

Technical Reference Document Listing Antimicrobial Agents of Veterinary Importance for Bovine Animals

An appendix to the WOAHA List of Antimicrobial Agents of Veterinary Importance

Scope

The objective of this *Technical Reference Document Listing Antimicrobial Agents of Veterinary Importance for Bovine Animals* (hereafter, the Technical Reference Document) is to provide additional, species-specific information without serving as a treatment guideline. By identifying antimicrobial agents authorised for use in cattle and/or water buffaloes, the technical reference document can aid in evaluating accessibility to veterinary medicinal products needed to treat common infectious diseases in these species, contribute to the development and update of national treatment guidelines and essential medicines lists, inform stewardship programs, as well as risk management and prioritisation actions to minimise and contain antimicrobial resistance (AMR).

It should be borne in mind that the antimicrobial agents listed in this technical reference document may not be available in all countries or be appropriate for use in all types of production systems. This technical reference document acknowledges that extra-label/off-label use of antimicrobial agents is not common in bovine animals but may still occur in some countries and regions where access to antimicrobials may be problematic or when managing infectious diseases in high-value animals. It is recognised that the legal frameworks and contexts in which veterinarians and other animal health professionals operate vary across regions, countries and territories regarding licensing, drug access, off-label/extra-label use of veterinary medicinal products, AMR patterns and public health engagement; therefore, the general information provided in this document should be interpreted in light of the local context.

Relevant recommendations for bovine animals described in the World Organisation for Animal Health (WOAH) Standards and the WOAHA List of Antimicrobial Agents of Veterinary Importance should be considered alongside this document. Furthermore, the technical reference document can be used by countries' competent authorities to identify antimicrobial agents to be considered as part of national surveillance systems for antimicrobial use (AMU) and AMR in animals and in the reporting of AMU data for bovine animals to WOAHA's ANIMUSE in alignment with the WOAHA's Strategy on Antimicrobial Resistance and the Prudent Use of Antimicrobials.

Methodology used to prepare this document

Ad-hoc group recruitment process

Experts participating in the *ad hoc* group for bovine animals were selected through an open call process and were nominated by the Director General of WOAHA. The *ad hoc* group was chaired by a member from the WOAHA's Antimicrobial Resistance Working Group (AMRWG). The experts represented geographical areas with sizeable bovine populations and different areas of expertise in bovine medicine and veterinary microbiology and pharmacology.

The members of the *ad-hoc* group were:

- Prof Moritz van Vuuren (Chair, ex-AMRWG), South Africa
- Dr Guilherme de Souza, Brazilian Agricultural Research Corporation (EMBRAPA), Brazil
- Prof Yang Wang, China Agricultural University, China
- Dr Damien Bouchard, France, ANSES (WOAH Collaborating Centre), France
- Dr Grace Murilla, Kag East University, Kenya
- Dr Claire Burbick, Washington State University, USA

As a first step, an evidence-guided rapid literature review was undertaken by the *ad hoc* group to prepare a preliminary table of important bacterial and protozoal pathogens of bovine animals and the antimicrobial agents used to treat infections caused by these pathogens. The table compiled from this rapid review included 44 pathogens of bovine animals, including 43 bacteria at genus and strain levels and one protozoal genus. Furthermore, the experts conducted searches of regulatory approvals of veterinary medicinal products containing antimicrobial agents in their respective countries and regions to identify from the existing [WOAH list of antimicrobial agents of veterinary importance](#) (hereafter, the WOA List) which antimicrobial agents were authorised for use in cattle and/or water buffaloes. Antimicrobial agents were only included in the technical reference document if they were included in formulations as the sole antimicrobial agent with antibacterial action or as part of well-established combinations (e.g., trimethoprim-sulphonamides) and were authorised for use in at least one country or region. Antimicrobial agents and classes not included in the WOA List but identified as authorised for use in bovine animals were added to the technical reference document. The importance of antimicrobial classes and subclasses was retained as per the WOA List.

The end product was a table presenting the following information:

- Antimicrobial class;
- Antimicrobial sub-class;
- Antimicrobial agent and/or well-established combination of two or more antimicrobial agents;
- Authorisation status for bovine animals (stated as “Used” or “Not used”) in one or more countries;
- Comments and other considerations regarding the importance of the antimicrobial class for animal and/or public health based on current scientific evidence and recommendations of the WOA List.

Once this table was established by the *ad hoc* group, the technical reference document was developed by the group and shared with the AMRWG for feedback. After consolidation, the technical reference document was shared with a panel of external experts, WOA Collaborating Centres and stakeholder organisations with whom the WOA has established a cooperation agreement. External experts were identified through the shortlist of experts that had been created during the recruitment process of the *ad hoc* group. The external experts, Collaborating Centres and stakeholder organisations were asked to address gaps in knowledge identified by the *ad hoc* group and to provide feedback concerning the tables of antimicrobial agents authorised for use, list of major pathogens and diseases and the proposed indications for use of antimicrobial groups against common infectious diseases in bovine animals.

The group took into consideration the feedback provided by external experts to consolidate the technical reference document. The final version of the technical reference document was submitted for consideration and endorsement by the AMRWG and WOA hierarchy prior to publication in the WOA website.

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Abbreviations:

The animal species in which antimicrobial agents are used and categories of antimicrobials of veterinary importance are abbreviated as follows:

AVI: Avian
API: Bee
BOV: Bovine
CAN: Canid
CAP: Caprine
CAM: Camel
CRU: Crustaceans
EQU: Equine
FEL Feline
LEP: Rabbit
OVI: Ovine
PIS: Fish
SUI: Swine
VCIA: Veterinary Critically Important Antimicrobial Agents
VHIA: Veterinary Highly Important Antimicrobial Agents
VIA: Veterinary Important Antimicrobial Agents

Note: more information on the categorisation of antimicrobial agents according to importance to veterinary medicine can be found in the [WOAH List of Antimicrobial Agents of Veterinary Importance](#).

