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FOOD AND AGRICULTURE
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Agenda Item 8

CX/RVDF 09/18/8
March 2009

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

Eighteenth Session

Natal, Brazil, 11-15 May 2009

DRAFT PRIORITY LIST OF VETERINARY DRUGS REQUIRING EVALUATION OF RE-EVALUATION BY JECFA AND WORKING DOCUMENT LISTING VETERINARY DRUGS OF POTENTIAL INTEREST

(Report of the electronic Working Group on Priority List of Veterinary Drugs Requiring Evaluation or Re-evaluation)

Governments and international organizations wishing to submit comments on Draft Priority list of veterinary drugs requiring evaluation of re-evaluation by JECFA and working document listing veterinary drugs of potential interest are invited to do so **no later than 20 April 2009** 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 (Telefax: +1 202 720 3157 ; or *preferably* E-mail: uscodex@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 (Telefax: +39.06.5705.4593; E-mail: Codex@fao.org, *preferably*).

Background

1. At the most recent (17th) session of CCRVDF, Breckenridge, Colorado, USA; 3-7 September 2007, the Committee agreed to request the Codex Secretariat to prepare a Circular Letter requesting members and observer organizations to: i) provide comments and information on the priority list of veterinary drugs requiring evaluation or re-evaluation by the Joint Expert Committee on Food Additives (JECFA); and ii) provide information and comments on Annex 1 of document CX/RVDF 07/17/12 "Starting Point for a Priority List of Veterinary Drugs for Discussion at the 17th CCRVDF" (paragraph 91 of ALINORM 08/31/31).

2. The Committee further agreed to establish an electronic Working Group, under the leadership of Australia, working in English only and open to all members and observers. The Committee agreed that the electronic Working Group, based on the replies to the Circular Letter would:

- prepare a Priority List of Veterinary Drugs for Evaluation or Re-evaluation by JECFA with a view to reaching a decision on the safety of residues in food by:
 - developing maximum residue limits (MRLs) or
 - informing risk managers on the safety of residues in food, if it is likely that an ADI or MRL cannot be recommended
- prepare a working document listing veterinary drugs of potential interest, based on Annex 1 to document CX/RVDF 07/17/12 "Starting Point for a Priority List of Veterinary Drugs for Discussion at the 17th CCRVDF" (paragraph 93 of ALINORM 08/31/31).

3. The Committee also requested the electronic Working Group to include the proposal submitted by the Delegations of Guatemala and Japan, as contained in document CX/RVDF 07/17/12 Add.2, in the working document listing veterinary drugs of potential interest. It agreed that the report of the electronic Working

Group should be made available in a timely manner to allow consideration and comments by all members and observer organisations.

Membership

4. The electronic Working Group on Priority is open to all members and observers. Participating countries and observer organisations were invited to identify experts and forward their name and email addresses to the Australian Codex contact point by 30 June 2008.

5. The following members and observers participated in the electronic Working Group on Priority: Antigua and Barbuda, Argentina, Australia (chair), Canada, Costa Rica, Croatia, France, Germany, Iran, Japan, New Zealand, Poland, Spain, Sweden, the United Kingdom, the United States of America, Zimbabwe, the International Federation of Animal Health, the Food and Agriculture Organisation, the World Health Organisation and the International Dairy Federation.

Schedule of work

6. The draft Priority List of Veterinary Drugs for Evaluation or Re-evaluation by the JECFA and the draft working document listing veterinary drugs of potential interest, based on comments received in response to CL2007/42-RVDF and including previous comments from Japan and Guatemala were provided to participants on 29 August 2008. Comments were received from the United Kingdom, the United States of America, the International Dairy Federation and the International Federation of Animal Health.

7. This document contains the final report of the electronic Working Group on Priority based on comments received to date. Annex 1 contains the "Priority List of Veterinary Drugs for Evaluation or Re-evaluation by JECFA". Annex 2 shows the responses received in relation to drugs of potential interest (Starting Point for a Priority List of Veterinary Drugs for Discussion at the 18th CCRVDF).

Recommendations

Consideration of the draft Priority List of Veterinary Drugs for Evaluation or Re-evaluation by JECFA

8. In order for a veterinary drug to be evaluated/re-evaluated by JECFA, adequate scientific data needs to be supplied by the drug manufacturer, the FAO/WHO Member State that initially requested the evaluation/re-evaluation or other contributing sources. For the compounds included in the draft Priority List (29 August 2008) to be evaluated/re-evaluated in this session, all data was required to have been provided to the electronic working group by 31 October 2008. As this did not occur for any of the compounds on the draft Priority List, it is proposed that **all** of the compounds be removed and returned to the Starting List. This includes the following compounds:

- Virginiamycin
- Diclazuril
- Amprolium
- Boldenone undecyclenate
- Nandrolone
- Ivermectin + Zeranol
- Ivermectin + vitamins and minerals
- Ivermectin + closantel
- Nonylphenol + amitraz

9. In accordance with the Codex Procedural Manual 17th Edition (Risk Analysis Principles Applied By the CCRVDF, section 3.1.2.13), before the inclusion of a substance on CCRVDF Priority List, it needs to satisfy certain criteria, including the commitment that a dossier be made available. It is recommended that in future, a closer adherence to the Codex Procedural Manual is followed and that 'cleaner' lists of compounds are nominated for inclusion on the Priority List for review – i.e. only compounds with sufficient available

data are to be submitted for consideration. Further consideration needs to be given to the circumstances by which compounds are included.

10. A number of nominations to the Priority List include combinations of compounds. Such nominations present particular difficulties for evaluation by JECFA – the simultaneous availability of data for multiple drugs is questionable and the complexity of the synergistic actions cannot be established without significant investment of limited resources. It is especially true for ambiguous terms such as ‘vitamins and minerals’ – the breadth of investigations required would significantly overwhelm the capacity of JECFA and may only provide limited insights into the safety of the drug combination in food production. It is recommended that in future, only single compounds are nominated for evaluation.

