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CODEX ALIMENTARIUS COMMISSION

Food and Agriculture Organization of the United Nations

World Health Organization

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Agenda Item 7 **CX/RVDF 23/26/7**

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JOINT FAO/WHO FOOD STANDARDS PROGRAMME

CODEX COMMITTEE ON RESIDUES OF VETERINARY DRUGS IN FOODS

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Portland, Oregon, United States of America

EXTRAPOLATION OF MAXIMUM RESIDUE LIMITS FOR VETERINARY DRUGS TO ONE OR MORE SPECIES

(At Step 4)

(Prepared by the Electronic Working Group chaired by the European Union and co-chaired by Costa Rica)

Codex members and observers wishing to submit comments at Step 3 on the

- proposed extrapolated MRLs for veterinary drugs to one or more species in accordance with the *Approach for the extrapolation of maximum residue limits for veterinary drugs to one or more species*
- extrapolation of bovine milk MRL for ivermectin to goat and sheep milk and
- extrapolation of MRLs of veterinary drugs for edible offal

should do so as instructed in CL 2022/76-RVDF available on the Codex webpage/Circular Letters[1] or CCRVDF/Related Circular Letters[2]

INTRODUCTION

1. The 25th Session of the Codex Committee on Residues of Veterinary Drugs in Foods (CCRVDF25, 2021) agreed to forward the *Approach for the extrapolation of maximum residue limits for veterinary drugs to one or more species*[3] to the Codex Alimentarius Commission for adoption and inclusion as Annex C to the *Risk Analysis Principles Applied by CCRVDF*. The 44th Session of the Commission (CAC44, 2021) adopted[4] the Approach as proposed by CCRVDF25.

2. CCRVDF25 further agreed to request the Codex Secretariat to issue the proposed extrapolated MRLs for comments through a circular letter (CL). This was done by CL 2021/98-RVDF in December 2021 with a deadline of 25 March 2022 for replies.

TERMS OF REFRENCE

3. CCRVDF25 decided to establish an Electronic Working Group (EWG), chaired by the European Union (EU) and co-chaired by Costa Rica with the following terms of reference:

- To continue discussing the extrapolated MRLs taking into account the comments submitted to CL2021/98-RVDF, and prepare revised proposals for consideration by CCRVDF26[5].
- To consider the extrapolation of MRLs for ivermectin in goat and sheep milk[6].
- To develop a suitable approach for the extrapolation of MRLs for residues of veterinary drugs for offal tissues[7]

1 http://www.fao.org/fao-who-codexalimentarius/resources/circular-letters/en/
2 http://www.fao.org/fao-who-codexalimentarius/committees/committee/related-circular-letters/en/?committee=CCRVDF
3 REP21/RVDF25, para. 105(i), App. III
4 REP21/CAC44, App. II
5 REP21/RVDF25, para. 105(iv)
6 REP21/RVDF25, para. 150(iii)
7 REP21/RVDF25, para. 150(vi)

WORK PROCESS: PARTICIPATION AND METHODOLOGY

4. Member countries, Observer organizations and FAO registered to participate in the EWG. The list of participants is attached as Appendix III.

5. The EWG Chairs circulated the first message to the EWG on 17 September 2022 in English and in Spanish. In line with the terms of reference of the EWG, the document contained an analysis of comments received in response to CL 2021/98-RVDF, an analysis on the extrapolation of MRLs for ivermectin in goat and sheep milk and a proposal for possible approach to the extrapolation of MRLs for residues of veterinary drugs for offal tissues.

6. Two Members provided their comments. On the basis of the comments, the EWG Chairs prepared a draft report and circulated it to the EWG on the 15 November 2022. One Member sent comments on the draft draft.

