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World Health Organization

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JOINT FAO/WHO FOOD STANDARDS PROGRAMME

CODEX COMMITTEE ON RESIDUES OF VETERINARY DRUGS IN FOODS

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REPORT OF THE INFORMAL ONLINE DISCUSSION FORUM ON EXTRAPOLATION OF MAXIMUM RESIDUE LIMITS FOR VETERINARY DRUGS TO ONE OR MORE SPECIES

(Prepared by the European Union)
This CRD should be read in conjunction with CX/RVDF 21/25/8

INTRODUCTION

1. On 25 April 2021, the European Union (EU), as lead country of the Electronic Working Group (EWG) established by the 24th Session of the Codex Committee on Residues of Veterinary Drugs in Foods (CCRVDF24, 2018) on extrapolation of maximum residue limits (MRLs) for veterinary drugs to one or more species, invited Codex members and observers to participate in an informal online discussion forum. The forum was to consider technical issues raised in reply to CL 2020/42-RVDF concerning the policy framework to the extrapolation of maximum residue limits of veterinary drugs to one or more animal species and the MRL proposals derived on the basis of this approach in order to facilitate their consideration by CCRVDF25.

PARTICIPATION AND METHODOLOGY

2. The online forum was joined by 17 Codex Members. The List of Participants is presented in Appendix III.

3. On 18 May 2021, the chair circulated to the participants a response to the comments received in reply to CL 2020/42-RVDF and a revised version of the proposed approach and the MRL proposals prepared on the basis of the comments received. The participants had until 28 May to provide further comments. On 7 June, the chair provided a response to the comments and a slightly revised approach prepared on the basis of the comments with a deadline for further comments by 14 June. On 30 June, the chair provided a report of the discussion and the proposed approach together with the MRL proposals to the Codex Secretariat.

SUMMARY OF DISCUSSION

4. A number of countries expressed their support for the proposed approach including the proposals made in the pilot on extrapolation of MRLs identified in the priority list Part D. A number of other countries made comments suggesting clarifications and/or addition of definitions without suggesting changes to the proposed approach. The comments were accommodated in the revised document wherever possible.

5. In addition, a number of more substantive comments were received:

a) One comment suggested that the description of species within a related species group, particularly the non-ruminant mammal group, should be further refined. The response pointed out that current proposal already relates to a defined (and rather limited) set of criteria that provides a high degree of confidence that metabolism is similar across species and consequently further restricting the species within a group seems unnecessary.

b) Two comments were received suggesting addition of guidance in relation to extrapolation in more complicated scenarios than those currently envisaged. The response noted that, at this time, the aim is to see if it is possible to reach agreement for the most straight forward cases. More complicated scenarios could be considered as a follow up activity.

c) A comment was received suggesting that consideration was needed in relation to different consumption patterns of livestock products in different regions and countries. The response noted that CCRVDF has traditionally assumed the same intake pattern for all mammals. Furthermore, the current proposal recommends that the most conservative set of MRLs established within a category of related species should be extrapolated. Taking these factors into consideration, further consideration of consumption patterns seems unnecessary.

d) Two members supported the approach in principle but pointed out that, for a number of the substances included in the pilot, full residues packages were not available for 2 related species as the Joint FAO/WHO Expert Committee on Food Additives (JECFA) had extended the MRLs (and M:Ts) from one species to another based on only a limited data set. The response suggested that if the data reviewed by JECFA were considered strong enough to allow CCRVDF to draw conclusions on the MRLs and M:Ts, then it would be reasonable to use these conclusions for the further extrapolation of MRLs. To do otherwise, would seem to cast doubt on CCRVDF's earlier conclusions.

e) Two members commented that, where JECFA has the ratio of market to total residues of (toxicological) concern, this value could be used in place of the M:T. This was accepted and the proposed approach was amended.

f) One member suggested that the condition indicating that if the M:T = 1 in all tissues, extrapolation may take place based on residues in a single species, could be amended to indicate that a M:T approaching 1 would also be acceptable. This change was taken on board.

g) One country supported the approach in principle but raised concerns over the potential for trade issues resulting from the possibility that the extrapolated MRLs may not truly reflect depletion characteristics in the concerned species. The response highlighted that, as long as products are used in compliance with good veternary practice (GVP) (ie in compliance with an appropriate withdrawal period), the relevant MRLs will be respected and trade difficulties should be avoided.

