

# CODEX ALIMENTARIUS COMMISSION



Food and Agriculture  
Organization of the  
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World Health  
Organization

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Agenda Items: 5, 6.1, 6.2, 7, 8,

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**JOINT FAO/WHO FOOD STANDARDS PROGRAMME**  
**CODEX COMMITTEE ON RESIDUES OF VETERINARY DRUGS IN FOODS**  
**Twenty-fourth Session**  
**Comments Submitted By: the Philippines**

**AGENDA ITEM 5: (REP17/RVDF App. II) DRAFT RMR FOR GENTIAN VIOLET COMMENTS AT STEP 6**

## **Background**

The CAC40 adopted the RMR for gentian violet at Step 5, noting that members and observers would have ample opportunity to further develop and discuss the RMR at CCRVDF24, in April 2018 and took note of the reservations of Ecuador, Honduras, Peru, Philippines and the United States of America.

## **General Comments:**

The Philippines remains to support the Option 2 text as discussed in the CCRVDF23.

“In view of the JECFA conclusions on the available scientific information, there is no safe level of residues of gentian violet or its metabolites in food that represent an acceptable risk to consumers. For this reason, competent authorities should prevent residues of gentian violet in food. (Gentian Violet is an effective treatment of skin disease in animal.)”

## **Rationale:**

As discussed in CCRVDF 23, the delegations in favor of Option 2 reiterated that: the language used in the last sentence of the RMR was overly restrictive and it could limit national authorities from applying other risk management measures they considered more appropriate; the application of the RMR as adopted by CAC 40 in Step 5, could introduce further expenses to national control programs; gentian violet was very efficient for the topical treatment of skin and eye lesions; Codex should provide broad guidance as the selection of specific risk management measures is in the remit of national authorities.

In the Philippines, registration of products with Gentian violet is both listed in the pharmaceutical and veterinary products list, banning of the product particularly for use in food-producing animals but has existing permission for use to non-food producing animals and humans, would complicate monitoring programs of the competent authorities.

The committee may consider the option to give flexibility to regulatory authorities to classify the use of Gentian violet in the food animals, moreover, in the JECFA evaluation; we would like to inquire if there is a possibility to establish the risk of residues of Gentian violet if this is only used as a topical treatment to skin and eye diseases and not as a systemic introduction to the animal.

In the fishery sector, the regulatory authority has already issued a policy guideline on its control measures in the use of Gentian violet in aquaculture settings by virtue of ***BFAR Administrative Order 256 series of 2015: Declaring malachite green and gentian violet as health hazards and prohibiting their use in food fish production and trade.*** In the animal feeds there is no approval for use of Gentian violet as mold inhibitor in feeds.

**AGENDA ITEM 6.1: (REP17/RVDF App. V) PROPOSED DRAFT MRLS FOR ZILPATEROL HYDROCHLORIDE (CATTLE FAT, KIDNEY, LIVER, MUSCLE) 81ST JECFA AT STEP 4**

The Philippines would like to thank the 81<sup>st</sup> JECFA for the evaluation of the supplemental data provided for zilpaterol hydrochloride.

**General Comments**

The JECFA evaluation has provided a robust scientific data and evaluation mechanism to establish the recommended MRLs of zilpaterol hydrochloride.

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

<b>Species</b>	<b>Tissue</b>	<b>MRLs (<math>\mu\text{g}/\text{kg}</math>)</b>	<b>Step</b>	<b>JECFA</b>
Cattle	Kidney	3.3	4	81
Cattle	Liver	3.5	4	81
Cattle	Muscle	0.5	4	81

In the Philippines, there is no approved use by the competent authority for Zilpaterol hydrochloride in cattle, in this light, we support for the establishment of MRL for this drug and observe the discussion that would transpire during the general session as there are still clarification in its chemical nature being a  $\beta$ 2 adrenoreceptor agonist.

**AGENDA ITEM 6.2: (CX/RVDF 18/24/6) PROPOSED DRAFT MRLS FOR AMOXICILLIN (FINFISH FILLET, MUSCLE); AMPICILLIN (FINFISH FILLET, MUSCLE); FLUMETHRIN (HONEY), LUFENURON (SALMON AND TROUT FILLET), MONEPANTEL (CATTLE FAT, KIDNEY, LIVER, MUSCLE) (85TH JECFA) AT STEP 3**

**General Comments:**

The Philippines would like to thank the 85<sup>th</sup> JECFA for the evaluation of the MRLs for amoxicillin (finfish fillet, muscle); ampicillin (finfish fillet, muscle); flumethrin (honey); lufenuron (salmon and trout fillet), monepantel (cattle fat, kidney, liver, muscle).