7. The EWG Chairs finalised the discussion paper and submitted it to the Codex Secretariat on 30 November 2022.

SUMMARY OF DISCUSSIONS

The proposed extrapolated MRLs

8. Comments received from Codex members in response to CL 2021/98-RVDF are attached in Appendix II. The EWG noted wide support for the proposed extrapolated MRLs. There were two substantial comments which the EWG addressed as follows:

- *Benzylpenicillin - Thailand:* Thailand pointed out that there is in error in Annex to CL 2021/98-RVDF, i.e. it indicates that MRLs for benzylpenicillin exist in sheep. The EWG noted that Thailand was correct. In fact, this error was highlighted before CCRVDF25 and corrected in Appendix 2 of CRD3 (the species sheep was replaced by chicken) presented for CCRVDF25. However, despite the error noted by Thailand, the recommendation that MRLs can be extrapolated to all ruminants adhered to the agreed approach on extrapolation. This was because it complied with the requirement that the the marker 'M' to total residues of toxicological concern 'T' (M:T) is 1 in all commodities, and consequently extrapolation from a single reference species was acceptable.
- *Tilmicosin - Kenya:* Kenya did not support extrapolation of the MRL for kidney because different M:Ts were used by the Joint FAO/WHO Expert Committee on Food Additives (JECFA) for cattle and sheep kidney. The EWG noted that the MRLs recommended by JECFA for cattle and sheep kidney were identical. Therefore, in line with the agreed approach on extrapolation, the MRL can be extrapolated despite the fact that the M:Ts are not identical in cattle and sheep.

The EWG further considered the following issues:

Cyhalothrin

9. The EWG agreed that the extrapolation criteria had been met. However, it was noted that the current Codex MRLs for bovine liver (20 µg/kg) and ovine liver (50 µg/kg) differ. The EWG was concerned that the proposed MRL of 20 µg/kg in liver for all ruminants might cause some confusion regarding which value applies to ovine liver (*i.e.*, 20 µg/kg or 50 µg/kg). Therefore, the EWG agreed that a note should be inserted in the veterinary drug MRL database and CX/MRL 2 to the liver MRL for all ruminants indicating that the liver MRL of 20 µg/kg applies to all ruminants except sheep.

Cypermethrin

10. The EWG agreed that the criteria had been met for extrapolating the cattle and sheep MRLs for muscle, fat, liver, and kidney to all ruminants. However, the EWG noted that the MRL for bovine milk does not meet the extrapolation criteria because M:T was not 1 as required by the Specific Criterion 3(v) of *Approach for the extrapolation of maximum residue limits for veterinary drugs to one or more species*.

11. The EWG also noted that there is some confusion over the existence of a Codex MRL for sheep milk as inconsistent information is published. CX/MRL 2 makes no reference to an MRL for sheep milk but the following WHO overview states that there is one: https://apps.who.int/food-additives-contaminants-jecfa-database/Home/Chemical/876

Deltamethrin

12. The EWG agreed that the criteria was met for extrapolating the bovine and sheep MRLs for muscle, fat, liver, and kidney to all ruminants. However, the EWG was unsure whether the extrapolation criteria had been met for milk (i.e., Specific Criterion 3(v)). JECFA52 (1999) (WHO TRS 893) reported that parent deltamethrin was 42 to 55% of the total residue in milk fat. In addition, the Theoretical Maximum Daily Intake (TMDI) calculation performed by JECFA52 did not provide an M:T ratio for milk. JECFA52 also reported that most of the deltamethrin residues are distributed predominantly in milk fat. This suggested that differential fat composition among ruminants could affect residue disposition. Later, JECFA60 (2003) (WHO TRS 918) did not report an M:T value for milk either.

13. On the other hand, the EWG noted that residues in cattle milk were <LOQ (limit of quantification), and on this basis JECFA did not even include them in the TMDI calculation. The fact that residues in cattle milk were <LOQ indicates that they do not make a significant contribution to the intake calculation. On this basis it could be argued that, even if the fat composition of milk varies across species and even without a statement from JECFA specifying the M:T in milk, establishing the same MRL in milk of ruminants as currently exists for cattle would not represent a consumer safety concern, particularly in light of the statement by JECFA52 that residues other than the parent compound will have reduced toxicity compared to that of the parent.

14. So a case could still be made for supporting the milk MRL extrapolation although this would not be following the rules specified in the *Approach for the extrapolation of maximum residue limits for veterinary drugs to one or more species*. Nevertheless, the EWG agreed that that CCRVDF should seek advice from JECFA on whether the appropriate M:T value in bovine milk is 1 before extrapolating the bovine milk MRL to all ruminants.

