AMR – When the problem brings solutions

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Head of AMR & Veterinary Products Department

Aquatic Animal Webinar Series
Alternatives to Antimicrobials & Vaccination
June 14th 2023

World Organisation for Animal Health
Founded as OIE

Organisation mondiale de la santé animale
Fondée en tant qu'OIE

Organización Mundial de Sanidad Animal
Fundada como OIE

Antibiotics – A conversation with my father

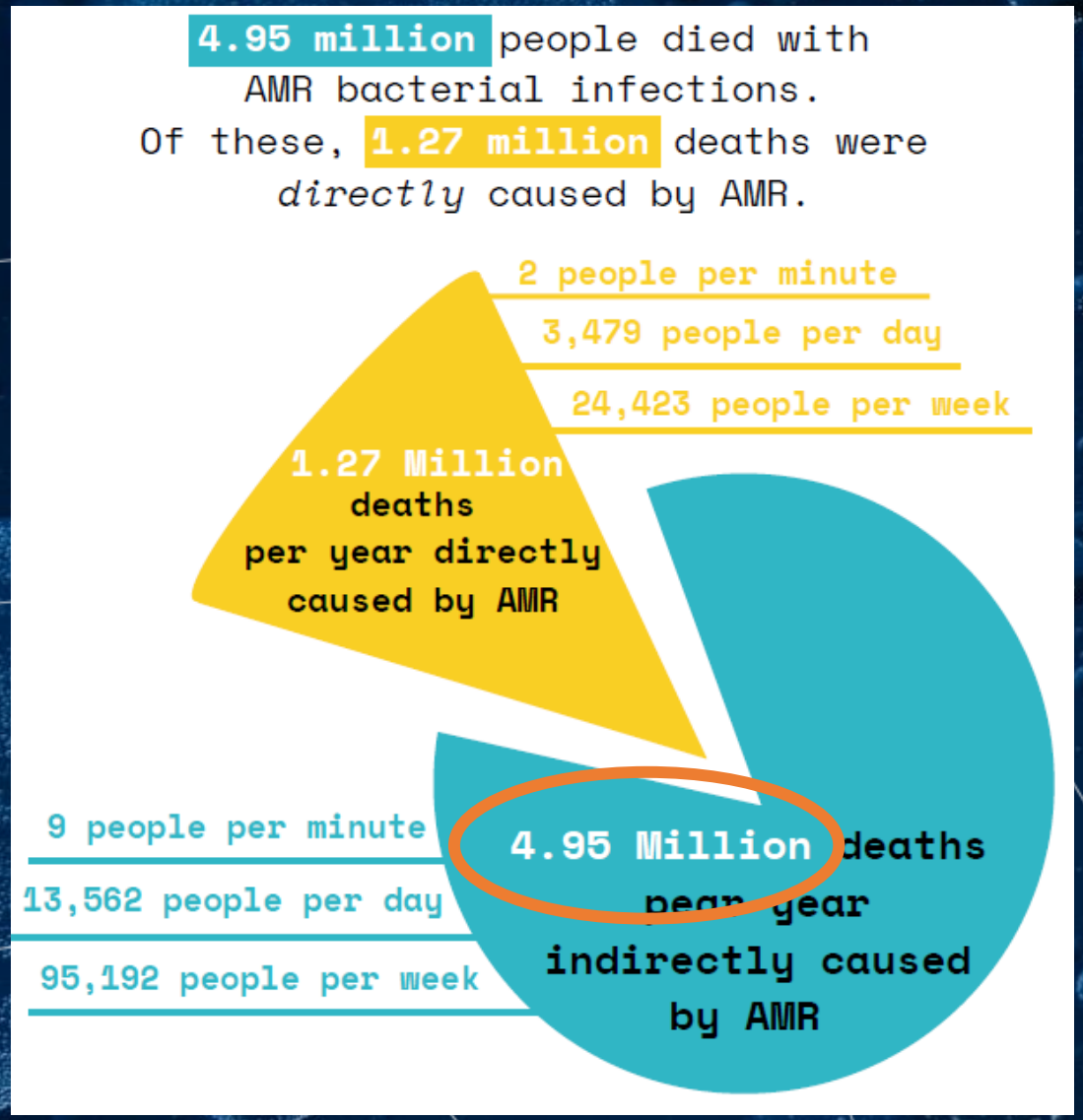
1940s

ADAPTATION

ADAPTATION

2010s

AMR – Some figures



3

2

10

6*

AMR is a silent pandemic

*20 million people are estimated to have died because of COVID since 2020 (WHO data – May 2023)

AMR – A complex matter, a right balance to find, a matter of adaptation

ACCESS

INNOVATION

CONSERVATION

Strategies for achieving global collective action on antimicrobial resistance

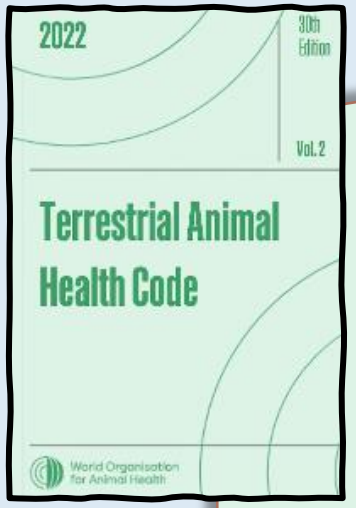
Steven J Hoffman,[a] Grazia M Caleo,[b] Nils Daulaire,[c] Stefan Elbe,[d] Precious Matsoso,[e] Elias Mossialos,[f] Zain Rizvi[g] & John-Arne Røttingen[h]

Abstract Global governance and market failures mean that it is not possible to ensure access to antimicrobial medicines of sustainable effectiveness. Many people work to overcome these failures, but their institutions and initiatives are insufficiently coordinated, led and financed. Options for promoting global collective action on antimicrobial access and effectiveness include building institutions, crafting incentives and mobilizing interests. No single option is sufficient to tackle all the challenges associated with antimicrobial resistance. Promising institutional options include monitored milestones and an inter-agency task force. A global pooled fund could be used to craft incentives and a special representative nominated as an interest mobilizer. There are three policy components to the problem of antimicrobials – ensuring access, conservation and innovation. To address all three components, the right mix of options needs to be matched with an effective forum and may need to be supported by an international legal framework.

