OIE STANDARDS AND GUIDELINES FOR VETERINARY MEDICINAL PRODUCTS

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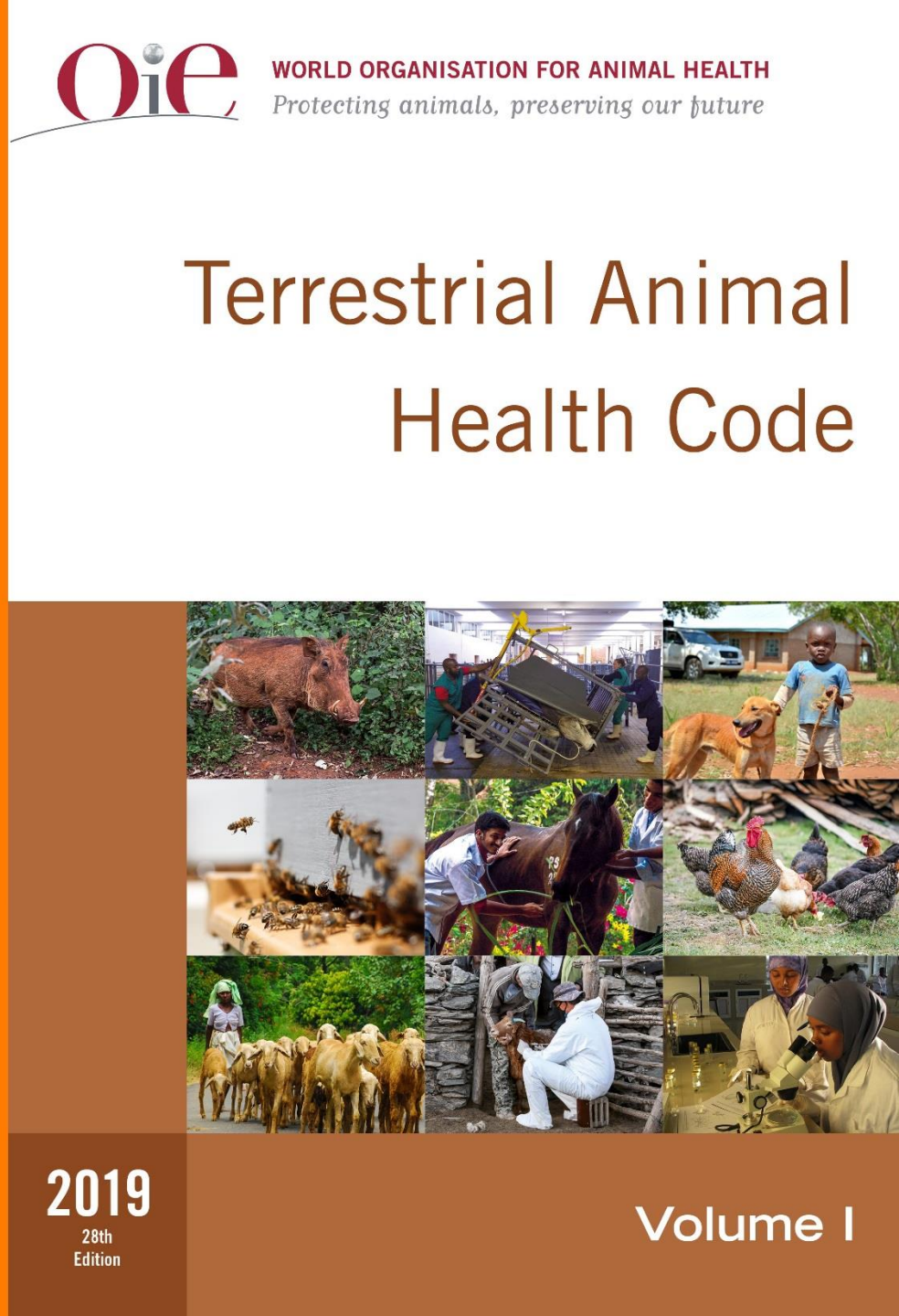
Outline

Terrestrial Code Chapter 3.4
Veterinary legislation

- Update on OIE standards and guidelines related to vaccines
- Update on OIE standards and guidelines related to antimicrobial resistance (AMR)
- Currently no OIE standards or guidelines related to antiparasitic products



Update on OIE standards and guidelines related to vaccines

Update on OIE standards and guidelines related to vaccines

OIE Technical standards for manufacturing and quality control of veterinary vaccines.

