CODEX ALIMENTARIUS COMMISSION

Food and Agriculture Organization of the United Nations

World Health Organization

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Agenda item 6 **CX/RVDF 24/27/6**

October 2024

JOINT FAO/WHO FOOD STANDARDS PROGRAMME

CODEX COMMITTEE ON RESIDUES OF VETERINARY DRUGS IN FOODS

27th Session
21-25 October 2024

Omaha, Nebraska, United States of America

MRLs FOR VETERINARY DRUGS IN FOODS ARISING FROM JECFA98 (2024)

Comments in reply to CL 2024/65-RVDF

Comments by Brazil, Canada, Chile, Costa Rica, European Union (EU), Guatemala, Kenya, Morocco, Paraguay, Philippines, United Kingdom (UK)

Background

1. This document compiles comments received through the Codex Online Commenting System (OCS) in response to CL 2024/65-RVDF[1] issued in August 2024. Under the OCS, comments are compiled in the following order: general comments are listed first, followed by comments on specific sections.

Explanatory notes on the Annex

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

1 https://www.fao.org/fao-who-codexalimentarius/resources/circular-letters/en/
https://www.fao.org/fao-who-codexalimentarius/committees/committee/related-circular-letters/en/?committee=CCRVDF

ANNEX

GENERAL COMMENTS

COMMENT	MEMBER / OBSERVER
Request for comments at Step 4 MRLs for veterinary drugs. **MRLs for Comments at Step 4** Brazil congratulates JECFA for its diligent work and supports the advancement of MRLs for clopidol, fumagillin, and imidacloprid to step 5/8 at the Codex Committee on Residues of Veterinary Drugs in Foods (CCRVDF26). Despite the incomplete data packages submitted by the sponsors for clopidol and fumagillin, and JECFA's adoption of a simplified risk assessment approach, we believe consumer safety has been maintained due to the high safety factors applied. Brazil views JECFA's simplified approach for assessing veterinary drug residues with incomplete data packages as pragmatic and necessary. However, there are some concerns as to the safety factors adopted and if they could end up being so high that the MRLs generated would become too restrictive. Anyways, we see some key benefits to this approach, listed below. **Flexibility in Risk Assessment** - Adaptable Framework: It provides a structured yet adaptable framework to address various scenarios, including older drugs, drugs with no commercial sponsor. **Systematic Collection of Prior Knowledge** - Identifying Data Gaps: By systematically collecting and evaluating existing data, JECFA can identify critical data gaps and focus on obtaining the most relevant additional information. - Evidence-Based Assessments: This ensures that the risk assessment is based on the best available evidence, even if it is not complete. **Decision-Tree Approach** - Clear Pathway: The decision-tree approach provides a clear and logical pathway for risk assessment, helping to ensure consistency and transparency in the evaluation process. - Alternative Methods: It allows for the use of alternative methods, such as the Threshold of Toxicological Concern (TTC) approach and Margin of Exposure (MOE), to assess risk when traditional data are lacking. **Communication and Transparency** - Clear Communication: The guidance emphasizes the importance of clearly communicating the outcomes, limitations, and uncertainties of the risk assessment to risk managers. - Building Trust: This transparency helps build trust in the risk assessment process and ensures that risk managers have the information they need to make informed decisions.	**Brazil**

COMMENT	MEMBER / OBSERVER
Protection of Public Health - Conservative Assumptions: By using conservative assumptions and additional safety factors when data are incomplete, JECFA ensures that the recommended MRLs are protective of public health. - Balanced Approach: The approach balances the need for thorough risk assessment with the practicalities of data availability, ensuring that safety evaluations are both rigorous and feasible.	
Request for comments on maximum residue limits (MRLs) for veterinary drugs in foods: Chile thanks JEFCA for its work during its 98th meeting and does not have comments on the MRL drafts. We therefore support advancing: - Clopidol in chickens for the kidney, liver, muscle, and skin/fat matrices; - Fumagillin dicyclohexylamine (DCH) in fish for the fillet matrix, as well as the honey matrix; and - Imidacloprid in Atlantic salmon and rainbow trout for the fillet matrix (muscle with skin in natural proportions) or muscle. Rationale: It is important for Codex to move forward with the analysis and establishment of MRLs for the active ingredients that are regularly used in animals, and for which Codex has not yet established an MRL in the respective matrix or completed a reevaluation.	**Chile**
Costa Rica supports the adoption of the developed MRLs given the importance of having new MRLs to facilitate the drug registration and availability processes.	**Costa Rica**
Guatemala agrees.	**Guatemala**
Kenya commends the evaluation work undertaken by JECFA98 for clopidol, fumagillin dicyclohexylamine, and imidacloprid. Further, Kenya agrees with the proposed MRLS for clopidol and fumagillin as proposed by JECFA98.	**Kenya**
The Philippines appreciates the efforts of the JECFA98 for the extensive work to evaluate the safety of imidacloprid, clopidol and fumagillin dicyclohexylamine. The Philippines generally supports the recommended MRLs and its advancement to Step 4 as it is. These recommended MRLs have been meticulously developed through extensive scientific research and risk assessments conducted by JECFA98. The establishment of MRLs for the three veterinary drugs is crucial in safeguarding public health by minimizing potential exposure to harmful residues. Additionally, these MRLs will play a key role in facilitating trade and ensuring that food products adhere to the safety standards. By lending support to these MRLs, the Philippines is able to uphold stringent food safety standards while simultaneously bolstering its agricultural trade opportunities.	**Philippines**

