

Antimicrobial Resistance in Food Safety The Role of WHO to address this issue Globally

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**World Health
Organization**

Introduction

- The emergence and spread of antibiotic resistance is one of the greatest public health threats of the 21st century.
- Antibiotics are a unique class of drugs since they have effects on both the individual and society. Use and misuse of antibiotics by individuals leads to selection of antibiotic resistance in bacteria that may spread to others and thus compromise effective treatment also for other members of society.
- The frequency of antibiotic resistance, especially multidrug resistance, continues to increase globally leading to higher health-care costs, failed treatments, and deaths.



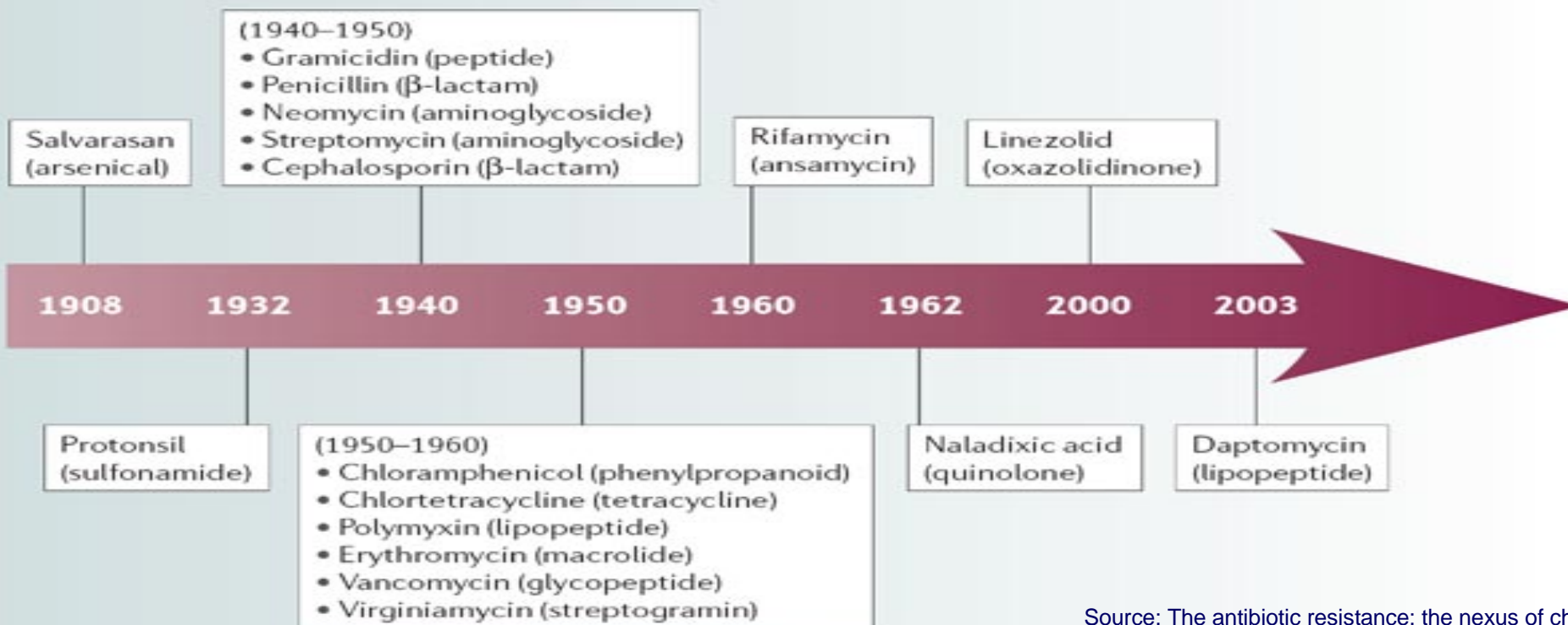
AMR in Food Safety Perspective

- Widespread use of antimicrobials in livestock productionnot only from therapeutic purposes
- Same classes of antimicrobials are used both in humans and animals..
- Few new antibiotics are being developed to replace those becoming ineffective through resistance
- Food is generally considered to be the most important vector for spread of resistance between humans and animals
- Globalization of food trade, need for international action



Discovery of antibiotics: a faltering pipeline

Timeline | Antibiotic drug discovery



The class of the antibiotic is shown in brackets.

Source: The antibiotic resistance: the nexus of chemical and genetic diversity. Gerard D. Wright. *Nature Reviews Microbiology* 5, 175-186 (March 2007)

How does antibiotic resistance develop?

- Some bacteria are naturally resistant; new resistances also arise spontaneously by chance mutations and these resistant strains then multiply.
- Some resistances can be passed from one bacterium to another, spreading resistance between species. Loops of DNA (called plasmids) carry the resistance genes from one bacterium to another.
- When an antibiotic is given, it kills the sensitive bacteria, but any resistant ones can survive and multiply.
- The more antibiotics are used (in animals and agriculture as well as in man) the greater will be the "selective pressure", favoring resistant strains. This is an example of Darwin's Theory of evolution, operating the "survival of the fittest".
- Antibiotics don't 'cause' resistance; rather, they create an environment which favors the growth of resistant variants which already exist in nature or arise by chance.