Advice on Veterinary Drugs for which it is Unlikely that an ADI or MRL can be Recommended by JECFA

11. The Priority List can include compounds for which CCRVDF wishes to seek JECFA’s advice other than recommendation for ADI or MRL (17th CCRVDF). However, the advice that CCRVDF seeks is required to be framed appropriately in order for JECFA to respond. According to the Codex Procedural Manual 17th Edition (Risk Analysis Principles Applied By the CCRVDF, section 2.6), JECFA is primarily responsible for providing the risk assessments to CCRVDF through the evaluation of available scientific data on veterinary drugs. As such, adequate data must be available if aspects such as the history of safe use for a veterinary drug, good veterinary practices, and the threshold of toxicological concern are required by CCRVDF.

PRIORITY LIST OF VETERINARY DRUGS FOR EVALUATION OR RE-EVALUATION BY JECFA

Name of the compound	Question(s) to be answered	Data availability	Proposed by	Comments
Virginiamycin	Request to establish ADI and recommend MRLs in poultry (tissues, eggs) and pigs (tissues)	Require commitment for data availability by 31 October 2008 or will be removed from Priority List and returned to the Starting List	Peru	As no data were received by 31 October 2008, this compound was deleted from the Priority List and returned to the Starting List.
Diclazuril	Request to establish ADI and recommend MRLs in poultry (tissues and eggs)	Require commitment for data availability by 31 October 2008 or will be removed from Priority List and returned to the Starting List	Peru	Codex MRLs already exist for sheep, rabbit and poultry tissues, and in the absence of additional/new data for poultry eggs being received by 31 October 2008, this compound was deleted from the Priority List. In order for residues in eggs to be a valid concern, the nominating country needs to verify that the compound is in fact registered for use in laying hens.
Amprolium	Request to establish ADI and recommend MRLs in poultry (tissues and eggs)	Require commitment for data availability by 31 October 2008 or will be removed from Priority List and returned to the Starting List	Peru	As no data were received by 31 October 2008, this compound was deleted from the Priority List and returned to the Starting List.
Boldenone undecylenate	Request to establish ADI and recommend MRLs in cattle (tissues)	Require commitment for data availability by 31 October 2008 or will be removed from Priority List and returned to the Starting List	Guatemala	As no data were received by 31 October 2008, this compound was deleted from the Priority List and returned to the Starting List.
Nandrolone	Request to establish ADI and recommend MRLs in cattle (tissues)	Require commitment for data availability by 31 October 2008 or will be removed from Priority List and returned to the Starting List	Guatemala	As no data were received by 31 October 2008, this compound was deleted from the Priority List and returned to the Starting List.
Ivermectin + Zeranol	Request to examine synergistic effect	Require commitment for data availability by 31 October 2008 or will be removed from Priority List and returned to the Starting List	Guatemala	As no data were received by 31 October 2008, this compound was deleted from the Priority List. Also, multiple compound evaluations have not previously been conducted by JECFA. The evaluation of combinations for synergistic effects has not been scientifically justified.
Ivermectin + vitamins and minerals	Request to examine synergistic effect	Require commitment for data availability by 31 October 2008 or will be removed from Priority List and returned to the Starting List	Guatemala	As no data were received by 31 October 2008, this compound was deleted from the Priority List. Also, multiple compound evaluations have not previously been conducted by JECFA. The evaluation of combinations for synergistic effects has not been scientifically justified. Additionally, vitamins and minerals are not considered veterinary drugs.

Name of the compound	Question(s) to be answered	Data availability	Proposed by	Comments
Ivermectin + closantel	Request to examine synergistic effect	Require commitment for data availability by 31 October 2008 or will be removed from Priority List and returned to the Starting List	Guatemala	As no data were received by 31 October 2008, this compound was deleted from the Priority List. Also, multiple compound evaluations have not previously been conducted by JECFA. The evaluation of combinations for synergistic effects has not been scientifically justified.
Nonylphenol + amitraz	Request to examine synergistic effect	Require commitment for data availability by 31 October 2008 or will be removed from Priority List and returned to the Starting List	Guatemala	As no data were received by 31 October 2008, this compound was deleted from the Priority List. Also, multiple compound evaluations have not previously been conducted by JECFA. The evaluation of combinations for synergistic effects has not been scientifically justified.

Annex 2**STARTING POINT FOR A PRIORITY LIST OF VETERINARY DRUGS FOR DISCUSSION AT THE 18TH CCRVDF****Explanatory notes:**

- Substances highlighted in grey have already been evaluated by JECFA (veterinary drugs).
- ☉ indicates that evaluation by JECFA (veterinary drugs) did not result in an MRL recommendation.
- The ‘country code’ indicates which country suggested the veterinary drug be included in this list.

The following veterinary drugs have been removed from this list because they have been included in the ‘Priority List of Veterinary Drugs for Evaluation or Re-evaluation by JECFA’:

- **Dexamethasone, tylosin, avilamycin, malachite green, tilmicosin and monensin**
 - moved to Priority List at 17th session of CCRVDF, September 2007.