In this light, the Philippines would like to express its support for the establishment of MRLs for amoxicillin (finfish fillet, muscle) and ampicillin (finfish fillet, muscle) as these are the common antimicrobials being used in the aquaculture settings. For flumethrin (honey); lufenuron (salmon and trout fillet), monepantel (cattle fat, kidney, liver, muscle).

**AMOXICILLIN (antimicrobial agent)**

Microbiological Acceptable Daily Intake (mADI)	0.005 mg/kg bw based on microbiological effects on the intestinal microbiota
Acute Reference Dose (ARfD)	0.14 µg/kg bw per day (for the general population), which represents 7% of the upper bound of the mADI
Estimated Chronic Dietary Exposure (GECDE)	1.4 µg/kg bw (for the general population), which represents 28% of the microbiological ARfD
Estimated Acute Dietary Exposure (GEADE)	1.6 µg/kg bw (for children), which represents 31% of the microbiological ARfD

Residue Definition: **Amoxicillin**

Species	Tissue	MRLs (µg/kg) recommended by the 85 <sup>th</sup> JECFA	Step	JECFA
Finfish <sup>a</sup>	Fillet <sup>b</sup>	50	3	85
	Muscle	50	3	85

<sup>a</sup> The term "finfish" includes all fish species.

<sup>b</sup> Muscle plus skin in natural proportion.

**AMPICILLIN (antimicrobial agent)**

Microbiological Acceptable Daily Intake (mADI)	0–0.003 mg/kg bw based on a no-observed-adverse-effect level (NOAEL) equivalent to 0.025 mg/kg bw per day for increase in population(s) of ampicillin-resistant bacteria in the gastrointestinal tract in humans, and using a safety factor of 10 (for the variability in the composition of the intestinal microbiota within and between individuals).
Acute Reference Dose (ARfD)	0.012 mg/kg bw based on the microbiological end-point.
Estimated Chronic Dietary Exposure (GECDE)	0.29 µg/kg bw per day (for the general population), which represents 10% of the upper bound of the ADI.
Estimated Acute Dietary Exposure (GEADE)	1.9 µg/kg bw per day (for the general population), which represents 16% of the ARfD. 1.7 µg/kg bw per day (for children), which represents 14% of the ARfD

Residue Definition: **Ampicillin**

Species	Tissue	MRLs (µg/kg) recommended by the 85 <sup>th</sup> JECFA	Step	JECFA
Finfish <sup>a</sup>	Fillet <sup>b</sup>	50	3	85
	Muscle	50	3	85

<sup>a</sup> The term “finfish” includes all fish species.<sup>b</sup> Muscle plus skin in natural proportion.

Note: The 85th JECFA recommended an MRL of 50 µg/kg for ampicillin in finfish muscle and in finfish muscle plus skin in natural proportion, the same as that recommended for amoxicillin, because the modes of action, the physicochemical properties and the toxicological and pharmacokinetic profiles of amoxicillin and ampicillin are very similar.

**FLUMETHRIN** (insecticide)

Microbiological Acceptable Daily Intake (mADI)	0–0.004 mg/kg bw based on the NOAEL of 0.37 mg/kg bw per day for skin lesions in parental animals and reduced survival and body-weight gain in pups in a two-generation toxicity study in rats, and using a safety factor of 100 (10 for interspecies variability and 10 for intraspecies variability)
Acute Reference Dose (ARfD)	0.005 mg/kg bw based on the NOAEL of 0.5 mg/kg bw for salivation in dams in a developmental toxicity study in rats, and using a safety factor of 100 (10 for interspecies variability and 10 for intraspecies variability)
Estimated Chronic Dietary Exposure (GECDE)	0.008 µg/kg bw per day (for the general population), which represents 0.2% of the upper bound of the ADI. 0.006 µg/kg bw per day (for children), which represents 0.2% of the upper bound of the ADI. Note: As flumethrin is also used as pesticide the overall dietary exposure was estimated. The assumptions and detailed results will be displayed in the JECFA 85 report. Results below are only for use as veterinary drug
Estimated Acute Dietary Exposure (GEADE)	0.1 µg/kg bw per day (for the general population), which represents 2.2% of the ARfD. 0.1 µg/kg bw per day (for children), which represents 2.2% of the ARfD

Residue Definition: Flumethrin (trans-Z1 and trans Z2 diastereomers at a ratio of approximately 60:40)

Species	Tissue	MRLs (µg/kg) recommended by the 85 <sup>th</sup> JECFA	Step	JECFA
	Honey	6	3	85