Moxidectin

15. The EWG agreed that the extrapolation criteria had been met. However, it was noted that the current Codex MRLs for bovine muscle (20 µg/kg) and ovine muscle (50 µg/kg) differ. The EWG was concerned that the proposed MRL of 20 µg/kg in muscle for all ruminants might cause some confusion regarding which value applies to ovine muscle (i.e., 20 µg/kg or 50 µg/kg). Therefore, the EWG agreed that a note should be inserted in the veterinary drug MRL database and CX/MRL 2 to the muscle MRL for all ruminants indicating that the muscle MRL of 20 µg/kg applies to all ruminants except sheep.

Tilmicosin

16. The EWG noted a typographical error for the reported chicken kidney MRL in CL 2021/98-RVDF as it reported an MRL of 300 µg/kg for chicken kidney while CX/MRL 2 reported an MRL of 600 µg/kg for chicken kidney. However, the EWG further noted that this error did not impact on the outcome of the proposed extrapolation.

Extrapolation of bovine milk MRL for ivermectin to goat and sheep milk

17. The EWG agreed that the criteria of the *Approach for the extrapolation of maximum residue limits for veterinary drugs to one or more species* did not allow the extrapolation of the bovine milk MRL for ivermectin to goat and sheep milk because MRL for milk has only been established in 1 species and the M:T is not 1. Some uncertainty was also expressed with regards to whether ivermectin B1a can be considered to be the same as the parent compound.

Extrapolation of MRLs for residues of veterinary drugs for offal tissues

18. In the absence of experience in setting MRLs for offal tissues other liver and kidney, it was suggested as a possible pragmatic approach to extrapolate the lowest MRL established in liver or kidney to all offal tissues while noting that this was not based on data confirming the validity of such an approach. The following specific concerns were raised on the suggested approach:

    1. Extrapolating an MRL from one edible offal tissue to another does not consider the additional source of dietary exposure resulting from the consumption of the edible offal tissue with the now extrapolated MRL. In other words, this approach would not involve a dietary exposure assessment that considers the new source of exposure plus the current sources of exposure in relation to the health based guidance value (HBGV). Consequently, this approach would result in MRLs that lack a science based demonstration of consumer safety.

    2. There was no data demonstrating that the M:T value determined in liver or kidney is applicable to other edible offal tissues. An appropriate M:T value is needed to conduct a dietary exposure assessment. Similar to point 1, without an M:T value, this approach would establish MRLs without the benefit of a science based demonstration of consumer safety.

    3. There was no data demonstrating that the disposition (e.g., kinetics, binding, etc.) of a marker residue in kidney or liver is similar to that in other edible offal tissues. If the disposition of the marker residue is different in the extrapolated tissue than in kidney or liver, then the concentration of the marker residue could exceed the extrapolated MRL even when good veterinary practices (GVPs) are followed. That is, the extrapolated MRL might not be compatible with the established GVPs. Thus, extrapolating the kidney or liver MRL to other edible offal tissues might inadvertently create trade barriers even when established GVPs are followed.

19. In response to these concerns, and in particular concern no 1, it was noted that historically CCRVDF and JECFA relied on a standard food basket to estimate consumer exposure. Food commodities other than those in the standard basket were not considered in the dietary exposure calculation. This did not mean that such commodities were never eaten. Rather, the MRLs established for the commodities in the food basket were considered to be sufficiently conservative to provide a margin of safety that adequately addressed uncertainty arising from exposure via other commodities. The assumption would seem to be that if other commodities are ingested (e.g. cheese and other offal tissues) this would mean that less of the standard food basket commodities are ingested. If CCRVDF is content to make this assumption, then there is no need to consider ingestion of offal tissues other than liver and kidney as adding to the overall consumer exposure to residues.

20. Due to the outstanding concerns and lack of experience and data on setting MRLs for offal tissues other than liver and kidney, the EWG was not able to develop a suitable approach for the extrapolation of MRLs for residues of veterinary drugs for offal tissues at this time.

CONCLUSIONS

21. The EWG agreed that:

i. the proposed extrapolated MRLs in Appendix I comply with the rules specified in the *Approach for the extrapolation of maximum residue limits for veterinary drugs to one or more species*;

ii. the *Approach for the extrapolation of maximum residue limits for veterinary drugs to one or more species* does not allow the extrapolation of the bovine milk MRL for ivermectin to goat and sheep milk; and

iii. further discussions at CCRVDF26 level would be helpful on how to generate MRLs in edible offal tissues other than kidney and liver.