The following veterinary drugs have been suggested for inclusion in the ‘Priority List of Veterinary Drugs for Evaluation or Re-evaluation by JECFA’, but have not been considered for the reasons cited below:

- **Avermectins**
 - several avermectins have already been evaluated by Codex (e.g. ivermectin, doramectin, moxidectin, abamectin, eprinomectin)
- **Benzimidazoles**
 - several benzimidazoles have already been evaluated by Codex (e.g. fenbendazole, albendazole, oxfendazole, flubendazole, thiabendazole, triclabendazole)
- **Clenbuterol**
 - has already been evaluated by JECFA/CCRDVF and has a recently reviewed Codex status
- **Hormonal growth promoters**
 - trenbolone acetate, zeranol, progesterone, oestradiol-17 β and testosterone have a Codex status
 - melengestrol acetate is currently at step 7 of the Codex step procedure.
- **Pirlimycin**
 - Codex MRLs exist with the following footnote “JECFA evaluated the effect of pirlimycin residues on starter cultures and for this reason recommended an MRL of 100 μ g/kg of milk. Codex Members may therefore adapt national/regional MRLs in order to address this technological aspect for trade of fresh liquid milk intended for processing using starter culture”.
- **Sulfadimidine**
 - Codex MRLs exist
- **Tetracycline**
 - Codex MRLs exist
- **Dinitolamide, Ethion, Malathion, Spinosad, Temephos and Triflumuron** were identified as pesticides and therefore deleted from the list

Abbreviations

Animal species		Country Code		Miscellaneous	
AVI	Avian	AUS	Australia	ADI	Acceptable daily intake
API	Bee	BRA	Brazil	AB	Antibiotic/antimicrobial
BOV	Bovine	CAN	Canada	AP	Anaesthetic/pain killer
CAM	Camel	CR	Costa Rica	CM	Codex members
CAP	Caprine	DE	Denmark	CC	Compendium of methods of analysis identified as suitable to support Codex MRLs, ALINORM 06/29/31, Appendix X
EQU	Equine	FR	France	D	JECFA has confirmed that there are data gaps that need to be filled in order to set MRLs
LEP	Rabbit	GE	Germany	E	Not evaluated by JECFA yet
PIS	Fish	JAP	Japan	HO	Hormone
SUI	Swine	NL	The Netherlands	PA	Antiparasitic
OVI	Ovine	ROK	Republic of Korea	PG	Priority Group: A = recent re-evaluation by next JECFA; B = on priority list for next JECFA
		SE	Sweden	Z	Candidate for exclusion from uses in food producing species
		TH	Thailand		
		UK	United Kingdom		
		US	United States of America		

STARTING POINT FOR A PRIORITY LIST OF VETERINARY DRUGS FOR DISCUSSION AT THE 18TH CCRVDF

Veterinary drug	Group	Class	Objective	Necessity for the treatment/prevention of disease in animals	Consumer health protection concerns	Trade concerns	Agronomic impact	Data identified as missing	Data offer 16th CCRVDF	Analytical methods	Recommendation to 18th CCRVDF	Priority
Altrenogest (synthetic hormone) (AUS)	HO	E	Use EQU	Suppression of oestrus EQU	?	Different MRL/ residue status among Codex members	?	?	No	?	The CCRDVDF should not recommend this substance for JECFA evaluation as there is not enough information available. Substance will be deleted from this list if no further specifications are made	Low
Amitraz (CR)	PA	E	Use ?	Widely used for treatment of animal ectoparasites	Slightly toxic to mammals if ingested orally	Different MRL/ residue status among Codex members	?	Not evaluated yet	No	?	The CCRVDF should not recommend this substance for JECFA evaluation as there is not enough information available. Substance will be deleted from this list if no further specifications are made	Low

Veterinary drug	Group	Class	Objective	Necessity for the treatment/ prevention of disease in animals	Consumer health protection concerns	Trade concerns	Agronomic impact	Data identified as missing	Data offer 16 th CCRVDF	Analytical methods	Recommendation to 18th CCRVDF	Priority
Amoxicillin (aminopenicillin antimicrobial) (CR)	AB	E	Use BOV, SUI, AVI, PIS	Widely used in AVI, BOV, CAP, EQU, OVI, PIS, SUI		Different MRL/ residue status among Codex members	?	Not evaluated yet	?	?	The CCRVDF should not recommend this substance for JECFA evaluation as there is not enough information available. Substance will be deleted from this list if no further specifications are made	Low
Ampicillin (aminopenicillin antimicrobial) (SE)	AB	E	Use BOV, SUI, AVI, PIS	Important antimicrobial (AVI,BOV,CAP,E QU,OVI, PIS, SUI)	?	Different MRL/ residue status among Codex members	?	Not evaluated yet	?	?	The CCRVDF should not recommend this substance for JECFA evaluation as there is not enough information available. Substance will be deleted from this list if no further specifications are made	Low

Veterinary drug	Group	Class	Objective	Necessity for the treatment/prevention of disease in animals	Consumer health protection concerns	Trade concerns	Agronomic impact	Data identified as missing	Data offer 16 th CCRVDF	Analytical methods	Recommendation to 18 th CCRVDF	Priority
<p>Bacitracin (polypeptide antimicrobial) (CR, BR) Evaluated: 12th JECFA Recommended MRLS in milk, meat, and eggs</p>	AB	D	Use AVI, SUI	Bacitracin is used against necrotic enteritis (AVI) septicaemias, colibacillosis, salmonellosis and urinary infections (AVI, BOV, LEP, SUI)		Different MRL/ residue status among Codex members	?	?	BRA	CAN	The CCRVDF should not recommend this substance for evaluation as there is not enough information available unless BR confirms that she is willing to provide data	?
<p>Carbadox (SE) Evaluated: 38th and 60th JECFA. Temporary ADI and MRL not extended.</p>	AB	ZC	None, not to be used in food producing animals	None, growth promoter	Genotoxic carcinogen. No dose identifiable that presents acceptable risk to consumers has been found by JECFA	Prohibited for use in food producing animals by several Codex members. Approved for use in the United States of America.	?	Re-evaluation will only be justified if significant new data are presented which question the validity of previous evaluations	?	CAN	The CCRVDF should confirm that this substance should not be used in food producing animals and agree that Codex does not recommend either an MRL or extra-label/off label use due to concern for toxicity to the human consumer	High