Appendices:

Appendix 1: List of major pathogens and diseases affecting bovine animals.

Appendix 2: Antimicrobial classes used in veterinary medicine for infections in bovine animals.

Appendix 3: List of external experts involved in the revision of the technical reference document.

Appendix 4: List of Collaborating Centres involved in the revision of the technical reference document.

Appendix 5: List of organisations and professional associations involved in the revision of the technical reference document.

ANTIMICROBIAL AGENTS OF VETERINARY IMPORTANCE AUTHORISED FOR USE IN BOVINE ANIMALS

Antimicrobial Agents (Class, Sub-class and Substance by International Nonproprietary Name [INN])	Categorisation			Molecules	Species	Authorised for use in cattle and/or water buffaloes	Specific comments by class
	VCIA	VHIA	VIA				
AMINOCOUMARIN			x	Novobiocin (vet only)	AVI, CAP, OVI	No	This class is currently only used in animals.
AMINOCYCLITOL	x			Spectinomycin	AVI, BOV , CAN, CAP, EQU, FEL, LEP, OVI, SUI	Yes	Aminocyclitol is used to treat infections of the respiratory system a caused by <i>Mannheimia haemolytica</i> , <i>Mycoplasma</i> spp., and <i>Pasteurella</i> spp.
AMINOGLYCOSIDES	x			Dihydrostreptomycin	AVI, BOV , CAN, CAP, EQU, FEL, LEP, OVI, SUI	Yes	Oral aminoglycosides are used to treat bacterial gastrointestinal infections in cattle.
				Streptomycin	API, AVI, BOV , CAN, CAP, EQU, FEL, LEP, OVI, SUI	Yes	
AMINOGLYCOSIDES + 2 DEOXYSTREPTAMINE	x			Amikacin (synonyms: amikacillin, amikacin)	BOV , CAN, EQU, FEL	Yes	Aminoglycosides are used via intramammary route for the treatment of subclinical and subacute mastitis due to <i>Staphylococcus aureus</i> , <i>Streptococcus agalactiae</i> , <i>Streptococcus dysgalactiae</i> , <i>Streptococcus uberis</i> and <i>Escherichia coli</i> . Parenteral and intramammary veterinary medicinal products containing aminoglycosides should be used with caution due to their extensive withdrawal periods.
				Apramycin (vet only)	AVI, BOV , LEP, OVI, SUI	Yes	
				Astromycin (synonym: fortimycin)	LEP, OVI	No	
				Framycetin	CAN, CAP, FEL, OVI	No	
				Gentamicin	AVI, BOV , CAM, CAN, CAP, EQU, FEL, LEP, OVI, SUI	Yes	
				Kanamycin	AVI, BOV , CAN, EQU, FEL, SUI	Yes	
				Neomycin	API, AVI, BOV , CAN, CAP, CRU, EQU, FEL, LEP, OVI, PIS, SUI	Yes	
				Paromomycin	AVI, BOV , CAN, CAP, FEL, LEP, OVI, SUI	Yes	
				Tobramycin (synonym: tobramycin)	CAN, EQU, FEL	No	

Antimicrobial Agents (Class, Sub-class and Substance by International Nonproprietary Name [INN])	Categorisation			Molecules	Species	Authorised for use in cattle and/or water buffaloes	Specific comments by class
	VCIA	VHIA	VIA				
AMPHENICOLS	x			Chloramphenicol	CAN, FEL	No	Amphenicols are used to prevent and treat respiratory disease caused by <i>Actinobacillus pleuropneumoniae</i> , <i>Histophilus somni</i> , <i>Mannheimia haemolytica</i> , <i>Mycoplasma bovis</i> and <i>Pasteurella multocida</i> ; to treat foot rot, acute interdigital necrobacillosis, infectious pododermatitis associated with <i>Fusobacterium necrophorum</i> and <i>Prevotella melaninogenica</i> .
				Florfenicol (vet only)	AVI, BOV , CAN, CAP, CRU, EQU, FEL, LEP, OVI, PIS, SUI	Yes	
				Thiamphenicol	AVI, BOV , CAN, CAP, FEL, OVI, PIS, SUI	Yes	
ANSAMYCINS - RIFAMYCINS		x		Rifampicin (synonym: rifampin)	EQU	No	Ansamycins are used via intramammary route to treat subclinical and clinical mastitis due <i>Staphylococcus aureus</i> , <i>Streptococcus agalactiae</i> , <i>Streptococcus dysgalactiae</i> and <i>Streptococcus uberis</i> .
				Rifaximin*	BOV , CAN, CAP, EQU, FEL, LEP, OVI, SUI	Yes	
ARSENICALS			x	Nitarsonsone (vet only)	AVI, SUI	No	Note: Arsenicals have been withdrawn from the market in some countries/regions due to the detection of tissue residues containing inorganic arsenic, a carcinogen. This class is currently only used in animals.
				Roxarsone (vet only)	AVI, SUI	No	
BICYCLOMYCIN			x	Bicozamycin (synonym: bicyclomycin)	SUI	No	
CEPHALOSPORINS		x					First and second generation cephalosporins are used to treat clinical and subclinical mastitis caused by, <i>Corynebacterium</i> spp., <i>Pasteurella</i> spp., <i>Staphylococcus</i> spp., <i>Streptococcus agalactiae</i> , <i>Streptococcus dysgalactiae</i> , <i>Streptococcus uberis</i> , <i>Trueperella pyogenes</i> .
Cefacetriple* (synonyms: cephacetriple, cefacetril, cephacetril)				BOV	Yes		
Cefalexin* (synonyms: cephalexin, cephalillin, cephalexine, cefalexine)				AVI, BOV , CAN, CAP, EQU, FEL, OVI, SUI	Yes		
Cefalonium* (vet only) (synonyms: cephalonium, cefalonum)				BOV , CAN, CAP, OVI	Yes		
Cefalotin*				BOV , CAN, EQU	Yes		

