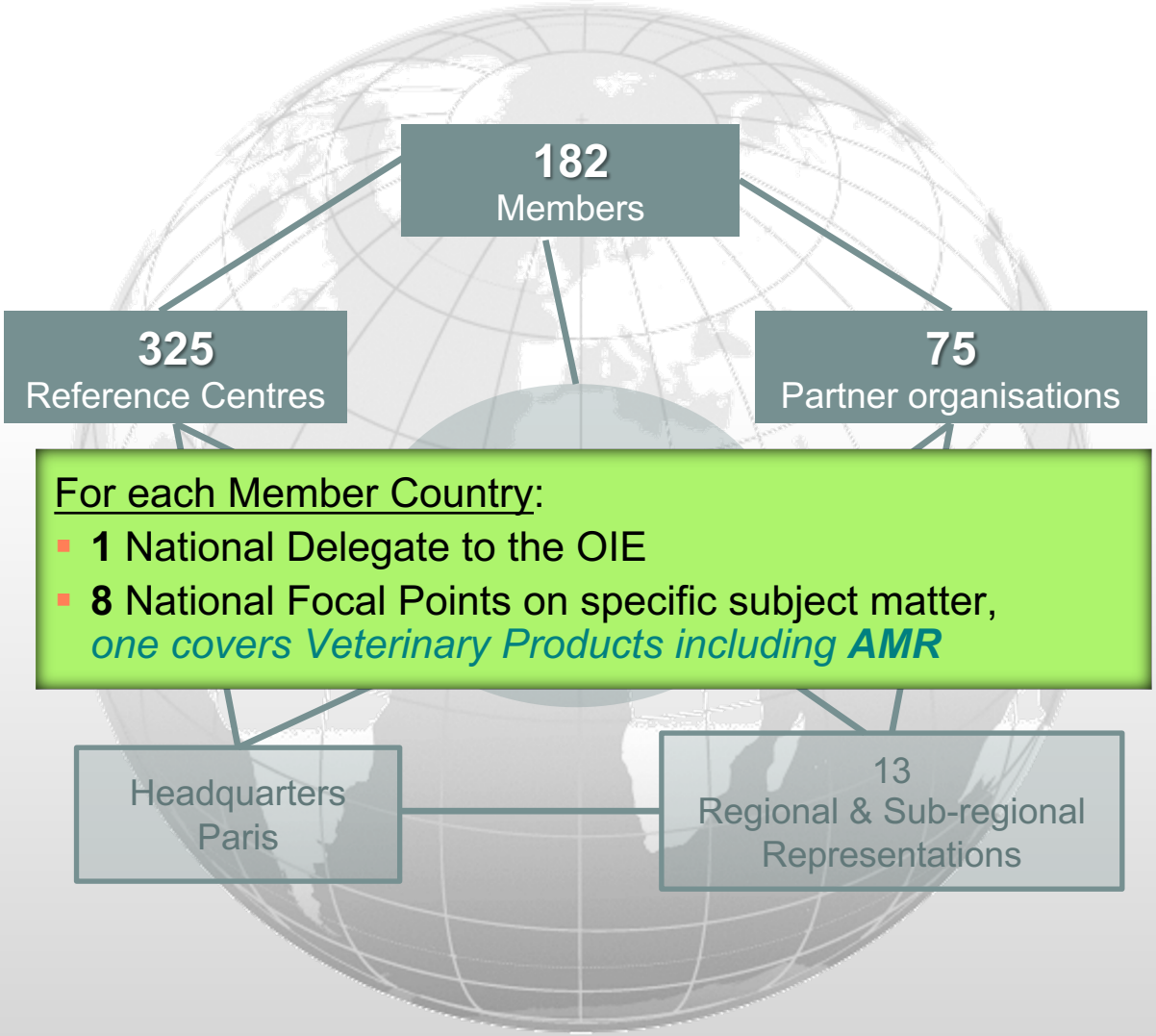
Dr Jorge Pinto Ferreira
Deputy Head, Antimicrobial Resistance and Veterinary Products Department

OIE AMR & AMU standards and activities

FAO/WHO/CODEX webinar on FAO and WHO activities to support monitoring and surveillance of antimicrobials resistance in the food and agriculture sectors
March 16th, 2021

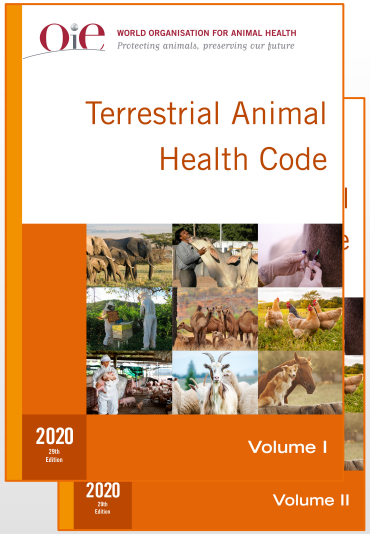
World Organisation for Animal Health (OIE): 2021

