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Vaccination as a tool to reduce antimicrobial resistance worldwide

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Prioritisation of Diseases for which Vaccines Could Reduce Antimicrobial Use in Animals

Vaccine Technology VI Congress
"One Health Round Table"

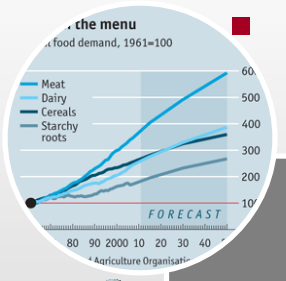
Albufeira (Portugal)
16th June 2016

Outline

- Background on antimicrobial resistance (AMR)
- Main activities on animal health policies preventing and fighting antimicrobial resistance (AMR) through Intergovernmental standards and guidelines
- Focus on the OIE *ad hoc* Group on prioritisation of diseases for which vaccines could reduce antimicrobial use in animals
- Conclusion

Background

- +1 billion people by 2050



- Demand for animal protein, increase by more than 50%

Demand for food

- Focus on developing countries

Population growth

Globalisation

- Unprecedented movement of people and commodities

ARCHAEOLOGY

Antibiotic-Resistant Genes Found in Mummy

OCT 20, 2015 03:50 PM ET // BY ROSSELLA LORENZI

http://news.discovery.com/history/archaeology/antibiotic-genes-found-in-mummy-151020.htm

The *One Health* collaboration

Food and Agriculture Organization of the United Nations

Global leader for food and agriculture

WORLD ORGANISATION FOR ANIMAL HEALTH

Global leader for animal health and welfare standards

World Health Organization

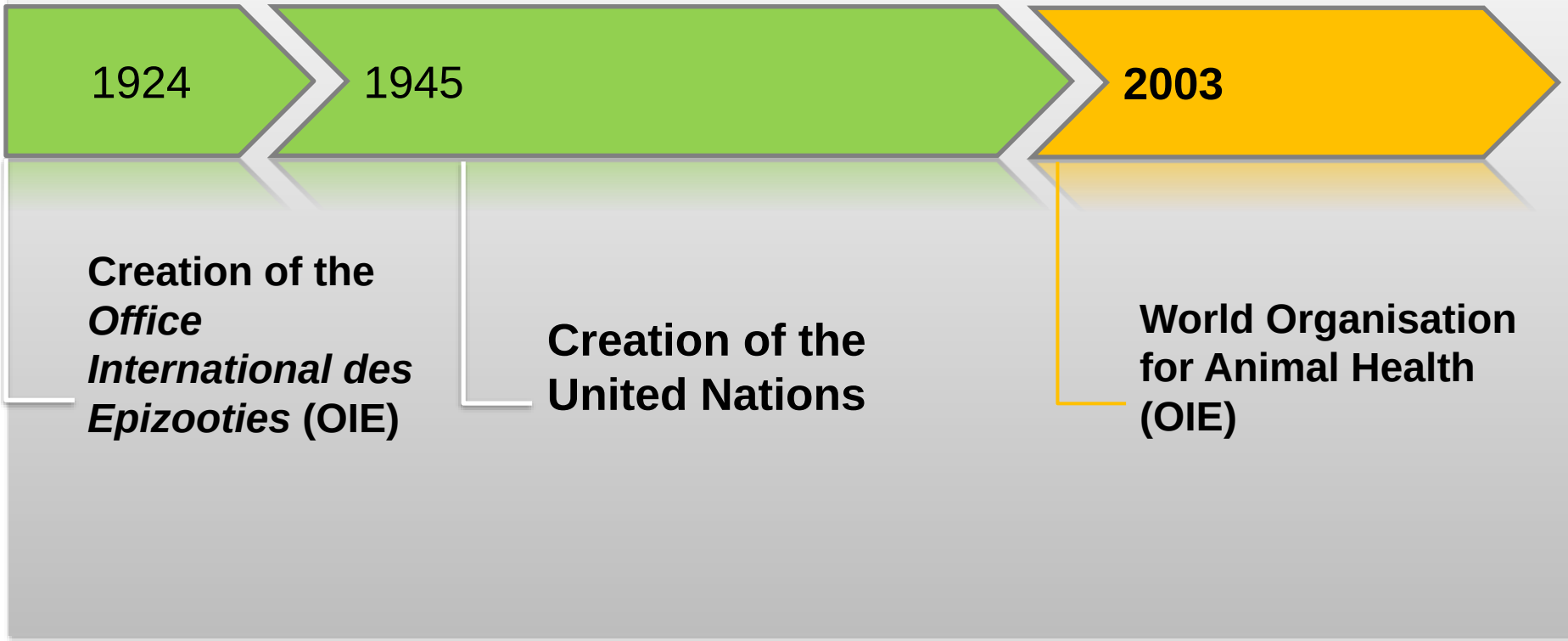
Global leader for human health

Tripartite agreement
Collaborations
Joint priorities including Antimicrobial resistance (AMR)