Note: the 85th JECFA set an MRL for honey of 6 µg/kg, which is twice the limit of quantification (LOQ; 3 µg/kg) of the most reliable analytical method (liquid chromatography coupled with tandem mass spectrometry; LC– MS/MS) used in the residues studies

**LUFENURON (insecticide)**

Microbiological Acceptable Daily Intake (mADI)	0–0.02 mg/kg bw based on the NOAEL of 1.93 mg/kg bw per day for tonic-clonic seizures and findings in lungs, gastrointestinal tract, liver and urinary tract in a 2-year dietary study in rats, and using a safety factor of 100 (10 for interspecies variability and 10 for intraspecies variability)
Acute Reference Dose (ARfD)	Unnecessary, in view of lufenuron low acute oral toxicity and the absence of developmental toxicity and other toxicological effects likely to be elicited by a single dose
Estimated Chronic Dietary Exposure (GECDE)	1.1 µg/kg bw per day (for the general population), which represents 5.5% of the upper bound of the ADI. As lufenuron is also used as pesticide the overall dietary exposure was estimated. The assumptions and detailed results will be displayed in the JECFA 85 report. Results below are only for use as veterinary drug.

Residue Definition: Lufenuron

Species	Tissue	MRLs (µg/kg) recommended by the 85 <sup>th</sup> JECFA	Step	JECFA
Salmon	Fillet <sup>a</sup>	1,350	3	85
Trout	Fillet <sup>a</sup>	1,350	3	85

<sup>a</sup> Muscle plus skin in natural proportion.

**MONEPANTEL (anthelmintic)**

Microbiological Acceptable Daily Intake (mADI)	0–0.02 mg/kg bw based on the NOAEL of 1.93 mg/kg bw per day for tonic-clonic seizures and findings in lungs, gastrointestinal tract, liver and urinary tract in a 2-year dietary study in rats, and using a safety factor of 100 (10 for interspecies variability and 10 for intraspecies variability)
Acute Reference Dose (ARfD)	Unnecessary
Estimated Chronic Dietary Exposure (GECDE)	13.7 µg per kg bw per day (for the general population), which represents 68% of the upper bound of the ADI. 5.0 µg per kg bw per day (for children), which represents 22% of the upper bound of the ADI. 4.4 µg per kg bw per day (for infants), which represents 25% of the upper bound of the ADI.

Residue Definition: Monepantel sulfone, expressed as monepantel

Species	Tissue	MRLs (µg/kg) recommended by the 85 <sup>th</sup> JECFA	Step	JECFA
Cattle	Fat	7,000	3	85
Cattle	Kidney	1,000	3	85
Cattle	Liver	2,000	3	85
Cattle	Muscle	300	3	85

**AGENDA ITEM 7: (CX/RVDF 18/24/7) DISCUSSION PAPER ON MRLS FOR GROUPS OF FISH SPECIES****Issues**

The absence of MRLs for veterinary drugs in fish species raises challenges for appropriate protection of human health and fair trade practices. So far, there are only five compounds with established MRLs.

Lack of MRLs for fish species reduces the variety of drugs available to treat diseases, and thus affects the possibility of maintaining good fish health by veterinary treatments in aquaculture. Extrapolating to several fish would contribute to expand the variety of available drugs for fish. Extrapolating MRLs will also reduce the number of studies performed with animals and thus follow the principles of replacement, refinement and reduction principles for animal welfare.

For fish there are a wide range of species farmed as food-producing animals, compared to farmed mammals or birds. A residue study on all species for any drug is costly and therefore extrapolating MRLs is considered necessary.

The challenges of extrapolating MRLs to other fish species have been raised by JECFA at several sessions of CCRVDF based on the understanding that there might be a need for grouping.

**General Comment:**

The Philippines would like to thank the EWG for the discussion paper with preparations led by Norway and Japan, with the assistance of Argentina, Belgium, Brazil, Chile, Canada, France, Japan, Peru, Thailand and United States.

The Philippines would like to provide comments on the recommendations provided by the EWG and support Option C in order to set the most strategic way for JECFA or the respective competent authority to address the need for MRLs in fish species:

- C. No grouping, but discuss further guidance on national risk management options as this might seem an effective way forward.

On the other issues raised by the EWG members, the Philippines would like to provide comments on the issues raised:

1. Grouping of drugs: Metabolism of drugs is driven by chemical nature. Small differences can cause different metabolism pathway. Based on the feedback from EWG members, it does not look like grouping of drugs neither should be essential nor necessary when extrapolating MRLs

**Comment: The Philippines support the EWG members' observation that the grouping of drugs has no direct effect on the extrapolation of MRLs as the metabolism of drugs is dependent in its chemical nature.**

2. Marker Residue: Extrapolation is generally possible if the marker residue is identical and the same food basket is used for the species of one group, in this case the ADI cannot be exceeded.