Veterinary drug	Group	Class	Objective	Necessity for the treatment/prevention of disease in animals	Consumer health protection concerns	Trade concerns	Agronomic impact	Data identified as missing	Data offer 16 th CCRVDF	Analytical methods	Recommendation to 18th CCRVDF	Priority
Cefoperazone (cephalosporin antimicrobial) (CR)	AB	E	Use	Treatment of septicemias, respiratory infections, and mastitis (BOV, CAP, OVI)	?	Different MRL/ residue status among Codex members	?	Not evaluated yet	?	?	The CCRVDF should not recommend this substance for JECFA evaluation as there is not enough information available	Low
Cefuroxime (CAN/JAP) ⊗ Evaluated: 62 nd JECFA Temporary ADI and MRLs for cefuroxime in milk not extended therefore withdrawn.	AB	D	Use in dairy animals	Clinical mastitis (BOV) in lactating animals and for dry-cow therapy	Unidentified residues in milk	Differing MRL/ residue status among Codex members	?	Insufficient toxicity data on unidentified residues in milk, metabolism in milk, inadequate depletion study (cows)	?	?	The CCRVDF should confirm that this substance should not be used in dairy animals and agree that Codex does not recommend either an MRL or extra-label/off label use due to concern for toxicity to the human consumer	Medium

Veterinary drug	Group	Class	Objective	Necessity for the treatment/prevention of disease in animals	Consumer health protection concerns	Trade concerns	Agronomic impact	Data identified as missing	Data offer 16 th CCRVDF	Analytical methods	Recommendation to 18th CCRVDF	Priority
Cephalosporins (group includes e.g. Cefoperazone Cefitiofur Ceftriaxone) (ROK)	AB	E	Use BOV, SUI	Widely used treatment of septicaemias, digestive infections, puerperal fevers, interdigit phlegmon, respiratory infections and mastitis	Canada recommends that antimicrobial resistance risk be used as a key criterion for the determination of the priority status of individual cephalosporins and fluoroquinolones. May also be referred to the Codex Intergovernmental Task Force on Antimicrobial Resistance	Different MRL/ residue status among Codex members	?	?	?	?	The CCRVDF should not recommend this substance for JECFA evaluation as there is not enough information available	Low

Veterinary drug	Group	Class	Objective	Necessity for the treatment/prevention of disease in animals	Consumer health protection concerns	Trade concerns	Agronomic impact	Data identified as missing	Data offer 16 th CCRVDF	Analytical methods	Recommendation to 18th CCRVDF	Priority
Chloramphenicol (NL, DE, US, ROK) ⊕ Evaluated: 42 nd and 62 nd JECFA	AB	ZC	None, not to be used in food producing animals	Antimicrobial effective against a wide variety of micro-organisms	Concern for aplastic anaemia, carcinogenicity, and inability to establish MRL	Numerous rejected consignments worldwide	Still very widely used in low income countries as it is very cheap	Re-evaluation will only be justified if significant new data are presented which question the validity of previous evaluations	?	CAN	The CCRVDF should confirm that this substance should not be used in food producing animals and agree that Codex does not recommend either an MRL or extra-label/off label use due to concern for toxicity to the human consumer	High

Veterinary drug	Group	Class	Objective	Necessity for the treatment/prevention of disease in animals	Consumer health protection concerns	Trade concerns	Agronomic impact	Data identified as missing	Data offer 16 th CCRVDF	Analytical methods	Recommendation to 18 th CCRVDF	Priority
Chlorpromazine (CAN) ☉ Evaluated: 38 th JECFA	AP	D	Use/ban	Used as a pre-anaesthetic and muscle relaxant in BOV, CAP, OVI, SUI	Long persistence of substance in humans, small doses may cause behavioural change	Use prohibited by several Codex Members	?	In-sufficient toxicity data	?	EC multi method for tranquilizers LOD 5µg/kg	Two options: 1) The CCRVDF should confirm that this substance should not be used in food producing animals and that Codex does not recommend either an MRL or extra-label/off label use due to concern for toxicity to the human consumer. 2) Observers/ Codex members make firm commitment for data for new evaluation	Medium

Veterinary drug	Group	Class	Objective	Necessity for the treatment/ prevention of disease in animals	Consumer health protection concerns	Trade concerns	Agronomic impact	Data identified as missing	Data offer 16 th CCRVDF	Analytical methods	Recommendation to 18th CCRVDF	Priority
Cloxacillin (antistaphylococcal penicillin) (ROK)	A B	E	Use BOV	Used for treating infectious keratoconjunctivitis, puerperal fevers, respiratory infections, clinical mastitis in cattle, used against staphylococci producing betalactamase (BOV, CAP, EQU, OVI, SUI)	Devoid of serious toxicity except for allergic reactions	Different MRL/ residue status among Codex members	?	?	?	?	The CCRVDF should not recommend this substance for JECFA evaluation as there is not enough information available. Substance will be deleted from this list if no further specifications are made	Low
Danofloxacin (ROK/JAP) Evaluated: 48 th JECFA Codex MRLs for BOV, AVI, SUI, muscle, liver, kidney and fat	AB	D	Use for which purpose other than covered by MRLs?	Synthetic broad spectrum fluoroquinolone widely used in the treatment of respiratory disease and colibacillosis (AVI, BOV, CAP, LEP, OVI, SUI)	Induction of anti-microbial resistance- is not a health concern that can be addressed by JECFA. It is an issue for Codex Task Force on Antimicrobial Resistance			?	?	?	The CCRVDF should not recommend this substance for JECFA evaluation as there is not enough information available. Substance will be deleted from this list if no further specifications are made	Low