- An Intergovernmental Organisation
- Mandate to Improve Animal Health, Welfare and Veterinary Public Health
- **Sets international standards recognised by the WTO**



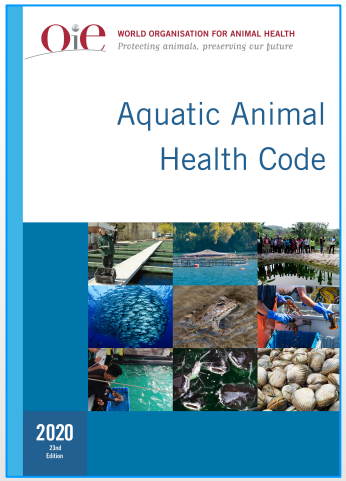
OIE Standards related to AMR and AMU

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

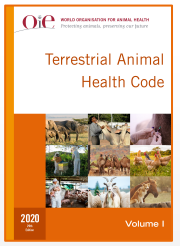
AMU standards

Monitoring of the quantities and usage patterns

Terrestrial Code Chapter 6.8. / Article 6.9.1;

- *The purpose of the recommendations in this chapter is to describe an approach to the monitoring of the quantities of antimicrobial agents used in food-producing animals*.

- *In order to evaluate antimicrobial exposure in food-producing animals, quantitative information should be collected to monitor usage patterns by animal species, antimicrobial agents or class of antimicrobial agents, route of administration and type of use: veterinary medical (to treat, control or prevent infectious disease) or non veterinary medical (including growth p*romotion).



Terrestrial Code: Chapter 6.8: https://www.oie.int/index.php?id=169&L=0&htmfile=chapitre_antibio_monitoring.htm

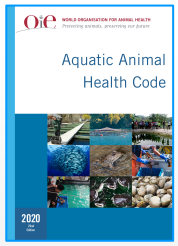
Monitoring of the quantities and usage patterns

Aquatic Code Chapter 6.3. / Article 6.3.1;

- *The purpose of these recommendations is to describe approaches to the monitoring of quantities of antimicrobial agents used in aquatic animals, including species reared for food and ornamental purposes.*

- These recommendations are intended for use in the collection of objective and quantitative information to evaluate usage patterns by antimicrobial class, route of administration and *aquatic animal* species in order to evaluate exposure of microorganisms to *antimicrobial agents*

- The collection of data on the use of *antimicrobial agents* in *aquaculture* may be constrained in some countries by the lack of available resources, lack of accurately labelled products, poorly documented distribution channels and lack of professional consultation or supervision.



Aquatic Code: Chapter 6.3
https://www.oie.int/index.php?id=171&L=0&htmfile=chapitre_antibio_quantities_usage_patterns.htm

AMR standards

CHAPTER 6.8.

HARMONISATION OF NATIONAL ANTIMICROBIAL RESISTANCE SURVEILLANCE AND MONITORING PROGRAMMES

Table 1. Examples of sampling sources, sample types and output

Source	Type	Output	Additional information required or additional stratification
Herd or flock of origin	Faeces or bulk milk	Prevalence of resistant bacteria originating from animal populations (of different production types). Relationship between resistance and antimicrobial use	Age categories, production types, etc. Antimicrobial use over time
Slaughterhouse/Abattoir	Faeces	Prevalence of resistant bacteria originating from animals at slaughter	
	Caeca or intestines	As above	
	Carcass	Prevalence of resistant bacteria after carcass dressing, representative of the hygiene of the process and the contamination during slaughter	
Processing, packing	Food products	Prevalence of resistant bacteria after processing, representative of the hygiene of the process and the contamination during processing and handling	
Point of sale (Retail)	Food products	Prevalence of resistant bacteria originating from food, exposure data for consumers	
Various origins	Animal feed	Prevalence of resistant bacteria originating from animal feed, exposure data for animals	
Various origins	Environment	Occurrence of resistant bacteria originating from the animal-immediate or the wider environment	

Table 2. Examples of target animal species and animal bacterial pathogens that may be included in resistance surveillance and monitoring programmes

Source	Respiratory pathogens	Enteric pathogens	Udder pathogens	Other pathogens
Cattle	*Pasteurella multocida*	*Escherichia coli*	*Staphylococcus aureus*	
	Mannheimia haemolytica	*Salmonella* spp.	*Streptococcus* spp.	
Pigs	*Actinobacillus pleuropneumoniae*	*Escherichia coli*		*Streptococcus suis*
		Salmonella spp.		
Poultry		*Salmonella* spp.		*Escherichia coli*

Source: https://www.oie.int/index.php?id=169&L=0&htmfile=chapitre_antibio_harmonisation.htm

CHAPTER 6.4.