h) There was a comment that a template similar to the *current Template for Information Necessary for Prioritization by Codex Committee on Residues of Veterinary Drugs in Foods* should be used for suggesting substances for which extrapolation should be considered. No objection to this was raised.

i) The comment was also made that, in order to allow extrapolation, the drug should already be approved for use in the species for which extrapolation is requested in at least one country and GVP should have been established. The response noted that the primary benefit of extrapolation would be that it allows establishment of MRLs in species for which data are unlikely to be available (as sponsors have not chosen to develop products for these species). It therefore seems likely that authorised uses and GVP will rarely be available. A requirement for such conditions would greatly limit opportunities to use extrapolation and seems unnecessary from a consumer safety perspective.

j) There was a comment suggesting that, if an extrapolation approach is agreed, an electronic working group should be formed to apply the criteria and the proposed draft MRLs should be circulated for comment at Step 3. The response was that for those substances included in Part D of the Priority List agreed by CCRVDF24, proposals for MRLs extrapolated based on the proposed approach have already been circulated for comments at step 3 with CL 2020/42-RVDF (Rev 1). An electronic working group could be formed to conduct future extrapolations.

k) There was a comment that an analytical method should be available for the extrapolated Codex MRLs in the concerned species. The response was that the existence of an analytical method in the reference species would already provide assurance that it would also be possible for monitoring authorities to measure the substance in the concerned species also. It was noted that in practice residue monitoring authorities use multi-residue methods which are not usually those reviewed by JECFA. Consequently, for residue monitoring purposes, some work is, in any case, almost always required by the monitoring laboratory in order to incorporate detection/measurement of a marker residue into an existing multi-residue method.

6. Concerning the question how the proposed approach on extrapolation could be formalised provided that it were agreed by CCRVDF25. The chair suggested in his contribution of 7 June to the particpants of the online forum that the proposed approach would be added as an annex to the *Risk Analysis Principles Applied by the Codex Committee on Residues of Veterinary Drugs in Foods* in the Procedural Manual with a title reading "*Risk Management Policy applied by CCRVDF for the Extrapolation of MRLs to One or More Animal Species*" thus making a clear distinction to the extrapolation recommended by JECFA. The chair further suggested making an appropriate reference to the new annex in the second indent of paragraph 30 of the Principles. No comments were received in response to these proposals.

CONCLUSIONS

7. There was wide support in the online forum for the proposed approach for extrapolation as presented in Appendix I and for the proposed draft MRLs in Appendix 2. Amendments to the corresponding texts in working document CX/RVDF 21/25/8 are indicated in track changes.

8. Concerning the formalisation of the proposed approach, in the absence of any objections it is suggested that the proposed approach is added as Annex C to the *Risk Analysis Principles Applied by the Codex Committee on Residues of Veterinary Drugs in Foods* in the Procedural Manual with a title "*Risk Management Policy applied by CCRVDF for the Extrapolation of MRLs to One or More Animal Species*". An appropriate reference to the new Annex C should be made in the second indent of paragraph 30 of the Principles.

RECOMMENDATIONS

9. Codex members and observers are invited to consider:

a) the proposed approach for extrapolation as presented in Appendix I;

b) the proposed draft MRLs in Appendix 2; and

c) the proposal to insert the proposed approach as a new Annex C to the *Risk Analysis Principles Applied by the Codex Committee on Residues of Veterinary Drugs in Foods* in the Procedural Manual with an appropriate reference to the new Annex C in the second indent of paragraph 30 of the Principles.

Appendix I

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

General criteria for extrapolation:

1. Extrapolation should take place only between the same tissues/food commodities in the reference and concerned species (e.g. muscle to muscle, fat to fat etc.).

2. Extrapolation of reference species MRLs to a concerned species on a one to one basis should be considered only if **all** of the following are satisfied:

   (i) the reference and concerned species are related (see "A note on terminology" below),

   (ii) the marker residue in the reference species is the parent compound only, or is the same as the total residues of toxicological concern, or the Codex MRL status in the reference species is 'unnecessary' and there is an expectation that the active substance will be used under the same conditions (i.e. by the same administration routes and at similar doses) in both species.

   (iii) the M:T[1] (the marker 'M' to total residues of toxicological concern 'T') established for the reference species can be applied to the concerned species.

Specific criteria for extrapolation

3. In order to ensure that the third of the above-mentioned three general criteria is satisfied, the following specific criteria are proposed.