Outline

- Background
- OIE and activates on preventing and fighting antimicrobial resistance (AMR)
- Focus on the OIE *ad hoc* Group on prioritisation of diseases for which vaccines could reduce antimicrobial use in animals
- Conclusion

OIE: an intergovernmental organisation founded in 1924 : 180 Member Countries in 2016



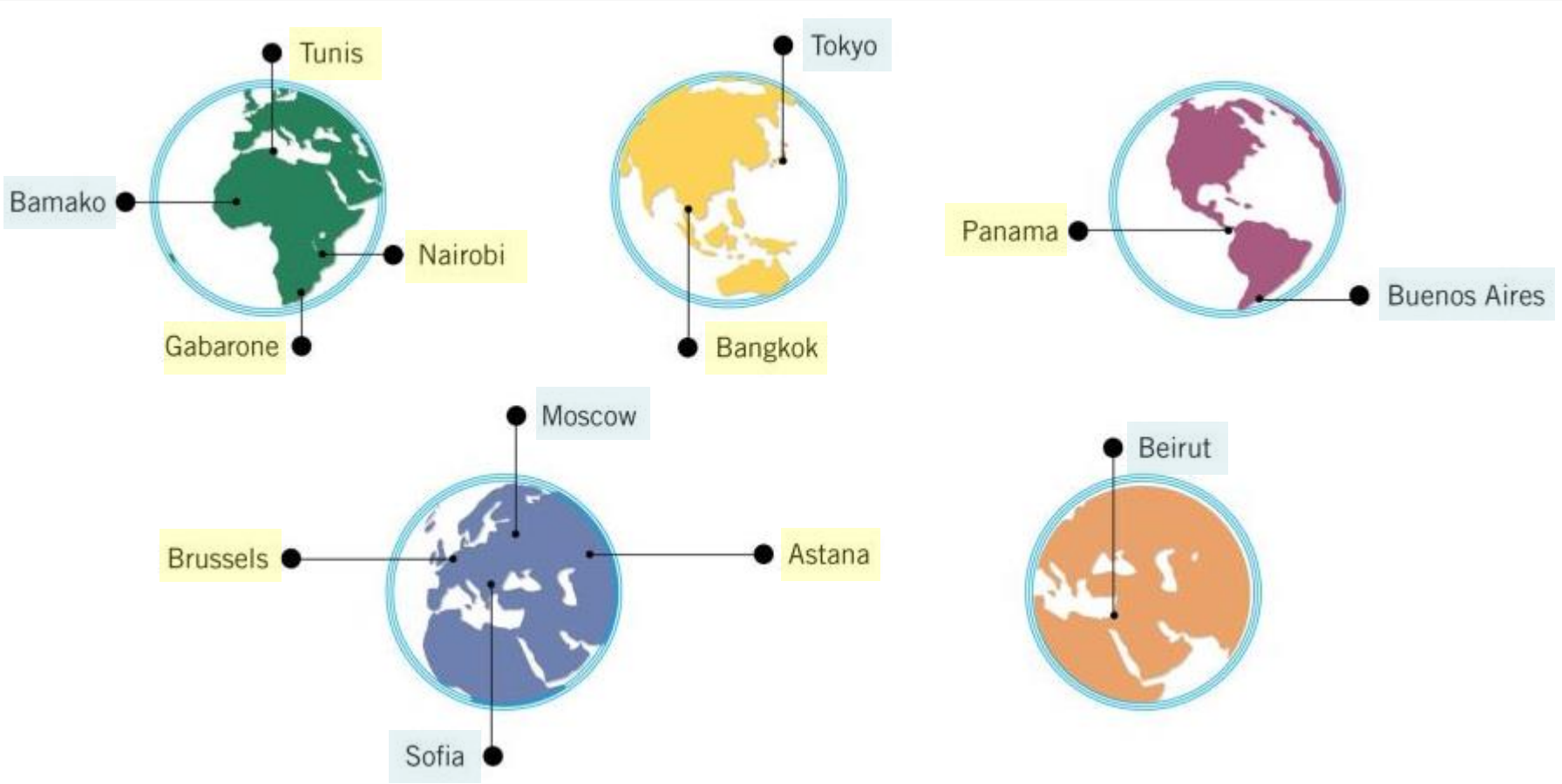
180 Member Countries in 2016

17 Regional and Sub-regional Representations

OIE Headquarters in Paris (France)

