



JOINT FAO/WHO FOOD STANDARDS PROGRAMME

CODEx COMMITTEE ON RESIDUES OF VETERINARY DRUGS IN FOODS

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REPORT OF THE WORKING GROUP ON THE PRIORITY LIST OF VETERINARY DRUGS REQUIRING EVALUATION OR RE-EVALUATION BY JECFA

Introduction

1. The physical working group (PWG) on the priority list of veterinary drugs requiring evaluation or re-evaluation by JECFA was held on 20 October 2024 and chaired by James Deller (Australia). The Chair reminded the EWG on the prioritization criteria and advised the PWG that document CX/RVDF 24/27/10 had been prepared for CCRVDF27 to communicate comments received in response to circular letter CL 2024/66-RVDF which was issued in July 2024. The Chair also advised that the Republic of Korea, in their conference room document (CRD10), nominated two compounds for the priority list of veterinary drugs for evaluation or re-evaluation by JECFA.

Part I. Veterinary drugs for inclusion in the Priority List for JECFA evaluation / re-evaluation

2. Amoxicillin in chicken tissues: Amoxicillin has previously been evaluated by JECFA and an ADI and ARfD set. The request for MRLs to be established for chicken tissues was originally made by Chile in response to CX/RVDF 23/26/11. In response to CL 2024/66-RVDF, Chile indicated that data should be available before the next deadline for data submission to JECFA. At the PWG, Chile confirmed that residue depletion data and validated analytical methods should be available by 31 March 2025. Further details on this nomination are provided in Appendix 2. The working group recommended that amoxicillin in chicken tissues should be included on the priority list for evaluation.
3. Amoxicillin in chicken eggs: The Republic of Korea nominated amoxicillin for use in laying hens via drinking water in CRD10 and confirmed that metabolism and residue depletion studies for eggs can be submitted by 30 September 2025. Further details on this nomination are provided in Appendix 3. The working group recommended that amoxicillin in chicken eggs should be included on the priority list for evaluation.
4. Fumagillin dicyclohexylamine (DCH) in trout tissues: Fumagillin DCH was assessed by JECFA98 in 2024. The Republic of Korea nominated Fumagillin DCH for use in rainbow trout in CRD10 and confirmed that additional metabolism, residue depletion and analytical method studies for DCH in trout can be submitted by 31 December 2026. Further details on this nomination are provided in Appendix 4. The working group recommended that fumagillin DCH should be included on the priority list for evaluation.

Recommendation 1: Approve the nominations for amoxicillin in chicken tissues, amoxicillin in chicken eggs and Fumagillin DCH in trout tissues for inclusion on the priority list (see also Appendix 1).

5. Environmental inhibitor compounds: In response to CL 2024/66-RVDF, New Zealand highlighted the growing relevance and interest in environmental inhibitors and the likelihood of one or more compounds being submitted for evaluation by JECFA. New Zealand commented that while there is no specific environmental inhibitor compound ready for prioritisation at this time, it is likely that a compound could be submitted to the JECFA between now and the next meeting of the CCRVDF. At the PWG, the Chair noted that while environmental inhibitor compounds could be included onto the priority list for evaluation by JECFA, the nomination procedure requires that specific compounds be nominated and that knowledge about when a dossier could be available for submission was important. The PWG Chair recommended that any Member with an interest in nominating an environmental inhibitor compound onto the priority list of veterinary drugs for evaluation by JECFA should do so as part of the priority list process that will take place for CCRVDF28 in 2026.

Part II. Veterinary drugs for which data availability should be confirmed at next CCRVDF

6. Ethoxyquin: Following inclusion on the priority list at CCRVDF21 (2013), ethoxyquin had been retained on the priority list pending confirmation that data is available to enable an evaluation by JECFA. At CCRVDF26, India indicated that data was available and it was included on the priority list. Ethoxyquin was included on the agenda for JECFA98 in 2024 but was withdrawn as no data was submitted. No update on the potential for ethoxyquin data to be submitted for JECFA evaluation was provided in response to CL 2024/66-RVDF or at the PWG. As this compound had been on the priority list for 10 years without confirmation that data will be submitted for JECFA evaluation, the working group agreed to remove it from Part II of the priority list. Should a Member have data that they wish to submit for ethoxyquin, another nomination could be made in the future.
7. Norfloxacin: Norfloxacin (Cattle, Camelids, Equines, Goats, Pigs, Poultry and Sheep) was include on the priority list at CCRVDF25 (2021). A timeframe for data submission was not included with the original proposal and an update on the potential for data submission was not provided at CCRVDF26, in response to CL 2024/66-RVDF, or at the PWG. As this compound had been on the priority list for 4 years without confirmation that data will be submitted for JECFA evaluation, the working group agreed to remove it from Part II of the priority list. Should a Member have data that they wish to submit for norfloxacin, another nomination could be made in the future.