Bull World Health Organ 2015;93:867–876 | doi: http://dx.doi.org/10.2471/BLT.15.153171

1. Responsible use

RESPONSIBLE USE - WOAH International Standards for AMR



https://www.woah.org/en/what-we-do/standards/codes-and-manuals/terrestrial-code-online-access/

Ch.6.7. Introduction to the recommendations for controlling antimicrobial resistance

Ch.6.8. Harmonisation of national AMR surveillance and monitoring programmes

Ch.6.9. Monitoring of the quantities and usage patterns of antimicrobial agents used in food-producing animals

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

https://www.woah.org/en/what-we-do/standards/codes-and-manuals/aquatic-code-online-access/

Ch. 6.1. Introduction to the recommendations for controlling antimicrobial resistance

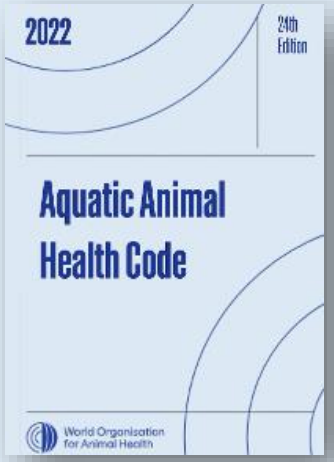
Ch.6.2. Principles for responsible and prudent use of antimicrobial agents in aquatic animals

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

RESPONSIBLE USE – Chapter 6.2 Aquatic Animal Health Code



Article 6.2.1.

Purpose

These principles provide guidance for the responsible and prudent use of *antimicrobial agents* in *aquatic animals*, with the aim of protecting both animal and human health. The *Competent Authorities* responsible for the registration and marketing authorisation of products and the control of all organisations involved in the production, distribution and use of *antimicrobial agents* have specific obligations.

Article 6.2.2.

Objectives of responsible and prudent use

Responsible and prudent use includes a set of practical measures and recommendations intended to reduce the risk associated with the selection and dissemination of antimicrobial resistant microorganisms and antimicrobial resistance determinants in *aquatic animal* production to:

1) maintain the efficacy of *antimicrobial agents* both for veterinary and human medicine and to ensure the rational use of antimicrobials in *aquatic animals* with the purpose of optimising both their efficacy and safety;

2) comply with the ethical obligation and economic need to keep *aquatic animals* in good health;

3) prevent or reduce the transfer of both resistant microorganisms and resistance determinants from *aquatic animals* to humans and terrestrial animals;

4) prevent antimicrobial residues that exceed the established maximum residue limit (MRL) occurring in the food.

RESPONSIBLE USE - WOAH List of Antimicrobials of Veterinary Importance

Criterion 1 : Response rate of the questionnaire regarding Veterinary Important Antimicrobial Agents (more than 50% identified the importance of the antimicrobial class)

Criterion 2 : Treatment essential against specific infections and lack of sufficient therapeutic alternatives

VCIA (Veterinary Critically Important Antimicrobial)

Both Criteria (1 & 2) are met

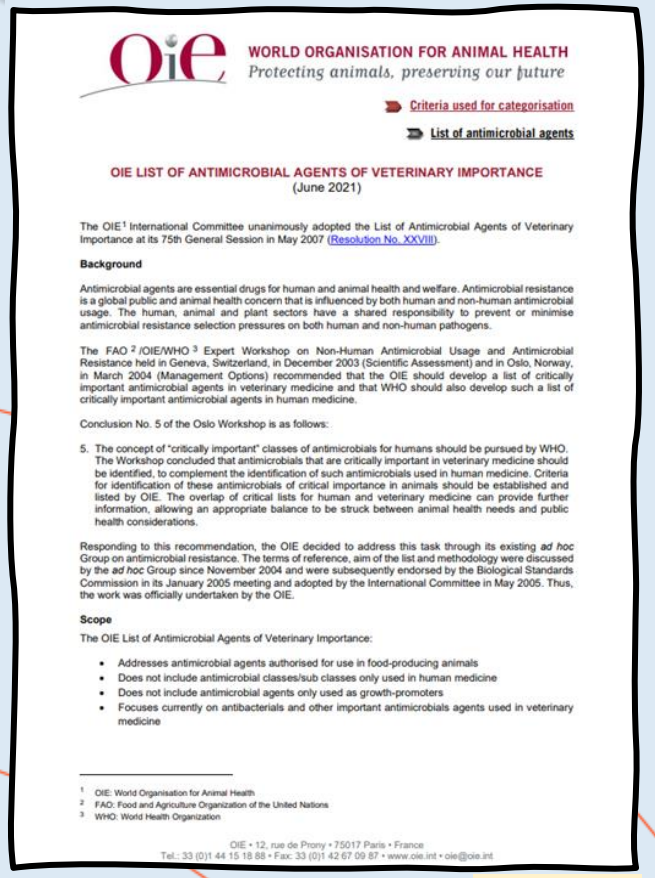
VHIA (Veterinary Highly Important Antimicrobial)

One Criterion (1 or 2) is met

VIA (Veterinary Important Antimicrobial)

No Criteria (1 nor 2) are met

WOAH's list of antimicrobials of veterinary importance



OIE 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
(June 2021)

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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Finalised :