Veterinary drug	Group	Class	Objective	Necessity for the treatment/prevention of disease in animals	Consumer health protection concerns	Trade concerns	Agronomic impact	Data identified as missing	Data offer 16 th CCRVDF	Analytical methods	Recommendation to 18th CCRVDF	Priority
Enrofloxacin Quinolone (TH, ROK, CR, KR, JAP) ☉ Evaluated: 48 th JECFA	AB	D	Use AVI, BOV, SUI	Wide use in the treatment of chronic respiratory disease (<i>E. coli</i>) and colibacillosis (AVI, BOV, CAP, EQU, LEP, OVI, PIS, SUI)	Induction of anti-microbial resistance-is not a health concern that can be addressed by JECFA. It is an issue for Codex Task Force on Antimicrobial Resistance	Different MRL/ residue status among Codex members		Important data missing			The CCRVDF should not recommend this substance for JECFA evaluation as there is not enough information available	Low
Flavofosfolipol (CR, BR)	AB	E	Use as growth promoter (AVI, SUI)	None, growth promoter (AVI, SUI, BOV)	?	Different MRL/ residue status among Codex members	?	?	BR	?	The CCRVDF should not recommend this substance for JECFA evaluation as there is not enough information available unless BR confirms that she is willing to provide data	Medium

Veterinary drug	Group	Class	Objective	Necessity for the treatment/prevention of disease in animals	Consumer health protection concerns	Trade concerns	Agronomic impact	Data identified as missing	Data offer 16 th CCRVDF	Analytical methods	Recommendation to 18th CCRVDF	Priority
Flunixin, Flunixin Meglumin (non-steroidal anti-inflammatory drug /analgesic) (CR, SE)	AP	E	Use BOV, EQU	Inflammation, pyrexia, and colic (EQU), fever and inflammation (BOV)	?	Different MRL/ residue status among Codex members	?	?	?	CAN	The CCRVDF should not recommend this substance for JECFA evaluation as there is not enough information available. Substance will be deleted from this list if no further specifications are made	Low
Fosfomycin (CR)	AB	E	Use (PIS), BOV	Critically important for infections in fish. Several bacterial infections in cattle	?	authorised only by a few Codex members	?	?	?	?	The CCRVDF should not recommend this substance for JECFA evaluation as there is not enough information available. Substance will be deleted from this list if no further specifications are made	Low

Veterinary drug	Group	Class	Objective	Necessity for the treatment/prevention of disease in animals	Consumer health protection concerns	Trade concerns	Agronomic impact	Data identified as missing	Data offer 16 th CCRVDF	Analytical methods	Recommendation to 18 th CCRVDF	Priority
Glycopeptides (ROK) -vancomycin, -teicoplanin -avoparcin	AB	E	Ban	None growth promoter (AVI)	Induction of antimicrobial resistance	authorised only by a few Codex members and expressly prohibited in others	?	?	?	?	The CCRVDF should not recommend this substance for JECFA evaluation as there is not enough information available. Substance will be deleted from this list if no further specifications are made	Low
Isoeugenol (clove oil) (AUS) Evaluated by 61 st JECFA as flavouring agent	AP	E	Use PIS	Widely used as anaesthetic (PIS)	Potentially toxic to humans: e.g. carcinogenicity, reproductive and developmental toxicity, neurotoxicity, and acute toxicity. No safety concern when evaluated by 61 st JECFA as flavouring agent		?	?	?	?	The CCRVDF should not recommend this substance for JECFA evaluation as there is not enough information available. Substance will be deleted from this list if no further specifications are made	Low

Veterinary drug	Group	Class	Objective	Necessity for the treatment/prevention of disease in animals	Consumer health protection concerns	Trade concerns	Agronomic impact	Data identified as missing	Data offer 16 th CCRVDF	Analytical methods	Recommendation to 18 th CCRVDF	Priority
Josamycin (Macrolide antibiotic) (CR)	AB	E	Use AVI, PIS, SUI	Mycoplasma infection (SUI, AVI), Streptococcal infection (PIS)	?	Different MRL/ residue status among Codex members	?	?	?	?	The CCRVDF should not recommend this substance for JECFA evaluation as there is not enough information available. Substance will be deleted from this list if no further specifications are made	Low
Kanamycin (Macrolide antibiotic) (ROK) ⊗ Evaluated: 12 th JECFA	AB	D	Use in BOV, OVI, EQU (tissues, milk); AVI, SUI, PIS (tissues)	Widely used to treat Mycoplasma infections (AVI, SUI), Staphylococcus infection and colibacillosis (AVI), hemorrhagic digestive disease (SUI and BOV), liver abscesses (<i>Fusobacterium necrophorum</i>), and mastitis (BOV), respiratory infections (BOV, SUI)	?	?	?	Important data on toxicology missing	ROK	?	The CCRVDF should not recommend this substance for JECFA evaluation as there is not enough information available unless ROK confirms that she is willing to provide data	Medium

Veterinary drug	Group	Class	Objective	Necessity for the treatment/ prevention of disease in animals	Consumer health protection concerns	Trade concerns	Agronomic impact	Data identified as missing	Data offer 16 th CCRVDF	Analytical methods	Recommendation to 18th CCRVDF	Priority
Kitasamycin (CR) (AUS)	AB	E	Use AVI, SUI, BOV	Widely used to treat Mycoplasma infections (pig, poultry) haemorrhagic digestive disease (pigs) and liver abscesses (<i>Fusobacterium necrophorum</i>) (cattle), respiratory infections in (cattle)	?	Different MRL/ residue status among Codex members	?	?	?	?	The CCRVDF should not recommend this substance for JECFA evaluation as there is not enough information available. Substance will be deleted from this list if no further specifications are made	Low
Maduramycin (CR)	AB	E	Use AVI	Control of intestinal parasitic coccidiosis. (<i>Eimeria</i> spp.)	?	Different MRL/ residue status among Codex members	?	?	?	?	The CCRVDF should not recommend this substance for JECFA evaluation as there is not enough information available. Substance will be deleted from this list if no further specifications are made	Low

