FAO Regional Office for Asia and the Pacific, 2013

REPORT of the Regional Expert Workshop on Harmonization and Standardization of Antimicrobial Resistance Monitoring in the Asia-Pacific Region

Bangkok, 14-15 May 2013

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FOOD AND AGRICULTURE ORGANIZATION OF THE UNITED NATIONS
REGIONAL OFFICE FOR ASIA AND THE PACIFIC
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BACKGROUND

Antimicrobial resistance (AMR) is a growing global threat across drug classes and around the world. Although much of the evolving antimicrobial resistance can be attributed to (mis-)use of antimicrobials in humans, research by international scientific bodies supports the conclusion that the overuse of drugs in food animal production is a threat for continued availability of effective treatment of human and animal diseases.

Little systematic research and analysis on the use of antimicrobials (AMU) and AMR in micro-organisms associated with food animals is available for the Asia-Pacific region while individual studies on AMR in food borne pathogens such a *Salmonella spp*. and *Campylobacter spp.* suggest fairly widespread AMR to commonly used antimicrobials.

Against this background, APHCA delegates, at the 36th Session held in Negombo, Sri Lanka, recognised that action in each member country was needed to underpin regional and global AMR risk reduction measures. Delegates however also noted that AMR can only be tackled through a collective effort requiring a degree of harmonization and standardization of approach.

To foster a process of harmonization and standardization for the management of AMR, FAO is convening an Expert Workshop, bringing together national and international experts to exchange information and deliberate on ways forward.

The workshop has the following objectives:

- Exchange information about various protocols for AMU and AMR monitoring / surveillance used in countries of the Asia Pacific region (participants to provide brief report on protocol(s) / approach(es) applied in their country);
- Review approaches for monitoring of AMU in livestock that allows identification (and quantification) of risk factors for the development and occurrence of AMR;
- Review approaches to antimicrobial susceptibility testing (antimicrobial agents, test ranges, interpretive criteria, etc);
- Familiarize participants with methods for AMR risk assessment and risk management;
- Based on the OIE guidelines for AMR surveillance develop proposal for standardized AMR monitoring protocols;
- Identify country-specific support requirements to implement / move towards implementation of the above proposed protocols.

MODULE OUTLINES

THE GLOBAL PROBLEM OF AMR AND CRITICAL ANTIMICROBIALS FOR USE IN HUMANS (J. WAGENAAR)

Objective: To provide the participants with an overview of the discovery and development of antimicrobials over time and the development and trends of AMR parallel to the use of antimicrobials. The problems in humans and animals due to resistant microorganisms will be discussed as well as the relation between human and animal domain. Persistence and containment of resistance from a practical perspective will be covered.

Content: Relation usage-resistance; co-resistance; transfer of resistance (genes or microorganisms) between animals and humans; burden of resistance in animals and humans; persistence of resistance in the presence and absence of antimicrobials; geographical containment of resistance.

Key Points to be covered: Use of antimicrobials will induce resistance and human and animal domains are hardly separated from resistance point of view.

BASIC MICROBIOLOGY TO SET THE STAGE FOR AMR MONITORING AND RISK ASSESSMENT (S. SIMJEE)

Objective: To provide participants with an overview of key food-borne and commensal bacteria of importance to human health. Additionally the module will cover antibiotics, their mode of action and the mechanisms of antibiotic resistance. Genetics of resistance gene transfer will also be covered. This should help set the scene for understanding various aspects of risk assessment.

Content: Basic microbiology so no reference material will be required.

Key points covered:

- Fundamental microbiology
- Antimicrobial mechanism of action
- Antimicrobial mechanism of resistance
- Genetics of resistance

OIE ACTIVITIES ON AMR AND RECOMMENDATIONS OF THE GLOBAL CONFERENCE ON THE RESPONSIBLE AND PRUDENT USE OF ANTIMICROBIAL AGENTS FOR ANIMALS (H.T. MYINT)

Objective: To provide participants with an overview of OIE activities on AMR, inform them on the recommendations of the OIE Global Conference on the Responsible and Prudent Use of Antimicrobial Agents for Animals and follow up actions.

Content: OIE standards on terrestrial and aquatic animals, OIE list of Antimicrobial Agents of Veterinary Importance, Questionnaire an results on monitoring of the quantities of antimicrobial agents used in animals in OIE Member Countries, recommendations of the OIE Global Conference, follow up actions.

Key Points to be covered:

- Updates on OIE codes and standards and the OIE list of Antimicrobial Agents of Veterinary Importance
- Questionnaire and results
- Recommendations of the OIE Global Conference and follow up actions

AMU AND AMR MONITORING FOR AMR RISK ASSESSMENT AND RISK MANAGEMENT (T. SHRYOCK)

Objective: To provide participants with an overview of risk assessment processes, data inputs and application for risk management intervention selection in order to facilitate implementation.

Content: The OIE Terrestrial Code Risk Analysis document, the Vose et al., 2003 paper and the Codex GL77 will be referenced, as will national regulatory risk assessment guidelines from the US and Australia.

Key points to be covered:

- Prerequisites for risk assessment
- OIE vs. Codex risk analysis approaches
- Practical considerations for implementation
- Where to begin?
- Next steps

APPROACHES TO AMU AND AMR MONITORING / SURVEILLANCE AND THEIR LIMITATIONS (D. PFEIFFER)

Objective: To provide participants with an introduction to methods for monitoring / surveillance of AMU and AMR

Content: Complexity of livestock production and food systems; linking risk assessment and monitoring/surveillance; bias and error in surveillance; surveillance/monitoring approaches

Key Points to be covered:

- Production/food system characteristics
- Drivers of AMU and AMR
- Risk and surveillance programme design
- Sources of bias
- Surveillance and monitoring approaches

ANTIMICROBIAL SUSCEPTIBILITY TESTING (AST) WITH LIMITED RESOURCES (S. SIMJEE)

Objective: To provide an understanding of the key methods currently approved for AST. Help participants understand how best to perform AST with limited resources. The session will wrap up with methods currently available to interpret AST data and the need for harmonization for data comparison between regions.

Content: The CLSI M31, M37 and X08-R documents and the Franklin et al (2001) OIE paper will be referenced throughout the presentation.

Key points covered:

- AST Methods
- AST data interpretation
- The need for harmonization

RESPONSIBLE USE / CLINICAL PRACTICE GUIDELINES (T. SHRYOCK)

Objective: To provide participants with an overview of Responsible Use Guidelines from WHO, OIE and Codex that describe stakeholder responsibilities and to provide Clinical Practice guidelines consistent with the World

Veterinary Association and regional / country veterinary medical organizations. The guidelines provide a roadmap to appropriate antimicrobial product use and can be used to change behaviors of those who administer antimicrobial products to animals.

Content: The WHO, OIE and Codex Responsible Use guidelines will be referenced, as will WVA and other veterinary practice guidelines, with supplemental documents also provided.

Key Points to be covered:

- Common themes among the documents for stakeholder responsibilities
- Clinical practice guidelines – consensus principles outlined
- Practical considerations for implementation
- Next steps

THE GLOBAL PROBLEM OF AMR AND CRITICAL ANTIMICROBIALS FOR USE IN HUMANS

J. Wagenaar

The global problem of AMR and critical antimicrobials for use in humans

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Faculty of Veterinary Medicine, Utrecht University, Utrecht - NL

Central Veterinary Institute, Lelystad - NL
j.wagenaar@uu.nl

Outline

- Antimicrobial resistance: the problem
- Impact of veterinary use
  - MRSA
  - ESBLs
- What can we do to control increasing resistance
- The future and the way forward

BMC Infectious Diseases

RESEARCH ARTICLE Open Access

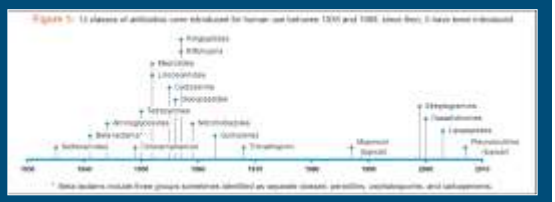
Antimicrobial susceptibility and genetic characteristics of *Neisseria gonorrhoeae* isolates from Vietnam, 2011

BMC Infectious Diseases

RESEARCH ARTICLE Open Access

Antimicrobial susceptibility and genetic characteristics of *Neisseria gonorrhoeae* isolates from India, Pakistan and Bhutan in 2007–2011

Development of antimicrobials



Resistance

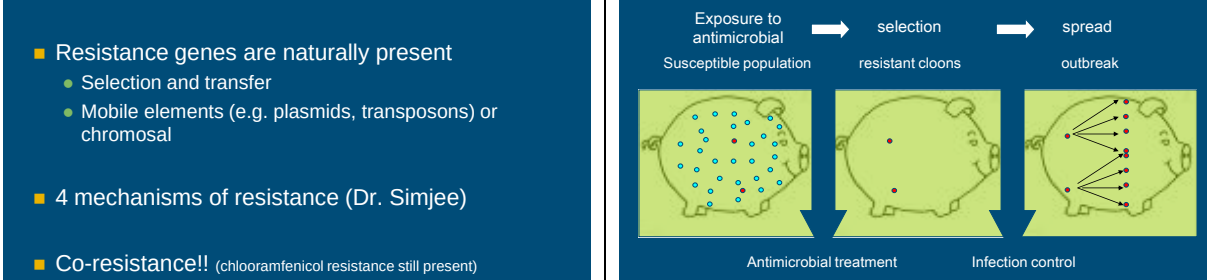
Consequence of use:

- Resistance to penicillin 1947
- Resistance to methicillin 1960 (3 months after introduction)

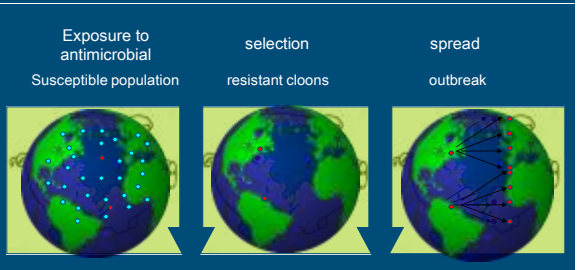
Presence of resistance

- Resistance genes are naturally present
  - Selection and transfer
  - Mobile elements (e.g. plasmids, transposons) or chromosal
- 4 mechanisms of resistance (Dr. Simjee)
- Co-resistance!! (chlooramfenicol resistance still present)

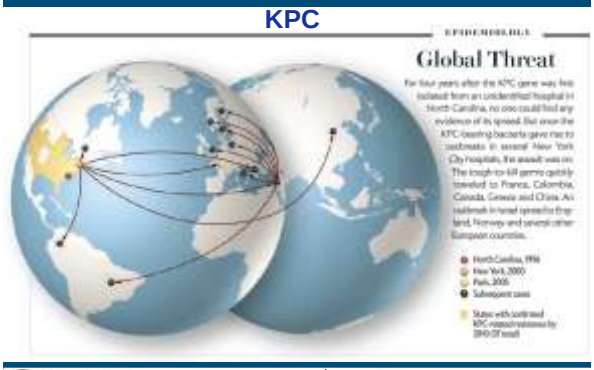
Selection and spread of resistance



Selection and spread of resistance



Carbapenemase positive Klebsiella (KPC)



Antimicrobials:

the more you use, the faster you lose

regardless if the use is in animals or in humans

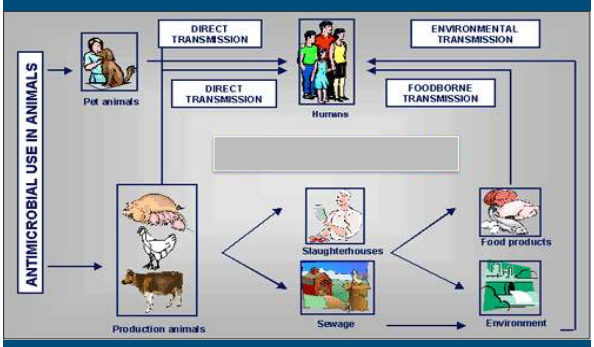
Humans are just another type of animal….

Bacteria may transfer between animals to humans

- Pathogens:
  - *Salmonella*
  - *Listeria*
- Commensals (gut-flora = reservoir of resistance genes and transfer of resistance genes)
  - *E. coli*

Human, animal and environmental microbial compartments are not separated

Antimicrobial resistant microorganisms (and genes!) can transfer between compartments



Problem for public health

- Public Health threat: the emergence and spread of antibiotic resistance
- Use and misuse of antibiotics by individuals: threat to others
- antibiotic resistance: increased health-care costs, failed treatments, and deaths.

Problem for animal health

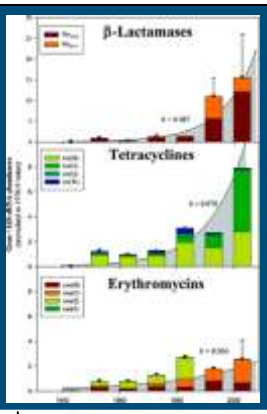
- Resistance in animal pathogens?
  - Treatment of *E. coli* in poultry?
  - Treatment of respiratory pathogens?

