



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

Twenty-second Session

San José, Costa Rica, 27 April – 1 May 2015

PROPOSED DRAFT MRLS FOR DERQUANTEL, EMAMECTIN BENZOATE, IVERMECTIN, LASALOCID
SODIUM AND MONEPANTEL

At Step 3

Governments and international organizations wishing to submit comments at Step 3 on the proposed draft Maximum Residues Limits for Veterinary Drugs arising from the 78th JECFA Meeting (see Annex 1) are invited to do so **no later than 1 March 2015** as follows: U.S. Codex Office, Food safety and Inspection Service, US Department of Agriculture, Room 4861, South Building, 14th Independence Avenue, S.W., Washington DC 20250, USA (E-mail: CCRVDf-USSEC@fsis.usda.gov), with a copy to the Secretary, Codex Alimentarius Commission, Joint FAO/WHO Food Standards Programme, Viale delle Terme di Caracalla, 00153 Rome, Italy (E-mail: Codex@fao.org).

BACKGROUND

1. The 78th Meeting of the Joint FAO/WHO Expert Committee on Food Additives (JECFA) was convened in Geneva, Switzerland, from 5 to 14 November 2013 to evaluate residues of certain veterinary drugs in foods. The full report of the meeting is published in the WHO Technical Report Series (TRS 988)¹. Toxicological monographs summarising the data that were considered by the Committee are published in *WHO Food Additives Series No.69*²; residue monographs summarising the data that were considered by the Committee are published in *FAO JECFA Monographs No. 15*³.

2. Annex 1 to this document presents the recommendations of the 78th JECFA Meeting on numerical Maximum Residues Limits (MRLs) for the veterinary drugs: derquantel, emamectin benzoate, ivermectin, lasalocid sodium and monepantel. Recommendations on other veterinary drugs i.e., gentian violet, recombinant bovine somatotropins and zilpaterol hydrochloride for which the 78th JECFA has not recommended MRLs as well as other considerations are provided in the document CX/RVDF 15/22/4 (Matters of Interest arising from FAO/WHO and from the 78th Meeting of the Joint FAO/WHO Expert Committee on Food Additives (JECFA)).

3. CCRVDF21 agreed to hold the draft MRLs for monepantel in sheep tissues and the proposed draft MRLs for derquantel in sheep tissues at Step 7 and 4 respectively⁴, for consideration at its next session in the light of the 78th JECFA recommendations, which are presented in Annex 1 (Ref. REP14/RVDF paras 36-40, 44-45 and Appendices II and III).

4. CCRVDF21 also submitted new provisions on the use of a Concern Form by CCRVDF to the 37th Session of the Codex Alimentarius Commission through the Committee on General Principles for inclusion in the *Risk Analysis Principles Applied by the CCRVDF* (Ref. REP14/RVDF paras 105-121 and Appendix IX). The provisions were endorsed by CCGP28 (April 2014)⁵ and adopted by CAC37 (July 2014).⁶ The revised *Risk Analysis Principles Applied by the CCRVDF* will be included in the 23rd Edition of the Procedural Manual (currently under preparation).

¹ http://apps.who.int/iris/bitstream/10665/127845/1/9789241209885_eng.pdf?ua=1

² http://apps.who.int/iris/bitstream/10665/128550/1/9789241660693_eng.pdf?ua=1

³ <http://www.fao.org/3/a-i3745e.pdf>

⁴ These MRLs are presented in shaded font in Annex 1.

⁵ REP14/GP, para. 15.

⁶ REP14/CAC para. 36 and Appendix II.

Annex 1

**PROPOSED DRAFT MAXIMUM RESIDUE LIMITS (MRLs) FOR VETERINARY DRUGS
(AT STEP 3)**

Recommendations arising from the 78th JECFA

DERQUANTEL (anthelmintic agent)

Acceptable Daily Intake (ADI): 0-0.3 µg/kg body weight on the basis of a lowest-observed-adverse-effect level (LOAEL) of 0.1 mg/kg body weight per day for acute clinical observations in dogs, consistent with antagonistic activity on the nicotinic acetylcholine receptors. A safety factor of 300 was applied to the LOAEL (75th JECFA, 2011).

Estimated Dietary Exposure (EDI): There were insufficient data to calculate an EDI, and the TMDI approach was used. Using the model diet and the MT:TR approach, these MRLs result in an estimated dietary exposure of 6.8 µg/person, which represents approximately 38% of the upper bound of the ADI.

Residue Definition: Derquantel.

Species	Tissue	MRLs(µg/kg) recommended by the 75 th JECFA	Step	JECFA	MRLs (µg/kg) recommended by the 78 th JECFA	Step	JECFA
Sheep	Muscle	0.2	4	75	0.3	3	78
Sheep	Liver	2.0	4	75	0.8	3	78
Sheep	Kidney	0.2	4	75	0.4	3	78
Sheep	Fat	0.7	4	75	7.0	3	78

In shaded font are the MRLs held at Step 4 by CCRVDF21.