   (i) Where identical Codex MRLs have been established in at least two related species on the basis of JECFA recommendations, these Codex MRLs can be extrapolated to other related species (e.g. extrapolate from cattle and sheep to all ruminants).

   Explanatory note: *The existence of identical MRLs in two related species provides grounds upon which to base the assumption that metabolism does not vary significantly within the group of related species—i.e. that the M:T established for the reference species can be applied to the concerned species.*

   (ii) Where identical M:T values have been used in JECFA calculations for two related species but the MRLs recommended (by JECFA) differ, the most conservative set of Codex MRLs (i.e. the MRLs from the species associated with the lowest consumer exposure estimate) can be extrapolated to other related species (e.g. where different MRL values have been established for cattle and sheep and extrapolation is considered to goats, the lowest set of MRLs should be used for extrapolation).

   Explanatory note: *The fact that JECFA considered it appropriate to use identical M:T values in two related species provides grounds upon which to base the assumption that metabolism does not vary significantly within the group of related species—i.e. that the M:T established for the reference species can be applied to the concerned species.*

   (iii) Where the M:T established by JECFA is 1 or approaching 1 in all tissues in a single reference species, the same Codex MRLs can be extrapolated to related species.

   Explanatory note: *The fact that the M:T is 1 in all tissues/food commodities indicates that the marker residue includes all the compounds of concern.~~substance is not metabolised to any significant degree.~~ It is considered reasonable to assume that this would also be the case in the concerned species.*

   Finally, while the above criteria can be used in all cases, the following additional criteria are proposed for fish, milk and eggs (i.e. extrapolation for fish, milk and eggs may be based on the above criteria OR based on the additional criteria below):

[1] EHC 240 (1) defines the marker residue as: The parent drug, or any of its metabolites, or a combination of any of these, with a known relationship to the concentration of the total residue in each of the various edible tissues at any time between administration of the drug and the depletion of residues to safe levels. Where 'total residues of toxicological concern' are not defined, 'total residue' may be used where 'Total residue' is defined CAC/MISC 5-1993 (2): the total residue of a drug in animal derived food consists of the parent drug together with all the metabolites and drug based products in the food after administration of the drug to food producing animals. The amount of total residues is generally determined by means of a study using the radiolabelled drug, and is expressed as the parent drug equivalent in mg/kg of the food'.

(iv) For fish, where the MRL in muscle/fillet recommended by JECFA was established based on the LoQ (e.g., twice the LoQ), the Codex MRL can be extrapolated to all bony fish.

Explanatory note: *The fact that the MRL in muscle/fillet is below the LoQ indicates that residues in muscle/fillet are not measurable and so do not make a significant contribution to the intake calculation. Even if there are differences in metabolism between fish species, the possibility that they will be so dramatic as to result in a level of residues in muscle/fillet sufficiently high to significantly impact on overall consumer exposure is considered unrealistic.*

(v) For milk and eggs, where the M:T established by JECFA is 1 (in milk or eggs of a reference species), the milk/egg Codex MRL of the reference species can be extrapolated to milk of other ruminants and eggs of other domesticated poultry species, respectively, even if the M:T is not 1 in tissues.

Explanatory note: *For milk and eggs, there may be a concern that the fat content differs between related species. However, if the M:T is 1 in the reference species this indicates that the M:T is not significantly influenced by the fat content.*

A note on terminology

- 'Reference species' is used to refer to a species in which Codex MRLs have been established based on a scientific evaluation by JECFA
- 'Concerned species' is used to refer to a species for which extrapolation is being considered
- 'Related species' means species belonging to the same category of food producing species of ruminant and non-ruminant mammals*, birds or bony fish** (Osteichthyes)
- 'Unrelated species' is used to refer to species belonging to different categories of food producing species

* The category of non-ruminant food producing mammals is considered to include pigs, horses and rabbits

** Three distinct classes of fish are usually identified: (i) jawless fish (Agnatha), (ii) cartilaginous fish (Chondrichytes) and (iii) bony fish (Osteichthyes). To date, MRL data have been provided only for bony fish, and it is these that are predominantly farmed and eaten. Consequently, it is proposed that MRL extrapolations in fish should be limited to this class.

Reporting extrapolated MRLs

4. Where CCRVDF agrees to extrapolate MRLs, it should be clear that these MRLs were established by extrapolation rather than on the basis of a substance/species specific JECFA assessment. An appropriate symbol should be included next the relevant values reported in the MRL database. Moreover, extrapolated MRLs should be reconsidered in case the reference MRLs are modified or new data/information on the active substance in question becomes available.

