

The OIE International Committee unanimously adopted the List of Antimicrobials of Veterinary Importance at its 75<sup>th</sup> General Session in May 2007 (Resolution No. XXVIII).

### Background

Antimicrobial agents are essential drugs for human and animal health and welfare. Antimicrobial resistance is a global public and animal health concern that is influenced by both human and non-human antimicrobial usage. The human, animal and plant sectors have a shared responsibility to prevent or minimise antimicrobial resistance selection pressures on both human and non-human pathogens.

The FAO/OIE/WHO Expert Workshop on Non-Human Antimicrobial Usage and Antimicrobial Resistance held in Geneva, Switzerland, in December 2003 (Scientific Assessment) and in Oslo, Norway, in March 2004 (Management Options) recommended that the OIE should develop a list of critically important antimicrobials in veterinary medicine and that WHO should also develop such a list of critically important antimicrobials in human medicine.

Conclusion No. 5 of the Oslo Workshop is as follows:

5. The concept of “critically important” classes of antimicrobials for humans should be pursued by WHO. The Workshop concluded that antimicrobials that are critically important in veterinary medicine should be identified, to complement the identification of such antimicrobials used in human medicine. Criteria for identification of these antimicrobials of critical importance in animals should be established and listed by OIE. The overlap of critical lists for human and veterinary medicine can provide further information, allowing an appropriate balance to be struck between animal health needs and public health considerations.

Responding to this recommendation, the OIE decided to address this task through its existing ad hoc Group on antimicrobial resistance. The terms of reference, aim of the list and methodology were discussed by the ad hoc Group since November 2004 which was subsequently endorsed by the Biological Standards Commission in its January 2005 meeting and adopted by the International Committee in May 2005. Thus, the work was officially undertaken by the OIE.

### Preparation of the draft list

The Director General of the OIE sent a questionnaire prepared by the ad hoc Group accompanied by his

letter explaining the importance of the task to OIE Delegates of all Member Countries and international organisations having signed a Co-operation Agreement with the OIE in August 2005.

Sixty-six replies were received. This response rate highlights the importance given by OIE Member Countries from all regions to this issue. These replies were analyzed first by the OIE Collaborating Centre for Veterinary Drugs, then discussed by the ad hoc Group at its meeting in February 2006. A list of proposed VCIA was compiled together with an executive summary. This list was endorsed by the Biological Standards Commission and circulated among Member Countries aiming for adoption by the OIE International Committee during the General Session in May 2006.

### Discussion at the 74<sup>th</sup> International Committee in May 2006

The list was submitted to the 74<sup>th</sup> International Committee where active discussion was made among Member Countries. Concerns raised by Member Countries include: 1) the list includes substances that are banned in some countries; 2) some of the substances on the list are not considered “critical”; 3) nature of the list – is this mandatory for Member Countries?; and 4) the use of antimicrobials as growth hormone is included. While many Member Countries appreciated the work, it was considered appropriate to continue refinement of the list. The list was adopted as a preliminary list by Resolution No. XXXIII.

### Refinement of the list

The *ad hoc* Group was convened in September 2006 to review the comments made at the 74<sup>th</sup> General Session of the OIE International Committee, and Resolution No. XXXIII adopted at the 74<sup>th</sup> General Session. Based on the further analysis provided by the OIE Collaborating Centre for Veterinary Medicinal Products, the *ad hoc* Group prepared its final recommendations of the list of antimicrobials of veterinary importance together with an executive summary. Once again, this was examined and endorsed by the Biological Standards Commission in its January 2007 meeting and circulated among member Countries.

### Adoption of List of Antimicrobials of Veterinary Importance

The refined list was submitted to the 75<sup>th</sup> International Committee during the General Session in May 2007 and adopted unanimously by Resolution No. XXVIII.

## CRITERIA USED FOR CATEGORISATION OF VETERINARY IMPORTANT ANTIMICROBIALS

### Introduction

### List of antimicrobials

In developing the list, the *ad hoc* Group agreed that any antimicrobial authorised for use in veterinary medicine according to the criteria of quality, safety and efficacy as defined in the *Terrestrial Animal Health Code* (Appendix 3.9.3. Guidelines for the responsible and prudent use of antimicrobial agents in Veterinary Medicine) is important. Therefore, the Group decided to address all antimicrobials used in food-producing animals to provide a comprehensive list, divided into critically important, highly important and important antimicrobials.