Veterinary drug	Group	Class	Objective	Necessity for the treatment/prevention of disease in animals	Consumer health protection concerns	Trade concerns	Agronomic impact	Data identified as missing	Data offer 16 th CCRVDF	Analytical methods	Recommendation to 18th CCRVDF	Priority
Mebendazol (CR)	AB	E	Use	Used to combat pinworms, roundworms and hookworms (BOV, OVI, CAP, SUI, AVI)	?	Different MRL/ residue status among Codex members	?	?	?	?	The CCRVDF should not recommend this substance for JECFA evaluation as there is not enough information available. Substance will be deleted from this list if no further specifications are made	Low
Metamizol (SE)	AP	E	Use	Important for the treatment of severe pain in pig, cattle and equidae	?	?	?	?	?	?	The CCRVDF should not recommend this substance for JECFA evaluation as there is not enough information available. Substance will be deleted from this list if no further specifications are made	Low

Veterinary drug	Group	Class	Objective	Necessity for the treatment/prevention of disease in animals	Consumer health protection concerns	Trade concerns	Agronomic impact	Data identified as missing	Data offer 16 th CCRVDF	Analytical methods	Recommendation to 18th CCRVDF	Priority
<p>Nitrofurans (NL, UK, DE, US, ROK, FR)</p> <p>-furazolidone</p> <p>-nitrofurazone</p> <p>⊗ Evaluated: 40th JECFA</p>	AB PA	Z	<p>2 options:</p> <ul style="list-style-type: none"> ◦ Use in BOV, SUI, AVI, PIS, API - MRL => all relevant tissues, eggs, milk, honey ◦ Ban, not to be used in food animals 	<p>Gastrointestinal and dermatological infections including salmonellosis in BOV, SUI, AVE, PIS. Infectious bacterial diseases, API</p>	<p>Concern for carcinogenicity</p>	<p>Prohibited for use in food producing animals by several Codex members. Numerous rejected consignments worldwide</p>	<p>Still very widely used in low income countries as it is very cheap</p>	<p>In-sufficient residue data</p>	FR	CAN	<p>Two options:</p> <ol style="list-style-type: none"> 1) CCRVDF should confirm that this substance should not be used in food producing animals and agree that Codex does not recommend either an MRL or extra-label/off label use due to concern for toxicity to the human consumer. 2) Observers/ Codex members make firm commitment for data for new evaluation and agree that substances will be deleted from this list if data are not presented to JECFA by 11/07 	High

Veterinary drug	Group	Class	Objective	Necessity for the treatment/prevention of disease in animals	Consumer health protection concerns	Trade concerns	Agronomic impact	Data identified as missing	Data offer 16 th CCRVDF	Analytical methods	Recommendation to 18th CCRVDF	Priority
<p>Nitroimidazoles (e.g. Ronidazole, ⊗ Evaluated: 34th, 42nd JECFA Iprnidazole, Dimetridazole, ⊗ Evaluated: 34th JECFA Metronidazole (UK, D, US, SE) ⊗ Evaluated: 34th JECFA</p>	AP	Z	2 options: ◦ Use AVI ◦ None, not to be used in food producing animals	Used against protozoal disease caused by <i>Histomonas meleagridis</i> , which is especially lethal to turkeys	Concern for systemic toxicity and carcinogenicity	?	?	Important data on toxicology missing	?	?	Two options: 1) CCRVDF should confirm that this substance should not be used in food producing animals and agree that Codex does not recommend either an MRL or extra-label/off label use due to concern for toxicity to the human consumer. 2) Observers/ Codex members make firm commitment for data for new evaluation and agree that substances will be deleted from this list if data are not presented to JECFA by 11/07	Medium

Veterinary drug	Group	Class	Objective	Necessity for the treatment/prevention of disease in animals	Consumer health protection concerns	Trade concerns	Agronomic impact	Data identified as missing	Data offer 16 th CCRVDF	Analytical methods	Recommendation to 18th CCRVDF	Priority
Novobiocin (CAN/JAP) ⊗ Evaluated: 12 th JECFA	AB	D	Use BOV, CAP, OVI, PIS (only used in animals)	Used in the treatment of mastitis in the form of intra-mammary creams and in sepsis of fishes.	?	Different MRL/residue status among Codex members	?	No detectable residues in food with recommended methods?	?	?	To be deleted from this list if no further specifications are made	Low
Nystatin (CAN) ⊗ Evaluated: 12 th JECFA	AB	E	Use ?	Treatment of cutaneous fungal (yeast) infections and <i>Cryptococcus</i> ; in combination with corticosteroid widely used to treat ear infections	?	?	?	No detectable residues in food by recommended methods?	?	?	To be deleted from this list if no further specifications are made	
Olaquinox (ROK, AU) Evaluated: 36 th and ⊗ 42 nd JECFA: ADI but no MRL. Limited acceptance of residues when used in food-producing animals under conditions of good practice in the use of veterinary drugs		Z	2 options: ◦ Use in SUI ◦ Ban, not to be used in food producing animals	None, growth promoter (SUI)	Genotoxic potential of the parent compounds and possibly metabolites	Use prohibited by many Codex members	?	JECFA: absence of specific toxicity studies on metabolites → no ADI could be allocated		CAN	The CCRVDF should confirm that this substance should not be used in food producing animals and agree that Codex does not recommend either an MRL or extra-label/off label use due to concern for toxicity to the human consumer	High