Resistance is a Consequence of Usage

- The widespread use of antibiotics both inside and outside of medicine is playing a significant role in the emergence of resistant bacteria
- Selective pressure from the use of antimicrobials is a major driving force behind the emergence of resistance
- This resistance will "resist" to phylogenetic, geographic or ecologic barriers; therefore once resistance emerge, resistant bacteria can be found in different ecosystems



More than 50% of all antimicrobials are used non-therapeutically in animal husbandry

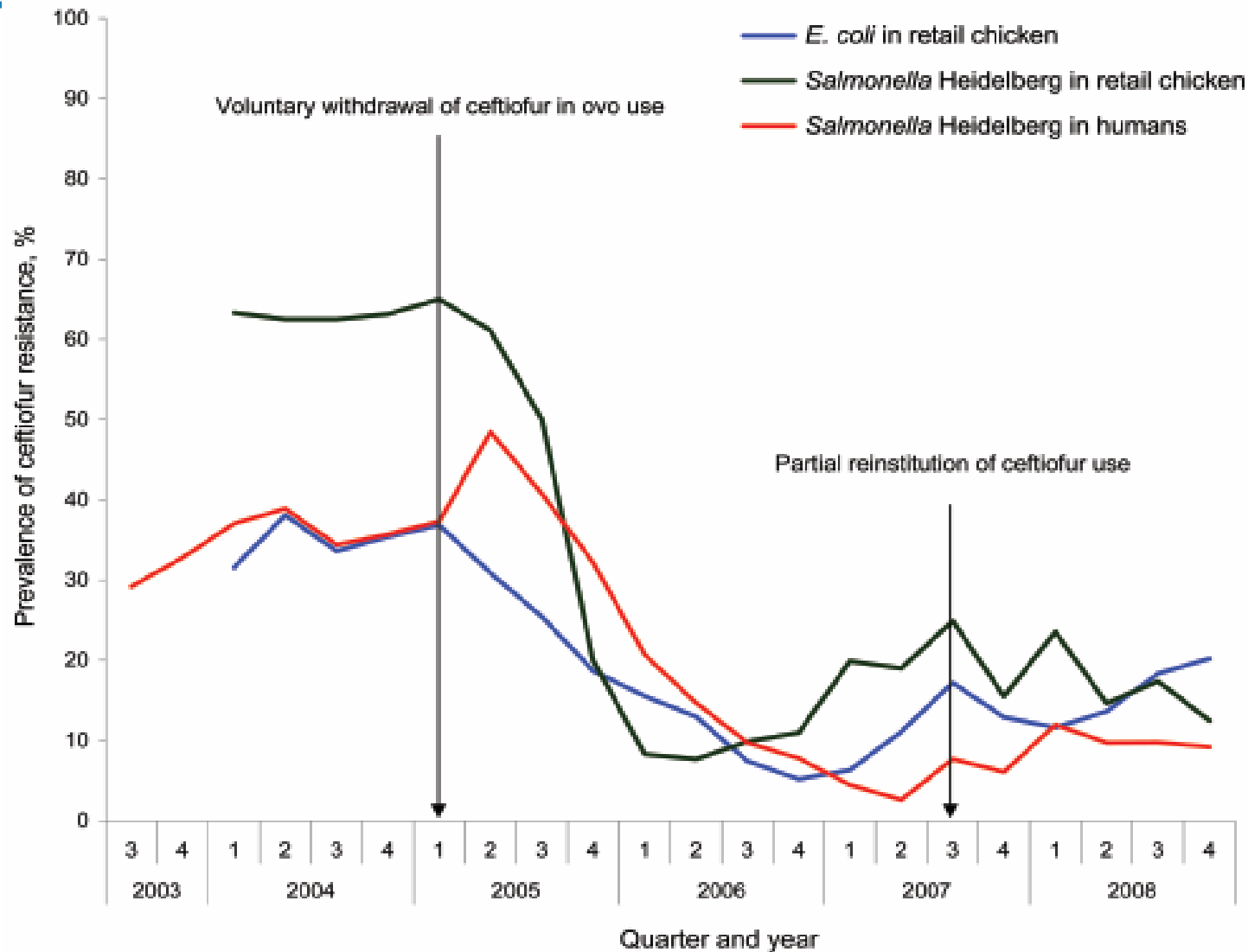
Use of antimicrobials in food animals can lead to **Antimicrobial Resistance (AMR)** in human pathogen.



- In industrial production, antibiotics are added to drinking water to decrease diseases of crowding and as growth promoters
 - When microbes are exposed to antibiotics, the bacteria resistant to these drugs live to reproduce which resulted in **Antimicrobial Resistance**

Antibiotics... "the more you use them, the faster you lose them"

Ceftiofur in ovo use and prevalence of ceftiofur resistance among retail chicken *Escherichia coli*, and retail chicken and human clinical *Salmonella enterica* serovar Heidelberg isolates during 2003–2008 in Québec, Canada



Summary on the importance of the animal reservoir

- Larger selective pressure
- Most important reservoir for antimicrobial resistant *Salmonella* and *Campylobacter*.
- An increasingly important reservoir for MRSA
- Important, but not quantified reservoir for *E. coli*
- Transferable genes



**More than one decade (2
decades?...) of WHO Activities
on Containment of Food-related
Antimicrobial Resistance**

The First alert...1990

- Realising that modern livestock production throughout the world relied heavily on the use of antimicrobial substances (treatment, prophylaxis, growth promotion), WHO already in 1990 called for action.
- This was the first alert pointing at an increase of antimicrobial resistance in zoonotic and foodborne pathogens and the first call for action, intersectoral collaboration and harmonization of methods for monitoring and surveillance across sectors.
- An international, multidisciplinary working group was established by WHO to elaborate guidelines for uniform, regular and systematic monitoring and surveillance of antimicrobial resistance susceptibility testing worldwide.
- The result was The Guidelines for Surveillance and Control of Antimicrobial Resistance (WHO, 1990).