Antimicrobial resistance: some considerations

- Widespread use of antimicrobials in livestock production ….not only for therapeutic purposes
- Same classes of antimicrobials in humans and animals
- Few new antimicrobials in the pipeline
- Globalization (food trade, travel): need for international action
- Spread of resistant organisms (and genes!) through environment and food


Evidence of Increasing Antibiotic Resistance Gene Abundances in Archived Soils since 1940

Environ. Sci. Technol 2010, 44, 580–587



Use of antibiotics in animals

- Therapeutic use: to treat sick animals
- Prophylactic use: to prevent infection in animals
- Metaphylactic use: to treat preventively when spread is likely
- Growth promoters:
  - To improve feed utilization, production (economics!): antimicrobials used in subtherapeutic concentrations
  - Control of chronic diseases in intensively-reared animals
- More than 50% of all antimicrobials are used non-therapeutically in animal husbandry

2 examples

- MRSA (Methicillin Resistant *Staphyloccus aureus*)
- ESBL (Extended Spectrum Beta Lactamase producing bacteria)

LA-MRSA

- Dominated by ST398 (EU, US) ST9 (Asia)
- Recently introduced (‘invented’ in NL) 2005
- No problem for animal health but exposed humans may become carrier
- Health risks for humans and increased costs for health care
- In the Netherlands: strict infection control in hospitals (virtually no MRSA)
- Farmers experienced problems by themselves!!


NEWSFOCUS

From Pigs to People: The Emergence of a New Superbug

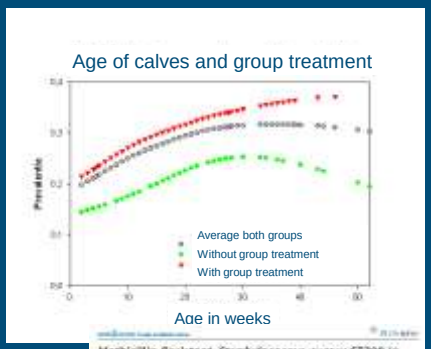
Science (329), 27 August 2010

Prevalence MRSA veal farms: 88%

People living at veal farms on average 16%
- Farmers: 33%
- Family members: 8%

Prevalence MRSA on pig farms: >70%

People living on pig farms on average 14%
- Farmers: 49%
- Family members: 3%



Methicillin Resistant *Staphylococcus aureus* ST398 in Veal Calf Farming: Human MRSA Carriage Related with Animal Antimicrobial Usage and Farm Hygiene

ESBL Problem

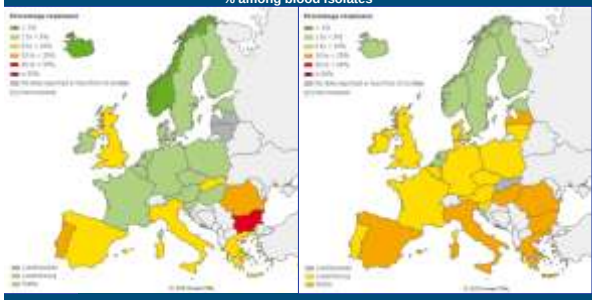
- Enzymes in Gram-negative bacteria (*E. coli, Klebsiella*)
- ESBLs are resistant to all beta-lactams (penicillines and cefalosporines) and usually to many other classes of antimicrobials
- Increasing prevalence of ESBLs in human infections (general population and health care facilities)
- Rapid spread of resistance (genes on plasmids)
- The diversity of genes is huge!!

ESBL results from the Netherlands

- Almost all broilers are carrier of ESBLs in the gut.
  Most poultry meat is contaminated (≥ 90%)
- About 40% of the pig farms is positive
  - Pork ± 15% contamination
- 50% of batches of veal calves are positive at slaughter
- 20% of clinical isolates from humans are genetically indistinguishable from poultry isolates

Dutch patients, retail chicken meat and poultry share the same ESBL genes, plasmids and strains

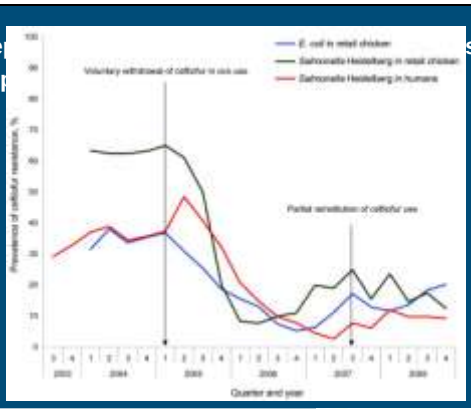
2005 % among blood isolates 2009



Escherichia coli, resistant to third generation cephalosporins (~ ESBL positive)

The European Surveillance System (TESSy, ECDC)

Ce se in p

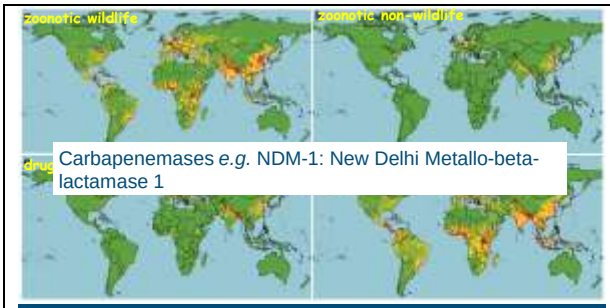


Changes needed

- How to change the farmer/veterinarian?
- How to change the husbandry system?
- What are the drivers behind these changes?
  - Economics
  - Media attention (with political consequences)
  - Farmers experience problems themselves

Future threats, predictions….

- Predicting outbreaks and new introductions of infectious diseases and antimicrobial resistance is difficult



Global distribution of relative risk of an EID event

KE Jones et al., Nature 2008

Way forward

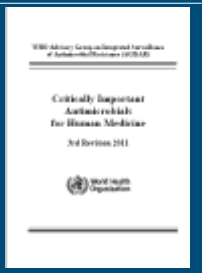
- ''More than 50% of all antimicrobials are used non-therapeutically in animal husbandry''
- Need for better control over use of antibiotics in husbandry (reduction!!): changes in the production system
- Keep animal and human antimicrobials separated (critically important antimicrobials for human medicine)
- Joined forces between WHO-FAO-OIE
- Active surveillance of evolution of microbes and resistance trends
- It is a global problem and all countries have their responsibility
- Development of new agents

For the near future…

- There is an urgency for action.
- Awareness at farmer/veterinarian and policy level.
- How to get it prioritized?
- Provide decision makers with data on usage and resistance

Critically important antimicrobials for human medicine

- Improved management of the use of antimicrobials in food animals, particularly reducing those *critically important* for human medicine, is an important step towards preserving the benefits of antimicrobials for people. The World Health Organization (WHO) has developed and applied criteria to rank antimicrobials according to their relative importance in human medicine.
- Collaboration between WHO, OIE and FAO!


Critically Important Antimicrobials for Human Medicine

Don't say:

- it all comes from abroad….
  - Local policy is effective!!
- A big proportion of the problem comes from humans, they have to do something….
  - that is true but it will not reduce our responsibility in animal production sector

INTRODUCTION TO MICROBIOLOGY, ANTIBIOTICS AND ANTIBIOTIC RESISTANCE

S. Simjee

Introduction to Microbiology, Antibiotics and Antibiotic Resistance

Dr Shabbir Simjee
Microbiologist
Elanco Animal Health
Basingstoke
England
simjeess@lilly.com

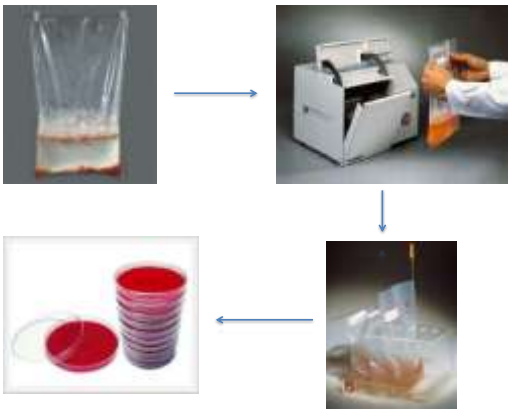
APHCA AMR Expert Workshop
Bangkok, Sukosol Hotel, 14 to 15 May 2013

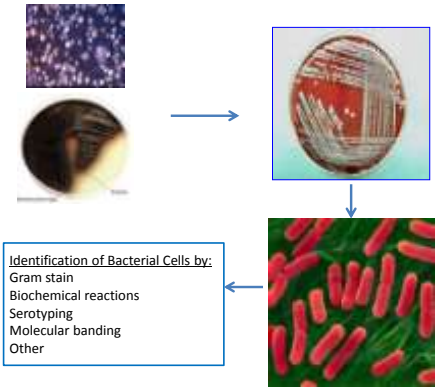
FAO's AMR Capacity Development Pillars

1. Policies
   - Support for development and implementation of policies that create the enabling environment for AMR prevention and control and prudent use of antimicrobials in animal production and human medicine
2. Support for institutional capacity development:
   - Strengthening of institutional framework and arrangements;
   - enhance institutional capacities e.g. labs for generation of AMR data, of AMR surveillance and AM usage monitoring; and data sharing between sectors;
3. Support Technical Capacity development: AMR Detection, surveillance, AMU Monitoring,
4. Support/advice to value chain operators and stakeholders - Good animal husbandry & health practices, good hygienic practices

Patrick Otto, *Animal Health Officer (Veterinary Public Health) FAO, Rome*

From Food Animal to MIC Data



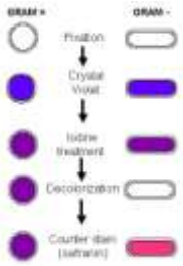


Identification of Bacterial Cells by:
Gram stain
Biochemical reactions
Serotyping
Molecular banding
Other

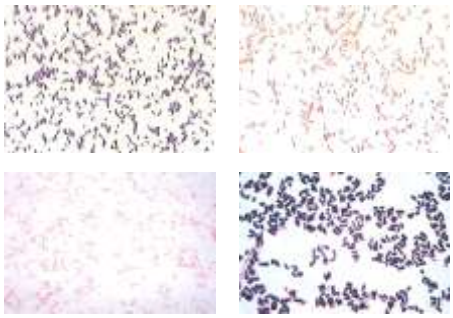
www.xenopus.com/disease.htm

Gram stain

1844 Danish bacteriologist, Hans Christian Gram, devised method to stain and visualise bacteria

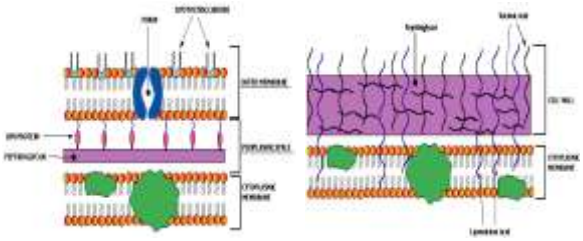


G+ and G- Bacteria



Cell Wall Architecture

Staining differences are explained by cell wall differences



Gram-negative cell wall

Gram-positive cell wall

Typing Methods: Biotyping

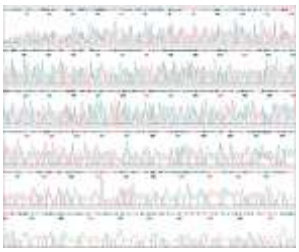
Speciation using biochemical testing

Cost:
Commonly used API strips ~ £180 for a pack of 25
Additional costs of around £12-£25 for reagents
Additionally labour intensive (5 mins per strip)

DNA Sequencing confirmation

PCR of 16S ribosomal subunit followed by DNA sequencing

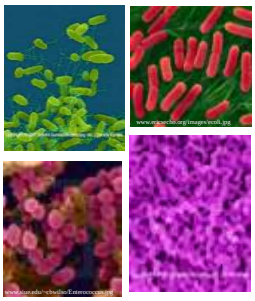
ABI 3700



Cost:
Market cost around £95 for one isolate for region between 1 and 750bp

MALDI-TOF Biotyper System – Cost: market cost around £8 per isolate

Which Bacteria?



- *Salmonella*
- *E. coli*
- *Campylobacter*
- *Enterococcus*

Animal pathogenic bacteria that are targeted by the antibiotic are not the issue

E. coli O157:H7

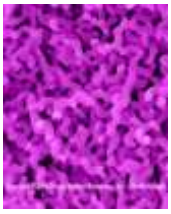
- *E. coli* usually commensal; indicator organism
- Enterohemorrhagic (EHEC) serotype O157:H7 toxin causes hemorrhagic colitis and hemolytic uremic syndrome
- Not treated with antibiotics because that will kill the bacteria and release more toxin

www.ericsecho.org/images/ecoli.jpg

Nontyphoidal *Salmonella enterica*

- Gram-negative pathogen; high morbidity, and some mortality
- Treatment options include fluoroquinolones, 3rd generation cephalosporins, etc.
- Multi-drug resistance e.g. ACSSuT and others

Campylobacter jejuni



• Gram-negative pathogen; high morbidity but low mortality

• Treatment options include: Fluoroquinolones (empiric), macrolides (diagnosed), etc.