RECOMMENDATIONS

22. CCRVDF is invited to:

i. consider the proposed extrapolated MRLs in Appendix I;

ii. seek advice from JECFA on whether the appropriate M:T value for residues of deltamethrin in bovine milk is 1;

iii. note that the *Approach for the extrapolation of maximum residue limits for veterinary drugs to one or more species* does not allow the extrapolation of the bovine milk MRL for ivermectin to goat and sheep milk; and

iv. consider ways forward to extrapolate MRLs for residues of veterinary drugs for offal tissues other than kidney and liver.

APPENDIX I

EXTRAPOLATION OF MRLs
IN ACCORDANCE WITH THE
APPROACH FOR THE EXTRAPOLATION OF MAXIMUM RESIDUE LIMITS FOR VETERINARY DRUGS TO ONE OR MORE SPECIES
(For comments: Proposed MRLs,
the remaining information in the tables is for information only)

1. Amoxicillin – extrapolation to ruminants

Which species have MRLs been established in?		**Cattle (µg/kg)**	**Sheep (µg/kg)**	**Pig (µg/kg)**	**Finfish**
	Muscle	50	50	50	50**
	Fat*	50	50	50	-
	Liver	50	50	50	-
	Kidney	50	50	50	-
	Milk	4	4	-	-
Were the MRLs established on the basis of a full evaluation undertaken by JECFA?	Yes				
Is the marker residue the parent compound?	Yes				
What are the M:Ts	The JECFA report (WHO TRS 969(10)) establishes a microbiological ADI and indicates that the only microbiologically active residue is the parent substance. The M:T in all tissues and milk is therefore considered to be 1 in all species				
Can the MRLs be extrapolated to ruminants?	Yes, as the M:T is 1 in all commodities and, in addition, identical MRLs already exist in 2 ruminant species				
Proposed MRLs:	Muscle	50 µg/kg			
	Fat*	50 µg/kg			
	Liver	50 µg/kg			
	Kidney	50 µg/kg			
	Milk	4 µg/kg			

* Fat/skin for pigs
** This value applies to finfish fillet

2. Benzylpenicillin – extrapolation to ruminants

Which species have MRLs been established in?		Cattle (µg/kg)	Chicken (µg/kg)	Pig (µg/kg)
	Muscle	50	50	50
	Fat	-	-	-
	Liver	50	50	50
	Kidney	50	50	50
	Milk	4	-	-
Were the MRLs established on the basis of a full evaluation undertaken by JECFA?	Yes			
Is the marker residue the parent compound?	Yes			
What are the M:Ts	The JECFA report (WHO TRS 799(10)) uses a M:T of 1 in all tissues and milk of all species			
Can the MRLs be extrapolated to ruminants?	Yes, as the M:T is 1 in all commodities			
Proposed MRLs:	Muscle	50 µg/kg		
	Fat	-		
	Liver	50 µg/kg		
	Kidney	50 µg/kg		
	Milk	4 µg/kg		

3. Tetracyclines - extrapolation to ruminants

Which species have MRLs been established in?		Cattle (µg/kg)	Sheep (µg/kg)	Pigs (µg/kg)	Poultry (µg/kg)	Fish* (µg/kg)	Giant prawn* (µg/kg)
	Muscle	200	200	200	200	200	200
	Fat	-	-	-	-	-	-
	Liver	600	600	600	600	-	-
	Kidney	1200	1200	1200	1200	-	-
	Milk	100	100	-	-	-	-
	Eggs	-	-	-	400	-	
Were the MRLs established on the basis of a full evaluation undertaken by JECFA?	Yes						
Is the marker residue the parent compound?	Yes						
What are the M:Ts	The JECFA report (WHO TRS 888(10) uses a M:T of 1 in all tissues, milk and eggs						
Can the MRLs be extrapolated to ruminants?	Yes, as the M:T is 1 in all tissues, milk and eggs and, in addition, identical MRLs already exist in 2 related ruminant species						
Proposed MRLs:	Muscle	200 µg/kg					
	Fat	-					
	Liver	600 µg/kg					
	Kidney	1200 µg/kg					
	Milk	100 µg/kg					