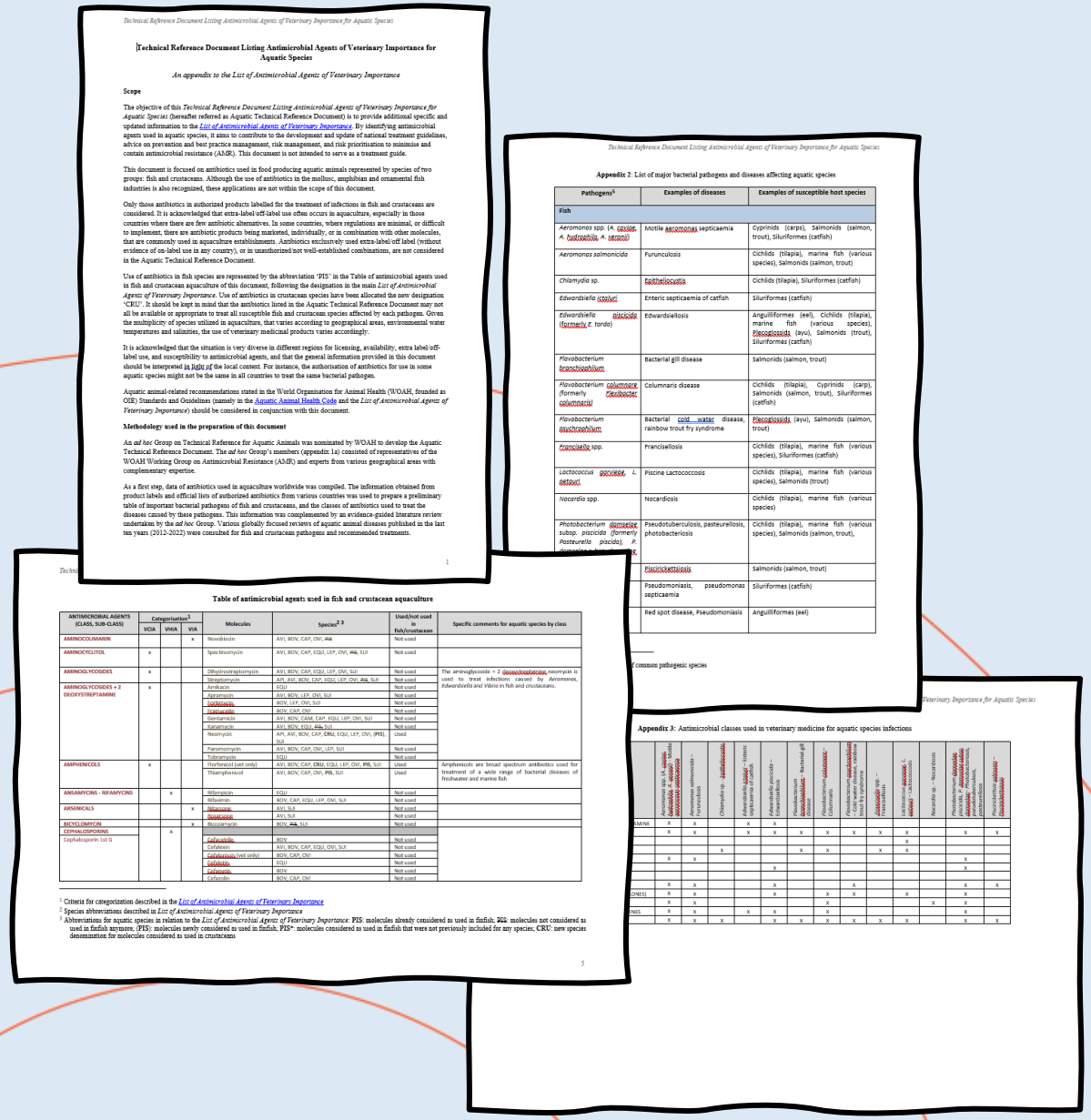
Working Group on Antimicrobial Resistance - WOAH

In progress :

Aquatic animal component of List of Antimicrobial Agents of Veterinary Importance fine-tuned

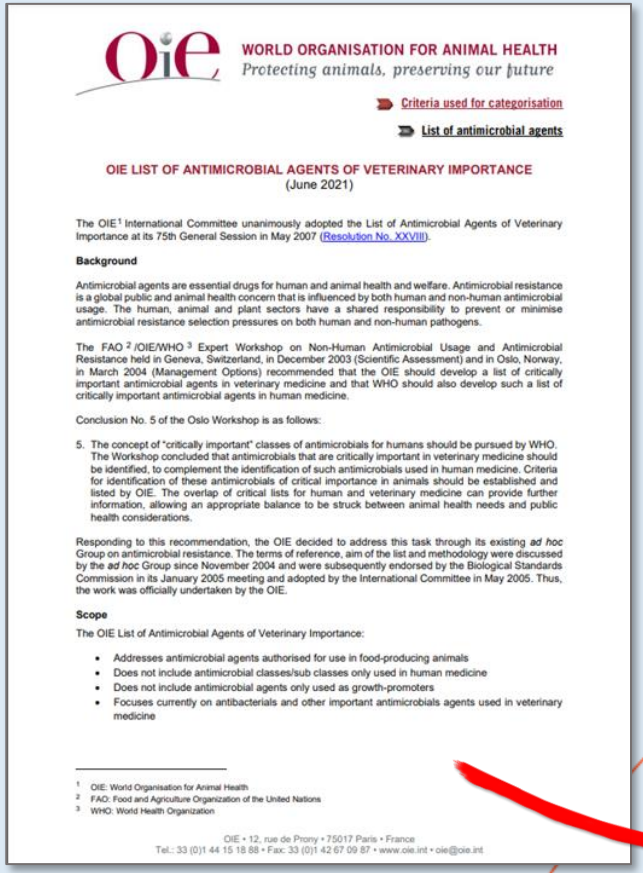
Technical Reference Document Listing Antimicrobial Agents of Veterinary Importance for Aquatic Species

- Introductory text
  - Scope: **Authorized antibiotics for food-producing fish and crustaceans**
  - Methodology: **Developed by AHG, reviewed by ext. experts**
- Table of antimicrobial agents: **26 antibiotics**
- List of main bacterial pathogens/diseases
  - **23 for fish**
  - **5 for crustacean**
- List of antimicrobial classes/sub-classes used to treat main diseases
  - **12 for fish diseases**
  - **4 for crustacean diseases**