Recommendation 2: Delete ethoxyquin and norfloxacin from the Part II of the priority list.

Part III. Veterinary drugs for which additional data/information is necessary to complete the JECFA evaluation

8. Ethion: JECFA (85th meeting, 2018) requested additional data/scientific argument to enable MR and MR:TRR to be determined as well as analytical methodology. At CCRVDF26, Argentina indicated that data generation had been delayed but was expected at the time to be completed by CCRVDF27. At the PWG, Uruguay provided an update that data generation had been further delayed but was underway and was expected to be completed by 31 December 2025. The working group recommended that ethoxyquin should be included on the priority list for re-evaluation.

Recommendation 3: Approve ethion for inclusion on the priority list (see also Appendix 1).

9. Flumethrin: JECFA (88th meeting, 2019) requested additional data/scientific argument to enable MR and MR:TRR to be determined, residue depletion data, identity of metabolite in milk data and data relevant to the toxicological profile. At the PWG, the EU as the original nominator, provided an update that additional data to allow for the JECFA assessment to continue was not available. As additional data is not available for submission to JECFA, the working group agreed to remove flumethrin from Part III of the priority list.

Recommendation 4: Delete flumethrin from the Part III of the priority list.

10. Fosfomycin: Fosfomycin was originally nominated by Peru and included on the priority list at CCRVDF24 (2018). JECFA (88th meeting, 2019) requested additional data/scientific argument to enable a mADI to be set, additional data/scientific argument to enable MR and MR:TRR to be determined and analytical methodology. Fosfomycin was then included in Part III of the priority list at CCRVDF25 (2021). An update on if the data that was requested by JECFA is available for submission was not provided in response to CL 2024/66-RVDF or at the PWG. Noting that Argentina, Paraguay and Peru were not present at the PWG, a conclusion on if fosfomycin should be retained in Part III of the priority list until CCRVDF28 or be deleted at CCRVDF27 was not made by the PWG. Efforts will be made to seek an update on the potential for data availability prior to or during the plenary discussion on the priority list at CCRVDF27. If an update on data availability is not made for this compound which was previously included on the priority list and for which a JECFA assessment has commenced, a decision on if it will be retained in Part III of the priority list until CCRVDF28 to allow more time to seek information on data availability, or be deleted, will be made during the plenary discussion on the priority list (Agenda Item 10) at CCRVDF27.

Part IV. Parallel review – Evaluation of a new compound

11. Umifoxolaner: The request was made for an ADI to be established along with MRLs for cattle tissues using the parallel review process. The nominator, Brazil, has confirmed that toxicology, metabolism, residue depletion and analytical method studies should be available for submission to JECFA by December 2024 and that GVP should be available prior to the next JECFA meeting. Further details on this nomination are provided in Appendix 5. The working group recommended that umifoxolaner should be included on the priority list.

Recommendation 5: Approve umifoxolaner for inclusion on the priority list (see also Appendix 1).

12. Selamectin: JECFA (94th meeting, 2022) concluded that MRL recommendations could not be made without full registration in a Member state, including GVP. At the PWG, and Observer provided an update that national approval and GVP was not expected to become available. As the information that was requested by JECFA, namely GVP, is not available, the working group agreed to remove selamectin from Part IV of the priority list.

Recommendation 6: Delete selamectin from the Part IV of the priority list.

Part V. Extrapolation

13. No new nominations to the priority list for the extrapolation of MRLs were received in response to CL 2024/66-RVDF, or at the PWG.