* Applies only to oxytetracycline

4. Cyhalothrin - extrapolation to ruminants

Which species have MRLs been established in?		Cattle (µg/kg)	Sheep (µg/kg)	Pigs (µg/kg)
	Muscle	20	20	20
	Fat	400	400	400
	Liver	20	50	20
	Kidney	20	20	20
	Milk	30	-	-
Were the MRLs established on the basis of a full evaluation undertaken by JECFA?	Yes			
Is the marker residue the parent compound?	Yes			
What are the M:Ts	The JECFA report (WHO TRS 900(10) uses the same M:T values in all species (1 in muscle, fat and milk, 0.06 in liver and 0.2 in kidney)			
Can the MRLs be extrapolated to ruminants?	Yes, as the M:Ts established for cattle and sheep are identical, the more conservative set of MRLs (cattle) can be extrapolated to other ruminants. As the M:T for cattle milk is 1, the MRL can be extrapolated to milk of other ruminants			
Proposed MRLs:	Muscle	20 µg/kg		
	Fat	400 µg/kg		
	Liver	20 µg/kg*		
	Kidney	20 µg/kg		
	Milk	30 µg/kg		

*The liver MRL of 20 µg/kg applies to all ruminants except sheep. The liver MRL for sheep is 50 µg/kg

5. Cypermethrin - extrapolation to ruminants

Which species have MRLs been established in?		**Cattle (µg/kg)**	**Sheep (µg/kg)**
	Muscle	50	50
	Fat	1000	1000
	Liver	50	50
	Kidney	50	50
	Milk	100	-
Were the MRLs established on the basis of a full evaluation undertaken by JECFA?	Yes		
Is the marker residue the parent compound?	Yes		
What are the M:Ts	The JECFA reports use the following values: 0.3 in muscle, 0.8 in fat, 0.1 in liver, 0.05 in kidney and 0.95 (WHO TRS 911 and FAO FNP 41/16) The same values appear to have been used for cattle and sheep		
Can the MRLs be extrapolated to ruminants?	For tissues, yes, as the M:Ts established for cattle and sheep are identical and, in addition, identical MRLs already exist in 2 ruminant species. For milk, no, as the M:T established for cattle milk is 0.95 and an MRL has only been established in milk of 1 ruminant species		
Proposed MRLs:	Muscle	50 µg/kg	
	Fat	1000 µg/kg	
	Liver	50 µg/kg	
	Kidney	50 µg/kg	
	Milk	-	

6. Deltamethrin - extrapolation to ruminants

Which species have MRLs been established in?		Cattle (µg/kg)	Sheep (µg/kg)	Chicken (µg/kg)	Salmon (µg/kg)
	Muscle	30	30	30	30
	Fat	500	500	500	-
	Liver	50	50	50	-
	Kidney	50	50	50	-
	Milk	30	-	-	-
	Eggs	-	-	30	-
Were the MRLs established on the basis of a full evaluation undertaken by JECFA?	Yes				
Is the marker residue the parent compound?	Yes				
What are the M:Ts	The JECFA reports (WHO TRS 893 and 918) use the following values: 0.6 in fat, 0.04 in liver, 0.03 in kidney. No M:T is reported for milk. M:T for muscle not reported but equivalent values were applied in all species				
Can the MRLs be extrapolated to ruminants?	For tissues, yes, as the MRLs for cattle and sheep are identical. For milk, no, as the M:T for cattle milk is unreported				
Proposed MRLs:	Muscle	30 µg/kg			
	Fat	500 µg/kg			
	Liver	50 µg/kg			
	Kidney	50 µg/kg			
	Milk*	-			

*In relation to milk, see comments in body of report

7. Moxidectin - extrapolation to ruminants

Which species have MRLs been established in?		Cattle (µg/kg)	Sheep (µg/kg)	Deer (µg/kg)
	Muscle	20	50	20
	Fat	500	500	500
	Liver	100	100	100
	Kidney	50	50	50
	Milk	-	-	-
Were the MRLs established on the basis of a full evaluation undertaken by JECFA?	Yes			
Is the marker residue the parent compound?	Yes			
What are the M:Ts	The JECFA report (WHO TRS 888) uses the following values: 0.75 for fat, 0.4 for muscle, 0.4 for liver and kidney for all three species			
Can the MRLs be extrapolated to ruminants?	Yes, as the M:Ts are the same in all three species (identical MRLs were originally established for cattle, sheep and deer [TRS 864] but the muscle MRL for sheep was subsequently raised following a new residue study in sheep with the M:T remaining unchanged)			
Proposed MRLs:	Muscle	20 µg/kg		
	Fat	500 µg/kg		
	Liver	100 µg/kg		
	Kidney	50 µg/kg		
	Milk	-		