•Not multi-drug resistant

Enterococcus

• Gram positive bacterium, usually commensal; indicator organism for resistance genes

• Does not cause a true foodborne disease

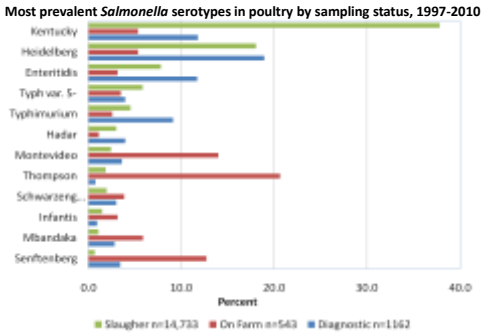
• Nosocomial infections: UTI, intra-abdominal, pelvic, and soft tissue infections, bacteremia, endocarditis

• Treatment options: vancomycin, streptogramins, ampicillin-gentamicin, oxazolidinones, etc.

www.siue.edu/~cbwilso/Enterococcus.jpg

Sample Collection

If food animal samples then need to consider collection point



(Paula Cray, USDA, 2011)

Sample Origins

If the bacterial isolates will undergo susceptibility testing with the goal of using the data for risk assessment then the samples must originate from appropriate sources to provide data for the relevant steps of the risk assessment

•Release
Samples should come from the farm

•Exposure
Samples should come from slaughter houses or retail meat

•Consequence
Samples should come from humans, ideally pre-treatment samples

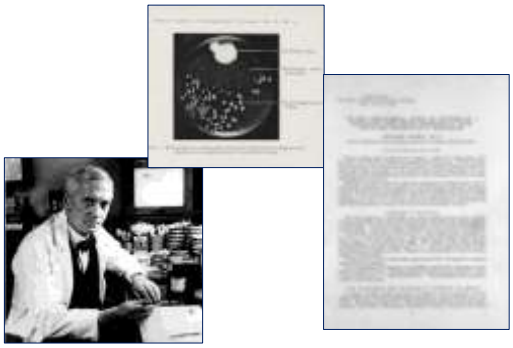
Bacterial Storage

Bacterial Freezing Kit allow for a simple and convenient method for preserving bacteria directly from culture. Each vial contains sterile 3 mm glass beads and 250µl 30% glycerol. Simply add 250µl of culture broth with actively growing cells, mix, label and freeze.

These tubes can be used for any temperature storage, though ultralow and cryogenic temperatures are most effective for long-term viability of bacteria.

Commercial cost : £125/100 ready made tube, cheaper to make in-house

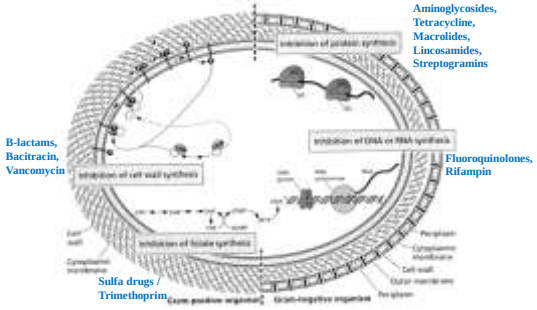
Antibiotics



Major Classes of Antibiotics (cross-resistance)

- β-lactams (Penicillins and cephalosporins)
  amoxicillin, ceftriaxone; ceftiofur
- Macrolides and Lincosamides
  erythromycin; tylosin, tilmicosin, lincomycin
- Glycopeptides
  vancomycin, teicoplanin; avoparcin
- Aminoglycosides
  gentamicin; neomycin, apramycin
- Fluoroquinolones
  ciprofloxacin; enrofloxacin
- Tetracyclines
  doxycycline, tetracycline; oxytetracycline
- Sulfonamides-trimethoprim
  sulfamethoxazole; sulfonamide + trimethoprim
- Streptogramins
  quinupristin/dalfopristin; virginiamycin
- Polypeptides
  bacitracin
- Orthosomycin
  avilamycin, evernimicin
- Polyether Ionophores
  monensin, narasin

Antibiotic Targets



Walsh, C. T. 2003. Antibiotics: Actions, origins, resistance

4 Mechanisms of Action

4 Mechanisms of Resistance

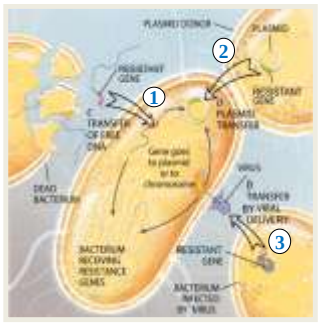
- **Antibiotic inactivation**
  - –Beta-lactams, Aminoglycosides, Chloramphenicol, Streptogramins
- **Alteration of target enzyme**
  - –Sulfa drugs, Fluoroquinolones
- **Alteration of target binding site**
  - –Streptomycin, Erythromycin
- **Reduced cellular uptake; active efflux**
  - –Tetracycline, Macrolides, Fluoroquinolones, Phenicols, B-lactams

New Strain Development

New traits *e.g.* antibiotic resistance or virulence are acquired by:

- Chromosomal mutation:
  - – Results in vertical transfer from parent to daughter cell
- Mobile DNA :
  - – Plasmids, Transposons or Integrons
  - – Results in both vertical and horizontal transfer
    - Horizontal transfer = transfer between bacteria of same species, same genus or different genus

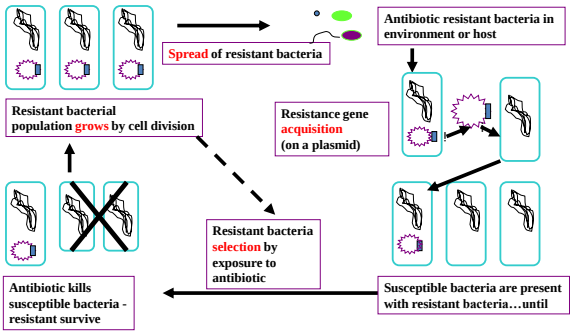
Gene Transfer



1. Transformation
2. Conjugation
3. Transduction

Levy, S.B. 1998. *The Challenge of Antibiotic Resistance*. Scientific American.

Antibiotic Resistance Cycle (co-selection)



Why Targeted Spectrum First Line?

Targeted spectrum act predominantly on one category

Gram negative

Gram positive

Broad spectrum act on both

Questions?

OIE ACTIVITIES ON AMR AND RECOMMENDATIONS OF THE 'GLOBAL CONFERENCE ON THE RESPONSIBLE AND PRUDENT USE OF ANTIMICROBIAL AGENTS FOR ANIMALS'

H.T. Myint

OIE activities on AMR and Recommendations of the Global Conference on the Responsible and Prudent Use of Antimicrobial Agents for Animals

APHCA Expert Workshop, Bangkok, 14-15 May 2013

Dr Hirofumi Kugita, Dr Hnin Thidar Myint
OIE Regional Representation for Asia and the Pacific

Contents

- OIE activities on prudent and responsible use of antimicrobial agents
- OIE list of Antimicrobial Agents of Veterinary Importance
- Questionnaire and results on monitoring of the quantities of antimicrobial agents used in animals in OIE Member Countries
- Recommendations of the OIE Global Conference
- Ongoing and future global collaboration

OIE Global Mandate: "to improve animal health veterinary public health and animal welfare world-wide"

Responsible and Prudent Use of Antimicrobial Agents

- In accordance with its mandate, **OIE considers the use of antimicrobial agents in food producing animals as a key issue for human health, animal health and animal welfare**
- Since a decade, the OIE has been working actively on this issue

Actions of the OIE

In promoting the responsible and prudent use of antimicrobial agents in veterinary medicine

- Reinforcement of **good governance of Veterinary Services** for better control in registration, import, distribution and on-farm use of antimicrobials
- **Develop and update standards** for the containment of antimicrobial resistance & the responsible and prudent use of antimicrobial agents
- Encourage **international coordination and solidarity** programmes
- Support of **capacity building**
- **Condemning the marketing** and use of fake products

OIE Standard and Guidelines

- **Section – 6: Veterinary Public Health**
  - **Chapter 6.6. Introduction to the recommendations for controlling antimicrobial resistance**
  - **Chapter 6.7. Harmonisation of national antimicrobial resistance surveillance and monitoring programmes**
  - **Chapter 6.8. Monitoring of the quantities and usage patters of antimicrobial agents used in food producing animals**
  - **Chapter 6.9. Responsible and prudent use of antimicrobial agents in veterinary medicine**
  - **Chapter 6.10. Risk assessment for antimicrobial resistance arising from the use of antimicrobial agents in animals**

http://www.oie.int/en/international-standard-setting/terrestrial-code/access-online/

OIE Standard and Guidelines

Chapter 6.7. Harmonisation of national antimicrobial resistance surveillance and monitoring programmes

- Criteria for development of national antimicrobial resistance surveillance and monitoring programmes
- Harmonisation of existing programmes in food producing animals and in products for human consumption
- Surveillance and monitoring programmes of the prevalence of resistance in bacteria in animals, food and environment is a critical part of animal health and food safety strategy
- Monitoring of bacteria from products of animal origin intended for human consumption collected at different steps of the food chain are also considered.

OIE Standard and Guidelines

Chapter 6.8. Monitoring of the quantities and usage patterns of antimicrobials agents in food producing animal

- Monitoring the quantities and usage patters of Antimicrobial Agents in food producing animals is essential for antimicrobial resistance risk analyses and for planning purposes
- Development and standardization of monitoring systems considering the sources of antimicrobial data, the types of use and reporting formats
- Essential elements when conducting risk assessments, as described in Chapter 6.10

OIE Standard and Guidelines

Chapter 6.9. Responsible and prudent use of antimicrobial agents in veterinary medicine

- Responsible and prudent use is principally determined by the outcome of marketing authorization and by the distribution, prescription and administration of veterinary medicinal products containing antimicrobial agents. Recommendations are provided for each of the parties involved:
  - regulatory authority
  - veterinary pharmaceutical industry
  - wholesale and retail distributors
  - veterinarians
  - food-animal producers

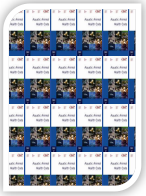
OIE Standard and Guidelines

Chapter 6.10. Risk assessment for antimicrobial resistance arising from the use of antimicrobial agents in animals

- Analysis of risks to human health, and
- Analysis of risks to animal health:
  - Definition of the risk
  - Hazard identification
  - Release assessment
  - Exposure assessment
  - Consequence assessment
  - Risk estimation
  - Risk management options

OIE Standard and Guidelines

- **Section – 6: Veterinary Public Health**
  - **Chapter 6.2. Introduction to the recommendations for controlling antimicrobial resistance**
  - **Chapter 6.3. Principles for responsible and prudent use of antimicrobial agents in aquatic animals**
  - **Chapter 6.4. Monitoring of the quantities and usage patterns of antimicrobial agents used in aquatic animals**
  - **Chapter 6.5. Development and harmonisation of national antimicrobial resistance surveillance & monitoring programmes for aquatic animals**
  - **Chapter 6.x. Risk assessment for antimicrobial resistance arising from the use of antimicrobial agents in aquatic animals (under development)**



http://www.oie.int/en/international-standard-setting/aquatic-code/access-online/

OIE Standard and Guidelines

- **Part 3: General Guidelines:**

  3.1. Laboratory methodologies for bacterial antimicrobial susceptibility testing

http://www.oie.int/en/international-standard-setting/terrestrial-manual/access-online/

OIE Expertise

- **Network of 236 OIE Reference Laboratories and 41 OIE Collaborating Centres**
- Amongst this network:
  - **Collaborating Centre for Veterinary Medicinal Products (France)**
  - **Collaborating Centre for Diagnosis and Control of Animal Diseases and Related Veterinary Product Assessment in Asia (Japan)**
  - **Collaborating Centre for Veterinary Drug Regulatory Programmes (USA)**
  - **Reference Laboratory on Antimicrobial Resistance (UK)**

Communication/Training

- Publications
- International and regional conferences
- Regional training for OIE National Focal Points on veterinary products

OIE List of Antimicrobial Agents of Veterinary Importance

- FAO/OIE/WHO Expert Workshop on Non-Human Antimicrobial Usage and Antimicrobial Resistance in 2003 & 2004 recommended the OIE to develop the List
- The OIE sent a questionnaire to Member countries, responses were analyzed by experts, the List developed in 2006
- **The International Committee unanimously adopted the List at its May 2007 General Session (Resolution XXVIII)**

OIE List of Antimicrobial Agents of Veterinary Importance

Based on the response rate to the questionnaire and treatment of serious animal diseases, and availability of alternative antimicrobial agents, the following categories were established:

- Veterinary Critically Important Antimicrobial Agents **(VCIA)**
- Veterinary Highly Important Antimicrobial Agents **(VHIA)**
- Veterinary Important Antimicrobial Agents **(VIA)**

OIE List of Antimicrobial Agents of Veterinary Importance

- The OIE *ad hoc* Group on Antimicrobial Resistance met in July 2012 to review and update the List, taking into account the top three critically important antimicrobials of the WHO list for human medicine
- The revised list was endorsed by the Scientific Commission and will be submitted for adoption by the General Assembly in May 2013

Recommendations:

- Any use of antimicrobial agents in animals should be in accordance with OIE standards on responsible and prudent use laid down in Chapter 6.9 of the Code
- Antimicrobial agents in the OIE List should be classified according to the three categories (VCIA, VHIA and VIA)

OIE List of Antimicrobial Agents of Veterinary Importance

2012 Revision of the List to be presented at 2013 General Assembly

For a number of Antimicrobial Agents there are no or few alternatives for the treatment of diseases in target species. In this context, particular attention paid on VCIA and VHIA.