SPECIFIC COMMENTS

COMMENT	MEMBER / OBSERVER
Clopidol (Coccidiostat)	
The MRLs recommended by JECFA98 for clopidol in edible chicken tissues are lower than those established in Canada. However, Canada is supportive of the proposed MRLs as the methodology used is sufficiently conservative to protect human food safety in the absence of better data.	**Canada**
The EU cannot support, at this stage, the proposed MRLs for clopidol in chicken (kidney, liver, muscle, and skin/fat) due to the lack of data at the EU level and pending the outcome of the review by the EU of the JECFA monographs, once available.	**EU**
Following JECFA's evaluation, Morocco supports the recommended MRLs	**Morocco**
Paraguay does not have objections to the recommended MRLs and supports their advancement.	**Paraguay**
It is noted that the JECFA evaluation was completed based on a limited data package; JECFA noted that no reliable studies of reproductive performance were identified, and the only reproductive toxicity data available were from a summary of a three-generation reproductive toxicity study. It is noted that an additional safety (uncertainty) factor of 5 was applied to account for uncertainties in the data but it is unclear whether this is adequate to address the data gaps, including the lack of a prenatal developmental toxicity study in rabbits. Additionally, the ADI would be exceeded when evaluating the proposed MRLs using the TMDI approach. Nevertheless, we have no plans to adopt these MRLs in the UK and we do not intend to object to the progression of the standard to the next step.	**UK**

COMMENT	MEMBER / OBSERVER
Fumagillin dicyclohexylamine (DCH) (Mycotoxin)	
Fish As fumagillin is administered solely as the dicyclohexylamine (DCH) salt in veterinary medicine, human consumers may be exposed to residues of both moieties in edible products from treated animals. As such, Canada has concerns regarding the lack of metabolism and residue depletion data available for DCH in finfish. Without data from applicable studies, it cannot be concluded that the MRL recommended for fumagillin in fish fillet would correspond to a safe concentration of total DCH residues when GVP conditions are observed. In addition, without a validated analytical method available for the quantification of DCH (and its possible metabolites) in fish fillet, it is not currently feasible to ensure that total DCH residues will not exceed the target level (1000 µg/kg) compatible with the upper bound of the ADI. **Honey** While recognizing that parent fumagillin is not an appropriate marker residue for monitoring total fumagillin residues in honey, Canada has concerns that DCH may also not be a suitable marker due to external sources of DCH in the environment that are not related to the use of fumagillin in honeybees. This concern is supported by peer-reviewed literature1-3 as well as Canadian monitoring of DCH in honey. 1. van den Heever, J.P., Thompson, T.S., Curtis, J.M. et al. (2015) Determination of Dicyclohexylamine and Fumagillin in Honey by LC-MS/MS. Food Anal. Methods 8, 767–777 (2015). doi:https://doi.org/10.1007/s12161-014-9956-x 2. van den Heever, J. P., Thompson, T. S., Curtis, J. M., & Pernal, S. F. (2015). Stability of dicyclohexylamine and fumagillin in honey. Food Chemistry, 179, 152-158. doi:http://dx.doi.org/10.1016/j.foodchem.2015.01.111 3. van den Heever, J. P., Thompson, T. S., Otto, S. J. G., Curtis, J. M., Ibrahim, A., & Pernal, S. F. (2016). The effect of dicyclohexylamine and fumagillin on Nosema ceranae-infected honey bee (Apis mellifera) mortality in cage trial assays. Apidologie, 47(5), 663-670. doi:10.1007/s13592-015-0411-9	**Canada**
The EU cannot support, at this stage, the proposed MRLs for fumagillin dicyclohexylamine in fish fillet and honey due to the lack of data at the EU level and pending the outcome of the review by the EU of the JECFA monographs, once available.	**EU**
Residues of DCH (including any potential metabolites) should be monitored when fumagillin DCH preparations are used in fish to ensure that the concentration is < 1000 µg/kg, a target level compatible with the upper bound of the ADI. A suitable analytical method for the determination of DCH in fish fillets would need to be developed (JECFA98, 2024). Guatemala agrees.	**Guatemala**
Fumagillin is administered only as dicyclohexylamine (DCH) salt in veterinary medicine, but as the fumagillin DCH salt dissociates into the two moieties, consumers would be exposed to residues of both moieties. Overall, there also seems to be a lack of conclusive data on aspects such as metabolism and genotoxicity, and no information on depletion of DCH in fish. Nevertheless, we have no plans to adopt this MRL in the UK and we do not intend to object to the progression of the standard to the next step.	**UK**

COMMENT	MEMBER / OBSERVER
Imidacloprid (Neonicotinoid parasiticide)	
Canada is supportive of the Committee recommended MRL for Atlantic salmon and rainbow trout fillet (muscle with skin in natural proportions) and/or muscle of 600 µg/kg.	**Canada**
The EU supports the proposed MRLs for imidacloprid in Atlantic salmon and rainbow trout. The MRL recommended by JECFA is coincidental to that already in place in the EU. Tissue: Fillet (muscle with skin in natural proportions) and/or muscle Recommended MRLs (µg/kg): 600	**EU**
Following JECFA's evaluation, Morocco supports the recommended MRLs	**Morocco**
The UK is content for this MRL to proceed to the next stage, as the proposed MRL is set at the same level as the UK MRL.	**UK**