Antimicrobial Agents (Class, Sub-class and Substance by International Nonproprietary Name [INN])	Categorisation			Molecules	Species	Authorised for use in cattle and/or water buffaloes	Specific comments by class
	VCIA	VHIA	VIA				
Cephalosporin 2nd Generation				Cefapirin* (synonyms: cephapirin, cefapyrin)	BOV	Yes	
				Cefazolin* (synonyms: cephazolin, cephaloline, cephazolidin)	BOV, CAP, OVI, SUI	Yes	
				Cefuroxime	BOV	Yes	
Cephalosporin 3rd Generation	x			Cefixime	CAN, FEL	No	<p>Third and fourth generation cephalosporins are critically important for human health and subject to specific recommendations in the WOA List of Antimicrobial Agents of Veterinary Importance. Their use in animals should only occur when the pathogen is resistant to the first choice antimicrobial; its use should be supported by antimicrobial susceptibility testing whenever possible.</p> <p>Extra-label/off label use should be limited and reserved for instances where no alternatives are available and in agreement with national legislation.</p>
				Cefoperazone*	BOV, CAP, OVI	Yes	
				Cefovecin (vet only)	CAN, FEL	No	
				Cefpodoxime	CAN	No	
				Ceftiofur (vet only)	AVI, BOV, CAN, CAP, EQU, LEP, OVI, SUI	Yes	
				Ceftriaxone	BOV, CAN, OVI, SUI	Yes	
Cephalosporin 4th Generation				Cefquinome (vet only)	BOV, CAP, EQU, LEP, OVI, SUI	Yes	
							<p>Third and fourth generation cephalosporins are used in bovine animals to treat respiratory disease caused by <i>Histophilus somni</i>, <i>Mannheimia haemolytica</i>, <i>Pasteurella multocida</i>; acute interdigital necrobacillosis caused by <i>Fusobacterium necrophorum</i> and <i>Prevotella melaninogenica</i>; post-partum metritis caused by <i>Trueperella pyogenes</i>, <i>E. coli</i>, and <i>Fusobacterium necrophorum</i>; septicemia in calves caused by <i>Escherichia coli</i>.</p> <p>Third and fourth generation cephalosporins are also used topically to treat clinical mastitis caused by: <i>Escherichia coli</i>, <i>Klebsiella</i> spp., <i>Pseudomonas aeruginosa</i>, <i>Staphylococcus aureus</i>, <i>Streptococcus agalactiae</i>, <i>Streptococcus dysgalactiae</i>, <i>Streptococcus uberis</i>, <i>Trueperella pyogenes</i>.</p>

Antimicrobial Agents (Class, Sub-class and Substance by International Nonproprietary Name [INN])	Categorisation			Molecules	Species	Authorised for use in cattle and/or water buffaloes	Specific comments by class
	VCIA	VHIA	VIA				
FUSIDANE			x	Fusidic acid	CAN, EQU, FEL	No	
IONOPHORES		x		Lasalocid (vet only)	AVI, BOV , LEP, OVI	Yes	Ionophores are used to prevent and treat coccidiosis (e.g., <i>Eimeria</i> spp.) in bovine animals. This class is currently only used in animals.
				Maduramicin (vet only)	AVI	No	
				Monensin (vet only)	API, AVI, BOV , CAP	Yes	
				Narasin (vet only)	AVI	No	
				Salinomycin (vet only)	AVI, LEP	No	
				Semduramicin (vet only)	AVI	No	
LINCOSAMIDES		x		Clindamycin	CAN, FEL	No	Lincosamides are used to treat pyelonephritis caused by <i>Corynebacterium renale</i> ; enterotoxaemia caused by <i>Clostridium perfringens</i> ; <i>Clostridium tetani</i> ; mastitis caused by <i>Trueperella pyogenes</i> , <i>Staphylococcus aureus</i> and <i>Nocardia asteroides</i> .
				Lincomycin	API, AVI, BOV , CAN, CAP, FEL, OVI, PIS, SUI	Yes	
				Pirlimycin (vet only)	BOV	Yes	
MACROLIDES	x						Macrolides are very important antimicrobials for bovine medicine. Macrolides are used to treat respiratory infections caused by <i>Histophilus somni</i> , <i>Mannheimia haemolytica</i> , <i>Mycoplasma bovis</i> , <i>Pasteurella multocida</i> ; infectious keratoconjunctivis (IBK) associated with <i>Moraxella bovis</i> ; necrobacillosis in calves. Macrolides are also used topically to treat mastitis caused by <i>Staphylococcus aureus</i> , <i>Streptococcus uberis</i> , <i>Streptococcus agalactiae</i> and <i>Streptococcus dysgalactiae</i> .
Macrolides 14-membered ring				Erythromycin	API, AVI, BOV , CAN, CAP, EQU, FEL, LEP, OVI, PIS, SUI	Yes	
Macrolides 15-membered ring				Oleandomycin		No	
				Azithromycin	CAN	No	
				Gamithromycin (vet only)	BOV , SUI	Yes	
Macrolides 16-membered ring				Tulathromycin (vet only)	BOV , SUI	Yes	
				Carbomycin	AVI	No	
				Josamycin	SUI	No	
				Kitasamycin (vet only)	AVI, PIS, SUI	No	
				Mirosamicin (synonyms: mirosamycin, miporamycin)	API, AVI, SUI	No	