In selecting the criteria to define veterinary important antimicrobials, one significant difference between the use of antimicrobials in humans and animals has to be accounted for: the many different species that have to be treated in veterinary medicine.

The following criteria were selected to determine the degree of importance for classes of veterinary antimicrobials.

#### **Criterion 1. Response rate to the questionnaire regarding Veterinary Critically Important Antimicrobials**

This criterion was met when a majority of the respondents (more than 50%) identified the importance of the antimicrobial class in their response to the questionnaire.

#### **Criterion 2. Treatment of serious animal disease and availability of alternative antimicrobials**

This criterion was met when compounds within the class were identified as essential against specific infections and there was a lack of sufficient therapeutic alternatives.

On the basis of these criteria, the following categories were established:

- Veterinary **Critically Important Antimicrobials**: are those that meet **BOTH** criteria 1 **AND** 2
- Veterinary **Highly Important Antimicrobials**: are those that meet criteria 1 **OR** 2
- Veterinary **Important Antimicrobials**: are those that meet **NEITHER** criteria 1 **OR** 2

#### **Abbreviations:**

Animal species in which these antimicrobials are used are abbreviated as follows:

AVI:	avian	EQU:	Equine
API:	bee	LEP:	Rabbit
BOV:	bovine	OVI:	Ovine
CAP:	caprine	PIS:	Fish
CAM:	camel	SUI:	Swine

VCIA:	Veterinary Critically Important Antimicrobials
VHIA:	Veterinary Highly Important Antimicrobials
VIA:	Veterinary Important Antimicrobials

# CATEGORISATION OF VETERINARY IMPORTANT ANTIMICROBIALS FOR FOOD-PRODUCING ANIMALS

## Introduction

## Criteria used for categorisation

ANTIMICROBIAL FAMILY	SPECIES	% quotations	Specific comments	C1: Quotation > 50%	C2: Essential or Few alternatives	VCIA	VHIA	VIA
<b>AMINOGLYCOSIDES</b> <b>AMINOCYCLITOL</b> Spectinomycin  <b>AMINOGLYCOSIDES</b> Streptomycin  Dihydrostreptomycin  Framycetin  Kanamycin  Neomycin  Paromomycin  Apramycin  Gentamicin  Tobramycin Amikacin	AVI, BOV, CAP, EQU, LEP, OVI, PIS, SUI  API, AVI, BOV, CAP, EQU, LEP, OVI, PIS, SUI  AVI, BOV, CAP, EQU, LEP, OVI, SUI  BOV, CAP, OVI  AVI, BOV, EQU, PIS, SUI  API, AVI, BOV, CAP, EQU, LEP, OVI, SUI  CAP, OVI, LEP  AVI, BOV, LEP, OVI, SUI  AVI, BOV, CAM, CAP, EQU, LEP, OVI, SUI  EQU EQU	77,1%	The wide range of applications and the nature of the diseases treated make aminoglycosides extremely important for veterinary medicine. Aminoglycosides are of importance in septicaemias; digestive, respiratory and urinary diseases.  Gentamicin is indicated for <i>Pseudomonas aeruginosa</i> infections with few alternatives. Spectinomycin is used only in animals. Few economic alternatives are available.	Y	Y	Y		
<b>ANSAMYCIN – RIFAMYCINS</b> Rifampicin Rifaximin	EQU BOV, CAP, EQU, LEP, OVI, SUI	30%	This antimicrobial class is authorised only in a few countries and with a very limited number of indications (mastitis) and few alternatives, e.g. treatment of <i>Rhodococcus equi</i> infections in foals.  <b>Rifampicin is critically important in equines.</b>	N	Y		Y	
<b>BICYCLOMYCIN</b>  Bicozamycin	BOV, PIS	1,4%	Biclomycin is listed for digestive and respiratory diseases in cattle and septicaemias in fish.	N	N			Y