DEVELOPMENT AND HARMONISATION OF NATIONAL ANTIMICROBIAL RESISTANCE SURVEILLANCE AND MONITORING PROGRAMMES FOR AQUATIC ANIMALS

Article 6.4.5.

Design of surveillance and monitoring programmes for microorganisms in or on aquatic animal products intended for human consumption

For details of the sampling protocols and analytical procedures required for surveillance and monitoring programmes for antimicrobial resistance in microorganisms present in *aquatic animal products* intended for human consumption, Chapter 6.8. of the OIE *Terrestrial Animal Health Code* should be consulted.

It is important to note that the word 'commensal' as used in Chapter 6.8. of the OIE *Terrestrial Animal Health Code* has less relevance due to the transient nature of the intestinal microflora of *aquatic animals*. The inclusion of intestinal microflora in surveillance and monitoring programmes should only be considered when there is evidence that these are resident for sufficient time to be a risk factor affected by *antimicrobial agents*.

When designing a sampling programme it is important to consider that contamination of *aquatic animal products* with resistant microorganisms that are capable of infecting humans may arise from sources other than the *aquatic animal*. All sources of contamination should be taken into account, for example entry of raw manure into the aquatic environment. The number of such microorganisms associated with *aquatic animals* is much less than that found in terrestrial animals. However the following species should be included, as a minimum, in a surveillance and monitoring programme:

1) *Salmonella* spp.;
2) *Vibrio parahaemolyticus*;
3) *Listeria monocytogenes*.

Source: https://www.oie.int/index.php?id=171&L=0&htmfile=chapitre_antibio_development_harmonisation.htm

Table 1. *Phenotypic susceptibility testing methods available and their features*

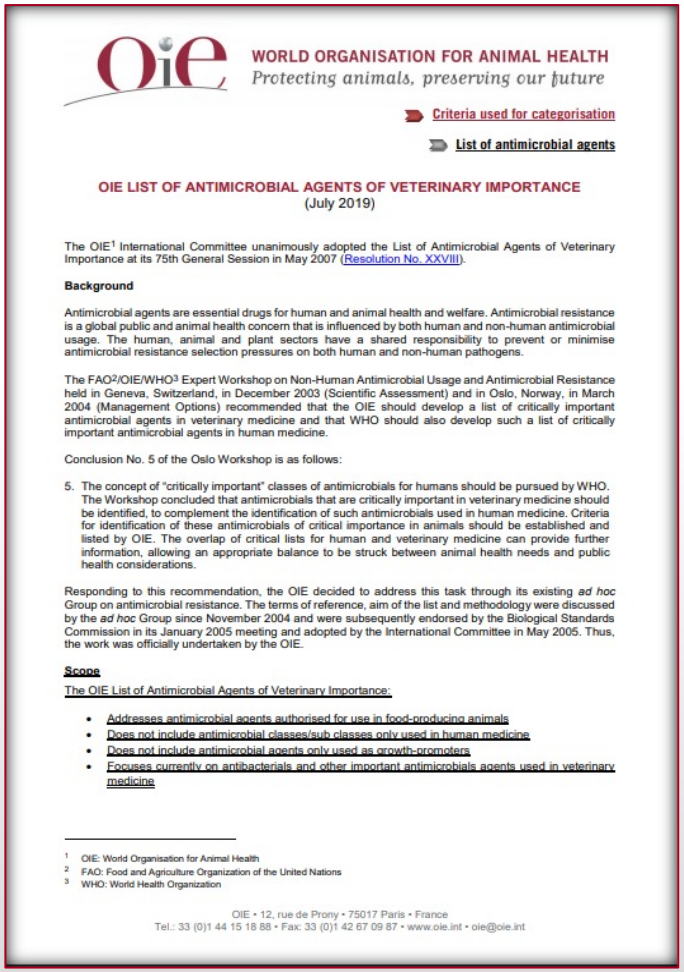
Susceptibility testing method	International standard available	Published methods available	Use in national surveillance programmes	Use in susceptibility testing for therapeutic purposes	Breakpoints that may be applied	Test output	Comparability of outputs	Features
Broth (micro) dilution MIC determination	Yes (ISO 20776-1), CLSI, EUCAST	Yes (CLSI, EUCAST)	Yes, broth microdilution MIC determination is preferred	Yes	Clinical breakpoints or epidemiological cut-off values (ECOFFs)	MIC	High	Current reference method. Recording MIC values allows interpretation of the test outputs using different breakpoints (e.g. clinical breakpoint or ECOFF), as well as re-evaluation of historical data if changes occur to breakpoints and evaluation of shifts in MIC. Numerous national surveillance programmes adopt this method. The MIC value can sometimes indicate the likely mechanism of resistance (e.g. high-level amikacin resistance and rRNA methylases) or provide an epidemiological marker. Currently, this is the only method suitable for determining susceptibility to colistin.
Agar dilution MIC determination	No	Yes (CLSI, EUCAST)	Not widely used	Yes	Clinical breakpoints or ECOFFs	MIC	Dependent on congruity of methods used	Reference method. The breakpoints appropriate for broth dilution may not be directly applicable to agar dilution. Currently used in particular for testing certain fastidious organisms.
Breakpoint method	No	Yes (scientific literature)	Not widely used	Yes	The test is performed at a set breakpoint	Resistant or susceptible at selected breakpoint	Dependent on congruity of methods used	Changes to breakpoints in this method result in the inability to interpret historical data. Shifts in susceptibility within the S or R categories cannot be detected. The breakpoint method relies on the growth or absence of growth of bacteria in broth or on agar containing an antimicrobial at a single (breakpoint) dilution.
Gradient strip method	No	Yes (manufacturer)	Not widely used	Yes	Clinical breakpoints or ECOFFs	MIC	High	Provide a convenient alternative method of determining MIC with minimal additional equipment required.
Disc diffusion test	No	Yes (CLSI, EUCAST) A number of different methods are available. These are not in general equivalent.	May be used, but broth microdilution MIC determination is preferred	Yes	Clinical breakpoints (ECOFFs are also available for the EUCAST disc diffusion method).	Diameter of zone of inhibition, interpreted as resistant or susceptible according to test guidelines	Dependent on congruity of methods used	Frequently used to provide an indication of susceptibility for therapeutic purposes. Versatile in that different discs can be used, according to the antimicrobials authorised for treatment. Different methods are not usually equivalent (zone sizes obtained using one method cannot be interpreted using criteria from another, different method). The collection of zone size data can allow shifts in susceptibility to be detected. Disc diffusion methods may be harmonised to a degree with other methods, by using the same breakpoint.