*The muscle MRL of 20 µg/kg applies to all ruminants except sheep. The muscle MRL for sheep is 50 µg/kg

8. Spectinomycin -extrapolation to ruminants

Which species have MRLs been established in?		Cattle (µg/kg)	Sheep (µg/kg)	Pig (µg/kg)	Chicken (µg/kg)
	Muscle	500	500	500	500
	Fat	2000	2000	2000	2000
	Liver	2000	2000	2000	2000
	Kidney	5000	5000	5000	5000
	Milk	200	-	-	--
	Eggs	-	-	-	2000
Were the MRLs established on the basis of a full evaluation undertaken by JECFA?	Yes				
Is the marker residue the parent compound?	Yes				
What are the M:Ts	The JECFA report (WHO TRS 888) uses the following values: 0.25 for liver and 1 for all other tissues, milk and eggs in all species				
Can the MRLs be extrapolated to ruminants?	Yes, as the M:Ts are the same in all species and, in addition, identical MRLs already exist in 2 related ruminant species. In relation to milk, the M:T is 1.				
Proposed MRLs:	Muscle	500 µg/kg			
	Fat	2000 µg/kg			
	Liver	2000 µg/kg			
	Kidney	5000 µg/kg			
	Milk	200 µg/kg			

9. Levamisole extrapolation to ruminants

Which species have MRLs been established in?		Cattle (µg/kg)	Sheep (µg/kg)	Pig (µg/kg)	Poultry (µg/kg)
	Muscle	10	10	10	10
	Fat	10	10	10	10
	Liver	100	100	100	100
	Kidney	10	10	10	10
	Milk	-	-	-	-
	Eggs	-	-	-	-
Were the MRLs established on the basis of a full evaluation undertaken by JECFA?	Yes				
Is the marker residue the parent compound?	Yes				
What are the M:Ts?	The JECFA report (WHO TRS 851) uses the following values: 0.024 for all tissues				
Can the MRLs be extrapolated to ruminants?	Yes, as the M:Ts are the same in all species and, in addition, identical MRLs already exist in 2 related ruminant species				
Proposed MRLs:	Muscle	10 µg/kg			
	Fat	10 µg/kg			
	Liver	100 µg/kg			
	Kidney	10 µg/kg			
	Milk	-			

10. Tilmicosin extrapolation to ruminants

Which species have MRLs been established in?		Cattle (µg/kg)	Sheep (µg/kg)	Pigs (µg/kg)	Chicken* (µg/kg)	Turkey* (µg/kg)
	Muscle	100	100	100	150	100
	Fat	100	100	100	250	250
	Liver	1000	1000	1500	2400	1400
	Kidney	300	300	1000	600	1200
	Milk	-	-	-	-	-
	Eggs	-	-	-	-	-
Were the MRLs established on the basis of a full evaluation undertaken by JECFA?	Yes					
Is the marker residue the parent compound?	Yes					
What are the M:Ts?	The JECFA report (WHO TRS 876) uses the following values: 0.05 for cattle and sheep liver, 0.10 for sheep kidney, 0.25 for cattle kidney, 0.10 for cattle and sheep muscle and fat, 0.50 for pig liver and kidney, 0.10 for pig muscle and fat					
Can the MRLs be extrapolated to ruminants?	Yes, although there is a difference in the M:T for cattle and sheep kidney, the MRLs recommended for these 2 species were identical					
Proposed MRLs:	Muscle	100 µg/kg				
	Fat	100 µg/kg				
	Liver	1000 µg/kg				
	Kidney	300 µg/kg				
	Milk	-				