https://www.woah.org/app/uploads/2022/12/a-woah-wg-amr-report-oct-2022-2.pdf

RESPONSIBLE USE – A word on Highest Priority Critically Important Antimicrobials



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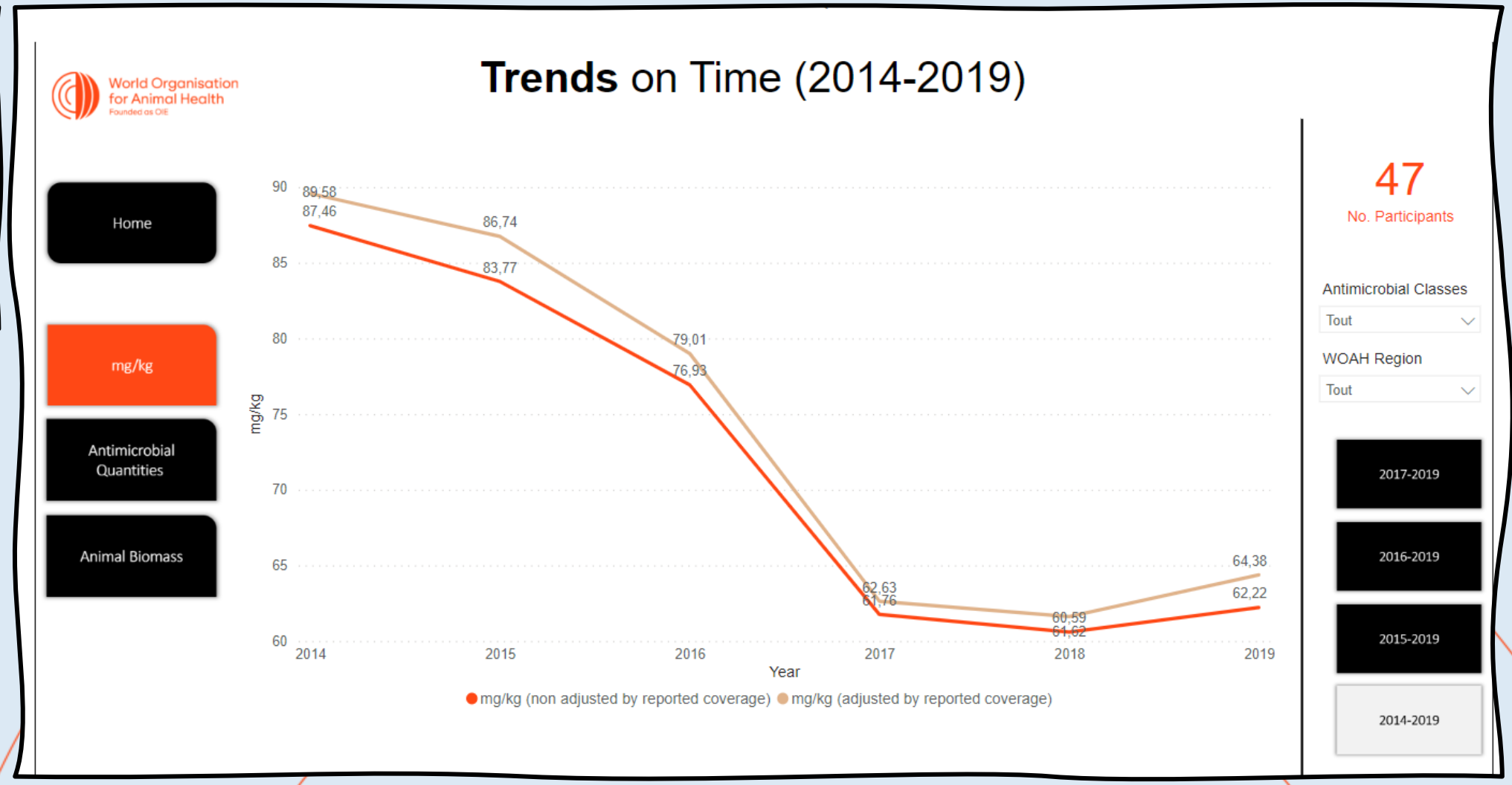
WOAH's list of antimicrobials of veterinary importance

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.

ANTIMICROBIAL USE – Are we responsible ? Enough?



Since 2015, the [World Organisation for Animal Health (WOAH, founded as OIE)], has taken the lead to build a global database on antimicrobial agents intended for use in animals (AMU). In 2022, WOAH transformed this into an online customized database system: **ANIMUSE Global Database (ANImal antiMicrobial USE).**