The susceptibility testing method selected should provide details of the method, appropriate controls and quality control ranges and breakpoints. The comparability of outputs obtained in surveillance programmes is not only dependent on the laboratory methodology used but is also dependent on the target population of livestock included in the study and method of sampling.

Source: https://www.oie.int/fileadmin/Home/eng/Health_standards/tahm/2.01.01_ANTIMICROBIAL.pdf

AMU activities

OIE List of Antimicrobial Agents of Veterinary Importance:



WORLD ORGANISATION FOR ANIMAL HEALTH
Protecting animals, preserving our future

Criteria used for categorisation

List of antimicrobial agents

OIE LIST OF ANTIMICROBIAL AGENTS OF VETERINARY IMPORTANCE
(July 2019)

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.

Scope

The OIE List of Antimicrobial Agents of Veterinary Importance:

- Addresses antimicrobial agents authorised for use in food-producing animals
- Does not include antimicrobial classes/sub classes only used in human medicine
- Does not include antimicrobial agents only used as growth-promoters
- Focuses currently on antibacterials and other important antimicrobials agents used in veterinary medicine

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

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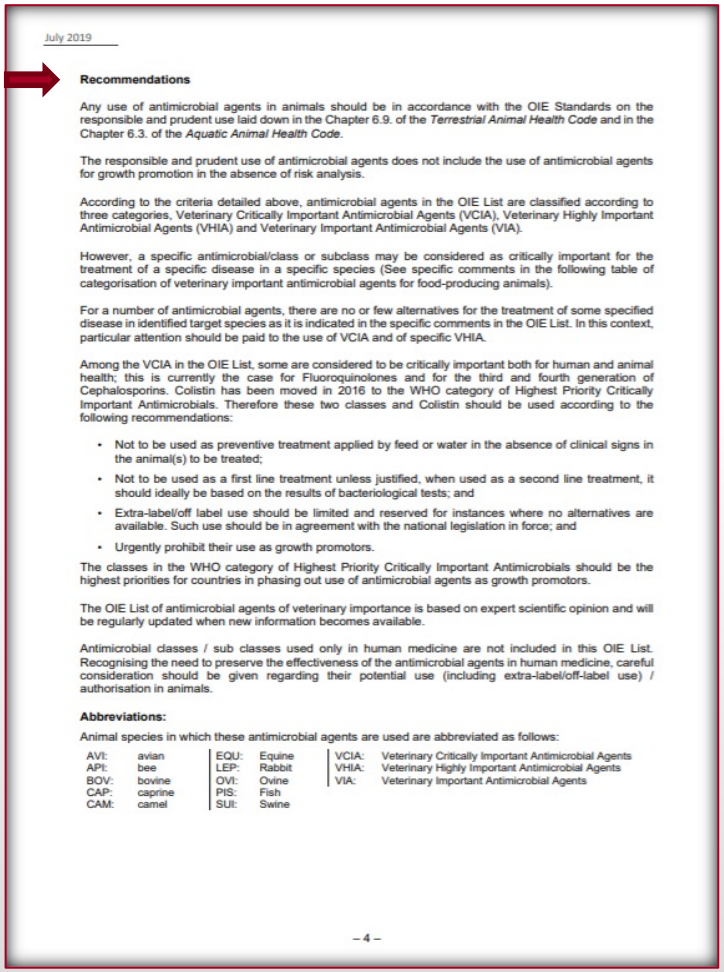