- Compilation of seven vaccine-related chapters from the *Terrestrial Code* and *Terrestrial Manual.* Published in 2019.
- Handbook intended to serve as a readily accessible technical resource for vaccine manufacturers and regulatory officials to
  - Advance global awareness and implementation of the established science-based standards for the quality, safety, and efficacy of veterinary vaccines
  - Maximize the quality and availability of veterinary vaccines that are required for prevention and control of animal diseases.

Available for purchase from OIE online bookshop as a paperback book or downloadable pdf file at
http://web.oie.int/boutique/index.php

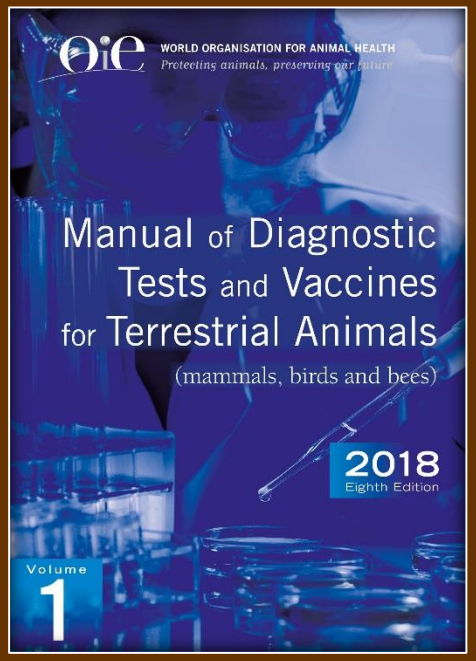
http://web.oie.int/boutique/index.php

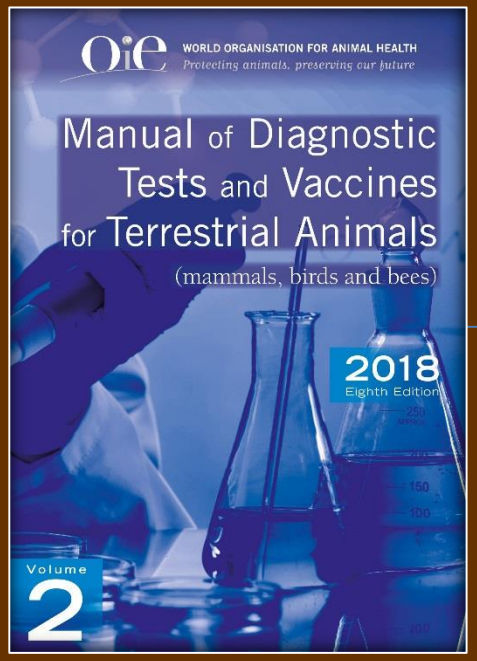
Available in English, French, or Spanish

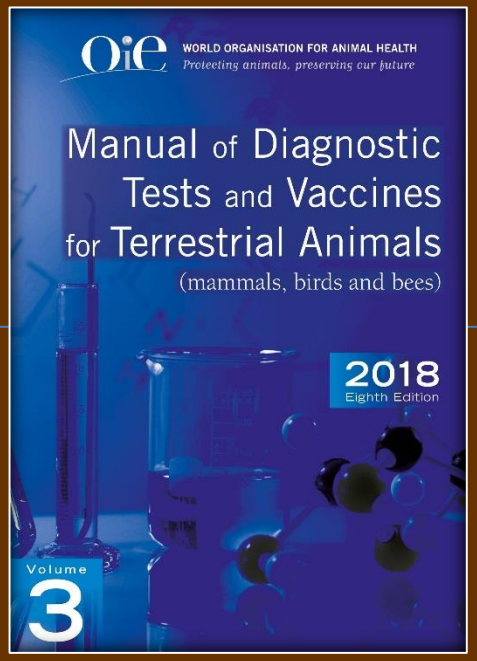
Update on OIE standards and guidelines related to vaccines