ANTIMICROBIAL FAMILY	SPECIES	% quotations	Specific comments	C1: Quotation > 50%	C2: Essential or Few alternatives	VCIA	VHIA	VIA
<b>CEPHALOSPORINS</b>								
<b>CEPHALOSPORIN 1G</b>								
Cefacetile	BOV							
Cefalexin	BOV, CAP, EQU, OVI, SUI							
Cefalotin	EQU							
Cefapirin	BOV							
Cefazolin	BOV, CAP, OVI							
Cefalonium	BOV, CAP, OVI	58,6%	Cephalosporins are used in the treatment of septicemias, respiratory infections, and mastitis. Alternatives are limited in efficacy through either inadequate spectrum or presence of antimicrobial resistance.	Y	Y	Y		
<b>CEPHALOSPORIN 2G</b>								
Cefuroxime	BOV							
<b>CEPHALOSPORIN 3G</b>								
Cefoperazone	BOV, CAP, OVI							
Ceftiofur	AVI, BOV, CAP, EQU, LEP, OVI, SUI							
Ceftriaxone	AVI, BOV, OVI, SUI							
<b>CEPHALOSPORIN 4G</b>								
Cefquinome	BOV, CAP, EQU, LEP, OVI, SUI							
<b>FOSFOMYCIN</b>								
Fosfomicin	AVI, BOV, PIS, SUI	7,1%	This antimicrobial is authorised only in a few countries. Fosfomicin has a limited number of alternatives in some fish infections. <b>Critically important for fish<sup>1</sup>.</b>	N	Y		Y	
<b>FUSIDIC ACID</b>								
Fusidic acid	BOV, EQU	1,4%	Fusidic acid is used in the treatment of ophthalmic diseases in cattle and horses.	N	N			Y
<b>IONOPHORES</b>								
Lasalocid	AVI, BOV, LEP, OVI							
Maduramycin	AVI							
Monensin	API, AVI, BOV, CAP	42,9%	Ionophores are essential for animal health because they are used to control intestinal parasitic coccidiosis. ( <i>Eimeria</i> spp.) where there are few or no alternatives available. <b>Ionophores are critically important in poultry. Ionophores are used only in animals</b>	N	Y		Y	
Narasin	AVI							
Salinomycin	AVI, LEP							
Semduramicin	AVI							

<sup>1</sup> Under study

ANTIMICROBIAL FAMILY	SPECIES	% quotations	Specific comments	C1: Quotation > 50%	C2: Essential or Few alternatives	VCIA	VHIA	VIA
<b>LINCOSAMIDES</b> Pirlimycin Lincomycin	BOV API, AVI, BOV, CAP, OVI, PIS, SUI	51,4%	Lincosamides are essential in the treatment of Mycoplasma pneumonia, infectious arthritis and hemorrhagic enteritis of pigs.	Y	N		Y	
<b>MACROLIDES</b> <b>AZALIDE</b> Tulathromycin  <b>MACROLIDES C14</b> Erythromycin  <b>MACROLIDES C16</b> Josamycin Kitasamycin Spiramycin  Tilmicosin  Tylosin  Mirosamycin Terdecamycin	BOV, CAP, LEP, OVI, SUI  API, AVI, BOV,CAP, EQU, LEP, OVI, PIS, SUI  AVI, PIS AVI, SUI AVI, BOV, CAP, EQU, LEP, OVI, PIS, SUI AVI, BOV, CAP, LEP, OVI, SUI API, AVI, BOV, CAP, LEP, OVI, SUI API, AVI, SUI AVI	77,1%	Macrolides are used to treat Mycoplasma infections in pig and poultry, hemorrhagic digestive disease in pigs and liver abscesses ( <i>Fusobacterium necrophorum</i> ) in cattle, where they have very few alternatives. Macrolides are also used for respiratory infections in cattle	Y	Y	Y		
<b>NOVOBIOCIN</b> Novobiocin	BOV, CAP, OVI, PIS	31,4%	Novobiocin is used in the treatment of mastitis in the form of intramammary creams and in sepsis of fish. <b>Novobiocin is only used in animals</b>	N	N			Y
<b>ORTHOSOMYCINS</b> Avilamycin	AVI, LEP	4,3%	Avilamycin is used for digestive diseases of poultry and rabbits: avilamycin is used to treat necrotic enteritis in chickens where available. <b>The antimicrobial class is used only in animals.</b>	N	N			Y