Among the VCIA, some are also considered of critical importance for human and animal health (**third and fourth generation Cephalosporins, and Fluoroquinolones**):

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

OIE Global Conference

on the Responsible and Prudent use of Antimicrobial Agents for Animals
Paris, 13 – 15 March 2013

Objectives

- Present an **overview** of the current global situation regarding antimicrobial use in animals and antimicrobial resistance
- Inform on **initiatives** taken by the OIE and other international organisations to promote prudent and responsible use of antimicrobial agents in animals at national, regional and international level
- Promote **good governance practices** and encourage international cooperation;
- Foster and strengthen **cooperation** with Veterinary Statutory Bodies, the veterinary profession and veterinary education establishments
- Present **scientific findings** on the alternatives that could be used in animal production replacing antimicrobial agents

Feedback from Global Conference: Questionnaire

Questionnaire divided into two parts:

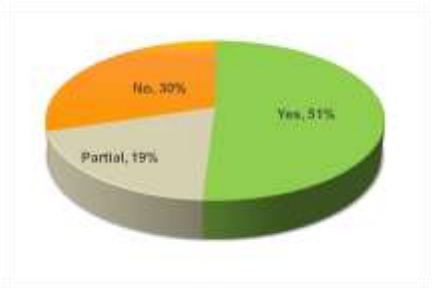
1. **General context** (three main questions - legislation covering Veterinary Medicinal Products (VMP) - use of growth promoters in Member Countries - a system for collecting quantitative data on antimicrobial agents used in animals)
2. **Implementation of the OIE standard** (Chapter 6.8. of the *Terrestrial Code*) – 2 sub-parts:
   - One part for those countries that do not have an official system for collecting quantitative data on antimicrobial agents used in animals (seven main questions)
   - One part for those countries that have an official system for collecting quantitative data on antimicrobial agents used in animals (nine main questions)

Feedback from Global Conference: Questionnaire

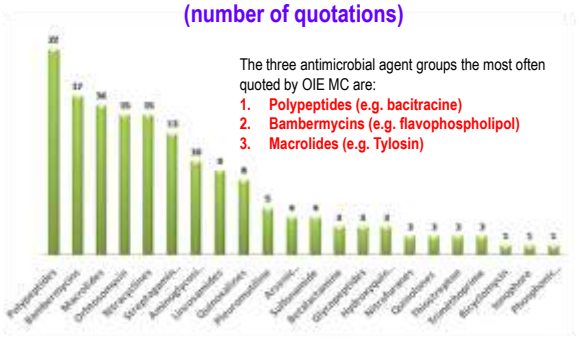
Replies and analysis

- Sent to all the OIE Delegates and copied to the OIE National Focal Points for Veterinary Products in June 2012 (final deadline September 2012)
- 152 questionnaires received from 178 OIE Member Countries = **85% replied**
- OIE National Focal Points for Veterinary Products were mainly in charge of filling in the Questionnaire

Proportion of OIE Member Countries banning the use of antimicrobial agents as growth promoters



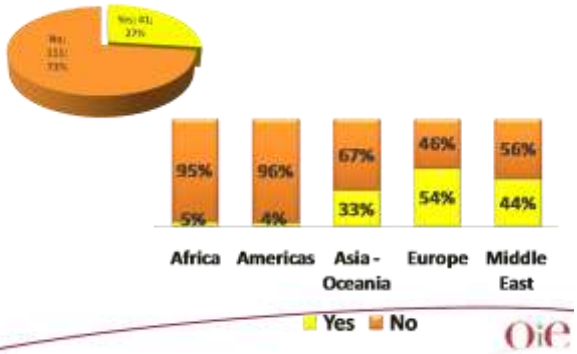
Growth promoters named by OIE Member Countries (number of quotations)



The three antimicrobial agent groups the most often quoted by OIE MC are:

1. **Polypeptides (e.g. bacitracine)**
2. **Bambermycins (e.g. flavophospholipol)**
3. **Macrolides (e.g. Tylosin)**

Proportion of OIE Member Countries with an official system for collecting quantitative data



Recommendations of the OIE Global Conference

To the OIE Member Countries

3. To **develop and set up an official harmonised national system** for collecting data on the monitoring of antimicrobial resistance in relevant animal pathogens and quantities of antimicrobial agents used in food producing animals at the national level based on the OIE standards

11. To **contribute and to participate in global or regional cooperation** aiming at developing measures for responsible and prudent use of antimicrobial agents in animals

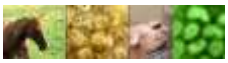
Recommendations of the OIE Global Conference

To the OIE Member Countries

12. To **promote good agriculture and aquaculture practices** including the use of vaccines where applicable and interact with all relevant interested parties while ensuring **compliance with OIE and Codex Alimentarius standards** to minimise the development and spread of antimicrobial resistance

Need for common actions!

- A stronger collaboration between WHO, FAO and OIE through the Tripartite agreement
- Sharing responsibilities and coordinating global activities to address health risks at the animal-human-ecosystems interfaces
- Three 'flagship' topics:
  - Zoonotic influenza
  - Rabies
  - **Antimicrobial resistance (AMR)**



Conclusion: Antimicrobial Use in Animals

Problems related to AMR are linked to antimicrobial use in any environment, including human and non-human usages. Antimicrobial resistance is not a recent phenomenon, but it is critical to take action now to keep antimicrobial agents effective and useful to combat disease.

- Animal health and welfare must be sustained
- Food security and food safety must be ensured
- Practices at risk such as the use of antimicrobial agents for animal growth promotion should be carefully evaluated
- No universal optimal solution for the delivery of antimicrobial agents at farm level worldwide, the well qualified veterinarian is the key actor
- International solidarity is crucial in a globalised world

AMU AND AMR MONITORING FOR AMR RISK ASSESSMENT AND RISK MANAGEMENT

T.R. Shryock

Risk Assessment & Risk Management AMU and AMR Inputs

Thomas R. Shryock, Ph.D.
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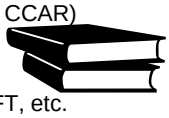
May, 2013
FAO-APHCA AMR Expert Workshop,
Bangkok, Thailand

Risk Assessment Workshop Outline

- Risk Analysis Overview
  - Codex & OIE approaches to Risk Analysis
  - Applications
- Risk Analysis Guidelines
- Hazard Characterization / Risk Profile
- Your Journey Begins…

Global "authority" Reports/Recommendations since 1997

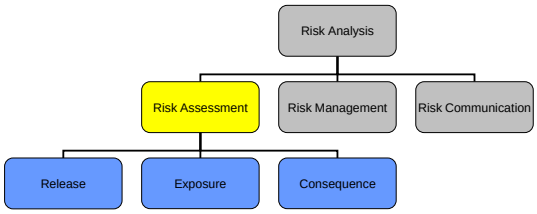
- WHO (Berlin, FQ, Global Principles of Use, Use Monitoring, Aquaculture)
- Europe (CVMP, EFSA, Health Ministers, etc.)
- Australia (JETACAR)
- U.S. (CDC, FDA, GAO, IOM, Public Health Action Plan, etc.)
- Canada (Adv. Com. Report, CCAR)
- OIE
- Codex
- Other reports from APUA, IFT, etc.



Summary of Actions and Recommendations International and National Level

- Responsible Use
  - Appropriate veterinary antibiotic use practices described; education, disease prevention
- Resistance Monitoring
- Antibiotic sales Monitoring
- Regulatory Controls
  - Risk assessment-based regulatory decisions on microbial food safety guide decisions on product use:
    - Approval with appropriate label indications and use, prescription
- Research
  - New products

Risk Analysis Components



What Should Risk-Based Evaluations Do?

- Provide detailed description of risk-generating system (causal pathway)
  - Requires multiple experts to be involved
  - Each step of the pathway is identified
  - Data gaps and research needs are noted
- Estimate of the probability and magnitude of consequence
  - This estimate can be used to support decisions
- Provide Risk Managers with intervention options to choose from based on their likelihood of efficiently reducing risk
  - Risk Assessors should ask Risk Managers what do they want? Value? What resources are available? [Risk Communication]
  - Need to provide a means to evaluate the effectiveness of the intervention option!

What do you Want to Manage? (Application of Risk Assessment)

- Reduce food borne bacterial disease
  - Reduce microbial contamination on food
  - Reduce microbial load in animals on farm
- Reduce AMR food borne bacterial disease or commensals
  - Reduce the subset of AMR microbial food contamination
  - Reduce the subset of AMR bacteria on farm
- Provide antibiotic product regulation?
  - Ensure Responsible Use of antibiotics by Regulation
- Reduce AMR animal pathogens?

National Regulatory Risk Assessments

Risk Management - Guided by Risk Assessment

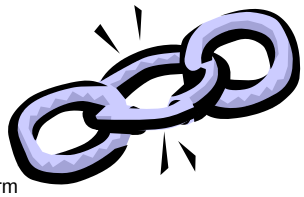
- How large will the risks and benefits to human (or animal) health caused by animal antimicrobial use become *in the future* in the absence of intervention i.e. maintain status quo?
- How would risk management *changes* in current use affect human (or animal) health risks and benefits now and later?
  - For example, restrictions on some uses, better food hygiene
  - Focus on decisions and their future consequences, not on blame/attribution of past health effects
  - The perspective is *not* (situation → action), but rather (action → predicted consequence) → recommendation

Risk Management (choose, do, measure, check)

1. **Risk evaluation** - the process of comparing the *risk* estimated in the *risk assessment* with the appropriate level of protection.
2. **Option evaluation** - the process of identifying, evaluating the efficacy and feasibility of, and selecting measures to reduce the *risk* associated with an importation in order to bring it into line with the Members appropriate level of protection. The efficacy is the degree to which an option reduces the likelihood and/or magnitude of adverse health and economic consequences. Evaluating the efficacy of the options selected is an iterative process that involves their incorporation into the *risk assessment* and then comparing the resulting level of *risk* with that considered acceptable. The evaluation for feasibility normally focuses on technical, operational and economic factors affecting the implementation of the *risk management* options.
3. **Implementation** - the process of following through with the *risk management* decision and ensuring that the *risk management* measures are in place.
4. **Monitoring and review** - the ongoing process by which the *risk management* measures are continuously audited to ensure that they are achieving the results intended

OIE Terrestrial Code 2.1

Risk assessment starts by connecting the causal chain



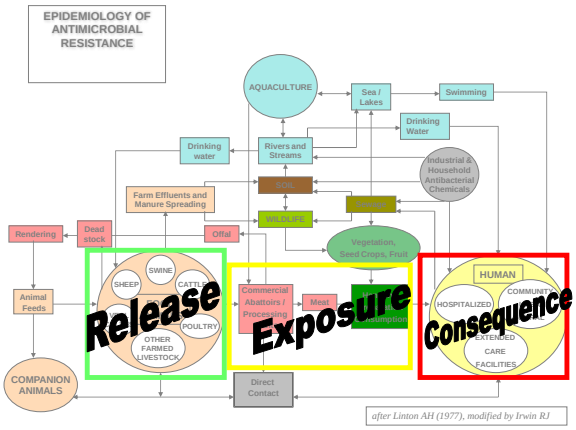
Adverse treatment outcomes In humans

Antibiotic Use on-farm

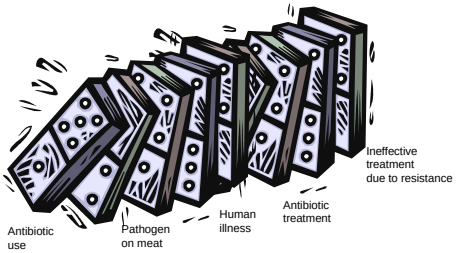
If there is NO connection there is NO RISK

The 3-step RA Process

- ✓ An antibiotic must select for foodborne bacteria that acquire antibiotic-resistance in food animals during treatment
  - ✓ Release
- ✓ A person must ingest meat from a treated animal that is contaminated with those same antibiotic-resistant foodborne bacteria
  - ✓ Exposure
- ✓ The person that ingests these bacteria must become sick with a bacterial infection that cannot be appropriately treated with antibiotics as a result of those animal-derived antibiotic-resistant bacteria
  - ✓ Consequence



Remove any one element and risk is ZERO



GL77 Risk Analysis Outline

Preliminary Foodborne AMR Risk Management Activities
- Identification of an AMR food safety issue
- Development of a foodborne AMR risk profile
- Ranking of the food safety issues and setting priorities for risk assessment and management
- Establishment of preliminary risk management goals
- Establishment of a risk assessment policy
- Commission a foodborne AMR risk assessment

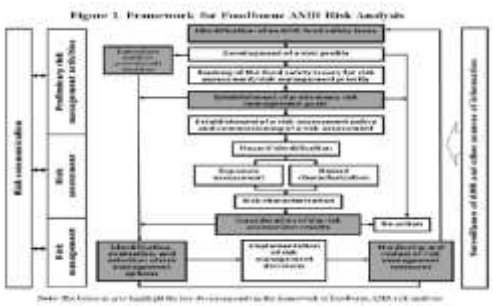
Foodborne AMR Risk Assessment
- Sources of information
- Process of foodborne AMR risk assessment
- Hazard identification
- Exposure assessment
- Hazard characterization
- Risk characterization

Foodborne AMR Risk Management
- Consideration of the foodborne AMR risk assessment results
- Identification of foodborne AMR RMOs
- Evaluation of foodborne AMR RMOs
- Selection of foodborne AMR RMOs
- Implementation of foodborne AMR risk management decision(s)
- Monitoring and review of foodborne AMR risk management measures

Surveillance of Use of Antimicrobial Agents and AMR Microorganisms and Determinants

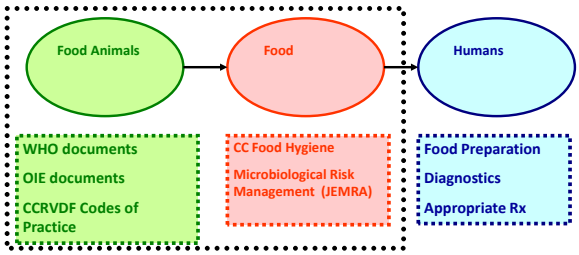
Foodborne AMR Risk Communication
- Foodborne Risk Communication as a Risk Management Tool

CODEX GUIDELINES FOR RISK ANALYSIS OF FOODBORNE ANTIMICROBIAL RESISTANCE
CAC/GL 77- 2011
www.codexalimentarius.net/input/download/standards/11776/CXG_077e.pdf



Continuum of Codex Risk Management Options

"All interventions guided by National Risk Assessments"



Measurements to determine the effectiveness of actions to protect human and animal health?