	Glossary of Terms
Chapter 1.1.8	Principles of Veterinary Vaccine Production (2018)
Chapter 1.1.9	Tests for Sterility and Freedom from Contamination of Biological Materials Intended for Veterinary Use (2017)
Chapter 1.1.10	Vaccine Banks (2016)
Section 2.3	Recommendations for the Manufacture of Vaccines (2016)
Chapter 2.3.3	Minimum Requirements for the Organisation and Management of a Vaccine Manufacturing Facility (2016)
Chapter 2.3.4	Minimum Requirements for the Production and Quality Control of Vaccines (2018)
Chapter 2.3.5	Minimum Requirements for Aseptic Production in Vaccine Manufacture (2016)

Terrestrial Manual is available online at
http://www.oie.int/standard-setting/terrestrial-manual/access-online/







TERRESTRIAL MANUAL

Eighth Edition published in 2018 in three volumes

Part 1 • General Standards chapters available online in English, French and Spanish

Part 2 • Specific Recommendations chapters available online in English, French and Spanish

Resolution No. 14

Amendment to the *Manual of Diagnostic Tests and Vaccines for Terrestrial Animals*

Chapter 1.1.8

Principles of veterinary vaccine production
(VICH guidelines 50 and 55 referenced in Chapter 2.2, criteria to characterize thermotolerance claims)

Chapter 2.3.2

The role of official bodies in the international regulation of veterinary biologicals
(EU, Japan USA and VICH texts updated)

Chapter 2.3.4

Minimum requirements for the production and quality control of vaccines

(Adopted by the World Assembly of OIE Delegates during their 86th General Session May 2018)

Recent update on OIE standards and guidelines on vaccines

Waiving or not waiving Target Animal Batch Safety Tests (TABST)?

- **The OIE Biological Standard Commission,** concluded that, rather than completely eliminating all references to the TABST, references to the TABST in the *Terrestrial Manual* should be revised to include a note that the prescribed TABST could be eliminated in situations where other quality control measures are in place.
- BSC implemented its decision regarding TABST by modifying chapters 1.1.8 and 2.3.4, and amending the relevant disease chapters when they are updated.

Update on OIE standards and guidelines related to vaccines

Reasons

- Potential variability of quality assurance systems currently employed by manufacturers in OIE Member Countries

- Potential for residual toxicity of some vaccines

It would be inappropriate to completely eliminate all references to the TABST in OIE guidelines such as the *Terrestrial Manual*

Update on OIE standards and guidelines related to vaccines

Biological Standards Commission

Developed a revised glossary definition and expanded guidance for characterizing thermotolerant vaccine in the *Terrestrial Manual.*

*"**Thermotolerant**: For vaccines, the term is used to describe the ability to retain protective immunogenicity after exposure to temperatures above the storage temperature required according to the manufacturer's recommendations. Claims of thermotolerance must be supported by data."*

Further information is provided in Chapter 1.1.8 Principles of Veterinary Vaccine Production. Stability Tests.

Update on OIE standards and guidelines related vaccines

To determine the minimum standards for thermotolerant vaccines, participants at the Peste des petits ruminants (PPR) - Global Eradication Programme Thermotolerant PPR Vaccines Workshop Rome, December 2017, agreed that minimum requirements should be set for manufacturers to be able to use the term “thermotolerant vaccine”.

AU-PANVAC was asked to develop a draft Standard Operating Procedure to describe the process for testing thermotolerance of PPR vaccines.