ANTIMICROBIAL FAMILY	SPECIES	% quotations	Specific comments	C1: Quotation > 50%	C2: Essential or Few alternatives	VCIA	VHIA	VIA
<b>PENICILLINS</b> <b>NATURAL PENICILLINS</b> Benzylpenicillin Penethamate hydroxide Penicillin procaine  <b>AMINOPENICILLINS</b> Mecillinam  <b>AMINOPENICILLINS</b> Amoxicillin Ampicillin Hetacillin  <b>AMINOPENICILLIN PLUS BETA-LACTAMASE INHIBITOR</b> Amoxicillin_Clavulanic Acid  <b>CARBOXYPENICILLINS</b> Ticarcillin Tobicillin  <b>UREIDO PENICILLIN</b> Aspoxicillin  <b>PHENOXYPENICILLINS</b> Phenoxymethylpenicillin Phenethicillin  <b>ANTISTAPHYLOCOCCAL PENICILLINS</b> Cloxacillin Dicloxacillin Nafcillin Oxacillin	AVI, BOV, CAM, CAP, EQU, LEP, OVI, SUI BOV, SUI BOV, CAM, CAP, EQU, OVI, SUI  BOV, SUI  AVI, BOV, CAP, EQU, OVI, PIS, SUI AVI, BOV, CAP, EQU, OVI, PIS, SUI BOV  AVI, BOV, CAP, EQU, OVI, SUI  EQU PIS  BOV, SUI  AVI, SUI EQU  BOV, CAP, EQU, OVI, SUI BOV, CAP, OVI BOV, CAP, OVI BOV, CAP, EQU, OVI	87,1%	Penicillins are used in the treatment of septicaemias, respiratory and urinary tract infections. They are very important in the treatment of many diseases in a broad range of animal species. Few economical alternatives are available.	Y	Y	Y		
<b>PHENICOLS</b> Florphenicol  Thiamphenicol	AVI, BOV, CAP, EQU, LEP, OVI, PIS, SUI AVI, BOV, CAP, OVI, PIS, SUI	51,4%	Phenicols are of particular importance in treating some fish diseases, in which there are no or very few treatment alternatives. Phenicols also represent a useful alternative in respiratory infections of cattle, swine and poultry. Phenicols, and in particular florfenicol, are used to treat pasteurellosis in cattle and pigs.	Y	Y	Y		

ANTIMICROBIAL FAMILY	SPECIES	% quotations	Specific comments	C1: Quotation > 50%	C2: Essential or Few alternatives	VCIA	VHIA	VIA
<b>PLEUROMUTILINS</b> Tiamulin Valnemulin	AVI, CAP, LEP, OVI, SUI AVI, SUI	48,6%	Pleuromutilins are used exclusively in animals. The class of pleuromutilins is essential against respiratory infections in pigs and poultry. <b>This family is critically important against swine dysentery (<i>Brachyspira hyodysenteriae</i>)</b> because there are no alternatives in many regions.	N	Y		Y	
<b>POLYPEPTIDES</b> Enramycin Gramicidin Bacitracin  <b>POLYPEPTIDES CYCLIC</b> Colistin Polymixin	AVI, SUI EQU AVI, BOV, LEP, SUI  AVI, BOV, CAP, EQU, LEP, OVI, SUI BOV, CAP, EQU, LEP, OVI, AVI	64,3%	Bacitracin is used against necrotic enteritis in poultry where available. Polypeptides are indicated in septicaemias, colibacillosis, salmonellosis, and urinary infections. Cyclic polypeptides are widely used against Gram negative digestive infections.	Y	N		Y	
<b>QUINOLONES</b> <b>QUINOLONES 1G</b> Flumequin  Miloxacin Nalidixic acid Oxolinic acid  <b>QUINOLONES 2G (FLUOROQUINOLONES)</b> Ciprofloxacin Danofloxacin  Difloxacin Enrofloxacin  Marbofloxacin  Norfloxacin  Ofloxacin Orbifloxacin	AVI, BOV, CAP, EQU, LEP, OVI, PIS, SUI  PIS BOV AVI, BOV, LEP, PIS, SUI  AVI, BOV, SUI AVI, BOV, CAP, LEP, OVI, SUI  AVI, BOV, LEP, SUI AVI, BOV, CAP, EQU, LEP, OVI, PIS, SUI  AVI, BOV, EQU, LEP, SUI  AVI, BOV, CAP, LEP, OVI, SUI  AVI, SUI BOV, SUI	68,6%	Quinolones of the 1st and of 2nd generations are used in septicemias and in infections such as colibacillosis, which cause serious losses in poultry, cattle, swine, fish and other species. Fluoroquinolones have no equally efficacious alternative in the treatment of chronic respiratory disease in poultry ( <i>E. coli</i> )	Y	Y	Y		
<b>QUINOXALINES</b> Carbadox	SUI	4,3%	Quinoxalines (carbadox) is used for digestive disease of pigs (e.g. swine dysentery).	N	N			Y