EMAMECTIN BENZOATE (antiparasitic agent)

Acceptable Daily Intake (ADI): ADI of 0–0.0005 mg/kg body weight established by the Joint FAO/WHO Meeting on Pesticide Residues (JMPR) in 2011, based on an overall no-observed-adverse effect level (NOAEL) of 0.25 mg/kg body weight per day for neurotoxicity from 14- and 53-week studies in dogs, supported by an overall NOAEL of 0.25 mg/kg body weight per day from 1- and 2-year studies in rats. An uncertainty factor of 500 was applied to the NOAEL, which includes an additional uncertainty factor of 5 to account for the steep dose–response curve and irreversible histopathological effects in neural tissues at the lowest-observed-adverse-effect level (LOAEL) in dogs, as used by JMPR and confirmed by the current Committee.

Estimated Dietary Exposure (EDI): The EDI is 11 µg/person per day, which represents approximately 37% of the upper bound of the ADI.

Residue Definition: Emamectin B1a.

Species	Tissue	MRLs (µg/kg) recommended by the 78 th JECFA	Step	JECFA
Salmon	Muscle	100	3	78
Salmon	Fillet ^a	100	3	78
Trout	Muscle	100	3	78
Trout	Fillet ^a	100	3	75

^a Muscle plus skin in natural proportion.

IVERMECTIN (antiparasitic agent)

Acceptable Daily Intake (ADI): 0-1 µg/kg body weight (40th JECFA, 1992).

Estimated Dietary Exposure (EDI): The fortieth meeting of the Committee (WHO TRS No. 832, 1993) included an estimate of the potential intake from muscle. No further assessment of dietary exposure was undertaken at the current meeting

Residue Definition: Ivermectin B1a.

Species	Tissue	MRLs (µg/kg) recommended by the 78 th JECFA		Step	JECFA
Cattle	Muscle	4	3		78

LASOLACID SODIUM (antiparasitic agent)

Acceptable Daily Intake (ADI): 0-5 µg/kg body weight on the basis of a NOAEL of 0.5 mg/kg body weight per day from a developmental toxicity study in rabbits and a multigeneration reproductive toxicity study in rats, with application of an uncertainty factor of 100 for interspecies and intraspecies variability (78th JECFA, 2013).

Estimated Dietary Exposure (EDI): An EDI of 80 µg/person per day was calculated, which represents approximately 27% of the upper bound of the ADI.

Residue Definition: Lasolacid A.

Species	Tissue	MRLs (µg/kg) recommended by the 78 th JECFA		Step	JECFA
Chicken	Muscle	400	3		78
Chicken	Liver	1200	3		78
Chicken	Kidney	600	3		78
Chicken	Skin + Fat	600	3		78
Turkey	Muscle	400	3		78
Turkey	Liver	1200	3		78
Turkey	Kidney	600	3		78
Turkey	Skin + Fat	600	3		78
Quail	Muscle	400	3		78
Quail	Liver	1200	3		78
Quail	Kidney	600	3		78
Quail	Skin + Fat	600	3		78
Pheasant	Muscle	400	3		78
Pheasant	Liver	1200	3		78
Pheasant	Kidney	600	3		78
Pheasant	Skin + Fat	600	3		78

NOTE: The 78th JECFA extended the MRLs in chicken to turkey and quail and extrapolated the MRLs in chicken to pheasant. No information was available for duck, including on approved uses. As the compound is not registered for use in laying hens, according to the sponsor, it is not appropriate to recommend MRLs for eggs

MONEPANTEL (anthelminthic)**Acceptable Daily Intake (ADI):**

0-20 µg/kg body weight on the basis of a lowest-observed-adverse-effect level (LOAEL) of 1.8 mg/kg body weight per day considering liver effects in mice, and a safety factor of 100, with rounding to one significant figure (75th JECFA, 2011).

Estimated Dietary Exposure (EDI):

Using the model diet and marker residue to total residue ratios of 1.00 for muscle and 0.66 for fat, liver and kidney, and applying a correction factor of 0.94 to account for the mass difference between monepantel sulfone (the marker residue) and monepantel, the EDI is 446 µg/person per day, which represents approximately 37% of the upper bound of the ADI. (78th JECFA, 2013).

Residue Definition:

Monepantel sulfone, expressed as monepantel.

Species	Tissue	MRLs(µg/kg) recommended by the 75 th JECFA	Step	JECFA	MRLs (µg/kg) recommended by the 78 th JECFA	Step	JECFA
Sheep	Muscle	300	7	75	500	3	78
Sheep	Liver	3000	7	75	7000	3	78
Sheep	Kidney	700	7	75	1700	3	78
Sheep	Fat	5500	7	75	13000	3	78

In shaded font are the MRLs held at Step 7 by CCRVDF21.