Update on OIE standards and guidelines related to vaccines

Thermotolerance Test for PPR Vaccines

Purpose: This procedure describes the process for the titration of PPR vaccine for thermotolerance testing of veterinary vaccines.

Performance of the test:

- Vaccines should be placed at any of the three temperature conditions for the determination of thermotolerance, i.e. 2-8ºC, 25ºC or 40ºC.
- Rapid evaluation of vaccines by AU-PANVAC to be carried out at 40ºC.
    - Conduct virus titrations at day 0,1, 2, 3, 4 and 5.
    - Titrations should be carried out at approximately same time each day.
    - Testing period can be extended if there is a need for further information.

Storage	Standard Cold Chain	Room	Field
Temperature	2 - 8° C	25° C	40° C
Period	2 years	10 days	5 days

Draft for consultation

African Union

Pan African Veterinary Vaccine Centre

(AU-PANVAC)

Recommended procedure for

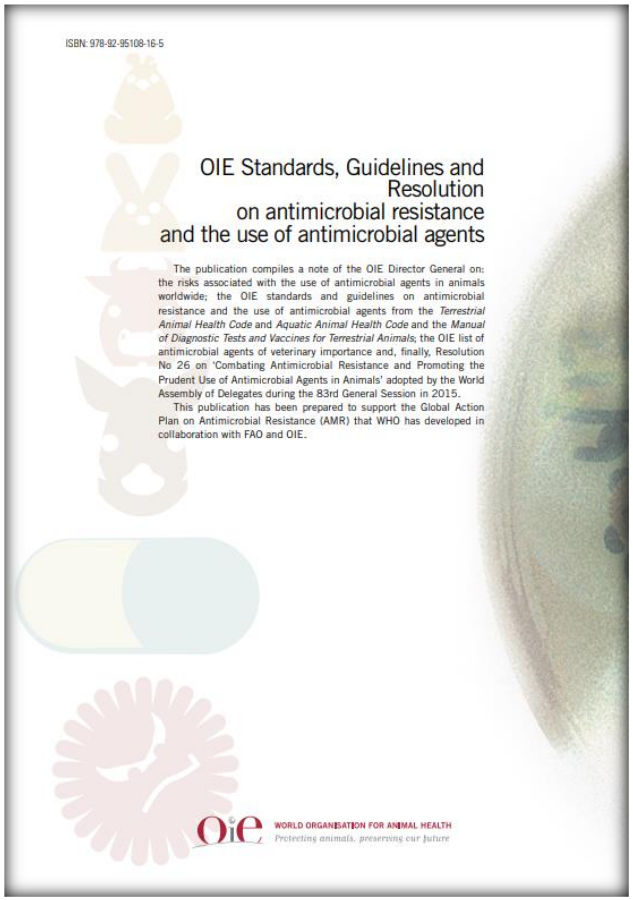
Peste des Petits Ruminants (PPR) Vaccine