1991...1st Meeting WHO WG on AMR

- The guidelines stated that "The occurrence of antimicrobial resistant pathogenic bacteria in clinical materials, as well as in the normal flora of humans, in food and the environment urgently require elucidation to solve the problem encountered in treating the numerous infections due to such bacteria. "
- As a result, a WHO Working Group on Antimicrobial Resistance was established and held its first meeting at the Central Veterinary Laboratory in Weybridge in 1991
- The WG elaborated a small pilot project on "surveillance and assessment of antimicrobial resistance in microorganisms derived from animals, public and environmental health, and clinical medicine" by applying a common methodology (1992).



Berlin 1997. Assessing the Medical Impact

- In 1997 WHO convened an expert meeting on “The Medical Impact of the Use of Antimicrobials in Food Animals”
- The experts acknowledged that antimicrobial use can select resistant forms of bacteria in the ecosystem and resistant bacteria and resistance genes can be exchanged between human, animal and other ecosystems. The following adverse consequences of selecting resistant bacteria in animals were identified:
 - 1. Transfer of resistant pathogens to humans via direct contact with animals or through the consumption of contaminated food or water.
 - 2. Transfer of resistance genes to human bacteria.
 - 3. Increased incidence of human infections caused by resistant pathogens.
 - 4. Potential therapeutic failures.



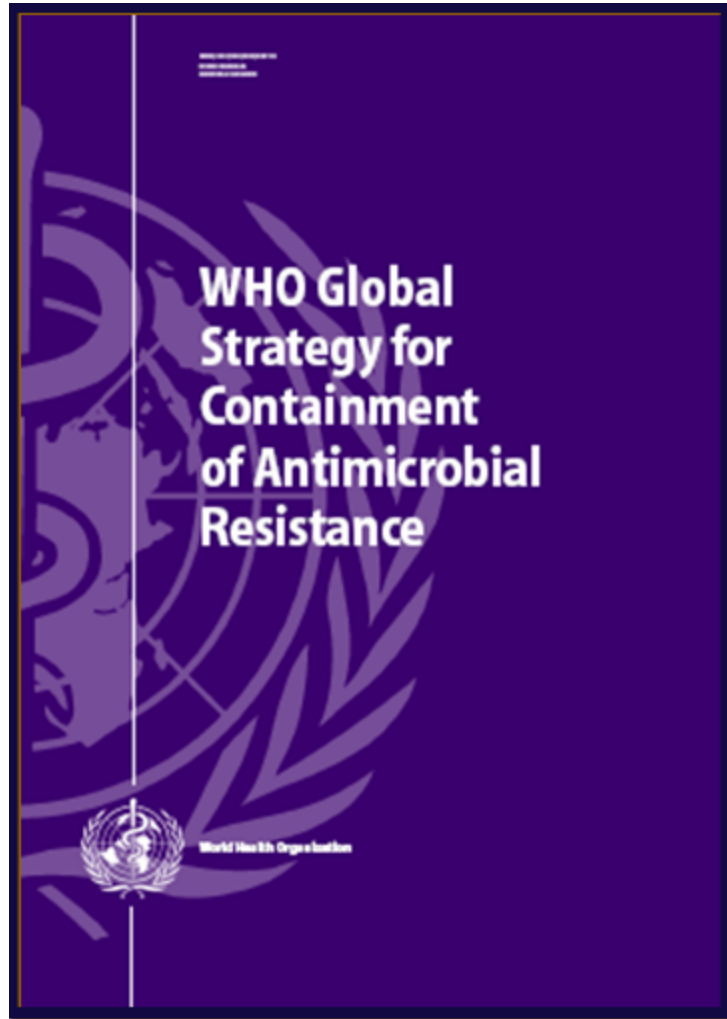
1998 WHA Resolution

● WHA 51.17

- Concerned by the extensive use of antibiotics in food production, which may further accelerate the development of antimicrobial resistance rendering treatment ineffective,
- the World Health Assembly urges Member States
- to develop programs for monitoring and containment of antimicrobial resistance
- to take measures to encourage the reduced use of antimicrobials in food-animal production"