Appendix 1: Priority list of veterinary drugs for evaluation or re-evaluation by JECFA

Name of Compound	Question(s) to be answered	Registration status	Proposed by	Comments	When will data package be available
PART I: Veterinary drugs for inclusion in the Priority List for JECFA evaluation / re-evaluation					
Umifoxolaner (Part IV – Parallel review)	The request is for an ADI to be established for umifoxolaner along with MRLs for cattle muscle, fat, liver and kidney.	Nominator noted that the review of the risk assessment for food safety dossier ongoing in Brazil. Approval is expected prior to the next JECFA meeting.	Brazil	Umifoxolaner has not been assessed by JECFA. A toxicological and residues dossier is required.	Residue and toxicological data is expected to be available December 2024
Amoxicillin	Request for MRLs for chicken muscle, skin/fat, liver and kidney.	Nominator noted that relevant registrations exist in the European Union, Canada and Chile.	Chile	ADI set by JECFA at 0-0.07 µg/kg bw (2011), ARfD 0.005 mg/kg bw (2017). Classified by WHO as a CIA and by the OIE as VCIA.	Residue data is expected to be available 31 March 2025
Amoxicillin	Request for MRL for chicken eggs	Nominator noted that relevant registrations exist in the Republic of Korea.	Republic of Korea	ADI set by JECFA at 0-0.07 µg/kg bw (2011), ARfD 0.005 mg/kg bw (2017). Classified by WHO as a CIA and by the OIE as VCIA.	Metabolism and residue depletion data is expected to be available 30 September 2025
Ethion (Part III – additional data required)	Request ADI and MRL for cattle tissue	Nominator noted that relevant MRLs are established in a number of countries.	Argentina, Costa Rica and Uruguay	JECFA85 requested additional data/scientific argument to enable MR and MR:TRR to be determined and analytical methodology	Metabolism studies to identify compounds of concern, validation of an analytical method and a radiolabel study to enable MR and MR:TRR to be determined are expected to be completed by 31 December 2025 .

Fumagillin dicyclohexylamine (DCH)	Request for MRL for Rainbow trout (fillets)	Nominator noted that relevant registrations exist in the Republic of Korea	Republic of Korea	JECFA98 (2024)	Metabolism, residue depletion and analytical method studies for DCH in trout is expected to be available 31 December 2026 .
Part II. Veterinary drugs for which data availability should be confirmed at the next CCRVDF					
Name of Compound	Question(s) to be answered	Proposed by	Comments	When will data package be available	
Ethoxyquin (feed additive use)	Request to establish MRL in shrimp muscle.	Philippines/India	Carried over from CCRVDF21 (2013). ADI 0-0.005 mg/kg bw (2005 JMPR). The ADI and the ARfD are applicable to ethoxyquin and its metabolites/degradation products methylethoxyquin (MEQ), dihydroethoxyquin (DHEQ), dehydrimethylethoxyquin (DHMEQ). ARfD 0.5 mg/kg bw (2005 JMPR).	Ethoxyquin to be removed from Part II as no indication on if data will become available has been provided.	
Norfloxacin	Request to establish MRLs for cattle, camelids, equines, goats, poultry, sheep and swine tissues.	Peru	Norfloxacin is classified by WHO as a CIA and by the OIE as a veterinary CIA.	Norfloxacin to be removed from Part II as no indication on if data will become available has been provided.	
Part III. Veterinary drugs for which additional data / information is necessary to complete the JECFA evaluation					
Name of Compound	Information required by JECFA	Proposed by	Comments	When will data package be available	
Ethion	See Part I above				

Flumethrin	Additional data/scientific argument to enable MR and MR:TRR to be determined, residue depletion data, identity of metabolite in milk and toxicological profile.	EU	ADI set by JECFA at 0-0.004 mg/kg bw (2017), ARfD 0.005 mg/kg bw (2017).	Flumethrin to be removed from Part III as it was confirmed that additional data will not be available.
Fosfomycin	Additional data/scientific argument to enable a mADI to be set, additional data/scientific argument to enable MR and MR:TRR to be determined, analytical method.	Argentina/Paraguay/Peru	JECFA (88 th meeting) could not establish an ADI.	No update provided to the PWG.
Part IV. Parallel review – Evaluation of a new compound				
Name of Compound	Information required by JECFA	Proposed by	Comments	When will data package be available
Umifoxolaner	See Part I above			
Selamectin	Confirmation of full registration in a Member state, including GVP.	Canada/US	Selamectin to be removed from Part IV as it was confirmed that GVP will not be available.	-
Part V. Extrapolation				
Name of Compound(s)	Extrapolation to	Proposed by	Indication that extrapolation principles could be met	
None proposed	-	-	-	