* The value for fat applies to skin/fat

11. Deltamethrin extrapolation to finfish

Which species have MRLs been established in?		Cattle (µg/kg)	Sheep (µg/kg)	Chicken (µg/kg)	Salmon (µg/kg)
	Muscle	30	30	30	30
	Fat	500	500	500	-
	Liver	50	50	50	-
	Kidney	50	50	50	-
	Milk	30	-	-	-
	Eggs	-	-	30	-
Were the MRLs established on the basis of a full evaluation undertaken by JECFA?	Yes				
Is the marker residue the parent compound?	Yes				
What are the M:Ts?	The JECFA report (WHO TRS 893) indicates that a M:T in muscle of salmon was not established. However, the concentrations of the marker residue and total residues were very low in muscle (of all species), with the MRL established based on twice the LoQ (From TRS 918): 0.04 for liver, 0.03 for kidney and 0.60 for fat)				
Can the MRLs be extrapolated to bony fish?	Yes, as residues in muscle of all species evaluated including salmon were very low (<LoQ) and do not make a significant addition to consumer exposure (Note that it was considered appropriate to extend the MRL for mammalian muscle to *Salmonidae* without metabolism data in this family)				
Proposed MRL:	Muscle	30 µg/kg			

12. Flumequine extrapolation to finfish

Which species have MRLs been established in?		Cattle (µg/kg)	Sheep (µg/kg)	Pigs (µg/kg)	Chicken (µg/kg)	Trout (µg/kg)
	Muscle	500	500	500	500	500
	Fat	1000	1000	1000	1000	-
	Liver	500	500	500	500	-
	Kidney	3000	3000	3000	3000	-
	Milk	-	-	-	-	-
	Eggs	-	-	-	-	-
Were the MRLs established on the basis of a full evaluation undertaken by JECFA?	Yes					
Is the marker residue the parent compound?	Yes					
What are the M:Ts?	The JECFA report (WHO TRS 900(10) uses the following values: Cattle: muscle, kidney and fat: 0.79, liver: 0.17 Sheep: muscle, kidney and fat: 0.4, liver: 0.06 Pigs: muscle, kidney and fat: 0.59, liver:0.07 Chickens: 0.82 in all tissues Trout: no measurable residues of flumequine metabolites, so most probably M:T = 1					
Can the MRLs be extrapolated to bony fish?	Yes, as the M:T in trout is most probably 1 (suggesting no significant metabolism in fish) and, in addition, identical MRLs have been established in multiple unrelated species.					
Proposed MRL:	Muscle	500 µg/kg				

APPENDIX II
Original Language Only

COMMENTS IN REPLY TO CL 2021/98-RVDF
(For information)

GENERAL COMMENTS

COMMENT	MEMBER / OBSERVER
On reviewing the proposed extrapolations, Australia notes the maximum residue limits proposed are in lines with the Approach for the Extrapolation of MRLs for Veterinary Drugs to One or More Species (REP21/RVDF25, Appendix III) which was supported by Australia. Australia supports all the proposed extrapolations	**Australia**
Canada does not establish/extrapolate MRLs for veterinary drugs to one or more species in the absence of a registered drug product i.e. without having an approved indication for the species in question. However, we acknowledge the need for MRLs in various commodities to facilitate international trade and protect human food safety and therefore, support the extrapolation of MRLs for the specific drugs included in the circular.	**Canada**
Chile apoya los LMR extrapolados propuestos en el anexo de la Carta Circular "CL 2021/98-RVDF". Adicionalmente, considerando que este anexo es la versión original que estuvo disponible para la reunión 25 CCRVDF y por razones de tiempo no se alcanzó a revisar en esa oportunidad, entendemos que no tiene incorporado las modificaciones de términos acordados en esa reunión y por lo tanto se deberá tener presente incluirlos para esta nueva etapa de comentarios. Justificación: Lo indicado en el reporte de la 25 CCRVDF, párrafo 102, 2° viñeta. 102. Además, el CCRVDF acordó lo siguiente:· Utilizar el término peces de aleta en lugar de peces óseos y suprimir la referencia a los nombres científicos, ya que los LMR del Codex actuales para medicamentos veterinarios se refieren principalmente a los peces de aleta.	**Chile**
Agreed	**China**
We support the proposed extrapolations as presented as they are based on the criteria agreed by CCRVDF. For prudent use, we would like to underline the importance of GVP and we would especially like to refer to the guidance dovuments on AMR (adopted 2021).	**Norway**
Saudi Arabia has no comments on the proposed draft of maximum residue limits for veterinary drugs extrapolated to one or more species	**Saudi Arabia**