Veterinary drug	Group	Class	Objective	Necessity for the treatment/prevention of disease in animals	Consumer health protection concerns	Trade concerns	Agronomic impact	Data identified as missing	Data offer 16 th CCRVDF	Analytical methods	Recommendation to 18th CCRVDF	Priority
Oleandomycin (macrolide) (CAN/JAP) ☉ Evaluated: 12 th JECFA	AB	D	Use SUI, BOV, PIS	None, growth promoter (SUI, BOV). Treatment of mastitis in BOV and streptococcal infection in PIS	Induction of anti-microbial resistance- is not a health concern that can be addressed by JECFA. It is an issue for Codex Task Force on Antimicrobial Resistance	Different MRL/ residue status among Codex members	?	No detectable residues in food by recommended methods			CCRVDF should identify data sources and confirm the necessity of the use of the substances. Substance will be deleted from this list if no further specifications are made	Low
Oxolinic Acid (quinolone) (SE) ☉ Evaluated: 43 rd JECFA	AB	D	Use BOV, SUI, AVI, PIS, LEP	Used in septicaemias and in infections such as colibacillosis, which cause serious losses in poultry, cattle, swine, fish and other species	?	Different MRL/ residue status among Codex members	Important anti-microbial for fish farming	Toxicology studies did not meet requirement	?	?	The CCRVDF should only suggest substance if sponsor presents data package	Medium

Veterinary drug	Group	Class	Objective	Necessity for the treatment/prevention of disease in animals	Consumer health protection concerns	Trade concerns	Agronomic impact	Data identified as missing	Data offer 16 th CCRVDF	Analytical methods	Recommendation to 18th CCRVDF	Priority
Oxytocin (CR)	HO	E	Use BOV, OVI, CAP, SUI, EQU	Used to facilitate birth and to increase milk production. Breeding disinfection in BOV, EQU, SUI	?	Different MRL/ residue status among Codex members	?	?	?	?	CCRVDF should identify data sources and confirm the necessity of the use of the substances and identify data sources. Substance will be deleted from this list if no further specifications are made.	Low
Penicillins (UK) Benzyl-penicillin Penethamate hydroxide Procaine penicillin (Penicillin G) Evaluated 36 th JECFA	AB	D	Use AVI, BOV, CAM, CAP, EQU, LEP, OVI, SUI	Treatment of septicaemias, respiratory and urinary infections. They are very important in the treatment of many diseases in a broad range of animal species	?	Different MRL/ residue status among Codex members	Few economically attractive alternatives available	?	CC: full recommendation (Benzyl-penicillin)		Remove this group entry and replace with individual antimicrobials when appropriate data packages are made available to CCRVDF OR Evaluate and set and ADI and MRL for benzyl-penicillin and extrapolate it to all penicillins	?

Veterinary drug	Group	Class	Objective	Necessity for the treatment/prevention of disease in animals	Consumer health protection concerns	Trade concerns	Agronomic impact	Data identified as missing	Data offer 16 th CCRVDF	Analytical methods	Recommendation to 18 th CCRVDF	Priority
Permethrin (SE) ⊗ Evaluated: 54 th JECFA	PA	D	Use BOV, EQU, OVI, CAP, SUI, AVI	Important for the treatment of ectoparasites populations of the deer tick <i>Ixodes scapularis</i>		The Codex MRL has already been set for this substance as pesticide		Important data on toxicology missing			The CCRVDF should not recommend this substance for JECFA evaluation as there is not enough information available. Substance will be deleted from this list if no further specifications are made.	Low
Phenylbutazone (SE)	AP	E	2 options: ○ Use BOV, EQU ○ Ban in food producing animals	Treatment of musculoskeletal disorders, including muscular sprain and strain, muscular overuse tendonitis, acute joint injury/ strain/ sprain, and arthritic conditions	Concern for carcinogenicity, blood dyscrasias and hypersensitivity reactions.	Not authorized for use by several Codex Members				CAN	CCRVDF should identify data sources and confirm the necessity of the use of the substances and identify data sources. Substance will be deleted from this list if no further specifications are made.	Low

Veterinary drug	Group	Class	Objective	Necessity for the treatment/prevention of disease in animals	Consumer health protection concerns	Trade concerns	Agronomic impact	Data identified as missing	Data offer 16 th CCRVDF	Analytical methods	Recommendation to 18th CCRVDF	Priority
Polymyxin B (CAN) ⊗ Evaluated: 12 th JECFA	AB	D	Use BOV, EQU, OVI, CAP, SUI	Used to treat infections of the eye	Induction of anti-microbial resistance is not a health concern that can be addressed by JECFA. It is an issue for Codex Task Force on Antimicrobial Resistance	?	?	No detectable residues in food by recommended methods	?	(CAN)	CCRVDF should identify data sources and confirm the necessity of the use of the substances and identify data sources	Low
Propionylpromazine (CAN) ⊗ Evaluated: 38 th JECFA	AP	D	Use BOV, SUI, EQU	Antiemetic, antipruritic, premedication for anaesthesia	Concern about high level of residues at injection site – issue to be considered by the CCRVDF Working Group on Risk Management.	?	?	In-sufficient toxicity and residue data	?	?	CCRVDF should identify data sources and consider how measures concerning injections site residues could be addressed in a JECFA assessment	Low