Monitoring (AMR and "Use") + Risk Assessment "Prediction"

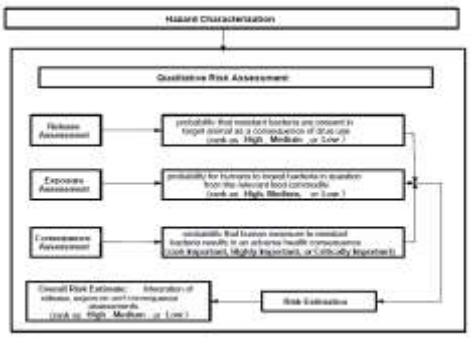
OIE Risk Analysis Methodology

Vose et al. Rev. sci. tech. Off. Int. Epiz., 2001, 20(3), 811-827

- The Ad hoc Group of experts on antimicrobial resistance, appointed by OIE, has developed an objective, transparent and defensible risk analysis process, providing a valid *basis for risk management decisions* in respect to antimicrobial resistance.
- The components of risk analysis and of different possible approaches in risk assessment (*qualitative, semi-quantitative, and quantitative*) are defined.
- The Ad hoc Group recommended the following: an *independent* risk assessment based on *scientific data*; an *iterative* risk analysis process; a qualitative risk assessment systematically undertaken *before* considering a quantitative approach; the *establishment of a risk assessment policy*; and the availability of technical assistance for developing countries.

Regulatory Risk Assessment

Inputs: AMR Monitoring and AB volume data + context data



From CVM Guidance 152

Figure 1: Components of a qualitative antimicrobial resistance risk assessment

The Components of Risk Analysis: a comparison of the systems used by Codex Alimentarius and OIE

Codex Alimentarius
- Risk Assessment
  - Hazard Identification
  - Hazard Characterization
  - Exposure Assessment
  - Risk Characterization
- Risk Management
- Risk Communication

OIE
- Hazard Identification
- Risk Assessment
  - Risk Release Assessment
  - Exposure Assessment
  - Consequence Assessment
  - Risk Estimate
- Risk Management
- Risk Communication

Vose et al. Antimicrobial resistance: risk analysis methodology for the potential impact on public health of antimicrobial resistant bacteria of animal origin *Rev. sci. tech. Off. int. Epiz.*, 2001, 20 (3), 811-827

Definitions

- Hazard: Human illness, caused by an antimicrobial-resistant bacteria, attributable to an animal-derived food commodity, and treated with the human antimicrobial drug of interest.
- Hazardous agent: Antimicrobial-resistant food-borne bacteria of human health concern that are in or on a food-producing animal as a consequence of the proposed use of the antimicrobial new animal drug.
- Risk: The probability that human food-borne illness is caused by an antimicrobial resistant bacteria, is attributable to an animal-derived food commodity, and is treated with the human antimicrobial drug of interest.

From CVM Guidance 152

Your Journey Begins…

- Start by making a list of Identified Food safety issues / or Risk Profile (GL77, Appendix 1 or a Hazard Characterization per OIE)
  - Identify key food borne bacteria of concern
  - Identify food animals, foods and human disease of concern
  - Identify key antibiotics to be evaluated
- THEN, choose one combination and begin to work on it
  - For example, fluoroquinolone resistant campylobacter from chickens
  - Assemble multi-disciplinary team
  - Consult available work already done on the combination
  - Prepare Risk Profile or Hazard Characterization
  - Move to next combinations on the list.
  - The Hazard Characterizations will show the need for Risk Assessments in priority order

Hazard Characterization (problem description 1)

A. Drug-specific information:

Chemical name and structure

1. Class of antimicrobial drug (e.g., macrolide)
2. Mechanism (e.g., protein synthesis inhibitor) and type of action (i.e., bactericidal vs. bacteriostatic)
3. Spectrum of activity (e.g., Gram-positive, Gram-negative, broad, or narrow spectrum, etc.)
4. Standardized antimicrobial susceptibility testing methodology *and specific* susceptibility data (i.e., minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC) data pertinent to the appropriate bacteria of human health concern). FDA recommends that if the sponsor does not use standardized susceptibility test methods, the sponsor should include a detailed description of the antimicrobial susceptibility testing method(s) used for determining the susceptibility of the bacterial isolates of concern and the reason(s) for the needed change. The methods should include the quality control organism(s), the dilution scheme used, and the source for the interpretive criteria for human or veterinary isolates. The methods may include citations, if available, of relevant laboratory standards such as the Clinical Laboratory Standards Institute (CLSI). Additional guidance on susceptibility testing may be obtained from recognized sources such as CLSI documents.
5. Relative importance of the drug in human medicine (see Appendix A of Guidance 152).

Hazard Characterization (problem description 2)

B. Bacterial resistance information:

Taking into account the target animal species to be treated with the drug, the conditions of intended animal use of the drug in animals, and the antimicrobial properties of the drug in question, FDA recommends that the sponsor identify:

1. Bacterial species and strains for which resistance acquisition has potential human health consequence.
2. Known resistance determinants or mechanisms associated with the antimicrobial drug(s) of interest. FDA recommends that information describing phenotypic and genotypic similarities with resistance determinants in other food-borne bacteria of human concern be identified.

Hazard Characterization (problem description 3)

C. Data gaps and emerging science:

The sponsor or FDA may identify data gaps and areas of emerging science that may be relevant to the microbial food safety assessment for the proposed conditions of use.

Key Components

- Food Animals
  - Beef, dairy, pigs, chickens, fish….
- Bacteria
  - Salmonella, campylobacter…*E. coli*, enterococci
- Antibiotics
  - Refer to WHO and OIE Importance Lists to prioritize or draft own list
- ❖ Each animal species, bacterial type and antibiotic class has to be evaluated separately
  - Product-specific evaluations not needed at this step
- Integration of antibiotic use data and AMR monitoring data in Hazard Characterization (as would be done for Release and Consequence sections; AMR monitoring data only in Exposure)
  - Note: if animal pathogen AMR is of interest or non-food borne routes are of interest, adjust the "pathway" appropriately

Key Point #1

"Risk Analysis Expertise Needed"

- Medical, food & veterinary microbiology
- Veterinary medicine
- Human infectious disease
- Food processing (e.g. HACCP)
- Epidemiology
- Risk Analysis
- Pharmacology
- Literature search specialist
  - Ongoing searches
  - Reprint repository

Other experts contribute as needed

Key Point #2

"Pre-screening" saves time and resources
The value of Hazard Characterization

- A list of animal-use antibiotic classes not used in human medicine is a valuable tool.
  - Be careful on cross-resistance
- Such antibiotics usually only require a Hazard Characterization to address risk concerns
- More time and effort can be spent generating and evaluating antibiotic classes that are cross-resistant with those used in human medicine

Key Point #3

"One size doesn't fit all"

- Product-specific risk or general antibiotic class?
- Research must be comprehensive
  - Literature, web-based data, reports, studies
- Data from monitoring programs is compiled
  - Resistance data
  - Antibiotic sales or use data
  - Disease data
- Data gaps need to be addressed

Other Risk Assessment Preparations

- National agencies need to be involved
  - Veterinary medicine regulatory agency
    - Risk-based product evaluation guidelines must be in place
    - Participation in national resistance monitoring programs
    - Desirable to have sales or use data on antimicrobials
    - Responsible Antibiotic Use guidelines for veterinarians
  - Food safety agency
    - On-farm disease prevention efforts
    - Contamination data for food
    - Participation in national resistance monitoring programs
  - Human disease agency
    - Surveys of food borne disease prevalence
    - Participation in national resistance monitoring programs
- Independent experts need to be recruited
  - Stakeholders along food chain bring unique inputs to consider
  - Expertise not available within an agency
  - Can lend credibility to the process and outcome

To Continue the Journey…

- A regulatory risk assessment guideline will be needed to continue.
  - Consult guidelines from other countries and Vose paper
  - Propose a Draft guideline for adoption
- Develop a list of agencies, experts and data sources needed
- Prepare a timeline of activities and responsibilities

What do you Want to Manage? (Application of Risk Assessment)

- Reduce food borne bacterial disease
  - Reduce microbial contamination on food
  - Reduce microbial load in animals on farm
- Reduce AMR food borne bacterial disease or commensals
  - Reduce the subset of AMR microbial food contamination
  - Reduce the subset of AMR bacteria on farm
- Provide antibiotic product regulation?
  - Ensure Responsible Use of antibiotics by Regulation
- Reduce AMR animal pathogens?

Critical Learning To Consider

1. Focus on causal pathway!
   - Farm → food / other → treatment failure.
   - Convert possibility to probability
   - Each bug-drug combination may be different
2. Assess impact of Risk Management options
   - Include a new section on benefits or value to animal health, welfare from proposed use of antibiotic
3. Multiple Risk Management Options should be considered

Demonstrate the connections in the causal pathway even if you cannot quantify the exact risk

- Start with data on human illness with resistant foodborne / other bacteria
  - Salmonella, Campylobacter or other
  - NOT Enterococcus
  - Are resistant infections a problem and,
  - Are they more difficult to treat than non-resistant infections?

Region-Specific Data Needs

Some data may be very difficult to find

- The incidence of campylobacteriosis
- Local surveillance data
- Meat consumption patterns
- HACCP and other contamination control measures that are used in processing

What agencies or organizations have relevant data? What is the quality?

Key Learning 4

Despite the abundance of available information, important data gaps still exist and research in this area should continue

- How are the antibiotics used in the field
- Antibiotic selection outcomes
- Pathogen load
- Dose response
- Human health consequences

APPROACHES TO AMU AND AMR MONITORING / SURVEILLANCE AND THEIR LIMITATIONS

D. Pfeiffer

Royal Veterinary College University of London

APHCA Expert Workshop - Monitoring of AMU and AMR in Animals in the Asia-Pacific Region. Bangkok, 14 -15 May 2013

Approaches to AMU and AMR Monitoring and their Limitations

Dirk Pfeiffer

Professor of Veterinary Epidemiology

Honorary Professor at London School of Hygiene & Tropical Medicine

United Nations - Food and Agriculture Organisation
Reference Centre for Veterinary Epidemiology

Outline

- general methodological principles
- systems perspective
- antimicrobial sales/usage
- antimicrobial resistance
- policy development
- conclusions

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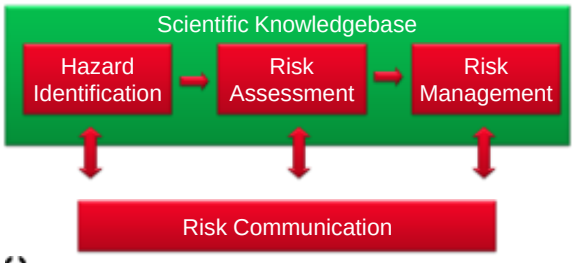
2

Risk Analysis or Risk-Based Decision Making



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after OIE Animal Health Code

4

Risk Management and Assessment Cycle

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5

Monitoring *versus* Surveillance

- monitoring
  - systematic, continuous or repeated, measurement, collection, collation, analysis and interpretation of animal health related data not associated with pre-defined plan of action
- surveillance
  - systematic, continuous or repeated, measurement, collection, collation, analysis, interpretation and timely dissemination of animal health related data, essential for describing health hazard occurrence and for planning, implementation, and evaluation of risk mitigation measures