July 2019

Recommendations

Any use of antimicrobial agents in animals should be in accordance with the OIE Standards on the responsible and prudent use laid down in the Chapter 6.9. of the *Terrestrial Animal Health Code* and in the Chapter 6.3. of the *Aquatic Animal Health Code*.

The responsible and prudent use of antimicrobial agents does not include the use of antimicrobial agents for growth promotion in the absence of risk analysis.

According to the criteria detailed above, antimicrobial agents in the OIE List are classified according to three categories, Veterinary Critically Important Antimicrobial Agents (VCIA), Veterinary Highly Important Antimicrobial Agents (VHIA) and Veterinary Important Antimicrobial Agents (VIA).

However, a specific antimicrobial/class or subclass may be considered as critically important for the treatment of a specific disease in a specific species (See specific comments in the following table of categorisation of veterinary important antimicrobial agents for food-producing animals).

For a number of antimicrobial agents, there are no or few alternatives for the treatment of some specified disease in identified target species as it is indicated in the specific comments in the OIE List. In this context, particular attention should be paid to the use of VCIA and of specific VHIA.

Among the VCIA in the OIE List, some are considered to be critically important both for human and animal health; this is currently the case for Fluoroquinolones and for the third and fourth generation of Cephalosporins. Colistin has been moved in 2016 to the WHO category of Highest Priority Critically Important Antimicrobials. Therefore these two classes and Colistin should be used according to the following recommendations:

- Not to be used as preventive treatment applied by feed or water in the absence of clinical signs in the animal(s) to be treated;
- Not to be used as a first line treatment unless justified, when used as a second line treatment, it should ideally be based on the results of bacteriological tests; and
- Extra-label/off label use should be limited and reserved for instances where no alternatives are available. Such use should be in agreement with the national legislation in force; and
- Urgently prohibit their use as growth promotors.

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.

The OIE List of antimicrobial agents of veterinary importance is based on expert scientific opinion and will be regularly updated when new information becomes available.

Antimicrobial classes / sub classes used only in human medicine are not included in this OIE List. Recognising the need to preserve the effectiveness of the antimicrobial agents in human medicine, careful consideration should be given regarding their potential use (including extra-label/off-label use) / authorisation in animals.

Abbreviations:

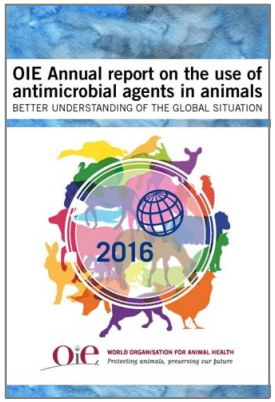
Animal species in which these antimicrobial agents are used are abbreviated as follows:

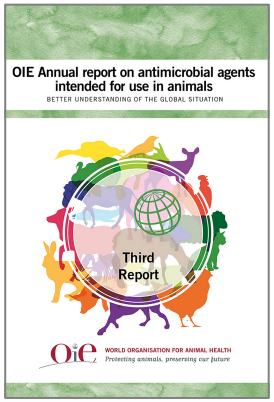
AVI:	avian	EQU:	Equine	VCIA:	Veterinary Critically Important Antimicrobial Agents
API:	bee	LEP:	Rabbit	VHIA:	Veterinary Highly Important Antimicrobial Agents
BOV:	bovine	OVI:	Ovine	VIA:	Veterinary Important Antimicrobial Agents
CAP:	caprine	PIS:	Fish		
CAM:	camel	SUI:	Swine		