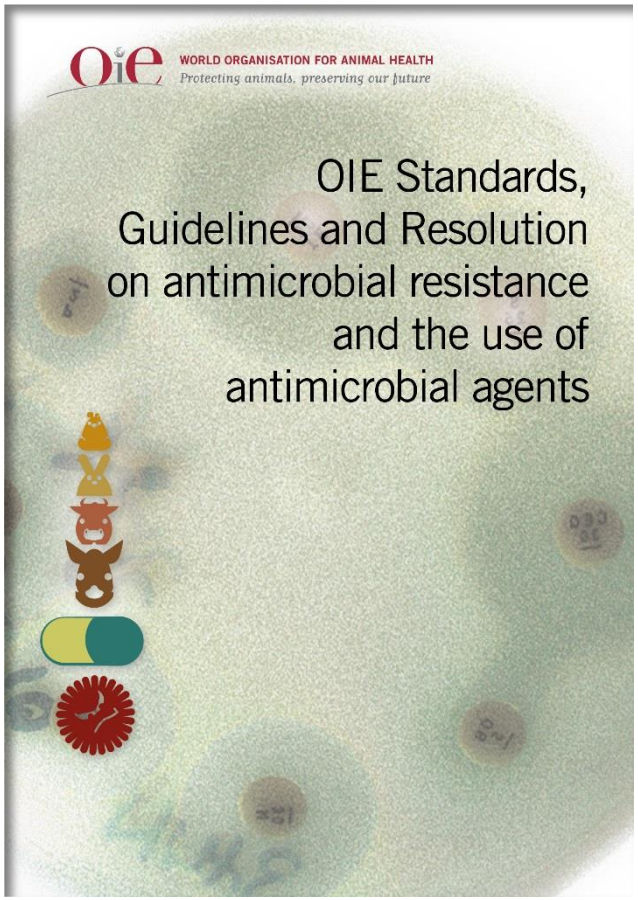
THERMOTOLERANCE TEST

As part of the PPR Global Eradication Program

Update on standards and guidelines related to antimicrobial resistance (AMR)

Update on OIE standards and guideline related to antimicrobial resistance (AMR)

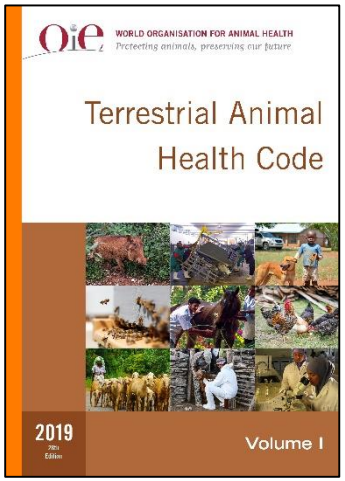




http://www.oie.int/fileadmin/home/eng/Media_Center/docs/pdf/PortailAMR/EN-book-AMR.PDF

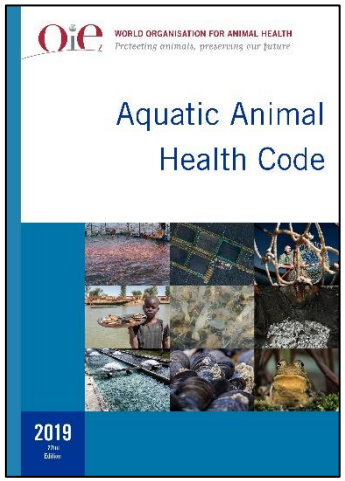
Update on OIE standards and guidelines related to AMR

Terrestrial Animal Health Code



- Ch.6.7. **Introduction** to the recommendations for controlling antimicrobial resistance
- Ch.6.8. Harmonisation of national AMR **surveillance and monitoring** programmes (updated in May 2018)
- Ch.6.9. **Monitoring of the quantities and usage patterns** of antimicrobial agents used in food-producing animals (Agreement on definitions)
- Ch.6.10. **Responsible and prudent use** of antimicrobial agents in veterinary medicine
- Ch.6.11. **Risk analysis** for AMR arising from the use of antimicrobial agents in animals

Aquatic Animal Health Code



- Ch.6.2. Principles for **responsible and prudent use** of antimicrobial agents in aquatic animals
- Ch.6.3. **Monitoring of the quantities and usage patterns** of antimicrobial agents used in aquatic animals
- Ch.6.4. Development and harmonisation of national AMR **surveillance and monitoring** programmes for aquatic animals
- Ch.6.5. **Risk analysis** for AMR arising from the use of antimicrobial agents in aquatic animals

Update on OIE standards and guidelines related to AMR
Definitions adopted in May 2018

Veterinary medical use of antimicrobial agents: means the administration of an antimicrobial agent to an individual or a group of animals to treat, control or prevent infectious disease from the *Terrestrial Code, Chapter 6.9* :

01

To treat: means to administer an antimicrobial agent to an individual or a group of animals showing clinical signs of an infectious disease

02

To control: means to administer an antimicrobial agent to a group of animals containing sick animals and healthy animals (presumed to be infected), to minimize or resolve clinical signs and to prevent further spread of the disease

03

To prevent: means to administer an antimicrobial agent to an individual or a group of animals at risk of acquiring a specific infection or in a specific situation where infectious disease is likely to occur if the drug is not administered.