5 Regional Representations

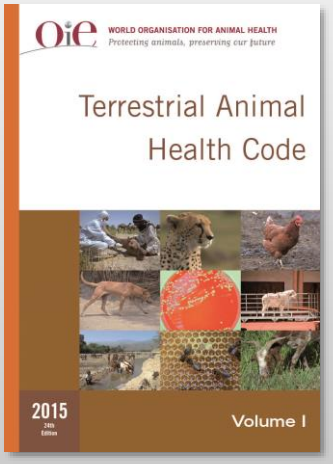
8 Sub-Regional Representations and Sub-Regional Offices

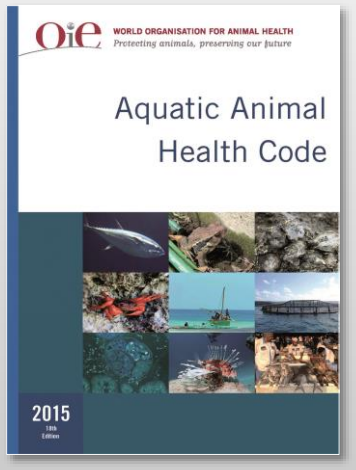


OIE intergovernmental Standards

CODES

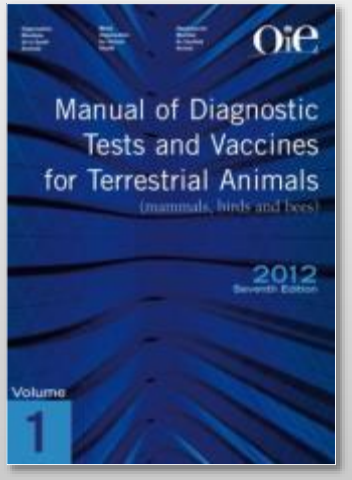
- Terrestrial
- Aquatic

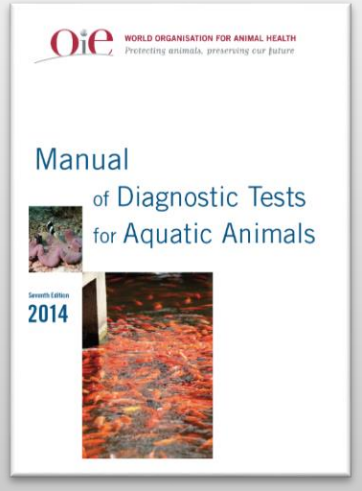




MANUALS

- Terrestrial
- Aquatic





***Codes* and *Manuals* available on the OIE website**

Terrestrial Manual - Purpose

- Describes internationally agreed standard laboratory methods for disease diagnosis
- Describes requirements for the production and control of vaccines and other biological products
- Available in full and up to date on line in English and Spanish at http://www.oie.int/en/international-standard-setting/terrestrial-manual/access-online/

Terrestrial Manual – Part 3

General Guidelines

3.1 Laboratory methodologies for bacterial antimicrobial susceptibility testing

3.2 Biotechnology in the diagnosis of infectious diseases

3.3 The application of biotechnology to the development of veterinary vaccines

3.4 The role of official bodies in the international regulation of veterinary biologicals

3.5 Managing biorisk: examples of aligning risk management strategies with assessed biorisks

3.6 OIE Validation Guidelines

OIE activities on preventing and fighting AMR

- Initiatives to improve good governance of veterinary services
- Global database on antimicrobials use in animals worldwide
- Contributing to the availability of quality assured antimicrobials and their prudent and responsible use
- List of antibiotics of critical importance for animal health
- *Ad hoc* Group on AMR and ***ad hoc* Group on prioritization of diseases for which vaccines could reduce AMR in animals**
- 2nd International Symposium on Alternatives to Antibiotics for Animal Production (USDA with the support of the OIE), 13-15 December 2016, Paris (France)

Outline

- Background
- OIE and activates on preventing and fighting antimicrobial resistance (AMR)
- Focus on the OIE *ad hoc* Group on prioritisation of diseases for which vaccines could reduce antimicrobial use in animals
- Conclusion