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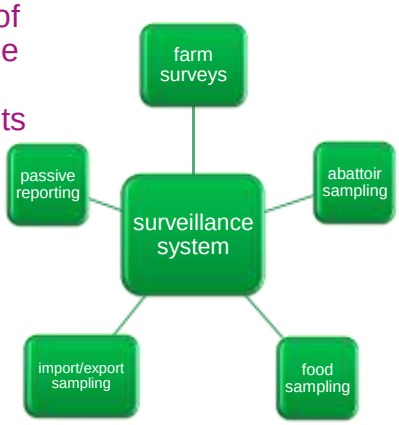
6

Examples of Surveillance System Components



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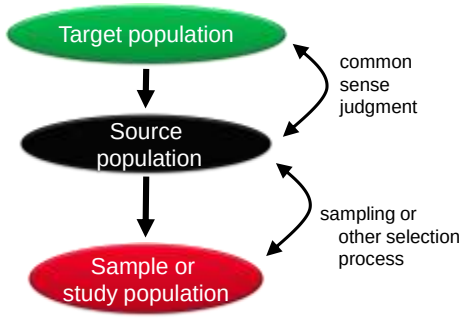
Populations and Sampling



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Criteria for Design of Integrated Surveillance Systems (based on AGISAR recommendations)

1. Study population
– Humans, retail meats, food producing animals

2. Sampling strategy
a. Representativeness
b. Sampling bias
c. Frequency of testing
d. Sample size
e. Sample source

3. Culture methodology
a. Target organisms
b. In vitro antimicrobial susceptibility testing methods
c. Antimicrobials to be used in susceptibility testing

4. Data management and reporting
a. Database design for appropriate data extraction
b. Type of data to be reported
c. Analysis and interpretation of data
d. Information sharing
e. Confidentiality policies should be established to protect proprietary data

from WHO AGISAR Antimicrobial Resistance Monitoring Subcommittee 2011

Systems Perspective on AM Usage

From: Comprehensive Reviews in Food Science and Food Safety - Antimicrobial Resistance: Implications for the Food System. Pages 71-137, 2 AUG 2006 DOI: 10.1111/j.1541-4337.2006.00004.x

Drug Value Chain

Pharmaceutical producers

↓

Regulating authorities, Retailers, Importers, Pharmacies, Private veterinarians, Government veterinarians, other animal health care providers, farmers, pet owners and others

↓

Animal treated with Antimicrobial

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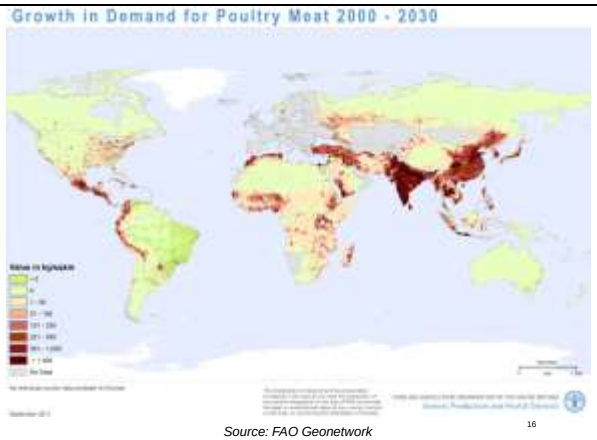
Structure of Poultry Production Systems in South-East Asia

Country	Commercial integrated	Commercial non-integrated	Semi-commercial and backyard
Thailand	70%	20%	10% (almost 99% of farms)
Vietnam	20-25%	10-15% (small number of farms)	65% (majority of farms)
Lao and Cambodia	3%	7%	>90%

Source Thailand: Rushton et al 2005 *Source Vietnam: Delquigny et al. 2004*



Source: FAO Geonetwork

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Monitoring Programme Design Questions

- product(s) to monitor
- data source
- data collection approach
  - complete data
  - sampling
- data analysis
  - detect change in quantity over time or in space

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Constraints to Cost-Effective AM Usage Monitoring in Low to Middle Income Countries

- ineffective regulation
  - poor enforcement
- poor reliability of livestock population data
- legal trade/usage
  - data quantity and poor quality
- illegal trade/usage
  - widespread
  - transboundary?

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Development of AM Usage Monitoring in Low to Middle Income Countries

- targeted monitoring
  - informed by risk assessment
  - temporal change in livestock population numbers
    - mortality reporting
    - census at meaningful intervals
- identify high risk groups for targeted surveys
  - livestock flow intensity
  - fluctuation in live animal prices?
  - disease-free compartments
  - specific livestock production sectors

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Development of AM Usage Monitoring in Low to Middle Income Countries *cont.*

- qualitative data collection to complement quantitative data
  - focus groups
  - participatory data collection
- target stakeholders involved in AM trade
  - describe value chain
    - determine most effective data collection approach

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AMR Surveillance Systems

- pathogen specific
  - appropriate indicator organisms
    - Campy, Salmonella, E-coli, Enterococcus
- syndromic
  - samples based on animals not responding to treatment
  - likely to be biased if lack of reporting incentive
- voluntary or compulsory sample submission
- data source
  - farm, slaughter house, food products

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Diagnostic Methods

- definition of 'resistance'
- antimicrobial susceptibility testing
  - genotypic or phenotypic
- molecular diagnostics
  - strain typing
    - e.g. pulsed-field gel electrophoresis (PFGE), whole-genome sequencing (WGS), multi-locus sequence typing (MLST)
  - genome sequencing

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Constraints to AMR Surveillance in Low to Middle Income Countries

- passive surveillance inadequate
  - need for representative surveys
- surveys are problematic
  - large sample sizes needed for representative data
  - often laboratory-based -> bias
  - expensive, time-consuming, labour-intensive

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Constraints to AMR Surveillance in Low to Middle Income Countries *cont.*

- laboratories
  - limited financial resources
  - limited laboratory capacity
  - issues of quality assurance

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Ideas for AMR Surveillance in Low to Middle Income Countries

- focus on detection and/or containment?
- sentinel surveillance networks
  - herds/population
    - target specific livestock production sectors
  - abattoirs/livestock markets
  - regional
  - emphasis on quality rather than quantity
    - data collection and diagnostics

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Ideas for AMR Surveillance in Low to Middle Income Countries *cont*.

- repeated surveys
  - abattoirs
  - livestock markets
  - disease-free compartments
  - specific livestock production sectors

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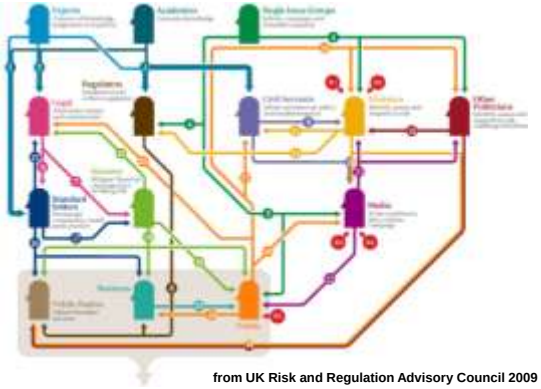
Actors involved in Risk Management



from UK Risk and Regulation Advisory Council 2009

Stakeholders and Impact of Risk Management

- impact is dependent on stakeholders continuing with current behaviour or accepting value making changes
- need to assess stakeholders' willingness to change
- behaviour change will occur if stakeholders accept that risk is their problem too and therefore want its management

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From: Falk, Wallace and Ndoen – Managing biosecurity across borders 2011 31

Challenges for Surveillance Policy Development in Low to Medium Income Countries

- engagement of all relevant stakeholders
  - understand drivers of behaviour
  - behaviour change
    - incentives to change
      - animal health management
  - tackle illegal trade and use
- avoid policy which is unlikely to be effective

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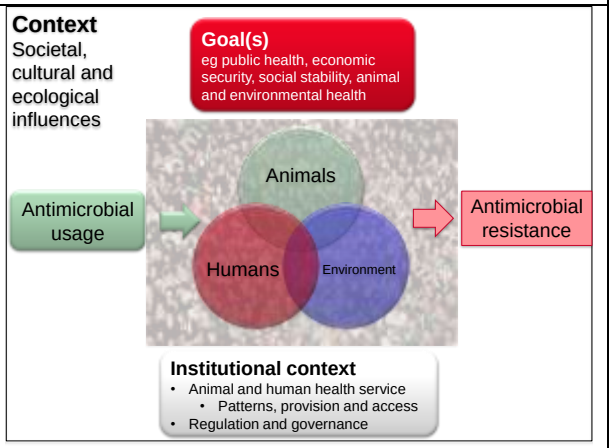

Conclusions

- monitoring / surveillance strategy
  - needs to be informed by transdisciplinary risk assessment
    - identify and ideally involve key stakeholders
    - AM trade value chain mapping
  - agree with stakeholders on monitoring / surveillance purpose

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Conclusions *cont.*

- monitoring / surveillance strategies
  - AM usage
    - sales monitoring
      - targeted data collection
    - predictive modelling
      - livestock density
  - AMR
    - national/regional sentinel surveillance
    - focus on specific livestock sectors
- monitoring / surveillance policy development
  - adapted to needs of local stakeholders

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ANTIMICROBIAL SUSCEPTIBILITY TESTING (AST) WITH LIMITED RESOURCES

S. Simjee

Antibiotic Susceptibility Testing and Data Interpretation

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APHCA AMR Expert Workshop
Bangkok, Sukosol Hotel, 14 to 15 May 2013

Agenda

1. Antibiotic Susceptibility Testing Methodology
2. Quality Control and Interpretive Criteria - Does it Matter?
3. Interpretation of Antibiotic Susceptibility Data - Are We Harmonised?
4. Q&A

What Are You Measuring?

Minimal Inhibitory Concentration (MIC)

The lowest concentration of an antimicrobial agent that prevents visible growth (to the naked eye) of a microorganism in an agar or broth dilution susceptibility test.

AST Methods

British Society of Antimicrobial Chemotherapy (BSAC)

European Committee on Antimicrobial Susceptibility Testing (EuCAST)

Clinical and Laboratory Standards Institute (CLSI)

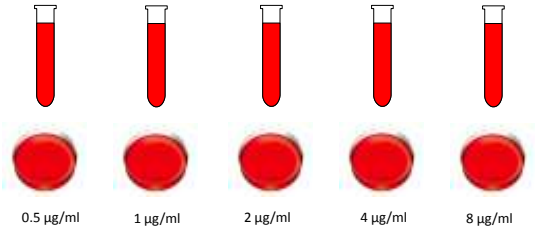
The basic for each method

Isolate bacterium in pure culture → **Inoculate broth** → **Standardize turbidity 0.5 McFarland**

Agar Dilution Susceptibility Test

An *in vitro* antimicrobial susceptibility test method conducted using serial concentration of an antimicrobial agent incorporated into an agar growth medium in separate Petri dishes that are inoculated with a bacterial suspension to determine the minimal inhibitory concentration.

Agar Dilution

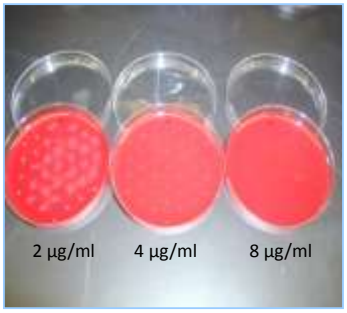


Agar Dilution

Agar Dilution

Incubate and record MIC

Agar Dilution



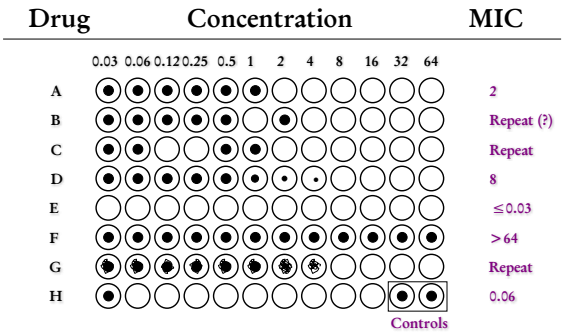
Broth Dilution Susceptibility Test

An *in vitro* antimicrobial susceptibility test conducted using serial concentrations of an antimicrobial agent incorporated in liquid nutrient media that are inoculated with a bacterial suspension to determine the minimal inhibitory concentration of an antimicrobial agent.

NOTE: When this procedure is carried out in test tubes, it is referred to as broth macrodilution; when performed in microdilution plates, it is called broth microdilution.

Broth Dilution

Broth Dilution



Approved AST methods

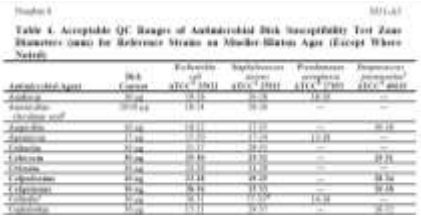
- A number of organisations have approved AST methods e.g. BSAC, EUCAST, CLSI
- Each one has slight differences in the methodology e.g. media used or incubation times. Each of these factors have some influence on the results and thus the interpretation of the data
- Use of a standard method ensures reproducibility of the AST and thus comparison of data between laboratories

- EUCAST have interpretive criteria BUT these are based on bacteria of human origin and against human use antibiotics
- CLSI is the only organisation that has veterinary specific interpretive criteria

Why use QC strains?