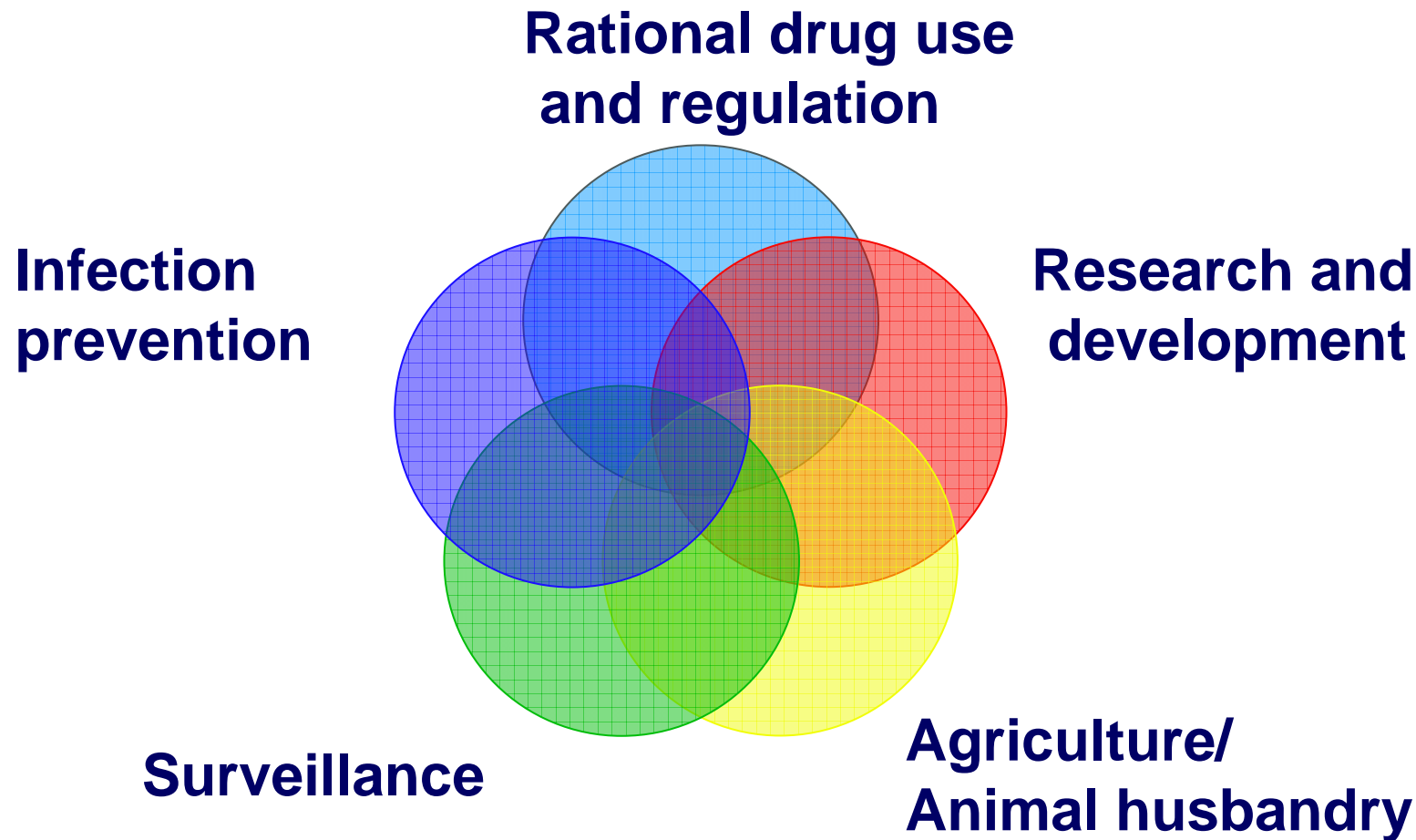


Preserving effectiveness of anti-microbial therapy: globally

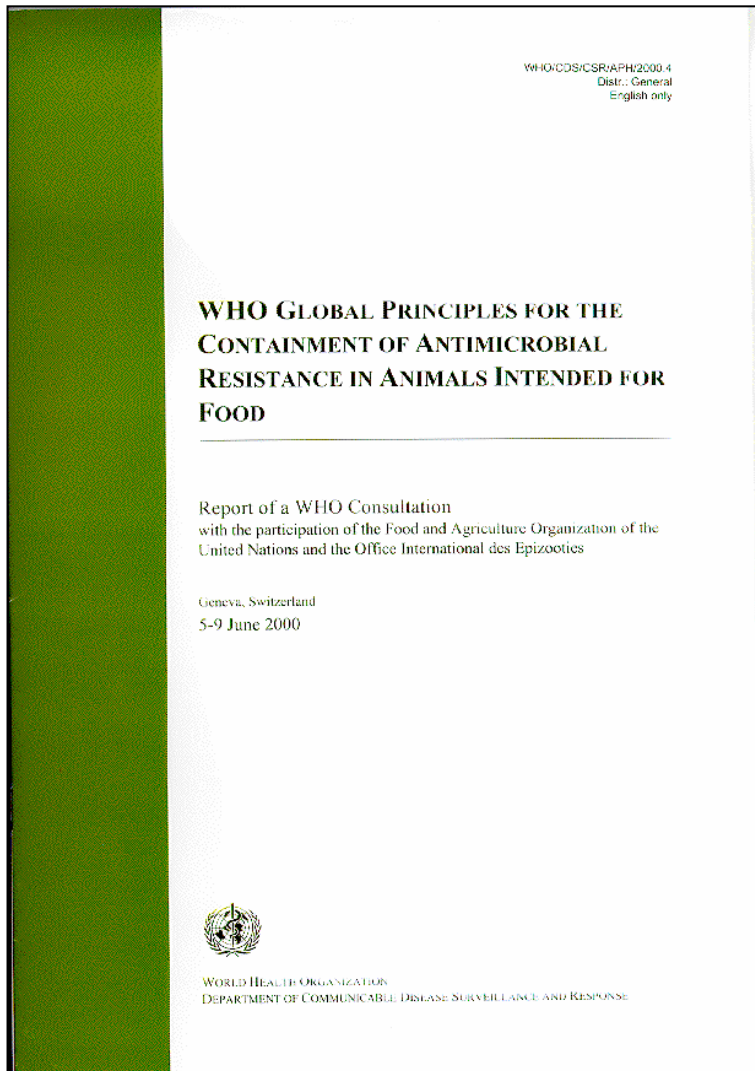


September
2001

The five key areas: global strategy for containment of antimicrobial resistance



WHO Global Principles for the Containment of AMR in food-animals



**To minimise the public health impact of
the use of antimicrobial agents in food
animals**

**and provide recommendations for their
safe and effective use in veterinary
medicine.**

Large consultation incl. stakeholders

**As chapter in the publication on WHO
Global strategy on Containment of
Antimicrobial Resistance - 2001**

WHO Global strategy for Prevention and Control of Foodborne Antimicrobial Resistance-1