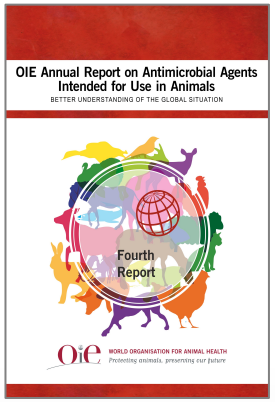
– 4 –

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

Monitoring of the quantities and usage patterns of antimicrobial agents used in animals

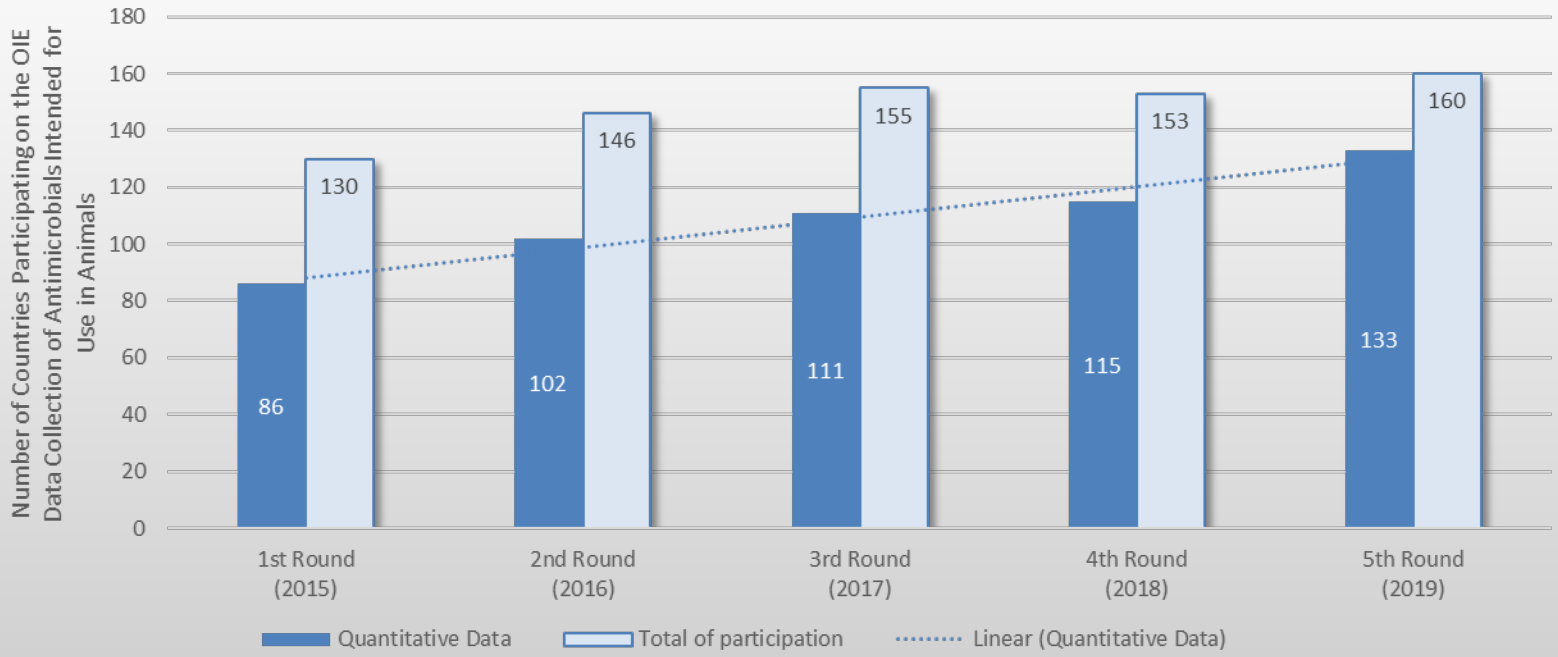






Fifth Report

https://www.oie.int/en/scientific-expertise/veterinary-products/antimicrobials/



OIE AMU Methodology

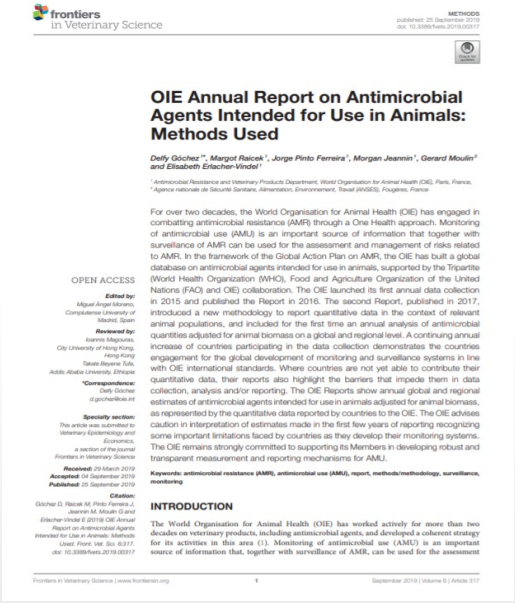
OIE Annual Report on Antimicrobial Agents Intended for Use in Animals: Methods Used