- QC = Quality Control strains, these can be considered 'positive controls'
- QC are bacterial isolates that have undergone rigorous testing to ensure that under a standard test system they will always give the same MIC range with a given antibiotic
- If a QC is out of range it invalidates the AST and indicates there are problems in the method e.g. pH, ion concentrations, temperature etc


Performance Standards for Antimicrobial Disk and Dilution Susceptibility Tests for Bacteria Isolated From Animals; Approved Standard—Third Edition




Performance Standards for Antimicrobial Disk and Dilution Susceptibility Tests for Bacteria Isolated From Animals; Approved Standard—Third Edition

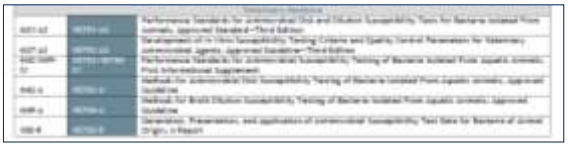
What does QC tell us…….

- As long as our QC strains are in range we have a valid test system
- It does NOT tell us if test bacteria are susceptible or resistant

What are interpretive criteria?

- These are commonly known as breakpoints; S, I, R (Susceptible, Intermediate, Resistant)
- **Susceptible**
  This category implies an infection due to the isolate may be appropriately treated with the dosage regimen of an antimicrobial agent recommended for that type of infection and infecting species, unless otherwise indicated.
- **Intermediate**
  This category implies an infection due to the isolate may be appropriately treated in body sites where the drug are physiologically concentrated or when a high dosage of drug can be used; also indicates a 'buffer zone' that should prevent small, uncontrolled, technical factors from causing major discrepancies in interpretation.
- **Resistant**
  Resistant isolates are not inhibited by the usually achievable concentrations of the agent with normal dosage schedules and/or fall in the range where specific microbial resistance mechanisms are likely, and clinical efficacy has not been reliable in treatment studies.


Performance Standards for Antimicrobial Disk and Dilution Susceptibility Tests for Bacteria Isolated From Animals; Approved Standard—Third Edition



Need for Harmonisation

Franklin *et al* (2001) published a guideline on the harmonisation of surveillance programmes in animals on behalf of the Office International des Epizooties (OIE)

a) animal species/categories (including age) to be sampled
b) for food sampling, the relative merits of sampling at the abattoir and retail outlet should be considered. In addition to food of domestic origin, food of foreign origin may also be considered, possibly at the port of entry of the products
c) sampling strategy to be employed, for example: active or passive collection of samples; random, stratified or systematically collected samples; statistically based sampling or opportunistic sampling
d) samples to be collected (faeces, carcass, raw and/or processed food)
e) bacterial species to be isolated
f) antimicrobials to be used in susceptibility testing
g) standardised susceptibility testing
h) quality control – quality assurance
i) type of quantitative data to be reported
j) database design for appropriate data extraction
***k*) analysis and interpretation of data**
l) reporting (consideration of transparency of reporting and interests of stakeholders)

Franklin A, Acar J, Anthony F, Gupta R, Nicholls T, Tamura Y, Thompson S, Threlfall EJ, Vose D, van Vuuren M, White DG, Wegener HC & Costarrica ML (2001). Antimicrobial resistance: harmonisation of national antimicrobial resistance monitoring and surveillance programmes in animals and in animal-derived food. Revue scientifique et technique (International Office of Epizootics) 20, 859-870

Need for Harmonisation

At the outset it is important to emphasise that all of the reviewed surveillance systems have merit, especially when considering resistance trends within the countries in which the surveillance has been instigated

The major challenge when analysing data across surveillance systems is a lack of harmonisation in sampling, susceptibility testing methods and in such basic terms as defining resistance

All these factors can confound data interpretation even when analysing data vertically within a country but in horizontal analysis, across countries, it can be become almost impossible

Definition of Resistance

National surveillance schemes do not all define resistance in the same way, there is considerable variability in what is defined as "resistant"

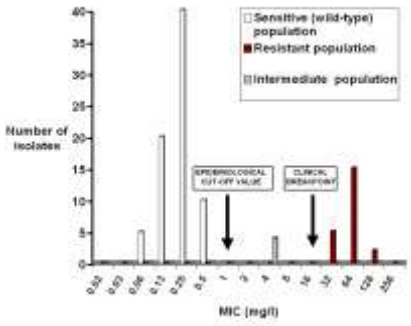
This means that it is not possible to simply compare resistant rates from different surveillance schemes as they are not measuring the same parameter

Indeed even within national surveillance schemes methods of analysis have changed over time such that % resistance values need to be viewed with caution

Clinical vs. Epidemiologic

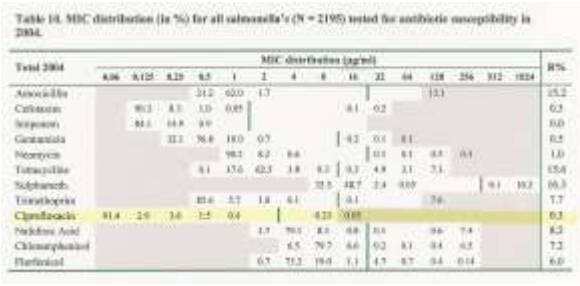
- **Clinical Resistance**
  - Isolates are not inhibited by the usually achievable concentrations of the agent with normal dosage schedules and/or fall in the range where specific microbial resistance mechanisms are likely (e.g. β-lactamases), and clinical efficacy has not been reliable in treatment studies
- **Epidemiological (Resistance)**
  - Isolate is defined as non-wild type (NWT) by the presence of an acquired or mutational resistance mechanism to the antibiotic. Isolates may or may not respond clinically to antimicrobial treatment

Clinical vs. Epidemiologic



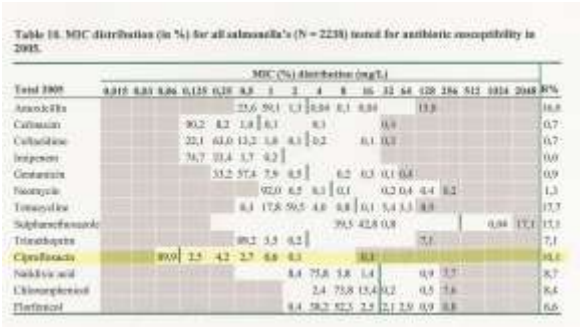
Lets Compare Data

within a country



Lets Compare Data

within a country

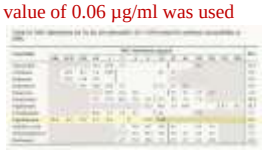


Lets Compare Data

within a country

In MARAN 2004, ciprofloxacin resistance in all *Salmonella* (n = 2195) was reported to be 0.3%, applying a clinical breakpoint of greater than 2 µg/ml

In MARAN 2005 ciprofloxacin resistance in all *Salmonella* (n = 2238) was reported to be 10.1%, as the epidemiological cut-off value of 0.06 µg/ml was used



Lets Compare Data

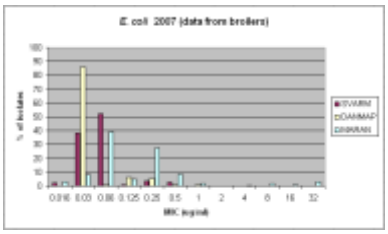
between countries

Ciprofloxacin resistance in *E. coli*

DANMAP (Denmark) uses >0.03 µg/ml

MARAN (Netherlands) and SVARM (Sweden) use >0.06 µg/ml

VAV (Spain) uses >2 µg/ml



CLSI Initiative on Harmonisation

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Generation, Presentation and Application of Antimicrobial Susceptibility Test Data for Bacteria of Animal Origin; A Report

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efsa European Food Safety Authority

ecdc

EFSA Journal 2011;9(7):2154

SCIENTIFIC REPORT OF EFSA AND ECDC

The European Union Summary Report on antimicrobial resistance in zoonotic and indicator bacteria from humans, animals and food in the European Union in 2009

European Food Safety Authority
European Centre for Disease Prevention and Control

ABSTRACT

The European Food Safety Authority and the European Centre for Disease Prevention and Control have analysed the information on antimicrobial resistance among zoonotic and indicator bacteria in 2009 submitted by 25 European Union Member States. This information covers antimicrobial resistance in *Salmonella and Campylobacter isolates from humans, food and animals, and in indicator Escherichia coli and enterococci* isolates from animals and food.

Page 17:

"*The results must therefore be interpreted with care and no direct comparison between countries should be made. Where countries have used the same method over the time period covered by the report, then an evaluation of trends is likely to be valid, though may lack sensitivity dependent on the specific breakpoint used.*"

Summary (page 4)

In 2010, 26 Member States submitted information on the occurrence of antimicrobial resistance in zoonotic bacteria to the European Commission, the European Food Safety Authority and the European Centre for Disease Prevention and Control.

Information on antimicrobial resistance was reported regarding *Salmonella* and *Campylobacter* isolates from human cases, food and animals, whereas data on indicator *Escherichia coli* and indicator *enterococci* isolates derived only from animals and food.

Data on antimicrobial resistance in isolates from human cases were mainly interpreted by using clinical breakpoints, while the quantitative data on antimicrobial resistance in isolates from food and animals were interpreted using harmonised epidemiological cut-off values defining the microbiologically resistant isolates.

However, the use of different thresholds, clinical breakpoints and epidemiological cut-off values, means that resistance data in isolates from humans and in isolates from animals and food are, in most cases, not directly comparable.

RESPONSIBLE ANTIBIOTIC USE

T.R. Shryock

Responsible Antibiotic Use

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May 14-15, 2013
FAO-APHCA AMR Expert Workshop,
Bangkok, Thailand

Responsible Antibiotic Use

- Overview of Recommendations
- Clinical practice guidelines
- Practical matters

Food Economics and Consumer Choice

An overview of the challenge ahead

1 Green, R. et al. January 2005. "Farming and the Fate of Wild Nature." Science 307.5709: 550-555; and Tilman, D. et al. August 2002. "Agricultural sustainability and intensive production practices." Nature 418.6898: 671-677.
2 "World Agriculture: toward 2015/2030." 2002. United Nations Food and Agriculture Organization, Rome. Accessed 12/8/08. <ftp://ftp.fao.org/docrep/fao/004/y3557e/y3557e.pdf>.

TECHNOLOGY'S ROLE IN THE 21ST CENTURY

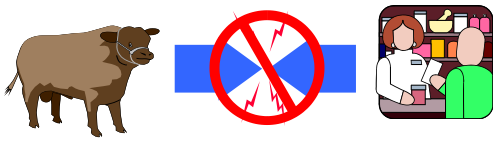
AVMA Veterinarians Oath

- "Being admitted to the profession of veterinary medicine, I solemnly swear to use my scientific knowledge and skills for the benefit of society through the protection of animal health and welfare, the *prevention and relief* of animal suffering, the conservation of animal resources, the *promotion of public health*, and the advancement of medical knowledge."

Effective 2010

The Problem

- Veterinary vs. Medical need for antimicrobials
- Selective pressure of antibiotic use in animals
- Zoonotic bacteria may be exposed to drug during antimicrobial use for food animal infections
  - Animal antibiotic use is not the source of all human antibiotic resistance!



Global "authority" Reports/Recommendations

since 1997

- WHO (Berlin, FQ, Global Principles of Use, Use Monitoring, Aquaculture)
- Europe (CVMP, EU SSC, UK ACMSF, UK H.Lords, Microbial Threat, etc.)
- Australia (JETACAR)
- U.S. (NRC, CDC, FDA, GAO, IOM, Public Health Action Plan, etc.)
- Canada (Adv. Com. Report, CCAR)
- OIE
- Codex -various
- Other reports from APUA, IFT, etc.

Summary of Actions and Recommendations
International and National Level

- Responsible Use
  - Appropriate veterinary antibiotic use practices described; education, disease prevention
- Resistance Monitoring
- Antibiotic sales Monitoring
- Regulatory Controls
  - Risk assessment-based regulatory decisions on microbial food safety guide decisions on product use:
    - Approval with appropriate label indications and use, prescription
- Research
  - New products

Objectives of Prudent Use (based on OIE)

- Prudent use includes a set of practical measures and recommendations intended to prevent and/or reduce the selection of antimicrobial-resistant bacteria in animals to:
- maintain the efficacy of antimicrobial agents and to ensure the rational use of antimicrobials in animals with the purpose of optimising both their efficacy and safety in animals.
- comply with the ethical obligation and economic need to keep animals in good health;
- prevent, or reduce, as far as possible, the transfer of micro-organisms (with their resistance determinants) within animal populations;
- maintain the efficacy of antimicrobial agents used in food-producing animals
- prevent or reduce the transfer of resistant micro-organisms or resistance determinants from animals to humans;
- maintain the efficacy of antimicrobial agents used in human medicine and prolong the usefulness of the antimicrobials;
- prevent the contamination of animal-derived food with antimicrobial residues that exceed the established maximum residue limit (MRL);
- protect consumer health by ensuring the safety of food of animal origin with respect to residues of antimicrobial drugs, and the ability to transfer antimicrobial drug resistant micro-organisms to humans.