2. Alternatives

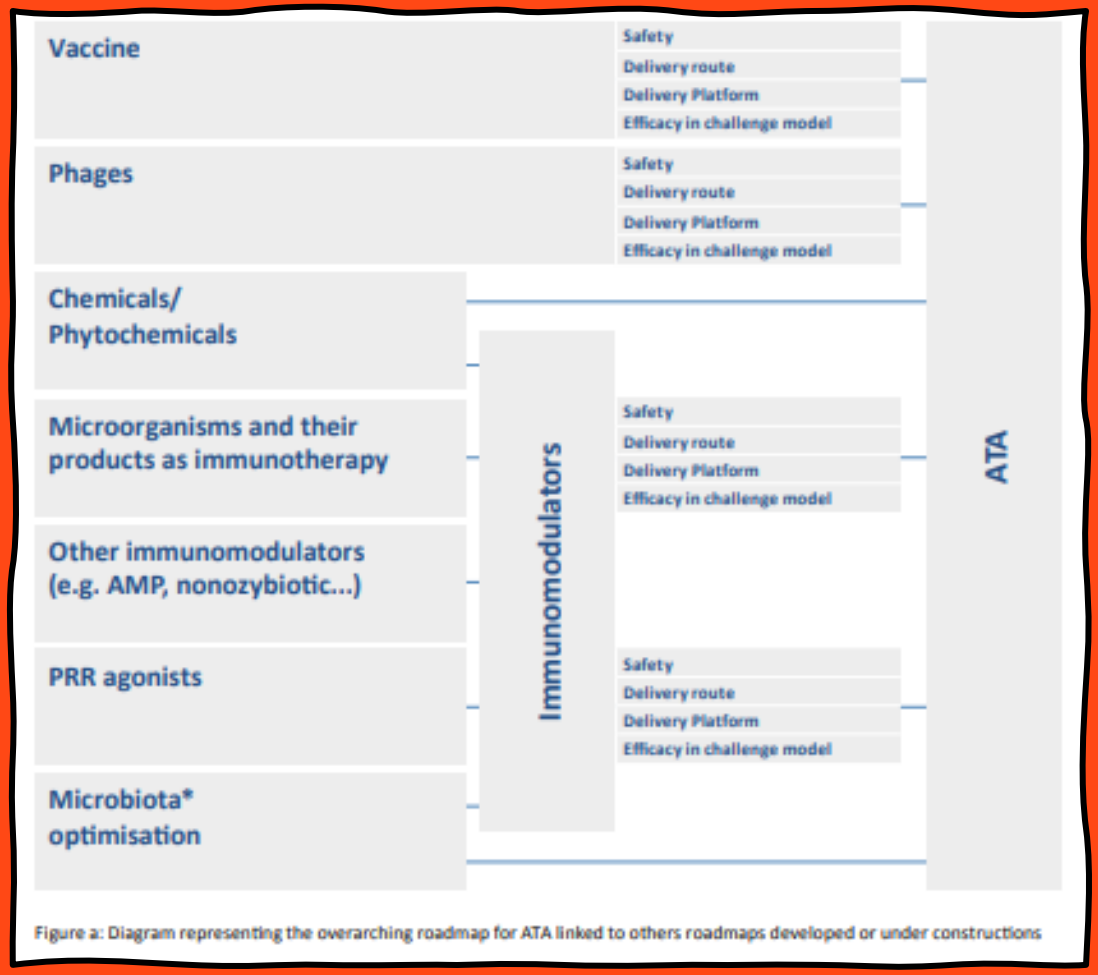
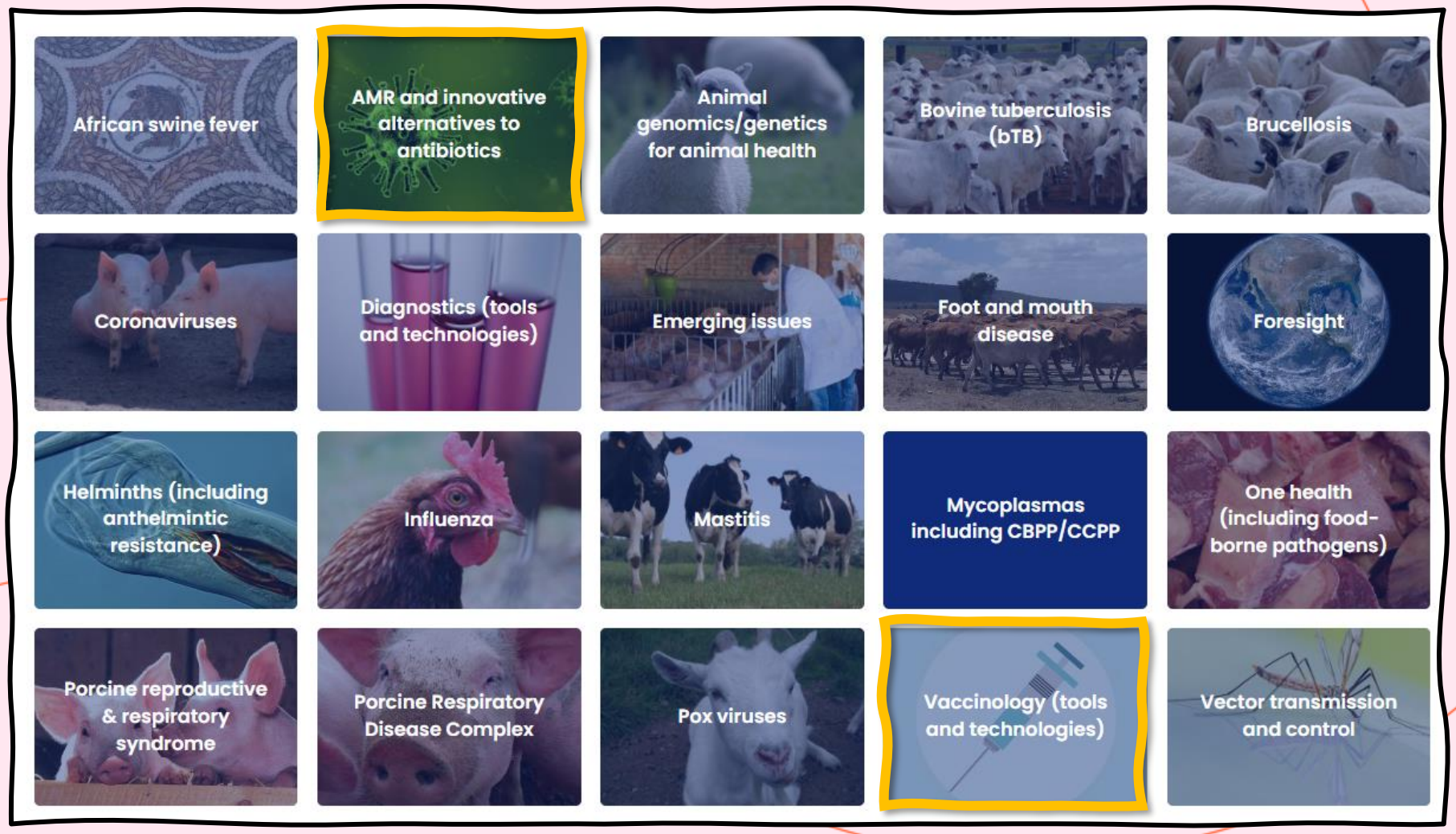


Figure a: Diagram representing the overarching roadmap for ATA linked to others roadmaps developed or under constructions

STAR-IDAZ – An International Research Consortium on Animal Health

STAR-IDAZ International Research Consortium on Animal Health

STAR-IDAZ International Research Consortium (IRC) is a global initiative to address the coordination of research programmes at an international level in the area of animal health and in particular infectious animal diseases including zoonoses