Antimicrobial Agents (Class, Sub-class and Substance by International Nonproprietary Name [INN])	Categorisation			Molecules	Species	Authorised for use in cattle and/or water buffaloes	Specific comments by class
	VCIA	VHIA	VIA				
Macrolides 17-membered ring				Spiramycin	AVI, BOV , CAP, EQU, LEP, OVI, SUI	Yes	
				Tildipirosin (vet only)	BOV , SUI	Yes	
				Tilmicosin (vet only)	AVI, BOV , CAP, LEP, OVI, PIS, SUI	Yes	
				Tylosin (vet only)	API, AVI, BOV , CAP, LEP, OVI, SUI	Yes	
				Tylvalosin (vet only)	AVI, SUI	No	
				Sedecamycin (synonym: lankacidin A)		No	
				Terdecamycin		No	
ORTHOSOMYCINS			x	Avilamycin (vet only)	AVI, LEP, SUI	No	This class is currently only used in animals.
PENICILLINS	x						
Natural penicillins (including esters and salts)				Benethamine penicillin		No	<p>The wide range of applications and the nature of the diseases treated make penicillins extremely important for bovine medicine.</p> <p>Penicillins are used to treat arthritis, skin infections, gastrointestinal infections, ocular infections, peritonitis, pododermatitis, respiratory infections, urogenital infections; septicaemia, tetanus, omphalophlebitis and joint-ill infections in calves caused by <i>Actinomyces bovis</i>, <i>Bacillus anthracis</i>, <i>Bacteroides</i> spp., <i>Clostridium</i> spp., <i>Corynebacterium</i> spp., <i>Erysipelothrix rhusiopathiae</i>, <i>Fusobacterium necrophorum</i>, <i>Leptospira</i> spp., <i>Listeria</i> spp., <i>Mannheimia haemolytica</i>, <i>Moraxella</i> spp., <i>P. multocida</i>, <i>Staphylococcus</i> spp., <i>Streptococcus</i> spp..</p> <p>Penicillins are used via intramammary route to treat subclinical and clinical mastitis caused by <i>Clostridium</i></p>
				Benzylpenicillin (synonyms: penicillin G, benzylpenicillin G, benzopenicillin, benzyl penicillin)	AVI, BOV , CAM, CAN, CAP, EQU, FEL, LEP, OVI, SUI	Yes	
				Procaine benzylpenicillin (synonyms: benzylpenicillin procaine, procaine G penicillin) Benzathine benzylpenicillin (synonyms: benzathine penicillin, benzathine penicillin G)	BOV , CAM, CAN, CAP, EQU, FEL, OVI, SUI	Yes	

Antimicrobial Agents (Class, Sub-class and Substance by International Nonproprietary Name [INN])	Categorisation			Molecules	Species	Authorised for use in cattle and/or water buffaloes	Specific comments by class
	VCIA	VHIA	VIA				
				Penethamate hydriodide (vet only)	BOV, CAN, SUI	Yes	spp., <i>Corynebacterium</i> spp., <i>Pasteurella</i> spp., <i>Staphylococcus</i> spp. and <i>Streptococcus uberis</i> , <i>Streptococcus dysgalactiae</i> , <i>Trueperella pyogenes</i> .
				Tobicillin		No	
Amidinopenicillins				Mecillinam (synonyms: amdinocillin, hexacillin, penicillin HX)		No	
Aminopenicillins				Amoxicillin (synonym: amoxycillin)	AVI, BOV, CAN, CAP, EQU, FEL, OVI, PIS, SUI	Yes	
				Ampicillin	AVI, BOV, CAN, CAP, EQU, FEL, OVI, PIS, SUI	Yes	
				Hetacillin (synonym: phenazacillin)	BOV	Yes	
Aminopenicillin plus betalactamase inhibitor				Amoxicillin + clavulanic acid	AVI, BOV, CAN, CAP, EQU, FEL, OVI, SUI	Yes	
				Ampicillin + sulbactam	BOV	Yes	
Carboxypenicillins				Ticarcillin	EQU	No	
Phenoxypenicillins				Pheneticillin (synonyms: phenethicillin, penicillin B)	EQU	No	
				Phenoxymethylpenicillin (synonyms: penicillin V, pen V, penicillin phenoxymethyl, phenoxymethyl penicillin, beromycin, oraxillin)	AVI, CAN, SUI	No	
Antistaphylococcal penicillins				Cloxacillin* (synonym: methocillin S)	BOV, CAN, CAP, EQU, FEL, OVI	Yes	
				Dicloxacillin (synonym: dicloxacycline)	BOV, CAP, EQU, OVI	Yes	
				Nafcillin (synonym: naphcillin)	CAP, OVI	No	

