 14 November 2013 to evaluate residues of certain veterinary drugs in foods. The full report of the meeting is published in the *WHO Technical Report Series (TRS 988)*. Toxicological monographs summarizing the data that were considered by JECFA are published in *WHO Food Additives Series No. 69*; residue monographs summarizing the data that were considered by the Committee are published in *FAO JECFA Monographs No. 15*.

Zilpaterol hydrochloride: JECFA78 established an ADI of 0–0.04 µg/kg body weight on the basis of a LOAEL of 0.76 µg/kg body weight for tremor in humans. An uncertainty factor of 20 was applied, comprising a default uncertainty factor of 10 for human individual variability and an additional uncertainty factor of 2 to account for the use of a LOAEL for a slight effect instead of a NOAEL. JECFA noted that the ADI is based on an acute effect. JECFA also noted that the upper bound of the ADI provides a margin of safety of at least 1250 with respect to the NOAEL of 50 µg/kg body weight per day for the formation of leiomyomas in rats.

Only limited data were available for tissues other than muscle, and JECFA was unable to determine a suitable marker residue in other edible tissues. JECFA used the highest concentrations of total residues to estimate dietary exposure, because no median residue levels could be determined and no marker residue in liver and kidney was defined. The calculations indicated that the dietary exposure was higher than the ADI for the withdrawal times for which data were provided. JECFA concluded that it was not possible to recommend MRLs for zilpaterol. The following data are needed to establish MRLs:

- results from studies investigating marker residue in liver and kidney;
- results from studies determining marker residue to total residue ratio in liver and kidney;
- results from depletion studies to enable the derivation of MRLs compatible with the ADI.

All such studies should use sufficiently sensitive validated analytical methods capable of measuring zilpaterol and its major metabolites in edible tissues of cattle.

After the publication of the report, the JECFA Secretariat has provided further clarifications in response to a series of questions received from the Zilpaterol sponsor, concerning both the toxicological and the residue part of the evaluation.

JECFA81 will be dedicated to the evaluation of veterinary drug residues in food, and will be held 17 to 26 November 2015. A call for data for to evaluations of ethoxyquin, sisapronil and to complete the evaluation of zilpaterol hydrochloride has been published, with a submission deadline of 15th March 2015.

⁴⁰ JECFA summary and full reports as well as toxicological and residue monographs, including databases, can be downloaded from the FAO and WHO websites as follows.

- FAO: <http://www.fao.org/food-safety/scientific-advice/jecfa/en/>
www.fao.org/food/food-safety-quality/scientific-advice/jecfa/en/
- WHO: www.who.int/foodsafety/publications/jecfa/en/
<https://www.who.int/foodsafety/databases/en/>

JECFA publications: <http://www.fao.org/food-safety/resources/publications/en/>

JECFA summary reports:

- FAO: <http://www.fao.org/food/food-safety-quality/scientific-advice/jecfa/summary-reports/en/>

JECFA full reports: Technical Report Series (TRSs):

- FAO: <http://www.fao.org/food/food-safety-quality/scientific-advice/jecfa/full-reports/en/>
- WHO: <https://www.who.int/foodsafety/publications/jecfa-reports/en/>

JECFA Monographs

Toxicological Monographs: WHO Food Additives Series (FAS)

- FAO: <http://www.fao.org/food/food-safety-quality/scientific-advice/jecfa/toxicological-monographs/en/>
- WHO: <https://www.who.int/foodsafety/publications/monographs/en/>

Residue Monographs: Compendium of FAO Food Additive Specifications

- FAO: <http://www.fao.org/food/food-safety-quality/scientific-advice/jecfa/jecfa-publications/en/>

⁴¹ CX/RVDF 15/22/4, paras. 4 and 28

JECFA81⁴² (2015) EXTRACTED

2. JECFA81 was held in Rome, Italy, from 17 to 26 November 2015 to evaluate residues of certain veterinary drugs in foods. The full report of the meeting is published in the WHO Technical Report Series (TRS 997). Toxicological monographs summarising the data that were considered by JECFA81 are published in *WHO Food Additives Series No. 72*; residue monographs summarising the data that were considered by JECFA are published in *FAO JECFA Monographs No. 18*.