Appendix 2: Nomination for amoxicillin in chicken tissues

The following information was provided in CX/RVDF 23/26/11:

Administrative Information

1. Member(s) submitting the request for inclusion: Chile
2. Veterinary drug names: Amoxicillin 50%
3. Trade names: Primavet 50% (Centrovét) Vetrimonix 50% (Ceva Santé animale) Neumotona 50% (Veterquímica) Amoxyvet (Intermedicavet) Amoxy-50 (Zagro)
4. Chemical names and CAS registry number (2S,5R,6R)- 6-[[[(2R)-2-amino- 2-(4-hydroxyphenyl)-acetyl]amino]- 3,3-dimethyl- 7-oxo- 4-thia- 1-azabicyclo[3.2.0]heptane- 24-carboxylic acid
5. Names and addresses of basic producers Centrovét Ltda. Avda. Los Cerrillos 602, Cerrillos, Santiago, Chile www.centrovét.com Veterquímica S.A. Camino a Lonquén 10387, Maipú, Santiago, Chile www.veterquímica.com Ceva Sante Animale Z.I. Tres Le Bois 22600, Loudéac, Francia

Purpose, Scope and Rationale

6. Identification of the food safety issue (residue hazard): Amoxicillin is a broad-spectrum antibiotic widely used for treating both human and animal diseases, and it belongs to a group that are excreted unchanged within urine and faeces; therefore, it is possible to find traces of this drug or its degradation products in environmental water bodies. In water, it is rapidly degraded by biotic and abiotic factors, yielding different intermediate products; these are suspected of being more resistant to degradation, and potentially more toxic, than the parent compound. Amoxicillin may bioaccumulate in muscle tissues, with the possibility of the occurrence of these drugs in food, leading to a passive consumption of this antibiotic resulting in undesirable effects on consumer health such as immunoallergic responses. However, the main problem related with the presence of this antimicrobial compounds in tissues is the possibility of inducing bacterial resistance genes.

7. Assessment against the criteria for the inclusion on the priority list: Amoxicillin, has been assessment twice by JECFA, 75 (2011) and 85 (2017) meetings. It currently MRLs for cattle, sheep, pigs and fish has been established, however, there is no Codex MRL in broiler chicken tissues. Chile at CCRVDF24, after the discussion of "DATABASE OF COUNTRY MRL NEEDS (Agenda Item 11)", offered to develop dossiers to support the JECFA assessment for amoxicillin in poultry. Chile proposes a reevaluation of this drug. GVPs were established and there are three products registered in the country for use in broiler chickens. Verified maximum residue limits are necessary to ensure food safety for domestic use and protect the commercial destinations of edible broiler chicken tissues. Chile CX/RVDF 23/26/11 4

Risk Profile Elements

8. Justification for use: For the treatment of Staphylococcosis and Avian Streptococcosis (Staphylococcus spp., Streptococcus spp.), Fowl Cholera (Pasteurella multocida), Infectious Coryza (Avibacterium paragallinarum), Avian Colibacillosis (Escherichia coli), Avian Salmonellosis and Paratyphosis (Salmonella spp.) and Clostridium perfringens.
9. Veterinary use pattern, including information on approved uses if available: Registered products are authorized for oral administration, dissolved in drinking water. Dosage of Amoxicillin 20 mg per kg bodyweight (bw) for day for 5 - 7 days.
10. Commodities for which Codex MRLs are required: Muscle, liver, kidney and skin and fat in natural proportions of broiler chickens.