Antimicrobial Agents (Class, Sub-class and Substance by International Nonproprietary Name [INN])	Categorisation			Molecules	Species	Authorised for use in cattle and/or water buffaloes	Specific comments by class
	VCIA	VHIA	VIA				
				Oxacillin (synonyms: oxazocillin, MPI-penicillin)	BOV, CAP, EQU, OVI	Yes	
Antipseudomonal penicillins				Aspoxicillin		No	
PHOSPHONIC ACID DERIVATIVES		x		Fosfomycin (synonyms: phosphomycin, phosphonomycin)	AVI, BOV, PIS, SUI	Yes	Phosphonic acid derivatives are critically important for human health and subject to specific recommendations in the WOAHP List of Antimicrobial Agents of Veterinary Importance. Their use in animals should only occur when the pathogen is resistant to the first choice antimicrobial; its use should be supported by antimicrobial susceptibility testing whenever possible. Extra-label/off label use should be limited and reserved for instances where no alternatives are available and in agreement with national legislation. Fosfomycin is used in some countries to treat <i>Escherichia coli</i> diarrhea and salmonellosis in bovine animals
PLEUROMUTILINS		x		Tiamulin (vet only) (synonym: thiamutillin)	AVI, CAP, LEP, OVI, PIS, SUI	No	
				Valnemulin (vet only)	SUI	No	
POLYPEPTIDES		x					Polypeptides are used to reduce incidence of liver abscesses in cattle caused by bacteria such as <i>Fusobacterium necrophorum</i> and <i>Trueperella pyogenes</i> .
Cyclic polypeptides				Bacitracin	AVI, BOV, CAN, FEL, LEP, OVI, SUI	Yes	
				Enramycin	AVI, SUI	No	
				Gramicidin	EQU	No	
Polymyxins				Polymyxin B (synonym: polymixin B)	CAN, CAP, EQU, FEL, LEP, OVI, SUI	No	Colistin is critically important for human health and subject to specific recommendations in the WOAHP List of Antimicrobial Agents of Veterinary Importance. Its use in animals should only occur when the pathogen is resistant to the first choice antimicrobial; its use should be supported by antimicrobial susceptibility testing
				Colistin (synonym: polymyxin E)	AVI, BOV, CAN, CAP, EQU, FEL, LEP, OVI, SUI	Yes	

Antimicrobial Agents (Class, Sub-class and Substance by International Nonproprietary Name [INN])	Categorisation			Molecules	Species	Authorised for use in cattle and/or water buffaloes	Specific comments by class
	VCIA	VHIA	VIA				
							whenever possible. Extra-label/off label use should be limited and reserved for instances where no alternatives are available and in agreement with national legislation. Colistin is used to treat intestinal infections caused by <i>Escherichia coli</i> in bovine animals.
QUINOLONES							
Quinolones 1 st generation		x		Flumequine (synonym: flumequin)	AVI, BOV , CAN, CAP, EQU, FEL, LEP, OVI, PIS, SUI	Yes	Quinolones are important antimicrobials for bovine medicine and are used to treat respiratory and gastrointestinal infections in bovine animals caused by <i>Campylobacter</i> spp., <i>Escherichia coli</i> , <i>Histophilus somni</i> , <i>Mannheimia haemolytica</i> , <i>Pasteurella multocida</i> and <i>Salmonella</i> spp.
				Miloxacin		No	
				Nalidixic acid (synonyms: nalixidate, nalidixinic acid, nalidic acid)		No	
				Oxolinic acid	AVI, BOV , LEP, OVI, PIS, SUI	Yes	
Quinolones 2 nd generation (Fluoroquinolones)	x			Ciprofloxacin	AVI, BOV , PIS, SUI	Yes	Fluoroquinolones are critically important for human health and subject to specific recommendations in the WOAHP List of Antimicrobial Agents of Veterinary Importance. Its use in animals should only occur when the pathogen is resistant to the first choice antimicrobial; its use should be supported by antimicrobial susceptibility testing whenever possible. Extra-label/off label use should be limited and reserved for instances where no alternatives are available and in agreement with national legislation. Fluoroquinolones are used to treat respiratory, gastrointestinal, urogenital system infections, septicaemia, arthritis and mastitis in bovine animals associated with <i>Campylobacter</i> spp., <i>Escherichia coli</i> , <i>Histophilus somni</i> , <i>Klebsiella</i> spp., <i>Mannheimia haemolytica</i> , <i>Mycoplasma</i> spp., <i>Pasteurella</i> spp., <i>Salmonella</i> spp., <i>Staphylococcus aureus</i> , <i>Yersinia</i> spp.
				Danofloxacin (vet only)	BOV , CAP, LEP, OVI, SUI	Yes	
				Difloxacin	AVI, LEP, SUI	No	
				Enrofloxacin (vet only)	AVI, BOV , CAN, CAP, CRU, EQU, FEL, LEP, OVI, PIS, SUI	Yes	
				Ibafloxacin	CAN, FEL	No	
				Levofloxacin	CAN	No	
				Marbofloxacin (vet only)	BOV , CAN, EQU, FEL, LEP, SUI	Yes	
				Norfloxacin	AVI, BOV , CAN, CAP, FEL, LEP, OVI, SUI	Yes	
				Ofloxacin	AVI, CAN, FEL, SUI	No	