Purpose of the *ad hoc* Group

- “Provide guidance on prioritisation of disease for which the use of already available and new vaccines could reduce antimicrobial use in animals, focusing the first step on pigs, poultry and fish “



- Identify actions to improve utilisation of such vaccines

- To support the WHO Global Action Plan on AMR which makes provision for such approach

Terms of Reference (ToR)

- Consider disease for which the availability and use of appropriate vaccines could reduce antimicrobial use in animals
- Rank bacterial disease in terrestrial (pig and poultry) and aquatic (fish) animals by animal group, which cause the highest use of antimicrobials in the animal concerned
- Refine the ranking by considering relevant factors impacting vaccine development, effectiveness or implementation of vaccination

Methodology

- Development of a template and guiding criteria for the ranking of diseases:
  - For the purpose of stimulating research into new or better adopted vaccines with the aim of reducing the use of antibiotics
  - The development of multivalent vaccines should potentially cover a broad range of issues and disciplines, including discovery of new aetiological agents

Methodology

Proposed chicken, swine and fish diseases where development or improvement of vaccines would have a high impact on antibiotic use :

Key principles:

1. Identification of the most prevalent and important bacterial infections in chickens, swine, and identification of fish species that are commonly farmed and associated with high antibiotic use, and associated prevalent bacterial infections in those species.
2. Identification of common non-bacterial infections in chicken, swine and fish (e.g. protozoal, viral) showing clinical signs that trigger empirical antibiotic treatment (e.g. for diarrhoea) and which also result frequently in bacterial co-infection.
3. An assessment of antibiotic use in response to the syndromic indication or diagnosed disease. This was categorised as high, medium or low in the context of considered use compared with the total use of antibiotics in that animal species.
4. The availability of a vaccine(s), and if available, their effectiveness.
5. The potential for a new or improved vaccine to reduce the need for antibiotic treatment

Tables: Infections for which new or improved vaccines would significantly reduce the need for antibiotic use (chicken, swine or fish)

01| Key syndrome

02| Primary pathogen(s) (disease)

03| Antibiotic use

04| Commercial vaccine exists

05| Major constraints to use of vaccine / vaccine development

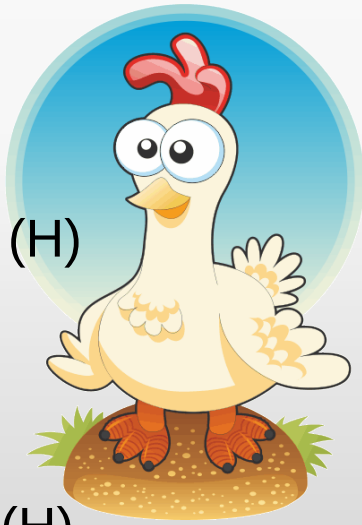
06| Vaccine research priority

Table 1: Infections for which new or improved vaccines would significantly reduce the need for antibiotic use in chickens

Key syndrome	Primary pathogen(s) (disease)	Antibiotic use	Commercial* vaccine exists	Major constraints to use of vaccine / vaccine development	Vaccine research priority
Systemic (Broilers)	*Escherichia coli* *(Yolk sac infection, airsacculitis, cellulitis)*	High	Yes	• Omphalitis: secondary bacterial infection – not a disease one can immunize against • Strain coverage limited • Airsacculitis, cellulitis: vaccines available, e.g. live aerosol vaccine. However, Serotype coverage limited and field efficay variable	High
	Infectious Bursal Disease virus *(secondary bacterial infections)*	Medium	Yes	• Issues with vaccine application • Short window of opportunity to vaccinate • Maternal antibody interference	Medium
Systemic (Breeders, Layers)	*Escherichia coli* *(airsacculitis, cellulitis, salpingitis and peritonitis)*	High	Yes	• Strain coverage limited	High
Enteric (Broilers, Breeders, and Layers)	*Clostridium perfringens,* type A (necrotic enteritis)	High	Yes	• Toxoid vaccine for layers providing only short-lasting passive immunity • Research needed to achieve active immunity. • Improved and/or more convenient (mass vaccination) vaccine needed for broilers	High
	Coccidiosis (secondary bacterial infections)	High	Yes	• Lack of cross-protection • Strains must be matched to infectious agent • Current vaccines are not attenuated and can produce low dose infection • Sub-unit vaccines have not been successful	High
	Infectious Bronchitis virus *(secondary bacterial infections)*	Medium	Yes	• Issues with strain matching and strain coverage • High mutation rate of virus	Medium

