CODEX ALIMENTARIUS COMMISSION

Food and Agriculture Organization of the United Nations

World Health Organization

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Agenda Item 8 **CX/RVDF 23/26/8-Add.1**

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JOINT FAO/WHO FOOD STANDARDS PROGRAMME

CODEX COMMITTEE ON RESIDUES OF VETERINARY DRUGS IN FOODS

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CRITERIA AND PROCEDURES FOR THE ESTABLISHMENT OF ACTION LEVELS FOR UNINTENDED AND UNAVOIDABLE CARRYOVER OF VETERINARY DRUGS FROM FEED TO FOOD OF ANIMAL ORIGIN

Comments in reply to CL 2022/77-RVDF

submitted by

Brazil, European Union (EU), Kenya, Peru, Uganda, United States of America (USA), African Union (AU) and Health for Animals

Background

1. This document compiles comments received through the Codex Online Commenting System (OCS) in response to circular letter CL 2022/77-RVDF[1] issued in December 2022. Under the OCS, comments are compiled in the following order: general comments are listed first, followed by comments on specific sections. For this CL, comments comprise general and specific comments.

Explanatory notes on the annexes

2. Comments submitted through the OCS are hereby annexed and presented in tabulated format.

[1] 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

Annex

GENERAL AND SPECIFIC COMMENTS

COMMENT	MEMBER/OBSERVER
Brazil congratulates and thanks the Chair and Co-chair of the EWG and acknowledges the efforts to set forth a methodology for the establishment of action levels for unintended and unavoidable carryover of veterinary drugs from feed to food of animal origin. Brazil considers that the document will facilitate the decisions to be taken by the competent authorities as a result of risk management measures. **Q.1 What methodology should be used by CCRVDF when setting action levels to accommodate presence of residues due to unavoidable and unintended veterinary drug carry-over in non-target animal feed?** Brazil considers that the methodology proposed is detailed and adequate for setting action levels for unintended and unavoidable carryover of veterinary drugs from feed to food of animal origin. **Q3. Are the proposed criteria suitable?** Brazil considers that the proposed 4 steps are suitable to establish the action levels of residues. **Q4. Which approach should be used to estimate the veterinary drug carry-over level in non-target animal feed for non-target animal (e.g., hypothetical carry-over rates, highest residue levels in feed from feed mills, etc.)?** Brazil proposes a combination of Option 1 and Option 2, starting from Option 1, with a series of hypothetical carry-over rates. We suggest starting the calculations from the highest % level and decreasing it until getting to a % that is deemed to be adequate in terms of diet exposure/ human consumption. The % carry over rate defined would then be tested by using option 2, to check whether, under the application of Good Manufacturing Practices, it is possible for the industry to be below this action level or a higher level is unavoidable. **Q5. What assumptions should be made in calculating TFs?** Brazil considers that the assumptions made under Notes – Step 2 are the needed assumptions to be made. **Q6. What level of importance should be given to monitoring data when relevant monitoring data is available?** Brazil considers that monitoring data is of great importance; however, the quality of the data should be assessed in the process. **Q7. What approach should be given to determining an appropriate MR:TR (Marker Residue: Total Residue of toxicological concern or microbiological concern) ratio when there is no specific radiolabelled data for a food commodity exposure via veterinary drug carry over?** Brazil considers that the ratio MR:TR could be extrapolated to similar species and does not envision, at this point of the discussion, other scientifically based approaches for different species. We will follow the discussion during the plenary meeting. **Q8. Are there other considerations that have not been considered in this risk assessment procedure?** Brazil does not have other considerations for the proposed procedure.	**Brazil**