Antimicrobial Agents (Class, Sub-class and Substance by International Nonproprietary Name [INN])	Categorisation			Molecules	Species	Authorised for use in cattle and/or water buffaloes	Specific comments by class
	VCIA	VHIA	VIA				
				Orbifloxacin (vet only)	BOV, CAN, FEL, SUI	Yes	
				Pradofloxacin (vet only)	BOV, CAN, FEL		
				Sarafloxacin		No	
QUINOXALINES			x	Carbadox (vet only)	SUI	No	<p>Note: Carbadox has been withdrawn from the market in some countries/regions due to the detection of carcinogenic tissue residues.</p> <p>This class is currently only used in animals.</p>
				Olaquinox (vet only) (synonym: olachinox)		No	
SULFONAMIDES	x			Phthalylsulfathiazole (vet only) (synonyms: sulfathalidine, phthalazol, phthalylsulphathiazole, phthalylsulfonazole)	CAN, FEL, SUI	No	<p>The wide range of applications and the nature of the diseases treated make sulfonamides very important for bovine animals.</p> <p>Sulfonamides can be used topically or systemically and are often used (\pm trimethoprim) to control infections of the respiratory tract, gastrointestinal system, urogenital system, skin (including pododermatitis), soft tissues, wounds and sepsis caused by: <i>Corynebacterium</i> spp., <i>Escherichia coli</i>, <i>Listeria</i> spp., <i>Pasteurella</i> spp., <i>Salmonella</i> spp., <i>Staphylococcus</i> spp. and <i>Streptococcus</i> spp.</p> <p>Sulfonamides are also used to treat mastitis caused by <i>Corynebacterium bovis</i>, <i>Klebsiella pneumoniae</i>, <i>Staphylococcus aureus</i>, <i>Streptococcus uberis</i>, <i>Streptococcus agalactiae</i>, <i>Streptococcus dysgalactiae</i>, <i>Streptococcus pyogenes</i>.</p> <p>In calves, sulfonamides (\pm trimethoprim) are used to treat coccidiosis (e.g., <i>Eimeria bovis</i>, <i>E. zuernii</i>) and <i>Escherichia coli</i> infections.</p>
				Sulfacetamide (synonyms: sulphacetamide, acetosulfamine, acetosulfamin, N- acetylsulfanilamide)	AVI, BOV, CAN, FEL, OVI, SUI	Yes	
				Sulfachlorpyridazine (synonym: sulfachloropyridazine)	AVI, BOV, SUI	Yes	
				Sulfadiazine (synonyms: sulphadiazine, sulfapyrimidine, sulfadiazin, sulfazine, sulfadiazene)	AVI, BOV, CAN, CAP, FEL, OVI, PIS, SUI	Yes	
				Sulfamethoxazole (synonyms: sulfadimethoxazole sulphamethoxazole, sulfisomezole)	AVI, BOV, CAN, FEL, SUI	Yes	
				Sulfadimethoxine (synonyms: sulphadimethoxine,	AVI, BOV, CAN, CAP, EQU, FEL, LEP, OVI, PIS,	Yes	

Antimicrobial Agents (Class, Sub-class and Substance by International Nonproprietary Name [INN])	Categorisation			Molecules	Species	Authorised for use in cattle and/or water buffaloes	Specific comments by class
	VCIA	VHIA	VIA				
				sulfadimethoxin, sulfadimethoxydiazine)	SUI		
				Sulfadimidine (synonyms: sulfamethazine, sulfadimethyldiazine, sulfamezathine, sulphamethazine, sulfadimerazine)	AVI, BOV , CAN, CAP, EQU, FEL, LEP, OVI, SUI	Yes	
				Sulfadoxine (synonyms: sulphadoxine, sulforthomidine, sulphormethoxine, sulfadoxin)	AVI, BOV , CAN, EQU, FEL, OVI, SUI	Yes	
				Sulfafurazole (synonyms: sulfisoxazole, sulphafurazole, sulfisoxazol, sulfafurazol)	CAN, PIS	No	
				Sulfaguanidine (synonyms: sulfaguanidin, sulphaguanidine, sulfanilguanidine, sulfoguanidine)	AVI, BOV , CAN, CAP, FEL, OVI, SUI	Yes	
				Sulfamerazine (synonyms: sulphamerazine, sulfamerazin, sulfamethyldiazine)	AVI, BOV , CAN, CAP, EQU, FEL, LEP, OVI, PIS, SUI	Yes	
				Sulfamethoxydiazine (synonyms: sulfamethoxine, sulfameter, sulfamethoxydiazine, sulfamethoxypyrimidine)	AVI	No	
				Sulfamonomethoxine (synonyms: sulfamonomethoxin, sulfamonmethoxine)	AVI, BOV , CAN, FEL, PIS, SUI	Yes	
				Sulfanilamide (synonyms:	BOV , CAN, CAP, FEL,	Yes	

Antimicrobial Agents (Class, Sub-class and Substance by International Nonproprietary Name [INN])	Categorisation			Molecules	Species	Authorised for use in cattle and/or water buffaloes	Specific comments by class
	VCIA	VHIA	VIA				
				sulphanilamide, sulfamine, sulfonamide)	OVI, SUI		
				Sulfapyridine (synonym: sulphapyridine)	BOV , CAN, FEL, SUI	Yes	
				Sulfaquinoxaline (synonyms: sulfabenzpyrazine, sulphaquinoxaline)	AVI, BOV , CAP, LEP, OVI, SUI	Yes	
				Sulfamethoxypyridazine (synonyms: sulphamethoxypyridazine, sulfapyridazine, sulfametoxipiridazine)	AVI, BOV , CAN, EQU, FEL, SUI	Yes	
Sulfonamides + diaminopyrimidines				Ormetoprim (synonyms: ormethoprim, ormetorprim) + sulfonamide	AVI, BOV , PIS, SUI	Yes	
				Trimethoprim (synonym: trimetoprim) + sulfonamide	AVI, BOV , CAN, CAP, EQU, FEL, LEP, OVI, PIS, SUI	Yes	
DIAMINOPYRIMIDINES				Baquiloprim		No	
				Ormetoprim (synonyms: ormethoprim, ormetorprim)	AVI	No	
				Trimethoprim (synonym: trimetoprim)	AVI, BOV , CAP, EQU, LEP, OVI	Yes	
STREPTOGRAMINS			x	Virginiamycin (vet only) (Synonym: Pristinamycin)	AVI, BOV , OVI, SUI	Yes	Streptogramins are used to reduce incidence of liver abscesses in cattle caused by bacteria such as <i>Fusobacterium necrophorum</i> and <i>Trueperella pyogenes</i> .
TETRACYCLINES	x			Chlortetracycline	AVI, BOV , CAN, CAP, EQU, FEL, LEP, OVI, PIS, SUI	Yes	The wide range of applications and the nature of the diseases treated make tetracyclines extremely important for bovine medicine.
				Doxycycline (synonyms:	AVI, BOV , CAM, CAN,	Yes	