Table summarising proposed MRL extrapolations

From reference species	To concerned species
Tissues of a ruminant (e.g. cattle, sheep, goats)	Tissues of all ruminants if the marker residue is the parent only or is the same as the total residues of toxicological concern* and one of the following apply: (i) identical Codex MRLs already exist in 2 ruminant species (ii) identical M:Ts exist in 2 ruminant species (iii) MRLs have been established in only 1 ruminant species but the M:T = 1 in all tissues.
Milk of a ruminant (e.g. cattle, goats)	Milk of all ruminants if the marker residue is the parent only or is the same as the total residues of toxicological concern* and one of the following apply: (i) identical Codex MRLs already exist in milk of 2 ruminant species (ii) identical M:Ts exist in milk of 2 ruminant species (iii) a milk Codex MRL has been established in only 1 ruminant species and the M:T = 1 in milk.
Tissues of a non-ruminant mammal (e.g. pigs)	Tissues of all non-ruminant mammals if the marker residue is the parent only or is the same as the total residues of toxicological concern* and one of the following apply: (i) identical Codex MRLs already exist in 2 non-ruminant mammal species (ii) identical M:Ts* exist in 2 non-ruminant mammal species (iii) Codex MRLs have been established in only 1 non-ruminant species but the M:T = 1 in all tissues.
Tissues of a bird (e.g. chickens)	Tissues of all birds if the marker residue is the parent only or is the same as the total residues of toxicological concern* and one of the following apply: (i) identical Codex MRLs already exist in 2 bird species (ii) identical M:Ts exist in 2 bird species (iii) Codex MRLs have been established in only 1 species but the M:T = 1 in all tissues.
Eggs from a bird (e.g. chickens)	Eggs from all birds if the marker residue is the parent only or is the same as the total residues of toxicological concern* and one of the following apply: (i) identical Codex MRLs already exist in eggs of 2 bird species (ii) identical M:Ts exist in eggs of 2 bird species (iii) Codex MRLs have been established in only 1 bird species but the M:T = 1 in eggs.

From reference species	To concerned species
Muscle/fillet of a bony fish (e.g. salmon)	Muscle/fillet of all bony fish if the marker residue is the parent only or is the same as the total residues of toxicological concern* and one of the following apply: (i) identical Codex MRLs already exist in muscle/fillet of 2 bony fish species (ii) identical M:Ts exist in muscle/fillet of 2 bony fish species (iii) Codex MRLs have been established in only 1 fish species but the M:T = 1 in the reference species (iv) the Codex MRL in the reference species was established based on twice the LoQ.

*The requirement that the marker residue is the parent only or is the same as the total residues of toxicological concern does not apply in cases where the MRL classification is 'unnecessary' as there is no marker residue in these cases.

Appendix 2

MAXIMUM RESIDUE LIMITS FOR VETERINARY DRUGS EXTRAPOLATED TO ONE OR MORE SPECIES

(Based on the approach described in Annex II and using compounds as identified in Part D of the Priority List of Veterinary Drugs)

1. Amoxicillin – proposed 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				
If so, what MRLs are proposed?	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 – proposed extrapolation to ruminants				
Which species have MRLs been established in?		Cattle (µg/kg)	Chicken~~Sheep~~ (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 ~~and, in addition, identical MRLs already exist in 2 ruminant species~~			
If so, what MRLs are proposed?	Muscle	50 µg/kg		
	Fat	-		
	Liver	50 µg/kg		
	Kidney	50 µg/kg		
	Milk	4 µg/kg		

3. Tetracyclines – proposed 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						
If so, what MRLs are proposed?	Muscle	200 µg/kg					
	Fat	-					
	Liver	600 µg/kg					
	Kidney	1200 µg/kg					
	Milk	100 µg/kg					

* Applies only to oxytetracycline

4. Cyhalothrin – proposed 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			
If so, what MRLs are proposed?	Muscle	20 µg/kg		
	Fat	400 µg/kg		
	Liver	20 µg/kg		
	Kidney	20 µg/kg		
	Milk	30 µg/kg		