METHODS ARTICLE

Front. Vet. Sci., 25 September 2019

| https://doi.org/10.3389/fvets.2019.00317

➔ *Develops the Methodology of the OIE AMU Data Collection and the OIE Calculation of the Animal Biomass*


frontiers in Veterinary Science

METHODS

OIE Annual Report on Antimicrobial Agents Intended for Use in Animals: Methods Used

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INTRODUCTION

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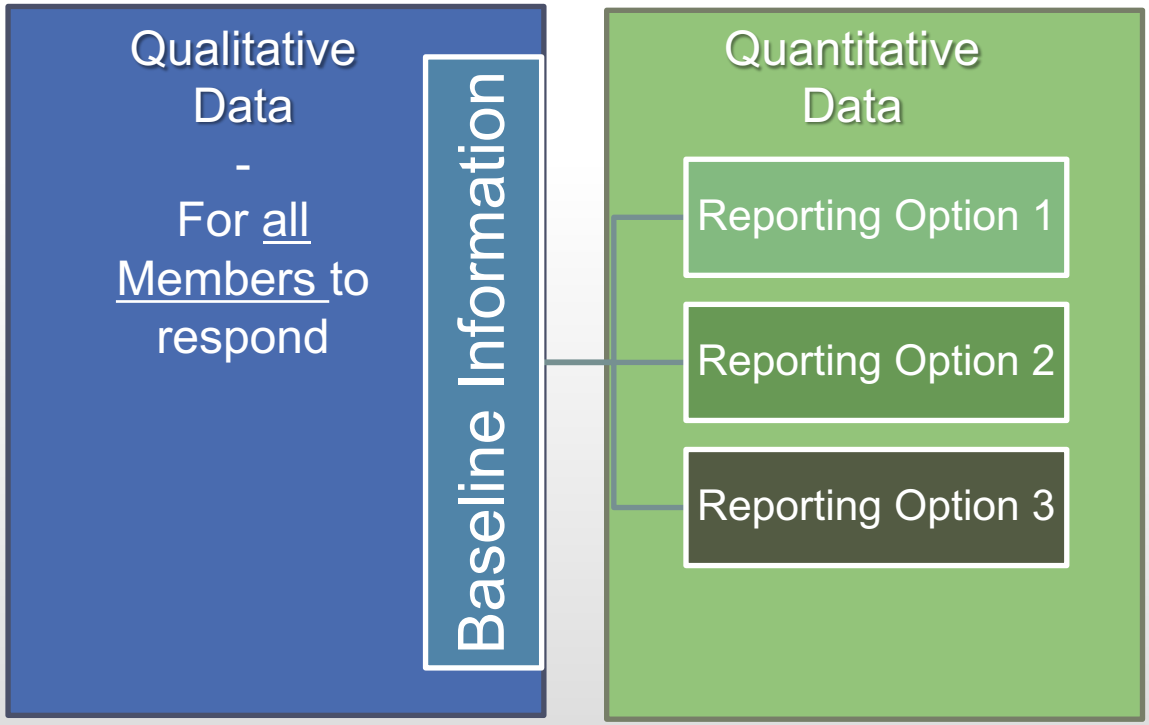
More on impact ›