Antimicrobial Agents (Class, Sub-class and Substance by International Nonproprietary Name [INN])	Categorisation			Molecules	Species	Authorised for use in cattle and/or water buffaloes	Specific comments by class
	VCIA	VHIA	VIA				
				doxytetracycline, doxycyclin)	CAP, EQU, FEL, LEP, OVI, PIS, SUI		Tetracyclines are used to treat navel-ill/joint-ill, infectious keratoconjunctivitis, intestinal, respiratory and genital infections, pododermatitis and septicaemia caused by <i>Anaplasma</i> spp., <i>Babesia</i> spp., <i>Bacillus anthracis</i> , <i>Campylobacter</i> spp., <i>Chlamydia</i> spp., <i>Corynebacterium</i> spp., <i>Erysipelothrix</i> spp., <i>E. coli</i> , <i>Fusobacterium</i> spp., <i>nechrophorum</i> , <i>Histophilus somni</i> , <i>Leptospira</i> spp., <i>Mycoplasma</i> spp., <i>Pasteurella multocida</i> , <i>Rickettsia</i> spp., <i>Salmonella</i> spp., <i>Staphylococcus</i> spp. and <i>Streptococcus</i> spp. Tetracyclines are used topically to treat ophthalmic infections and digital dermatitis and to prevent or treat infections of traumatic or surgical wounds.
				Oxytetracycline (synonyms: oxytetracycline, oxytetracyclin, oxitetracyclin) oxytetracyne)	API, AVI, BOV , CAM, CAN, CAP, CRU, EQU, FEL, LEP, OVI, PIS, SUI	Yes	
				Tetracycline (synonym: tetracyclin)	API, AVI, BOV , CAM, CAN, CAP, EQU, FEL, LEP, OVI, PIS, SUI	Yes	
THIOPEPTIDES			x	Nosiheptide	BOV	Yes	Thiopeptides are used to treat <i>Enterococcus</i> spp. and <i>Staphylococcus</i> spp. infections in bovine animals.
				Thiostrepton	CAN, FEL	No	
HALOGENATED HYDROXYQUINOLINES			x	Halquinol	SUI	No	
PSEUDOMONIC ACID				Mupirocin	CAN, FEL	No	
NITROIMIDAZOLES				Metronidazole	CAN, FEL	No	
				Ornidazole	CAN	No	
				Tinidazole	CAN, FEL	No	

*These antimicrobial agents are authorised for topical use in cattle and/or water buffaloes.

Appendix 1: List of major pathogens and diseases affecting bovine animals commonly treated with antimicrobials.

Pathogen	Examples of diseases and conditions
<i>Actinomyces bovis</i>	Actinomycosis (lumpy jaw)
<i>Bacillus anthracis</i>	Anthrax
<i>Bibersteinia trehalosi</i>	Pneumonia, Bovine Respiratory Disease (BRD)
<i>Borrelia burgdorferi</i>	Lyme disease, polysynovitis, lymphadenopathy, emaciation, interstitial myocarditis, nephritis, meningoencephalitis
<i>Clostridium novyi</i> type A	Malignant oedema
<i>Clostridium novyi</i> type B	Black disease
<i>Clostridium novyi</i> type D	Bacillary haemoglobinuria
<i>Clostridium perfringens</i> type A	Wound infections, enterotoxaemia in calves and water buffalo
<i>Clostridium perfringens</i> type B, <i>Clostridium perfringens</i> type C	Haemorrhagic enteritis
<i>Clostridium chauvoei</i>	Black quarter, myonecrosis of skeletal or cardiac muscles, severe toxæmia and high case fatality rate.
<i>Campylobacter jejuni</i>	Mastitis, diarrhoea, infertility and abortion
<i>Campylobacter fetus venerealis</i>	Bovine genital campylobacteriosis, infertility and abortion
<i>Corynebacterium</i> spp.	Mastitis, skin lesions
<i>Corynebacterium pseudotuberculosis</i>	Cutaneous granulomas, lymphangitis, mastitis
<i>Corynebacterium renale</i>	Cystitis and pyelonephritis
<i>Dichelobacter (Bacteroides) nodosus</i>	Interdigital necrobacillosis (foot rot), interdigital dermatitis and heel erosion
<i>Dermatophilus congolensis</i>	Senkobo disease (Dermatophilosis)
<i>Enterococcus faecalis</i>	Mastitis
<i>Escherichia coli</i>	Endometritis, enterotoxigenic infections, enteropathogenic infections, colisepticaemia
<i>Fusobacterium necrophorum</i>	Acute pneumonia (calves and young cattle), oral and laryngeal necrobacillosis, liver abscesses, metritis, necrobacillosis of the liver, interdigital necrobacillosis (foot rot), interdigital dermatitis and heel erosion
<i>Histophilus somni (Haemophilus somnus)</i>	Bacteraemia, myocardial abscesses, pleuritis, Bovine Respiratory Disease (BRD), meningitis, septicaemia
<i>Klebsiella pneumoniae</i>	Acute pneumonia (calves and young cattle), mastitis, endometritis
<i>Leptospira</i> spp.	Abortion, infertility, interstitial nephritis
<i>Listeria monocytogenes</i>	Abortion, encephalitis, meningitis
<i>Mannheimia haemolytica</i>	Bacteraemia, pleuritis, pneumonia, pneumonic pasteurellosis (i.e., BRD or 'shipping fever' in young animals), septicaemia, mastitis
<i>Moraxella bovis</i>	Infectious keratoconjunctivitis
<i>Mycoplasma mycoides</i> subspecies <i>mycoides</i>	Contagious bovine pleuropneumonia or CBPP
<i>Mycoplasma</i> spp. (<i>M. bovis</i> , <i>M. bovoculi</i> , <i>M. bovigenitalium</i> , <i>M. californicum</i> , <i>M.</i> <i>canadense</i> , <i>M. dispar</i> , <i>M. (Eperythrozoon)</i> <i>wenyonii</i>)	Anaemia, arthritis, otitis media, conjunctivitis, infertility, lymphadenopathy, mastitis, Bovine Respiratory Disease (BRD) (calves)
<i>Pasteurella multocida</i> serotype B	Haemorrhagic septicaemia in cattle and water buffalo (<i>Bubalus bubalis</i>)
<i>Pasteurella multocida</i> serotype E	East African haemorrhagic fever