**Comment: The Philippines supports the use of Marker Residues as one of the critical information in the determination of MRLs and ADI.**

3. Antimicrobials: The use of antimicrobials in food animals can create an important source of antimicrobial resistant bacteria that can spread to humans through the food supply. Improved management of the use of antimicrobials in food animals, particularly reducing those critically important for human medicine, is an important step towards preserving the benefits of antimicrobials for people.

: When discussing extrapolating of antimicrobial drugs the work on minimizing antimicrobial resistance must also be taken into account as described in the *Code of practice to minimize and contain antimicrobial resistance*

**Comment: The Philippines supports that strategies and policies on the use of antimicrobials in food animals should be guided by the existing codes of practice and guidelines that is already set by the international organizations such as Codex, FAO, OIE and WHO.**

#### **AGENDA ITEM 8: (CX/RVDF 18/24/8) DISCUSSION PAPER ON EDIBLE OFFAL TISSUES (POSSIBLE DEFINITION AND EDIBLE OFFAL TISSUES OF INTEREST IN INTERNATIONAL TRADE**

##### **Background:**

The 23rd Codex Committee on Residues of Veterinary Drugs in Foods (CCRVDF23) agreed to establish an Electronic Working Group (EWG), chaired by Kenya, working in English, to prepare a discussion paper in response to the request from 81st JECFA for CCRVDF to “provide a definition of edible offal”. The discussion paper will propose a possible definition of edible offal tissue and specify edible offal tissues of interest in international trade.

##### **Conclusions by the Discussion Paper of the EWG**

There is consensus on the general definition of offal tissue, which encompasses internal and external organs of an animal excluding the carcass. The Chair therefore proposes the general definition of offal as *fresh meat other than that of the carcass, including viscera, appendages and blood*.

With regards to edible offals, there was general consensus on considerations for the culture or customs of the respective countries, which had to be taken into account and the aspect of the organs being declared fit for human consumption. The chair therefore proposes that the definition of edible offals as *those parts of an animal apart from meat from the carcass that are considered fit for human consumption and they include the organs as described in paragraph 5*.

Based on the data submitted, it is observed that cattle, pigs and poultry are the species, which provide the bulk of edible offals, with liver, tripe and tongue being the most traded edible offals in cattle; Liver, tripe, trotters and heart in pigs; neck, liver, trotters, and heart in poultry; and tripe, casing, liver and kidney in sheep. These could be considered as edible offals of significance to international trade.

Cattle and pigs are the main contributors of international trade in liver and heart.

### **Recommendations by the EWG**

There is need for consensus by codex members on a harmonized definition of edible offals to facilitate elaboration of MRLs on tissues of international importance.

#### **General Comment:**

The Philippines would like to thank the EWG led by Kenya together with the comments from Members, Argentina Brazil, Canada, Chile, Egypt, France, Japan, Nigeria, Peru, Thailand, United States of America, United Republic of Tanzania, Health For Animals and International Meat Secretariat for the preparation of this discussion paper.

#### **Specific Comments on the Conclusions:**

The Philippines through the Department of Agriculture - Bureau of Agriculture and Fisheries Standards has an on-going project on the development of Philippine National Standard (PNS) Edible Offal of Swine in collaboration with the established Technical Working Group composed of relevant stakeholders. The draft standard, after series of in-country consultations, is up for finalization and expected to be adopted as PNS this year. The same was posted to WTO for notification last September 2017.

In view of the foregoing, the Philippines would like to offer its working definition (adopted in principle) of edible offal for swine as presented below.

**Edible offal** are the edible viscera (internal organs, glands and tissues), extremities, and other by-products that are separated from the carcass of swine, and which are enumerated below:

The parts listed below are the edible offal of swine:

- Heads and cuts thereof
  - Mask
  - Jowl
  - Ear, including ear drum
  - Cheek meat
  - Head meat
  - Lips
  - Snout
  - Tongue
  - Brain
- Feet/trotters
- Tail
- Heart
- Liver
- Kidneys
- Lungs, including trachea, throat, esophagus/weasand
- Diaphragm
  - Hanging tender
  - Skirt meat
  - Skirt sinew
- Skin
- Spleen
- Stomach
- Pancreas
- Omentum/mesentery
- Small intestine
- Large intestine, including rectum
- Reproductive organs

The TWG of the Philippines would also then consider if further work would be needed to develop specific national standards on the other commodities as also covered by the EWG.