Available Information

12. Countries where the veterinary drugs are registered: European Union, Canada and Chile.
13. National/Regional MRLs or any other applicable tolerances
European Medicines Agency (EMA) Muscle 50 µg/kg Liver 50 µg/kg Skin and fat 50 µg/kg Kidney 50 µg/kg
14. List of data available (pharmacology, toxicology, metabolism, residue depletion, analytical methods):
A novel developed optimized and validated analytical methodologies for the detection of beta-lactams (amoxicillin) in edible (muscle, liver, kidney and fat) and feathers of broiler chickens.
An extraction method was developed for the detection and quantification of Amoxicillin residues in broiler chicken muscle and skin plus fat matrices. This was based on the publication of Benito-Peña et al., 2009 and Gajda et al.,

2019. The analysis will be performed by high-performance chromatography coupled to tandem mass spectrometry (API 5500, AB SCIEX®). The methodology will be validated for the parameters of linearity of the calibration curve, trueness, precision, decision limit (CC α), matrix effect, specificity, stability and robustness, according to the recommendations of the European Union document: 2021/808/CE "Commission Implementing Regulation (EU) 2021/808 of 22 March 2021 on the performance of analytical methods for residues of pharmacologically active substances used in food-producing animals and on the interpretation of results as well as on the methods to be used for sampling and repealing Decisions 2002/657/EC and 98/179/EC".

In parallel, a methodology for the analysis of amoxicillin in kidney and liver is being optimized. However, the extraction of this compound has been more complicated to implement due to the properties of the analyte, such as its stability, interaction with these matrices and its protein binding capacity, among others. A depletion study of amoxicillin in muscle, liver, kidney and skin and fat in natural proportion, of broiler chicken treated with isotopically labelled standards. In order to determine the amoxicillin depletion time in the study matrices, an in vivo assay was performed with broiler chickens. For this, the birds were treated with a 50% amoxicillin pharmaceutical formulation, therapeutically as indicated on the label. The study was based mainly on a trial with 40 broiler chickens of Ross 308 genetics, which were raised until 42 days of age, controlling temperature and relative humidity according to the physiological requirements of the birds, as well as drinking water and feed ad libitum, according to their nutritional requirements. These were kept from the first day of life in rearing batteries with a raised wire floor. The chicks were randomly divided from day 21 of life into a treatment group and a control group. The treatment group consisted of 30 birds treated with amoxicillin trihydrate 50% (authorized and described in the Register of Veterinary Medicines of the Agriculture and Livestock Service to be administered to broilers) at a therapeutic dose of 40 mg/kg/day for 7 days by orogastric tube, while the control or blank group consisted of 10 birds that did not receive treatment. After treatment, the matrices of interest were sampled on days 1, 2, 5, 9 and 18. For each sampling point, six samples of muscle, liver, kidney and fat plus skin were obtained. Once the solid-liquid extraction of amoxicillin residues from the study matrices has been performed, as indicated in the previous point, the samples are analyzed by HPLC-MS/MS in order to obtain the concentrations of these analytes, using the standards Amoxicillin (certified with purity greater than 95%) and Amoxicillin D4 (as internal standard).

The study has the Biosafety Certificate N°184 of the Biosafety Committee of the Faculty of Veterinary and Livestock Sciences of the University of Chile, and the certificate N° 23643 – VET – UCH of the Institutional Animal Care and Use Committee (CICUA), issued by the same faculty. The euthanasia method was guided according to the recommendations of "The AVMA Guidelines for the Euthanasia of Animals" (2013), and Regulation No. 1099/2009 associated with the protection of animals at the time of killing of the European Commission (2009). For the depletion study and the determination of the withdrawal period in the matrices, the guidelines of the document "Guideline on determination of withdrawal periods for edible tissues" of the European Medicines Agency (2018) will be followed.

Timetable

15. Date when data could be submitted to JECFA

A novel developed optimized and validated analytical methodologies for broiler muscle, and skin and fat: December 2023
A novel developed optimized and validated analytical methodologies for broiler liver and kidney: July 2024

A depletion study of amoxicillin in muscle, and skin and fat in natural proportions, of broiler chicken: July 2024

A depletion study of amoxicillin in liver and kidney, of broiler chicken: July 2024
It is important to consider that we are currently working on the extraction method for broiler chicken liver and kidney matrices, so the dates of the validation and depletion study are subject to the achievement of the development of the method.

At the PWG prior to CCRVDF27, Chile provided the update that the data should be available by 31 March 2025.