Pathogen	Examples of diseases and conditions
<i>Pasteurella multocida</i>	Bacteraemia, mastitis, Bovine Respiratory Disease (BRD), septicaemia
<i>Prevotella melaninogenica</i>	Interdigital necrobacillosis (foot rot), interdigital dermatitis and heel erosion
<i>Salmonella Enterica</i> (e.g., <i>S. Dublin</i>)	Sepsis, pneumonia, severe diarrhoea in calves
<i>Serratia</i> spp.	Mastitis
<i>Staphylococcus aureus</i> , coagulase-negative <i>Staphylococcus</i>	Endometritis, mastitis, skin infections
<i>Streptococcus</i> spp.	Mastitis, endometritis
<i>Streptococcus agalactiae</i>	Mastitis
<i>Streptococcus dysgalactiae</i>	Joint infections (calves), mastitis
<i>Streptococcus uberis</i>	Mastitis
<i>Trueperella (Arcanobacterium) pyogenes</i>	Numerous pyogenic or suppurative conditions; Bovine Respiratory Disease (BRD)
<i>Yersinia pseudotuberculosis</i>	Abscesses, enterocolitis and haemorrhagic diarrhoea
Rickettsial diseases	
<i>Anaplasma marginale</i>	Bovine anaplasmosis
<i>Ehrlichia ruminantium</i>	Heartwater
Coccidia	
<i>Eimeria</i> spp. (e.g., <i>E. zuernii</i> , <i>E. bovis</i> , <i>E. ellipsoidalis</i> , <i>E. alabamensis</i> , <i>E. auburnensis</i> and <i>E. wyomingensis</i>)	Coccidiosis

Pathogens not included in the above list fulfil at least one of the following criteria:

- 1) Pathogens cause infections that are deemed very rare in bovine animals
- 2) Pathogens for which antimicrobials are not indicated for the control of disease

Pathogens and diseases not commonly treated with antimicrobials:

- *Actinobacillus lignieresii*
- *Babesia* spp. (Babesiosis)
- *Brucella* spp. (e.g. *Brucella abortus*)
- *Ehrlichia ondiri*
- *Coxiella burnettii*
- *Mycobacterium* spp. (including *M. bovis*)
- *Mycoplasma mycoides subspecies mycoides*
- *Proteus* spp.
- *Pseudomonas* spp.
- *Theileria annulata* (Tropical Theileriosis)
- *Theileria orientalis* (Bovine Infectious Anaemia)
- *Theileria parva* (East Coast Fever)
- *Trypanosoma* spp. (Trypanosomiasis)
- *Ureoplasma diversum*
- *Yersinia enterocolitica*

Appendix 2: Antimicrobial classes authorised for use for the treatment of bacterial and protozoal infections in bovine animals.

Table a. Antimicrobial classes authorised for use in bacterial and protozoal infections and by body system/organ.

[illegible]

Appendix 3: External expert involved in the revision of the technical reference document.

Dr Jing Li
China Agricultural University
CHINA

Appendix 4: List of Collaborating Centres involved in the revision of the technical reference document.

National Institute of Animal Health (NIAH)
JAPAN
<https://www.naro.go.jp/>

National Veterinary Assay Laboratory (NVAL)
JAPAN
<https://www.maff.go.jp/nval/english/>

École Inter-Etats des Sciences et Médecine Vétérinaires (EISMV)
SENEGAL
<https://www.eismv.org/>

Centre National de Veille Zoosanitaire (CNVZ)
TUNISIA
<http://cnvz.agrinet.tn/index.php/fr/>

Food and Drug Administration (FDA)
UNITED STATES OF AMERICA
<https://www.fda.gov/>

Appendix 5: List of stakeholder international non-governmental organisations involved in the revision of the technical reference document.

Brooke
UNITED KINGDOM
<https://www.thebrooke.org/>

HealthforAnimals
BELGIUM
<https://www.healthforanimals.org/>

International Dairy Federation (IDF)
BELGIUM
<https://fil-idf.org/>

World Veterinary Association (WVA)
BELGIUM
<https://worldvet.org/>