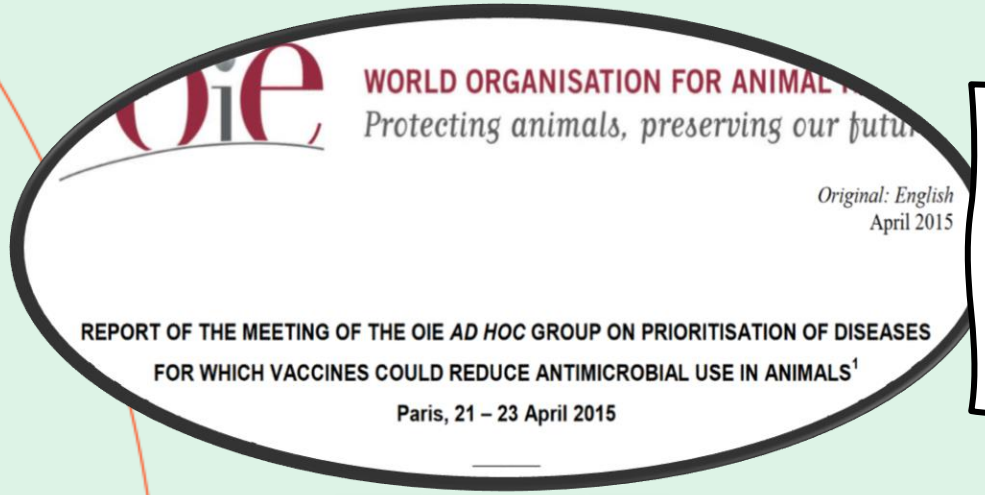


STAR-IDAZ – Research Priorities in Alternatives to Antimicrobials

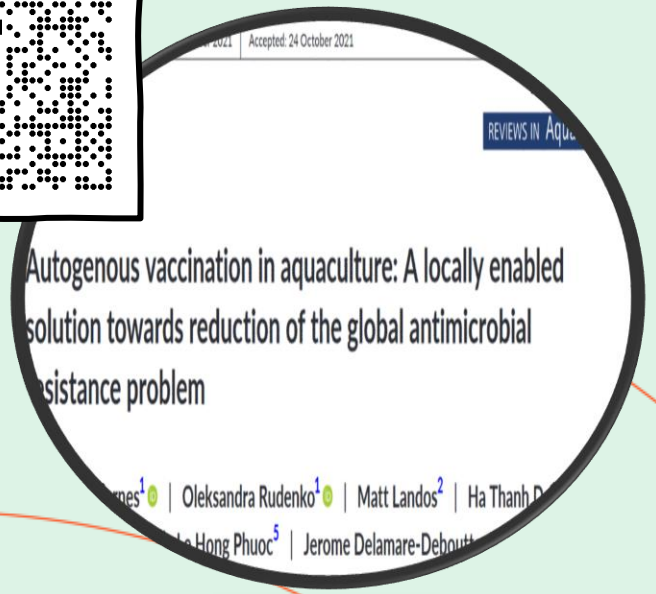
Topic:	Research priorities
Mechanisms behind antibiotics as growth promoters:	• Understand mechanisms of how AB work as growth promoters, to develop other alternatives • Create appropriate in-vivo/ex-vivo/in-vitro models • Basic research to better characterise microbiota • Defined standardized methods to test mechanism of subAbx and defined goal (growth vs feed conversion rate)
Phage technologies:	• Phage-bacteria interaction • In-vivo models and trials • Investigate phage survival in the animal and in the environment • Synthetic biology for retargetable phage-based platforms • Interaction between phage and the immune system • High throughput screening platforms for phage isolation/characterisation
Immunomodulators:	• Understand interaction between immune responses and inflammation • Mechanisms of host-microbial interaction • Kinetics and quantification of innate response stimulated by immunomodulators or by vaccines (non-specifically) • Functional studies of microbiota • Clearly define desired outcomes and best practices in testing immunomodulators
Microbiome:	• Increase knowledge on 'the microbiome', particulrly in different production forms/age-groups • Understanding mode of action of effective probiotics • Functional studies on the microbiome, linking taxonomy with function • Determine the impact microbiome shaping on vaccine efficacy and basic metabolic turnover

VACCINES – Three valuable reports worth to be rescued !

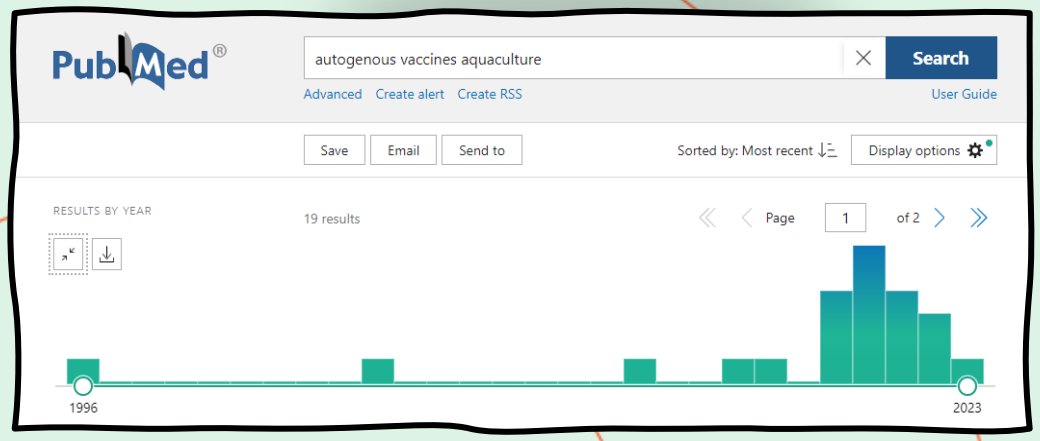
- Disease, antibiotic usage, availability of marketed vaccines, constraints for use or development, **priority**
- Freshwater cyprinids, marine salmonids, other marine fish, catfish
- Highest research priority assigned to
  - Freshwater cyprinids – *Aeromonas hydrophila* and other species, and *Pseudomonas* spp.
  - Marine fish - *Vibrio* spp., *Photobacterium* spp. and *Streptococcus* spp.
  - Catfish – *Edwardsiella ictaluri*, *E. tarda*, *Aeromonas hydrophila* and other species
- Research is needed on how to safely and affordably vaccines can be applied to large populations



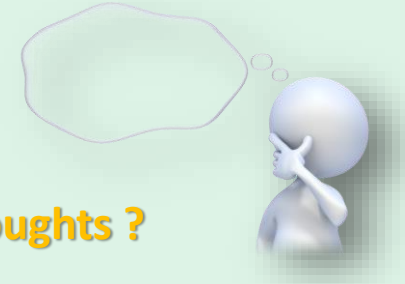
VACCINES – What about autogenous vaccines ?