Update on OIE standards and guidelines related to AMR

The OIE International Committee unanimously adopted the List of Antimicrobial Agents of Veterinary Importance at its 75th General Session in May 2007 (Resolution No. XXVIII).

This list was further updated and adopted in May 2013 and May 2015 by the World Assembly of OIE Delegates. WHO list of critically important antimicrobials was took into consideration

OIE List of Antimicrobial Agents of Veterinary Importance: Recommendations (additional adopted in May 2018 updated May 2019)

List of antimicrobial agents of veterinary importance

https://www.oie.int/fileadmin/Home/eng/Our_scientific_expertise/docs/pdf/AMR/A_OIE_List_antimicrobials_July2019.pdf

Recent update on OIE standards and guidelines on AMR

OIE LIST OF ANTIMICROBIAL AGENTS OF VETERINARY IMPORTANCE

The OIE[1] International Committee unanimously adopted the List of Antimicrobial Agents of Veterinary Importance at its 75th 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[2]/OIE/WHO[3] 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 antimicrobial agents in veterinary medicine and that WHO should also develop such a list of critically important antimicrobial agents 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.

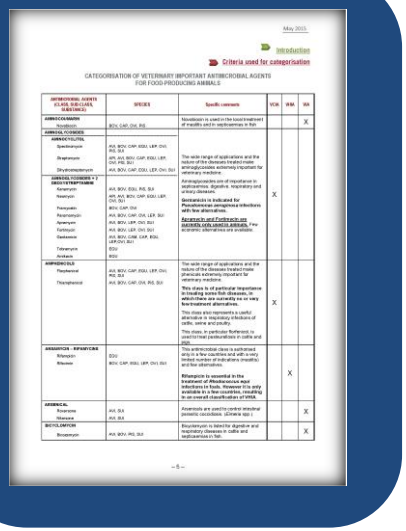
Responding to this recommendation, the OIE decided to address this task through its existing ad hoc Group on antimicrobial resistance. The terms of reference, aim of the list and methodology were discussed by the ad hoc Group since November 2004 and were subsequently endorsed by the Biological Standards 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 a 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 analysed 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 antimicrobial agents of veterinary importance 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.

1 OIE: World Organisation for Animal Health
2 FAO: Food and Agriculture Organisation of the United Nations
3 WHO: World Health Organisation