frontiers in Veterinary Science

Veterinary Epidemiology and Economics

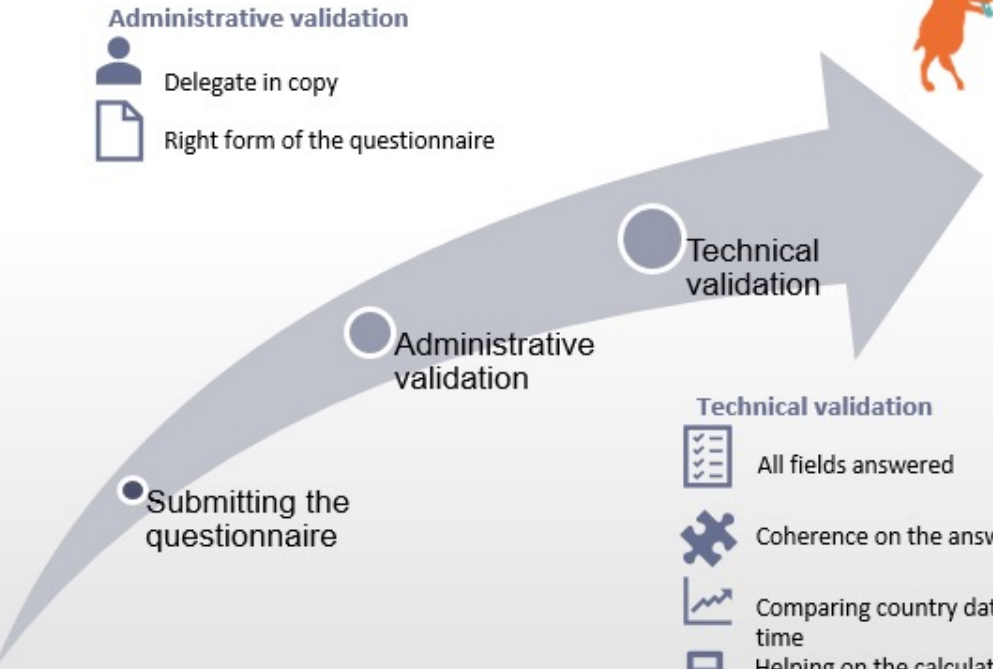
Reporting Options

The sections of the OIE Template named ‘Reporting Options’ 1, 2 and 3, collect the quantities of antimicrobial agents intended for use in animals.



* Type of use: veterinary medical use or growth promotion
**For the purposes of the OIE database, animal groups means: ‘terrestrial food-producing animals’, ‘aquatic food-producing animals’ or ‘companion animals’

Interaction with the Countries



Technical validation

- All fields answered
- Coherence on the answers
- Comparing country data over time
- Helping on the calculations of kg of active ingredient

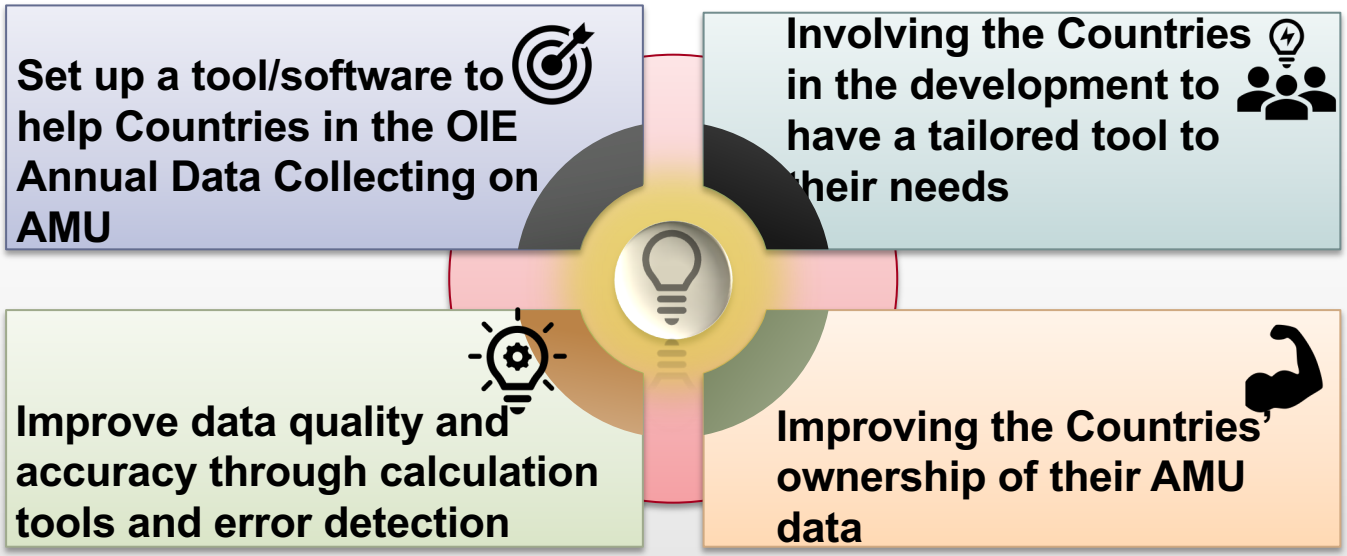
681 emails, **27** phone calls and **10** videoconferences exchanged with the Countries (mainly Focal Points for Veterinary Products)

- Africa: 194
- Americas: 190
- Asia, Far East and Oceania: 131
- Europe: 152
- Middle East: 14

Around 80% of the countries changed their original report after the clarifications:

- Data sources
- Quantities
- Antimicrobial growth promoters
- Reporting Option

Future of the OIE Data Collection: The AMU Database Project



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Thank you for your attention.

https://doi.org/10.20506/AMR.3138

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