COMMENT	MEMBER/OBSERVER
Q9. Are the proposed roles and responsibilities appropriate in establishing action levels? Brazil considers that the proposed roles and responsibilities are appropriate in establishing action levels. **Q10. Any other considerations not addressed in the above questions that could further assist the consideration of this item.** Brazil has no further considerations for the time being.	
Proposal The criteria and procedures for the establishment of action levels for unintended and unavoidable carry-over of veterinary drugs from feed to food of animal origin as presented in document CX/RVDF 23/26/8 are overall acceptable for the EU. However, they should in a first phase be limited to veterinary drugs other than antimicrobial active substances. The unintended and unavoidable carry over of antimicrobial active substances could then be considered in a second phase in which, besides food safety concerns related to residues in edible parts of non-target animal species, would also consider the avoidance of antimicrobial resistance (AMR) as a public health outcome, in conjunction with other relevant Codex texts on AMR. **Q3. Are the proposed criteria suitable?** The proposed criteria are acceptable. **Q4. Which approach should be used to estimate the veterinary drug carry-over level in non-target animal feed for non-target animal (e.g., hypothetical carry-over rates, highest residue levels in feed from feed mills, etc.)?** As regards the options for animal dietary exposure assessments, it seems appropriate to consider hypothetical carry-over rates of x% of the highest authorised dose (1 %, 2.5% or 3 %). The rate of 5 % should not be considered as this rate is too high in case all good practices, including the application of appropriate mitigation steps, at the different stages of the feed chain are applied. If monitoring data provide evidence that lower levels of carry-over can be achieved than the hypothetical carry-over rates, then these lower levels of carry-over should be considered. In case effective data indicate higher levels of carry-over than the hypothetical carry-over rates, then the hypothetical carry-over rate are to be used and feed business will have to strengthen their good practices, including the application of appropriate mitigation steps, to achieve these hypothetical carry-over rates. Experience in the EU have demonstrated that when good practices are applied the carry over rates of 1 and 3 % (depending on the mitigation measures applied) are achievable and this independently from the size and the nature of the feed manufacturing plants. **Q6. What level of importance should be given to monitoring data when relevant monitoring data is available?** • For the data on the carry over in feed: see the reply to Q4. • For the residue levels in food of animal origin: in case extensive monitoring data demonstrate that the levels of residues are (much) lower than the calculated action levels using estimated TF factors, then the used assumptions as regards carry-over level in non-target feed and for the calculation of the TF factor might need closer examination and reconsideration. In case monitoring data indicate higher levels than the calculated action level, then an examination of the assumptions can also be done but much more cautiously given that there is no evidence that these monitoring data are the result of applying good practices, including the appropriate mitigation measures, all along the feed chain.	**EU**

COMMENT	MEMBER/OBSERVER
Q8. Are there other considerations that have not been considered in this risk assessment procedure? Antimicrobial active substances should be excluded from the scope of this document because in addition to food safety concerns, AMR concerns as a consequence of carry over antimicrobial active substances need to be considered. In addition, a prioritisation of new work proposals of action levels should be considered. A valid criterion for prioritisation should be the proven occurrence (combined with frequency of occurrence) of residues of the veterinary drug in edible commodities from non-target animals. **Q9. Are the proposed roles and responsibilities appropriate in establishing action levels?** The proposed roles and responsibilities are acceptable. **Q10. Any other considerations not addressed in the above questions that could further assist the consideration of this item.** Although CCRVDF and Codex do not deal with animal health, it would be appropriate to mention explicitly that the necessity to limit the unintended cross-contamination of non-target feed is not only very important for food safety/public health but also for animal health as certain non-target animal species might be very sensitive to the presence of traces of certain veterinary drugs. To do so, as an overarching principle, it could be mentioned that relevant World Organisation for Animal Health (WOAH, founded as OIE) standards need to be considered for all animal health aspects.	
General Comment: Kenya commends the EWG for developing the criteria and procedures for the establishment of action levels for residues of veterinary drugs in foods linked to the unintended and unavoidable carryover of veterinary drugs from non-target feed to food of animal origin. **General criteria on the proposed approach** Kenya supports the "general criteria or rules" on the proposed approach for establishing action levels for veterinary drug residues in food products from non-target animals linked to the unintended and unavoidable carry-over of veterinary drugs in nontarget animal feed. Rationale: The proposal to have CCVRDF to request JECFA to conduct an appropriate Human dietary exposure assessment based on the proposed action level will mitigate the risk to human health that could arise from residues of veterinary drugs in food of non-target species caused by unavoidable and unintended veterinary drug carry-over in non-target animal feed. **Q3. Are the proposed criteria suitable?** Position: Kenya further supports the proposed four step procedure for setting the Action Levels for residues of veterinary drugs detected in foods of animal origin (i.e. from non-target animals) determined to be caused by unavoidable and unintended veterinary drug carry-over in nontarget animal feed based on the Guidelines on the Application of Risk Assessment for Feed (CXG 80- 2013) and risk assessment approaches. Kenya also supports the inclusion of an option to use default low levels of carry-over from medicated to un-medicated feed provided that this is supported by data from studies/surveys undertaken in feed mills operating under good manufacturing practice conditions. Rationale: Animal feed and its ingredients should be obtained and stored under suitable conditions to prevent their contamination by pests or chemical contaminants, physical or microbiological or other undesirable substances during their production, handling, storage and transportation. Animal feed should be in good condition and meet the standards of generally accepted quality. Good agricultural practices (GAP), Good Manufacturing Practices (GMP) and principles of Hazard Analysis Critical Control Points (HACCP) should be followed to control the risks that may appear in food.	**Kenya**