Introduction
Criteria used for categorisation

CATEGORISATION OF VETERINARY IMPORTANT ANTIMICROBIAL AGENTS FOR FOOD-PRODUCING ANIMALS

ANTIMICROBIAL AGENTS (CLASS, SUBCLASS, SUBSTANCE)	SPECIES	Specific comments	VCIA	HVIA	VIA
AMINOCYANDIN		Nourobiocin is used in the local treatment of mastitis and in septicaemias in fish			X
Nourobiocin	BOV, CAD, OVI, EQU				
AMINOGLYCOSIDES					
AMINOCYCLITOL					
Spectinomycin	AVI, BOV, CAP, EQU, LEP, OVI, PIG, SUI				
Streptomycin	AVI, BOV, CAP, EQU, LEP, OVI, PIG, SUI	The wide range of applications and the nature of the diseases treated make aminoglycosides extremely important for veterinary medicine.			
Dihydrostreptomycin	AVI, BOV, CAP, EQU, LEP, OVI, SUI				
AMINOGLYCOSIDES + 2 DEOXYSTREPTAMINE		Aminoglycosides are of importance in septicaemias, digestive, respiratory and urinary diseases.			
Gentamycin	AVI, BOV, EQU, PIG, SUI	**Gentamicin is indicated for Pseudomonas aeruginosa infections with few alternatives.**			
Neomycin	AVI, BOV, CAP, CAT, EQU, LEP, OVI, SUI	**Apramycin and Paromomycin are used in veterinary medicine only.** Few antibiotic alternatives are available.	X		
Framycetin	AVI, BOV, CAP, CAT, EQU, LEP, OVI, SUI				
Paromomycin	AVI, BOV, CAP, CAT, EQU, LEP, OVI, SUI				
Apramycin	AVI, BOV, LEP, OVI, SUI				
Kanamycin	AVI, BOV, LEP, OVI, SUI				
Gentamicin	AVI, BOV, CAM, CAP, EQU, LEP, OVI, SUI				
Tobramycin	EQU				
Amikacin	EQU				
AMPHENICOLS					
Thiamphenicol	AVI, BOV, CAP, EQU, LEP, OVI, PIG, SUI	The wide range of applications and the nature of the diseases treated make phenicols extremely important for veterinary medicine.			
Florfenicol	AVI, BOV, CAP, OVI, PIG, SUI	**This class is of particular importance in treating some fish diseases, in which there are currently six or very few treatment alternatives.**	X		
		This class also represents a useful alternative in respiratory infections of cattle, swine and poultry.			
		This class, in particular florfenicol is registered to treat pasteurellosis in cattle and pigs.			
ANSAMYCIN – RIFAMYCINS					
Rifampicin	EQU	This antimicrobial class is authorised only in a few countries and with a very limited number of indications (mastitis) and few alternatives.			
Rifaximin	BOV, CAP, EQU, LEP, OVI, SUI	**Rifampicin is essential in the treatment of Mycobacterial infections of Equids. However it is only available in a few countries, resulting in an overall classification of VHIA**		X	
ARSENICAL					
Roxarsone	AVI, SUI	Arsenicals are used for control intestinal parasitic coccidiosis. (Chlamydia spp.)			X
Nitarsone	AVI, SUI				
BICYCLAMYCIN					
Bicozamycin	AVI, BOV, PIG, SUI	Bicozamycin is listed for digestive and respiratory diseases in cattle and septicaemias in fish			X

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OIE List of Antimicrobial Agents of Veterinary Importance

- Any use of antimicrobial agents in animals should be in accordance with OIE standards on responsible and prudent use.This does not include the use of antimicrobial agents for growth promotion in the absence of risk analysis.

- The classes in the WHO category of Highest Priority Critically Important Antimicrobials should be the highest priorities for countries in phasing out use of antimicrobial agents as growth promotors

Update on OIE standards and guidelines related to AMR

OIE List of Antimicrobial Agents of Veterinary Importance (May 2018)

Among the Veterinary Critically Important Antimicrobial Agents, some are also of critical importance for human health (third and fourth generation *Cephalosporins*, and *Fluoroquinolones*).

Colistin has been moved in 2016 to the WHO category of Highest Priority Critically Important Antimicrobials.

Therefore these two classes and *Colistin* should:

- **Not to be used** as preventive treatment in feed or water or in absence of clinical signs
- **Not to be used** as first line treatment, unless justified and bacteriological test
- **Extra label/off label limited** and reserved for instances no alternatives are available
- Urgently prohibit their use as **growth promoters**

Conclusion

1 We made a **significant progress** since December 2017, (Regional Seminar for OIE National Focal Points for Veterinary Products (Cycle V) Bangkok , 20 – 22 March 2018)

2 OIE staff and Focal Points for Veterinary Products need to continue to **work together with partners and stakeholders** to have **high quality, practical global standards and guidelines** for veterinary medicinal products (VMPs)

3 How can the OIE **contribute** to support Member Countries to implement the standards and guidelines for VMPs?

4 Do we need **new** or **updated** OIE standards and guidelines for VMPs?

Thank you for your attention!

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WORLD ORGANISATION FOR ANIMAL HEALTH
Protecting animals, preserving our future