Amoxicillin MRLs extrapolated to ruminants

Comment: Kenya supports the extrapolation Justification: Based on the deliberations of JECFA MRLs M: T is 1 in all commodities and, in addition, identical MRLs already exist in 2 ruminant species.	**Kenya**
Agreed	**India**

Benzylpenicillin MRLs extrapolated to ruminants

Comment: Kenya supports the extrapolation Justification: Based on the evaluations of JECFA MRLs M: T is 1 in all commodities and, in addition, identical MRLs already exist in 2 ruminant species.	**Kenya**
Agreed	**India**
We would like to reiterate our observation that the Codex MRLs for benzylpenicillin are given only for cattle, chicken and pig tissues as shown in the Codex online databases, the RVDF/25 INF/01, Part A (Codex MRLs and Risk Management Recommendations (RMRs) for Veterinary Drugs) adopted by the CAC41, report of the 23rd Session of the Codex Alimentarius Commission and report of the 50th Meeting of Joint FAO-WHO Expert Committee Report on Food Additives. In this regard, the proposed extrapolation of MRLs for benzylpenicillin in cattle and sheep tissues to all ruminant species tissues should be reconsidered because the Codex MRLs for benzylpenicillin in sheep is not established. The approach for the extrapolation of MRLs relevant to the existence of identical Codex MRLs must adhere to the specific criteria for extrapolation (i) in Annex C the Approach for the extrapolation of maximum residue limits for veterinary drugs to one or more species of the Risk Analysis Principle applied by CCRVDF, which was adopted by CAC44.	**Thailand**

Tetracyclines MRLs extrapolated to ruminants

Comment: Kenya supports the extrapolation Justification: Based on the evaluations of JECFA MRLs M: T is 1 in all tissues, milk, eggs and, in addition, identical MRLs already exist in 2 ruminant species.	**Kenya**
Agreed	**India**

Cyhalothrin MRLs extrapolated to ruminants

Comment: Kenya supports the extrapolation Justification: Based on the evaluations of JECFA MRLs M: T and their recommendation for extrapolation	**Kenya**
Agreed	**India**

Cypermethrin MRLs extrapolated to ruminants

Comment: Kenya supports the extrapolation Justification: Based on the evaluations of JECFA MRLs M: T and their recommendation for extrapolation	**Kenya**
Agreed	**India**

Deltamethrin MRLs extrapolated to ruminants

Comment: Kenya supports the extrapolation Justification: Based on the evaluations of JECFA MRLs for cattle and sheep, and their recommendation for extrapolation.	**Kenya**
Agreed	**India**

Moxidectin MRLs extrapolated to ruminants

Comment: Kenya supports the extrapolation Justification: Based on the evaluations of JECFA MRLs M: T and their recommendation for extrapolation	**Kenya**
Agreed	**India**

Spectinomycin MRLs extrapolated to ruminants

Comment: Kenya supports the extrapolation Justification: Based on the evaluations of JECFA MRLs M: T and their recommendation for extrapolation	**Kenya**
Agreed	**India**

Levamisole MRLs extrapolated to ruminants

Comment: Kenya supports the extrapolation Justification: Based on the evaluations of JECFA MRLs M: T ratios, and their recommendation for extrapolation	**Kenya**
Agreed	**India**

Tilmicosin MRLs extrapolated to ruminants

Comment: Kenya does not support the proposal for extrapolation as presented given differences in the M: Ts of Cattle and sheep kidneys, although the MRLs are identical. Kenya requests JECFA to provide additional guidance on other criteria that can be used to extrapolate. Comment: Kenya supports the extrapolation in the muscle, Fat and Liver. Justification: Based on the evaluations of JECFA MRLs M: T ratios, and their recommendation for extrapolation	**Kenya**
Agreed	**India**

Deltamethrin MRL extrapolated to finfish

Comment: Kenya supports the extrapolation Justification: Based on the evaluations of JECFA MRLs M: T ratios, and their recommendation for extrapolation in bony fish.	**Kenya**
Agreed	**India**

Flumequine MRL extrapolated to finfish

Comment: Kenya supports the extrapolation Justification: Based on the evaluations of JECFA MRLs M: T ratios, and their recommendation for extrapolation.	**Kenya**
Agreed	**India**

APPENDIX III

LIST OF PARTICIPANTS

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