COMMENT	MEMBER/OBSERVER
(General Comment) Peru does not have comments on the proposed approach to establishing action levels for veterinary drug residues in food products from non-target animals linked to unintended and unavoidable veterinary drug carry-over in non-target animal feed.	**Peru**
Uganda supports the "general criteria or requirements" for establishing action levels for veterinary drug residues in food products from non-target animals linked to the unintended and unavoidable carry-over of veterinary drugs in non-target animal feed. The EWG put into consideration all relevant factors such as authorized veterinary drugs, feed production mechanisms, established Codex MRLs, availability of analytical methods e.t.c The proposed four step procedure for setting the Action Levels for residues of veterinary drugs detected in foods of non-target animals determined to be caused by unavoidable and unintended veterinary drug carry-over in non-target animal feed should be adopted by CCRVDF26. This is because it is based on the already established Codex Guidelines on the Application of Risk Assessment for Feed (CXG 80-2013) and risk assessment approaches. Specific comments • Step 1: Animal dietary exposure assessment. We propose that Option 2 is adopted i.e. the highest residue levels in feed determined by feed mills is used to estimate the veterinary drug carry-over level in non-target feed for non-target animal. • When calculating Transfer Factors (TFs) it may be assumed that metabolism of the drug takes places in the different tissues and the level of residues in the tissue or commodity of interest is low. • The proposed roles and responsibilities for CCRVDF and JECFA are very appropriate since each committee has the requisite expertise. b. A pilot study using Nicarbazin residues in chicken eggs, as presented in the discussion paper, which illustrates the proposed approach for estimating action levels as presented in Appendix I, Part II The proposed action level of 0.220 mg/kg for Nicarbazin in Chicken Eggs be adopted by CCRVDF26 since the human dietary exposure to Nicarbazin residues was assessed using the JECFA TMDI (Theoretical Maximum Daily Intake) which is a conservative approach.	**Uganda**
Q4. Which approach should be used to estimate the veterinary drug carry-over level in non-target animal feed for non-target animal (e.g., hypothetical carry-over rates, highest residue levels in feed from feed mills, etc.)? The United States supports deriving action levels only when data indicate that unavoidable and unintended carryover occurs and results in residues in edible commodities from non target species. In the absence of such data, CCRVDF would be setting action levels when no evidence of carryover exists. Without evidence of carryover, the action levels would be accounting for misuse of veterinary drugs rather than unavoidable and unintended carryover of veterinary drugs into the feed of non target species. To this end, the United States supports the proposed approach that uses actual data indicating the occurrence of carryover (i.e., Option 2 in the animal dietary exposure assessment outlined in CX/RVDF 23/26/8). **Q7. What approach should be given to determining an appropriate MR:TR (Marker Residue: Total Residue of toxicological concern or microbiological**	**USA**