ANTIMICROBIAL FAMILY	SPECIES	% quotations	Specific comments	C1: Quotation > 50%	C2: Essential or Few alternatives	VCIA	VHIA	VIA
<b>SULFONAMIDES</b>								
Sulfachlorpyridazine	AVI, SUI	70%	Several sulfonamides alone or in combination with diaminopyrimidines are very essential because of diseases covered (bacterial, coccidial and protozoal infections), and use in multiple animal species. This is essential for treatment of cattle, pigs, sheep, poultry, fish or other species. Few economical alternatives are available.	Y	Y	Y		
Sulfadiazine	BOV, CAP, OVI, SUI							
Sulfadimerazin	AVI, BOV, LEP							
Sulfadimethoxine	AVI, BOV, CAP, EQU, LEP, OVI, PIS, SUI							
Sulfadimidine	AVI, BOV, CAP, EQU, LEP, OVI, SUI							
Sulfadoxine	EQU, SUI							
Sulfafurazole	PIS							
Sulfaguandine	CAP, OVI							
Sulfamethazine	SUI							
Sulfadimethoxazole	AVI, BOV, SUI							
Sulfamethoxine	AVI, PIS, SUI							
Sulfamonomethoxine	AVI, PIS, SUI							
Sulfanilamide	BOV, CAP, OVI							
Sulfaquinoxaline	AVI, BOV, CAP, LEP, OVI							
<b>SULFONAMIDES+DIAMINOPYRIMIDINES</b>								
Sulfamethoxypyridazine	AVI, BOV, EQU							
Trimethoprim+Sulfonamide	AVI, BOV, CAP, EQU, LEP, OVI, PIS, SUI							
<b>DIAMINOPYRIMIDINES</b>								
Baquiloprim	SUI							
Trimethoprim	AVI, BOV, CAP, EQU, LEP, OVI, SUI							
<b>STREPTOGRAMINS</b>								
Virginiamycin	AVI, BOV, OVI, SUI	5.7%	Virginiamycin is an important antimicrobial in the prevention of necrotic enteritis ( <i>Clostridium perfringens</i> )	N	N			Y
<b>TETRACYCLINES</b>								
Chlortetracycline	AVI, BOV, CAP, EQU, LEP, OVI, SUI	87,1%	Tetracyclines are very important in the treatment of many bacterial and chlamydial diseases in a broad range of animal species. There are no alternatives to tetracyclines in the treatment of animals against heartwater ( <i>Ehrlichia ruminantium</i> ) and anaplasmosis ( <i>Anaplasma marginale</i> ). Few economical alternatives are available	Y	Y	Y		
Doxycycline	AVI, BOV, CAM, CAP, EQU, LEP, OVI, PIS, SUI							
Oxytetracycline	API, AVI, BOV, CAM, CAP, EQU, LEP, OVI, PIS, SUI							
Tetracycline	API, AVI, BOV, CAM, CAP, EQU, LEP, OVI, PIS, SUI							



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12 rue de Prony 75017 Paris France • tel.: 33(0)1 44 15 18 88 • fax: 33(0)1 42 67 09 87 • [ois@ois.int](mailto:ois@ois.int) • [www.ois.int](http://www.ois.int)