Appendix 3: Nomination for amoxicillin in eggs

The following information was provided in CRD10 for CCRVDF27:

Administrative Information

1. Member submitting the request for inclusion: Republic of Korea
2. Veterinary drug name: Amoxicillin, Amoxicillin trihydrate
3. Trade names: Amoxicillin
4. Chemical names and CAS registry number:
Amoxicillin: 26787-78-0, Amoxicillin trihydrate: 61336-70-7F
5. Names and addresses of basic produces: Woogene B&G, 230, Jeongmunsongsan-ro, Yanggam-myeon, Hwaseong-si, Gyeonggi-do, Korea

Purpose, Scope and Rationale

6. Identification of the food safety issue (residue hazard)
 - Residues (including any potential metabolites) of amoxicillin in eggs of laying hens after oral administration of amoxicillin
7. Assessment against the criteria for the inclusion on the priority list:
 - The eighty-fifth JECFA assessed Amoxicillin (See WHO Technical Report Series 1008)
 - The Committee did not assess residues (including any potential metabolites) of amoxicillin in eggs after oral administration of amoxicillin via feed admixture or drinking water for lack of data.

Risk Profile Elements

8. Justification for use: Treatment or control of bacterial infections in animals (including pigs, cattles, milking cows, goats, sheep, chicken, laying hens and etc) and human
9. Veterinary use pattern, including information on approved uses if available:
 - Laying hens: Incorporate it in feeds or drinking water and provide it at 100 mg per kg body weight twice per day for 5 days
10. Commodities for which Codex MRLs are required: Eggs

Risk Assessment Needs and Questions for the Risk Assessors

11. Specific request to risk assessors:
 - Residues of amoxicillin (including any potential metabolites) in eggs are required to be monitored when amoxicillin preparations are used in laying hens

Available Information

12. Countries where the veterinary drugs are registered: Republic of Korea
13. National/Regional MRLs or any other applicable tolerances:
 - In poultry muscle, liver, kidney and fat 0.05 mg/kg for the MR amoxicillin as Korea's national MRL
 - In egg of 0.01 mg/kg for the MR amoxicillin as Korea's national MRL
14. List of data available:
 - Metabolism study of amoxicillin to determine the quantity and identify the nature of amoxicillin in eggs of laying hens after oral administration of amoxicillin hydrate.
 - Residue depletion data of amoxicillin in eggs of laying hens after oral administration of amoxicillin hydrate via feed admixture or drinking water

Timetable

15. date when data could be submitted to JECFA: September 30 2025

Appendix 4: Nomination for fumagillin DCH

The following information was provided in CRD10 for CCRVDF27:

Administrative Information

1. Member submitting the request for inclusion: Republic of Korea
2. Veterinary drug name: Fumagillin dicyclohexylamine
3. Trade names: Fumidil-B
4. Chemical names and CAS registry number: Fumagillin, 23110-15-8
5. Names and addresses of basic producers: KBNP, 415 Heungandae-ro, Dongan-gu, Anyang-si, Gyeonggi Province, RoK

Purpose, Scope and Rationale

6. Identification of the food safety issue (residue hazard)
 - Residues (including any potential metabolites) of dicyclohexylamine in fillet of rainbow trout after oral administration of Fumagillin dicyclohexylamine.
7. Assessment against the criteria for the inclusion on the priority list:
 - The ninety-eight JECFA assessed Fumagillin DCH (See WHO Technical Report Series 1055)
 - The Committee could not assess residues (including any potential metabolites) of dicyclohexylamine in trout fillet after oral administration of Fumagillin dicyclohexylamine for lack of data and without suitable analytical method for DCH in fish fillet.

Risk Profile Elements

8. Justification for use: Treatment for Sphaerospora sp or Myxobolus cerebralis in rainbow trouts
9. Veterinary use pattern, including information on approved uses if available:
 - Fish: Incorporate it in feeds at 300g~1kg/day/ton of fish weight or 1.2kg/ton of water weight for 5 days
10. Commodities for which Codex MRLs are required: Fish fillet

Risk Assessment Needs and Questions for the Risk Assessors

11. Specific request to risk assessors:
 - Residues of DCH (including any potential metabolites) are required to 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 of DCH (0-0.02 mg/kg bw).
 - A suitable analytical method for determination of DCH in fish fillet is need to be developed.