Zilpaterol hydrochloride: JECFA81 recommended MRL⁴³ for the following veterinary drugs: ivermectin, teflubenzuron and zilpaterol hydrochloride.

JECFA85⁴⁴ (2017) EXTRACTED

3. JECFA85 was held in Geneva, Switzerland, from 17 to 26 October 2017 to evaluate residues of certain veterinary drugs in foods. The full report of the meeting is published in the WHO Technical Report Series (TRS 1008). A fully edited pre-publication report was circulated through the Codex Electronic Distribution List on 7 December 2017. Toxicological monographs summarising the data that were considered by JECFA will be published in *WHO Food Additives Series No. 76*; residue monographs summarising the data that were considered by JECFA will be published in *FAO JECFA Monographs No. 21*.

Zilpaterol hydrochloride: JECFA81 accounted for limited oral bioavailability of only the non-extractable (bound) zilpaterol residues in cattle tissues. The remaining (extractable) zilpaterol residues were considered to be fully bioavailable. The new bioavailability data submitted to JECFA85, support the approach used in the previous assessment. Following evaluation of these data, the MRLs recommended by JECFA81 remain unchanged.

⁴² CX/RVDF 16/23/3, para. 3

⁴³ CX/RVDF 16/23/6

⁴⁴ CX/RVDF 18/24/3, para. 18

2. MRLs for ZILPATEROL HYDROCHLORIDE

PROPOSED DRAFT MRLs FOR VETERINARY DRUGS

ZILPATEROL HYDROCHLORIDE⁴⁵

(β2-adrenoceptor agonist)

(Held at Step 4 by CCRVDF24)

ADI: ADI is 0-0.04 µg/kg body weight established at JECFA78 (WHO TRS No. 988, 2014) and reaffirmed at JECFA81 (2015) and JECFA85 (2017).

ARfD: ARfD is 0.04 µg/kg body weight based on a lowest-observed-adverse-effect level (LOAEL) of 0.76 µg/kg body weight for acute pharmacological effects observed in a single-dose human study, with application of an uncertainty factor of 20, comprising a default uncertainty factor of 10 for human individual variability and an additional uncertainty factor of 2 to account for use of a LOAEL for a slight effect instead of a NOAEL (JECFA81).

GEADE: GEADE is 1.9 µg/day for the general population, which represents approximately 80% of the ARfD. The GEADE is 0.57 µg/day for children, which represents approximately 94% of the ARfD (JECFA81).

Residue Definition: Zilpaterol (free base) in muscle, liver and kidney.

Species	Tissue	MRLs (µg/kg)	Step	JECFA
Cattle	Kidney	3.3	4	81
Cattle	Liver	3.5	4	81
Cattle	Muscle	0.5	4	81

⁴⁵

As evaluated by JECFA78, 81 and 85.

As submitted for consideration by CCRVDF23 (2016) in CX/RVDF 16/23/6 and shown in REP16/RVDF, Appendix V and further considered by CCRVDF24 (2018) and shown in REP18/RVDF, Appendix III

PART V**ACRONYMS USED IN THIS DOCUMENT**

ADI	Acceptable Daily Intake
ArfD	Acute Reference Dose
AU	African Union
CAC	Codex Alimentarius Commission
CCEXEC	Executive Committee
CCFA	Codex Committee on Food Additives
CCGP	Codex Committee on General Principles
CCRVDF	Codex Committee on Veterinary Drugs in Foods
CL	Circular Letter
CRD	Conference Room Document
EU	European Union
EWG	Electronic Working Group
FAO	Food and Agriculture Organization
GAP(s)	Good Agricultural Practice(s)
GEADE	Global Estimated Acute Dietary Exposure
GVP(s)	Good Veterinary Practice(s)
JECFA	Joint FAO/WHO Expert Committee on Food Additives
JMPR	Joint FAO/WHO Meetings of Pesticide Residues
LOAEL	Lowest-Observed-Adverse-Effect Level
MRL(s)	Maximum Residue Limit(s)
NOAEL	No-Observed-Adverse-Effect Level
PM	Procedural Manual
PWG	Physical Working Group
SoP	Statements of Principle
USA	United States of America
WG	Working Group
WHO	World Health Organization
WTO	World Trade Organization
WTO/SPS	WTO Agreement on Sanitary and Phytosanitary Measures