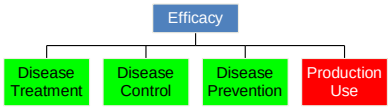
Stakeholder Responsibilities

- Regulatory Authorities
- Veterinary Pharmaceutical Industry
- Wholesale and Retail Distributors
- Veterinarians
- Food Animal Producers

Codex CAC/RCP 61-2005
Code of Practice for Responsible Use

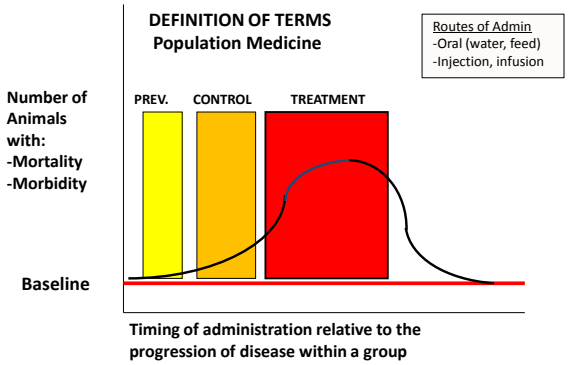
- Responsibilities of stakeholders
  - Regulatory
  - Manufacturers
  - Veterinarians
  - Producers
- Expect implementation at national level
- In general, OIE and WHO guidelines are in alignment
  - OIE Terrestrial Code
    - http://www.oie.int/index.php?id=169&L=0&htmfile=chapitre_1.6.9.htm
  - WHO Responsible Use Guidelines
    - http://apps.who.int/iris/bitstream/10665/68931/1/WHO_CDS_CSR_APH_2000.4.pdf

Approved Antibiotic Label Indications

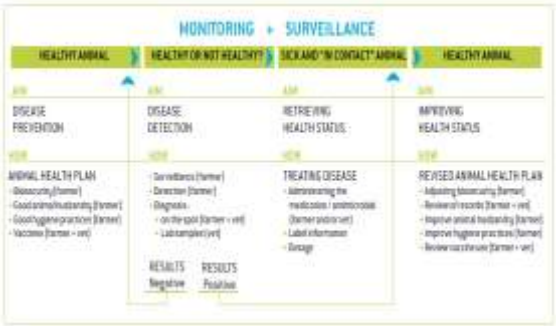


- **Therapeutic**
  - **–Treatment**
  - **– Disease control**
  - **– Disease prevention**
- **Production (not in EU, some other locations)**
  - **– Nutritional, Physiological and Immunological effect on Average Daily Gain and Feed Efficiency**

Based on Guidance 209



Ensuring Animal Health



Perspectives on Antibiotics in Animals

Consensus Principles
(directed to veterinarian)

- Prevention strategies emphasized
  - Minimize environmental contamination; vaccinate; biosecurity, nutrition, housing, management at high levels
- Minimize therapeutic use
  - Treat only at-risk or ill animals
- Utilize only licensed products by label directions; exercise clinical judgment for off-label usages
- Utilize culture and sensitivity
- Use narrow spectrum antibiotics when possible
- Vet-client-patient relationship encouraged
- Record keeping
- Periodically review usage practices

Extralabel Use (AVMA)

(does not apply to feeds)

Why Veterinarian Oversight?

- Veterinarians are viewed as having the necessary experience and accountability to prescribe antibiotics – just like physicians
  - Therapeutic indications!
- Disease presentation, diagnostics, client relationship and other considerations require veterinary expertise to integrate into a medication decision
- Consistent with Responsible Use Principles
- May need to consider non-vets or vet technicians with certifications to "cover" remote areas

Biosecurity Poster USDA

Quality Products

- Quality (potency, formulation, etc.)
- Cost
- Distribution (storage conditions, market channels)
- Technical service support
- Counterfeit or other product quality issues

Retailer Antibiotic use Policy

McDonald's Global Policy on Antibiotic[1] Use in Food Animals[2]

Introduction

Executive Summary

Practical Actions to Take

- Communication and Education
  - Inform veterinarians and producers of:
    - Actions they can take to minimize disease (biosecurity)
    - The need to follow clinical practice guidelines
  - Seek support from veterinary medical organizations, schools of veterinary medicine, food production companies and others
- Improve diagnostic capabilities and capacity
  - Laboratory or quick-test applications to guide antibiotic use decisions
  - Use of CLSI clinical breakpoints when possible

DEVELOPING NATIONAL AMU & AMR MONITORING / SURVEILLANCE PLANS

M.J. Otte

Developing National AMU & AMR Monitoring / Surveillance Plans

Joachim Otte (FAO)

AMU & AMR Expert Workshop
Bangkok, 14-15 May 2013

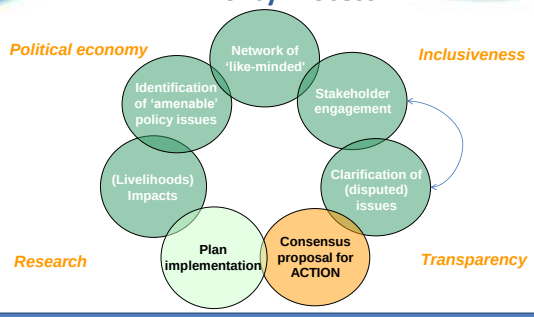
Threats of rapid livestock sector growth

- Environment
  - Natural resource erosion
  - Pollution
  - GHG emission associated with livestock production
- Health
  - Infectious diseases affecting animals (PRRS, FMD)
  - Emerging zoonotic diseases (e.g. HPAI)
  - Proliferation of antimicrobial resistance (AMR)
- Social
  - Marginalization of small-scale producers
  - Exploitation of 'cheap' labour

Consequences of AMR in the USA

- Longer hospitalization (11 days)
- Increased treatment cost (US$20,000)
- **Higher case fatality rates (2.2 fold)**
- General therapy shift to more expensive drugs (even for non-AMR-resistant cases)

'PPLPI Policy Process'



Suggested Approach

1. Analysis: what are the strengths and weaknesses of 'your' current system of AMU & AMR monitoring?
2. Setting Targets: What do you see as priority issues needing to be addressed in the short term (12 to 24 months)?
3. Action Plan: What actions need to be taken to address the priority issues?

Some Questions

- Does 'your' AMR monitoring system have a clearly defined purpose?
- What risk(s) do 'you' want to manage?
- What links exist between results of AMR monitoring and actions?
- Does the system provide the information needed to guide actions?

Some more Questions

- What can / will you do to improve the system?
- How can you mutually support each other?
- What can FAO (OIE) do to support you?

RECOMMENDATIONS

DEVELOPING NATIONAL AMU AND AMR MONITORING ACTION PLANS

The key objective of in each country is to develop detailed and costed country-specific 'action plans' to enhance national AMU and AMR monitoring and management capacity over a 12 and 24 months horizon. The following steps are suggested.

Step 1 – Analysis of current situation: In light of the information presented, review the strengths and weaknesses of the current national system for AMU and AMR monitoring and management, covering the aspects of:

1. Licensing of antimicrobials for use in food animals
2. Monitoring of sales of antimicrobials for use in food animals
3. Monitoring of use of antimicrobials in food animals
4. Sample collection from food animals / animal products for AMR testing
5. Testing protocols for micro-organisms isolated from food animals
6. Collation and analysis of AMR test results
7. Information on AMR infections of humans with farm animal related micro-organisms
8. Use of information for AMR management

Step 2 – Setting targets: Where would you like national AMU and AMR monitoring and management capacity to be with regards to the above in 12 and in 24 months? It would probably be useful to restrict the target to key food-borne bacteria of concern, key food animals, foods and human diseases of concern and key antimicrobials.

Step 3 – Identifying necessary and sufficient actions: Identify key actions that need to take place to move from the current situation to the 12 and 24 month targets, who needs to take these actions and their financial, political and social implications (stakeholder analysis and involvement).

Item	Current situation	Target 12 / 24 months	Actions	Who	Cost
1					
2					
3					
4					
5					
6					
7					
8					

WORKING GROUP ON VETERINARY AMR RISK MANAGEMENT (VAMRRM)

Objective

The objective of the working group is to advocate for increased national and regional policy development and action in APHCA member countries on the issue of AMR in bacteria of food animal origin (including pathogens of food animals, zoonotic bacteria and commensals).

A core group of invited experts will assist selected APHCA country representatives to draft and implement actions per the Terms of Reference.

Terms of Reference

- Develop educational and information materials on AMR and risk management approaches to facilitate discussions on policy and funding
    - Identify key decision-makers in each country
    - Identify key stakeholders in each country
    - Prepare communication / outreach plan to engage in dialogue
- Develop context-specific guidelines for the responsible and prudent use of antimicrobials in food animal production tailored to the situation prevailing in FAO and APHCA member countries
- Propose harmonised science-based guidelines for AMR monitoring programme development:
    - The appropriate collection methodology of samples for the isolation of farm animal-related bacteria to be assessed for AMR
    - Use standardized laboratory methods for the assessment of AMR
    - Collation, analysis and reporting of AMR laboratory results on a regular basis
- Propose science-based guidelines for AM sales/use data programme development
    - Harmonized reporting among countries as much as possible, depending on data sources, availability, etc.
- Develop national or regional regulatory agency AMR risk assessment for antimicrobial products that guide risk management decisions
    - Will take into consideration the AMR monitoring and AM sales/use data
- Establish an information / data base on alternatives to antimicrobial use in food animal production
    - Disease prevention practices; biosecurity, consumer hygiene practices, etc.
    - Alternative disease interventions locally available
- Share the results of the work conducted via symposia, web posting or other means
- Seek financial support to enhance national AMR management capabilities and capacities

International Expert Members

- Myint, H.T. – International Standards on AMR risk management and prudent use of antimicrobials
- Pfeiffer, D.U. – Surveillance & Epidemiology
- Simjee, S. – Microbiology & AMR Surveillance
- Shryock, T.R. – Regulatory Affairs (e.g. Risk Assessment, etc)
- Wagenaar, J.A. – Evolutionary Biology of AMR

National Expert Members

- To be nominated by each country

SYSTEMATIC REVIEW OF ANTIMICROBIAL RESISTANCE IN THE ASIA PACIFIC REGION

Background

Awareness about the threat of AMR development and spread is low among public authorities and professionals involved with animal production and few countries in the region have systems in place to monitor AMU and AMR, carry out necessary risk assessments and put in place evidence-based policies for AMR management. The aim of this literature review is to enhance current knowledge on the extent and patterns of AMR in different countries in the Asia-Pacific region as basis for devising strategies for AMR management.

Outputs

1. A review of published and unpublished literature on antimicrobial resistance in bacterial micro-organisms isolated from livestock and livestock products in the Asia-Pacific region;
2. An interim report on specifying the search / inclusion criteria to be used as well as classification criteria to apply for synthesizing study;
3. An electronic archive (CD) of compiled literature;
4. A final report on methodology and findings.

Suggested Approach

1. Define study inclusion criteria, search algorithm and databases
2. Determine classification criteria to use for synthesizing study results
3. Identify, compile and review the literature, both published and unpublished, on the subject
4. Extract and assemble relevant information
5. Analyse and critically discuss findings
6. Write and submit a report in MS Word format

TIMETABLE

Tuesday 14 May

Time	Topic	Speaker
08:30 – 09:00	*Registration*	
09:00 – 09:30	Opening remarks	DG DLD APHCA Secretary
09:30 – 10:15	The global problem of AMR and critical antimicrobials for use in humans	Prof. J. Wagenaar
10:15 – 10:45	*Group Photo & Coffee / tea break*	
10:45 – 11:30	Basic microbiology to set the stage for AMR monitoring and risk assessment	Dr S. Simjee
11:30 – 12:15	OIE activities on AMR and recommendations of the 'Global Conference on the Responsible and Prudent Use of Antimicrobial Agents for Animals'	Dr H.T. Myint
12:15 – 13:45	*Lunch break*	
13:45 – 14:15	AMU and AMR monitoring for AMR risk assessment and risk management	Dr T. Shryock
14:15 – 14:45	Approaches to AMU monitoring and their limitations	Prof. D. Pfeiffer
14:45 – 15:15	*Coffee / tea break*	
15:15 – 15:45	Antimicrobial susceptibility testing (AST) with limited resources	Dr S. Simjee
15:45 – 16:15	Responsible use / clinical practice guidelines	Dr T. Shryock
16:15 – 16:45	Template for the development of national AMU / AMR monitoring plans	Dr J. Otte
17:30 – 19:00	*Hosted dinner courtesy of DLD*	

Wednesday 15 May

Time	Topic	Speaker
09:00 – 09:15	Recap of day 1 and presentation of day 2 work plan	Tbd
09:15 – 12:00	Country delegates to develop structured 'Action Plan' for stepwise improvement of national AMR management system	Delegates assisted by workshop leaders
12:00 – 13:30	*Lunch*	
13:30 –15:30	Presentation and discussion of country 'Action Plan' proposals Identification of common themes with possibility of regional collaboration	Delegates and workshop leaders
15:30 – 16:00	*Coffee / tea break*	
16:00 – 16:30	Wrap-up / next steps / feedback / closure	

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