- **National and international interdisciplinary cooperation**
- **Prudent use of antimicrobial agents in all sectors**
 - **No use of antimicrobial agents for growth promotion**
 - EU banned all growth promoters as of January 1, 2006
 - **A good regulatory system for approval and licensing**
 - **Prescription-only**
 - **Practitioners not having economic profit from prescription**
 - **Routine prophylactic use of antimicrobials should be never be used as a substitute for health management**
 - **Accurate diagnosis and antimicrobial susceptibility testing**
 - **Appropriate antimicrobial product and administration route**
- **Infection control**
 - **Successful disease control relies on a holistic approach encompassing hygiene, animal husbandry and management, nutrition, animal welfare, and vaccination**



WHO Global strategy for Prevention and Control of Foodborne Antimicrobial Resistance-2

- Antimicrobials identified as critically important in human medicine (WHO, 1998, 2005, 2007) to be used in animals **only if justified**
 - Fluoroquinolones, 3 + 4 generation cephalosporins
- Monitoring of antimicrobial resistance and antimicrobial usage in human and animals
 - Useful information on prevalence and trends
 - Input for risk assessment and risk management
 - A basis for choosing, implementing and evaluating interventions

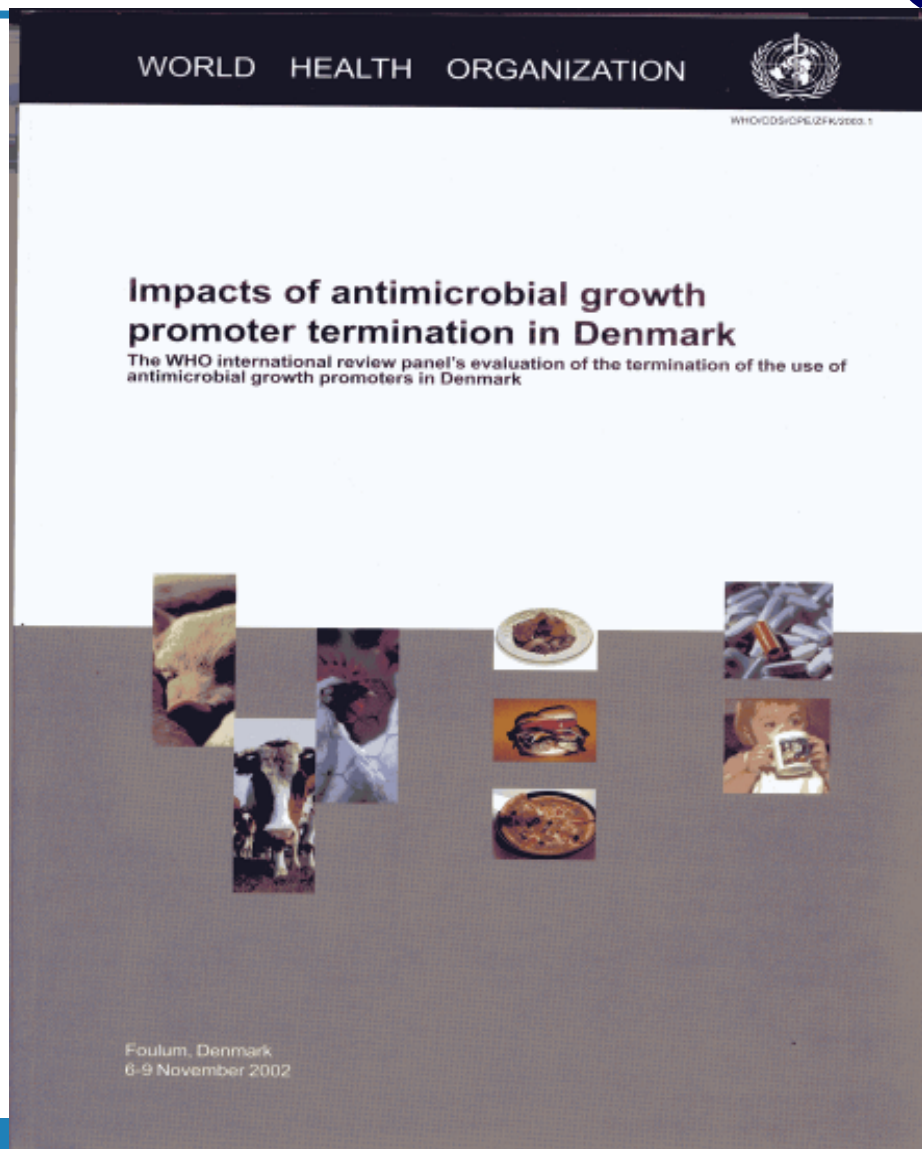


Joint FAO/WHO/OIE consultative process on Non-human use of antimicrobials and antimicrobial resistance (Requested by codex)



- 1st Workshop on scientific risk Assessment, Geneva, December, 2003
- 2nd workshop on risk management options, Oslo, March 2004
- WHO Expert Consultations on critically important antimicrobials for Human Health, Canberra 2005 and Copenhagen 2007-2009
- Joint Expert Consultation on use of antimicrobials in aquaculture and antimicrobial resistance, Seoul, June 2006
- Joint Expert Consultation on critically important antimicrobials, Rome 2007

WHO-panel on impacts of growth promoter termination in Denmark (2003)



- **Independent interdisciplinary review panel;**
- **Assessed impacts on human health, AH and welfare, animal production and economic consequences.**

Achievements 1997-2010

- International collaboration established
 - Codex, FAO, OIE, WHO
- 15+ expert meetings and consultations
- Codex Ad Hoc Intergovernmental task Force on Antimicrobial resistance (2007-2010)
- WHO list of Critically Important Antimicrobials for Human Health developed
- Establishment of an Advisory Group on Integrated Surveillance of Antimicrobial Resistance (AGISAR)