Available Information

12. Countries where the veterinary drugs are registered: Republic of Korea
13. National/Regional MRLs or any other applicable tolerances:
 - In fish fillet of 0.01 mg/kg for the MR fumagillin as Korea's national provisional MRL
14. List of data available:
 - Metabolism study of DCH to determine the quantity and identify the nature of DCH in rainbow trout after oral administration of Fumagillin DCH.
 - Residue depletion data of DCH in fillet of rainbow trout after oral administration of Fumagillin DCH via feed admixture
 - Residue analytical method for determination of DCH in fish fillet

Timetable

15. date when data could be submitted to JECFA:
 - Until December 31 2026

Appendix 5: Nomination for umifoxolaner in beef tissues

The following information was provided in CX/RVDF 24/27/10:

ADMINISTRATIVE INFORMATION

Member(s) submitting the request for inclusion: BRAZIL

Veterinary drug names: UMIFOXOLANER (INN)

Trade names: SOLECTUS®

Chemical names and CAS registry number:

IUPAC (International Union of Pure and Applied Chemistry) Nomenclature: 4-[(5S)-5-[3-chloro-4-fluoro-5-(trifluoromethyl)phenyl]-4,5-dihydro-5-(trifluoro-methyl)-3-isoxazolyl]-N-[2-oxo-2-[(2,2,2-trifluoroethyl)amino]ethyl]-1-naphthalene-carboxamide

Synonyms: ML-3,032,878, ML-878 and MR-026, CLM2317

CAS number: 2021230-37-3

International Non-proprietary Name (INN): umifoxolaner

Names and addresses of basic producers: BOEHRINGER INGELHEIM ANIMAL HEALTH DO BRASIL LTDA, Avenida Doutor Roberto Moreira, n° 5005, Recanto dos Pássaros, CEP 13148-914, Paulínia/SP – Brazil

PURPOSE, SCOPE, AND RATIONALE

Identification of the food safety issue (residue hazard):

The food safety issue concerns the potential for residues of umifoxolaner to be remained in food products (cattle tissues) consumed by humans. Residues could pose health risks and therefore it is necessary to establish ADI (Acute Daily Intake), ARfD (Acute Reference Dose) and Maximum Residue Limits (MRLs) to ensure that any residue present in food are within safe levels for human consumption.

Umifoxolaner is a novel veterinary drug that has not yet been evaluated by the Joint FAO/WHO Expert Committee on Food Additives (JECFA) for use in veterinary medicine, and there is currently no established ADI, ARfD and MRLs for its residues in cattle tissues.

Assessment against the criteria for the inclusion on the priority list:

The MAPA registration procedure will be performed in parallel to the JECFA/CCRVDf review. Currently the risk assessment for food safety dossier is under review at ANVISA.

Umifoxolaner is intended to be registered in Brazil, Argentina, Colombia, Uruguay, Bolivia, Paraguay, Mexico, Australia, New Zealand, South Africa, Botswana, Namibia, Zimbabwe, Kenya, Tanzania, Uganda, Ethiopia, Nigeria, Egypt, Algeria and Morocco member states for use in cattle. Relevant data are available on toxicology, metabolism, pharmacokinetics, and residue depletion studies conducted with both radiolabeled and non-radiolabeled forms of the drug in the target species. A comprehensive dossier will be provided for the risk assessment.

RISK PROFILE ELEMENTS

Justification for use:

Treatment and control of infestations caused by single-host ticks *Rhipicephalus (Boophilus) microplus*.

Treatment and control of infestations caused by larvae of *Dermatobia hominis*.

Prevention of infestations caused by *Cochliomyia hominivorax* larvae (screwworm myiasis), including prevention of postoperative wound myiasis and prevention of umbilical myiasis of newborn calves.

Treatment and control of infestations caused by chewing lice (*Bovicola bovis*).

Veterinary use pattern, including information on approved uses if available (*this should include product labels or other evidence of official use authorization*):

It is recommended to administer Solectus® in cattle, in a subcutaneous injection of 0.6 mg of umifoxolaner per kg of body weight (BW), equivalent to 1 mL of product per 100 kg of body weight (BW).

Solectus® is indicated for beef cattle and can be given to all ages of animals including one-day-old calves.

The recommended withdrawal period is 105 days.

Do not use the product on dairy cows producing milk for human consumption (Milk depletion studies are currently in progress).

Commodities for which Codex MRLs are required: Cattle Liver, kidney, fat, muscle.