- **Autogenous (auto) vaccines are custom vaccines produced from pathogens isolated directly from affected farm(s)** on which the vaccines are subsequently deployed under a minor use or restricted permit.
- Alternative in cases where value of produced fish is low, when diversity of diseases is high, and evolution of diseases is fast
- Already used in terrestrial animals, as well as in aquatic environments
  - Atypical *Aeromonas*,
  - Novel biotypes of *Yersinia ruckeri* infections in salmonids,
  - Streptococcal pathogens in barramundi and stingrays and, in Tilapia,
  - Intracellular pathogen *Francisella noatuensis* …
- Evidence-based formulation is critical – Enhanced diagnostics capacities
- Enable local production & blended vaccination strategies



- Very scarce scientific literature
- Currently, no international standard
- In the workplan from the AMR Working Group



What are your thoughts ?

3. Reducing the need

BIOSECURITY – Chapter 4.1 Aquatic Animal Health Code

- **Biosecurity** is a set of **management and physical measures** which, when used together, cumulatively **reduce the risk of infection** in aquatic animal populations within an aquaculture establishment. Planning and implementation requires identification of risks and cost-effective measures.
- The measures required will vary among aquaculture establishments, depending on factors such as likelihood of exposure to pathogenic agents, the species of farmed aquatic animal, the category of aquaculture production system, husbandry practices, environmental conditions and geographical location.
- **Chapter 4.1 (updated in 2021)** describes recommendations on biosecurity to be applied to aquaculture establishments, including semi-open, semi-closed and closed systems

Article 4.1.5.
Categories of aquaculture production systems

Article 4.1.6.
Area management

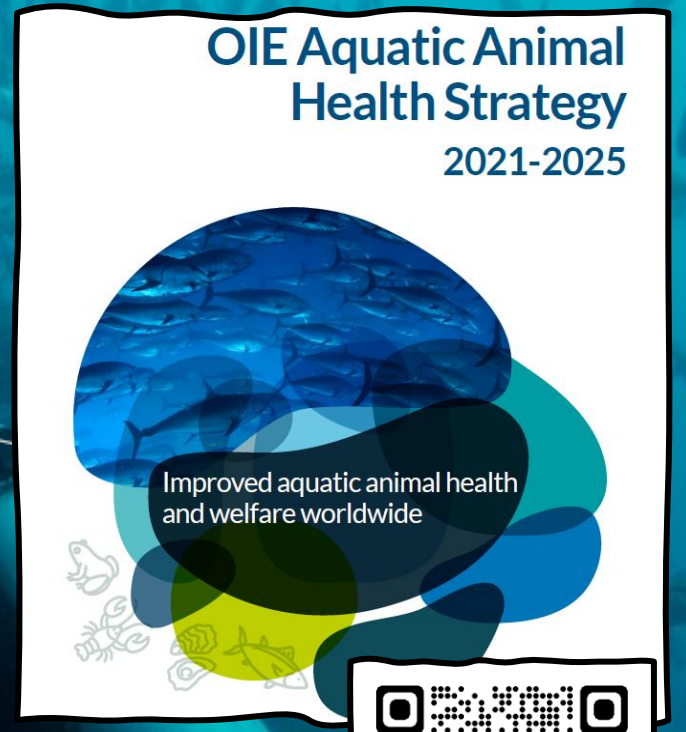
Article 4.1.7.
Transmission pathways and mitigation measures

Article 4.1.8.
Risk analysis

Article 4.1.9.
Biosecurity plan development

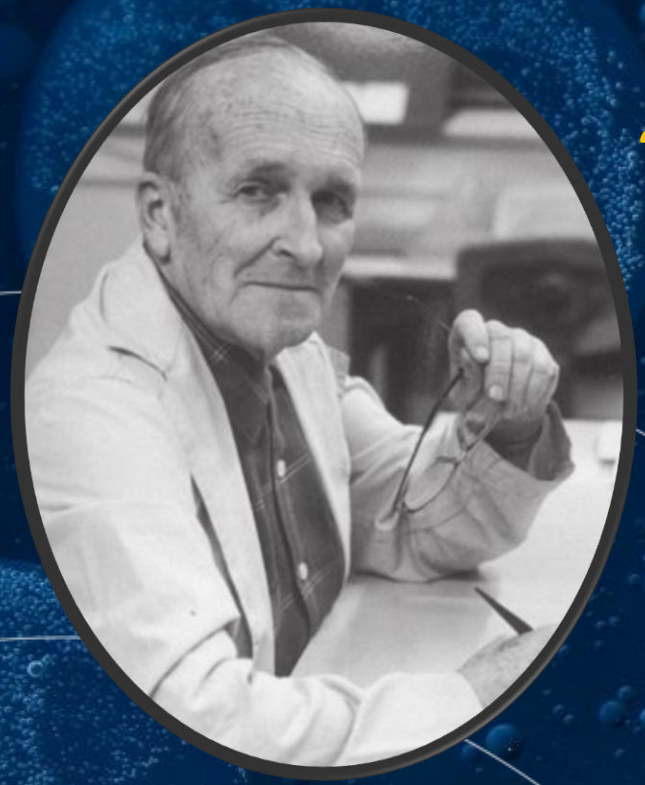
Aquatic Animal Health Strategy

This Aquatic Strategy is a call to action to address some of the WOAH Community's greatest challenges in managing ***aquatic animal health and welfare****. It will identify and coordinate actions that address the highest-priority common needs and focus resources on activities that will provide enduring impacts*