Integrating Surveillance Systems AGISAR

A group of experts working in veterinary, food and public health disciplines advising WHO on ensuring globally containment of foodborne antimicrobial resistance through integrated surveillance of antimicrobial usage and antimicrobial resistance in the animal, food and human sectors



First AGISAR meeting Copenhagen, June 2009

- 1) Update the WHO list of critically important antimicrobials (CIA) for human medicine
- 2) Develop a WHO strategic plan for containment of food-borne AMR



Integrated surveillance a key element of AGISAR- AMR Containment strategy

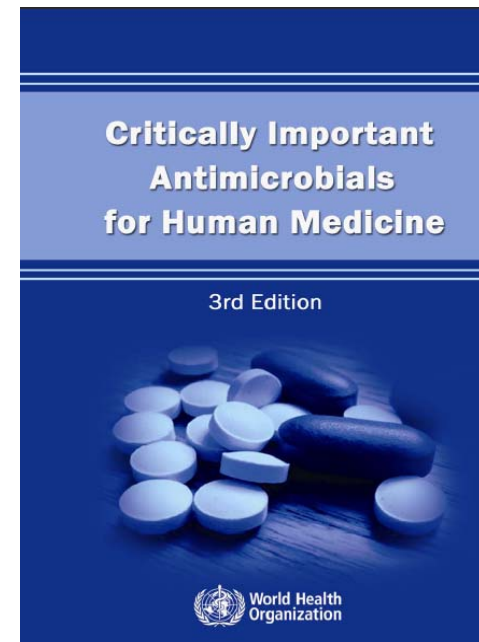
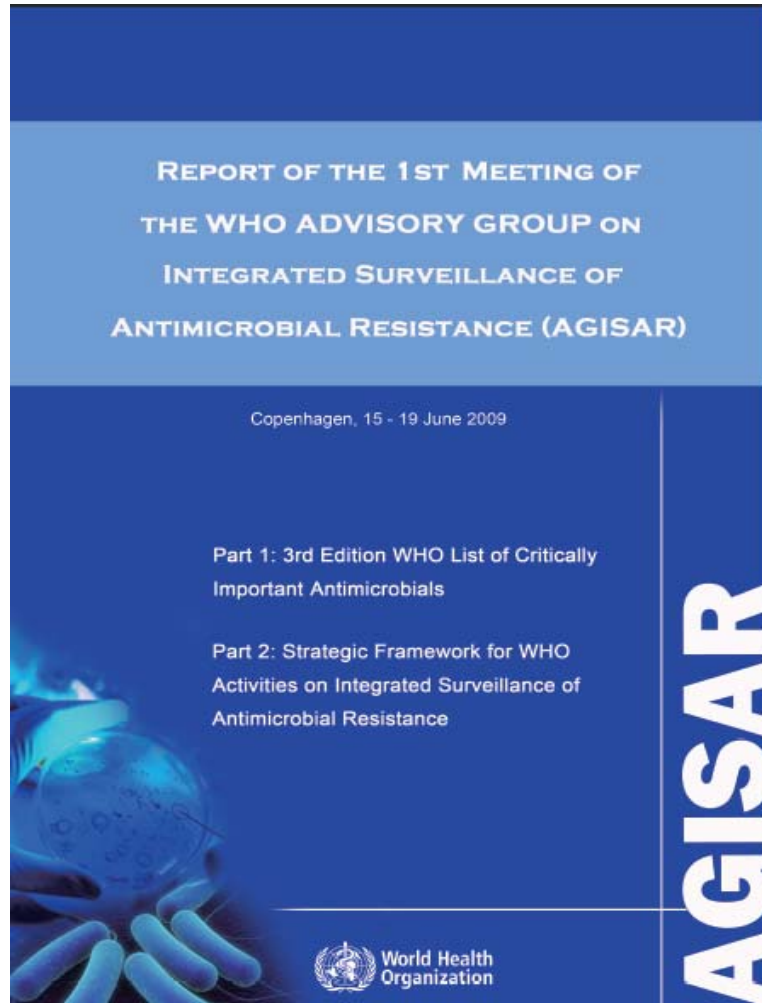
- - *Documentation of the situation*
- - *Identification of trends*
- - *input data for:*
 - *Establishing associations antimicrobial usage and antimicrobial resistance*
 - *risk assessment*
 - *evaluation of effectiveness of interventions*
- - *identify need for interventions*
- - *Basis for focused and targeted research”*
- - *Basis for communication*



