



JOINT FAO/WHO FOOD STANDARDS PROGRAMME
CODEX COMMITTEE ON RESIDUES OF VETERINARY DRUGS IN FOODS
Twenty-fourth Session

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)

At Step 3

Codex members and Observers wishing to submit comments at Step 3 on the proposed draft Maximum Residues Limits for Veterinary Drugs arising from the 85th JECFA Meeting (see Annex 1) should do so as instructed in CL 2017/85-RVDF available on the Codex webpage/Circular Letters 2017: <http://www.codexalimentarius.org/circular-letters/en/>. Comments will only be accepted through the online commenting system within the deadline indicated in the CL 2017/85-RVDF

BACKGROUND

1. The 85th Meeting of the Joint FAO/WHO Expert Committee on Food Additives (JECFA) was convened 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)¹. Toxicological monographs summarising the data that were considered by the Committee are published in *WHO Food Additives Series No. 76*²; residue monographs summarising the data that were considered by the Committee are published in *FAO JECFA Monographs No. 21*³.

2. Annex 1 to this document presents the recommendations of the 85th JECFA Meeting on numerical Maximum Residues Limits (MRLs) for the veterinary drugs: amoxicillin (finfish fillet, muscle); ampicillin (finfish fillet, muscle); flumethrin (honey), lufenuron (salmon and trout fillet), monepantel (cattle fat, kidney, liver, muscle). Recommendations on other veterinary drugs i.e. halquinol, ethion and sisapronil for which the 85th JECFA has not recommended MRLs as well as other considerations are provided in the document CX/RVDF 18/24/3 (Matters of Interest arising from FAO/WHO and from the 85th Meeting of the Joint FAO/WHO Expert Committee on Food Additives (JECFA).

3. CCRVDF23 agreed to hold the proposed draft MRLs for zilpaterol hydrochloride (cattle fat, kidney, liver, muscle) at Step 4 for consideration at its next Session in light of the JECFA evaluation of the additional studies (Ref. REP17/RVDF para. 74 and Appendix V). The MRLs for zilpaterol hydrochloride and the 85th JECFA recommendations will be considered under Agenda Item 6.1

¹ To be published on WHO website: <http://www.who.int/foodsafety/publications/jecfa-reports/en/>. A fully edited pre-publication of the report of the 85th JECFA has been distributed to all Codex Members and Observers through Codex email list.

² To be published on WHO website: <http://www.who.int/foodsafety/publications/jecfa-reports/en/>

³ To be published on FAO website: <http://www.fao.org/food/food-safety-quality/scientific-advice/jecfa/jecfa-publications/en/>

Annex 1

**PROPOSED DRAFT MAXIMUM RESIDUE LIMITS (MRLs) FOR VETERINARY DRUGS
(at Step 3)**

AMOXICILLIN (antimicrobial agent)

Microbiological Acceptable Daily Intake (mADI)	0–0.002 mg/kg body weight (bw) based on the effects of amoxicillin on the intestinal microbiota.
Acute Reference Dose (ARfD):	0.005 mg/kg bw based on microbiological effects on the intestinal microbiota
Estimated Chronic Dietary Exposure (GECDE):	0.14 µg/kg bw per day (for the general population), which represents 7% of the upper bound of the mADI
Estimated Acute Dietary Exposure (GEADE):	1.4 µg/kg bw (for the general population), which represents 28% of the microbiological ARfD. 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 th JECFA	Step	JECFA
Finfish ^a	Fillet ^b	50	3	85
	Muscle	50	3	85

^a The term “finfish” includes all fish species.

^b 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 th JECFA	Step	JECFA
Finfish ^a	Fillet ^b	50	3	85
	Muscle	50	3	85

^a The term “finfish” includes all fish species.

^b 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)

Acceptable Daily Intake (ADI)	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. <u>Note:</u> 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 th 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)

Acceptable Daily Intake (ADI) 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 th JECFA	Step	JECFA
Salmon	Fillet ^a	1 350	3	85
Trout	Fillet ^a	1 350	3	85

^a Muscle plus skin in natural proportion.

MONEPANTEL (anthelmintic)

Acceptable Daily Intake (ADI) 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 th JECFA	Step	JECFA
Cattle	Fat	7 000	3	85
	Kidney	1 000	3	85
	Liver	2 000	3	85
	Muscle	300	3	85