* does not cover autogenous vaccines

Report of the meeting of the OIE *ad hoc* Group on Prioritisation of Diseases for which Vaccines could Reduce Antimicrobial Use in Animals



Poultry diseases

- *Escherichia coli* (Yolk sac infection, airsacculitis, cellulitis) (H)
- *Clostridium perfringens*, type A (necrotic enteritis) (H)
- Coccidiosis (secondary bacterial infections) (H)
- Infectious bronchitis virus (secondary bacterial infections) (H)
- Infectious bursal disease virus (secondary bacterial infections) (M)

Table 2: Infections for which new or improved vaccines would significantly reduce the need for antibiotic use in swine

Key syndrome	Primary pathogen(s) (disease)	Antibiotic use	Commercial* vaccine exists	Major constraints to use of vaccine / vaccine development	Vaccine research priority
Systemic (respiratory)	*Streptococcus suis*	High	Yes	• Strain coverage too narrow • Lack of cross-protection • Poor immunogenicity due to being a capsule based vaccine	High
	Haemophilus parasuis	Medium	Yes	• Serotype specific with variable cross-protection • Maternal antibody interference	Medium
Respiratory	*Pasteurella multocida (for pneumonic disease)*	High	No	• No vaccine with approved label claim for pneumonia (There is a vaccine for atrophic rhinitis)	High
	Mycoplasma hyopneumoniae	High	Yes	• Does not completely prevent lung lesions • Animals continue to shed pathogen • Diagnostics not always accurately done	Low
	Actinobacillus pleuropneumoniae	High	Yes	• Limited coverage • Good immunity only if serotype specific • Sub-unit vaccine which affords cross-protection	High
	Porcine Reproductive and Respiratory Syndrome virus (secondary bacterial infections)	High	Yes	• Strain coverage limited • High virus mutation rate • Modest cross-protection • Vaccine evasion	High
	Swine Influenza Virus (secondary bacterial infections)	High	Yes	• Strain matching • Vaccine-associated enhanced respiratory disease (VAERD) • Lack of cross-protection • Efficacy in piglets limited	High
Enteric – neonatal	*Escherichia coli*	High for the syndrome, Low for *E. coli*	Yes	• Maternal vaccine provides effective lactogenic immunity • Coverage of enterotoxigenic *E. coli* may occasionally need to be updated	Low
Enteric (weaners/finishers)	*Escherichia coli*	High	Yes	• Maternal antibody interference • Short window for induction of immunity	High
	Lawsonia intracellularis	High	Yes	• Other pathogens in the syndrome (*Brachyspira*) not included • Antibiotic-free window for vaccination required (live attenuated oral vaccine)	Low (see also *Brachyspira*)
	Brachyspira spp *B. hyodysenteriae,* *B. pilosicoli*	Medium-high	No	• Low current research investment as changes in husbandry largely eliminated the disease • Technical barriers to vaccine development	High
	Rotaviruses (secondary bacterial infections)	High	Yes	• Reasons limiting wider adoption unknown	High

Report of the meeting (contd)

Swine diseases

- *Streptococcus suis* (H)
- *Pasteurella multocida* (for pneumonic disease) (H)
- *Actinobacillus pleuropneumoniae* (H)
- Porcine reproductive and respiratory syndrome virus (H)
- Swine influenza virus (H)
- *E. coli* (H)
- *Brachyspira* spp. including *B. hyodysenteriae* and *B. pilosicoli* (H)
- Rotaviruses (secondary bacterial infections) (H)
- *Haemophilus parasuis* (M)

Table 3: Infections for which new or improved vaccines would significantly reduce the need for antibiotic use in fish