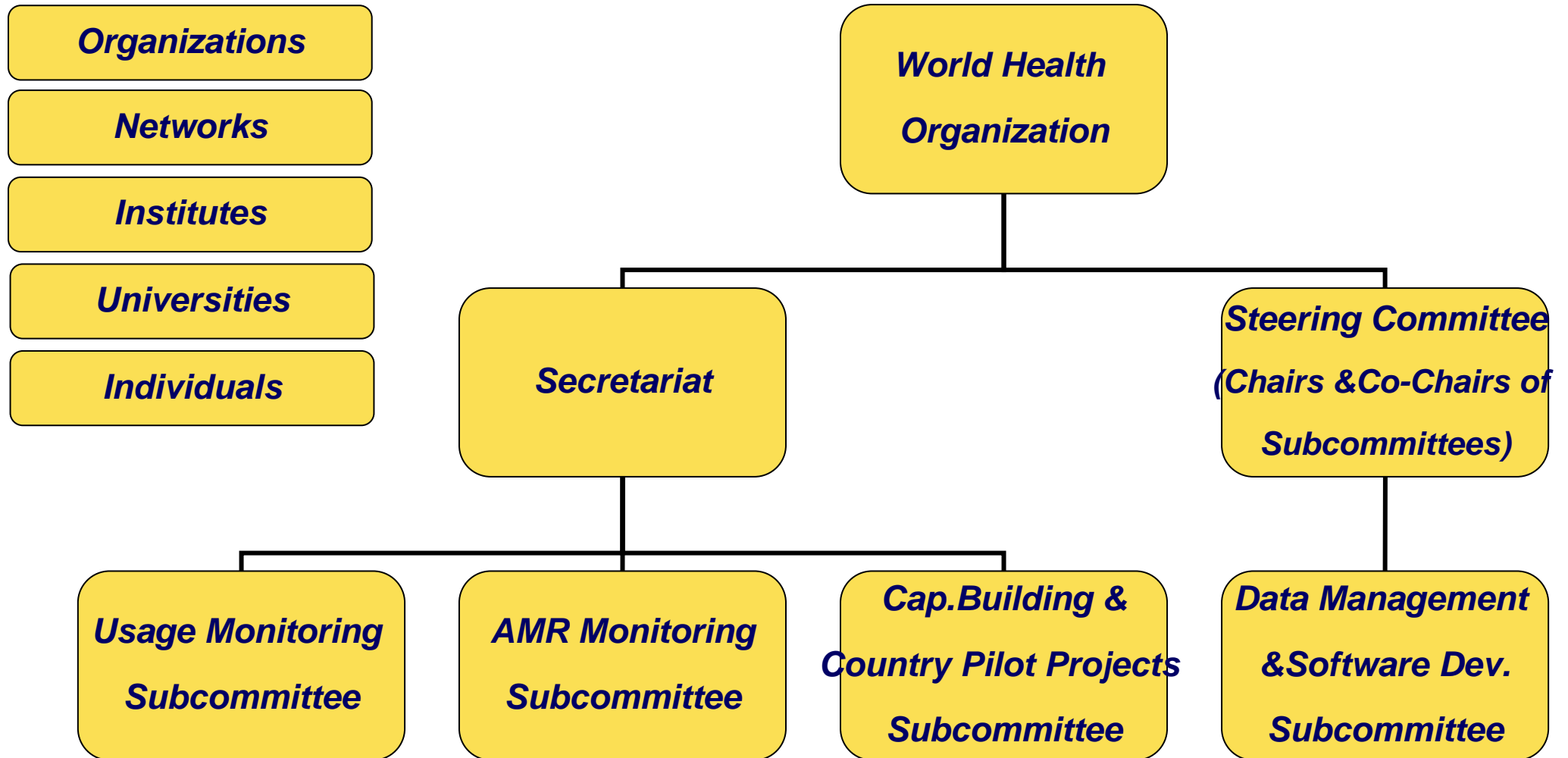
Outputs of AGISAR1

-Meeting Report

-3rd Edition of the WHO List of Critically Important Antimicrobials for Human Medicine



Governance of AGISAR



AGISAR 2 Meeting 5-7 June 2010, Guelph Canada

- Discuss emerging antimicrobial threats from the food-chain (ESBL *E.coli*)
- Discuss WHO-AGISAR's role in promoting global harmonization of antimicrobial usage monitoring and antimicrobial resistance
- Define future work plans for the four WHO-AGISAR working subcommittees





Antimicrobial Usage Monitoring SC

- The main aim of the sub-committee's work is to support and promote collection of standardized data on the usage of antibacterial agents for humans and animals, including aquatic species at regional/national levels.
- Approach :
 - Identify the AM products on the market
 - Identify channels of AM distribution that give representative data coverage
 - Decide on which AM to be included
 - Decide which data to collect for each product
 - Decide on confidentiality politics
 - Selection of sources for population data (denominator)



Software Development and Data Management SC

- Objective : improve the data management and analysis capabilities of the WHONET software in order to support the WHO AGISAR's objectives for integrated surveillance of AMR
 - Inventory of websites and reports for integrated surveillance of antimicrobial resistance
 - Identification of a useful set of fields and code lists from existing surveillance programs and use them as a basis for discussion and planning.
 - Development 2 sets of codes/fields
 - 1) fairly comprehensive set of fields/codes to support a variety of surveillance needs and projects
 - 2) a short list of highest priority fields/codes recommended for implementation by most surveillance program.



Software Development SC

Phase I: Determine specifications for the AGISAR software

Phase II: Implement specifications into the software based on WHONET

Phase III: Dissemination of the software.

- Joint FAO/OIE/WHO Expert Workshop on Non-human Antimicrobial Usage and Antimicrobial Resistance: Scientific assessment
- Second Joint FAO/OIE/WHO Expert Workshop on Non-human Antimicrobial Usage and Antimicrobial Resistance: Management options
- DANMAP 2008 report
- NORM/NORM-VET 2008 report
- CIPARS 2006 report
- NARMS (USDA) 2006 report
- NARMS (FDA) 2007 report
- FINRES-Vet 2006 report
- MARAN 2007 report
- SVARM 2007 report
- Others

- Expert advices from AGISAR members



- General information
- Sample Categories
- Antimicrobial and sample selection
- Measurement fields (data collection)
- Suggested output format (data analysis)



World Health
Organization

Antimicrobial Resistance Monitoring SC

- Develop recommendations for international harmonization of integrated AMR monitoring systems of food borne bacteria, including both pathogenic and commensal organisms.
- Provide guidance on surveillance and monitoring priorities and minimum requirements for integrated monitoring systems and for AGISAR pilot monitoring projects.
- Provide guidance on sampling strategies.
- Disseminate guidelines and standards on laboratory testing methods and quality assurance.
- Propose components of reporting and information sharing systems that permit regional and international comparison of findings.
- Communicate recommendations through GFN training courses, AGISAR pilot projects, and through other partnerships.