Veterinary drug	Group	Class	Objective	Necessity for the treatment/ prevention of disease in animals	Consumer health protection concerns	Trade concerns	Agronomic impact	Data identified as missing	Data offer 16 th CCRVDF	Analytical methods	Recommendation to 18th CCRVDF	Priority
Pyrimethamin (ROK)	PA	E	Use LEP, SUI, AVI	Treatment of coccidiosis and bacterial infections, Toxoplasmosis (SUI), Leucocytozoonosis (AVI)	?	?	?	?	?	?	CCRVDF should identify data sources and confirm the necessity of the use of the substances and identify data sources. Substance will be deleted from this list if no further specifications are made	Low
Robenidin (CR)	PA	E	Use LEP	Treatment of coccidiosis and bacterial infections	?	Different MRL/ residue status among Codex members	?	?	?	?	CCRVDF should confirm the necessity of the use of the substances and identify data sources. Substance will be deleted from this list if no further specifications are made	Low

Veterinary drug	Group	Class	Objective	Necessity for the treatment/ prevention of disease in animals	Consumer health protection concerns	Trade concerns	Agronomic impact	Data identified as missing	Data offer 16 th CCRVDF	Analytical methods	Recommendation to 18th CCRVDF	Priority
Roxarsone (Phenylarsonic organic arsenical) (SE)	PA	E	Use AVI	Prevention of coccidiosis caused by <i>Eimeria spp</i> and necrotic enteritis and growth promoter AVI	Arsenic compound = poison with low safety tolerance	Different MRL/ residue status among Codex members	?	?	?	?	CCRVDF should confirm the necessity of the use of the substances and identify data sources. Substance will be deleted from this list if no further specifications are made	Low
Salinomycin (CR)	PA	E	Use AVI	Prevention of coccidiosis caused by <i>Eimeria ssp.</i>		Different MRL/ residue status among Codex members	?	?	?	CAN	CCRVDF should confirm the necessity of the use of the substances and identify data sources. Substance will be deleted from list if no further specifications are made	Low

Veterinary drug	Group	Class	Objective	Necessity for the treatment/prevention of disease in animals	Consumer health protection concerns	Trade concerns	Agronomic impact	Data identified as missing	Data offer 16 th CCRVDF	Analytical methods	Recommendation to 18th CCRVDF	Priority
Semduramycin (CR)	PA	E	Use ?	Prevention of coccidiosis caused by <i>Eimeria ssp.</i>		Different MRL/ residue status among Codex members					CCRVDF should confirm the necessity of the use of the substances and identify data sources. Substance will be deleted from this list if no further specifications are made	Low
Stilbenes, Diethylstilbestrol (DES) (NL, UK, US) ⊗ Evaluated: 5 th JECFA	HO	Z	Ban = not to be used in food producing animals	None, growth promoter	Concern for developmental toxicity and carcinogenicity	Prohibited by many Codex members	None			CAN	The CCRVDF should confirm that this substance should not be used in food producing animals and agree that Codex does not recommend either an MRL or extra-label/off label use due to concern for toxicity to the human consumer	Low

Veterinary drug	Group	Class	Objective	Necessity for the treatment/prevention of disease in animals	Consumer health protection concerns	Trade concerns	Agronomic impact	Data identified as missing	Data offer 16 th CCRVDF	Analytical methods	Recommendation to 18 th CCRVDF	Priority
Sulphonamides other than Sulfadimidine (UK, SE, ROK, AU)	AB	E	Use BOV, OVI, SUI, AVE, PIS	Alone or in combination with diamino-pyrimidines are essential because of diseases covered (bacterial, coccidial and protozoal infections), BOV, OVI, SUI, AVI, PIS	?	?	Few economically viable alternatives available	?	?	?	The CCRVDF should not recommend this substance for JECFA evaluation as there is not enough information available	Low
Thiamphenicol (CAN) ⊗ Evaluated: 52 nd , 58 th JECFA. Temporary MRLs were not extended.	AB	D	Use BOV, SUI, AVI, PIS	Treatment of infectious diseases in BOV, SUI, AVI, PIS	?	?	?	ADI = 5µg/kg. Insufficient depletion studies, inadequate methods of analysis	?	CAN	The CCRVDF should not recommend this substance for JECFA evaluation as there is not enough information available	Medium (high if depletion studies are available)
Thyrostatic substances	HO	Z	Ban = not to be used in food producing animals	None, growth promoter	Concern for carcinogenicity	Prohibited by many Codex members	None	?	?	CAN	The CCRVDF should confirm that this substance should not be used in food producing animals	High

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Tiamulin (CR)	AB	E	Use SUI	Dysentery associated with <i>Brachyspira hyodysenteriae</i> , pneumonia due to <i>Actinobacillus pleuropneumoniae</i> SUI		Different MRL/ residue status among Codex members	?	?	?	?	The CCRVDF should not recommend this substance for JECFA evaluation as there is not enough information available	Low
Tobicillin (JAP)	AB	D	Use in PIS	Treatment of septicaemias, respiratory and urinary infections. They are very important in the treatment of many diseases in a broad range of animal species	?	Different MRL/ residue status among Codex members					The CCRVDF should not recommend this substance for evaluation as there is not enough information available. Substance will be deleted from this list if no further specifications are made	

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Trimethoprim (diamino-pyrimidine) (ROK)	AB	E	Use AVI, BOV, CAP, EQU, LEP, OVI, SUI	Widely used	?	?	?	?	?	?	The CCRVDF should not recommend this substance for JECFA evaluation as there is not enough information available. Substance will be deleted from this list if no further specifications are made	Low
Xylazine (CAN, NZ, DE) ☹ Evaluated: 47 th JECFA	AP	D	Use in BOV (tissues, milk) and deer (tissues). Use EQU	Analgesia and sedation in BOV and EQU	?	?	?	Insufficient toxicity data, inadequate data on metabolism - residue data not sufficient to identify marker residue, inadequate depletion studies	DE, NZ	CAN	The CCRVDF should not recommend this substance for JECFA evaluation as there is not enough information available unless NZ, DE and CAN confirm that they are willing to provide data	Medium