5. Cypermethrin – proposed 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 (WHO TRS 911(10) and 1 in milk (TRS 925(10) The same values appear to have been used for cattle and sheep		
Can the MRLs be extrapolated to ruminants?	Yes, as the M:Ts established for cattle and sheep are identical and, in addition, identical MRLs already exist in 2 ruminant species. As the M:T for cattle milk is 1, the MRL can be extrapolated to milk of other ruminants		
If so, what MRLs are proposed?	Muscle	50 µg/kg	
	Fat	1000 µg/kg	
	Liver	50 µg/kg	
	Kidney	50 µg/kg	
	Milk	100 µg/kg	

6. Deltamethrin – proposed 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(10) use the following values: 0.6 in fat, 0.04 in liver, 0.03 in kidney and 1 in milk M:T for muscle not reported but equivalent values were applied in all species				
Can the MRLs be extrapolated to ruminants?	Yes, the MRLs for cattle and sheep tissues are identical and so can be extrapolated. While the MRL for milk has only been established in one species, the M:T used for milk was 1 and consequently the MRL can be extrapolated to milk of other ruminants				
If so, what MRLs are proposed?	Muscle	30 µg/kg			
	Fat	500 µg/kg			
	Liver	50 µg/kg			
	Kidney	50 µg/kg			
	Milk	30 µg/kg			

7. Moxidectin – proposed 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(10) 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(10)] but the muscle MRL for sheep was subsequently raised following a new residue study in sheep with the M:T remaining unchanged)			
If so, what MRLs are proposed?	Muscle	20 µg/kg		
	Fat	500 µg/kg		
	Liver	100 µg/kg		
	Kidney	50 µg/kg		
	Milk	-		

8. Spectinomycin – proposed 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(10)) 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.				
If so, what MRLs are proposed?	Muscle	500 µg/kg			
	Fat	2000 µg/kg			
	Liver	2000 µg/kg			
	Kidney	5000 µg/kg			
	Milk	200 µg/kg			

9. Levamisole – proposed 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(10) 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				
If so, what MRLs are proposed?	Muscle	10 µg/kg			
	Fat	10 µg/kg			
	Liver	100 µg/kg			
	Kidney	10 µg/kg			
	Milk	-			

10. Tilmicosin – proposed 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	300	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(10) 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					
If so, what MRLs are proposed?	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

** Value not shown in database, but it was in the recommendation from JECFA

11. Deltamethrin – proposed extrapolation to bony fish					
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(10) 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(10): 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)				
If so, what MRLs are proposed?	Muscle	30 µg/kg			

12. Flumequine – proposed extrapolation to bony fish						
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.					
If so, what MRLs are proposed?	Muscle	500 µg/kg				

13. Teflubenzuron – proposed extrapolation to bony fish		
Which species have MRLs been established in?		Salmon (µg/kg)
	Muscle	400
	Fillet*	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 997(10) uses 0.8 for both muscle and fillet	
Can the MRLs be extrapolated to bony fish?	No, as the M:T is not 1 (i.e. there is metabolism) and as the MRLs are not based on the LoQ (indicating that residues make a significant contribution to the overall consumer intake)	

* Muscle and skin in natural proportions

Appendix 3

List of participants[2]

Australia	Dugald MacLachlan
Belgium	Florentina Pardo
Brazil	Suzana Bresslau
Canada	Bryn Shurmer
Canada	Manisha Mehrotra
Chile	Claudio Nunez Contardo
Denmark	Katja Kragelund
Ecuador	Lenin Ernesto Moreno Galvez
Germany	David Schumacher
Iran	Ehsan Zayerzadeh
Japan	Hajime Toyofuku
Japan	Takashi Kozasa
Maroc	Tahri Samah
New Zealand	Warren Hughes
Portugal	Ines Martins de Almeida
Portugal	Miguel Jose Oliveira Cardo
Republic of Korea	Kim ji hyun
Republic of Korea	Soyoung Lee
Thailand	Mintra Lukkana
Thailand	Dawisa Paiboonsiri
Thailand	Namaporn Attaviroj
The Netherlands	Nicholas Jarrett
Uganda	George William Nasinyama
Uganda	Ruth Awio
United States	Brandi Robinson
United States	Richard TenEyck
United States	Jonathan Greene
United States	Holly Erdely
United States	Jacqueline Killmer
Uruguay	Maria Natalia Baccino De Souza
Uruguay	Diego Moreira

[2] Please contact the focal point of the Member Country or Observer Organization for the details of the delegates. The list of Codex contact points for members and observers are available from the Codex website at: http://www.fao.org/fao-who-codexalimentarius/about-codex/members/en/ http://www.fao.org/fao-who-codexalimentarius/about-codex/observers/observers/obs-list/en/