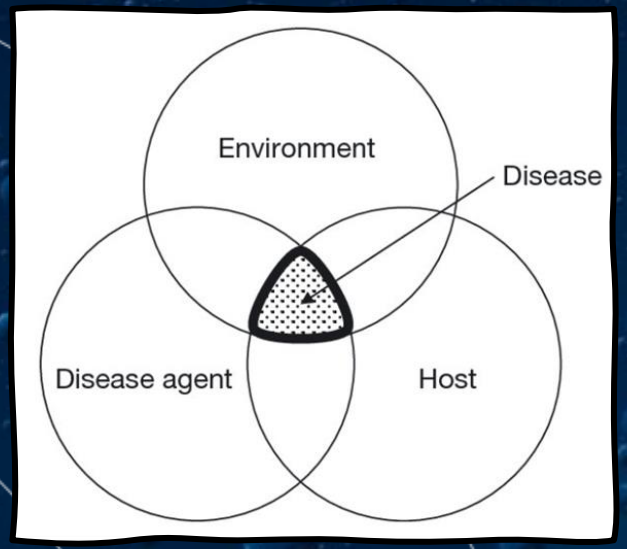
Activity 1.3 - Review the scientific basis of existing aquatic animal welfare standards. This Activity will review the science of aquatic animal welfare to evaluate whether standards continue to provide recommendations that are scientifically sound and meet the needs of Members. Priorities include assessing the developing science on sentience in aquatic animals and evaluating contemporary industry practices to promote welfare. This Activity will complement the OIE Animal Welfare Strategy and contribute to **increased understanding of aquatic animal welfare and its promotion through relevant standards.**

Animal Health & Animal Welfare – Interconnected tools against AMR



"Don't simply look at the pathogen as the source of the problem, but rather look at the disease as the symptom of the problem"

Dr Stalisnas Sniezko (1902–1984)



Animal welfare is an integral part of animal health, and improvement measures can contribute to decreasing the need for antimicrobials. Best practices in animal welfare align with measures recognized as imperative in the fight against antimicrobial resistance.

And if things go wrong...please communicate, inform about it !!

CHAPTER 1.4.

AQUATIC ANIMAL DISEASE SURVEILLANCE

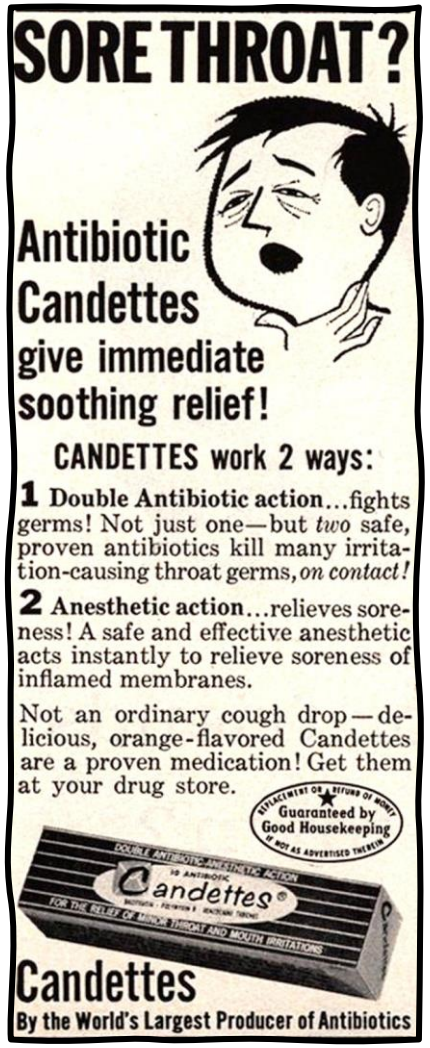
Article 1.4.1.

Purpose

This chapter provides guidance on the *surveillance* approaches to be used by a *Competent Authority* to make and maintain a *self-declaration of freedom from disease* or to confirm the occurrence of a *listed disease* or an *emerging disease*.

Antimicrobials – A conversation with you, today

1958



ADAPTATION

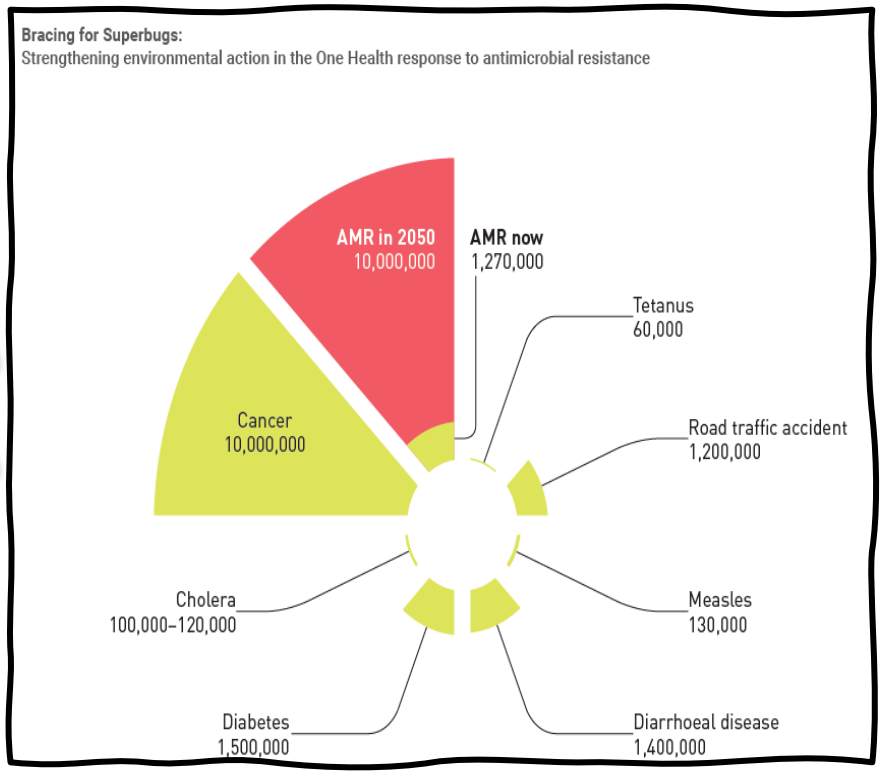
ADAPTATION

2016

ADAPTATION

ADAPTATION

2050



We can still avoid that scenario !

We need dynamic adaptation !

Gracias!
Thank you!
Merci!

ACKNOWLEDGEMENTS TO

- Dante Mateo
- Bernita Giffin
- Melanie Allan
- Elisabeth Erlacher-Vindel

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