Key syndrome or disease	Primary pathogen(s)	Antibiotic use	Commercial* vaccine exists	Major constraints to use of vaccine / vaccine development	Vaccine research priority
Freshwater cyprinids					
Systemic bacterioses	*Aeromonas hydrophila* and other species	High	No	• Disease is caused by a wide range of serotypes	High
Dermal bacterioses / red spot disease	*Pseudomonas* spp.	High	No	• Disease is caused by a range of species and wide range of strains and serotypes	High
Columnaris	*Flavobacterium columnare*	Medium	Yes	• Limited uptake by some countries for unknown reasons	Low
Freshwater cichlids					
Systemic/dermal bacterioses	*Aeromonas hydrophila* and other species	Medium	No	• Disease is caused by a range of species and wide range of strains and serotypes	Medium (not low because of projected increase in production)
	Streptococcus inae, S. agalactiae	Medium	Yes	• Industry awareness of need is low (first vaccine only became recently available)	Medium
Freshwater salmonids					
Systemic bacterioses	*Aeromonas salmonicida, Yersinia rukerii, Flavobacterium psychrophilum, Vibrio anguillarum*	Medium	Yes (multivalent, injectable)	• cost of vaccine is high relative to harvest value	Low
Marine salmonids					
Salmon Rickettsia Syndrome	*Piscirickettsia salmonis*	Medium	Yes	• Multivalent vaccine which provides low protection for *P. salmonis* compared to other pathogens included in the vaccine.	Unknown because the recent introduction of an oral monovalent vaccine booster may improve the level of protection
Other marine fish					
Systemic / dermal bacterioses	*Vibrio* spp., *Photobacterium* spp.	Medium	Yes	• Disease is caused by a wide range of serotypes • Industry awareness is low in some countries	High
	Streptococcus spp.	Medium	Yes	• Disease is caused by a wide range of serotypes • Industry awareness is low in some countries	High
Catfish					
Systemic	*Edwardsiella ictaluri, E. tarda*	Medium	Yes (for Channel catfish)	• Vaccines are not available for African catfish (an important farmed species) • Vaccines have very recently become available for Tra catfish and yet to be adopted by the industry	High (for African catfish)
Systemic	*Aeromonas hydrophila* and other species	Medium	No	• Disease is caused by a wide range of serotypes	High

Report of the meeting (contd)

Fish diseases

- *Aeromonas hydrophila* and other species (Freshwater cyprinids) (H)
- *Pseudomonas* spp. (Freshwater cyprinids) (H)
- *Vibrio* spp., (Marine fish) (H)
- *Photobacterium* spp. (Marine fish) (H)
- *Streptococcus* spp. (Marine fish) (H)
- *Edwardsiella ictaluri, E. tarda (Catfish) (H)*
- *A. hydrophila* and other species (Catfish) (H)
- *Streptococcus inae*, and *S. agalactiae* *(*Freshwater cichlids**)** *(M)*

Outcome

- In vaccine research could have a significant impact, particularly if it addressed the following four priority gaps:
  - Maternal antibody interference
  - Cross-protection or inclusion of relevant strains in vaccine formulations
  - Occurrence of immunological interference in multivalent vaccines
  - Innovative delivery systems to enable mass-vaccination

CONCLUSION

- A global vaccine research network should be created to pull resources and expertise to address gaps for each of the priority diseases listed in Table 1-3. ***(Annex 5 of the Scientific Commission Report)***

http://www.oie.int/fileadmin/Home/eng/Internationa_Standard_Setting/docs/pdf/SCAD/A_SCAD_Sept2015. pdf

- Call for encouragement for development for new technologies and handle the major shift on how vaccine discovery research may provide new opportunities for addressing the challenges

- Need to invest for new or improved vaccines in order to reduce antibiotic use in the animals (as presented in details in the report and tables).

- Public-Private partnership are key

Information is available at the OIE website

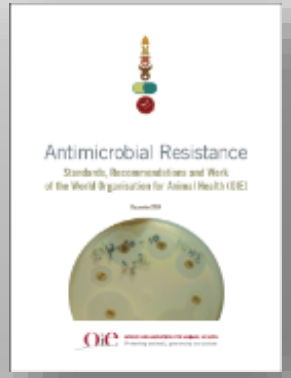
ANTIMICROBIAL RESISTANCE (AMR)

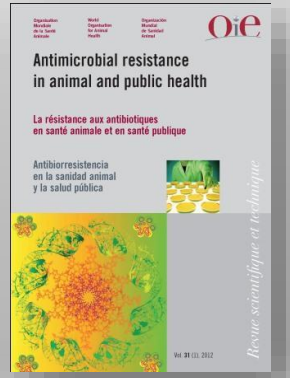
http://www.oie.int/en/our-scientific-expertise/veterinary-products/antimicrobials/

- http://www.oie.int/en/for-the-media/amr/multimedia-ressources/

REPORT

- http://www.oie.int/fileadmin/Home/eng/Internationa_Standard_Setting/docs/pdf/SCAD/A_SCAD_Sept2015.pdf





THANK YOU FOR YOUR ATTENTION !

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