COMMENT	MEMBER/OBSERVER
concern) ratio when there is no specific radiolabelled data for a food commodity exposure via veterinary drug carry over? The United States supports the approach described in CX/RVDF 23/26/8 in which CCRVDF asks JECFA to conduct a human dietary exposure assessment when deriving action levels (i.e., Step 4). The United States also supports the specific requests that CCRVDF will ask of JECFA outlined in item 3 a, b, c and d of the Proposed Procedure found in CX/RVDF 23/26/8. However, the United States recognizes that radiolabeled data might not be available to allow JECFA to estimate an MR:TR ratio. In the request to JECFA, the United States suggests that CCRVDF ask JECFA to conduct a margin of exposure (MOE) assessment in lieu of the standard dietary exposure assessment models (e.g., TMDI, EDI, GECDE) if an MR:TR ratio cannot be estimated. The MOE assessment would account for the dietary exposure resulting from the established MRLs and the proposed action level. Then, based on the outcome of the MOE assessment, CCRVDF can make a risk management decision on whether to establish the action level in the absence of an MR:TR ratio. The proposed approach is outlined below for situations in which JECFA cannot estimate an MR:TR ratio. 1. CCRVDF proposes an action level value. 2. CCRVDF asks JECFA to conduct an MOE assessment that accounts for the dietary exposure resulting from the established MRLs and the proposed action level. a. For the dietary exposure resulting from the edible tissues with established MRLs, CCRVDF would ask JECFA to estimate this value as they would normally, relying on the available residue data (e.g., marker residue and MR:TR ratio) and consumption data. b. For the dietary exposure resulting from the proposed action level, CCRVDF would ask JECFA to estimate this value using the proposed action level value and the available consumption data. It is important to note that this value only would represent an exposure value for the marker residue, not total residues. c. CCRVDF would then ask JECFA to generate an MOE value that is ratio between the Health Based Guidance Value (HBGV) and sum of the two values in 2a and 2b. 3. CCRVDF then makes a risk management decision based on the MOE value. Specifically, CCRVDF would decide whether the MOE is sufficiently large to reasonably to conclude that the total residue exposure from the established MRLs and proposed action level will not exceed the HBGV despite not knowing the MR:TR associated with the proposed action level. 4. If CCRVDF determines that the MOE is sufficiently large, then CCRVDF moves forward with establishing the proposed action level.	
AU supports the “proposed criteria or rules” on the proposed approach for establishing action levels for veterinary drug residues in food products from non-target animals linked to the unintended and unavoidable carry-over of veterinary drugs in non-target animal feed. In addition to establishing action levels, animal feed and its ingredients should be obtained and stored under suitable conditions to prevent their contamination by pests or chemical contaminants, physical or microbiological or other undesirable substances during their production, handling, storage and transportation. Animal feed should be in good condition and meet the standards of generally accepted quality. Good agricultural practices (GAP), Good Manufacturing Practices (GMP) and principles of Hazard Analysis Critical Control Points (HACCP) should be followed to control the risks that may appear in food. AU supports the proposed four-step procedure for setting the Action Levels for residues of veterinary drugs detected in foods of animal origin (i.e. from	**AU**

COMMENT	MEMBER/OBSERVER
non-target animals) determined to be caused by unavoidable and unintended veterinary drug carry-over in non-target animal feed based on the Guidelines on the Application of Risk Assessment for Feed (CXG 80-2013) and risk assessment approaches.	
HealthforAnimals urges the EWG to please consider the implementation of the Code of Practice on Good Animal Feeding (CAC/RCP 54-2004) to advance the objectives of the Committee instead of developing new criteria, methods, or regulatory constructs. The Code of Practice on Good Animal Feeding includes detailed information on controls and approaches to avoid contamination between batches of feed that include a veterinary medicine. The Code highlights the need to have procedures to avoid cross-contamination between batches, such as flushing, sequencing, and physical clean-out. HealthforAnimals is not aware of any significant trade issues from the adventitious presence of very low levels of veterinary medicines in feed of non-target species and subsequent impact on foods of animal origin. HealthforAnimals is concerned that the development of tolerances or action limits could introduce standards that are more restrictive than necessary to protect public and animal health – and thereby, restrict access to feed. The ability to support the health of animals by incorporating medicine in their feed provides a unique channel to provide therapy and many key diseases. <u>JECFA As Source of Scientific Advice</u> CCRVDF should continue to rely on JECFA as the primary responsible entity for providing independent scientific advice to the Committee. JECFA assists the CCRVDF by evaluating the available scientific data on the veterinary drug prioritised by the CCRVDF. The work of this EWG and the methodology considered should also reflect the Codex Procedural Manual's Risk Analysis section as prescribed for CCRVDF. JECFA relies on evidence and data to inform its risk assessments. The method should be derived from data and study instead of theory and extrapolation. <u>Relevance to Codex Objectives</u> The Codex Procedural Manual's Article 1(a) states that the purpose of Codex is "protecting the health of the consumers and ensuring fair practices in the food trade;". The EWG should consider guidance for the CCRVDF that addresses the two conditions in that statement. Guidance should consider its work as it relates to the Procedural Manual. A specific quantifiable outcome or level may not be the most relevant marker for advancing the goals of Codex. A qualitative goal may apply in this matter. Specifically, it is reasonable for the EWG to consider supporting implementation of the Code of Practice on Good Animal Feeding instead of determining an acceptable maximum level of unavoidable cross-contamination in feed.	**Health for Animals**