Capacity Building and Country Pilot Projects SC

- Objectives : Facilitate capacity building through GFN for the integrated surveillance of foodborne pathogens and commensal antimicrobial drug usage and AMR across sectors (animal, food, human), particularly in developing countries.
 - Identify and make available relevant resources for antimicrobial usage monitoring and integrated antimicrobial resistance surveillance
 - Identify potential training sites for AGISAR/GFN
 - Develop and facilitate implementation of training modules for postgraduate interdisciplinary intersectoral audiences
 - Encourage participation in external quality control systems to address proficiency/data gaps in laboratories monitoring AMR in foodborne pathogens during AGISAR/GFN training courses.
- Facilitate pilot studies focusing on integrated surveillance of AMR in foodborne pathogens and commensals , as well as antimicrobial drug use, with appropriate interventions in one or more developing countries (China, Kenya, Columbia).



Global Foodborne Infections Network (GFN)

A network of professionals working in veterinary, food and public health disciplines committed to enhancing capacity of countries to conduct integrated surveillance of foodborne and other enteric infections, incl. antimicrobial resistance

GFN Steering Committee



Public Health
Agency of Canada

Agence de la santé
publique du Canada



University of Utrecht



GFN main activities

🌐 (Inter)national Training Activities

🌐 Reference Services

🌐 External Quality Assurance System (EQAS)

🌐 Focused Regional and National Projects

🌐 Country Data Bank (CDB)

🌐 Communication



❖ ~ 1 600 Members

❖ > 700 Institutions

❖ 177 Member States

(Inter)national Training Courses

Microbiology training

- Global/Region-specific pathogens
(e.g. *Salmonella*, *Campylobacter*, *E. coli*, *V. cholerae*, *S. Typhi*, *Brucella*, *Shigella*, *Listeria*, *C. botulinum*)
- Quality assurance
- Biosafety
- Antimicrobial Susceptibility Testing

Epidemiology training

- Outbreak detection and response
- Evaluation of surveillance systems
- Study design
- Source attribution
- Burden of disease

Joint Epidemiology and Laboratory

- Joint case studies
- Integrated surveillance
- Risk assessment
- Country Plans of Action
- Advocacy and communication
- Information sharing networks



AMR Containment : The way forward

- *The WHO list of critically important antimicrobials updated every two years.*
- Harmonized protocols for monitoring antimicrobial usage and resistance in animal, food and human developed and disseminated.
- Software to support data collection and analysis developed and disseminated.
- Support WHO capacity-building activities in Member countries through GFN training courses.
- Data generated through country pilot projects (Kenya, China, Columbia) and add AMR data to the GFN country databank



More information at :

http://www.who.int/foodborne_disease/resistance

World Health Organization

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Antimicrobial Resistance

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Foodborne disease surveillance home

Strategies in surveillance and control

Burden of disease

Antimicrobial agents are essential for human health. Antimicrobial resistance is a major public health problem, caused by the continuing emergence, development and spread of antimicrobials that are resistant to antimicrobials. WHO's involvement in controlling antimicrobial resistance is essential.

Information resources

WHO strategy to ensure the prudent use of antimicrobials includes:

- Develop and promote good antimicrobial use in food production
- Develop a list of Critical Risk Management Strategies

Meetings

2nd meeting (WHO-AGISA) 16 October 2010

The 3rd Session 16 October 2010

First Meeting (AGISAR), 15-19 June 2009

The 2nd session 24 October 2010

Joint FAO/WHO November 2010

Joint FAO/OIE November 2010

Publications

Home | **Foodborne Disease Surveillance**

WHO > Programmes and projects > Foodborne Disease Surveillance > Antimicrobial Resistance

Printable version

WHO list of Critically Important Antimicrobials (CIA)

2nd edition WHO list of CIA [pdf 450kb]

The list may be found in the report of the 2nd WHO Expert Meeting on Critically Important Antimicrobials for Human Health

1st edition WHO list of CIA [pdf 214kb]

The list may be found in the report of the 1st WHO Expert Meeting on Critically Important Antimicrobials for Human Health

WHO Advisory Group on Integrated Surveillance of Antimicrobial Resistance (AGISAR)

Home | **Foodborne Disease Surveillance**

WHO > Programmes and projects > Foodborne Disease Surveillance > Antimicrobial Resistance

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WHO Advisory Group on Integrated Surveillance of Antimicrobial Resistance (AGISAR)

AGISAR members

- AGISAR subcommittees
- First Meeting of the WHO Advisory Group on Integrated Surveillance of Antimicrobial Resistance (AGISAR), 15-19 June 2009
- List of Critically Important Antimicrobials
- Global Foodborne Infections Network (GFNI) training courses

Burden of disease

Use of antimicrobials in food animals is an important public health issue. The first WHO Antimicrobial Resistance (AMR) training module for the Global Foodborne Infections Network (GFNI) training courses is currently available.

The first WHO Antimicrobial Resistance (AMR) training module for the Global Foodborne Infections Network (GFNI) training courses is currently available.

Information resources

Local intranet

- General information
- Codex ad hoc Intergovernmental Task Force of Antimicrobial Resistance
- List of Critically Important Antimicrobials
- WHO Advisory Group on Integrated Surveillance of Antimicrobial Resistance (AGISAR)
- Publications
- Meetings

WHO Advisory Public Health Workshop, 4-5 October 2010, Hong Kong