Specific request to risk assessors

Request for establishment of ADI, ARfD and MRLs for umifoxolaner for cattle muscle, liver, kidney and fat using the parallel review process.

AVAILABLE INFORMATION

Countries where the veterinary drugs are registered: Under review by Naonal Authorities in Brazil, Argentina and Uruguay.

National/Regional MRLs or any other applicable tolerances:

Review of the risk assessment for food safety dossier ongoing in Brazil (by ANVISA) and in Australia (APVMA Technical Assessment).

List of data (pharmacology, toxicology, metabolism, residue depletion, analytical methods) available (*this should include a list of the data available with the full study titles and whether the compound is also registered as pesticide and, as appropriate, has been evaluated or scheduled for evaluation or re- evaluation by JMPR*):

The compound is not registered as pesticide and has not been evaluated or scheduled for evaluation by JMPR. The list of data is as follows:

TOXICOLOGY

Genotoxicity Studies

Bacterial Reverse Mutation Assay.

In Vitro Mammalian Cell Micronucleus Assay in TK6 Cells.

In Vivo Mammalian Erythrocyte Micronucleus Assay in Mice.

Position paper on carcinogenicity study.

Acute Toxicity studies

Acute Oral Toxicity in Sprague Dawley Rats.

A Single-Dose Oral Gavage Maximum Tolerated Dose (MTD) Study in Sprague Dawley Rats.

Acute Dermal Toxicity Study in Albino Rats.

Acute Dermal Irritation Study in Albino Rabbits.

Acute Ocular Irritation Study in Albino Rabbits.

Subacute Toxicity

7-Day Oral Gavage Toxicity Study in Sprague Dawley Rats.

Escalating-Dose Phase and 7-Day Repeated-Dose Phase Study by Oral Capsule in Beagle Dogs.

28-Day Oral (Dietary) Toxicity Study in Sprague Dawley Rats.

28 Day Repeated-Dose Study by Oral Capsule in Beagle Dogs.

90 Day Oral Dietary Toxicity Study in Sprague Dawley Rats.

90-day oral toxicity study in Beagle Dogs.

Chronic Toxicity Studies

A 52-Week Oral Dietary Toxicity Study in Sprague Dawley Rats.

Toxicity Studies on Reproduction and Development

Oral (Gavage) Prenatal Developmental Toxicity Study in Sprague Dawley Rats.

Oral (Gavage) Prenatal Developmental Toxicity Study in New Zealand White Rabbits.

Oral (Gavage) Two-Generation Reproductive Toxicity Study in Sprague Dawley Rats.

Additional studies

MIC study on Human Gastrointestinal Tract Microbiota (to be ready in October 2024).

PHARMACOLOGY, METABOLISM and RESIDUES

Comparative Metabolism Study following Repeated Oral (Gavage) Administration to Rats.

Comparative Metabolism Study following Repeated Oral (Gavage) Administration to Dogs.

28-Day Pharmacokinetic Study of ML-3,032,878 by Intravenous Injection and Oral Gavage in Sprague Dawley Rats.

Study to Determine the Pharmacokinetic Profiles in Plasma of Cattle Administered a Single Intravenous Dose at 0.6 mg/kg body weight or a Single Subcutaneous Dose at 0.3, 0.6 or 1.2 mg/kg body weight.

Pivotal Radio-Residue Metabolism and Depletion Study in Beef Cattle Following a Single Subcutaneous Injection at 0.6 mg/kg Body Weight.

In Vitro Metabolite Profiling in HuREL Rat, Mouse, Dog, Cattle and Sheep Hepatocytes Co-cultures.

Plasma Protein Binding in Cattle, Sheep, Dog, Rat and Mouse Plasma.

Marker Residue Depletion Studies in Bovine Edible Tissues after a Single Subcutaneous Dose.

ANALYTICAL METHOD

Validation of an LC-MS/MS Method for the Quantification of ML-3,032,878 in Bovine Plasma.

Validation of an LC-MS/MS Method for the Quantitation of ML-3,032,878 in bovine edible tissues.

Long-Term stability of Umifoxolaner in bovine edible tissues During Storage in Freezer set at -20°C.

TIMETABLE

15. Date when data could be submitted to JECFA: December 2024