Vaccination as a tool to reduce antimicrobial resistance worldwide

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Recommended Citation
Bernard VALLAT and Elisabeth Erlacher, "Vaccination as a tool to reduce antimicrobial resistance worldwide" in "Vaccine Technology VI", Laura Palomares, UNAM, Mexico Manon Cox, Protein Sciences Corporation, USA Tarit Mukhopadhyay, University College London, UK Nathalie Garçon, BIOASTER Technology Research Institute, FR Eds, ECI Symposium Series, (2016).
http://dc.engconfintl.org/vaccine_vi/34

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Prioritisation of Diseases for which Vaccines Could Reduce Antimicrobial Use in Animals
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%
- Focus on developing countries
- Demand for food
- Unprecedented movement of people and commodities

Population growth

Globalisation
Antibiotic-Resistant Genes Found in Mummy

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

The One Health collaboration

Global leader for food and agriculture

Global leader for animal health and welfare standards

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

1924: Creation of the Office International des Epizooties (OIE)
1945: Creation of the United Nations
2003: World Organisation for Animal Health (OIE)
180 Member Countries in 2016
17 Regional and Sub-regional Representations

**OIE Headquarters in Paris (France)**

- Tunis
- Bamako
- Gabarone
- Nairobi

**5 Regional Representations**

- Tokyo
- Bangkok

**8 Sub-Regional Representations and Sub-Regional Offices**

- Panama
- Buenos Aires
- Moscow
- Astana
- Brussels
- Sofia
- Beirut
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/](http://www.oie.int/en/international-standard-setting/terrestrial-manual/access-online/)
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

<table>
<thead>
<tr>
<th>Key syndrome</th>
<th>Primary pathogen(s) (disease)</th>
<th>Antibiotic use</th>
<th>Commercial* vaccine exists</th>
<th>Major constraints to use of vaccine / vaccine development</th>
<th>Vaccine research priority</th>
</tr>
</thead>
</table>
| **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 efficacy 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

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

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


- 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/for-the-media/amr/multimedia-ressources/

REPORT

THANK YOU FOR YOUR ATTENTION !